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Expert insight

Using the Vascular Autonomic Signal to Guide Diagnosis and Treatment in Auricular Medicine.

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Abstract

Many chronic conditions arise not from isolated structural pathology but from dysregulation within autonomic, neuroendocrine, inflammatory, and limbic control systems. Auricular Medicine, as developed by Nogier and later expanded within the German medical tradition, uses the auricle as a diagnostic interface reflecting these regulatory states. Central to this approach is the Vascular Autonomic Signal (VAS), a transient, autonomically mediated modulation of arterial pulse amplitude elicited by stimulation of clinically relevant auricular zones. This article presents a condensed, physiology-based framework for VAS-guided auricular diagnosis and its integration with photobiomodulation (PBM). By identifying the regulatory layer actively under strain and applying targeted laser stimulation only to VAS-responsive points, treatment is individualised, adaptive, and system-oriented. Clinical illustrations demonstrate how symptoms often arise from non-local regulatory disturbances and resolve when the appropriate regulatory level is addressed.

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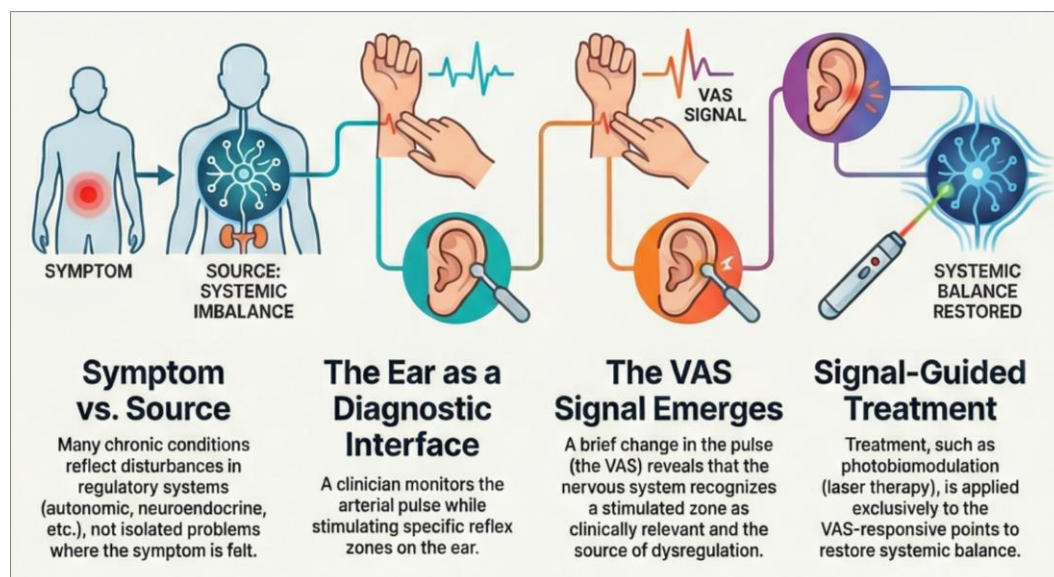
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Keywords: Auricular Medicine; Vascular Autonomic Signal; Autonomic Regulation; Central Autonomic Network; Photobiomodulation; Laser Acupuncture.

1. Introduction

Chronic pain, functional disorders, vasomotor instability, and stress-related conditions frequently reflect disturbances in higher-order regulatory systems rather than isolated peripheral pathology. In such cases, symptoms represent downstream expressions

of dysregulation within autonomic, neuroendocrine, inflammatory, or limbic networks ¹⁻³.

Auricular Medicine originated with Paul Nogier's description of a somatotopic representation of the body on the external ear ⁴. The German school of Auricular Medicine subsequently developed this concept into a structured diagnostic system by introducing regulatory-layer interpretation, systematic use of the VAS, and integration with modern neurophysiology ^{5,6}.

Because the auricle is richly innervated and connected to central autonomic and limbic centres, it functions not only as a somatotopic map but also as a real-time indicator of systemic regulatory activity ⁷⁻⁹. The VAS allows clinicians to identify which regulatory layer is actively engaged in a patient's condition, enabling treatment to be directed toward the origin of dysregulation rather than the site of symptom perception ^{5,10,11}.

2. Physiological Basis of the Vascular Autonomic Signal

The VAS is a brief, involuntary modulation of arterial tone elicited by minimal stimulation of auricular reflex zones. It reflects central autonomic network processing rather than a local vascular phenomenon ^{5,11,12}.

Afferent input from the auricle is transmitted primarily via the auricular branch of the vagus nerve, trigeminal nerve branches, facial nerve fibres, and cervical plexus contributions. These signals converge in the *nucleus tractus solitarius* and are relayed to higher autonomic centres, including the hypothalamus, amygdala, and brainstem cardiovascular nuclei ¹³⁻¹⁵.

Efferent modulation from these centres results in a rapid, localised change in peripheral vascular resistance, perceived clinically as a short increase in pulse amplitude ¹⁶⁻¹⁸. The VAS typically occurs within less than one second of stimulation and represents a specific regulatory response rather than a generalised cardiovascular reaction ^{19,20}.

Clinically, the VAS is interpreted as an indicator of active regulatory engagement. It provides information about autonomic balance, inflammatory tone, and neuroendocrine or limbic involvement, allowing the clinician to distinguish between functional regulatory disturbances and stable or compensated systems ^{5,21,22}.

3. Diagnostic Rationale of Auricular Medicine

Auricular Medicine is based on the observation that the auricle contains reflex zones corresponding not only to anatomical structures but also to functional regulatory states ^{7,23}. These zones are neurovascularly linked to the central autonomic network, which coordinates cardiovascular regulation, stress responses, endocrine activity, immune modulation, and interoception ^{7,9,24}.

Within the German Auriculomedicine model, auricular findings are interpreted according to regulatory layers. These layers represent reproducible physiological response patterns rather than fixed anatomical entities ^{23,25,26}. Commonly evaluated domains include ²⁷⁻³¹:

- Structural–somatic regulation;
- Autonomic–vegetative balance;
- Inflammatory–immune activity;
- Neuroendocrine–stress regulation;
- Emotional–limbic processing.

The purpose of auricular diagnosis is not to label disease but to identify which regulatory layer is currently under adaptive strain. This shifts clinical reasoning from symptom localisation toward systemic pattern recognition.

4. Clinical Assessment Using the VAS

The VAS functions as a real-time indicator of how the autonomic nervous system responds to sensory input. When stimulation of an auricular zone elicits a VAS response, it indicates that the nervous system recognises that zone as clinically relevant at that moment³²⁻³⁴.

Importantly, the absence of a VAS does not imply incorrect anatomy or lack of symptoms; it indicates that the system is not allocating regulatory attention to that region at the time of assessment. Thus, the pulse serves as a physiological monitor of active dysregulation rather than a measure of symptom severity^{5,35,36}.

4.1 Baseline and Selectivity

Before diagnostic testing, a quiet and stable pulse baseline must be established. If the autonomic system reacts indiscriminately to multiple stimuli, this reflects global stress activation, and meaningful diagnostic interpretation is not possible. In such cases, regulatory intervention precedes further assessment³⁷⁻⁴⁰.

Once selective responsiveness is confirmed, auricular zones are stimulated sequentially. The first clear and reproducible VAS response identifies the dominant regulatory layer currently driving the patient's condition^{5,41}.

5. Regulation Before Diagnosis

A core principle of VAS-guided practice is that regulation precedes diagnosis. When the autonomic system is overloaded, it produces non-specific reactions that obscure meaningful signalling.

In the regulation phase, only points that elicit a VAS response are treated. Laser stimulation or acupuncture is applied selectively to restore autonomic flexibility. Successful regulation is indicated by the disappearance of VAS responses at previously reactive points and the return of a quiet pulse baseline. Only then does detailed diagnostic mapping proceed⁴²⁻⁴⁴.

This step prevents misinterpretation of global sympathetic activation as clinically specific information and ensures that subsequent diagnosis reflects true regulatory priorities.

6. VAS-Guided Auricular Diagnosis

VAS-guided diagnosis is founded on a simple principle: the nervous system expresses recognition of a relevant disturbance through a measurable vascular response. The presence of a VAS identifies the regulatory origin of a symptom, which may be distant from the site of pain or discomfort^{5,45}.

For example, musculoskeletal pain may not elicit a VAS response at its corresponding somatotopic zone but may instead activate autonomic, inflammatory, or interference-field zones. This indicates that the symptom is compensatory rather than primary⁴⁶.

Accordingly, treatment is directed toward the regulatory cause identified by the VAS, not toward the anatomical location of symptom expression.

Clinical Meaning of VAS-Identified Patterns

VAS-guided assessment consistently demonstrates that symptoms do not necessarily arise from the tissues where they are perceived. Rather, symptoms represent outputs of regulatory strain, while the VAS identifies the source of that strain^{5,47}.

This distinction explains why treatment at non-local auricular zones often results in rapid systemic improvement, including changes in pain perception, sleep quality, emotional stability, and autonomic tone. By restoring balance at the appropriate regulatory level, compensatory symptoms resolve as adaptive capacity is regained^{48,49}.

7. Integration of Auricular Diagnosis, VAS, and Laser Therapy

Auricular mapping provides the anatomical and functional interface, the VAS identifies active dysregulation in real time, and photobiomodulation serves as a targeted regulatory intervention^{50,51}.

PBM influences mitochondrial metabolism, microcirculation, inflammatory signaling, and autonomic balance. When applied exclusively to VAS-responsive points, laser therapy reinforces the regulatory correction the nervous system is already attempting to achieve⁵²⁻⁵⁴.

Laser frequency selection may also be guided by the VAS. Frequencies that stabilise or strengthen the VAS response are considered supportive, whereas those that diminish it are avoided. This maintains a closed-loop, physiology-led treatment process^{55,56}.

8. Final remarks

VAS-guided auricular medicine offers a structured approach to understanding symptoms as expressions of systemic regulatory imbalance rather than isolated pathology. By aligning diagnosis and treatment with real-time autonomic signalling, interventions become individualised, efficient, and adaptive⁵ (Figure 1).

This model is particularly valuable in chronic pain, stress-related disorders, neuroendocrine imbalance, inflammatory syndromes, and psychosomatic presentations, where symptom location often obscures regulatory origin⁵.

The method does not replace conventional medical diagnostics but complements them by providing insight into functional regulation and adaptive capacity.

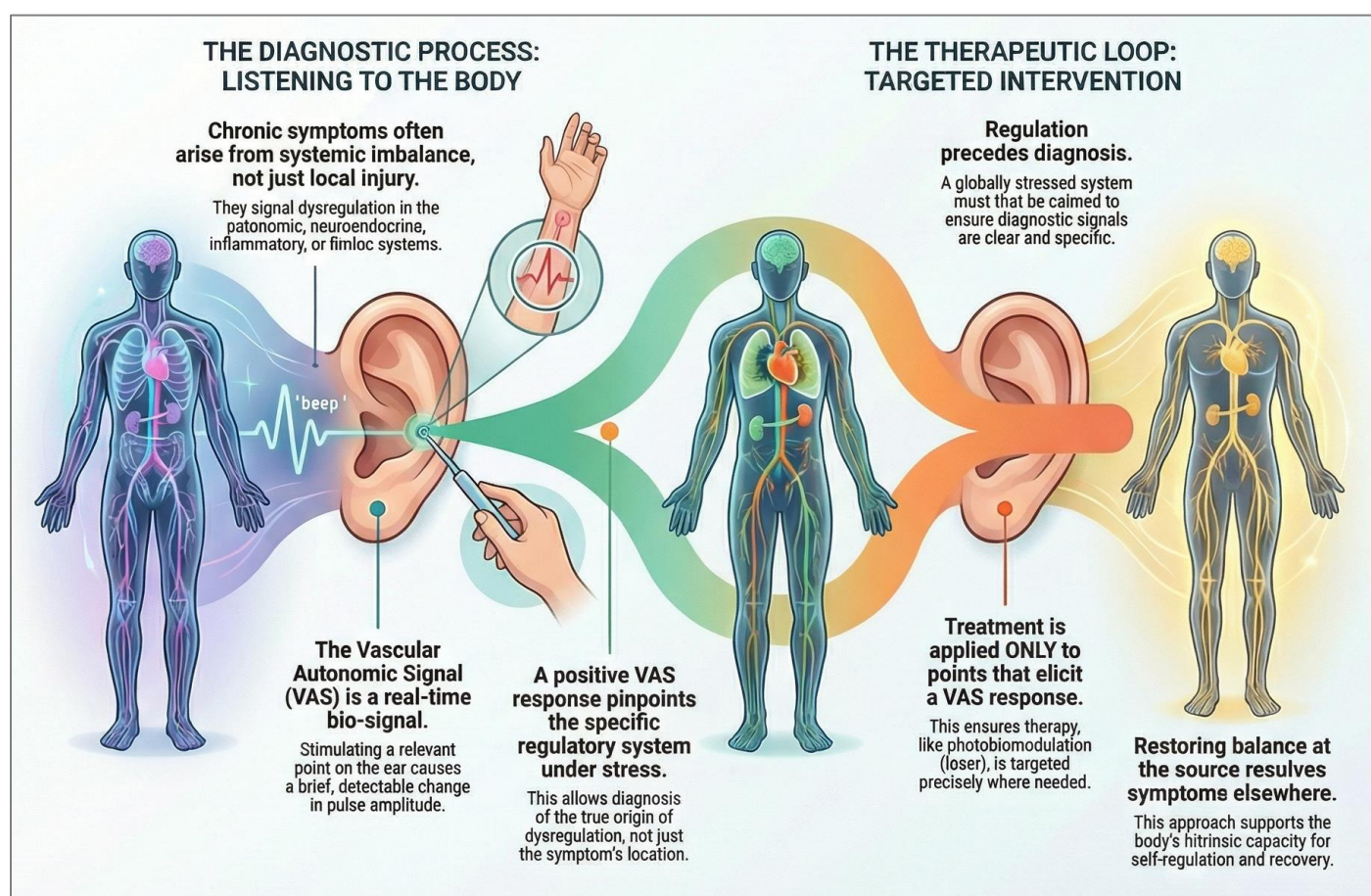


Figure 1. From the diagnosis to therapy.

9. Conclusion

VAS-guided auricular diagnosis represents a shift from symptom-based treatment toward regulation-based clinical reasoning. The Vascular Autonomic Signal identifies where the organism is failing to adapt, allowing intervention to be directed precisely at the active regulatory disturbance.

When combined with targeted laser therapy, this approach supports restoration of autonomic coherence, neuroendocrine balance, and systemic resilience. Rather than imposing treatment, the clinician follows the nervous system's own signalling. In doing so, therapy becomes not only diagnostic but also restorative, supporting the organism's intrinsic capacity for self-regulation and recovery.

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Multisystemic Proteomic Reprogramming and Haematopoietic Regeneration: A Naturopathic Framework for the Supervised Seven-Day Fast.

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Abstract

Fasting is an ancient therapeutic practice currently being redefined by modern molecular research. This article explores the physiological and clinical impact of a supervised seven-day fasting protocol, bridging traditional naturopathic principles with recent breakthroughs in systems biology. Following the depletion of glycogen stores within the first 24 to 48 hours, the body transitions into a state of nutritional ketosis characterised by the production of β -hydroxybutyrate. This metabolic switch activates key sensors, including AMPK and sirtuins, which trigger intensive autophagy and "multisystemic proteomic reprogramming". Central to the protocol is the regenerative peak observed around the 72-hour mark, involving leukocyte recycling and haematopoietic stem cell activation. Clinical evidence demonstrates significant improvements in glycaemic control, lipid profiles, and blood pressure normalisation. However, the study emphasises that the safety and efficacy of prolonged fasting are contingent upon rigorous clinical screening and structured refeeding to mitigate the risk of Refeeding Syndrome, in accordance with UK General Medical Council (GMC) and NICE standards. By integrating complementary practices such as hepatobiliary phytotherapy and mindful breathing, supervised fasting emerges as a potent, evidence-based tool for metabolic restoration and cellular renewal within contemporary naturopathic practice.

Keywords: Autophagy; β -Hydroxybutyrate; Haematopoietic Regeneration; Metabolic Flexibility; Naturopathy; Proteomic Reprogramming; Refeeding Syndrome.

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1. Background

Fasting has accompanied humanity since its earliest days, being recognised as a natural practice of purification, balance, and renewal ¹⁻³. From a naturopathic perspective, it represents a period of digestive rest that allows the body to focus energy on the processes of cleansing, cellular regeneration, and metabolic reorganisation. During this interval, the body eliminates accumulated waste, restores neuro-hormonal sensitivity, and reinforces the efficiency of its self-regulatory mechanisms ⁴⁻⁷.

Current scientific research demonstrates consistent benefits for cardiovascular ⁸, cognitive ⁹, and immune ¹⁰ parameters when fasting is conducted with discretion and proper supervision ¹¹. A seven-day protocol can provide significant metabolic transformations without exceeding physiological safety limits in well-selected individuals ¹¹⁻¹³. This article brings together the primary mechanisms, progressive effects, and safety measures, offering a solid foundation for integrating fasting into modern naturopathic clinical practice.

2. Physiological Foundations of Prolonged Fasting

In the first twenty-four hours, the body primarily utilises glycogen stores and initiates gluconeogenesis to maintain blood glucose levels ¹⁴⁻¹⁶. From twenty-four to forty-eight hours, a gradual transition to fatty acid oxidation and the production of ketone bodies is observed ^{13,17}, notably β -hydroxybutyrate, which becomes an efficient energy source for the brain and muscles ¹⁸⁻²¹. Caloric restriction activates metabolic sensors such as AMPK and sirtuins ^{22,23}, triggering processes of autophagy, mitochondrial biogenesis, and an increase in endogenous antioxidant capacity ²⁴⁻²⁸. These mechanisms contribute to cellular recycling, the reduction of oxidative stress, and the improvement of overall metabolic efficiency. Recent clinical studies demonstrate that seven-day fasts induce multisystemic proteomic reprogramming, with consistent results in body weight reduction, improved lipid profiles, glycaemic control, and the normalisation of blood pressure within supervised protocols ^{11,29-32}. Additional trials further indicate significant immune modulation and haematopoietic regeneration following prolonged fasting cycles, with experimental evidence of haematopoietic stem cell regeneration described in the context of extended fasting ^{10,33-37}.

Table 1 summarizes the progressive day-by-day benefits.

Table 1. Evolution of the physiological actions during a 7-day fasting.

Day	Physiological Changes and Observed Benefits
1	Initial reduction in blood glucose; glycogen consumption; transient hunger; onset of metabolic "cleansing".
2	Glycogen depletion; stable transition into ketosis; increased mental clarity and sustained energy.
3	Intensive autophagy and signs of immune renewal: leukocyte recycling and stimulation of haematopoietic stem cells (~72 h).
4	Decline in insulin and triglycerides; normalisation of blood pressure; improvement in hepatic and inflammatory markers.
5	Loss of 2–5% of body weight with relative preservation of lean mass; mental focus and a sense of well-being.
6	Continued cellular regeneration; enhanced antioxidant defences; acid-base and emotional stability.
7	Reinforced homeostasis; serenity; preparation for gradual and mindful reintroduction of food.

3. Precautions and Contraindications

Prolonged fasting always requires prior clinical screening and qualified professional supervision ^{12,32,38}. Throughout the process, adequate hydration must be ensured (ideally between 1.5 and 2.5 litres of water per day) and, where necessary, electrolyte supplementation (sodium, potassium, and magnesium) ^{32,39,40}.

There are specific situations where prolonged fasting is contraindicated, including pregnancy, lactation, Type 1 diabetes, and hepatic or renal failure, eating disorders, and states of malnutrition ^{11,32,41-43}. For individuals on continuous medication, a medical consultation is indispensable before starting any protocol ^{29,44}.

The refeeding phase is critical and must be carried out in a gradual and structured manner ⁴⁵. On the first day after the fast, the consumption of vegetable broths and water-rich fruits is recommended. On the second day, cooked vegetables and small portions of lean protein, such as eggs or white fish, may be introduced. By the third day, the individual can return to a wholefood, balanced eating pattern (ideally Mediterranean-inspired – Figure 1) focusing on natural and unprocessed foods ^{3,32}.

Mediterranean diet pyramid: a lifestyle for today
guidelines for adult population

Serving size based on frugality
and local habits



Wine in moderation
and respecting social beliefs



Figure 1. The mediterranean diet pyramid ⁴⁶.

In the UK, the GMC and various nutritional therapy bodies emphasise that electrolyte balance is the most critical safety factor during the refeeding stage to prevent Refeeding Syndrome ^{47,48}.

Professional guidance ensures that fasting remains a practice of metabolic regeneration rather than an experience of excessive deprivation. Thus, clinical supervision and "listening to one's body" are essential to reap the physiological and spiritual benefits of fasting in total safety.

4. Discussion

From a naturopathic perspective, fasting acts as a profound stimulus to the vital force and the innate capacity for self-regulation ⁴⁹⁻⁵¹. By reducing digestive overload, it optimises metabolic signalling and creates favourable conditions for tissue repair and regeneration ^{52,53}.

The phenomenon frequently described as "immune renewal", observed around the third day, aligns with data demonstrating haematopoietic regeneration and leukocyte recycling during periods of fasting ³³. The intensity of these effects, however, depends on individual factors such as age, nutritional status, and the level of metabolic adaptation ^{3,39,54}.

The clinical integration of fasting must respect the principles of biological individuality, gradual progression, and appropriate nutritional education. Complementary practices may be combined, including hepatobiliary phytotherapy ^{55,56}, mindful breathing techniques ^{57,58}, and sleep hygiene routines ^{59,60}, which reinforce the body's capacity for detoxification and organic restoration.

As observed previously in this work, current scientific evidence supports the significant clinical utility of supervised fasting, with documented improvements in metabolic and inflammatory parameters across various clinical studies. However, generalisations should be avoided, and a progressive, balanced reintroduction of food must always be guaranteed.

Moreover, although scientific evidence regarding prolonged fasting has increased in recent years, many available studies remain observational and have limited sample sizes. Additional controlled clinical trials will be essential to further clarify the physiological mechanisms and long-term effects of this intervention.

5. Conclusion

A seven-day fast represents a sophisticated intersection between ancient therapeutic tradition and modern molecular biology. Far from being a mere exercise in caloric restriction, prolonged fasting triggers a profound multisystemic proteomic reprogramming and immune reset that peaks around the third day. By shifting the body from an anabolic state of growth to a catabolic state of repair and autophagy, this protocol offers a powerful mechanism for metabolic restoration, blood pressure normalisation, and cellular renewal.

However, the clinical success of this intervention hinges entirely on meticulous safety protocols. In line with UK clinical standards and GMC guidelines, professional screening and structured refeeding are not optional extras but essential components to prevent complications such as refeeding syndrome. When conducted within these supervised boundaries, fasting transcends simple "detoxification" to become a high-precision tool for improving long-term healthspan.

Ultimately, the integration of supervised fasting into contemporary Naturopathy provides a biological "reset button" that respects the biological individuality of the patient. While further large-scale controlled trials are needed to map the long-term horizons of this practice, the current evidence suggests that a mindful, gradual, and professionally guided 7-day fast can be a transformative pillar of systemic health and organic vitality.

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Clinical cases

Vascular Autonomic Signal-Guided Photobiomodulation: Mechanisms and Clinical Applications in Autonomic Dysregulation.

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Abstract

Background: Dysregulation of the autonomic nervous system contributes to chronic conditions including insomnia, anxiety, chronic pain, and vertigo. Auricular stimulation can modulate autonomic, limbic, and sensorimotor pathways via cranial and cervical nerve afferents, influencing neurotransmitter release and anti-inflammatory signalling. The Vascular Autonomic Signal (VAS) provides real-time, feedback-driven identification of physiologically active auricular points through transient changes in radial pulse amplitude.

Methods: This review synthesises the origins, physiology, and clinical applications of the VAS, integrating evidence from historical observations, experimental models, and imaging studies. The synergistic application of photobiomodulation (PBM) to VAS-responsive points is examined, highlighting mechanisms including mitochondrial activation, nitric oxide signalling, microcirculatory modulation, and stem-cell mobilisation.

Results: Clinical illustrations demonstrate that VAS-guided PBM can stabilise autonomic tone, enhance sleep, reduce neuropathic pain, and improve functional outcomes. Personalised dosing guided by VAS attenuates overstimulation while promoting parasympathetic dominance and regenerative processes.

Conclusions: VAS-guided PBM represents a precise, non-invasive, and adaptive approach for modulating autonomic function and supporting regenerative mechanisms. Structured training and potential automated detection systems are essential to enhance reproducibility. Although preliminary evidence is promising, larger controlled trials are required to define optimal parameters, effect sizes, and condition-specific protocols. This integrative modality offers a real-time, patient-specific tool for autonomic modulation within evidence-informed practice.

Keywords: Vascular Autonomic Signal; Auricular Medicine; Photobiomodulation; Autonomic Dysregulation; Neuroimmune Modulation; Personalised Therapy.

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1. Background

Dysregulation of the autonomic nervous system is implicated in a wide range of chronic conditions, including insomnia, anxiety, chronic pain and vertigo ¹⁻⁴. Vertigo and dizziness alone affect approximately 20–30% of adults at some point in life, and in many cases are associated with autonomic imbalance ⁵. Auricular medicine seeks to influence autonomic, limbic and sensorimotor pathways through stimulation of specific points on the external ear ^{6,7}. Anatomically, the auricle is innervated by branches of the vagus (auricular branch of the vagus nerve), trigeminal (auriculotemporal nerve), facial nerve, and the greater and lesser auricular nerves ⁸⁻¹⁰. Stimulation of these fibres projects to brainstem

nuclei involved in autonomic regulation, and has been shown to modulate neurotransmitter release, including glutamate, γ -aminobutyric acid (GABA), acetylcholine and nor-adrenaline, as well as anti-inflammatory signalling pathways¹¹⁻¹⁴. These neurophysiological mechanisms provide a plausible basis for auricular therapeutic effects.

Conventional auricular charts map numerous predefined points, yet inter-individual variability means that fixed prescriptions may not always identify the most responsive sites. The VAS provides a dynamic alternative¹⁵. When a physiologically active auricular point is touched or exposed to a micro-stimulus, the examiner palpating the radial artery perceives a brief, transient change in pulse amplitude or tension, typically within one to three heartbeats¹⁶. This real-time feedback allows clinicians to locate reactive points and to titrate stimulation intensity according to the patient's autonomic responsiveness^{17,18}.

PBM introduces an additional dimension to VAS guided practice. PBM involves delivering low-intensity red or near-infrared light to biological tissues. Photons in this range are absorbed primarily by mitochondrial chromophores such as cytochrome-c-oxidase, enhancing electron transport, increasing adenosine triphosphate (ATP) synthesis and promoting the release of nitric oxide (NO)¹⁹⁻²¹. These photochemical effects trigger secondary signalling cascades, including controlled reactive oxygen species formation and modulation of gene expression and neuroimmune function^{19,22}. When PBM is applied to autonomic nerve-rich regions, measurable shifts in heart-rate variability have been reported, including increased parasympathetic indices (RSA, RMSSD) and reduced sympathetic stress markers, reflecting a shift toward parasympathetic dominance^{23,24}. Furthermore, PBM has been shown to mobilise endogenous stem cells, including neural and hematopoietic progenitors, in both preclinical and clinical studies²⁵⁻²⁷.

When PBM is delivered to auricular points identified through VAS palpation, the intervention can be tailored to the patient's current autonomic state^{15,28}. This combined approach supports gentle rebalancing of sympathetic and parasympathetic tone and may facilitate regenerative processes without the need for needles^{19,29,30}. The purpose of this article is therefore to review the origins, physiology and clinical application of the VAS, to summarise emerging research that objectively characterises the reflex, and to illustrate how PBM can be personalised using VAS feedback to optimise therapeutic outcomes.

1.2. René Leriche's Early Observation

The earliest documented description of a stimulus-induced pulse change originates from the French vascular surgeon René Leriche, who in 1941 observed an unusual phenomenon while examining a patient following surgery for an arteriovenous aneurysm³¹. When the skin overlying the femoral artery was touched, the arterial pulse exhibited a transient amplification; when the skin contact ceased, the pulse returned to baseline. Leriche interpreted this as evidence that cutaneous sensory input could influence vascular tone through reflexive autonomic pathways^{28,31,32}. At the time, the clinical relevance of the observation remained largely theoretical, and the phenomenon did not enter therapeutic practice.

1.3. Paul Nogier and the *Réflexe Auriculo-Cardiaque*

Two decades later, the French physician Paul Nogier rediscovered and formalised this reflex within the emerging field of auriculotherapy¹⁶. While palpating the radial pulse during examination, Nogier noted that touching specific points on a patient's ear produced a brief, reproducible change in pulse amplitude. He termed this response the *Réflexe Auriculo-Cardiaque* (RAC) and demonstrated that the reflex could be used to locate physiologically active auricular points in real time¹⁶. Nogier further observed that the change occurred within one to three heartbeat cycles, implicating rapid autonomic modulation rather than mechanical or hemodynamic changes.

2. Evolution of VAS Terminology

Over the decades following Nogier's discovery, clinicians and researchers sought terminology that more accurately reflected the underlying physiology of the reflex. Early descriptions referred to the phenomenon simply as a pulse reaction or retained Nogier's original French term RAC¹⁶. However, this terminology implied a primarily cardiac origin and suggested that the ear–heart connection was unique. Subsequent investigations showed that similar reflexive pulse changes could be elicited by cutaneous micro-stimulation at other body sites, indicating that the response reflected a broader autonomic regulation of vascular tone rather than a direct cardiac reflex³³.

As physiological studies in the 1970s and 1980s clarified the roles of arterioles, metarterioles and arteriovenous shunts in shaping pulse-wave propagation, several European researchers, including members of the German Academy of Acupuncture, introduced the term Vascular Autonomic Signal (VAS)^{33,34}. This designation emphasised that the reflex represents autonomic modulation of vascular resistance, detectable as a transient change in pulse amplitude, and that it can be recorded objectively using methods such as Doppler ultrasound and plethysmography, rather than being merely a subjective sensation in the examiner's fingers.

Today, the terms RAC and VAS are sometimes used interchangeably, but subtle distinctions persist. In French-speaking practice, RAC typically denotes the clinical palpation technique used to detect the reflex^{28,32}. In German- and English-language literature, VAS is preferred to describe the physiological neurovascular event itself^{28,32}. Some practitioners deliberately reserve VAS for the objectively measurable component and RAC for the manual technique used to elicit it. This evolving terminology reflects the field's progression from anecdotal clinical observation toward a mechanistic, research-driven interpretation of the reflex.

2.2. Physiological Basis

Pulse Wave Dynamics

When the left ventricle contracts, it generates two overlapping mechanical phenomena within the arterial system. The first is a rapidly propagating pressure or pulse (shock) wave that travels along the arterial wall at approximately 5–10 m/s^{35–37}. This wavefront reflects at points of branching and changes in vessel calibre, producing forward and retrograde components that combine constructively and destructively to shape the resulting waveform^{36,37}. The second phenomenon is the slower bulk flow of blood, which moves the fluid column itself at only a few centimetres per second. In central arteries these two phenomena are relatively distinct; however, in the peripheral vasculature, their interaction generates the palpable arterial pulse perceived at the wrist^{37,38}.

At the radial artery, the pulse felt under the examining finger represents a composite of the primary forward wave generated by ventricular ejection and multiple reflected waves arising from the arteriolar and capillary beds. The contour and perceived tension of the pulse are influenced by arterial elasticity, blood volume and the functional state of metarterioles and arteriovenous (AV) shunts, which determine how blood is distributed between capillaries and the superficial venous plexus. Shifts in microvascular tone can considerably alter the ratio of forward to reflected waves, even when cardiac output remains stable^{39,40}.

Auricular and cutaneous stimulation interface with this system through the peripheral nervous system. The auricle receives sensory innervation from branches of the vagus, trigeminal and facial nerves, as well as from the greater and lesser auricular nerves⁸. When a physiologically active auricular point is touched or illuminated, afferent signals project to the nucleus *tractus solitarius* (NTS) and related brainstem autonomic centres⁴¹. These centres adjust efferent sympathetic and parasympathetic output to the microvasculature. A brief surge in sympathetic tone can constrict metarterioles and AV shunts, increasing reflected wave amplitude and producing a palpable “hump.” Conversely, a shift

toward parasympathetic influence or vasodilatory signalling can soften the pulse, producing a transient “dip”^{8,41}.

A defining feature of the Vascular Autonomic Signal is that the response is rapid and self-limiting. Because the reflex is mediated by short-loop autonomic feedback circuits, the pulse change typically lasts only one to three cardiac cycles before returning to baseline³⁶. This distinguishes the VAS from slower vasomotor responses driven by metabolic, hormonal or emotional influences. The speed, subtlety and reversibility of the VAS make it well suited as a real-time clinical feedback mechanism, allowing practitioners to determine immediately whether a stimulus is engaging the autonomic system without significantly altering systemic haemodynamics.

2.3. Neurovascular and biochemical pathways

The VAS reflects not only mechanical modulation of arterial pulse dynamics but also complex neurovascular and biochemical signalling. Auricular stimulation activates afferent fibres from several cranial nerves, including the auricular branch of the vagus nerve, the auriculotemporal branch of the trigeminal nerve, and contributions from the facial, greater auricular and lesser occipital nerves^{7,41-43}. These afferent signals project to the nucleus NTS and associated brainstem autonomic centres, where they are integrated and relayed to sympathetic and parasympathetic efferent pathways^{44,45}.

Stimulation of the vagal afferents is known to influence the release of several neurotransmitters and neuropeptides, including glutamate, aspartate, GABA, acetylcholine and noradrenaline, particularly within limbic and cortical regulatory circuits⁴⁶⁻⁴⁸. Activation of the cholinergic anti-inflammatory pathway further modulates immune function by reducing the release of pro-inflammatory cytokines and influencing nitric-oxide synthesis⁴⁹⁻⁵¹. These neurochemical effects translate into measurable autonomic outcomes: increased vagal tone enhances heart-rate variability and promotes relaxation, while sympathetic activation decreases variability and increases cardiovascular tension⁵²⁻⁵⁴.

In the context of the VAS, a brief sympathetic surge can constrict metarterioles and arteriovenous shunts, generating the palpable “hump” response. A shift toward parasympathetic dominance can cause transient vasodilation, resulting in a “dip” in pulse tension. The reflex is rapid and self-limiting, consistent with short-loop autonomic feedback circuits^{18,28,33,55}.

PBM interacts with these pathways in a complementary manner. Absorption of red or near-infrared photons by mitochondrial cytochrome c oxidase leads to the dissociation of NO from the enzyme, restoring electron transport and ultimately increasing ATP production and mitochondrial membrane potential^{21,56,57}. PBM also up-regulates nitric-oxide synthase, promoting NO-mediated vasodilation and improved microcirculation⁵⁸⁻⁶⁰. Reactive oxygen species produced at low physiological levels act as second messengers, triggering transcriptional pathways that up-regulate anti-inflammatory and antioxidant responses⁶¹⁻⁶³.

Stem and progenitor cells have been shown to be particularly sensitive to PBM-induced signalling, which can enhance their mobilisation, differentiation and tissue repair functions in both animal and human studies⁶⁴⁻⁶⁶.

By combining auricular stimulation with PBM, clinicians influence both afferent neural regulation and mitochondrial bioenergetics. This dual action helps rebalance sympathetic–parasympathetic tone, improve microvascular perfusion and promote cellular repair. These physiological mechanisms help explain why subtle stimulation applied to the ear can evoke a reproducible, transient change in radial pulse tension detected during VAS palpation.

2.4. Palpation Technique

Reliable detection of the VAS requires both tactile sensitivity and a standardised, reproducible method⁶⁷.

Finger selection and placement

The VAS is typically palpated at the right radial artery using the left thumb, allowing the examiner's right hand to perform auricular stimulation. The thumb should be relaxed and slightly flexed (approximately 110–120°), with the oval, sensitive portion of the thumb tip placed gently over the arterial wall. Excessive pressure must be avoided, as it can either dampen or fully occlude the pulse, masking the transient modulation associated with the VAS⁶⁷⁻⁶⁹.

Practitioners with thickened or calloused skin may need to lightly abrade the thumb pad to enhance tactile acuity. For those who initially struggle to perceive subtle pulse changes, the three-finger technique, lightly placing the index, middle and ringfingers over the artery, can enlarge the contact area and make the brief pulse deviation easier to detect⁷⁰.

2.5. Body positioning and environment

The patient should be placed supine or seated with the forearm supported. The examiner stabilises the patient's arm to reduce muscular tension and maintains a relaxed posture to prevent wrist and shoulder strain. A quiet, low-stimulus environment is essential, as external noise, temperature shifts or conversation can alter autonomic tone and confound the pulse response⁷⁰.

If attention or tactile clarity decreases, the practitioner should pause briefly and resume, rather than continuing with degraded sensitivity.

2.6. Micro-stimulation and observation

Auricular stimulation may be delivered via a gentle probe pressure, touch, auricular seed placement, or a brief PBM exposure. Stimulation is applied for one to two cardiac cycles only.

If the auricular point is physiologically active, a transient modulation in pulse amplitude or tension is perceived within one to three beats. Stimulation must be reduced or stopped immediately once the VAS attenuates, to avoid overstimulation. When PBM is incorporated, wavelength, pulsing frequency, and exposure duration may be adjusted while monitoring the VAS to individualise dosing.

2.7. Sources of error and skill development

Common barriers to reliable VAS detection include (Table 1):

Table 1. Source of error and effect on examination.

Source of Error	Effect on Examination
Excessive thumb pressure	Pulse dampening or total occlusion (blocking the signal).
Calloused or desensitised skin	Reduced tactile perception; inability to feel subtle changes.
Incorrect finger angle or broad contact surface	Loss of waveform differentiation (blurring the "hump" vs. "dip").
Patient movement or muscle tension	Irregular pulse contour (noise) complicating signal detection.
Examiner fatigue or distraction	Decreased sensitivity and higher risk of misinterpretation.

Structured training significantly improves detection accuracy. Mentored practice is considered essential during skill acquisition^{71,72}.

Some training programs utilise analogue vascular models (fluid-filled elastic tubes) to demonstrate how changes in vascular impedance alter pulse waveforms. Electronic auricular point locators and high-resolution pulse imaging can serve as useful adjuncts, providing objective confirmation while tactile sensitivity develops. Even experienced clinicians benefit from periodic recalibration to maintain precision ⁷³.

3. Integration with Photobiomodulation

When PBM is applied to auricular points identified through VAS palpation, the two modalities become synergistic ^{15,74}. VAS determines which points are actively engaged in autonomic regulation at that moment and PBM provides a gentle, non-invasive stimulus that modulates cellular and vascular responsiveness at those same sites.

This produces a precision-guided, patient-specific intervention, rather than a generalised or fixed-protocol stimulation approach.

3.1. Mechanistic Synergy with Autonomic Regulation

PBM has measurable effects on autonomic nervous system balance. In a controlled study, laser stimulation of the lumbar and sacral regions resulted in increased parasympathetic tone, reflected by higher RSA and RMSSD, and reduced sympathetic stress index indicating a shift toward parasympathetic dominance ⁷⁵.

Because the VAS itself is a real-time reflection of autonomic tone, monitoring VAS during PBM allows the practitioner to titrate dose until the autonomic system begins to rebalance.

Once the VAS attenuates, stimulation is stopped, preventing sympathetic overstimulation and ensuring dosing remains within the patient's adaptive capacity ⁷⁶.

Furthermore, NO-mediated vasodilation induced by PBM may enhance the VAS amplitude by altering pulse-wave propagation, improving perceptual clarity for the practitioner.

3.2. PBM and Endogenous Stem-Cell Mobilisation

An emerging area of interest is PBM's influence on stem-cell activation and recruitment.

In animal models, near-infrared PBM has been shown to expand neural stem-cell pools and promote dendritic arborisation and neuronal repair ⁷⁷⁻⁷⁹. Moreover, in a human pilot study, PBM applied to the tibial bone marrow increased circulating CD34+ stem cells from approximately 7.8% to 29.5%, while macrophage populations increased from 7.8% to 52.1% within 2–4 days ⁸⁰.

These findings suggest that PBM delivered to VAS-responsive auricular points may support both autonomic regulation and regenerative capacity, offering potential benefit for chronic pain, neuroinflammation and neurodegenerative conditions.

4. Clinical Illustrations

4.1. Case Study 1: Chronic Insomnia and Autonomic Hyperarousal

A 70-year-old woman presented with a 20-year history of insomnia, characterised by difficulty initiating sleep, frequent nocturnal awakenings and daytime fatigue. Conventional pharmacological therapies had provided only short-term relief without improving sleep quality.

During assessment, VAS palpation of the radial pulse identified reactive auricular points at Shen Men, Limbic System, Thalamus, and micro-areas corresponding to Heart and San Jiao, indicating autonomic hyperarousal with limbic involvement.

PBM at 810 nm was applied in pulsed mode to each reactive point. Stimulation at each site was discontinued once the VAS attenuated, preventing overstimulation.

Over six sessions delivered across four weeks (one to two weekly treatments), the patient reported:

- Faster sleep onset;
- Fewer night-time awakenings;
- Improved morning refreshment and daytime function.

Follow-up treatments every four weeks maintained clinical improvement without pharmacological support.

This case demonstrates how VAS-guided PBM can stabilise autonomic tone and improve sleep regulation in chronic insomnia.

4.2. Case Study 2: Neuropathic Pain and Autonomic Dysregulation

A 55-year-old man presented with five years of neuropathic low back pain secondary to lumbar disc herniation. Symptoms included burning dysaesthesia, hypersensitivity and sleep disturbance. Prior interventions— including analgesics, physiotherapy and nerve blocks—provided only temporary relief.

VAS-guided auricular mapping identified strong responses at Lumbar Spin Sciatic Nerve, and Sympathetic Chain auricular zones.

PBM at 810 nm was applied to the identified auricular points and to the paraspinal muscles, stopping each application when the VAS response diminished.

After eight sessions over four weeks, the patient reported:

- Marked reduction in pain intensity;
- Improved mobility and daily function;
- Normalised sleep quality.

These improvements were sustained at a three-month follow-up.

This case suggests that VAS-guided PBM may be clinically valuable for chronic neuropathic pain, likely by modulating both peripheral inflammation and central autonomic dysregulation.

5. Final remarks

VAS represents a practical and reproducible interface between peripheral microstimulation and autonomic vascular regulation. By condensing complex haemodynamic and neurochemical processes into a transient pulse response, VAS palpation enables real-time, feedback-driven assessment at a single, anatomically defined site. Objective evidence from analogue vessel models, Doppler ultrasound, plethysmography, and high-resolution optical imaging confirms that the VAS reflects genuine autonomic modulation rather than a subjective tactile impression.

Integration with PBM enhances the therapeutic potential of VAS-guided interventions. PBM modulates mitochondrial activity, nitric oxide signalling, microcirculation, and neuroimmune balance, allowing tailored, feedback-responsive dosing that aligns with personalised medicine principles. Clinical observations suggest potential benefit in conditions characterised by autonomic dysregulation, including chronic pain, insomnia, vertigo, anxiety, and neuropathic dysfunction.

Effective application of VAS-guided PBM requires structured training, tactile sensitivity, and consistent technique.

Although preliminary evidence is encouraging, larger controlled trials are needed to establish effect sizes, optimal PBM parameters, and condition-specific protocols. Continued mechanistic research linking autonomic physiology, vascular dynamics, and neuro-immune modulation will strengthen the scientific basis of this approach. Ultimately, VAS-guided PBM offers a precise, adaptive, and evidence-informed modality, providing clinicians with a real-time tool to modulate autonomic tone while supporting the body's intrinsic self-regulatory capacity.

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Clinical cases

Mitochondrial Bioenergetics and Systemic Regeneration: A Narrative Review and Clinical Case Series of Photobiomodulation-Assisted Stem-Cell Therapy.

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Abstract

Background: Photobiomodulation (PBM) is a non-thermal light therapy that enhances mitochondrial efficiency by targeting cytochrome-c oxidase, thereby increasing ATP production and reducing oxidative stress. Stem cells rely heavily on these mitochondrial metabolic transitions to determine lineage commitment, migration, and reparative function. This article reviews the bioenergetic rationale for combining PBM with stem-cell therapy and explores the potential of this synergistic approach to treat conditions characterised by autonomic dysregulation, chronic inflammation, and impaired cellular repair.

Methods: A narrative critical review was conducted to synthesise literature regarding PBM mechanisms, stem-cell bioenergetics, and marrow-directed phototherapy. Furthermore, a clinical case series evaluated the practical application of PBM-assisted autologous stem-cell therapy in three patients. PBM was applied to the proximal tibial bone marrow to stimulate progenitor mobilisation, as well as to autonomic regulatory sites. Outcomes were assessed using validated measures.

Results: Mechanistically, PBM was found to improve mitochondrial oxygen utilisation and support stem-cell viability, paracrine signalling, and systemic mobilisation. Clinically, the combined therapy yielded significant improvements across all cases. The vasomotor case demonstrated reduced hot flash frequency and normalised sleep continuity. The fibromyalgia patient reported a reduction in pain intensity (VAS decreased from 8 to 4) and improved functional capacity. The anxiety case showed a reduction in GAD-7 scores from moderate (15) to mild (6), indicating improved autonomic stability.

Conclusion: PBM and stem-cell therapy likely operate in synergy through shared mitochondrial, immune-regulatory, and neuroendocrine pathways. PBM acts as a metabolic primer, creating an optimal microenvironment for stem-cell function and systemic repair. While these early findings are encouraging for treating complex conditions involving autonomic dysfunction, further controlled trials and standardised dosing protocols are necessary to fully validate this therapeutic strategy.

Keywords: Photobiomodulation; Stem-cell Therapy; Mitochondrial Bioenergetics; Autonomic Dysregulation; Synergistic Therapy.

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1. Introduction

PBM refers to the therapeutic use of low-irradiance red and nearinfrared (NIR) light to modulate cellular activity in ways that enhance physiological function without producing thermal tissue damage. The therapeutic potential of light in biology was first proposed in the late 19th century, but modern PBM research emerged following Mester's work in

the 1960s demonstrating accelerated wound healing and hair growth in animals exposed to low-power laser light. Since then, PBM has developed into a clinically and mechanistically validated therapeutic modality with applications in wound healing, neurorehabilitation, pain modulation, and regenerative medicine ¹⁻⁵.

The primary molecular target of PBM is cytochrome-c oxidase in the mitochondrial electron transport chain. This enzyme catalyses the final step of oxidative phosphorylation, transferring electrons to molecular oxygen. Under conditions of cellular stress, hypoxia, inflammation, or oxidative imbalance, nitric oxide may competitively bind to cytochrome-c oxidase, displacing oxygen and reducing ATP production. PBM has been shown to photodissociate nitric oxide from this binding site, restoring oxygen utilisation and electron transfer efficiency. The resulting increase in mitochondrial membrane potential leads to enhanced ATP synthesis, improved oxygen consumption efficiency, and controlled reactive oxygen species (ROS) signalling that acts as a transcriptional regulator rather than as a cytotoxic agent ⁶⁻⁸.

These mitochondrial changes initiate a cascade of cellular and systemic effects including modulation of redox balance, stabilisation of calcium signalling, activation of pro-survival transcription factors, increased synthesis of growth factors, and normalisation of inflammatory mediator release. PBM therefore influences not only energy metabolism but also cell phenotype, tissue repair processes, and immune system behaviour ⁹⁻¹¹.

Stem cells occupy a central role in tissue repair and systemic homeostasis, and their functional behaviour is tightly regulated by mitochondrial metabolic state. Pluripotent and undifferentiated stem cells rely primarily on glycolysis, while lineage commitment and maturation require a shift toward oxidative phosphorylation ¹²⁻¹⁶. This bioenergetic switch is not merely a reflection of cellular metabolic needs; it is a regulatory checkpoint that determines whether stem cells proliferate, migrate, differentiate, or adopt a trophic signalling role within their microenvironment ¹⁷⁻¹⁹.

Studies demonstrate that PBM enhances stem-cell viability, proliferation capacity, and resistance to oxidative stress by improving mitochondrial respiratory efficiency, supporting membrane potential stability, and modulating intracellular signalling pathways involved in cell fate determination ²⁰⁻²³. PBM also influences the secretome of mesenchymal stem cells (MSCs), increasing the release of anti-inflammatory cytokines, neurotrophic factors, and angiogenic signals that mediate many therapeutic effects traditionally attributed to cell engraftment ^{21,24,25}.

In vivo, PBM may further act on the regenerative niche, modifying the extracellular environment in ways that promote stem-cell retention, homing, and functional performance. Moreover, skeletal regions containing abundant red marrow, such as the proximal tibia, serve as accessible and responsive sites for PBM delivery. Research suggests that PBM applied over the tibial bone marrow can stimulate the mobilisation of endogenous progenitor cells into systemic circulation, reflecting not only local mitochondrial activation but also a coordinated systemic regenerative response ²⁶⁻²⁸.

Taken together, these mechanisms provide a coherent biological rationale for combining PBM with stem-cell-based therapies. PBM may enhance stem-cell treatment outcomes by optimising cellular metabolism, reducing inflammatory interference, and improving both local tissue environments and systemic immune-regulatory conditions. The integration of these approaches represents a promising direction for regenerative medicine, particularly in conditions characterised by mitochondrial dysfunction, chronic inflammation, neuroimmune dysregulation, and reduced adaptive repair capacity ²⁹⁻³³.

2. Mitochondrial Mechanisms of Photobiomodulation

The therapeutic effects of PBM originate primarily at the level of the mitochondrion, which serves as a central regulator of cellular respiration, redox balance, calcium handling, and apoptosis. Because these processes influence cell survival, immune activation, and repair capacity, even small improvements in mitochondrial function can have clinically significant systemic consequences ^{31,34-36}.

2.1. Cytochrome-c Oxidase as the Primary Photoacceptor

Cytochrome-c oxidase (Complex IV) is the principal photoacceptor for red and near-infrared light in the electron transport chain^{37,38}. Under hypoxic or inflammatory conditions, nitric oxide (NO) can bind to cytochrome-c oxidase and block oxygen utilisation, leading to impaired ATP production². PBM photodissociates NO from this binding site, restoring electron flow, mitochondrial membrane potential, and ATP synthesis³⁹⁻⁴¹.

2.2. Regulation of Redox Signaling and Controlled ROS Production

While excessive ROS can cause oxidative damage, low-level ROS is a physiologic signalling molecule involved in adaptive cellular communication. PBM increases mitochondrial ROS only within controlled ranges, generating a redox-signalling response rather than oxidative stress^{2,42-443}. This signalling activates transcriptional regulatory pathways including:

- Nrf2 – Upregulation of endogenous antioxidant defences⁴⁵.
- NF-κB – Modulated and not suppressed inflammatory signalling⁴⁶.
- CREB – Enhancement of neuronal plasticity and cellular repair⁴⁷.

This controlled redox modulation contributes to reduced inflammatory cytokine expression and enhanced tissue recovery⁴⁸.

2.3. Modulation of Calcium Homeostasis

Mitochondria regulate intracellular calcium in coordination with the endoplasmic reticulum. PBM stabilises the mitochondrial membrane potential ($\Delta\Psi_m$), increasing mitochondrial calcium buffering capacity and improving intracellular calcium rhythm regulation⁴⁹⁻⁵³. These effects protect neurons from excitotoxicity, stabilise synaptic signalling, reduce inflammatory cytokine secretion, and promote balanced cellular metabolism.

This is directly relevant in nociplastic pain, sleep dysregulation, and autonomic imbalance, where calcium-signalling abnormalities are central to symptom persistence.

2.4. ATP-Driven Support for Repair, Immunity, and Neuroendocrine Regulation

ATP availability determines whether cells maintain function or engage in repair. When ATP is scarce, cells adopt a conservation mode. By restoring mitochondrial ATP production, PBM shifts cells toward pro-repair and pro-regeneration metabolic states. This results in improved protein synthesis and extracellular matrix remodelling, enhanced angiogenesis and microcirculation, restoration of immune tolerance patterns, and stabilisation of hypothalamic autonomic regulation centres^{54,55}.

Thus, PBM acts not only locally but also systemically through mitochondrial–neuroendocrine coupling.

2.5. Implications for Stem-Cell Biology

Stem cells exhibit metabolic plasticity in which mitochondrial state determines fate (Table 1).

Table 1. Mitochondrial State and corresponding Stem-Cell Behaviour⁵⁶⁻⁶¹.

Mitochondrial State	Stem-Cell Behaviour
Low oxidative phosphorylation; glycolysis dominant	Self-renewal / pluripotency
Higher oxidative phosphorylation, stable $\Delta\Psi_m$	Directed differentiation and reparative signalling

Therefore, PBM may support stem-cell function by:

- Increasing mitochondrial ATP output ⁶²;
- Reducing oxidative stress susceptibility ^{63,64};
- Enhancing survival and migration to injury sites ^{65,66};
- Increasing release of trophic anti-inflammatory and angiogenic factors ^{67,68}.

This suggests the reasons for the positive clinical synergy observed when PBM is combined with stem-cell therapy.

3. Rationale for Photobiomodulation Targeting the Tibial Bone Marrow

The proximal tibia contains a high concentration of active red bone marrow, which houses both mesenchymal stem cells (MSCs) and hematopoietic stem/progenitor cells (HSPCs). Unlike deeper marrow reservoirs such as the pelvis or vertebral bodies, the tibial metaphysis has relatively thin cortical bone, low adipose interference, and close proximity to the skin surface. This anatomical configuration allows red and near-infrared wavelengths to penetrate adequately into the marrow cavity when delivered with appropriate irradiance and contact coupling ^{69,70}.

Bone marrow is not a static storage site for progenitor cells; it is a dynamic immunometabolic organ responsible for cellular regeneration, immune coordination, and inflammatory adaptation. The marrow microenvironment includes a network of stromal cells, endothelial niches, sympathetic innervation, and metabolic gradients that collectively determine stem-cell activation, quiescence, and release into systemic circulation ⁷¹⁻⁷³.

3.1. Evidence for PBM-Induced Stem-Cell Mobilisation

Preclinical studies have demonstrated that PBM directed to bone marrow activates intrinsic regenerative pathways ⁷⁴, accelerated tissue repair following cardiac and neural injury ⁷⁵⁻⁷⁷, and enhanced survival and differentiation of MSCs in vivo ^{78,79}.

More recent clinical data provide translational support. A human pilot trial reported that PBM applied to the proximal tibia produced a measurable increase in circulating CD34⁺ progenitor cells, with peak mobilisation occurring 2–4 days post-treatment, indicating a coordinated biological release rather than transient photostimulation ⁸⁰.

3.2. Systemic Immunoregulatory Effects of Marrow-Directed PBM

Bone marrow stimulation influences not only cell quantity but also immune phenotype and inflammatory signalling. PBM to marrow regions has been associated with:

- Mobilisation of regenerative mononuclear cell populations ⁸¹⁻⁸³;
- Shift toward M2 (pro-repair) macrophage phenotype expression ⁸⁴;
- Reduction of pro-inflammatory cytokines including TNF- α and IL-6 ²;
- Improvement of vagal-sympathetic balance and neuroimmune responsiveness ^{85,86}.

This systemic signalling likely arises from coordinated interplay between mitochondrial metabolic restoration, endothelial nitric oxide regulation, anti-inflammatory paracrine factor release by MSCs, and autonomic regulation of marrow immune activity ⁸⁷⁻⁹⁰.

3.3. Why the Tibial Site is Clinically Advantageous

The tibial marrow site offers several practical advantages in therapeutic settings (Table 2).

Table 2. Clinical considerations for the benefits of using the tibial site.

Clinical Consideration	Justification
Biological accessibility	Thin cortical bone enables therapeutic light penetration with predictable dose delivery.
High progenitor density	Contains both MSC and HSPC populations relevant to systemic regeneration.
Consistent anatomy	Provides reproducible and standardised patient positioning.
Comfort & safety	Minimally invasive, does not require imaging or invasive access.
Systemic therapeutic reach	Allows body-wide modulation through marrow-derived cell signalling.

PBM applied to the proximal tibia penetrates cortical bone and reaches the red marrow, where it enhances mitochondrial function in mesenchymal and hematopoietic stem cells. Improved metabolic signaling promotes CD34+ progenitor mobilisation, M2 macrophage polarisation, and regenerative cytokine modulation, enabling systemic therapeutic effects from a localised treatment site ^{91,92} (Figure 1).

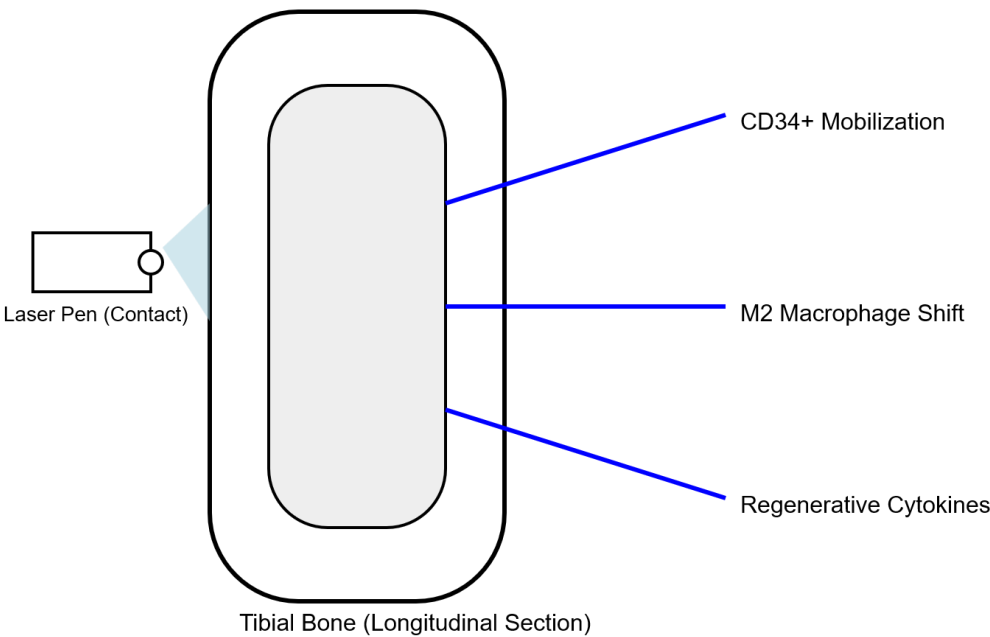


Figure 1. Tibial Bone Marrow PBM Mechanism

4. Clinical Synergy of Photobiomodulation and Stem-Cell Therapy

The therapeutic interaction between PBM and stem cell therapy arises from their complementary effects on mitochondrial metabolism, immune regulation, tissue repair, and neuroendocrine balance. PBM does not replace the function of transplanted or mobilised stem cells. Rather, it creates a metabolic and microenvironmental context in which endogenous or administered stem cells can survive, signal, and integrate more effectively ^{65,78,93-95}.

Stem cells require adequate mitochondrial function to transition between quiescence, proliferation, and differentiation. Mitochondrial bioenergetics therefore determine the reparative capacity of stem-cell populations. PBM enhances electron transport chain efficiency at cytochrome-c oxidase, restores ATP production, and regulates nitric-oxide availability, which improves mitochondrial performance in both stem cells and the host tissue milieu ^{36,96-98}.

At the immunological level, PBM induces a regulatory shift characterised by reduced proinflammatory cytokines (IL-1 β , IL-6, TNF- α) and increased anti-inflammatory mediators (IL-10, TGF- β). This environment supports mesenchymal stem-cell driven modulation of macrophage phenotype and promotes regenerative M2 polarisation. The combined result is reduction of inflammatory burden and support of tissue remodelling in chronic and nociplastic conditions^{97,99-103}.

PBM also promotes angiogenesis through upregulation of VEGF and stabilisation of endothelial cell metabolism. Enhanced microvascular perfusion improves the trophic signalling efficiency of stem cells, particularly in tissues with autonomic dysregulation, metabolic exhaustion, or chronic inflammation⁸².

Finally, PBM influences neuroendocrine centres including the hypothalamus, locus coeruleus, and brainstem autonomic nuclei. By improving cellular energy availability and modulating inflammatory signalling that reaches the central nervous system, PBM contributes to stabilisation of sleep cycles, vasomotor tone, pain perception, and affective regulation¹⁰⁴⁻¹⁰⁷.

This integrated framework explains the multimodal improvements observed in sleep stability, vasomotor symptom reduction, nociplastic pain reduction, and reduced anxiety in the clinical cases presented.

4.1. Autonomic Nervous System Modulation and Sleep Physiology

Chronic pain, anxiety, and vasomotor instability share a characteristic pattern of sympathetic dominance with insufficient parasympathetic recovery. This dysregulated autonomic tone is reinforced by inflammatory cytokine signalling and disrupted hypothalamic feedback loops. PBM improves mitochondrial efficiency in limbic, hypothalamic, and brainstem autonomic circuits, increasing inhibitory neurotransmission and vagal parasympathetic tone. These effects contribute to reduced hyperarousal, improved sleep consolidation, and stabilisation of thermoregulatory control¹⁰⁸⁻¹¹³.

Stem-cell derived immunomodulatory and neurotrophic factors introduce longer-term stabilisation of autonomic activity by decreasing microglial-driven cytokine release and promoting a shift toward regenerative M2 macrophage states. This reduces the neuroimmune drivers of sympathetic overactivation often implicated in nociplastic pain, vasomotor symptoms, and anxiety-related physiological patterns.

Sleep architecture depends on adequate mitochondrial ATP availability. Deep non-REM sleep requires synchronised low-energy neuronal states. When ATP is insufficient, cortical networks maintain light, fragmented, or hypervigilant sleep. PBM enhances oxidative phosphorylation and restores mitochondrial coupling, supporting metabolic transitions required for deep, continuous sleep cycles¹¹⁴⁻¹¹⁶.

5. Clinical Case Series

5.1. Methods

Three clinical cases were documented to illustrate the functional interaction between PBM and autologous stem-cell therapy in endocrine, nociplastic pain, and anxiety-related presentations. Low-burden, validated scales were used to standardise symptom tracking and reduce subjective interpretation bias:

- Hot Flash Score (HFS) and Pittsburgh Sleep Quality Index (PSQI) for vasomotor and sleep symptoms;
- Visual Analogue Scale (VAS) and Revised Fibromyalgia Impact Questionnaire (FIQ-R) for nociplastic pain and functional status;
- Generalised Anxiety Disorder 7-item scale (GAD-7) for anxiety severity.

Treatments included autologous stem-cell therapy and PBM directed to the proximal tibial bone marrow, consistent with strategies shown to mobilise mesenchymal and hematopoietic progenitors into systemic circulation¹¹⁷. PBM was also applied to symptom-

relevant regulatory regions (e.g., cervical sympathetic chain, thoracic paraspinals, abdomen, auricular autonomic points) depending on presentation. Treatment intervals were once weekly.

Photobiomodulation Parameters

PBM was delivered in contact mode to the proximal tibia to target active red marrow. Approximately 1000 J was delivered per tibial site per session. This approach is consistent with marrow-directed PBM protocols designed to influence stem-cell mobilisation and systemic immunoregulatory signaling²³. Additional PBM was applied to autonomic and regional pain-modulating sites as clinically indicated.

Frequency Modulation Protocol

Frequency-modulated PBM followed clinical neuromodulation practices derived from Nogier and Bahr. Two primary modulation frequencies were used:

- 2442 Hz, applied to support stem-cell metabolic activation and trophic signalling;
- 4625 Hz, applied to support autonomic stabilisation and self-regulatory recovery processes.

These frequencies are not presented as disease-specific codes but as structured bioenergetics modulation domains influencing cellular redox tone and neuroimmune balance.

Rationale for Frequency Selection

Mesenchymal stem cells depend on controlled redox signalling and mitochondrial respiration to transition between quiescence, proliferation, and differentiation¹⁶. PBM delivered at frequencies in the 2–3 kHz range has been associated with increased mitochondrial coupling, enhanced oxidative phosphorylation efficiency, and increased release of paracrine repair mediators such as SDF-1, VEGF, and IL-10¹¹⁸⁻¹²⁰. This mechanistic profile aligns with the regenerative orientation attributed to 2442 Hz.

Autonomic dysregulation plays a central role in vasomotor instability, nociplastic pain, and anxiety disorders^{121,122}. PBM frequencies in the 4–5 kHz domain have been associated with enhanced vagal tone, reduced sympathetic drive, and modulation of hypothalamic-limbic circuits linked to sleep and affective stability. This corresponds to the clinical use of 4625 Hz to promote systemic regulatory recalibration¹²³⁻¹²⁵.

These frequency selections are reported to support transparency and reproducibility. The parameters remain exploratory and require controlled clinical trials.

5.2. Case 1: Vasomotor Instability and Sleep Disruption

A 50-year-old woman presented with new-onset hot flashes, night-time thermal dysregulation, and fragmented sleep. Baseline assessment demonstrated elevated Hot Flash Score and PSQI, consistent with impaired sleep quality and hypothalamic autonomic instability.

Following the first session of PBM-directed stem-cell therapy, the patient reported her first uninterrupted night of sleep in several weeks. By the fifth session, the Hot Flash Score demonstrated a marked reduction in both frequency and intensity of vasomotor episodes, and PSQI scores indicated clinically meaningful improvement in sleep continuity and depth.

These clinical changes align with mechanistic models in which PBM enhances mitochondrial coupling and redox stability within hypothalamic thermoregulatory centres, reducing erratic autonomic discharge. Stem cell derived paracrine signalling likely further reduced neuroinflammatory tone and contributed to stabilisation of hypothalamicpituitary.

tary feedback dynamics. Notably, improvement in sleep quality preceded vasomotor normalisation, consistent with evidence that restoration of non-REM metabolic quieting is a prerequisite for neuroendocrine homeostasis.

5.3. Case 2: Fibromyalgia and Nociceptive Pain

A patient with chronic widespread musculoskeletal pain, fatigue, and sensory hypersensitivity consistent with fibromyalgia underwent PBM-supported autologous stem cell therapy. At baseline, VAS pain score was approximately 8/10 with reduced functional capacity reflected in FIQ-R scores.

After three treatments, VAS pain decreased to approximately 4/10, and FIQ-R functional domains improved, indicating enhanced activity tolerance and decreased nociceptive amplification.

This pattern aligns with PBM-mediated microglial downregulation, reduced cytokine-driven central sensitisation, and restoration of mitochondrial efficiency in dorsal horn and limbic circuits. Stem cell derived immunoregulatory factors further supported sustained reduction in inflammatory signalling and facilitated repair of neuromuscular microenvironments.

5.4. Case 3: Anxiety and Autonomic Dysregulation

A patient with generalised anxiety and episodic autonomic reactivity was evaluated using GAD-7, with a baseline score of ~15, consistent with moderate anxiety severity.

After five treatments, GAD-7 decreased to ~6, within the mild range, accompanied by the patient's report of improved emotional regulation, reduced somatic tension, and a subjective sense of restored internal coherence.

Observed changes are consistent with PBM-mediated enhancement of limbic inhibitory neurotransmission and improved vagal tone, combined with stem-cell driven attenuation of neuroinflammatory signalling, resulting in recalibration of autonomic balance.

5.5. Interpretation

Across all three cases, the observed improvements appear to reflect shared mitochondrial-neuroimmune regulatory mechanisms rather than isolated symptomatic effects.

PBM functioned as a metabolic primer, enhancing mitochondrial oxidative phosphorylation, restoring ATP availability, and modulating nitric-oxide and redox-mediated cellular signalling. These changes support normalisation of hypothalamic and limbic autonomic centres, reduction of sympathetic hyperactivation, and stabilisation of sleep regulation and thermoregulatory control.

Stem-cell therapy contributed a longer-duration immunological and reparative influence by releasing paracrine mediators that reduce microglial-driven cytokine signalling, promote M2 macrophage polarisation, and support neural-endocrine tissue resilience. The resulting environment favours recovery of neurovascular tone, nociceptive modulation, and restoration of homeostatic autonomic patterns associated with emotional and pain regulation.

The consistency of improvement across conditions as diverse as vasomotor dysregulation, nociceptive pain, and anxiety suggests involvement of a common physiological convergence point: improved mitochondrial energy status, reduced neuroinflammation, and rebalancing of autonomic nervous system dynamics.

This integrated pattern aligns with contemporary models in which endocrine instability, chronic pain, and anxiety share overlapping bioenergetic and neuroimmune dysregulation pathways rather than being independent disease entities. The clinical trends observed here therefore support the rationale for combined PBM and stem-cell approaches aimed at restoring systemic regulatory stability, rather than targeting isolated symptoms.

6. Limitations

The clinical observations presented in this case series are uncontrolled and exploratory, and therefore cannot establish causality. Improvements may reflect the combined influence of PBM, stem-cell therapy, placebo responsiveness, natural symptom fluctuation, or concurrent lifestyle factors. Controlled studies with randomisation, comparator groups, and blinded outcome assessment are required to determine the magnitude and specificity of the therapeutic effects.

PBM delivered to bone marrow presents dosimetric challenges. Variations in tibial cortical bone thickness, marrow vascularity, and individual tissue optical properties may influence the penetration and bioavailability of near-infrared light. Standardised dosing models for marrow-targeted PBM are not yet established, and the 1000 J per tibial site protocol used here should be interpreted as a clinically derived approach, not a validated standard.

Similarly, stem-cell preparations are heterogeneous. Differences in cell source, concentration, preparation technique, viability, and paracrine secretome composition may influence outcomes and limit reproducibility across clinical settings. The cases described here used autologous preparations, which reduce immunological risk but do not control for biological variability.

Outcome measures relied on self-reported and functional scales (HFS, PSQI, VAS, FIQ-R, GAD-7). While these instruments are validated, they may still be influenced by expectancy, context, and regression to the mean. Future studies should incorporate objective physiological biomarkers, such as heart rate variability for autonomic balance, cytokine and inflammatory panel assays, and mitochondrial functional indices.

The sample size was small and spanned heterogeneous diagnostic categories. While this diversity supports exploration of shared regulatory mechanisms, it limits conclusions regarding condition-specific responsiveness, optimal dosing frequency, and treatment sequencing.

These limitations underscore the need for prospective, protocol-standardised, multi-centre trials evaluating the combined application of PBM and stem cell therapy, including clear mechanistic endpoints and long-term follow-up.

7. Conclusion

The synergistic integration of PBM and stem cell therapy appears to restore systemic homeostasis by optimising shared mitochondrial and neuroimmune pathways. By addressing the bioenergetic roots of autonomic dysregulation, this combined strategy offers a promising, mechanism-based approach for treating complex, multi-system disorders.

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Clinical case study

Effects of Complementary and Integrated Therapies on Performance and Recovery in Mountain Ultra-Endurance Running: A Case Study.

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Abstract

Mountain ultra-endurance running represents one of the most physiologically demanding sports, combining biomechanical stress, cardiorespiratory demands, metabolic strain, and psychological resilience. This study provides a comprehensive case analysis of a 44-year-old male athlete specialising in races exceeding 100 km, with a competitive history including distances up to 308 km. The investigation integrates Western physiological insights with Traditional Chinese Medicine (TCM) diagnostic frameworks and therapeutic approaches. Biomechanical and physiological mechanisms underlying performance and injury risk are described, followed by a longitudinal clinical assessment of recurrent musculoskeletal complaints, systemic imbalances, and therapeutic interventions. Treatments included acupuncture, auriculotherapy, moxibustion, manual therapy, and Chinese herbal medicine, combined with modern supplementation strategies. Results suggest that integration of TCM-based interventions with conventional physiological understanding may support endurance athletes in injury prevention, recovery, and performance stability.

Keywords: Biomechanics; Endurance Physiology; Trail Running; Traditional Chinese Medicine; Acupuncture; Moxibustion; Ultra-Marathon; Sports Injuries.

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1. Introduction

Trail running, as an organised sport, has its origins in informal competitions along natural routes, with historical references dating back to the late 19th century and gaining its modern form in the 20th century through emblematic races such as the Dipsea Race in the USA and similar initiatives in Europe and Asia. The field evolved rapidly from short trail and hill challenges to the ultra-endurance events seen today, marked by distances well beyond the marathon, significant elevation change, technical terrain, and exposure to variable environmental conditions ¹⁻³. Ultra-endurance trail events differ fundamentally from road running and standard marathons due to the multidimensional physiological, mechanical, and psychological demands involved. Athletes must contend with uneven surfaces, steep ascents and descents, extreme weather, sleep deprivation, and prolonged periods of muscular and metabolic stress. This leads to multi-systemic responses, potentially affecting the cardiovascular, renal, musculoskeletal, immunological, and nervous systems in ways not observed in conventional endurance events ⁴⁻⁶.

Despite the growing popularity of trail running, there remains uncertainty regarding the physiological responses elicited by different uphill locomotion strategies, particularly when contrasting running and walking on steep inclines. Key factors such as maximal oxygen uptake (VO₂max), running economy (Cr, defined as the energy cost of running,

or the amount of energy required to transport the body a given distance), and the proportion of VO₂ sustained throughout the race have demonstrated considerable variability across studies, often due to differences in testing protocols and athlete populations ⁷.

Additionally, important biomechanical and metabolic determinants, including muscle strength, architecture, fibre recruitment patterns, and terrain characteristics, influence the energetic cost of running uphill. The interplay between individual athlete characteristics and the topographical profile of each race further complicates the prediction of performance and fatigue. Given these complexities, comparative studies conducted in realistic trail running conditions remain scarce. Despite the surging popularity and participation in ultra-trail events, the energetic demands and physiological responses experienced by athletes in these extreme contexts remain inadequately characterised, particularly in real-world racing conditions. The complexity of continuously measuring metabolic and cardiopulmonary parameters over several consecutive days has contributed to a paucity of field-based research. Consequently, much of current understanding is derived from laboratory studies or short-duration outdoor experiments, limiting ecological validity. Recently, case studies ^{6,7} conducted in actual events have begun to shed light on the metabolic cost, efficiency of locomotion, and adaptive strategies athletes employ during mountain ultra-marathons. Preliminary findings suggest that, contrary to expectations, well-adapted athletes may sustain exercise intensities and mechanical efficiency even as fatigue accumulates, potentially through progressive locomotor adaptations over the course of the race. However, the interplay between environmental challenges, race strategies, and physiological adaptations deserves further investigation to inform training, preparation, and recovery protocols for trail endurance athletes.

Therapeutic interventions for ultra-endurance trail runners have traditionally centred on conventional sports medicine, focusing on acute injury management (e.g., musculoskeletal injuries), hydration strategies, nutritional protocols, and physiotherapy. Therapies such as cryotherapy, non-steroidal anti-inflammatory drugs, and physical therapy remain predominant among these athletes, with studies indicating more than 90% of ultra-endurance runners use such conventional treatments regularly. However, despite the widespread adoption of these conventional methods, challenges remain in prevention, recovery, and management of chronic fatigue, overtraining, and subtle metabolic-immune imbalances ^{5,6,8}.

TCM is increasingly considered a complementary or alternative therapeutic modality for endurance athletes. Clinical and experimental evidence highlights TCM's holistic framework, incorporating herbal therapy, acupuncture, *tuina* massage, and dietary modifications, as supporting energy balance (*Qi*), accelerating recovery, and addressing not only acute musculoskeletal complaints but also underlying systemic fatigue and immune modulation. However, surveys and recent systematic reviews suggest that, globally, less than 10% of ultra-endurance athletes consistently incorporate TCM interventions compared to conventional treatments ⁹⁻¹³.

Within TCM, the meridians and organs most often affected by ultra-endurance trail running include the Spleen and Stomach (responsible for nourishment and energy transformation), Liver (governing tendons and smooth flow of *Qi*), Kidney (basis of endurance and bone strength), and Heart (regulating circulation and mental resilience). Excessive physical exertion, environmental exposure, and inadequate recovery are believed to deplete Spleen *Qi*, injure Kidney Jing, stagnate Liver *Qi*, and disturb Heart *Shen*, resulting in chronic fatigue, muscle/tendon injuries, oedema, suboptimal recovery, and psychological imbalance. TCM's targeted interventions, especially when mapped to these meridians and organ systems, may offer distinct benefits: improving nutritional assimilation, promoting musculoskeletal resilience, enhancing immune recovery, and facilitating psychological adaptation to the rigors of ultra-endurance sports. These advantages justify further integration and rigorous comparative study of TCM within sports medicine for this unique population ¹¹⁻¹³.

2. Case presentation

This case study details the therapeutic management of an ultra-endurance athlete who sustained two significant musculoskeletal injuries during multi-stage ultra-distance events in 2023 and 2024. The case illustrates the integration of acupuncture, moxibustion, cupping therapy, manual therapies, and phytotherapy guided by the principles of TCM to facilitate recovery and performance maintenance.

The subject is a male trail runner affiliated with EDV Viana Trail Club from Portugal, renowned for participation and success in national and international trail endurance competitions. His body weight is within the normative range for high-performance endurance athletes, and he regularly competes at distances requiring significant aerobic and musculoskeletal adaptation.

Given the extreme demands and endurance-specific hazards of the scheduled ultra-trail events, the clinical and sports intervention team opted for a comprehensive, longitudinal monitoring approach. The aim was early detection and management of potential musculoskeletal, metabolic, or systemic physiological deteriorations that may occur over high cumulative training and competitive loads. It should be noted that the athlete is an amateur who works in an environment with climate control set to cold temperatures. A notable factor in this case is the athlete's occupational exposure to a cold working environment. This chronic exposure to cold temperatures is recognised as a primary contributing factor to the development of Internal Cold and *Yang* Deficiency syndrome. Such environmental stress leads to impairment of *Yang* energy, resulting in symptoms including cold intolerance, reduced metabolic function, and compromised circulation. This syndrome heavily influenced the subsequent treatment protocols, with warming therapies such as moxibustion and the use of warming herbal formulas being central to the therapeutic strategy.

Over the course of several weeks the athlete underwent regular clinical evaluations and performance monitoring. These included musculoskeletal examinations, nutritional assessments, physiological and biochemical testing, and continuous feedback during preparatory and competitive phases. The intervention team's objective was to safeguard the athlete's physical integrity, optimise performance, and scientifically document adaptive or pathological changes in the context of repeated high-load exposures.

As a non-professional elite-level competitor, the athlete demonstrated meticulous preparation and commitment to peak performance, seeking to represent his club at the highest standard. The clinical oversight allowed prompt identification of fatigue, injury, or maladaptive responses, supporting targeted interventions and personalised therapeutic strategies throughout the period of observation.

A dedicated follow-up team was established to provide monitoring and intervention throughout the observation period, particularly in anticipation of musculoskeletal injury or physiological decline. This multidisciplinary team was tasked with real-time assessment of the athlete's physiological and musculoskeletal condition, enabling therapeutic interventions as required.

The need for targeted therapeutic intervention arose on multiple occasions during the monitored races, as well as in the recovery phases between competitions. Acute and subacute therapies were employed in response to emerging symptoms, including musculoskeletal discomfort, functional decline, or general fatigue.

Therapeutic strategies included a combination of acupuncture sessions, with the selection and combination of acupuncture points tailored according to the athlete's clinical presentation at each intervention. The set of acupuncture points used varied case by case, depending on ongoing physical findings, energetic assessment, or specific complaints. Additional supplemental therapies were incorporated as indicated, most notably, vitamin D supplementation and other micronutrients were prescribed as needed, according to biochemical screening and fatigue status.

Other therapeutic interventions, such as manual therapy, trigger point release, physiotherapy modalities, and nutritional adjustments, were utilised based on the prevailing

clinical scenario and individual response. This dynamic and adaptive approach aimed to optimise recovery, minimise injury risk, and promote overall functional resilience throughout the period of intense physical demand.

Pain assessment was systematically performed using the Numerical Rating Scale (NRS) for pain, as recommended by the Portuguese Directorate-General of Health (DGS)¹⁴. This validated tool allowed quantitative documentation of pain intensity at each assessment point, facilitating objective monitoring and individualised adjustments to the therapeutic strategy. The perception of fatigue was assessed using the Rating of Fatigue (ROF) scale, a validated tool for quantifying subjective fatigue intensity in athletic populations¹⁵. The NRS and the ROF are validated patient-reported outcome measures that use an 11-point numeric scale ranging from 0 to 10. For both scales, 0 represents the absence of NRS for pain or ROF, while 10 indicates the worst imaginable pain or fatigue. These scales provide a simple, reliable means to quantify symptom intensity, facilitating clinical assessment and monitoring of treatment efficacy.

2.1. First Injury and Initial Presentation

In September 2023, following a 100 km race, the athlete reported pain localised on the anterior aspect of the left leg along the femoral nerve path, more specifically corresponding to the saphenous nerve. Palpation revealed altered muscle tone without incapacitating features, allowing continued training despite discomfort. At the conclusion of the race, pain corresponded anatomically to the liver meridian between points F5 and F6. Clinical pulse and tongue signs indicate liver *Qi* stagnation and damp heat.

2.2. Second Injury and Progression

In December 2023, during a 308 km race (ALUT- Algarviana Ultra Trail), the athlete developed digestive complaints, oedema and pain in the right calf, secondary to a compensatory protective posture. Post 15-day rest, muscular pain in the right leg persisted with symptoms reflective with palpatory tenderness along the Kidney, Bladder, and Liver meridians.

2.3. Acute Heat Stroke

The athlete experienced a heat stroke during the race, which occurred on a 281 km trail event called PT 281. During an intensely hot period, he went for approximately three hours without access to fluid replacement on a section of the trail where autonomous hydration was the athlete's responsibility. This prolonged lack of hydration under extreme heat conditions led to the onset of heat-related illness. Heat stroke, an imbalance characterised by excessive internal heat and *Yin-Qi* deficiency compromising thermoregulation.

3. Therapeutic Interventions and results

3.1. 1st injury - September 2023

Table 1. Acupuncture points and meridians used in the treatment sessions, as well as the treatment procedure

Treatment Session	Point/Meridian Selection	Procedure Target	Meridian-Based Rationale	NRS Before	NRS After
2 weekly sessions	GB34, ST40, SP9, ST34, LR2, LR3, LR5 (unilateral)	Tendon influence, oedema, <i>Qi</i> circulation, liver fire dispersion	GB34 ("Master point of tendons") targets pain/stiffness in lower limb tendons; LR2/LR3 disperse Liver <i>Qi</i> /fire and treat tension near the saphenous nerve; ST40 clears dampness/oedema; SP9 supports lower limb fluid/oedema; ST34 <i>Xi</i> -cleft acts on acute pain and mobility; LR5 connects meridian influence at the level of the injury.	8	2

The athlete reported partial pain relief but did not adhere to rest recommendations, continuing intensive training.

3.2. 2nd injury - December 2023

Table 2. Points and meridians used in the treatment sessions, as well as the treatment procedure

Timing & Session	Point/Meridian Selection (or Auriculotherapy Region)	Procedure Target	Meridian/Ear Point Rationale	NRS Before	NRS After
During race (acute phase)	Auriculotherapy: calf, stomach, liver, spleen, <i>shenmen</i>	To relieve pain and digestive complaints	Auricular points mapped to lower limb (calf), digestion (stomach, spleen), Liver for muscle-tendon regulation, <i>shenmen</i> to modulate pain and emotional/physiological stress; engages vagus and cranial nerves for systemic pain/digestive modulation in acute demand.	9	8
During race (acute phase)	Lymphatic drainage massage	Reduce oedema and clear lactic acid	Method enhances peripheral circulation, mobilises tissue fluid, and improves recovery in acute musculoskeletal overload scenarios.	—	—
4 sessions weekly, 15 days post-race	LI4, LR3, GB30, SP6, ST36, GB34 (bilateral use)	Muscular recovery, pain, overall <i>Qi</i> /blood support	LI4 (disperses <i>Qi</i> stagnation), LR3 (Liver <i>Qi</i> movement), GB34 (tendon/muscle pain), ST36 & SP6 (digestive & stamina), GB30 (deep gluteal, sciatica relief). Rationale: synergy for pain, recovery, and resolving both local and systemic stasis after endurance injury.	7	0

The pain was resolved fully after multiple sessions.

3.3. Follow-up: February 2024-May 2024

Table 3. Points and meridians used in the treatment sessions, as well as the treatment procedure.

Timing & Sessions	Point/Meridian Selection	Procedure Target	Meridian-Based Rationale	ROF Before	ROF After
16 weekly sessions (general support)	BL62, SP3, GB34, KI3, LR8, LR3, ST36, SI3 (bilateral)	Nourish <i>Qi</i> , blood, <i>Yang</i> ; support stomach, spleen, kidney, liver	BL62 and SI3 harmonise <i>Du</i> pathway (<i>Yang Qiao/Wei</i>); GB34, LR3, LR8 support Liver-blood and muscle recovery; ST36 and SP3 strengthen Spleen, KI3 nurtures kidney essence and <i>Yang</i> . Synergistic protocol for restoring energy and organ function post-endurance stress.	6	3

3.4. Treatment after acute Heat Stroke – July 2024 – August 2024

Table 4. Points and meridians used in the treatment sessions, as well as the treatment procedure.

Schedule	Point/Meridian Selection	Procedure Target	Meridian-Based Rationale	NRS/ROF Before	NRS/ROF After
3 sessions weekly	GV20, KI6, CV6, LI11	Heat exhaustion cooling, <i>Yin</i> support, and <i>Qi</i> regulation	GV20 (<i>Baihui</i>) stimulates brain and clears <i>Yang</i> heat; KI6 nourishes Kidney <i>Yin</i> and moistens dryness post-heat; CV6 (<i>Qihai</i>) boosts <i>Yuan Qi</i> and circulation; LI11 (<i>Quchi</i>) is a strong heat-clearing point, reduces fever and inflammation by releasing excess heat from the body.	—	—

Subsequent tongue changes reflected increased moisture, evidencing therapeutic effect.

3.5. Recovery and Maintenance: September-December 2024

Table 5. Points and meridians used in the treatment sessions, as well as the treatment procedure.

Timing & Sessions	Point/Meridian Selection	Procedure Target	Meridian-Based Rationale	ROF Before	ROF After
16 weekly sessions	CV4, CV6, CV12, ST36, SP6, KI3 + moxibustion	Strengthen spleen and kidney function	Points CV4, CV6, and CV12 support Ren Mai (Conception Vessel) for central <i>Qi</i> and <i>Yin-Yang</i> balance; CV12 aids upper digestion and spleen ST36 and SP6 enhance digestion, <i>Qi</i> and blood production; KI3 supports Kidney essence and <i>Yang</i> ; Moxa adds warming and <i>Yang</i> reinforcement.	9	0

Post heat stroke, the athlete undertook multiple races ranging from 49 km to 300 km with intermittent digestive complaints and fatigue. Treatment focused on strengthening spleen (BP) and kidney (KI) function using acupuncture points CV4, CV6, CV12, ST36, SP6, and KI3, complemented by moxibustion and phytotherapy. Throughout the treatment period, the athlete reported progressive improvements in perceived fatigue and exhaustion levels.

Given the athlete's daily exposure to cold environments, treatment emphasised expelling internal cold, supporting *Qi* and *Yang* of spleen and kidney, primarily via acupuncture with moxibustion Points included KI3, SP6, ST36, CV4, and CV6.

Phytotherapeutic intervention included a formula known as *Qi Hai Yao Fang* (Sea of *Qi*), a modern traditional Chinese medicine formulation designed to supplement and invigorate the *Qi* and *Yang* of the spleen and kidney, support digestive and metabolic functions, and address chronic deficiency syndromes, combined with *Ashwagandha*.

In this period, the athlete completed multiple races without injury, reporting improved energy and physical conditioning post-treatment.

4. Laboratory Findings and Supplementation

Serum analysis in March 2024, revealed vitamin D deficiency, elevated cortisol, and normal but low-end testosterone levels for an athlete. Supplementation with Chinese phytotherapy (*Qi Hai Yao Fang*), *Ashwagandha* (for cortisol modulation), vitamins (D, K2), marine minerals, zinc, EPA, and DHA were initiated to address biochemical imbalances.

Table 6. Integrative mapping between Western physiological findings and corresponding TCM syndromes.

Western Medical Finding	TCM Syndrome	TCM Syndrome Interpretation
Elevated cortisol, chronic fatigue	Kidney Jing/ <i>Yin</i> Deficiency	Loss of deep vital energy and regulatory essence; manifests as exhaustion, poor recovery, hormonal dysregulation.
Low testosterone	Kidney <i>Yang</i> Deficiency	Impaired warming and activating energy; causes cold intolerance, low vitality, and poor hormonal output.
Vitamin D deficiency, cold exposure	Spleen/Kidney <i>Yang</i> Deficiency	Weak transforming and activating force; results in metabolic slowing, susceptibility to cold, low resilience.
Poor digestion, persistent fatigue, lab abnormalities (spleen, kidney)	Spleen <i>Qi</i> Deficiency, Kidney <i>Qi</i> Deficiency	Deficient energy for nutrient assimilation and reserve replenishment; manifests as fatigue, weakness, impaired recovery.
Oedema, musculoskeletal complaints post-exertion	<i>Qi</i> stagnation, Liver <i>Qi</i> disharmony	Blockage in energy movement and regulation; causes swelling, muscle pain, emotional irritability.

5. Final remarks

Ultra-endurance trail running ranks among the most physiologically demanding athletic endeavours, demanding sustained cardiovascular, metabolic, musculoskeletal, and psychological adaptations under extreme and variable environmental conditions. The

present case illustrates these challenges, emphasising the cascading impacts of intense prolonged exertion compounded by environmental factors such as heat stress, dehydration, and terrain complexity. As these unique stressors precipitate multi-system perturbations encompassing energy metabolism, endocrine regulation, immune function, and neuromuscular integrity, standard sports medicine approaches targeting isolated clinical manifestations often fail to adequately address the complex, interdependent dysfunctions evident in ultra-endurance athletes.

Consistent with the introduction, the multifactorial nature of fatigue, systemic inflammatory activation, and musculoskeletal overload in ultra-trail performance necessitates multimodal assessment and individualised intervention. Conventional injury management and nutritional support (while foundational) leave a gap in addressing chronic fatigue syndromes, subclinical immune dysregulation, and autonomic imbalances frequently emerging during ultra-endurance competition cycles. Moreover, this case supports emerging evidence for the complementary use of TCM techniques, which offer holistic frameworks integrating organ system energetics with symptom amelioration.

Notably, acupuncture and moxibustion interventions targeting the Spleen, Kidney, Liver, and Stomach meridians address fundamental TCM pathogeneses consistent with Western markers identified in the athlete, such as vitamin D deficiency and cortisol excess. These therapies potentially restore *Qi* and *Yang*, enhance microcirculation, alleviate inflammation and oedema, and support psychological resilience, domains which are aligned with the pathophysiology of overtraining syndrome and chronic fatigue states. The patient's progressive subjective fatigue reduction as quantified by ROF scores and functional recovery verifies the physiological and psychophysical value of integrating TCM with standard protocols.

The addition of phytotherapeutic agents, including *Ashwagandha* for cortisol modulation, and tonic warming formula, *Qi Hai Yao Fang* can potentiate metabolic homeostasis and endocrine normalisation, underscoring the necessity of tailored nutritional supplementation in comprehensive ultra-endurance athlete care. The combined biochemical improvements and clinical amelioration observed advocate for early, preventive screening and intervention strategies encompassing nutrient status and hormonal balance.

This case further delineates a prospective protocol emphasising continuous, multidimensional monitoring including precise ROF, detailed musculoskeletal evaluation, biochemical screening, and dynamic therapeutic adjustment. Such a protocol enables preemptive mitigation of overtraining risks, supports sustained athletic performance, and may extend athletic longevity.

Future randomised controlled trials should explore integrative approaches combining TCM and evidence-based conventional medicine, specifically characterising mechanistic pathways, dose-response relationships, and long-term outcomes. Additionally, sport-specific adaptations of TCM diagnostic frameworks and treatment regimens merit refinement to optimise efficacy and athlete acceptance.

Given the rising popularity and competitive intensity of ultra-endurance trail running, this integrative care model could become a pivotal anchor in athlete health management, reducing injury burdens, improving recovery trajectories, and enhancing performance through multidimensional synergy.

To the best of our knowledge, there are no other studies regarding the use of TCM on performance and recovery in mountain ultra-endurance running.

6. Conclusion

This case study highlights the complex physiological demands and multisystem challenges faced by ultra-endurance trail runners, especially under extreme environmental conditions such as heat stress and prolonged exertion. The integrative therapeutic approach, combining conventional sports medicine practices with TCM, including acupuncture, moxibustion, and phytotherapy, demonstrated promising outcomes in managing musculoskeletal injuries, fatigue, and systemic imbalances.

The targeted modulation of key meridians and organ systems facilitated symptom relief, improved functional capacity, and enhanced subjective fatigue perception. Supplementation with phytochemicals and micronutrients addressing identified biochemical deficiencies complemented the treatment spectrum.

This holistic protocol underscores the potential benefits of integrating Eastern and Western therapeutic frameworks to optimise athlete recovery, minimise injury risk, and sustain high-level performance in ultra-endurance trail events. Nevertheless, further rigorous, controlled investigations are warranted to validate these findings and refine standardised integrative protocols tailored to the unique needs of ultra-endurance athletes.

Effective multidisciplinary management combining objective monitoring and personalised interventions represents a vital evolution in the care of athletes undertaking the physiological extremities of ultra-endurance trail running.

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Clinical case series study

Acupuncture and Traditional Chinese Medicine in Surf Sports: Case Series on Recovery, Performance, and Chronic Conditions.

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Abstract

Acupuncture, rooted in Traditional Chinese Medicine (TCM), has been practiced for millennia to treat a variety of conditions, including pain, inflammation, anxiety, insomnia, and other chronic disorders. In recent decades, it has gained increasing recognition within integrative medicine for its role in enhancing physical recovery, regulating autonomic function, and promoting overall well-being. In the context of sports, and particularly in surfing (a discipline marked by intense physical demand and environmental exposure), acupuncture offers potential benefits such as improved muscle recovery, reduced fatigue, relief of musculoskeletal tension, enhanced circulation, and improved flexibility, balance, and endurance. It may also contribute to emotional regulation, energy support, and the mitigation of chronic conditions that could compromise athletic performance.

This exploratory and descriptive case series investigates whether individualised acupuncture treatment, combined with other TCM modalities such as herbal medicine, *Tui Na* massage, and dietetic therapy, can support recovery, prevent symptom recurrence, and optimise resilience in surf athletes. A brief review of recent literature supports the relevance of acupuncture in musculoskeletal and neurovegetative regulation; however, evidence specific to surf athletes remains scarce.

The clinical cases presented demonstrate that acupuncture, when tailored to the athlete's constitution and sport-specific demands, may lead to significant improvements in physical recovery, emotional balance, and overall vitality. These findings support the integration of acupuncture as a safe, adaptable, and cost-effective strategy within holistic athlete care, particularly in sports involving environmental stress and high physical load, such as surfing.

Keywords: Acupuncture; Sports Medicine; Traditional Chinese Medicine; Surf Athletes; Muscle Recovery; Performance Optimisation.

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1. Introduction

Acupuncture and TCM have gained increasing relevance within sports medicine as integrative approaches to pain management, recovery and overall physiological regulation ¹⁻³. Athletes frequently benefit from non-pharmacological methods capable of modulating fatigue, improving musculoskeletal function and supporting autonomic balance ⁴⁻⁷, particularly in sports that combine repetitive physical load with environmental stressors. When performed according to appropriate sterile procedures, acupuncture is regarded as a safe therapeutic option for both adults and children ^{8,9}.

Surfing presents a unique constellation of physical and environmental demands ¹⁰, including prolonged paddling, rapid changes of movement, rotational forces on the spine and joints, and continuous exposure to cold water and wind. These factors may contribute

not only to acute injuries but also to chronic musculoskeletal tension, delayed recovery, respiratory vulnerability, sleep disturbances and emotional dysregulation¹⁰. The holistic perspective of TCM is particularly suited to understanding these multifactorial presentations¹¹⁻¹⁴, integrating physical symptoms, emotional dynamics and environmental influences within individualised diagnostic patterns.

Despite the increasing use of acupuncture among athletes, clinical documentation focusing specifically on surf practitioners remains limited. This case series aims to illustrate the role of individualised TCM assessment and treatment in supporting recovery, resilience and chronic condition management in surfers across different age groups and health contexts. The following four cases exemplify the clinical reasoning, therapeutic strategies and outcomes observed in practice.

2. Case 1 – Spleen *Qi* Deficiency with Dampness in an Active Female Surfer

2.1. Presentation

A.B. is a 30-year-old French female surfer who also works as a fitness coach and pole dance instructor, maintaining a routine of high-intensity daily training. She reported delayed muscle recovery, recurrent lumbar pain and frequent muscular swelling, complaints that had not been resolved by previous physiotherapy. Her medical history included a disabling lumbar blockage in 2021 and a complicated urinary tract infection associated with fluctuating renal function. She had been using oral contraceptives since adolescence and experienced recurrent urinary infections and candidiasis approximately twice per year. Additional symptoms included dizziness while surfing, oily skin with a history of acne, hair loss, constant thirst, difficulty maintaining concentration and a tendency toward ruminative thought patterns. She described an overall positive mood, occasional alcohol use, non-smoking habits and a preference for warm climates.

The tongue was observed to be moist and shiny with pronounced teeth marks on the edges, and the pulse indicated Spleen deficiency with Kidney weakness. Musculoskeletal palpation revealed significant tension in the lumbar region. No recent imaging exams were available.

2.2. Diagnosis

From a TCM perspective, the clinical presentation reflected a combination of underlying energetic imbalances. The primary diagnosis included Spleen *Qi* deficiency with internal dampness^{11,15,16}, suggested by the delayed muscle recovery, heavy limbs, digestive and urinary susceptibility, moist tongue coating and teeth marks. Liver *Qi* stagnation was identified in association with chronic physical overexertion and emotional tension, contributing to dizziness, irritability, difficulty focusing^{11,13} and musculoskeletal tightness. Kidney deficiency (likely aggravated by long-term contraceptive use, recurrent infections and intensive training) was considered relevant to her history of lumbar weakness and poor recovery¹¹. Together, these patterns revealed a functional disharmony between Spleen, Liver and Kidney, with secondary damp accumulation obstructing physiological recovery mechanisms¹⁴.

2.3. Methods and Treatment Logic

Treatment aimed to support Spleen and Kidney *Qi*, resolve internal dampness, regulate Liver *Qi*, support the lumbar region, enhance post-exertion recovery and improve mental clarity. Acupuncture was applied using a combination of local, distal and systemic points based on the treatment principles^{1,2,4-7}. Points included GV20, CV17, CV4, KI3, SP6, SP3, SP9, GB34, GB39, LR3, BL60, LI11 and GB20^{17,18}. Supporting and harmonising techniques were selected to strengthen the Spleen, nourish Kidney resources, calm the Shen^{11,12}, transform dampness, promote the smooth flow of Liver *Qi* and reduce musculoskeletal tension. LI11 and GB20 were emphasised to address post-exercise inflammation and dizziness related to surf practice.

Tui Na massage was incorporated during periods of muscular overload, focusing on the lumbar region to release tension, regulate *Qi* and Blood circulation³ locally and support recovery. Lifestyle and dietetic recommendations complemented the treatment. These included prioritising rest between training sessions, consistent hydration and a diet oriented toward reducing dampness^{15,16,19}. Warm, cooked meals based on whole grains and seasonal vegetables were encouraged, along with moderate intake of light animal protein and fermented foods. Warming digestive spices such as ginger were recommended. Foods known to increase dampness, such as dairy products, fried foods, refined sugars, cold or raw meals, excess tropical fruits, processed wheat products and cold beverages, were discouraged.

2.4. Results and Discussion

After only two acupuncture sessions, A.B. reported significant improvements, including reduced thirst, enhanced mental clarity and complete resolution of lumbar pain. Her post-training muscle recovery improved markedly. A subsequent episode of muscular discomfort following an intensive training trip abroad did occur but was considerably milder than her previous baseline. These changes suggest both symptomatic improvement and increased resilience.

This clinical evolution is consistent with current literature supporting the use of acupuncture to improve circulation, modulate inflammation and enhance musculoskeletal recovery in athletes undergoing high-intensity training^{1,2,5-7}. It also aligns with TCM theory, in which Spleen and Kidney deficiencies contribute to chronic lumbar weakness^{11,12,14} and delayed muscle recovery, especially when exacerbated by damp accumulation and overexertion. By addressing these underlying energetic patterns and optimising the body's transformation and transportation functions, acupuncture and *Tui Na* facilitated both immediate symptom relief and longer-term functional improvement.

This case demonstrates the potential of an integrative TCM approach to support the physical demands of high-performance athletes, particularly when treatment is individualised to constitutional patterns and environmental stressors, such as cold-water exposure, repetitive strain and intensive physical routines typical of surf sports.

3. Case 2 – Spleen *Qi* Deficiency with Phlegm-Damp in Obstructive Sleep Apnoea

3.1. Presentation

The patient is a 55-year-old male surf journalist and instructor who leads a highly irregular professional schedule marked by frequent exposure to cold water, long periods of sedentary work during event coverage and intermittent bouts of physical exertion. He sought treatment primarily for obstructive sleep apnoea (OSA), which manifested as loud snoring, frequent nocturnal awakenings, respiratory pauses confirmed by his partner and persistent non-restorative sleep. He also reported chronic morning fatigue, night sweats, constant thirst, dry mouth, sensations of internal heat and warm extremities. Additional symptoms included mild obesity, with an estimated BMI of 30–32 kg/m², seasonal ocular itching suggestive of allergic tendencies, confirmed gluten intolerance diagnosed five years earlier and intermittent shoulder and neck pain exacerbated by prolonged sitting or emotional stress. His emotional profile was characterised by mild anxiety, nocturnal agitation, irritability in response to perceived injustices, difficulty setting boundaries and a recurring sense of frustration. His lifestyle was inconsistent, marked by an irregular diet high in refined carbohydrates and low in fresh whole foods, moderate alcohol consumption and a history of smoking cessation ten years earlier.

On examination, the tongue exhibited a thick white coating with red edges, indicating internal dampness and Liver heat, while the pulse was slippery and slightly wiry^{11,12}. The patient expressed a clear therapeutic goal: to improve sleep quality, daytime energy, chronic fatigue and global body balance.

3.2. Diagnosis

Based on TCM pattern differentiation, the clinical presentation aligned primarily with Spleen *Qi* deficiency with phlegm-damp accumulation, reflected in the patient's obesity, thick tongue coating^{11,15,16}, digestive irregularity, fatigue and respiratory obstruction. The habitual exposure to cold water associated with surf practice and the prolonged sedentary episodes characteristic of his work contributed to impaired transformation and transportation of fluids, resulting in dampness accumulation and subsequent phlegm formation¹⁰. This phlegm obstructed the respiratory passages, manifesting as snoring, apnoeic events and fragmented sleep.

A secondary but significant pattern of Liver *Qi* stagnation with internal heat was evident through irritability, emotional frustration, nocturnal agitation, thirst, night sweating^{11,12} and the red tongue edges. Liver *Qi* stagnation, perpetuated by chronic stress and emotional tension, further contributed to phlegm formation and disrupted *Qi* movement in the chest and throat. The presence of Shen disturbance was indicated by nocturnal restlessness, mild anxiety and difficulty relaxing at night^{11,12}.

Together, these patterns revealed a multifactorial disharmony involving Spleen weakness, phlegm obstruction of the upper airways, Liver stagnation generating internal heat and emotional imbalance exacerbating systemic dysregulation.

3.3. Methods and Treatment Logic

The therapeutic plan combined acupuncture, *Tui Na* massage, cupping therapy, herbal medicine and dietetic guidance, applied with the aim of supporting Spleen *Qi*, resolving phlegm, moving Liver *Qi*, dispersing internal heat, relaxing musculoskeletal tension and harmonising the Shen.

Acupuncture was performed weekly. Points included ST36 to support Spleen *Qi* and reduce dampness; SP6 to nourish *Yin* and assist fluid metabolism; ST40 to transform phlegm; CV12 and SP9 to regulate digestion and fluid pathways; LR14 and GB34 to soothe Liver *Qi*; LU7 to open the chest and regulate Lung *Qi*; HT7 and *Anmian* to calm the Shen; CV17 and KI27 to support respiratory function; and GV20 to clear heat and anchor *Yang*. Local musculoskeletal complaints were addressed using GB21, LI15, SJ14 and *Ashi* points in the cervical and shoulder regions to improve circulation and relieve tension^{12,17,18}.

Tui Na massage and cupping therapy were introduced from the second session. Manual techniques focusing on the cervical and upper thoracic areas (BL18–BL21) reduced muscle tightness and supported Liver and Spleen pathways. Fixed cupping over GB21, LI15 and BL20 improved regional circulation, facilitated phlegm transformation and relieved mechanical strain contributing to disrupted breathing³.

Chinese herbal medicine was prescribed to complement acupuncture. *Ban Xia Hou Po Tang* targeted phlegm obstruction²⁰ and helped regulate the Lung and Stomach *Qi*, reducing upper airway blockage associated with OSA. *Jia Wei Xiao Yao San* was used to move Liver *Qi*, clear internal heat and calm the Shen. The patient adhered reasonably well to the herbal regimen, with adjustments made to accommodate his schedule.

Dietetic counselling emphasised Spleen-strengthening, gluten-free, warm and cooked foods, including brown rice, quinoa, *azuki* beans and cooked vegetables such as pumpkin and carrot. Warming spices were recommended to support digestive transformation, while damp and heat-promoting foods^{15,16,19}, dairy, refined sugar, greasy meals, cold beverages, alcohol, caffeine and spicy foods, were discouraged. Hydration was encouraged, as well as the inclusion of peppermint and chamomile teas to soothe Liver heat.

The lifestyle component included recommendations for consistent sleep routines, reduction of evening screen exposure, gentle physical activity on sedentary days and maintaining warmth after prolonged periods in cold water¹⁰.

3.4. Results and Discussion

Clinical progression over twelve weekly sessions was favourable and consistent. The patient experienced a substantial reduction in snoring intensity, fewer respiratory pauses

and significantly improved sleep continuity. Daytime fatigue diminished, with the patient reporting increased stability of energy levels and improved emotional regulation. Night sweats and sensations of internal heat were markedly reduced. Cervical and shoulder tension improved through the combined effect of acupuncture, *Tui Na* and cupping, allowing for better respiratory mechanics and general relaxation ^{1,2,5,8}.

Tongue and pulse examinations indicated progressive improvement: the thick tongue coating thinned significantly, and the pulse shifted from slippery and wiry to a more balanced quality. The patient tolerated treatment well, reporting no adverse reactions to acupuncture, herbal medicine or *Tui Na*. Minor post-cupping soreness resolved spontaneously within 24 hours.

Despite these improvements, partial adherence to dietary recommendations limited complete resolution of internal heat and prevented full regulation of Spleen function. His mixed routine, alternating between surf-related cold exposure and prolonged sedentary work, also posed challenges to maintaining consistent *Qi* movement and phlegm resolution.

Nevertheless, the intervention demonstrated clear clinical benefits. This case illustrates how a comprehensive TCM approach that integrates acupuncture, manual therapy, herbal medicine, diet and lifestyle guidance can effectively address complex, multifactorial presentations such as OSA associated with Spleen deficiency and phlegm obstruction ^{11,12}. The patient's improvements reflect both symptomatic relief and deeper regulation of systemic patterns, particularly the interplay between Spleen deficiency, phlegm accumulation and Liver heat. The case reinforces the importance of integrating emotional and lifestyle components into treatment to achieve more consistent long-term results.

4. Case 3 – Liver-Kidney Yin Deficiency with Internal Wind in an Epileptic Surfer

4.1. Presentation

The patient is a 26-year-old male competitive surfer who has practiced the sport since childhood and sought TCM treatment to improve resilience, recovery, emotional stability and seizure control. His medical history is significant for two chronic and lifelong conditions: Juvenile Myoclonic Epilepsy (JME), diagnosed in adolescence, and Alpha-1 Antitrypsin Deficiency (A1ATD), identified in infancy through Liver biopsy following intolerance to breast milk. These diagnoses create a complex physiological background in which neurological and metabolic vulnerabilities coexist ^{21,22}.

He reported that his epileptic manifestations began as mild childhood symptoms but progressed at age 18 to include tonic-clonic seizures occurring approximately five to six times per year. These episodes were typically preceded by sensations of internal heat in the upper limbs and followed by prolonged fatigue, amnesia, tremors and drowsiness. His most recent seizure occurred in November 2024, resulting in a minor motor vehicle accident. Throughout adulthood, emotional stress and psychological tension consistently acted as triggers ²¹.

At the time of consultation, he described a constellation of symptoms including vertex headaches, dizziness, dry eyes, insomnia, nocturnal sweating, irritability, jaw tension, pronounced thirst, sensations of internal heat especially in the palms and soles, recurrent lumbar and left knee pain and chronic post-surf musculoskeletal tightness related to cold-water exposure. He also reported persistent ruminative thinking, emotional sensitivity, a tendency toward internal agitation and chronic discomfort in the ears. He was under stable pharmacological management with levetiracetam and lamotrigine, with no recent imaging exams or laboratory tests conducted. Tongue examination revealed a red, dry and coatingless body with red borders, and his pulse was rapid and wiry.

This broad spectrum of neurological, musculoskeletal, constitutional and emotional manifestations provided a complex clinical portrait requiring individualised and cautious integration of TCM strategies.

4.2. Diagnosis

From a TCM pattern differentiation perspective, the clinical picture represented a multifactorial disharmony rooted primarily in Liver and Kidney *Yin* deficiency. The chronic dryness, insomnia, dizziness, nocturnal sweating, heat sensations¹¹⁻¹³ and red, coatingless tongue strongly indicated depletion of *Yin* fluids and internal cooling mechanisms. Kidney *Yin* deficiency was particularly relevant given the long-standing history of A1ATD and constitutional vulnerability.

This deficiency created the internal conditions necessary for the generation of internal heat and subsequently internal wind, both of which are traditionally associated with seizure activity^{11,12,14}. The rapid, wiry pulse and susceptibility to emotional triggers further supported this assessment^{11,12}. The presence of relative *Yang* excess, resulting from insufficient *Yin* anchoring, was evident in the upward-rising symptoms such as vertex headaches, irritability, tinnitus-like ear discomfort and intense internal heat in the extremities.

Secondary elements included phlegm-damp accumulation, consistent with his musculoskeletal heaviness, glandular congestion sensations and the chronic effects of repeated cold exposure during surf practice. Although phlegm was not the primary seizure trigger here, its presence may have exacerbated neurological instability, particularly during stress or fatigue.

Together, these patterns revealed a TCM diagnostic framework of Liver–Kidney *Yin* deficiency generating internal wind and heat, combined with phlegm-damp factors and rising *Yang* contributing to neurological instability and emotional reactivity.

4.3. Methods and Treatment Logic

Given the patient's chronic neurological diagnosis and ongoing antiepileptic medication, herbal medicine was considered but intentionally avoided due to the significant risk of herb–drug interactions²⁰. The primary therapeutic modality was acupuncture, applied with caution and adapted progressively as symptoms evolved. The treatment focused on nourishing Liver and Kidney *Yin*, clearing internal heat, extinguishing internal wind, regulating Liver *Qi*, supporting Jing, calming the Shen and harmonising the ascent and descent of *Yang Qi*.

Acupuncture point selection reflected these principles. GV24 was used for its classical indication in epilepsy and its ability to calm the Shen and regulate neurological activity^{1,2,5}. ST36 supported overall vitality and *Qi* regulation. KI6 and LR3 nourished *Yin* and harmonised Liver and Kidney function. GB21 contributed to the reduction of internal wind and muscular tension. LI4 and LI11 cleared heat and regulated *Qi* movement. CV4 strengthened Kidney essence and supported the foundational *Yin* and *Qi* reserves. GB39 nourished marrow and was selected to prevent the re-emergence of wind rooted in Kidney deficiency. GB40 and SP10 enhanced blood and *Qi* circulation, supporting Liver balance and muscular relaxation. SP9 and ST40 were included to transform dampness and phlegm, particularly relevant for an athlete frequently exposed to cold and moisture. CV17 and HT3 regulated Shen activity and emotional stability. GB34 was chosen for its role in harmonising sinews and alleviating musculoskeletal tension. GV20, GB8 and GB20 were applied to subdue *Yang* rising, regulate neurological activity and prevent the excessive ascent of heat and wind to the head^{12,17,18}.

Tui Na massage was used selectively during periods of muscular overload, mainly in the lumbar and thoracolumbar regions, to support circulation and reduce tension from surf-related overuse. Dietetic guidelines were introduced gradually due to the patient's limited availability for structured follow-up. Recommendations focused on *Yin*-nourishing foods, avoidance of heating items and the inclusion of mildly cooling fruits, steamed vegetables, whole grains and sufficient hydration^{15,16,19}.

Throughout treatment, care was taken to avoid overstimulation, which could destabilise neurological patterns or trigger seizures. Sessions were paced methodically and integrated with ongoing neurological management.

4.4. Results and Discussion

The patient demonstrated early and consistent improvements across several domains. He reported enhanced sleep quality, a reduction in vertex headaches and diminished irritability and emotional reactivity. Thirst and internal heat sensations became more manageable, and episodes of ruminative thinking diminished. Musculoskeletal tension in the lumbar and knee areas decreased, particularly during periods of reduced surf exposure.

Although seizure frequency could not yet be evaluated due to the short follow-up period, the patient described a subjective increase in resilience and a greater sense of internal stability. Improvements in sleep and emotional regulation are particularly significant given that stress and sleep deprivation are recognised triggers of JME episodes ²¹.

The therapeutic outcomes align with classical TCM principles and emerging literature suggesting that acupuncture may modulate cortical excitability, reduce sympathetic overactivity and improve quality of life in patients with epilepsy. By nourishing *Yin*, reducing internal wind and stabilising *Shen* activity, acupuncture may contribute to a more regulated neurological environment, even when pharmacological treatment remains primary ^{1,2,5}.

This case highlights the potential of individualised TCM interventions to support young adult athletes with chronic neurological and metabolic diagnoses. The coexistence of JME and A1ATD required a cautious, personalised approach, emphasising safety, emotional regulation and constitutional strengthening. The case also underscores the importance of long-term follow-up to evaluate seizure activity, systemic inflammation and the sustainability of improvements observed in the early phase of treatment.

5. Case 4 – Paediatric Lung *Qi* and Kidney Deficiency in a Young Surfer

5.1. Presentation

The patient is a 9-year-old male who has been a regular surf practitioner since the age of four and who is frequently exposed to cold water and ocean wind. Despite an overall balanced lifestyle, including a diet predominantly based on whole foods and the absence of dairy and soft drinks, he presented with recurrent upper respiratory tract infections, nocturnal respiratory noise, enuresis and night sweats. These symptoms were more frequent during colder seasons, particularly autumn and winter. On physical examination, the child appeared well-developed, active and without any delays in growth or psychomotor development. However, his parents reported intermittent nasal obstruction, loud breathing during sleep and a tendency toward emotional restlessness in cold weather. These recurring symptoms suggested underlying energetic vulnerability despite his apparently strong physical constitution.

5.2. Diagnosis

According to TCM pattern differentiation, the child's presentation corresponded primarily to Lung *Qi* deficiency with weakened *Wei Qi* ¹¹⁻¹³, as evidenced by recurrent respiratory infections, nasal obstruction and susceptibility to external cold-damp pathogens ⁹. Prolonged exposure to cold water and cold wind during surf practice played a central role in this vulnerability ¹⁰, undermining the natural defensive *Qi* and compromising the Lung's role in dispersing and descending *Qi*.

A secondary pattern of Kidney *Yin* deficiency was suggested by the presence of night sweats and enuresis ^{11,13,23}, two manifestations that, in paediatric TCM physiology, often reflect the immaturity or insufficient consolidation of Kidney essence. In children, Kidney deficiency more easily destabilises fluid metabolism, sleep regulation and *Wei Qi* activity.

Additionally, signs of residual phlegm obstructing the Lung, such as noisy breathing during sleep, indicated impaired descent of Lung *Qi* ^{15,16,19,24}. This phlegm likely originated from either Spleen weakness or incomplete resolution of previous external invasions. To-

gether, these patterns revealed an interaction between constitutional susceptibility, environmental exposure and immature paediatric organ systems, producing recurring respiratory and nocturnal symptoms.

5.3. Methods and Treatment Logic

Treatment was tailored to paediatric needs, ensuring gentle yet effective interventions. Acupuncture was applied once weekly using fine paediatric needles combined with laser stimulation on selected points for increased comfort. Points included DU20 to calm the Shen and support *Yang*; CV17 to regulate *Qi* and open the chest; KI3 to nourish Kidney *Yin*; LU7 to disperse wind and strengthen the Lung; KI27 to resolve phlegm and benefit the thorax; CV4 to support *Yuan Qi* and harmonise the Spleen–Kidney axis; and LV3 to regulate Liver *Qi* and stabilise emotional balance^{17,18}.

Moxibustion was used to warm the Kidney and Lung regions, particularly over the lower back and nasal pathway, to expel residual cold, support *Yang* and enhance *Wei Qi* defense^{12,13}. *Tui Na* massage was incorporated into each session, focusing on the thoracic and lumbar areas to promote circulation, improve *Qi* movement and relax the child before needling³.

Herbal medicine was introduced using paediatric-adapted doses. *Yu Ping Feng San* was prescribed to strengthen *Wei Qi* and reduce vulnerability to respiratory pathogens. *Bu Zhong Yi Qi Tang Jia Wei* was used to support Lung, Spleen and Kidney *Qi* while addressing enuresis through its supporting and ascending properties. These formulas were chosen for their safety, compatibility with paediatric physiology and proven efficacy in reinforcing immunity and addressing constitutional deficiencies^{12,20}.

Dietetic recommendations emphasised maintaining internal warmth through seasonal cooked meals, soups, porridges and warm beverages^{15,16,19,24}. Foods known to produce dampness or phlegm, such as sugar, fried items and processed snacks, were minimised. Supporting foods such as *azuki* beans, black beans and miso-based soups were introduced to support Spleen and Kidney function. The family received guidance on maintaining warmth after surf practice, including adequate clothing and warm foot baths, to counteract cold exposure.

5.4. Results and Discussion

Over an eight-week period, the child displayed marked clinical improvement. The frequency and intensity of respiratory infections decreased considerably, and noisy breathing during sleep resolved. Enuresis became infrequent and eventually ceased, and night sweats diminished substantially. The child also reported improved tolerance to cold environments and demonstrated greater vitality and emotional stability, particularly during colder days. Parents noted that his energy levels and mood became more consistent, and that he recovered faster from environmental exposure after surf sessions.

No adverse reactions were reported with acupuncture, laser stimulation, moxibustion or herbal medicine⁹. Herbal formulas were well tolerated, with no gastrointestinal discomfort or allergic manifestations. The absence of pharmacological treatments simplified the clinical approach and eliminated concerns about herb–drug interactions.

Although physical appearance suggested robust health, the case highlighted the discrepancy between outward vitality and internal energetic fragility typical of paediatric physiology. One challenge encountered was maintaining treatment regularity amidst school commitments and surf training schedules, which occasionally created delays. This raised important considerations regarding how to support long-term adherence in families with active lifestyles.

The case underscores the particular vulnerability of the paediatric Lung and Kidney system and demonstrates how TCM interventions can strengthen constitutional foundations, reduce susceptibility to external pathogenic factors and prevent recurrence of respiratory issues. Early intervention proved essential in preventing the progression of mild but persistent symptoms into more complex patterns in adolescence^{11,23}. Furthermore, the

combination of acupuncture, moxibustion, *Tui Na* and herbal medicine provided a comprehensive approach addressing both acute symptoms and constitutional weaknesses. This case highlights the importance of integrating parental education into paediatric care to ensure sustained benefits beyond the treatment period, particularly in children with regular exposure to cold, moisture and environmental stressors due to sports practice.

6. Final Remarks

This case series provides a detailed exploration of the therapeutic potential of Traditional Chinese Medicine in supporting the health, recovery and physiological regulation of surf athletes across a variety of clinical presentations. Although each case reflects a distinct medical and energetic profile, several unifying themes emerge that illuminate how acupuncture and complementary TCM modalities can address both acute and chronic conditions frequently observed in individuals exposed to high physical demand, cold environments and emotional stress.

Across all four cases, Spleen *Qi* deficiency and Liver *Qi* stagnation surfaced as recurrent patterns, often accompanied by dampness, phlegm, or internal heat. These patterns reflect the physiological strain imposed by surfing, a sport that combines vigorous muscular effort with repeated exposure to cold and instability, conditions that challenge the body's capacity for transformation, transportation and emotional regulation¹¹⁻¹³. The consistent improvement observed in symptoms such as musculoskeletal pain, delayed recovery, respiratory vulnerability, sleep disturbances, emotional agitation and autonomic imbalance suggests that individualised acupuncture treatments, when combined with supportive modalities such as *Tui Na*, cupping, herbal medicine and dietetic guidance, can meaningfully influence the regulatory systems that underpin athletic resilience.

Another key finding of this series is the relevance of addressing not only physical symptoms but also Shen-related manifestations, including anxiety, irritability, cognitive fatigue and lack of emotional regulation. Emotional load and stress emerged as central aggravating factors in several cases, particularly in the context of obstructive sleep apnea and epilepsy. TCM's holistic framework proved valuable in understanding these connections and in designing therapeutic strategies that integrate musculoskeletal, metabolic, neurological and emotional dimensions of care.

This case series also highlights the clinical importance of considering environmental exposure, particularly cold and wind, as major contributors to pathogenesis in surf athletes and paediatric surfers. Cold exposure affected respiratory function, damp accumulation, muscle tension and recovery capacity. Interventions targeting *Wei Qi*, body warmth and fluid metabolism were essential components of treatment plans¹⁰.

Despite the positive outcomes observed, this study is limited by several methodological factors inherent to case series designs. These include the absence of standardised outcome measures, the lack of laboratory or imaging follow-up in certain cases, and the reliance on qualitative symptom evolution rather than objective biomedical markers. Patient adherence, particularly regarding diet, lifestyle modifications and session regularity, varied across cases and influenced treatment trajectories. Furthermore, the small sample size and the individualised nature of TCM interventions restrict the generalisability of findings.

Nonetheless, the results indicate that acupuncture and TCM represent safe, non-invasive, adaptable and cost-effective tools that can complement conventional medical care for surf athletes. They offer a particularly relevant contribution in managing chronic or multifactorial conditions for which biomedical approaches may provide limited relief⁸ or rely heavily on pharmacological interventions. The positive clinical evolution observed across cases invites further research into the role of acupuncture in athletic performance, recovery, emotional regulation and resilience in sports involving extreme environmental exposure. Future studies would benefit from controlled designs, validated scales, longitudinal follow-up and incorporation of biomarkers related to inflammation, autonomic regulation and neuromuscular performance.

Overall, these findings support the integration of TCM into multidisciplinary sports medicine frameworks and underscore the importance of individualised care in optimising both health and athletic function in surf practitioners.

7. Conclusion

This case series suggests that individualised acupuncture and Traditional Chinese Medicine interventions can effectively support recovery, physiological regulation and emotional balance in surf athletes. The consistent clinical improvements observed across varied conditions highlight the potential of TCM as a safe and adaptable complement to sports medicine. Further controlled studies are needed to deepen the evidence base and validate these findings in larger and more diverse surf populations.

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Protocol

The Therapeutic Role of Acupuncture in Endometriosis-Related Pain Management: A Systematic Review and Meta-Analysis Protocol.

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Abstract

Background: Pain is the most common and debilitating symptom of endometriosis. Unrelieved pain can deprive female patients of comfort and severely impair their quality of life and psychological health. The limitations of currently available pharmacologic treatment options make the treatment of endometriosis-related pain (ERP) a great challenge. Acupuncture has shown great potential in the management of ERP, but convincing evidence is still lacking. This systematic review aims to synthesise the latest available evidence regarding the clinical efficacy and safety of acupuncture for ERP.

Methods: A systematic literature search of seven online databases will be conducted from its inception to July 2023, including PubMed, EMBASE, Cochrane Library, Chinese National Knowledge Infrastructure, SinoMed, VIP Database, and Wanfang Database. Randomised controlled trials (RCTs) investigating the efficacy of acupuncture for ERP and meeting our predefined eligibility criteria will be included. The primary outcome of this study is the change in ERP as assessed by a validated scale, and secondary outcomes include patient quality of life, serum CA-125 levels, and adverse events. Study screening and data extraction will be conducted independently by two reviewers. The quantitative synthesis of data will be performed through RevMan 5.4 software. If applicable, subgroup analyses and sensitivity analyses will be conducted to identify potential causes of heterogeneity. The strength of evidence will be graded through the GRADE system.

Discussion: This study will critically synthesise the evidence regarding the efficacy and safety of acupuncture for the treatment of ERP. The findings will influence evidence-based management decisions for clinicians in the treatment of ERP.

PROSPERO registration number CRD42023442373.

Keywords: Acupuncture; Endometriosis; Chronic Pelvic Pain; Systematic Review; Meta-analysis; Protocol; Traditional Chinese Medicine; Dysmenorrhea; Ectopic Endometrium; Evidence-based Medicine.

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1. Introduction

Endometriosis is a common chronic, inflammatory and oestrogen-dependent disease characterised by the presence of endometrial-like tissue outside the uterus ¹⁻³. Ectopic tissue causes immune cell infiltration and inflammation, which in turn lead to sensitisation of nociceptive paths, making women susceptible to pain and infertility ⁴. It is estimated that nearly 10 percent of women of reproductive age are afflicted by this condition, and the prevalence is as high as 50 percent among women seeking infertility treatment ^{5,6}.

However, the exact prevalence of endometriosis is uncertain as it requires laparoscopy or surgical visualisation for a definitive diagnosis ⁷.

Chronic pain, including dysmenorrhea, dyspareunia, and non-menstrual pelvic symptoms, is the most common and debilitating symptom of endometriosis ^{1,8,9}. It is reported that approximately 70%-90% of patients with pelvic pain are associated with endometriosis ¹⁰. The pathogenesis of pain production is complex, and possible mechanisms are related to chronic inflammation, recurrent bleeding from the lesion, and peripheral and central nervous sensitisation caused by abnormal growth of lesion tissue ^{6,11,12}. Persistent pain is recognised as a potentially disabling condition that affects the quality of life, mental health, sexuality, and productivity of women ¹³⁻¹⁶, and carries a heavy financial burden ¹⁷. A multi-centre prospective study across Europe and the USA found that the average total annual cost per woman with endometriosis, including the cost of healthcare and lost productivity, was close to €10,000 ¹⁸.

Guideline-recommended first-line pharmacologic treatment for endometriosis-related pain (ERP) primarily includes nonsteroidal anti-inflammatory drugs (NSAIDs) and progestin-containing oral contraceptives ⁹. However, a recent Cochrane systematic review showed insufficient evidence to support that NSAIDs are effective in managing endometriosis pain ¹⁹. In addition, prolonged use of contraceptives and progestin tends to cause drug resistance as well as bothersome side effects, such as irregular uterine bleeding, weight gain, and mood swings, which can lead to discontinuation of drug therapy ²⁰⁻²³. Surgical therapy is a potential method of ERP management after failed pharmacologic therapies, however, pain symptoms usually recur within 6 to 12 months after surgical treatment ^{1,24}. Consequently, the management of pain in patients with endometriosis usually requires repeated medications or multiple surgeries until menopause ^{9,25,26}. Concerns about the limited efficacy and side effects of conventional therapies make many pain patients seek complementary treatments with anti-inflammatory and analgesic effects.

Acupuncture, a traditional non-pharmacological therapy, involves the insertion of needles into the body to treat diseases. The World Health Organization (WHO) 2019 global report states that acupuncture is the most widely used traditional medical therapy in the world ²⁷. Acupuncture is widely used for pain management in many countries around the world and is becoming increasingly popular. In recent years, growing evidence has supported the use of acupuncture as an effective intervention for ERP management ^{28,29}. Moreover, clinical guidelines refer to acupuncture as a potential approach for ERP management and suggest that clinicians should discuss non-pharmacological treatment strategies such as acupuncture with ERP patients who are seeking pain treatment. However, the guidelines criticised the quality of evidence from previous studies and rejected recommendations for any specific non-pharmacological interventions for ERP, including acupuncture ^{27,30}.

In recent years, an increasing number of high-quality RCTs have investigated the efficacy of acupuncture for ERP ^{31,32}, and integrating these potentially eligible RCTs into the latest meta-analyses to update previous evidence is necessary. Therefore, we will conduct a meta-analysis of currently available RCTs to assess the efficacy of acupuncture for ERP.

2. Methods

2.1. Study registration

This protocol followed the Preferred Reporting Items for Systematic Reviews and Meta-Analysis Protocol (PRISMA-P) statement and has been registered at PROSPERO (No. CRD42023442373) ³³.

2.2. Inclusion and exclusion criteria

Type of study

All published RCTs investigating the effects of acupuncture for ERP will be included in this review. In addition, if there is a cross-over trial, we will include only pre-crossover

data to avoid carry-over effects. There are no restrictions on language or publication date. Case reports, reviews and animal experiments will be excluded.

Type of participants

Subjects will be women of reproductive age with a diagnosis of endometriosis confirmed by laparoscopy or surgery, all of whom have pain related to endometriosis not due to pre-existing pathologies or related to treatment. Studies will be excluded if the diagnosis of endometriosis cannot be confirmed by laparoscopy or histology.

Type of interventions and comparators

The only permitted experimental treatment is acupuncture, which can be used alone or in combination with a control intervention. In order to minimise heterogeneity in data synthesis from a clinical perspective, acupuncture in this study will be defined as traditional or modern acupuncture techniques involving needle insertion (eg, manual acupuncture and electroacupuncture). Therefore, non-invasive acupuncture techniques will be excluded, such as acupressure, moxibustion, and transcutaneous electrical stimulation. Differences in acupuncture materials, acupoint selection, and treatment duration will not be taken into account. Interventions in the control group will be conventional western medications such as NSAIDs, progestin, GnRH agonists, and contraceptives, with detailed reporting of dosage, and treatment duration. Studies comparing different acupuncture methods or comparing acupuncture with other non-pharmacological therapies will not be considered.

Types of outcomes

Primary outcomes: The primary outcome will be the change in endometriosis-related pain, including dysmenorrhea, non-menstrual pelvic pain, and dyspareunia, and the pain score will be measured by validated pain-related scale such as the visual analogue scale (VAS) and the numeric rating score (NRS).

Secondary outcomes: (1) Quality of life, measured by ERP-specific scales (such as the Endometriosis Health Profile (EHP) pain scores) or any validated health-related scale (such as the Patient Global Impression of Change (PGIC)). (2) Serum CA-125 levels, measured before and after acupuncture treatment using an enzyme-linked immunosorbent assay. (3) Adverse events, to assess the safety of acupuncture for ERP, we will record the occurrence of adverse events in the included trials.

2.3. Search methods for identification of studies

We will conduct a comprehensive search for available RCTs in three English online databases (PubMed, EMBASE, and Cochrane Library) and four Chinese online databases (SinoMed, VIP, Chinese National Knowledge Infrastructure and Wanfang database). The search time for each electronic database ranges from database establishment to July 2023. The following keywords by both Medical Subject Headings (MeSH) and free words will be used: "endometriosis"; "endometrioses"; "endometrioma"; "endometriomas"; "endometrio*"; "dysmenorrhea"; "dyspareunia"; "dyschezia"; "pelvic pain"; "dysuria"; "constipation"; "pain symptom"; "pain"; "acupuncture"; "electroacupuncture"; "electro-acupuncture"; "ear acupuncture"; "needling"; "Intradermal acupuncture"; "warm acupuncture"; "fire acupuncture". All available combinations of search terms will be used to maximise the comprehensiveness of the final included trials. Additionally, the reference lists of prior relevant narrative reviews and meta-analyses in this clinical topic will also be checked to minimise any possible omissions.

2.4. Data collection and analysis

Study selection

Data retrieved from each database will be imported into Endnote X9 software to delete duplicate documents. To ensure the comprehensiveness of the included studies and

minimise subjective influence, two independent investigators will review the titles, abstracts, and full text of the literature to identify eligible studies based on predetermined inclusion and exclusion criteria. Any disagreements about study selection will be resolved through a third investigator arbitration.

Data extraction

Two independent researchers will use a standardised spreadsheet to extract the following data from all eligible studies: (I) general information (first author, language, country, article title, publication year, study type, study design, number of centres, sample size and follow-up period); (II) patient information (average age, gender distribution, diagnosis, pain intensity before treatment); (III) intervention details (types of acupuncture, acupoint selection and treatment duration/ frequency/ session); (IV) comparator details (drug type, drug dose and treatment frequency/ session); (V) outcomes (primary and secondary outcomes, measured time points and data). If a study provides unclear or insufficient data, the corresponding author will be contacted for details. Any discrepancies raised will be resolved by a third investigator.

2.5. Quality assessment

The quality of the included trials will be assessed by two independent reviewers using the Cochrane Risk of Bias 2 (ROB2) tool based on the following five domains: (1) randomisation process, (2) deviations from intended interventions, (3) missing outcome data, (4) measurement of the outcome, and (5) selection of the reported results. The ROB for each item will be classified into three levels (low risk, high risk, and some concerns) based on the specific circumstances of the study, and the overall ROB for the assessment results will be predicted accordingly. Any dispute between the two reviewers will be resolved by consulting with a third reviewer for a final decision.

2.6. Data synthesis and analysis

Data analysis

The software RevMan (V.5.3) will be the primary instrument for data analysis, which will be used to measure the 95% confidence intervals (CIs) for treatment effects. The effect measures will be presented as risk ratios (RR) for dichotomous data and weighted mean difference (WMD) or standardised mean difference (SMD) for continuous data. The WMD will be used when the outcome indicator is measured using the same assessment scale or instrument, otherwise, the SMD will be used. Data pooling will be performed using the Mantel-Haenszel method and the inverse variance method for dichotomous and continuous data, respectively ^{34,35}.

Assessment of heterogeneity

Statistical heterogeneity between studies will be calculated using the Cochrane Q test and I^2 statistic ³⁶. A P -value of >0.1 and $I^2 <50\%$ is a prerequisite to using a fixed-effects model for pooled analyses, and this heterogeneity is considered acceptable; conversely, it indicates statistically significant heterogeneity between studies, and meta-analyses will be more conservatively assessed using a random-effects model. Subgroup or sensitivity analyses will be conducted to investigate possible sources of heterogeneity from both clinical and methodological perspectives. Narrative analysis of the data will be performed when quantitative synthesis is not appropriate.

Subgroup analysis

If heterogeneity is significant and available data are sufficient, we will explore the sources of clinical heterogeneity through subgroup analyses, which will be based on the following: (1) different acupuncture techniques (eg, hand acupuncture, electroacupuncture, auricular acupuncture, or warm acupuncture); (2) different acupuncture interventions (eg, acupuncture and acupuncture combined with drugs); (3) the initial severity of pain; and (4) the course of acupuncture treatment.

Sensitivity analysis

If subgroup analyses exclude the sources of clinical heterogeneity, a sensitivity analysis will be used to assess the robustness of the Meta-analysis results. This test will attempt to check whether any particular study contributes to the majority of the heterogeneity. In addition, the potential impact of statistical models on the robustness of the results will also be considered.

Publication bias

If no fewer than 10 trials reported the same outcome indicator, funnel plots will be generated to assess potential reporting bias by visual examination. Egger's regression test will be used to assess its asymmetry ³⁷.

Grading the quality of evidence

Two reviewers will independently assess the certainty of evidence using the GRADE system ³⁸. In accordance with the GRADE rating criteria, the assessment will determine the quality of evidence into four levels (high, moderate, low, or very low) based on five domains (risk of bias, inconsistency, indirectness, imprecision and publication bias). Any disputes will be resolved by a third reviewer.

2.7. Ethics and dissemination

Ethical approval is not required for this study and the findings will be published in a peer-reviewed journal.

3. Discussion

Endometriosis is an under-diagnosed and disabling condition in which pain is the dominant symptom and the most commonly reported symptom in primary care settings ³⁹. The chronic nature and varied presentation of pain seriously affect the quality of life of patients with endometriosis, which emphasises the importance of adequate medical support for pain management ⁴⁰. However, currently available first-line treatments often fail to reduce pain symptoms to a satisfactory degree with unpleasant side effects and high recurrence rates ⁴¹. In addition, a recent multicentre retrospective cohort study found that 45.4% of endometriosis patients were dissatisfied with their medical support, including pain management ⁴⁰. As a result, finding other effective alternative treatments for pain management is becoming an urgent priority for endometriosis patients.

Acupuncture, a traditional Chinese medicine therapy with a history of more than 3,000 years, has been widely used for chronic pain management due to its favourable analgesic effects and lack of side effects. Therefore, acupuncture is considered a potentially valuable complementary therapy to existing pain management strategies ⁴². With the global popularity of acupuncture therapy, research on the mechanisms of acupuncture analgesia has received extensive attention. Recent studies have provided laboratory-based evidence suggesting that acupuncture analgesia is a complex process involving the entire nervous system from periphery to centre ⁴³. Potential mechanisms of acupuncture analgesia may be associated with the interaction of multiple bioactive molecules in the pain process, including inflammatory mediators, neurotransmitters, neuropeptides, and cell signalling molecules, etc. ⁴²⁻⁴⁴.

Currently, acupuncture has been widely used clinically in the management of endometriosis pain. Although previous systematic reviews have attempted to assess the therapeutic effects of acupuncture for ERP ^{45,46}, however, the quality of evidence from previous studies is limited by the quality and number of included studies. With an increasing number of new RCTs published in recent years, it is necessary to update a systematic review in the field to generate more conclusive evidence of acupuncture for ERP. Inevitably, this systematic review may have some limitations. First, the methodological quality of the included original studies may affect the accuracy of the results in this study. Second, differences in the type of acupuncture and treatment protocols among the included studies may lead to significant clinical heterogeneity.

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Review

The Ethics of Informed Consent in Traditional Chinese Medicine Practice and Research: A Narrative Literature Review.

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Abstract

Background: Traditional Chinese Medicine (TCM), a complementary/non-conventional therapy, is increasingly being integrated into modern healthcare systems. However, its practice and research raise ethical challenges, particularly concerning Informed Consent (IC), an essential element for ensuring patient autonomy, transparency, and protection.

Objective: This study aimed to conduct a Narrative Literature Review to identify the use of IC in clinical practice and research within TCM, highlighting its necessity and importance for protecting patient rights and promoting the adoption of ethical standards (including respect for autonomy, cultural sensitivity, trust, safety, and risk management).

Informed Consent in TCM: IC is a fundamental ethical and legal requirement, defined as a voluntary process where an individual agrees to a procedure or treatment after fully understanding the risks, benefits, alternatives, and potential outcomes (disclosure, comprehension, and voluntariness). TCM, as a non-conventional therapy, is subject to legal frameworks requiring patient choice and informed consent for all professional acts. IC is especially critical in TCM to ensure clear, culturally adequate communication regarding holistic concepts like *Qi* and *Yin/Yang*.

Conclusion and Recommendations: The review confirms that IC is a central ethical and legal prerequisite for TCM. Despite being widely recognised, the study suggests that its practical application often lacks quality and transparency, sometimes being treated informally. To address this, IC must evolve from a mere formality into an essential communicative process. Therefore, investing in specific ethical training for TCM professionals and the standardisation of patient information materials is strongly recommended to strengthen the clinical and social legitimacy of these practices.

Keywords: Consent, Free and Informed; Traditional Chinese Medicine; Complementary Therapies.

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1. Introduction

Understanding how TCM emerged requires going back in time and history, as it is present in ancient medical practices. However, TCM has come a long way and, given its recognition as a medical practice, albeit non-conventional, it is beginning to be integrated into modern healthcare systems. And with its expansion on a global scale, its objective and meticulous readjustment to modern times is currently based on pragmatic concepts, aiming for better guidance in diagnosis and understanding of the subject ¹. In this sense, there is a need, in our opinion, urgent, to analyse the ethical issues that guide its practice, particularly in relation to IC. It should be recalled that, despite the increasing recognition of TCM as a medical practice, it is noted that, unlike conventional Western medicine, where established IC protocols exist, TCM faces some challenges, which arise from differences in cultural norms, as well as diagnostic approaches and treatment methods ²⁻⁴. However, like Western medicine, whether in TCM clinical practice or its research, IC is a crucial

element of ethical responsibility, ensuring respect for patient autonomy, as well as transparency between TCM professionals and their patients ⁵. In this line of thinking, it is important to highlight the importance of IC within the scope of TCM practice and research and, concomitantly, identify the ethical challenges associated with IC. This is because, by recognising and prioritising IC, professionals and researchers ensure that their practices uphold the rights, safety, and autonomy of patients and participants (in research), contributing to the assumption of ethical integrity in TCM, as well as its acceptance and integration into modern healthcare systems ^{2,4,5}. Thus, the aim is to carry out a narrative literature review that identifies the use of IC in clinical practice and research in TCM and that highlights the necessity and importance of IC to guarantee the protection of patients' rights and, at the same time, promote the adoption of ethical standards in TCM, both at the level of clinical practice and research in this health area, namely, in relation to respect for autonomy, cultural sensitivity, building a therapeutic relationship of trust and based on transparency, safety, and risk management, ethical research practices, and compliance with ethical standards established by contemporary healthcare systems.

2. Traditional Chinese Medicine

As Coimbra ⁶ explains, TCM is a system of diagnosis and healthcare that has developed over more than 3000 years, with the oldest records dating back to 1000 BC (before Christ), during the *Shang* dynasty, a time when complex medical issues were already being treated. It can be described as an ancient healthcare system that originated in China, based on a holistic approach to health and well-being with the aim of balancing the mind, body, and environment to promote healing and prevent disease. According to Williams *et al.* ⁷, TCM works on the premise that disease is created as a consequence of a disturbance that occurs in the person's emotional and mental body. Secondly, from a philosophical point of view, that healing is a process that must involve the whole body, that is, regardless of the physical point where the disease developed, it must be understood that the body is sick ⁷. This, which is one of several non-conventional therapies (NCTs), encompasses various practices and theories that differ from so-called conventional medicine, Western medicine, focusing on restoring the balance of the organism and not just treating specific symptoms, since TCM translates into a set of very sophisticated practices, aimed at curing disease and maintaining health and well-being ⁷. For a better understanding of what TCM is, it is important to introduce what are considered its fundamental concepts: *Qi* or *Chi* (energy); *Jing* (essence or ancestral energy); *Xue* (blood); *Shen* (spirit or consciousness); and organic Fluids ⁸. In terms of advantages, it is worth mentioning that TCM is effective in treating some chronic diseases; it adopts a holistic approach, addressing all aspects of the individual's health; it focuses on the fundamental cause of the disease and not merely on the visible symptoms ⁹. It can also be said that in practice, Chinese doctors differentiated the "root" of an illness, the pattern of energetic imbalance in the patient, from the "branches" that reached the apparent symptoms ^{9,10}. This therapeutic system does not depend on drug therapy, in some cases associated with unwanted side effects; it promotes the person's general health, in addition to treating specific diseases; it tends to be more economically accessible than conventional allopathic treatment; it can be used in conjunction with Western medicine, including to alleviate the adverse effects of Western therapies ^{10,11}.

2.1. Legal Framework

As previously mentioned, TCM is an NCT and is therefore regulated by Law No. 71/2013, of September 2nd ^{12,13}, which regulates access to and the exercise of professions within the scope of NCTs in the public or private sector, with or without profit, and which, in its Article 2, recognises TCM as an NCT. In this matter, it is also necessary to refer to Law No. 45/2003, of August 22nd ^{12,14}, which establishes the framework for the activity and exercise of professionals who apply NCTs, as defined by the World Health Organization (WHO). According to this legal diploma, NCTs are therapies that are based on a different

philosophy from conventional medicine and apply specific diagnostic and therapeutic processes (no. 1, article 3) ¹⁴. Considering the theme of the work, it is important to mention that this diploma denotes a concern with ethics in the practice and research of TCM as an NCT and with IC. Let us consider its Article 4, where its guiding principles are set out: The individual right to choose the therapeutic method, based on an informed choice, about the safety, quality, efficacy, and possible risks; The defence of public health, in respect of the individual right to health protection; The defence of users, which requires that NCTs be practiced with a high degree of responsibility, diligence, and competence, based on the professional qualification of those who practice them and their respective certification; The defence of the user's well-being, which includes complementarity with other health professions; The promotion of scientific research in the different areas of NCTs, aiming to achieve high standards of quality, efficacy, and effectiveness ¹⁴. At the same time, Article 13 is highlighted, which refers to the right of option and to information and consent, meaning that "citizens have the right to freely choose the therapies they deem appropriate" (no. 1) and that "non-conventional therapy professionals can only perform acts with the informed consent of the user" (no. 2) ¹⁴. Therefore, the necessity and importance of IC being used in the practice and research of TCM is immediately evident. Finally, we want to highlight Ordinance No. 45/2018 of February 9th ¹⁵, which emphasises the need for a degree in TCM to include adequate training in all areas, including ethics. In its Article 9, directed at the TCM practice training component, it highlights the need for this training to include respect for safe practice, ethical, and deontological standards, and in complementarity, its Article 10 (training in other areas) emphasises the duty of the study plan leading to a degree in TCM to ensure, across the different components, adequate training in the area of ethics and deontology, among other areas ¹⁵. Thus, TCM, even though it is not a conventional medicine, is also guided by ethical and deontological principles, similar to conventional medicine, which allows us to underline the necessity of using IC in its practice and research, just as in the practice and research of Western medicine. In addition to the aforementioned legal documents, it is important to highlight others that establish the obligation to respect the person and their rights, as IC intends to do: at a national level, the Constitution of the Portuguese Republic, the Penal Code, the Civil Code, and the Basic Health Law are also highlighted; and on the international stage, the Universal Declaration on Bioethics and Human Rights, the Convention on Human Rights and Biomedicine, and the Charter of Patient Rights and Duties ¹⁶.

3. Informed Consent

IC can be described as a process through which an individual voluntarily agrees to participate in a medical procedure, research, or treatment, after fully understanding the risks, advantages, possible alternatives, and the results that can be obtained ¹⁷. That is, IC translates into the process that requires the individual to receive information, possess the mental capacity to understand and evaluate it, and be free from any form of persuasion or coercion. Therefore, there are two basic elements of IC: comprehension and free clarification. The first concerns the provision of correct and clear information about the diagnosis and therapeutic alternatives, in a way that is understandable to the individual; the second refers to the act through which the individual, of their own free will, consents and authorises an intervention or their participation in research ¹⁸. Therefore, it is understood that IC serves the purpose of disclosure, that is, providing all-important information to the patient such as the risks, advantages, alternatives, and the objective of the intervention/treatment/research. However, as ERS refers ¹⁸, the information to be provided must take into account three parameters: the common practice in the profession; the expectations of a specific patient; and the needs of a specific individual. In addition, depending on the mentioned parameters, the information provided in an IC must respect:

- the diagnosis and description of the clinical condition;
- the description of the proposed treatment, its nature and objectives;
- the risks and possible complications that may result from the treatment in question;
- alternative treatments;
- the risks of non-treatment;
- the probability of treatment success ¹⁸.

Comprehension is equally important and serves to ensure that the individual understands all the information provided, which can be done through questioning. Here, the importance of communication is highlighted, as the fact that the process is based on good communication makes IC a procedure that can be modified and evolve throughout the treatment ¹⁸. Voluntariness is another inherent characteristic of IC, allowing the individual to make a voluntary decision, of their own free will and free from manipulation or influence from third parties. This is because, free consent is an intentional and voluntary act, which authorises someone, in this case, the healthcare provider, either individually or institutionally, to act in a certain way during the therapeutic act ¹⁸. Finally, competence is another important aspect to consider, as it is necessary to confirm whether the person has the mental and legal capacity to make the decision. Therefore, in urgent situations, in situations where patients are temporarily or definitively unable to decide (coma, mental disability, children), the IC will have to be carried out by their legal representatives ¹⁶. According to ERS ¹⁸, one of the reasons that supports the existence of informed consent is related to the fact that it is admitted to be a benefit for the patient to actively participate in decisions about the medical care they undergo. This benefit of patient involvement in decisions about their health results, on the one hand, from being proactive, avoiding interventions that the patient may consider potentially dangerous to their health, and, on the other hand, from contributing to their well-being. In fact, only advantages result from IC, and there are several reasons that justify its importance, as it ensures respect for the person and their fundamental rights: 1) ensures respect for the patient's essential right to self-determination; 2) protects the patient against possible physical and psychological harm that may result from the disease or treatment; 3) promotes the benefit of the patient's active participation in decisions related to the medical care they receive ¹⁹. Therefore, IC is a crucial ethical and legal requirement, particularly in the area of health and research, as is the case with TCM practice and research, because it ensures respect for the autonomy and right of the individual to make their own decisions regarding their body and health. Furthermore, it fosters trust, essential for any therapeutic relationship ¹⁹, and therefore IC reflects an exchange of ideas that strengthens the doctor-patient relationship ²⁰. The IC form is the document that materialises the IC itself, being an ethical and legal document that aims to inform the patient about the procedure the patient is going to undergo, with the purpose of the latter exercising their right to free autonomy, and at the same time, protecting the health professional ²¹, and therefore, it cannot be discredited or ignored, nor treated informally ²². For this very reason, we agree with the idea that assuming that informed consent should be based on comprehension and free consent, its correct application depends on the observance of these principles in the patient's decision-making process. As it is a process that involves not only the patient's autonomy and freedom, but also duty and responsibility, its application is not subject to precise evaluation, although strategies can be defined to implement its application and evaluate the rigor with which the process is approached ¹⁸.

3.1. The Four Ethical Principles

It has been argued, regarding IC, that TCM practice and research, even though not falling under conventional medicine, should be guided by IC protocols. In this line of thinking, it is recognised that the four ethical principles that currently prevail in Western medical ethics can and should be applied in the context of NCTs, such as TCM. They are: non-maleficence; beneficence; respect for autonomy; and justice ²³. Thus, respect for the

principle of non-maleficence is based on the idea of doing no harm ²⁴⁻²⁶. That is, it inherently carries the idea that the patient should not be harmed, ensuring that the health professional must avoid causing harm to the patient. For this very reason, there must be prevention of direct harm, as well as a cautious assessment of the risks arising from the intervention, in order to avoid complications and minimise any negative consequences. Conversely, the principle of beneficence is based on the idea of doing good ²⁴⁻²⁶, ensuring that the health professional acts in the best interest of the patient, in order to promote their well-being and maximise the benefits for their health and quality of life. In turn, the principle of respect for autonomy guarantees the patient's right to make their own decisions regarding their body and health, based on their beliefs, values, and preferences, that is, the person chooses ^{24,26}. Therefore, it allows the patient the freedom of decision, with knowledge of the facts and without coercion, through correct information ²⁵. To ensure this right, it is the responsibility of the health professional to correctly inform the patient about their disease, their state of health, existing treatments, and the risks and advantages associated with each of them, so that the patient can make an informed and voluntary decision. The principle of justice, in the context of medical ethics, advocates the fair and egalitarian treatment of all patients, regardless of their socioeconomic status, religion, political option, sexual orientation, among others. This principle is based on the idea of "prioritising equitably, using available resources judiciously" ^{24,26}. In this regard, Rosa *et al.* ²⁵, based on the contribution of other theorists, say that this principle refers to the equitable distribution of resources necessary for assistance, as well as guaranteeing access to healthcare for all citizens. This principle is extremely important, as it prioritises a fair distribution and access to health resources, that is, it guarantees access to healthcare and treatment without discrimination or any kind of favouritism. Although these principles apply to Western medical ethics, they can be transposed to TCM, assisting its professionals, just as happens in conventional medicine, in their decisions. Because the formulation of an ethical decision is based on the understanding of these fundamental principles of bioethics that apply to common problems of clinical practice and is facilitated when institutional and individual responsibility are well defined ²⁵. These principles guide health professionals, in the sense of seeking to find a balance between the rights and interests of patients and their responsibility and duties, and the limitations of the current health system which, although already beginning to recognise and integrate NCTs, are still not the object of the recognition they deserve.

3.2. The Importance of Informed Consent in TCM Practice and Research

IC is an essential process in the practice and research of TCM, due to ethical factors, which are the focus of this work, as well as clinical and cultural factors. Regarding the challenges of ethical review in TCM clinical research, Zhang *et al.* ²⁷ state that in China this is highly convergent with that of Western medicine, however, it lacks the characteristics and culture of TCM, which is particularly important when we think about the Portuguese reality, where it is necessary, in order to achieve this convergence between Western medicine and Eastern medicine, to have greater knowledge and regulation of TCM. Firstly, respect for patient autonomy has been widely referred to, and just as in conventional medicine, in the context of TCM too, patients have the right to make their own informed decisions about their health and body. At the same time, similar to what happens in Western medicine, where patients do not have medical knowledge about treatments, in TCM they also do not have knowledge of its practices and treatments. Therefore, IC ensures that they understand what they are agreeing to, and by being informed, they gain knowledge to make their informed choices based on their preferences, values, and beliefs. In this regard, it is worth mentioning the article by White *et al.* ²⁸, which underlines the right of patients to be informed about the risks and benefits of any examination or treatment and the obligation of doctors to obtain prior IC. The same authors also mention the importance of information about the risks and advantages of this technique being available to health professionals and patients, having designed an information leaflet that not only identifies

the risks but can also be adapted for the construction of an IC form ²⁸. TCM, as already mentioned, approaches health and disease holistically, prioritising the relationship between body, mind, and environment, and therefore its philosophy includes concepts such as *Qi* and the balance of *Yin* and *Yang*, concepts that can be difficult for patients unfamiliar with them to understand. In this sense, IC in TCM necessarily requires clear and culturally adequate communication, in order to ensure that patients understand the nature, objectives, and mechanisms of the treatment to follow. However, it is noted that IC for treatment such as acupuncture, for example, is treated as an informal matter, meaning that most of its practitioners probably only provide information about risks when asked, and IC is assumed by the fact that the patient appeared at the clinic and undressed to prepare for treatment ²⁹. On the other hand, it is important that patients seeking TCM are aware of the risks and benefits inherent in each treatment, and therefore IC allows them to be informed about the risks, advantages, and effectiveness results of the treatment in question. As White *et al.* ³⁰ emphasise, "theoretically, any health professional who does not respect the principle of informed consent may be the subject of a lawsuit by the patient and an action by their professional body. Touching a patient without valid consent, for example, can constitute a civil or criminal offense of assault. Furthermore, if health professionals fail to obtain informed consent and the patient subsequently suffers harm as a result of the treatment, this fact may be a factor in a negligence complaint against the professional." At the same time, ethical and legal responsibility is also present in TCM, and therefore IC establishes an ethical and legal basis that holds the health professionals who practice it accountable, ensuring that this intervention is practiced responsibly, contributing to greater patient safety and trust. For this very reason, the key principles of informed consent are that consent must be given by a patient a) voluntarily, b) who has the capacity to understand and c) who has been given appropriate information ³⁰. Finally, in terms of research, IC is important for protecting participants. That is, through IC, participants in a TCM study are informed about whether the treatment is experimental, what the objective of the study is, and what the inherent risks are. Furthermore, in this context, the patient's identity is normally protected, and IC serves precisely to guarantee their anonymity and the confidentiality of the information provided by them. Therefore, the importance of IC in practice and research within TCM is a step for it to assert itself at the level of conventional medicine and to regularise itself, being in tune with the ethical standards that are required in all forms of medical practice. IC is thus a crucial procedure to ensure that patients (clinical practice) and those investigated (research) understand the treatment they will undergo or the study they will participate in and with which they have agreed, finding that the general ethical principles are the basis of the ethical review of TCM, where IC appears as one of the aspects to be considered due to the characteristics of TCM²¹.

3.3. Importance and Necessity of Informed Consent in Non-Conventional Therapies

IC is a crucial aspect in NCTs not only because of the unique challenges they raise, but also because of the ethical considerations involved in treatments that, for the most part, are not part of conventional medicine guidelines. Going somewhat along the lines of what was previously mentioned regarding IC in TCM, in NCTs, which include TCM, respect for the patient's right to autonomy is also fundamental. In fact, NCTs cover a large set of practices (e.g., herbal medicine, homeopathy, acupuncture, TCM, etc.), and may include therapeutic approaches that are unfamiliar and unknown to many patients. In this way, IC gains particular relevance, as professionals, after clearly informing their patients about the various treatment alternatives (indicating only those that are appropriate for their disease/condition), allow them to make an informed choice based on their values and beliefs, respecting and ensuring the right to their autonomy and self-determination. ERS ¹⁸ refers that one of the fundamental reasons for the existence of informed consent is respect for the person. It is now an accepted fact in our societies that each of us is the holder of a set of principles and characteristics that makes us a unique being, whose dig-

nity involves being able to assume their own individuality. The individuality of the human being is associated with the concept of autonomy, which in this context cannot be dissociated from the capacity for choice and self-determination. Once the right to autonomy is recognised, understood as the capacity to ethically determine one's way of life, it would be an unacceptable ethical violation to condition their freedom of choice, inducing choices or refusing their active participation in making decisions that may affect their future. On the other hand, we want to underline the importance of IC in defining realistic expectations, in protection against exploitation, and in encouraging transparency and trust. Regarding expectations, it is noted that individuals may resort to NCTs as a result of the ineffectiveness of conventional medicine treatments. Therefore, IC serves for professionals to inform about the scientific evidence of these therapies, their effectiveness in the face of the illness in question, contributing to patients creating realistic expectations regarding treatment through NCTs. In relation to protection against exploitation, IC protects patients from unethical practices, ensuring that they understand the options available to them, as well as the associated financial costs. Regarding the encouragement of transparency and trust, IC allows health professionals to explain how a therapy works, demonstrating the honesty of their actions, as well as the openness to establishing a therapeutic relationship based on trust. A study carried out by Ieong²⁹ discusses the state of TCM in Portugal comparing it with the system in force in the country where it originated (China) and where it is recognised in legislative, administrative, educational, and practice terms. The study's conclusions show that, in national territory, the TCM regime is part of the inclusive system according to the WHO's definition and description for the integrative, inclusive, and tolerant system. This same study highlights the importance of IC in TCM practice in Portugal, emphasising its indispensable and special role, largely justified by the particularity of the diagnosis, prescription, and treatment method. Ieong²⁹ thus concludes that the NCT system in Portugal is still in a very remote phase, lacking development, with the purpose of improving and developing the realisation of the IC doctrine in this recently legalised domain.

4. Final remarks

It can be said that the four principles of IC are usually present in studies and in the literature that researches TCM, where IC operationalises respect for autonomy and contributes to beneficence and non-maleficence by informing the patient about risks/benefits and alternatives²⁴⁻²⁶. However, as expressed by Zhao *et al.*⁵, although many studies refer to IC, this does not guarantee that consent is, effectively, informed and that it complied with all ethical requirements, namely, communication of risks, voluntariness, possibility of withdrawal, among others. That is, although many trials mention the application of IC, there is no certainty about the quality of this process and whether it was documented in accordance with rigorous ethical standards⁵. In fact, several authors who comment on the IC process emphasise that consent is a communicative process and not a simple form, and must ensure the comprehension, voluntariness, and decision-making capacity of each participant^{31,32}. In this sense, Zhang *et al.*² defend the idea that in order to obtain high-quality IC in TCM clinical trials, it is necessary to improve transparency, language, relational care, and ensure that participants understand all relevant and inherent aspects of the study/intervention they are participating in. Empirical research⁵ found that only a small fraction of the reported trials mentioned clinical trial registration and that ethical approval was referred to in less than a quarter of the papers, which highlights a gap in practice and reporting. Thus, it is important here to emphasise the study by Zhao *et al.*⁵, which contemplated IC in its research and treated it as an object of investigation, insofar as they did not assume that IC was provided to participants, concerning themselves with this aspect by questioning them about how the process was. In the same sense, it is understood that Li *et al.*³³ developed a protocol that considers the necessary ethical requirements for research on human beings, including specifically informing participants about the objectives, procedures, possible risks, and benefits before signing the IC. TCM trial participants

ask for clear explanations about the proposed mechanisms, interactions with Western treatments, duration, visits, adverse effects, and alternatives to non-treatment ^{2,5}. This indicates that standard forms/leaflets used in the clinic should include these items in a simple and illustrative way, and tools such as the model leaflet by White *et al.* ³⁰ (for acupuncture) or the WHO models for the ICF can be adapted to include specific sections on "what TCM is applied here", "what are the differences in relation to Western treatment", "what are the expected effects and potential adverse effects" ^{30,32}. Regarding the study by Barros *et al.* ³⁴, it allows for highlighting gaps in conceptualisation among professionals/managers. Thus, to guarantee quality IC, it is necessary to invest in the ethical training of TCM professionals, not least because IC protects against practices that promise extraordinary cures without any scientific evidence. For this reason, IC should include an honest balance between the evidence (what is known and what is not known) and realistic expectations, preventing psychological and financial harm from false expectations.

5. Conclusion

This review confirms that IC is a fundamental ethical and legal prerequisite for the practice and research of TCM. While IC is recognised and commonly mentioned in protocols, significant deficiencies in its quality, transparency, and practical implementation may occur. The core finding is that IC must evolve from a mere formality to an essential communicative process to guarantee patient autonomy and trust. To strengthen TCM's ethical foundation, the standardisation of information materials and dedicated ethical training for professionals are strongly recommended, ensuring these practices align with contemporary healthcare standards.

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Review

Phytotherapy for Anxiety: A Narrative Review of Efficacy, Mechanisms and Clinical Considerations.

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Abstract

Background: Anxiety disorders are among the most prevalent mental health conditions worldwide, and current pharmacological treatments, although effective, are often associated with adverse effects and incomplete symptom remission. These limitations have intensified interest in complementary and alternative therapeutic approaches, including herbal medicine.

Objective: This narrative review examines the evidence supporting the use of medicinal plants for the management of anxiety, highlighting their mechanisms of action, clinical efficacy and safety considerations.

Methods: A search of the scientific literature was conducted to identify studies investigating medicinal plants traditionally used for anxiety treatment. Particular attention was given to findings related to phytochemical activity within the central nervous system, clinical outcomes and reported adverse effects.

Results: Several plants, including *Valeriana officinalis*, *Passiflora incarnata*, *Melissa officinalis*, *Matricaria chamomilla* L., *Withania somnifera* and *Lavandula angustifolia*, demonstrate anxiolytic effects supported by preclinical and clinical evidence. Their primary mechanisms involve modulation of GABAergic neurotransmission, alongside antioxidant and anti-inflammatory pathways. Despite these promising results, the literature shows considerable variability in study design, formulation standardisation and sample size, limiting the generalisability of findings.

Conclusions: Herbal medicine presents a valuable complementary approach to anxiety management, offering potential therapeutic benefits with generally favourable safety profiles. Nevertheless, further high-quality, standardised clinical trials are necessary to confirm efficacy, establish optimal dosages and ensure long-term safety. Integrating herbal therapies into broader healthcare frameworks requires strengthened regulation, professional training and informed public use.

Keywords: Anxiety; Herbal Medicine; Phytotherapy; Anxiolytic Plants; GABAergic Activity; Complementary Therapies.

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1. Background

Anxiety is a psychological condition and one of the most prevalent today, affecting millions of people worldwide and negatively influencing their quality of life (QoL). According to Lobo ¹, in Portugal, one in every five people suffers from some psychiatric disorder, with anxiety disorders being the most prevalent. Globally, Fernandes *et al.* ², drawing on data from the World Health Organization (WHO), report that the worldwide prevalence of anxiety disorder is 3.6%, reflecting the dynamics of contemporary society. Although several conventional therapeutic approaches exist for the treatment of anxiety, such as psychotherapy and pharmacology ³, these therapies are not always effective and may also entail undesirable side effects, for example, those arising from pharmacological

treatment. Given this scenario, interest in complementary and integrative approaches has been increasing. For example, Chinese herbal medicine is one of the pillars of Traditional Chinese Medicine (TCM) and uses medicinal herbs in order to restore energetic and functional balance in the body. That is, it forms part of an ancient medical system and is characterised by the use of leaves, flowers, fruits, roots, plant barks and minerals for therapeutic purposes ⁴⁻⁶.

Thus, in view of the increasing demand for safe and effective therapeutic alternatives, and given that anxiety is a disorder with high prevalence both globally and nationally, it is understood that studying the role of herbal medicine in the treatment of anxiety is pertinent. Therefore, this study reviews the efficacy, mechanisms and clinical considerations relevant to the topic.

2. The case of Traditional Chinese Medicine

TCM is a science with centuries of history and is grounded in knowledge based on accumulated empirical experience ⁶. It begins from the theory that disease is the consequence of an imbalance of the vital force (*Qi*) throughout the body ⁷. *Qi* is the main substance of the universe and of the body ⁸; it is the “root” of the human being ⁹ and, together with the body, forms a single entity ¹⁰. *Xue* corresponds to blood, but it is a functional concept that differs from the understanding in conventional medicine and is associated with *Qi* ¹¹. *Yin-Yang* refers to the balance and harmony of the body ^{12,13}. Therefore, TCM is grounded in a holistic view of the human being, where the body is an integrated whole, providing a framework for prevention, diagnosis and treatment, based on various theories related to nature and the human body ⁹.

2.1. Diagnosis in TCM

Diagnosis is the essence of medicine and means to know or understand a patient; after deducing and comprehending knowledge about the patient and their disease, its nature and possible course are discovered ¹⁴. To perform diagnosis, some basic aspects must be taken into account: observing (*wàng*); listening and smelling (*wén*); assessing the patient's history (*wèn*); palpating the pulse, thorax and abdomen, various parts of the body, channels and points (*qiè*). After these initial observations, and in order to obtain a concrete diagnosis, there is a vast range of diagnostic techniques that may be used within TCM: evaluating the energy flow in each channel through palpation of the radial artery in six different positions; observing the face, eyes and tongue; superficially examining the ear; noting the sound of the patient's voice; palpating the body, particularly the abdomen; comparing temperatures in different parts of the body; and observing the vein of the index finger in small children. It should also be noted that everything that can be observed without instruments or invasive techniques, such as the patient's health history and main complaints, must be included in the diagnostic process ¹⁴⁻¹⁷.

2.2. Herbal Medicine as a TCM Treatment Technique

Herbal medicine is one of the main therapeutic techniques in TCM, and due to growing public awareness, it is increasingly sought as a therapeutic alternative or complement to Western medicine ^{18,19}. Regarding its role within TCM, herbal medicine is extremely relevant when compared with acupuncture (perhaps the most well-known TCM therapeutic technique), since Chinese herbalists use only herbal medicine to treat their patients, but most acupuncturists rely on herbal medicine to combine with acupuncture treatments. Therefore, herbal medicine treats diseases based on energetic patterns identified through diagnosis (e.g., spleen *Qi* deficiency), and herbal formulas are selected to correct these patterns and restore harmony between *Yin* and *Yang*, *Qi*, *Xue* and the internal organs. The main objectives of this therapeutic technique are as follows: proven clinical efficacy; safety of use; therapeutic individuality; promotion of health and disease prevention; holistic approach; sustainability and environmental respect; integration with other therapies.

2.3. Herbal Prescription

Once the diagnosis has been made and the patient's condition understood, the herbal therapist prescribes the formula most suited to the symptomatic picture, usually prescribing combinations of five to fifteen herbs, as single-herb formulas are rare in Chinese medicine. However, to prescribe herbal medicinal products it is necessary to possess legal authorisation and technical-scientific competence, thus avoiding exposing the patient to risks.

Therefore, herbal prescription may be explained as the process of identifying and guiding the use of medicines produced mainly from medicinal plants, ensuring safety, efficacy and quality in treatment. Treatment does not rely on a single consultation; patients must return at least every seven to fifteen days so that their condition can be reassessed and dosages adjusted if necessary ⁸. Herbal medicines may be used as complementary treatment for diseases, but in some cases may replace medications, provided that prescriptions are made responsibly and by a qualified professional ²⁰. Thus, herbal prescription involves correct identification of the plant, preparation/extract type, standardisation/quality, mode of use and suitability to each case.

2.4. Categories of Plants

Although some plants have more applications than others do, they all play a role, since removing one plant or altering the dosage results in a different formula with different energetic characteristics. For example, in Chinese Medicine, herbs have different flavours (pungent, sweet, bitter, salty, sour and bland) and are also classified according to temperature (hot, cold, warm, neutral, cool and intermediate), whereby hot diseases should be treated with cold herbs and cold diseases treated with hot herbs ²¹. There are 18 categories of plants, including: hot and cold herbs that release the exterior; herbs that drain fire (cold herbs); purgatives; herbs that regulate water and drain dampness; herbs that dispel wind and dampness; herbs that transform phlegm and stop cough; aromatic herbs that transform and dissolve dampness; herbs that relieve food stagnation; herbs that regulate *Qi*; herbs that regulate *Xue*; herbs that warm the interior and expel cold; tonics; astringent herbs and substances that stabilise and calm the spirit; herbs that nourish the heart and calm the spirit; aromatic substances that open the orifices; substances that extinguish wind and stop tremors; herbs that expel parasites; and substances for external application ^{22,23}.

3. Legal and clinical considerations in the use of Herbal medicine

3.1. Legislation on Herbal Medicine

Regarding the legislative framework governing the use of herbal medicine and the profession of herbal therapist, four main regulatory documents should be highlighted. Law No. 45/2003 of 22 August ²⁴, also known as the Basic Legal Framework for Non-Conventional Therapies, establishes the regulation of the activity and professional practice of non-conventional therapies. Law No. 71/2012 of 22 August ²⁵ regulates Law No. 45/2003 concerning the professional practice of non-conventional therapies, including herbal medicine (Article 2). Concerning the profession of herbal therapist, Ordinance No. 207-E/2014 of 8 October ²⁶ defines the characterisation and functional content of the profession. Finally, Ordinance No. 172-B/2015 of 5 June ²⁷ regulates the general requirements for the degree programme leading to a Bachelor's degree in Herbal Medicine.

3.2. Plant–Drug Interactions

Scientific publications in recent years have addressed interactions between phytochemical compounds (herbal medicine), drug-metabolising enzymes and physiological functions. Based on plants' ability to inhibit or induce certain metabolic enzymes and/or transport proteins, the potential risks of interaction between plants and medicines can be assessed ²⁸. Regarding these interactions, the study by focused exclusively on this subject

and presents numerous examples based on empirical evidence. Some of these examples are shown in the table below.

Table 1. Examples of plant–drug interactions according to Faustino ²⁸.

Medicine	Plant	Interaction
Paracetamol	Wu Wei Zi (<i>Fructus Schisandrae Chinensis</i>).	Decrease in side effects: gomisin A lignan may have a liver-protective effect; hyperkalaemia when used with high doses of potassium-sparing diuretics; reduced effect of sodium bicarbonate, aluminium hydroxide, antibiotics, reserpine, caffeine, opiates, scopolamine and berbamine.
General anaesthetics	Sheng Jiang (<i>Rhizoma Zingiberis Officinalis Recens</i>); Gan Jiang (<i>Rhizoma Zingiberis Officinalis</i>).	Reduction of side effects, decreasing nausea.
Aspirin	Gan Cao (<i>Radix Glycyrrhiza Uralensis</i>).	Reduction of side effects, decreasing gastrointestinal irritation.
Caffeine	Ma Huang (<i>Herba Ephedrae</i>)	Increases heart rate and blood pressure.
Chemotherapy	Yun Zhi (<i>Sclerotium Coriolus Versicolor</i>) Ci Wu Jia (<i>Radix Eleutherococcus Senticosus</i>)	Reduction of side effects, strengthening immune cell production and improving dendritic and cytotoxic T-cell tumour infiltration. Reduction of effects, decreasing immune system depression and therapy toxicity.
Epinephrine	Ma Huang (<i>Herba Ephedrae</i>)	Potentiates drug effect due to the plant's ephedrine content.
Heparin	Dan Shen (<i>Radix salviae miltiorrhizae</i>)	Potentiates drug effect by increasing heparin absorption.
Influenza vaccine	Ren Shen (<i>Radix panax ginseng</i>)	Enhances vaccination effects.
Insulin	Hu Lu Ba (<i>Semem trigonella foenum-graecum</i>)	Potentiates drug effects: plant reduces glycaemia, urinary sugar excretion, cholesterol and triglycerides.
Fenelzine	Ma Huang (<i>Herba Ephedrae</i>) Ren Shen (<i>Radix panax ginseng</i>)	Potentiates effects of ephedrine, as fenelzine inhibits ephedrine metabolism, leading to accumulation. Increases side effects (insomnia, headache, tremor). Mechanism unknown.

4. Anxiety

4.1. Anxiety Disorders and Diagnosis

In the literature addressing the topic, anxiety appears as an emotional state characterised by apprehension, worry or unease in the face of real or imagined threat. This state involves multiple components (emotional, cognitive, physiological and behavioural), which may be beneficial, promoting adaptation, or pathological when intense, persistent and disproportionate to the triggering stimulus ^{1,29}.

Thus, adaptive anxiety and pathological anxiety are distinguished. The former, healthy, can help motivate people to prepare, practise and train; it may also encourage appropriate caution in potentially dangerous situations ³⁰. Hence, it is described as the anticipation of future threat and being more frequently associated with muscle tension and vigilance in preparation for future danger and cautious or avoidant behaviours ³¹. As well, pathological anxiety, on the other hand, is a future-oriented emotion, marked by a sense of uncontrollability and unpredictability about potential aversive events ³². To determine whether anxiety is adaptive or pathological, Castillo *et al.* ³³ suggest evaluating the anxious reaction, whether it is short-lived, self-limited and related to the stimulus.

Therefore, anxiety is universal, as everyone has felt anxious at some point in their lives, and it may occur at different stages of life ³⁴. As a disorder, it is diagnosed regardless of age or gender and is not always easy to comprehend ³⁵. However, when it causes dysfunction and suffering in the individual, it becomes maladaptive and therefore a psychiatric

disorder³⁰. The diagnosis of any anxiety disorder is based on the characteristic signs and symptoms listed in the DSM-V (Diagnostic and Statistical Manual of Mental Disorders), but it may be suspected when: anxiety is highly distressing; anxiety interferes with functioning; anxiety does not resolve spontaneously within a few days; and other causes have not been identified³⁰.

According to the APA³¹, the different anxiety disorders are distinguished mainly by the stimuli or circumstances that trigger fear, anxiety or avoidance behaviours, as well as the types of thoughts and beliefs associated with them. The DSM-V presents diagnostic criteria, risk factors, prognosis, functional consequences and differential diagnosis for each type of anxiety disorder, considering as anxiety disorders: separation anxiety disorder; selective mutism; specific phobia; social anxiety disorder (social phobia); panic disorder; agoraphobia; generalised anxiety disorder (GAD); substance/medication-induced anxiety disorder; anxiety disorder due to another medical condition; other specified anxiety disorder; and unspecified anxiety disorder³¹.

4.2. Herbal Medicine in the Treatment of Anxiety

Concerning the use of medicinal plants for the treatment of anxiety, the studies by Assi *et al.*³⁶ and Georg Jensen *et al.*³⁷ are noteworthy. The former highlights the high prevalence of popular use of plants for anxiety treatment, but also the need for education to promote a better-informed population and regulation regarding plant use for this purpose. Georg Jensen *et al.*³⁷, in turn, report that in the Middle East and African regions there are plants with considerable potential for anxiety treatment, with antioxidant, anti-inflammatory and neurotransmitter-modulating mechanisms, but acknowledge that empirical evidence is limited due to small and poorly standardised studies. In other words, although medicinal plants of cultural importance are widely used, scientific rigour is lacking, and as previously mentioned, two of the seven pillars of herbal medicine are precisely proven clinical efficacy and safety of use. Moreover, these findings highlight the importance of professional herbal prescription, performed by a qualified therapist based on the patient's symptoms and requiring legal accreditation and technical-scientific competence.

Medicinal Plants for the Treatment of Anxiety

Herbal medicine has attracted significant research interest as an alternative and/or complementary approach in the treatment of anxiety, using medicinal plants with anxiolytic, calming and relaxing properties^{38,39}. Indeed, many patients show no response to conventional pharmacological treatments or cannot tolerate their adverse effects⁴⁰.

Regarding anxiolytic plants, the literature shows that herbal products such as *Valeriana officinalis*, *Passiflora incarnata*, *Melissa officinalis* and *Piper methysticum* are effective in reducing anxiety symptoms, acting on neurochemical mechanisms that modulate the central nervous system (CNS), such as increasing the availability of GABA (gamma-aminobutyric acid), a crucial neurotransmitter in anxiety regulation^{39,41}.

Piper methysticum (Kava-kava) has been officially recognised and frequently used in clinical studies, being attributed an anxiolytic effect; however, it presents some long-term safety restrictions^{40,42}. This plant's anxiolytic action is attributed to the pharmacological activity of alpha-pyrones, and it also exhibits anticonvulsant, sedative and anaesthetic properties. The dried stem or rhizome, when chewed, acts as a local anaesthetic and stimulates saliva production, and no adverse effects associated with its use have been identified to date⁴³⁻⁴⁵.

The study by Savage *et al.*⁴⁶ indicates an anxiolytic effect without dependence or hepatotoxicity; although not conclusive, the study highlights the therapeutic potential of Kava-kava. These findings are unsurprising, as Juvino *et al.*⁴⁷ note that it is one of the species with the highest number of studies involving patients with anxiety disorders, demonstrating its efficacy, which justifies its use as an effective and promising therapy for anxiety.

On the other hand, *Valeriana officinalis* has sedative, anxiolytic and antioxidant effects clinically demonstrated^{39,40,42,43}. Due to its sedative action, it aids sleep, and beyond its use

in the treatment of GAD, it acts on the CNS by increasing GABA concentration ^{44,45}.

Passiflora incarnata (passionflower) is used in controlled form for mild to moderate intermittent anxiety as a natural tranquilliser ⁴⁰⁻⁴². It has sedative, calming, antidepressant, anxiolytic, hypnotic and antispasmodic effects ⁴⁴.

Melissa officinalis (lemon balm) has a relaxing effect, reducing physical symptoms of tension and stress ^{39,40,48}. This effect is associated with its action on the GABA_A system, acetylcholinesterase inhibition (AChE) and metalloproteinase-2 inhibition, with rosmarinic acid being the main component responsible for its anxiolytic effect ⁴⁹.

In addition to the plants mentioned above, Lobo ¹ adds the following for anxiety treatment: *Hypericum perforatum* (St John's Wort); *Humulus lupulus* (hops); and *Rauvolfia serpentina* (Indian snakeroot or Devil Pepper). The literature also includes *Withania somnifera*, *Lavandula angustifolia* (lavender) and *Matricaria chamomilla* L. (chamomile).

Regarding *Withania somnifera*, Pratte *et al.* ⁵⁰ found that it contributes to a significant reduction in anxiety and has greater efficacy than psychotherapy. Indeed, *Withania somnifera* appears in the literature associated with anxiety treatment, reducing stress symptoms that give rise to anxiety ⁵¹. The systematic review carried out by Campos ⁵² similarly shows that this plant significantly reduces symptoms of anxiety and stress, improving QoL and well-being.

Conversely, the studies by Keefe *et al.* ⁵³ and Mao *et al.* ⁵⁴ highlight *Matricaria chamomilla* as a therapeutic alternative. In the former, chamomile showed a positive effect on the treatment of anxiety and GAD, with good levels of tolerance among participants. This study supports the use of chamomile in anxiety treatment, with efficacy comparable to anxiolytic medications in some cases. As noted by Aguiar *et al.* ⁴⁰, many patients do not tolerate or do not respond to side effects of conventional pharmacological treatments, making it important to explore alternative therapies. Mao *et al.* ⁵⁴ also found that participants treated with chamomile experienced fewer relapses, fewer symptoms and longer time to relapse, with good tolerability. These results show that long-term chamomile use may be safe and help maintain GAD, as also demonstrated by Rocha *et al.* ⁵⁵, who report that chamomile's anxiolytic effect derives from secondary metabolites of the flavonoid class.

Another plant that may be used in anxiety treatment is lavender. In the study by Kasper *et al.* ⁵⁶, Silexan, a standardised extract of *Lavandula angustifolia* used for therapeutic purposes, reduced symptoms of subclinical anxiety and GAD, showing efficacy comparable to medications such as lorazepam and paroxetine. Furthermore, Silexan improved sleep, somatic and depressive symptoms, and was well tolerated, representing an effective and safe alternative with a mild adverse-effect profile. Similarly, Moller *et al.* ⁵⁷ found that Silexan significantly reduced subclinical anxiety and improved sleep and QoL, establishing itself as an effective and safe alternative for treating subclinical anxiety symptoms. These findings show that lavender may be an effective therapeutic option, as also confirmed by Andrade *et al.* ⁵⁸ and Silva *et al.* ⁵⁹. In the first study, the authors note the efficacy of lavender in anxiety treatment due to its stress-reducing and anxiolytic effects. In the second study, focusing on lavender oil, various effects are described: the psychological effects of inhaling lavender oil occur through conscious perception, belief and expectation, and the pharmacological effects occur through modulation of cyclic adenosine monophosphate activity (reduction of cyclic adenosine monophosphate outcomes with sedation) and inhibition of glutamate binding (sedative effects). Thus, the use of the oil is considered safe, except for rare allergic reactions, and may be beneficial in patients with anxiety and reduce the need for antipsychotic medications.

Similarly, Donelli *et al.* ⁶⁰ also concluded that lavender is beneficial for anxiety treatment and, being administrable in multiple forms, inhalation was found to be the most effective route, followed by massage and capsules. These results converge with those reported by Kang *et al.* ⁶¹, in which lavender was shown to reduce symptoms of perceived anxiety, particularly when inhaled (aromatherapy).

5. Conclusion

This narrative literature review indicates that herbal medicine represents a complementary or alternative therapeutic strategy with significant potential for the management of anxiety, offering clinically relevant benefits and, in many cases, fewer adverse effects compared with conventional pharmacological treatments. Several medicinal plants (such as *Valeriana officinalis*, *Passiflora incarnata*, *Melissa officinalis*, *Matricaria chamomilla* L., *Withania somnifera* and *Lavandula angustifolia*) have demonstrated efficacy in reducing anxiety symptoms, acting through diverse neurochemical mechanisms within the central nervous system, particularly via modulation of GABAergic activity.

Despite these promising findings, the literature highlights the need for caution. Long-term safety profiles, potential herb–drug interactions and the lack of standardisation in formulations and dosages remain important limitations, underscoring the necessity for further robust and well-designed clinical studies. In this context, the role of qualified herbal therapists is essential to ensure responsible prescription practices, compliance with existing legislation and the provision of treatments that prioritise efficacy, safety and quality.

Therefore, herbal medicine constitutes a viable therapeutic option for the treatment of anxiety and holds considerable potential for integration into complementary and integrative healthcare models. However, achieving this integration requires continued scientific research, strengthened regulatory frameworks, appropriate professional training and greater public education regarding the safe and informed use of medicinal plants.

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Review

The Therapeutic Potential of Phytotherapy: A Review of Efficacy, Cultural Value, and Challenges for Integration into Contemporary Healthcare.

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Abstract

Phytotherapy, one of the therapeutic modalities of Traditional Chinese Medicine (TCM), has gained significant prominence as a complementary therapeutic practice, being utilised in domestic settings and formal contexts such as healthcare services. Its therapeutic potential, demonstrated across various clinical conditions, has sparked interest and necessitated an analysis of its contribution to human health. Therefore, the aim of this study is to identify and discuss the benefits of phytotherapy for human health and to analyse the challenges associated with its integration into healthcare services.

This is a Narrative Literature Review (NLR), which incorporates 12 articles published between 2014 and 2025 and searched in PubMed and LILACS. The results revealed that phytotherapy is used across different populations (children, the elderly and even pregnant women) and for multiple clinical conditions, such as Type 2 Diabetes Mellitus (T2DM), gastrointestinal disorders, bronchitis, and breast cancer. The main motivational factors for its use include accessibility, low cost, cultural tradition, and the perception of safety. However, some gaps are notable concerning standardisation, safety, the quality of clinical trials, and communication between practitioners and patients. It is concluded that phytotherapy presents high therapeutic potential and cultural acceptance, and can complement conventional therapy. Nevertheless, its full integration into health systems requires more studies, regulation of its use, professional training, and the promotion of safe, evidence-based practices.

Keywords: Phytotherapy; Traditional Chinese Medicine; Primary Healthcare Integration; Clinical Efficacy; Safety and Regulation; Cultural Value; Health Professional Training.

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1. Introduction

Chinese phytotherapy is one of the pillars of TCM, and can be explained as an ancient therapeutic approach that uses plants and natural substances to promote health and treat various diseases. Over more than 4,000 years, this system has been refined and validated not only by tradition but also by recent studies, highlighting phytotherapy as a significant complementary alternative within the current context of integrative health ^{1,2}.

The therapeutic approach of phytotherapy is based on the philosophical principles of *Yin-Yang*, the Five Phases (or Five Movements), and the circulation of *Qi* (vital energy). This philosophy guides the selection and combination of medicinal plants, aiming not only to resolve immediate symptoms but also to restore the body's internal balance ^{3,4}.

In the literature on the subject, it is noted that phytotherapy contributes to human health in various pathological situations, such as in the control of metabolic syndrome ^{5,6}, inflammatory disorders ⁷ and as support for oncological treatment ⁸.

Given that phytotherapy has gained more prominence and that it is important to inform the public, both academic and non-academic, of its multiple health benefits, this article is an NLR that seeks to identify the benefits of phytotherapy for human health, analysing its integration into healthcare and public health strategies.

2. Traditional Chinese Medicine

It can be said that TCM's main concept is holism, based on original theories regarding aetiology, diagnosis, and treatment ⁹. It encompasses the signs and symptoms of the entire organism, including the organs, channels and collaterals, *Qi*, blood (*Xue*), and *Yin-Yang* ⁹.

Qi can be explained as the energy that manifests physically and spiritually, capable of passing through various states of aggregation ¹⁰, and is re-established through the balance of the opposing forces of *Yin* and *Yang*, which manifest in the body as heat and cold, internal and external, and deficiency and excess ¹¹. *Yin* and *Yang* symbolise opposing forces, where *Yin* represents the shaded side of the mountain—the dark, feminine, and negative forces, and *Yang* represents the sunny side of the mountain, the illuminated, masculine, and positive forces ^{4,11}.

TCM postulates that for balance to exist, *Yin-Yang* must be present, being responsible for the changes in the body that will restore balance ^{4,12}. Regarding diagnosis in TCM, it is carried out through a holistic and detailed approach, so that Chinese medicine, although difficult to practise, arrives at a more certain and more complete diagnosis, a diagnosis that incorporates all aspects of the patient's life, thus leading to a safer treatment than Western medicine ¹³.

This allows for the assessment of the body's energetic and functional state, not only for the purpose of identifying the disease but also to understand the internal imbalance that triggered its onset. According to Maciocia ¹³, this is based on the idea that there must be a fundamental *Yin* and *Yang* imbalance for illness to occur, and that this imbalance manifests in all areas of human experience. For example, the patient will show an imbalance in colour, movement, skin texture, food preferences, music, clothing, sports, or painting style. In the body, the channels, the Elements, the Blood, and the entire pathway through which the *Qi* flows will be influenced by the imbalance.

Therefore, the four diagnostic methods in TCM are: Observation; Inquiry; Palpation; and Auscultation and Olfaction ¹³.

3. Phytotherapy

Phytotherapy, as a therapeutic technique of TCM, stands out for the use of medicinal plants and minerals, aiming to re-establish the body's energetic balance, as well as to treat the patterns of imbalance diagnosed in light of TCM principles. This branch of TCM studies medicinal plants, their properties, their advantages, their toxicity, and their mode of action, using plants for the treatment of deficiency or excess ⁴.

Based on an ancient, holistic philosophy, phytotherapy is a practice that considers the symptoms and causes of illnesses, promoting physical, emotional, and spiritual well-being. It conceives of the individual as a whole, considering physical, emotional, mental, and spiritual aspects of health, seeking to balance and harmonise the organism to promote an optimal state of health ¹⁴⁻¹⁸.

In this sense, TCM categorised medicinal plants according to their own energetic principles, where the therapist prescribes single herbs or compound formulas according to the energetic patterns (syndromes) presented by each patient. Therefore, phytotherapy is used complementary to Western medicine or integrated into traditional and cultural medical systems, gaining increasing numbers of followers who seek a natural and holistic approach to health and who are interested in the sustainable use of plant resources ¹⁴⁻¹⁶.

3.1. A Brief Historical Note on the Use of Medicinal Plants

Etymologically, the word phytotherapy derives from the Greek words *therapeia*, meaning treatment, and *phyton*, meaning plant; thus, phytotherapy (or therapy by plants) is dedicated to the study of medicinal plants, their chemical compositions, and therapeutic properties ¹⁹.

The use of medicinal plants dates back to the earliest civilisations, with archaeological records proving their use since approximately 60,000 years ago. In China, ginseng was used by emperors for more than 3,000 years, and in ancient Egypt, papyri such as the Ebers Papyrus showed the cataloguing of hundreds of species and therapeutic recipes ²⁰⁻²³.

Phytotherapy remains, even today, one of the main and oldest disciplines of TCM and is widely used in China and worldwide ²⁴, having evolved through the integration of modern scientific methods that have validated the traditional uses of plants, where clinical studies, laboratory research, and government regulations have contributed to its recognition as a legitimate and effective practice ²⁵.

3.2. Popular, Traditional, and Scientific Phytotherapy

In the literature on phytotherapy, terms such as popular phytotherapy, traditional phytotherapy, and scientific phytotherapy appear. It is considered important, within the scope of this work, to briefly clarify these concepts. What mainly differentiates these herbal therapies is the method of use, the validation, and the basis of knowledge about medicinal plants ^{26,27}.

Popular phytotherapy can be defined as the tradition of domestic and community use of medicinal plants, transmitted orally in each local reality, from generation to generation. This popular wisdom, besides being a strategic source of 'clues' regarding the efficacy or toxicity of medicinal plants to inspire subsequent scientific studies, which then multiply in universities and the pharmaceutical market, constitutes, above all, an important cultural and civic contribution, and, no less importantly, a political one ²⁸.

Traditional phytotherapy, most often, relies on written records of its practice, which, depending on its origin, has existed for decades, centuries, or even millennia. But what truly delimits it as a matrix for phytotherapy, in our view, would be the fact that it is not practised in isolation, as a simple therapeutic resource or method, but is always 'coupled' to a context, as an integral part of 'medical systems' originating from peculiar cultures, within the context of a 'field of health knowledge and practice', recognised by the World Health Organization (WHO) as 'traditional medicine' ²⁸⁻³¹.

Scientific phytotherapy, in turn, consists of the integrated study of the clinical use of medicinal plants and herbal products for therapeutic, diagnostic, or prophylactic purposes, based on scientific data and evidence, even if initially drawn from popular and traditional knowledge ²⁸.

3.3. Its Integration into the Healthcare System

Mendes ³² draws attention to a particularly important aspect, and, relying on various authors, state that in China, where phytotherapy originates and is widely used, approximately 30 to 50% of the population has already used herbal products, and in Europe and North America, 50% of the population has used them. Statistics also show that approximately 80% of the world population perceives phytotherapy as their primary health system, especially in developing countries, and that it has been increasingly used in developed countries, demonstrating the importance and, consequently, the need for herbal products to be studied and consciously prescribed so that they are used safely ³² and integrated into healthcare services.

Regarding the integration of phytotherapy into healthcare, several studies address the issue. Filho *et al.* ³³, referring to the Brazilian context, stress the importance of regulating the use of medicinal plants and herbal products in the national policy on integrative and complementary practices and the national policy on medicinal plants and herbal

products. The country already has initiatives such as *Farmácia Viva* (Living Pharmacy), the National List of Essential Medicines, and the List of Medicinal Plants of Interest to the unified health system. Despite policies that promote the integration of herbal products and their safe use, many practitioners still do not feel confident prescribing them, highlighting the need for training to be better equipped ³³.

In the same line, Silva *et al.* ³⁴, in their Systematic Literature Review (SLR) on the challenges and strategies for the insertion of phytotherapy into Primary Care, report critical barriers in areas such as insufficient practitioner training, structural and political limitations, a lack of robust clinical evidence, restricted access to inputs, challenges in inter-sectoral partnerships, and cultural resistance. Therefore, the authors reinforced the need for greater alignment between guidelines and the daily practices of the health system.

By integrating herbal products into healthcare, a significant advance is made in promoting integrative and complementary practices, contributing to a healthcare system that provides effective and culturally relevant therapeutic alternatives ³³, making the importance of herbal products for the population using the health system visible ³⁵. However, it is understood that for the integration of phytotherapy into healthcare, it is essential that the services employ a phytotherapist (herbal medicine practitioner), who, according to Article 4 of Ordinance No. 207-E/2014, of 8 October ³⁶, states that the phytotherapist should be capable of: promoting health and preventing illness, assessing the client's state of health, as well as identifying patterns of imbalance and applying specific criteria of phytotherapy; recognising the limits of their practice, identifying situations that may require referral to other professionals; drawing up the therapeutic plan, defining principles and strategies; prescribing and administering medicinal plants, formulas, supplements, and advising on nutrition, dietetics, and lifestyle; recognising and intervening in adverse reactions; conducting an individualised analysis, investigating personal factors that influence health and well-being; educating for health, informing clients and the public to promote healthy habits and prevent diseases; applying therapeutic methods specific to phytotherapy and correctly identifying the properties of the plants; providing follow-up and monitoring progress, tracking results and adjusting treatment as necessary; establishing a therapeutic relationship; critically evaluating practice, reflecting, analysing cases, gathering feedback, and participating in audits; prioritising scientific integration, keeping up with the literature and applying new knowledge in practice; considering the individual as a whole, and not just isolated symptoms; recognising signs of dysfunction and developing appropriate strategies; prioritising continuous updating and permanent professional development; collecting, interpreting fundamental data and clinical decisions; preparing and presenting case studies; guiding colleagues and interns.

3.4. Legislation on Phytotherapy

In the scope of legislation on phytotherapy, four documents can be highlighted: Law No. 45/2003, of 22 August (The Framework Law for Non-Conventional Therapies); Law No. 71/2012, of 22 August; Ordinance No. 207-E/2014, of 8 October²⁸; and Ordinance No. 172-B/2015, of 5 June ³⁷.

Law No. 45/2003 establishes the framework for the activity and practice of practitioners who apply non-conventional therapies (Article 1), recognising phytotherapy as a non-conventional therapy (Article 3). Furthermore, according to this law, the practice of non-conventional therapies can only be carried out by practitioners holding the legally required qualifications and duly accredited for their practice (Article 10) ³⁸.

Law No. 71/2012 regulates Law No. 45/2003 regarding the professional practice of applying non-conventional therapies, which includes phytotherapy (Article 2). To perform the function of a non-conventional therapist, one must hold a degree in one of the areas (Article 5), as well as possess the professional card issued by the Central Administration of the Health System (ACSS) (Article 6) ³⁹.

With regard to the profession of phytotherapist exclusively, Ordinance No. 207-E/2014, of 8 October, states that phytotherapy is practised under the professional title of phytotherapist (Article 3), who must have knowledge of (Article 4) ³⁶:

- The specific theoretical foundations underpinning their diagnosis and therapeutic intervention;
- The indications and contraindications of phytotherapeutic treatment;
- The theory, practice, and principles of phytotherapy, demonstrating this through various approaches, selecting natural agents, techniques and procedures, or modifying treatment plans to meet the needs of people;
- Interpersonal communication, allowing for an adequate collection of relevant personal and family facts for the application of the therapy, the maintenance of a good relationship with clients, colleagues, and others related to the profession, and the prevention and resolution of conflict situations;
- Psychology and social determinants of health, enabling them to contextualise the therapeutic decision and the care to be provided;
- Behavioural sciences, allowing for appropriate and effective advice on healthy lifestyles;
- Physiology, pathology, pathophysiology, observation of signs and symptoms to identify situations where the person may need the intervention of another health professional.

Finally, in section three of Article 4, the principles of conduct by which the phytotherapist must be governed are set out, namely ³⁶:

- Adopting ethical conduct aimed at guaranteeing the quality of the provision of phytotherapy care;
- Basing the relationship with the client on trust and information, knowing how to communicate effectively to build and maintain a therapeutic relationship;
- Not deliberately causing harm or prejudicing the client, under any circumstances, within the scope of their profession;
- Referring the client, whenever necessary, to the health professional best qualified to treat their health condition;
- Not creating false expectations regarding the expected results of the treatment;
- Not treating people with conditions that are not susceptible to any improvement in their health status through phytotherapy;
- Applying only treatments useful and necessary for the maintenance or recovery of the person's health;
- Developing a treatment plan that involves the active and consented participation of the client, stating the prognosis, the results to be achieved, the therapeutic methods and techniques used, and the regular evaluation of their progress;
- Providing high-quality phytotherapy care, always ensuring client safety;
- Ensuring the confidentiality of health information, as well as secrecy, in accordance with legal norms;
- Accepting multiculturalism, without compromising respect for the principle of non-discrimination of patients, namely based on ancestry, sex, race, language, territory of origin, religion, political or ideological convictions, education, economic situation, social status, or sexual orientation;
- Being available to participate in training in the field of phytotherapy, namely by welcoming students and interns;
- Ensuring the timeliness, quality, rigour, and humanisation of phytotherapeutic healthcare;
- Ensuring the preparation and permanent updating of health information, and registering the treatments performed;

- Ensuring professional development through continuous training.

Ordinance No. 172-B/2015, of 5 June, regulates the general requirements that must be met by the study cycle leading to the Bachelor's degree in Phytotherapy, which is taught in polytechnic institutes, non-integrated polytechnic higher education schools, or polytechnic higher education schools integrated into a university (Article 3). The main components of training are fundamental sciences, clinical sciences and techniques, the principles of phytotherapy, and the practice of phytotherapy ³⁷.

4. Methodology

For the implementation of the study, the NLR was adopted as the methodology—a vital part of most empirical articles, dissertations, and funding proposals, performing a vital scientific function ⁴⁰. The narrative review is an "older" format (compared to the SLR) and allows for an analysis of the available literature on a subject of interest. As it is not systematic, there are no formal guidelines regarding its completion ⁴¹. Even without guidelines and protocols for the NLR, in this specific case, the research question was designed using the PICO acronym: **P**atient – patients; **I**ntervention – phytotherapy; **C**omparison – conventional medicine; **O**utcome (expected results) – therapeutic benefits of phytotherapy for human health. Given this, the question to be answered is: What are the benefits of phytotherapy for human health?

4.1. Inclusion and Exclusion Criteria

The inclusion and exclusion criteria are an important aid in the selection of the scientific evidence that will constitute the study sample. Thus, the inclusion criteria are: articles published between 2014–2025; full and free access; publications in English and Portuguese; articles that address the benefits of phytotherapy for human health. The exclusion criteria are: articles published before 2014; without full and free access; languages other than those mentioned; articles focusing on a therapeutic practice other than phytotherapy.

4.2. Explanation of the Search Method

Before proceeding to search for articles in databases, the Health Sciences Descriptors (DeCS) were searched, and three were selected: fitoterapia / phytotherapy; saúde humana / human health; atenção à saúde / delivery of health care. Subsequently, using Boolean operators, the following search phrase was formulated: fitoterapia AND saúde humana AND atenção à saúde (phytotherapy AND human health AND healthcare). The search for evidence was carried out in the PubMed and LILACS databases.

5. Results

This NLR includes 12 studies published between 2016 and 2025 that address the use and benefits of phytotherapy in various areas and diseases, as well as its integration into Primary Care (themes that emerged during the reading and analysis of the articles). Table 1 presents the synthesis of the results and their categorisation by themes/subjects.

Table 1. Synthesis and Categorisation of Scientific Evidence

Ref.	Field	Results	Conclusion
42	Paediatrics	- Origin and transmission of knowledge: the use of phytotherapy is a family legacy, passed down from generation to generation, mainly through oral transmission; - Frequency of use: 96% of respondents reported having used some phytotherapy resource for children and/or adolescents; - Most mentioned plants: fennel (sweet herb), boldo, mint, pineapple, citronella, garlic, lemon grass, ginger, etc.; - Indications: cough,	- The practice of phytotherapy in paediatrics in primary care is a culturally embedded practice, part of the family and community legacy, incorporating traditional knowledge and everyday experiences; - Rescuing and considering this tradition gives new meaning to healthcare, as it allows popular practices to be valued, integrated into the care system,

		abdominal pain, colic, calming effect, expectorant; fever, sore throat, ear and headache, diarrhoea, infections, deworming, and oral hygiene; - Motivation for use: easy access to the plant, high cost of conventional treatments, difficulty accessing medical services, belief in the power of plants as a therapy; - Meanings attributed to phytotherapy beyond cure/treatment: prevention of worsening, recovery of memories and experiences, integration with nature, social aggregation (strengthening community/family ties); - Perception of efficacy: of the 96%, some considered it always efficient and others sometimes efficient.	stimulating autonomy, community participation, and the rational use of medicinal plants.
43	Maternal and Child Health	- Statistically significant associations: topical use of almond oil associated with preterm birth; oral use of raspberry leaf associated with a higher probability of Caesarean section; intensive use of liquorice associated with early preterm birth; use of African herbal medicine called <i>mwanaephopo</i> associated with maternal morbidity and neonatal morbidity or mortality; - 14 studies reported no adverse effects.	- There is not enough strong evidence to guarantee the safety of using many herbal products during pregnancy or postnatally; - There are major gaps in the studies, in terms of variability in doses, pharmaceutical forms, lack of follow-up for adverse events, and the underreporting of events.
44	Maternal and Child Health	- Knowledge: 66.2% of pregnant women had a good level of knowledge about phytotherapy; - Attitude: 71.2% showed a positive attitude towards the use of medicinal herbs; - Use outside of pregnancy: 56.5% have used medicinal herbs at some point in their lives; - Use in current pregnancy: 40% used it during pregnancy; - Use in previous pregnancies: 16% confirmed using herbal products in previous pregnancies; - Time of use: many started using it at the beginning of the first trimester; - Motivations: tradition/culture, low cost, easy access, belief that they are natural and safe; - Perceptions of risk: some women considered potential dangers (lack of correct dose, risk of excess), but many believed that, being natural, they would be harmless; - Statistical associations: only marital status showed a significant association with the level of knowledge, while age, education, and occupation did not show a relevant association.	- Most pregnant women in Nsukka who participated in the study had good knowledge and a positive attitude towards the use of phytotherapy; - Effective use during pregnancy was not universal; many women used phytotherapy outside of pregnancy or had used it in previous pregnancies, and a smaller percentage used it currently; - It is recommended that health professionals incorporate guidance on phytotherapy in antenatal care, with specific education to fill knowledge gaps, and that there is open communication with pregnant women about the use of these products.
45	Gastrointestinal Disorders	- FGID emerge as one of the most important indications for phytotherapy, given the number of plants used, the accumulated evidence, and the tradition in Europe and beyond; - Plants used in FGID are classified according to their main mechanism or effect: bitters - plants that stimulate gastric secretions; aromatics - plants with essential oils, carminative, that combat spasms; bitter-aromatics - combination of both properties; antispasmodic or carminative plants (essential oils or antispasmodic alkaloids) to relieve colic, distension, gas; mucilaginous plants that soothe or protect the gastrointestinal mucosa; flavonoid-rich plants with anti-inflammatory properties; - Use of plant combinations to increase efficacy or specificity of effect, such as STW	- Phytotherapy, particularly through herbal and combined preparations, is a valid therapeutic option for FGID, even according to the standards of Evidence-Based Medicine; - Well-studied preparations like STW 5 are examples of how this integration can work; - Some gaps still exist, such as: the need for more solid clinical studies for various plants, better safety data, clear mechanisms, standardisation of preparations (dosage, quality, composition); - The use of phytotherapy in FGID is not merely traditional or an alternative, and can be rationally integrated into conventional therapies, when properly studied and practised by qualified practitioners.

		5; - Although there is a long tradition of use, the variation in the quality of evidence for different plants and combinations is notable.	
46	Bronchitis	- Facilitators to the use of phytotherapy: concern about antibiotic resistance, perception that herbal products may be less invasive or cause fewer side effects, relatively easy access, patients' willingness to try alternatives; - Barriers to use: doubts about efficacy compared to antibiotics, concerns about interactions with conventional medicines (safety and adverse effects), cost, taste/flavour; - Conditions for acceptance: reliable evidence, trust, need for guidance.	- Many patients and health professionals consider the use of phytotherapy for acute bronchitis to be acceptable, especially as an alternative to antibiotics, as there is reliable evidence and clinical guidelines supporting its use; - Phytotherapy can help with self-care, reduce unnecessary antibiotic use, and decrease antimicrobial resistance, provided it is used safely; - There is a need for more studies, preparation of local guidelines, and clarification of doses and preparations.
47	Breast Cancer	- Considerable adherence of participants to alternative therapies was observed, with emphasis on phytotherapy (highest prevalence); - Motivational factors: psycho-biological (seeking relief from physical side effects or unpleasant symptoms, improved bodily well-being), psycho-spiritual (faith, spiritual or transcendental dimensions that help face the disease), psycho-social (social support, cultural influence/tradition, desire for personal control over one's own health, popular knowledge).	- Patients with a history of breast cancer demonstrate increased motivation to seek alternative therapies, aiming to improve their quality of life in the face of adverse effects of conventional treatment; - Phytotherapy is the most used alternative therapy by this group of patients; - There is a need for health professionals to be better prepared to provide guidance on these practices, aiming for greater safety, comprehensive and knowledge-based use, reducing the risks of empirical use.
48	Diabetes	- <i>Nigella sativa</i> and fenugreek showed consistent beneficial effects on improving glycaemic control and lipid profile; - Ginger regulates enzymes involved in carbohydrate metabolism; - Curcumin demonstrated the ability to control glucose and lipids through its antioxidant effects, although there are challenges with bioavailability (how much curcumin actually reaches the tissues); - Cinnamon improves glucose transport and inhibits specific enzymes related to glucose metabolism; - <i>Nigella sativa</i> presented the most consistent effects of improvement across the various studies.	- The herbs examined have therapeutic potential and can be used in complementary treatments for T2DM, mainly in glycaemic control and improvement of the lipid profile; - The need for more studies, standardisation in doses and preparations, duration of use, and drug interactions is confirmed.
49	Diabetes	- High prevalence of phytotherapy use among participants; - Significant associations: educational level; socioeconomic level; place of residence; duration of T2DM; - Independent factors associated with the use of phytotherapy: age between 51 and 60 years.	- Patients with T2DM frequently resort to phytotherapy as an anti-diabetic therapy. Factors such as age between 51 and 60 years, low educational level, low socioeconomic level, and average duration of diabetes are associated with this use. It is necessary to evaluate the efficacy and adverse effects of phytotherapy in the treatment of this disease.
50	Diabetes	- Use of herbal products: 68% of patients use herbal products, the most common being: cinnamon, ginger, and fenugreek; - Sources of information: most patients obtained information about herbal products from family, friends, and social media; - Communication with doctors: 71.4% of patients did not inform their doctors	- The use of herbal products is common among patients with T2DM; - There is a patient-doctor communication failure regarding the use of herbal products; - Greater awareness and dialogue about the use of

		about the use of herbal products; - Patients' perceptions: 54% believe that herbal products are effective in controlling T2DM and 46% consider herbal products safe; - Doctors' perceptions: 66% routinely ask patients about the use of herbal products and 25% have a positive opinion about the use of herbal products in T2DM; some doctors expressed concerns regarding the safety and efficacy of herbal products.	herbal products need to be promoted to ensure safety and efficacy in the treatment of T2DM.
51	Integration into Primary Care	- Facilitators: cultural acceptance of phytotherapy in the community, availability of local medicinal plants, previous experience of health professionals with phytotherapy; - Barriers: lack of formal training and knowledge about phytotherapy, concerns about the safety and efficacy of herbal products, and lack of regulation and standards for the clinical use of phytotherapy.	- Although phytotherapy is widely used and culturally accepted in Ghana, there are several challenges to its integration into formal clinical practice; - Adequate training for health professionals and clear regulations for the safe and effective use of phytotherapy need to be developed.
52	Elderly Population	- The main plants used are (from most to least used): mint, chamomile, rue, matico, plantain, boldo, melissa, pennyroyal, paico, and lemon verbena; - Reasons for use: gastrointestinal, nervous, dermal, respiratory, metabolic, and genitourinary problems; - Acquisition methods: home cultivation was the most reported; - Forms of preparation: infusion was the most popular form; - Drug interactions: some plants mentioned have potential interactions that have already been described.	- The use of medicinal plants is common among the elderly attended at the primary health centres of Puente Alto; - It is fundamental to know the plant species used by the population to guide their rational and safe use, considering benefits, adverse effects, and drug interactions.
53	Integration into Primary Care	- Belief in therapeutic effect: 96.2% of professionals believe in the therapeutic effect of medicinal plants, but do not prescribe them; - Knowledge of the National Policy on Integrative and Complementary Practices (PNPIC): 65.6% of professionals know the PNPIC; - Knowledge about the presence of herbal products in the National List of Essential Medicines (RENAME): 85.4% of professionals are unaware of the presence of herbal products in the RENAME; - Origin of knowledge about medicinal plants: 93% of professionals acquired knowledge about medicinal plants through family; - Association between belief in therapeutic effect and family use: a significant difference was observed between professionals who believe in the therapeutic effect of plants and those who use medicinal plants in their families.	- Although most professionals believe in the therapeutic effect of medicinal plants, the majority do not prescribe them; - Knowledge about the PNPIC and the presence of herbal medicines in the RENAME is limited among professionals; - The origin of knowledge about medicinal plants is predominantly familial, indicating the importance of traditional knowledge; - There is a need for training for health professionals to effectively integrate phytotherapy practices into primary healthcare.

6. Discussion

The results presented in Table 1 show the use of phytotherapy in various clinical, population, and geographical contexts, also revealing the scope of phytotherapy practice and its implications for human health, demonstrating its application in the treatment of different diseases and the importance that phytotherapy has for people who use the health system ³⁵.

Firstly, with the results obtained, it is verified that phytotherapy is an ancient practice ^{20,24} and crosses different phases of the life cycle: from paediatrics ⁴², through pregnancy and the puerperium ^{43,44}, up to the elderly population ⁵². This evidence strengthens the culturally embedded nature of phytotherapy, transmitted between generations and practised in domestic contexts as well as in health systems. This transmission between generations

refers to what is called popular phytotherapy, often transmitted orally, or traditional phytotherapy, which often has written records ²⁸.

The motivation for the use of phytotherapy appears in several studies and aspects such as accessibility, low cost, cultural tradition, and the belief in safety are mentioned ^{42,44,52}. The perception that plants are "natural and harmless" is dangerous, as shown by the results of Muñoz Balbontín *et al.* ⁴³, there are associations between certain herbal medicines and obstetric risks, highlighting the idea that the use of phytotherapy without adequate follow-up can lead to serious consequences, hence the importance of the presence of a phytotherapist in the health system, who is qualified to promote health and prevent illness, assess the patient's state of health, as well as identify patterns of imbalance and apply specific criteria of phytotherapy ³⁶.

In terms of clinical conditions, the findings reveal that phytotherapy is used and studied in acute illnesses, such as bronchitis ⁴⁶, in chronic conditions, such as T2DM ⁴⁸⁻⁵⁰, and breast cancer ^{8,47}. The analysis thus shows that the search for phytotherapy is due, on the one hand, to reducing dependence on conventional drugs to avoid side effects or unnecessary antibiotic use, and on the other, to therapeutic complementarity, as in the case of chronic diseases like T2DM or oncological diseases like breast cancer, where patients seek greater control over their health and well-being.

Although there are some herbal products with proven efficacy and potential for evidence-based integration ^{45,48}, the results showed that gaps still exist: lack of standardisation of doses, variable quality of preparations, and the need for more clinical trials that attest to safety ^{46,52}. If, on the one hand, the literature recognises the therapeutic potential of phytotherapy in various conditions, capable of bringing benefits to human health, critical barriers persist that limit its integration into health systems ³⁴.

Another aspect that is worth mentioning is the relationship between patients and health professionals, as some studies reveal a lack of communication between these two parties, with patients not informing doctors about the use of herbal products ⁵⁰ and health professionals, despite recognising the efficacy of phytotherapy, the majority still do not prescribe it ^{33,53}. What emerges from these results is the compromise of safety and the possibility of integrating phytotherapy and conventional therapies. This is explained in the study by Asare *et al.* ⁵¹, where it was found that there is great acceptance of phytotherapy, but the lack of training and regulation is visible, which creates obstacles to the safe clinical practice of this ancient therapy.

In summary, the results highlighted three main themes associated with the use of phytotherapy and its benefits for human health: the cultural and social value of phytotherapy, present in different populations; the great therapeutic potential of phytotherapy in various areas and clinical conditions (T2DM, gastrointestinal disorders, bronchitis), but which still require more studies for safe use, both by health professionals and by patients; challenges for the integration of phytotherapy into health systems, namely the need for professional training, clear regulation, research, and reinforcement of patient-doctor communication.

Despite its benefits for human health, phytotherapy continues to face scientific, regulatory, and communicational barriers that need to be overcome so that its use is safe, effective, and integrated into healthcare.

7. Conclusion

The NLR allowed us to confirm that phytotherapy, as an ancient therapeutic practice of TCM, has strong cultural and social acceptance, being used in different phases of the life cycle and in various clinical conditions. The analysed studies highlight important therapeutic benefits, particularly in glycaemic and lipid control, in the case of T2DM, in the improvement of gastrointestinal, respiratory, and oncological symptoms (fewer side effects), as well as in supporting the general well-being of patients.

However, some challenges still persist for the practice and use of phytotherapy that compromise its integration into healthcare: absence of standardisation in doses and preparations, the need for more research to measure efficacy and safety, lack of regulation and training among health professionals, which, in the absence thereof, the presence of phytotherapists or TCM practitioners with phytotherapy training in health services is advocated for teamwork with health professionals.

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Review

Phytotherapy in the Management of Low Back Pain: A Comparative Analysis with Conventional Pharmacological Interventions.

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Abstract

Background: Low back pain (LBP) is a leading cause of global disability, affecting up to 80% of the population. While conventional pharmacological treatments (NSAIDs, paracetamol) are standard, their efficacy is often limited by side effects or insufficient relief, particularly in chronic cases. Consequently, interest in Traditional Chinese Medicine (TCM) and phytotherapy has increased.

Objective: To evaluate the clinical benefits of phytotherapy in the treatment of LBP and compare its efficacy and safety with conventional pharmacological interventions.

Methods: A narrative literature review was conducted, focusing on clinical guidelines, comparative studies, and TCM theoretical frameworks. The review analysed the aetiopathogenesis of LBP, the structure of herbal formulations (Emperor, Minister, Assistant, Envoy), and the comparative outcomes of botanical vs. synthetic drugs.

Results: Evidence suggests that conventional analgesics, such as paracetamol, often show no superiority over placebo for acute non-specific LBP. In contrast, phytotherapeutic agents, specifically *Boswellia serrata*, *Curcuma longa*, and the *Du Huo Ji Sheng Tang* formula, demonstrated significant reductions in pain intensity and functional disability. Studies indicated that combining phytotherapy with acupuncture (e.g., *Palmijihwang-hwan*) provides superior cost-effectiveness and clinical outcomes compared to isolated conventional therapies.

Conclusion: Phytotherapy is a viable and safe complementary alternative for managing LBP. It addresses the systemic and energetic imbalances (such as Kidney Yang deficiency or Qi stagnation) that conventional medicine often overlooks. While further longitudinal trials are needed to standardise dosages, integrating herbal medicine into multidisciplinary care offers a promising path for reducing the global burden of LBP.

Keywords: Low back pain; Phytotherapy; Traditional Chinese Medicine; Pharmacology; Analgesia.

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1. Introduction

LBP, defined as pain located in the lower lumbar region, constitutes one of the most prevalent and disabling musculoskeletal problems worldwide, affecting up to 80% of the population at some point in their lives. The impact of this clinical condition is significant, appearing as the second most frequent cause of medical consultations, surpassed only by respiratory infections. The causes of LBP are varied, ranging from the overloading of lumbar spine structures, "comfortable" posture, sedentary lifestyles, trauma, ageing, and ergonomic factors. It can be classified as acute, subacute, or chronic depending on the duration of the pain ¹⁻³.

LBP is a public health issue, primarily due to its high prevalence, which can exceed 70% over a lifetime, with a higher occurrence among women and the elderly population, interfering with a person's functionality and quality of life ³⁻⁵. In the university context, several studies point to prevalence rates above 60%, essentially associated with sedentary behaviour and inadequate lifestyles ⁶.

Conventional treatment for LBP encompasses pharmacological options, physiotherapy, postural guidance, and physical exercise, with surgical intervention only recommended for specific and refractory cases ^{7,8}.

In recent decades, there has been a growing interest in complementary therapeutic alternatives, such as phytotherapy (herbal medicine), considering the potential analgesic and anti-inflammatory effects of certain medicinal plants. According to Pinela ⁹, it plays a crucial role in the treatment of LBP, using mostly herbal formulas specifically designed for each patient's energetic diagnosis. Within the range of TCM practices, the most used techniques in the treatment of lumbar pain usually are acupuncture, phytotherapy, and Tuina. In this line of thought, a Narrative Literature Review is considered necessary to understand the benefits of phytotherapy in lumbar pain, comparing them with those of conventional treatments.

2. Low Back Pain

2.1. Definition and types

LBP is defined as pain or discomfort located in the lower lumbar region, between the costal margin and the gluteal folds, being one of the most prevalent musculoskeletal symptoms worldwide. It is not a specific disease, but rather a symptom that can involve various mechanisms and clinical conditions ^{1,10,11}.

Most pain is caused by disorders in the spinal column and the joints, muscles, ligaments, and nerve roots surrounding the spine or in the discs between the vertebrae ^{12,13}. The most common causes are: injuries to muscles and ligaments, osteoarthritis, vertebral compression fractures, ruptured or herniated discs, lumbar spinal stenosis, spondylolisthesis, and fibromyalgia ^{14,15}.

The classification of LBP can be based on criteria such as the duration of the pain, the etiopathogenic mechanism, and the pain pattern ^{2,16}.

Regarding duration, LBP is considered acute when it lasts no longer than four weeks, subacute when it lasts from four to 12 weeks, and chronic when it exceeds 12 weeks ¹⁷.

Regarding the etiopathogenic mechanism, LBP can be mechanical, which is the most common typology and is related to injuries, degeneration, or structural changes in the spine, representing about 97% of cases. This can be specific mechanical (e.g., herniated disc, fractures) or non-specific (e.g., muscle-ligament or degenerative injuries). Non-mechanical LBP, which is systemic, is caused by inflammatory, infectious, neoplastic, or metabolic pathology, covering about 3% of cases ¹⁸.

Regarding the pain pattern, LBP can be classified as nociceptive (resulting from injury or activation of tissue nociceptors), neuropathic (arising from injury or disease of the nervous system), or nociplastic (persistent pain without apparent injury, usually associated with central sensitisation) ².

Therefore, the classification of the type of LBP is essential for the diagnosis and for determining the most appropriate therapeutic approach and patient prognosis.

2.2. Diagnosis

The diagnosis of LBP is carried out through clinical evaluation, alongside a medical history (anamnesis), a focused physical examination, and, only in specific cases, complementary exams are necessary ^{2,7,18}. The anamnesis is crucial for understanding the characteristics of the pain (intensity, location, duration, relationship with activities, etc.) and identifying "red flags" for serious pathologies such as fractures, neoplasms, or infections ^{7,18}.

The physical examination involves checking posture, palpation of the lumbar spine (spinous processes, paravertebral muscles), assessment of range of motion, and specific tests such as: the Schober test, which measures lumbar mobility; sciatic nerve tension tests, including the Lasègue test (Straight Leg Raise), important in identifying radiculopathy; and neurological examination of the lower limbs (muscle strength, reflexes, sensitivity), performed even in the absence of radiating symptoms to detect neurological deficits ^{18,19}.

When a diagnosis has not yet been established at this stage, it becomes urgent to resort to complementary exams, such as ^{2,7}: plain X-rays, to assess bone changes in cases where fractures or deformities are suspected; Computed Tomography (CT) and Magnetic Resonance Imaging (MRI), used when complications are suspected, symptoms persist, or warning signs are present, allowing for a detailed assessment of bone structures and soft tissues; and functional, non-invasive exams, such as cypholordometry, which can be used in postural assessment and monitoring evolution, particularly in rehabilitation cases ²⁰.

Thus, the diagnosis, based on clinical guidelines and scientific evidence, ensures the identification of the main causes of LBP, guiding the subsequent steps, namely treatment. To guide the diagnosis, there are the Guidelines from the American College of Physicians and the American Pain Society for the diagnosis and treatment of LBP ²¹⁻²⁵.

2.3. Conventional treatment

Conventional treatment for LBP may begin with the avoidance of activities that overload the spine and cause pain ²⁶⁻²⁸. There are three types of treatment: non-pharmacological, pharmacological, and surgical.

In terms of pharmacological therapy, paracetamol is frequently recommended for pain relief, unless there is inflammation. Non-steroidal anti-inflammatory drugs (NSAIDs), whether over-the-counter or prescribed, can also relieve pain and simultaneously decrease inflammation ^{29,30}.

When these options fail, opioid analgesics may be prescribed, but these should be used for a short period as they can increase pain sensitivity, cause side effects (e.g., drowsiness), confusion, and constipation, with a risk of developing a substance use disorder. It is also possible to use muscle relaxants; carisoprodol, cyclobenzaprine, diazepam, metaxalone, or methocarbamol are some of the medications used to reduce muscle spasms, though they are not suitable for the elderly ³¹⁻³³.

Other forms of treatment may include the application of heat or cold, massage, and physiotherapy. In the case of chronic LBP, aerobic exercises can help. If analgesics are ineffective, other treatments may be considered, such as facet joint injections, epidural corticosteroid injections, and, in cases of herniated discs or severe spinal stenosis, surgery is recommended ³⁴.

Therefore, pharmacological options include analgesics, NSAIDs, and muscle relaxants, while physiotherapy utilises resources such as kinesiotherapy, electrotherapy, thermotherapy, and manual techniques, each presenting a varying degree of scientific evidence for pain reduction and functional improvement ^{35,36}.

Taking into account each type of LBP, as therapeutic options vary according to chronicity and severity, Lopes ³⁷ explains that for the treatment of: subacute LBP, in addition to the non-pharmacological therapeutic plan (exercises and psychotherapy), there are 1st-line treatments, characterised by the administration of NSAIDs and paracetamol, and 2nd-line treatments, which involve the administration of non-benzodiazepine skeletal muscle relaxants; chronic LBP, movement exercises and other interventions are recommended, with 1st-line treatment including NSAIDs and paracetamol and 2nd-line treatment including serotonin-noradrenaline reuptake inhibitor (SNRI) antidepressants, tricyclic antidepressants, and tramadol.

3. Phytotherapy

3.1. Traditional Chinese Medicine

TCM is an ancient medical system originating in China, involving a series of external practices for the understanding, diagnosis, treatment, and prevention of diseases, based on the dynamic balance between *Yin* and *Yang* forces and the circulation of vital energy (*Qi*)^{38,39}.

It is a medical system that practices holistic medicine, evaluating the person as a whole (physically, psychically, and environmentally) and based on philosophical principles such as *Yin-Yang* (the duality of opposing forces that must be balanced to ensure health), the Five Elements (wood, fire, earth, metal, and water), Meridian Theory (energy channels), *Zang-Fu* (*Zang* organs, which are *Yin*, and *Fu* viscera, which are *Yang*), *Qi* and *Xue* (blood) organs, and diagnosis by Syndrome Differentiation^{39,40}. Thus, one agrees with Maciocia⁴¹ when he states that Chinese medicine diagnosis is also strong in its holistic view of body and mind. Probably no other form of diagnosis is capable of making such a comprehensive, holistic, and detailed assessment of a patient in a relatively short time, gathering all the different elements of the diagnosis.

3.2. Phytotherapy

While conventional medicine resorts to pharmacological therapy, phytotherapy resorts to plants. Oliveira⁴² explains that in Western medicine, drugs usually consist of an active principle, which are responsible for the therapeutic effect, and excipients, which serve as vehicles, helping in the transport and guidance of the active principle to the desired site of action. In Chinese phytotherapy, the situation is similar: herbal formulas follow an organised structure, and the main function is performed by the plant designated as the Emperor, the "heart" of the formula, corresponding to the active principle that acts on the main symptom⁴²⁻⁴⁴. The remaining plants in the formula are designated as Minister, Assistant, and Envoy, acting in a complementary manner:

- The Minister reinforces the main effect (the action of the Emperor) and treats secondary symptoms;
- The Assistant, or auxiliary plant, is responsible for reinforcing the action of the Emperor and Minister, reducing potential adverse effects or toxicity, and treating secondary symptoms;
- The Envoy, or guide plant, directs the action of the plants in the body (to the affected meridian, system, or part of the body), promoting harmony in the therapeutic action. It is important to note that each formula may contain one or more plants from each category.

Phytotherapy treats pathologies based on energetic patterns identified during diagnosis, governed by seven pillars⁴⁵: Proven clinical efficacy; Safety of use; Therapeutic individuality; Health promotion and disease prevention; Holistic approach; Sustainability and environmental respect; and Integration with other therapies.

Plant-drug interactions are a topic of great relevance, as they can enhance benefits or cause clinical risks, altering the absorption, metabolism, transport, and action of drugs. It is crucial that phytotherapy is performed by a phytotherapist, a TCM specialist, or a health professional with knowledge in the field. This is because there is the assumption that medicinal plants, as well as natural products, do not pose a health risk. This concept, without scientific basis... ends up offering serious risks to the health of less enlightened people⁴⁶.

Regarding the categorisation of plants, there are 18 different types⁴², including: Exterior-releasing plants (hot and cold); Fire-draining plants (cold); Purgatives; Water-regulating and dampness-draining plants; Wind-and-dampness-dispelling plants; Phlegm-transforming and cough-stopping plants; Aromatic dampness-transforming plants; Food stagnation-relieving plants; *Qi*-regulating plants; *Xue*-regulating plants; Interior-warming

and cold-expelling plants; Tonic plants; Astringent/stabilising substances; Heart-nourishing and spirit-calming plants; Orifice-opening aromatic substances; Wind-extinguishing and tremor-stopping substances; Parasite-expelling plants; and External application substances.

3.3. Phytotherapy in the treatment of low back pain according to TCM

Phytotherapy treats both manifestations and causes, using formulas consisting of a variable number of plants based on their energetic characteristics. These preparations restore the patient's balance. However, it is important to underline that these must be prepared by a professional, especially since some herbs are prohibited during pregnancy as they may contribute to miscarriage ^{47,48}.

Furthermore, in phytotherapeutic prescription, it is necessary to consider the individual characteristics of the patient (e.g., weight and age) so that the effects of the active compounds are appropriate. A complete anamnesis is crucial ⁴⁹. These factors are essential from the perspective of the compound's bioaccessibility; if the dose is too low, bioavailability may be significantly reduced, compromising benefits, while an excess can be harmful ⁴⁹.

Regarding lumbar pain, it may arise due to Kidney *Yang* deficiency, affecting the warming and nutrition of this region; phytotherapy can be used to tonify Kidney *Yang* and strengthen the body's energy ⁹. Jahromi *et al.* ⁵⁰ explain that the formula *Du Huo Ji Sheng Tang* is widely used to warm the meridians, tonify Kidney *Yang*, and nourish *Xue*, showing efficacy in treating chronic LBP.

LBP can also arise due to *Qi* and *Xue* stagnation, which causes intense and localised pain; treatment serves to move *Qi* and *Xue*, relieving pain and restoring circulation in the meridians ⁵¹. To treat this condition, *Yan Hu Suo* (*Corydalis*) and *Chuan Xiong* (*Ligusticum*) can be used, herbs with analgesic properties that promote blood circulation ⁹.

Additionally, the invasion of cold and dampness, which can block the flow of *Qi* and *Xue* in the meridians of the lumbar region, can cause acute pain, stiffness, and a feeling of heaviness ⁵². The formula *Juan Bi Tang* can be used to disperse cold and dampness, stimulating *Qi* circulation and relieving pain ⁵⁰.

4. Phytotherapy vs. Pharmacology for the Treatment of Low Back Pain

Regarding treatment by phytotherapy, the article by Majumdar *et al.* ⁵³ stands out, finding that the combination of *Boswellia serrata* and *Curcuma longa* significantly reduced pain, disability, and inflammatory biomarkers, decreasing the need for analgesics. These findings confirm the anti-inflammatory and analgesic potential of medicinal plants, as mentioned by Pinela ⁹.

The study by Gupta *et al.* ⁵⁴ reinforces the idea of Pinela ⁹, showing that the *Rhuleave-K* formula provided rapid and substantial relief from postural lumbar pain, being safe and effective in the short term.

Similarly, Pham *et al.* ⁵⁵ demonstrated that the VH supplement, together with electroacupuncture, improved pain, mobility, and function, showing superior results compared to acupuncture alone. These results align with the TCM approach, which favours combined and integrated therapies. Sung *et al.* ⁵⁶ corroborate this perspective by showing that the use of *Palmijihwang-hwan* associated with acupuncture not only decreases pain and improves function but also presents an additional advantage in terms of cost-effectiveness.

Regarding pharmacological treatment, the results of the study by Saragiotto *et al.* ⁵⁷ reveal that paracetamol is not superior to placebo in non-specific acute LBP, questioning its use as a first line of treatment. Previously, Brazil *et al.* ⁷ had mentioned that the efficacy of some drugs is debatable.

Focusing on the use of systemic corticosteroids, Chou *et al.* ⁵⁸ indicate that these have limited short-term benefit only for radicular pain, but are not effective for non-radicular pain or spinal stenosis. Khankhel *et al.* ⁵⁹ found that oral ibuprofen is more effective than

topical diclofenac, but the combination of the two adds no benefit, demonstrating that pharmacological choice must be judicious and individualised.

In Wertli *et al.*⁶⁰, it is noted that NSAIDs are the class with the best results in LBP; however, they relieve but do not "remove" the pain, and prolonged use carries risks.

Regarding the use of antidepressants in the treatment of LBP, the study by Ferraro *et al.*⁶¹ concludes that pain improvement is modest and presents higher rates of adverse effects, requiring caution in their use.

Finally, the results obtained by McKenzie *et al.*⁶² reinforce the variety of results in this second theme, showing a lack of consensus among clinical guidelines, especially regarding pharmacological approaches. This reinforces the uncertainty and the need for complementary alternatives such as phytotherapy and acupuncture.

Therefore, and following the initial idea that LBP is highly prevalent and disabling^{1,3}. It is possible to see from the included studies that various therapeutic approaches relieve pain and improve quality of life and function^{53,55-57}. Conventional treatment includes drugs and physiotherapy, but surgery is an exception^{7,8}. Studies focusing on pharmacological treatment⁵⁷⁻⁶¹ confirm that, although exclusively used, they present limited efficacy or risks of adverse effects. Conversely, studies focused on phytotherapy⁵³⁻⁵⁶ present consistent results in terms of pain reduction, functional improvement, and safety, validating the perspective that phytotherapy can be a relevant complementary alternative in the treatment of LBP.

5. Conclusion

This review confirms that LBP is a complex global challenge requiring more than just standard "one-size-fits-all" treatments. While conventional drugs like NSAIDs are the norm, their limited efficacy in some cases and the risk of side effects highlight a clear need for better alternatives.

Phytotherapy, based on TCM, offers a scientifically viable solution. Studies show that herbal formulas (like *Du Huo Ji Sheng Tang*) provide significant pain relief and functional recovery with fewer risks. Furthermore, combining these herbs with acupuncture often proves more effective and cost-efficient than medication alone.

In summary, integrating phytotherapy into a multidisciplinary approach allows for more personalised care. While more clinical trials are needed to refine dosages, the current evidence strongly supports using these natural alternatives to improve patient quality of life and reduce the global burden of chronic pain.

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Review

Molybdenum and Sulphite Detoxification: Biochemical Foundations and Clinical Implications for Integrative Practice.

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Abstract

Background: Molybdenum (Mo) is an essential cofactor for sulphite oxidase, the enzyme responsible for converting reactive sulphites into sulphates. Functional insufficiency, driven by poor dietary intake, dysbiosis, inflammation, or genetic variants, may impair detoxification capacity and contribute to symptoms such as fatigue, headaches, bronchial reactivity, and gastrointestinal discomfort.

Objectives: To synthesise current evidence on dietary, metabolic, and clinical determinants of Mo status, and to outline integrative strategies for supporting sulphite detoxification within a Naturopathic framework.

Methods: This synthesis draws on biochemical, nutritional, and clinical literature addressing Mo physiology, sulphite metabolism, dietary intake patterns, genetic modifiers, and evidence-based naturopathic interventions. Emphasis is placed on functional assessment and therapeutic personalisation.

Results: Findings indicate that many individuals may exhibit functional Mo insufficiency despite meeting standard reference intakes. High sulphite exposure, impaired intestinal absorption, mitochondrial dysfunction, and specific polymorphisms (e.g., sulphite oxidase, MOCS1) may reduce sulphite oxidase activity. Integrative interventions, including Mo-rich diets, reduction of exogenous sulphites, antioxidant support, and targeted supplementation, can improve metabolic resilience when deployed with laboratory supervision.

Conclusions: Mo plays a pivotal role in sulphite metabolism and should be considered in patients presenting with unexplained intolerances or detoxification-related symptoms. A personalised approach that combines functional testing, nutritional optimisation, and lifestyle strategies can enhance clinical outcomes and reduce the burden of sulphite-related metabolic stress.

Keywords: Molybdenum; Sulphite Oxidase; Detoxification; Functional Nutrition; Naturopathic Medicine; Sulphite Intolerance; Mitochondrial Function; Oxidative Stress; Genetic Polymorphisms.

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1. Introduction

1.1. Rationale and Clinical Relevance

The accumulation of sulphites in the human body is an often-neglected phenomenon, despite presenting significant repercussions for mitochondrial, neurological, respiratory, and gastrointestinal function ^{1,2}. Sulphites arise both as endogenous by-products of sulphur amino acid metabolism and from the exogenous ingestion of food additives and drugs (E220–E228), necessitating efficient detoxification to prevent toxic effects. This process occurs mainly through the conversion of sulphites to sulphates, mediated by the enzyme sulphite oxidase, whose activity depends on Mo as an indispensable cofactor ³.

Despite this fundamental role, Mo remains a trace element frequently underestimated in clinical practice and complementary therapeutic approaches. Its functional deficiency can compromise enzymatic activity even in the presence of normal serum concentrations, affecting multiple organ systems ⁴. Evidence suggests that manifestations such as persistent fatigue, headaches, intolerance to sulphite-rich foods, gastrointestinal changes, and non-specific neurological signs may reflect alterations in this metabolic pathway ^{5,6}. The increasing environmental exposure to food additives, chemical pollutants, and sulphur compounds coincides with the rise in the prevalence of mitochondrial dysfunctions, chronic inflammatory processes, and multiple food intolerances. In this context, Mo emerges as a potential limiting factor in the body's detoxification capacity, silently influencing biochemical homeostasis ^{2,7,8}.

Thus, the choice of the present topic proves to be scientifically pertinent and clinically strategic. The analysis of the interaction between Mo and sulphite detoxification mechanisms contributes to clarifying an under-explored area but one of growing relevance in modern Naturopathy. By integrating precision biochemistry knowledge with contemporary research, space is opened for the development of more complete and evidence-based therapeutic approaches in integrative clinical practice.

Therefore, the objectives of this study are: (1) to evaluate the physiological and biochemical role of Mo in detoxification processes, with particular emphasis on its function as a cofactor for the sulphite oxidase enzyme, essential in the conversion of sulphites to sulphates; (2) to critically analyse recent scientific literature on the relationship between Mo deficiency, functional or absolute, and sulphite accumulation in the human body; (3) to investigate the clinical repercussions of dysfunction in this metabolic pathway, namely its association with systemic inflammatory processes, neurological manifestations, and sulphite-induced food intolerances; (4) to explore integrative therapeutic approaches based on functional Naturopathy, aimed at the prevention and correction of imbalances related to sulphur metabolism; and (5) to contribute to the clinical valorisation of Mo as a central element in regulating biochemical processes linked to oxidative stress, inflammation, and metabolic homeostasis.

2. Methodology

This study is based on a narrative literature review, oriented to integrate biochemical, physiological, clinical, and naturopathic data related to the role of Mo in sulphite detoxification. To ensure the reliability and currency of the information, recognised scientific databases (PubMed, Scopus, Web of Science, Google Scholar, and SciELO) were consulted in the period between January 2000 and June 2025.

The literature search was conducted using specific keywords, isolated or combined by Boolean operators (AND, OR), including: molybdenum, sulphite oxidase, sulphite detoxification, sulphite sensitivity, molybdenum deficiency, sulphite toxicity, molybdenum supplementation, mitochondrial dysfunction, sulphite oxidase gene, functional medicine, naturopathy detox, among others.

The selection of literature for this review was governed by three specific inclusion criteria. Firstly, all included publications must demonstrate direct relevance to the biochemical mechanisms of Mo or sulphite metabolism, ensuring the focus remains on the core subject matter. Secondly, to facilitate comprehensive analysis, the publications must be available in English, French, Spanish, or Portuguese. Finally, the selected works must exhibit clear methodological quality and recognised institutional affiliation, thereby ensuring the reliability and academic rigour of the evidence considered.

The following criteria were employed to exclude unsuitable literature and studies from the review:

- **Significant Methodological Limitations:** Articles with notable flaws in design, execution, or analysis that compromise the reliability or validity of their findings were excluded.

- Opinion Publications without Experimental Foundation: Works based solely on expert opinion, conjecture, or theoretical discussion that lacked underlying experimental data or empirical evidence were not included.
- Outdated or Duplicated Studies: Studies that were obsolete due to newer, more robust research or publications that were duplicates were filtered out.

Priority was given to review articles, clinical trials, case studies, and original research of direct relevance, with particular attention to publications from the last 20 years. Additionally, chapters from academic books and technical documents from international organisations, such as the European Food Safety Authority (EFSA) and the World Health Organization (WHO), were included whenever considered scientifically pertinent.

3. Molybdenum in the Human Body

3.1. Role as an Essential Trace Element

Mo is a trace element indispensable for human life, present in extremely small quantities in the body, but essential for the activity of several critical biochemical reactions⁹. Its main role is to act as a metallic cofactor for a specific group of enzymes, the molybdoenzymes, which catalyse fundamental redox reactions in the sulphur, purine, aldehyde, and various pharmacological compound cycles⁹⁻¹¹.

The Mo-dependent enzymes include:

- Sulphite Oxidase: Converts toxic sulphites into innocuous sulphates, constituting the final stage of cysteine metabolism and preventing the accumulation of potentially harmful intermediates¹².
- Xanthine Oxidase: Participates in the degradation of purines, promoting the conversion of hypoxanthine and xanthine into uric acid, a relevant plasma antioxidant, but which in excess is associated with hyperuricaemia and gout¹³.
- Aldehyde Oxidase: Acts in the oxidation of endogenous and xenobiotic aldehydes, playing an important role in drug metabolism and the elimination of potentially toxic compounds^{9,14}.

Mo integrates these enzymes through the molybdopterin cofactor, an organic structure that incorporates the metallic ion and allows the electronic transfer necessary for enzymatic catalysis^{15,16}. In the absence of this functional cofactor, the activity of molybdoenzymes is severely compromised, leading to the accumulation of toxic substrates and significant metabolic disturbances.

Although absolute Mo deficiency is considered rare in healthy individuals, functional deficiencies are increasingly described in the literature. These can result from insufficient intake, poor intestinal absorption, competition with other minerals, or increased metabolic utilisation in states of chronic inflammation. Conditions such as intestinal dysbiosis, industrialised diets poor in trace elements, and states of high oxidative stress can contribute to this functional deficit^{4,17}.

From an integrative clinical perspective, Mo assumes relevance not only for its isolated enzymatic role but also for the systemic impact it exerts. Through the metabolic pathways in which it participates, it influences sulphur metabolism¹², the modulation of oxidative stress¹³, hepatic detoxification processes^{9,14}, and the regulation of neurological and mitochondrial functions¹¹, standing out as a key micronutrient in global biochemical homeostasis⁴.

3.2. Mechanisms of Absorption, Transport, and Storage

Mo absorption occurs predominantly in the small intestine, especially in the jejunum, through mechanisms that are still not fully clarified. Evidence suggests that the process involves facilitated passive transport and, to a lesser extent, active transport dependent on ionic gradients¹⁸. The bioavailability of Mo is high, ranging between 80% and 90%

when ingested in soluble forms such as sodium molybdate, which makes it one of the most efficiently assimilated trace elements by the human body ⁴.

After absorption, Mo circulates in the plasma mainly as free molybdate, although it also transiently associates with albumin and other plasma proteins ^{9,14}. Metabolically active tissues rapidly capture this trace element, with intracellular transport dependent on mechanisms that are still poorly characterised, possibly involving anionic channels and specific transporters ^{19,20}.

In the intracellular environment, Mo is incorporated into the molybdopterin complex, its functional form, which acts as a cofactor for the molybdoenzymes ¹¹. The synthesis of the Mo cofactor (MoCo) depends on a specialised biochemical pathway, which requires the participation of specific enzymes and the availability of elements such as sulphur and iron. Thus, genetic, metabolic, or nutritional deficits of these cofactors can compromise Mo-dependent enzymatic activity, even when serum levels are within the normal range ^{21,22}.

Unlike minerals such as iron and zinc, Mo does not have significant body reserves. The main sites of temporary accumulation include the liver, kidneys, adrenal glands, and, to a lesser extent, the brain and mitochondria, reflecting the high biochemical needs of these tissues ¹³.

Mo homeostasis is regulated primarily via the renal route, through urinary excretion. This feature ensures the efficient elimination of excesses and contributes to its low toxicity potential in healthy individuals. However, it also means that chronic urinary losses, poor intestinal absorption, or changes in the microbiota can lead to subclinical states of deficiency, especially in situations of inflammatory bowel disease, alcoholism, severe dysbiosis, or restrictive diets ¹⁷.

3.3. Active Forms: Enzymatic Cofactors

The biological activity of Mo depends on its incorporation into specific enzymatic complexes, where it acts as a central atom in oxidation-reduction reactions. To perform its catalytic function, inorganic Mo absorbed in the form of molybdate (MoO_4^{2-}), needs to be converted into the Mo cofactor, resulting from the association of the metallic ion with an organic structure called molybdopterin. This process occurs through a complex and evolutionarily conserved biosynthetic pathway ^{11,22}.

Mo cofactor is indispensable for the activity of four human enzymes:

- Sulphite Oxidase: Catalyses the oxidation of sulphites to sulphates, an essential step in cysteine metabolism and the prevention of oxidative stress ^{23,24}.
- Xanthine Oxidase: Converts hypoxanthine and xanthine into uric acid, regulating purine degradation and contributing to antioxidant mechanisms and pathological conditions such as gout ^{25,26}.
- Aldehyde Oxidase: Intervenes in the oxidation of endogenous and xenobiotic aldehydes, including pharmacological metabolites ²⁷⁻²⁹.
- Mitochondrial Amidoxime Reducing Component: More recently identified, this enzyme is involved in the reduction of nitrogenous compounds and the modulation of reactive species ³⁰⁻³².

The absence of functional Mo or mutations affecting MoCo biosynthesis results in severe enzymatic deficiencies ^{33,34}. A paradigmatic example is congenital sulphite oxidase deficiency, a rare but fatal metabolic disorder in neonates due to the accumulation of sulphites and subsequent neurotoxicity ^{35,36}. Although hereditary cases are uncommon, functional or partial forms of deficiency, associated with states of intestinal dysbiosis, chronic intoxications, persistent inflammation, or malnutrition, are more prevalent and often under-diagnosed ³⁷⁻⁴⁰.

From a naturopathic perspective, the recognition of these functional deficiencies is fundamental for understanding diffuse clinical manifestations, food intolerances, and chronic conditions that do not respond to conventional therapies ¹⁷.

3.4. Excretion and Homeostatic Regulation

Mo homeostasis is ensured primarily by renal excretion, which regulates the balance between intestinal absorption and elimination, preventing both deficiency and toxicity. The mineral circulates in the plasma predominantly as free molybdate, being filtered in the glomeruli and excreted proportionally to its serum concentration and hydration status ^{41,42}.

Unlike minerals such as iron or copper, Mo does not have robust intracellular storage systems. Transient reserves are located mainly in the liver, kidneys, making the body dependent on a continuous dietary intake ¹³. Homeostasis is thus highly vulnerable in situations of nutritional deficiency, intestinal dysfunction, chronic renal failure, or excessive urinary losses ^{17,43}.

Reference plasma values range between 0.3 and 2.0 µg/dL, although there is considerable inter-laboratory variability and a lack of clinical standardisation ⁴⁴. Furthermore, normal serum concentrations do not exclude functional deficiencies, given that enzymatic activity depends on the integration of Mo into MoCo ¹¹.

Faecal excretion represents a secondary route, more relevant in cases of low intestinal absorption or excessive ingestion, while elimination via sweating appears to be insignificant ¹⁸. Regulation is non-hormonal but adaptive: sudden increases in intake result in greater urinary excretion, which explains its low acute toxicity. However, this same characteristic can lead to silent depletions in chronic marginal intake, aggravated by intestinal dysbiosis, chronic inflammation, or excessive alcohol consumption ^{37,45,46}.

In functional clinical practice, the assessment of Mo status should consider not only plasma levels but also indirect markers, such as urinary sulphite excretion, indicators of oxidative stress, liver enzymes, and glutathione, in order to obtain a more reliable perspective on the functional status of the mineral ⁴³.

4. Sulphites: Sources, Exposure, and Effects

4.1. Endogenous vs. Exogenous Sulphites

Sulphites are present in the human body in two main forms: endogenous, produced as a physiological by-product of metabolic processes, and exogenous, resulting from the ingestion of food additives, drugs, and environmental exposures. This distinction is fundamental for evaluating the total sulphite load and the individual efficiency of detoxification mechanisms ^{5,47,48}.

Endogenous Sulphites: By-products of Cellular Metabolism

Endogenous sulphites are generated mainly during the metabolism of sulphur amino acids, especially cysteine and, to a lesser extent, methionine. In the process of deamination and desulphurisation of cysteine, sulphur is initially converted into sulphite (SO₃²⁻), which is subsequently oxidised into sulphate (SO₄²⁻), by the enzyme sulphite oxidase. This step is essential to prevent the accumulation of toxic and unstable intermediates ^{9,49}.

This mechanism occurs continuously in tissues with high metabolic activity, such as the liver, kidneys, and brain, and is closely linked to the methionine-glutathione cycle, which is fundamental in antioxidant defence and hepatic detoxification processes. However, when sulphite oxidase activity is reduced, either due to Mo deficiency or intense oxidative stress, sulphite accumulation can induce metabolic dysfunctions and promote cellular inflammation ^{48,50,51}.

Exogenous Sulphites: Preservatives and Potential Risks

Exogenous sulphites are widely used as food additives (E220–E228) due to their antimicrobial, antioxidant, and bleaching properties. They are found in wines, dried fruits, frozen shrimp, processed potatoes, soft drinks, industrial sauces, and some drugs ⁵².

In individuals with reduced sulphite oxidase activity or under high cumulative toxic load, sulphite ingestion can exceed the body's detoxification capacity, leading to its accumulation in the blood, tissues, and mitochondria ⁵. Repeated exposure to these compounds has been associated with headaches, persistent fatigue, bronchospasms, gastrointestinal disturbances, and urticaria. In more severe cases, manifestations similar to asthma attacks or episodes of transient neurological dysfunction may occur ^{53,54}. These clinical manifestations are often misinterpreted, being attributed to non-specific food intolerances or psychosomatic conditions ^{5,54}.

4.2. Detoxification Capacity: An Individual Limit

The efficiency of sulphite detoxification varies widely among individuals and depends on factors such as sulphite oxidase expression, Mo availability, the integrity of the intestinal mucosa, and the total xenobiotic load. Genetics (e.g., sulphite oxidase gene polymorphisms), diet, the composition of the intestinal microbiota, alcohol consumption, chronic use of medications, and the presence of inflammatory or liver diseases are determinants in this process ⁵⁵.

Thus, the balance between endogenous production and elimination of sulphites must be understood not only as a biochemical mechanism but also as an indicator of metabolic resilience. This parameter also constitutes a strategic target in naturopathic intervention, especially in conditions of chronic fatigue, multiple hypersensitivities, and low-grade inflammation ⁵⁵.

4.3. Food, Pharmacological, and Environmental Sources

Exogenous exposure to sulphites is an omnipresent reality in contemporary society, resulting from the consumption of industrialised foods, use in pharmaceutical preparations, and presence in environmental pollutants. This external load adds to the physiological endogenous production and can exceed the detoxification capacity, especially in individuals with reduced sulphite oxidase enzyme activity ^{5,47,52}.

Food Sources

Sulphites are authorised as food additives under codes E220 to E228, performing antimicrobial, antioxidant, and bleaching functions ⁵². They are particularly present in the following foods:

- Wines, sparkling wines, and ciders – sulphur dioxide is added for microbiological stabilisation and oxidation prevention.
- Treated dried fruits (apricots, raisins, figs) – often preserved with sodium metabisulphite ⁵⁶.
- Processed potatoes – in the form of chips, frozen products, or industrial mash, where sulphites prevent enzymatic browning ⁵.
- Frozen seafood (particularly shrimp) – where sulphites inhibit enzymatic melanin reactions ⁵².
- Juices, industrial sauces, jams, pickles, and bakery products – frequently subjected to sulphite addition to prolong stability.

Studies indicate that, in susceptible individuals, the ingestion of doses higher than 10mg of sulphites per meal can trigger adverse reactions, including headaches, fatigue, gastric irritation, and respiratory symptoms ⁵.

Pharmacological Sources

Sulphites are also used as preservative excipients in various drugs, especially in injectable and inhaled formulations. The most relevant examples include:

- Injectable adrenaline (epinephrine) – frequently stabilised with metabisulphite ^{5,57}.
- Injectable or inhalable corticosteroids, such as methylprednisolone and budesonide ⁵⁶.
- Inhaled bronchodilators, used in asthma attacks, which paradoxically may contain sulphites as stabilisers ⁵⁸.
- Local anaesthetics and intravenous antibiotics, in which sulphites act as formulation preservatives.

These forms of exposure are clinically relevant in asthmatic patients or individuals with enzymatic deficits, potentially triggering bronchospasms, urticaria, or anaphylactoid reactions ^{52,58}.

Environmental Sources

Although less publicised, environmental sources represent an additional route of exposure:

- Industrial emissions (refineries, paper mills, textile industries), which release sulphur dioxide (SO₂), subsequently converted into endogenous sulphites in the lungs ^{59,60}.
- ^{61,62}.
- Contaminated indoor environments, such as spaces with mould or a high load of volatile organic compounds, which can compromise antioxidant defence and liver function ^{63,64}.

Chronic exposure to environmental sulphites has been associated with the exacerbation of inflammatory symptoms and the worsening of multiple chemical sensitivity conditions, especially in individuals with compromised mitochondrial and hepatic reserves ⁶⁵⁻⁶⁷.

4.4. Toxic Effects and Systemic Impact

The accumulation of sulphites in the human body can trigger multiple toxic effects at the cellular and systemic level, affecting mainly tissues with high mitochondrial activity and greater vulnerability to oxidative stress, such as the lungs, liver, brain, and gastrointestinal tract ^{5,68,69}. This toxicity largely results from the formation of reactive oxygen species (ROS) during the incomplete oxidation of sulphites, as well as their ability to interfere with cellular enzymes and lipid structures ^{50,70-72}.

Experimental studies demonstrate that sulphites (even at concentrations considered safe by regulatory authorities, can induce lipid peroxidation, DNA damage, cellular apoptosis, and mitochondrial dysfunction) effects exacerbated in the presence of deficiencies of Mo, selenium, or glutathione, essential nutrients for neutralising oxidative stress ^{73,74}.

Clinically, high or chronic exposure to sulphites has been associated with systemic manifestations, including:

- Recurrent headaches, persistent fatigue, and difficulty concentrating ⁵⁶.
- Respiratory symptoms, such as bronchospasm, dry cough, wheezing, and chest tightness, especially in asthmatics ⁵.
- Gastrointestinal changes, including nausea, cramps, diarrhoea, and reflux, attributed to irritation of the intestinal mucosa ⁵².
- Cutaneous manifestations, such as urticaria, pruritus, and rashes, often of a pseudo-allergic nature ^{57,66}.

- Systemic mitochondrial dysfunction, expressed as chronic fatigue, exercise intolerance, and cognitive changes ^{75,76}.

In the nervous system, recent evidence suggests that sulphites can interfere with glutamatergic neurotransmission and the activity of glial cells, promoting states of low-grade neurogenic inflammation, with possible implication in neurodegenerative diseases ^{77,78}. In animal models, sulphite exposure induced behavioural changes, neuronal loss, and dysfunction of the blood-brain barrier, effects attenuated after supplementation with Mo and antioxidants ^{79,80}.

It is important to note that sulphite toxicity depends not only on the dose ingested or inhaled but also on the individual's capacity for metabolism, modulated by factors such as genetic polymorphisms (e.g., mutations in the sulphite oxidase gene), liver status, intestinal microbiota composition, diet, and co-exposure to other xenobiotics ^{58,81-84}.

Thus, sulphite accumulation must be understood as a cumulative functional risk factor, whose clinical evaluation and management benefit from an integrative and personalised approach, in line with the principles of contemporary functional Naturopathy.

4.5. International Regulation (E220–E228)

Sulphites are internationally regulated as authorised food additives, classified under codes E220 to E228, which include compounds such as sulphur dioxide (E220), sodium, potassium, and calcium sulphites, metabisulphites, and hydrogen sulphites. These compounds are widely applied in the food and pharmaceutical industries due to their antioxidant, antimicrobial, and preservative properties, and are considered technologically indispensable in various products ⁵².

The European Food Safety Authority (EFSA) established, in 2021, an Acceptable Daily Intake (ADI) for sulphites of 0.7mg/kg of body weight per day (expressed as sulphur dioxide). This value was determined based on toxicological studies, clinical trials, and evidence of adverse effects in humans and animals ⁵². The dose was defined to be safe for the majority of the population, including children and adults who are regular consumers of processed foods.

However, population assessments have shown that certain groups can easily exceed the ADI, especially when ingesting several sulphite-rich foods on the same day, such as wine, dried fruits, and industrial sauces ⁸⁵⁻⁸⁷. Furthermore, individuals with reduced sulphite oxidase enzyme activity, including asthmatics, alcoholics, people with intestinal dysbiosis, or functional Mo deficiency, may manifest adverse reactions even with intakes lower than the dose considered safe ⁸⁸⁻⁹⁰.

In the United States, the Food and Drug Administration (FDA) requires mandatory labelling whenever the sulphite concentration exceeds 10ppm (parts per million). In the European Union, declaration is mandatory above 10mg/kg or 10mg/L, depending on the type of product ^{91,92}. Despite these measures, the majority of consumers remain poorly informed about their accumulated exposure to sulphites, especially when they regularly consume processed foods ⁹³⁻⁹⁵.

From a regulatory point of view, sulphites are considered safe in low doses. However, this assessment is based on population averages, not adequately contemplating individual vulnerabilities, such as genetic predisposition, states of chronic inflammation, and cumulative oxidative stress. Furthermore, the interaction with metabolic and environmental factors is not fully integrated into legal limits ⁹⁶⁻⁹⁹.

4.6. Naturopathic Perspective and Integrative Proposal

Sulphite toxicity does not depend exclusively on the ingested dose, but above all on the individual capacity for metabolism and elimination. In this framework, the concept of “sulphite intolerance” can be reinterpreted as an acquired or constitutional metabolic dysfunction, potentially reversible with adequate support for detoxification and redox balance ^{5,100}.

The accumulation of sulphites can be understood as an indirect biomarker of toxic overload, enzymatic cofactor deficiency, or hepato-mitochondrial dysfunction. These states are rarely detected in conventional laboratory tests, which contributes to their undervaluation in standard clinical settings ^{6,101,102}.

Key strategies proposed in this area include:

- Reduction of the exogenous sulphite load by eliminating or rotating industrialised foods and beverages containing additives E220, E228}, including wine, dried fruits, seafood, and commercial sauces ^{52,103,104}.
- Reinforcement of endogenous enzymatic capacity through Mo supplementation, with the goal of restoring sulphite oxidase activity, especially in individuals with chronic fatigue, recurrent headaches, or multiple hypersensitivities ^{31,36,79}.
- Mitochondrial and Antioxidant Support, using compounds such as glutathione, N-acetylcysteine (NAC), selenium, Coenzyme Q10 (CoQ10), and B vitamins, which mitigate the oxidative stress induced by sulphite accumulation ¹⁰⁵⁻¹⁰⁸.
- Correction of intestinal dysbiosis, as this can compromise the absorption of Mo, the biosynthesis of molybdopterin, and hepatic conjugation mechanisms, exacerbating the effects of sulphites even at moderate intake ^{31,109,110}.
- Individualised dietary planning, based on chrononutrition principles, anti-inflammatory strategies, and symptom monitoring after consuming sulphite-rich foods, particularly in individuals with low detoxification resilience ¹¹¹⁻¹¹⁴.

The monitoring of the clinical response should include symptom scales and complementary laboratory tests, such as urinary sulphite, plasma markers of oxidative stress, and reduced glutathione, as well as the evaluation of indirect signs, such as fatigue, abdominal distension, eczema, and alcohol intolerance ¹¹⁵⁻¹²⁰.

5. Sulphite Oxidase: The Molybdenum-Dependent Key Enzyme

5.1. Structure and Function

Sulphite Oxidase is the terminal enzyme in the catabolism of sulphurous amino acids in mammals, catalysing the oxidation of sulphite (SO_3^{2-}) to sulphate (SO_4^{2-}), an indispensable step to prevent the accumulation of toxic intermediates, such as cysteine, and to preserve cellular integrity ¹²¹⁻¹²⁴. In eukaryotic cells, it is located in the mitochondrial intermembrane space, where it executes the reaction $\text{SO}_3^{2-} + \text{H}_2\text{O} \rightarrow \text{SO}_4^{2-} + 2\text{H}^+ + 2\text{e}^-$ and transfers the released electrons to cytochrome *c*, coupling sulphite detoxification to the respiratory chain ⁷.

Structurally, sulphite oxidase is a homodimer; each monomer contains two catalytic centres: (i) an N-terminal heme- b_4 domain for electron transfer, and (ii) a C-terminal domain with Mo coordinated to the Mo cofactor inserted into molybdopterin, where sulphite oxidation occurs ^{7,125-127}. The intracatalytic electron flow proceeds from the Mo centre to the heme and then to exogenous cytochrome *c*, which re-oxidises the enzyme and delivers electrons to Complex IV, integrating it into energy metabolism ^{31,128,129}.

The maturation of sulphite oxidase is cofactor-dependent: import into the mitochondrion requires a bipartite signal sequence, and MoCo binding is necessary for retention in the intermembrane space; without MoCo, the processed protein may remain in the cytosol and not reach the functional state ¹³⁰⁻¹³³. Furthermore, heme insertion and dimerisation occur after MoCo integration, in a hierarchy that ensures correct folding and activity ¹³⁴.

The strict dependence on Mo stems from the fact that the metallic atom in MoCo alternates between oxidation states during the catalytic cycle, allowing the transfer of oxygen to the substrate and the subsequent sequential transfer of two electrons to the heme/cytochrome *c* ^{31,135}. In mammals, sulphite oxidase exhibits highest expression in the liver, kidney, and heart, reflecting the detoxification and metabolic demands of these tissues ^{7,136-138}.

Functional insufficiency of Mo (due to a failure in MoCo biosynthesis/binding) or defects in the sulphite oxidase gene reduce sulphite oxidase activity, favouring the accumulation of sulphite and S-sulphocysteine and the subsequent increase in oxidative stress and neuronal excitotoxicity^{35,36,139}.

5.2. Primary and Secondary Enzymatic Deficiency

Sulphite oxidase deficiency can occur in two distinct forms: primary (congenital), of genetic origin, and secondary (acquired), resulting from nutritional deficiencies, dysbiosis, metabolic diseases, or environmental intoxication. Both result in an inability to adequately convert sulphites to sulphates, leading to the accumulation of toxic compounds in the body^{104,115,140-143}.

Primary (Congenital) Deficiency

Congenital sulphite oxidase deficiency is an extremely rare autosomal recessive disease, resulting from mutations in the sulphite oxidase gene, located on chromosome 12, which codes for the functional subunit of the enzyme. In these cases, enzymatic activity is completely or almost completely absent from birth^{103,144}.

Clinically, this condition manifests with intractable neonatal seizures, developmental delay, hypotonia, progressive microcephaly, and liver dysfunction, often culminating in early death^{145,146}. Biochemical analysis reveals high levels of sulphites in the urine, low sulphate levels, and alterations in sulphurous amino acids, such as the accumulation of S-sulphocysteine^{51,103,147,148}.

Although there is no definitive cure, some cases with partial mutations may benefit from early supplementation with Mo and antioxidants, with modest but promising results in terms of neuroprotection and clinical stabilisation¹⁴⁹⁻¹⁵¹.

Secondary (Acquired) Deficiency

More prevalent, although often under-diagnosed, is the secondary functional sulphite oxidase deficiency, where the enzyme is present but its activity is compromised due to a lack of bioavailable Mo, alterations in molybdopterin biosynthesis, or interference with mitochondrial function¹⁵²⁻¹⁵⁵.

Key contributing factors to this dysfunction include:

- Dietary Mo deficiency, common in diets poor in legumes, whole grains, and vegetables⁴⁴.
- Intestinal dysbiosis and malabsorption syndromes, which reduce the bioavailability of trace minerals¹⁵⁶⁻¹⁵⁸.
- Excessive exposure to exogenous sulphites, which can saturate enzymatic capacity even when it is functionally active⁵.
- Partial genetic polymorphisms in the sulphite oxidase gene, associated with reduced activity in heterozygosity^{103,159}.

From a clinical perspective, this secondary form can manifest with diffuse neurological symptoms, chronic fatigue, chemical hypersensitivity, multiple food intolerances, gastrointestinal disturbances, and recurrent headaches. These cases are often not recognised as related to sulphite detoxification, being attributed to “functional syndromes” or “psychosomatic causes”^{58,160-164}.

5.3. Relationship with Oxidative Stress and Mitochondrial Dysfunction

Dysfunction or absence of sulphite oxidase leads to the accumulation of sulphite and S-sulphocysteine (SSC), a biochemical condition associated with elevated oxidative stress, disruption of bioenergetics, and accentuated tissue vulnerability in organs with high metabolic demand (brain, liver, lung)^{69,165,166}. In cellular and animal models, sulphite exposure promotes lipid peroxidation, DNA damage, and apoptosis, with reduced ATP production

and morphological changes in mitochondria (decreased cristae density, hyper-interconnected networks, and reduced motility) ¹⁶⁷⁻¹⁷¹.

At the molecular level, incomplete sulphite oxidation and secondary reactions with peroxide can generate sulphite radicals, amplifying oxidative injury; cytochrome *c* participates as an electron acceptor and, in the presence of peroxide, can catalyse the formation of additional reactive species ¹⁷²⁻¹⁷⁴. In parallel, reduced sulphur metabolites (e.g., H₂S, in contexts distinct from sulphites) inhibit Complex IV (cytochrome *c* oxidase), illustrating the susceptibility of the mitochondrial respiratory system to sulphur species and its redox regulation ^{175,176}.

In the nervous system, S-sulfocysteine acts as an agonist of the NMDA receptor, triggering Ca²⁺ influx, calpain activation, and excitotoxicity, a mechanism implicated in the neurodegeneration observed in MoCo/sulphite oxidase deficiency; pharmacological NMDA inhibition attenuates injury in animal models ¹⁷⁷. These pathways explain the early encephalopathy and neuronal loss described in isolated sulfite oxidase deficiency/MoCo deficiency ¹⁷⁸⁻¹⁸⁰.

In extra-neuronal tissues, sulphite accumulation depletes antioxidant systems (e.g., glutathione), promotes the inhibition of redox-sensitive enzymes, and can interfere with components of the respiratory chain, translating into low oxidative phosphorylation and bioenergetic capacity ^{1,181-183}. The intensity of toxicity depends on the total sulphite load and the individual metabolic capacity, modulated by genetics, Mo nutritional status, liver function, and concomitant xenobiotic exposure ¹⁸⁴⁻¹⁸⁷.

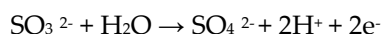
In humans, clinical series and reviews describe early seizures, progressive encephalopathy, movement disorders, and *ectopia lentis* in sulphite intoxication disorders (isolated sulfite oxidase deficiency/MoCo deficiency), with documentation of biomarkers (SSC, thiosulphate) and, in the case of MoCo deficiency, hypouricaemia/xanthinuria ^{178,188-191}. Experimental and observational reports also associate sulphite accumulation with mitochondrial dysfunction and neuroinflammation, reinforcing the central role of sulphite oxidase/MoCo in redox homeostasis ^{78,192,193}.

6. Biochemical Mechanisms of Sulphite Detoxification

The body primarily detoxifies sulphite SO₃²⁻, a potentially toxic compound, by oxidizing it to non-toxic sulphate SO₄²⁻, which is then excreted in the urine ^{68,194,195}.

6.1. Conversion to Sulphate (The Main Pathway)

Sulphite oxidase catalyses the oxidation of sulphite to sulphate, coupling this reaction to the cellular respiratory chain to produce ATP ^{141,196,197}.



Sulphite oxidase failure leads to sulphite accumulation and reduced ATP production, severely affecting high-energy demand tissues (e.g., brain), resulting in oxidative stress and neurotoxicity ^{198,199}. The resulting sulphate is mostly excreted, but some is recycled to form PAPS for hepatic sulphation reactions ²⁰⁰⁻²⁰².

Therefore, the efficiency of this process depends on:

- Mo availability.
- Mitochondrial integrity.
- Sulphite load.
- Antioxidants (e.g., Glutathione, Riboflavin).

6.2. Cofactors and Associated Reactions

Sulphite oxidase activity relies on a network of cofactors and antioxidant processes (Table 1).

Table 1. Cofactors and their role on sulphite detox.

Cofactor	Role in Sulphite Detoxification
Molybdenum (Mo)	Indispensable for forming MoCo, which is essential for sulphite oxidase function ³¹ .
Riboflavin (Vitamin B2)	Participates in regenerating cytochrome c and the mitochondrial respiratory chain; deficiency compromises electron transfer and energy function ²⁰³ .
Glutathione (GSH)	Neutralizes free radicals formed during sulphite oxidation; deficiency exacerbates associated oxidative stress ^{204,205} .
Selenium	Selenium Cofactor for GPx, which eliminates peroxides generated by general cellular metabolism and OS ^{206,207} .
Lipoic Acid, CoQ10, NADPH	Regenerate intracellular antioxidants, protect membranes, and provide essential reducing power for GSH recycling and sulphation ²⁰⁸⁻²¹¹ .

Substances like sulphonamides, paracetamol, anticonvulsants, and alcohol can interfere with sulphite oxidase or deplete antioxidants, promoting sulphite accumulation ²¹²⁻²¹⁵.

6.3. Integration with Sulphur Metabolism

Sulphite detoxification is functionally integrated with the Methionine Cycle and cellular antioxidant defense.

- **Methionine Cycle:** The transsulphuration pathway (converting homocysteine to cysteine, the GSH precursor) itself generates sulphite, which must be cleared by sulphite oxidase. Deficiencies in cofactors like Mo, B6, B12, or folate impair this cycle, raising both homocysteine and sulphite levels, which increases cardiovascular risk ²¹⁶⁻²¹⁸.
- **Glutathione:** Proper sulphite oxidase function *saves* GSH reserves. When sulphite oxidase is dysfunctional, excessive GSH consumption occurs to manage resultant ROS, leading to severe oxidative stress ²¹⁹⁻²²¹.
- **Lipid Peroxidation:** Accumulated sulphites generate ROS, initiating lipid peroxidation and producing harmful markers like MDA and 4-HNE ²²²⁻²²⁴.

The sulphite oxidase pathway must be understood as part of a complex biochemical network. Compromise in any link (e.g., cofactor deficiency, sulphite oxidase failure) can lead to systemic issues like fatigue, cognitive dysfunction, and chemical hypersensitivity.

7. Naturopathic Strategies for Supporting Sulphite Detoxification

The naturopathic approach prioritises dietary and metabolic optimisation to enhance sulphite detoxification, a process dependent on the activity of sulphite oxidase, for which Mo is the key cofactor.

A targeted nutrition plan aims to: (1) ensure sufficient Mo intake; (2) limit exogenous sulphites; and (3) reinforce hepatic, mitochondrial, and intestinal pathways that regulate sulphur metabolism ^{2,111}.

7.1. Functional Diet with Emphasis on Molybdenum

A functional dietary pattern for sulphite-sensitive individuals combines Mo-rich foods, reduction of sulphite-containing products, and support for detoxification and antioxidant systems.

7.2. Functional Eating and Detoxification Modulation

Cruciferous vegetables (broccoli, cauliflower, radish) supply indoles and isothiocyanates that balance Phase I cytochrome P450 activity and enhance Phase II sulphation and glutathione conjugation²²⁵⁻²²⁷. Foods providing methyl donors, such as spinach, beetroot, eggs, and liver, support the methionine cycle and glutathione synthesis^{228,229}. Avoiding ultra-processed foods containing sulphites (E220–E228) is essential, as cumulative exposure may overwhelm sulphite oxidase activity, while low-fibre, high-protein diets can increase colonic hydrogen sulphide and aggravate dysbiosis^{230,231}.

7.3. Microbiota and Antioxidant Support

Fermentable fibres from oats, flaxseed, artichoke, and apples promote short-chain fatty acids, improve mucosal integrity, and indirectly enhance sulphite clearance²³²⁻²³⁴. Regular intake of antioxidant-rich fruits (berries, pomegranate, citrus) and leafy vegetables augments endogenous defences against sulphite-induced oxidative stress²³⁵⁻²³⁷.

7.4. Molybdenum-Rich Foods

Legumes, whole grains, nuts, seeds, and organ meats provide 70–150 µg/100 g of Mo depending on soil composition²³⁸⁻²⁴⁰. Bioavailability is generally high but may be reduced by phytates, copper excess, or intestinal inflammation^{241,242}. Achieving the RDI of 45–70 µg/day is straightforward through consistent consumption of legumes and seeds^{243,244}.

7.5. Reduction of Exogenous Sulphites

Common dietary sources include dried fruits, wine, processed potatoes, sauces, and certain seafoods⁵². Although the ADI is 0.7 mg/kg/day, habitual wine or dried-fruit consumers can exceed this threshold. Sensitive individuals may react at much lower exposures, necessitating label vigilance and preference for minimally processed foods^{245,246}.

7.6. Liver and Intestinal Support

As sulphite oxidase operates in hepatic mitochondria, liver steatosis, inflammation, or medication overload can impair sulphite detoxification^{247,248}. Dysbiosis additionally increases luminal sulphite and hydrogen sulphide, exacerbating hepatic burden^{249,250}. Clinically, hepatoprotective botanicals (artichoke, milk thistle), fermented foods, and prebiotic fibres strengthen overall detoxification capacity^{251,252}.

7.7. Individualised Planning

Because sulphur metabolism varies considerably between individuals, personalised assessment, including dietary history, alcohol and drug exposure, intolerance symptoms, and where possible urinary sulphite or sulphite oxidase-related genetics, is recommended²⁵³. Intervention is typically structured into: an initial elimination phase, a stabilisation period with intensified Mo and cofactor intake, and a long-term maintenance plan emphasising microbiota stability and relapse prevention. However, no complementary and alternative medicine literature acknowledges high variability in protocols and lack of standardisation in detox practices²⁵⁴.

8. Final Remarks

The clinical use of Mo in the management of sulphite intolerance and related metabolic dysfunctions requires a comprehensive, individualised, and data-driven naturopathic approach. Functional testing provides essential insight into the narrow therapeutic window of this trace element and supports safe decision-making. Symptoms frequently overlooked in conventional care, such as recurrent headaches, asthma-like episodes, persistent fatigue, chemical sensitivity, or digestive irritability, should be integrated with dietary history, identification of exogenous sulphite exposure, and assessment of Mo-rich

food intake to detect potential subclinical deficits. Whenever indicated, laboratory markers including uric acid, urinary sulphates, antioxidant status, and genetic polymorphisms affecting the sulphite oxidase/MoCo pathway provide further precision in tailoring the intervention.

Dietary and lifestyle education remains central to long-term clinical success. Empowering patients to recognise hidden sources of sulphites and adopt anti-inflammatory, nutrient-dense eating patterns enhances metabolic resilience and reduces recurrent symptom burdens. Lifestyle strategies that support hepatic function, mitochondrial regeneration, microbiome balance, and autonomic regulation complement the nutritional intervention and reinforce the body's intrinsic detoxification systems.

Integrative supervision, incorporating periodic laboratory monitoring, is essential to ensure therapeutic effectiveness, prevent cumulative toxicity, and modulate dosing according to biochemical responses. Collaboration with conventional health professionals strengthens clinical safety, particularly in patients with genetic predispositions, comorbidities, or renal impairment. Within this interdisciplinary framework, naturopathy contributes unique value by identifying functional imbalances, addressing environmental and dietary determinants, and offering targeted support for individuals with subclinical sulphite intolerance, an area often insufficiently recognised in mainstream practice.

9. Conclusion

Mo plays a central role in sulphite detoxification, and functional insufficiency (often driven by low dietary intake, impaired absorption, inflammation, or genetic variants) can compromise sulphite oxidase activity even in the absence of overt deficiency. This imbalance contributes to symptoms such as headaches, respiratory reactivity, fatigue, and digestive irritability, which are frequently overlooked in conventional practice.

Given the widespread use of sulphite additives and the increasing metabolic burden associated with inflammation and xenobiotic exposure, supporting Mo-dependent pathways has growing relevance in Naturopathic care. Clinical integration requires careful assessment of dietary patterns, toxic load, intestinal health, and relevant biomarkers, ensuring safe and individualised use of supplementation.

Overall, Mo should be viewed as a key component of personalised detoxification strategies, complementing functional nutrition, antioxidant support, and lifestyle measures that collectively promote metabolic stability and symptom reduction.

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Review

Diagnosis in Paediatrics according to Traditional Chinese Medicine and its Application in the Therapeutic Approach and Treatments for Autism Spectrum Disorder.

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Abstract

Objective: To explore the theoretical foundations of Traditional Chinese Medicine (TCM) Paediatrics, analyse its specific diagnostic patterns, and review the application and potential of TCM therapeutic modalities as a complementary and integrative approach for Autism Spectrum Disorder (ASD).

Background: ASD is a complex neurodevelopmental disorder with heterogeneous manifestations. While Western medicine offers various symptomatic strategies, many families seek complementary alternatives. TCM adopts a holistic, individualised approach, interpreting ASD symptoms as manifestations of core energetic imbalances, such as deficiencies of Kidney *Jing*, Spleen *Qi*, and the presence of Phlegm Clouding the Heart.

Methods: This study employed a descriptive and exploratory literature review methodology, synthesising classical TCM paediatric concepts, including the "Five Delays" (*Wǔ Chí*) syndrome, with current preclinical and clinical research concerning the application of acupuncture, herbal medicine, cupping therapy, and *Tui Na* in the context of ASD.

Results: TCM diagnoses ASD based on patterns of energetic deficiency and stagnation. The "Five Delays" syndrome directly correlates with deficiencies in the Kidneys, Spleen, and Heart, which require specific therapeutic principles (e.g., Tonifying the Kidney *Jing*, Resolving Phlegm). On the other hand, TCM interventions demonstrate potential for modulating both behavioural and neurophysiological symptoms; Acupuncture showed efficacy in activating the hypothalamic oxytocinergic system, improving social deficits and emotional regulation. Herbal Medicine (e.g., Curcumin, *Acorus calamus*) showed neuroprotective potential in animal models, improving hippocampal neurogenesis and reducing autism-like behaviours. Moreover, *Tui Na* and Cupping were associated with improvements in sensory processing, sleep quality, and the reduction of maladaptive behaviours.

Conclusion: TCM offers a valuable, personalised, and holistic framework for the management of ASD, providing diagnostic tools and complementary therapeutic strategies that consider the child's energetic individuality. The integration of TCM with conventional Western care shows promise for enhancing therapeutic outcomes, supporting emotional stability, and improving the overall quality of life for children with ASD and their families. Further controlled clinical studies are necessary to validate the efficacy of specific TCM protocols and promote their adoption in interdisciplinary clinical settings.

Keywords: Traditional Chinese Medicine; Paediatrics; Autism Spectrum Disorder; Energetic Diagnosis; Complementary Therapies.

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1. Introduction

ASD is a neurodevelopmental disorder characterised by deficits in social communication and restricted, repetitive behaviours. According to the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) ¹, ASD presents a broad spectrum of manifestations, ranging from mild to more severe forms, significantly impacting the quality of life of individuals and their families.

The manifestation of ASD occurs early, with signs already observable in infancy. However, its evolution can be diverse, with different developmental patterns throughout life ²⁻⁴. Furthermore, ASD is frequently associated with other medical and psychiatric conditions, such as anxiety disorders, epilepsy, and motor difficulties ^{2,4-10}, which reinforces the need for integrative and personalised therapeutic approaches.

The aetiology of ASD is not yet fully elucidated; it is considered multifactorial, involving genetic predisposition and environmental factors ^{4,9}. Although Western medicine offers various therapeutic strategies to minimise the impact of symptoms, many patients and families seek complementary alternatives, such as TCM, to enhance the effects of conventional treatments.

TCM adopts a holistic view of health, considering the balance between *Yin*, *Yang*, and *Qi* as fundamental to the individual's well-being ¹¹⁻¹³. According to this approach, ASD may be related to energetic imbalances in specific organs and meridians, making it treatable through techniques such as acupuncture, cupping therapy, herbal medicine, and *Tui Na* massage ¹⁴⁻¹⁶.

Thus, this study aims to deepen the understanding of ASD from the perspective of TCM, exploring its possible therapeutic applications and its articulation with Western medicine. To this end, the theoretical foundations of TCM, its therapeutic principles, and the specific strategies used in the treatment of ASD will be presented. The challenges and potential of integrating TCM as a complementary approach in the context of conventional medical practice will also be discussed.

2. Diagnosis in Paediatrics according to TCM

According to Scott ¹⁷, the paediatric organism is still developing, with immature energetic systems and physiological functions. Although they function to meet the body's needs, it is fundamental to understand that a child is not a miniature adult, possessing their own unique physiological and pathological characteristics. The younger the child, the more immature their energetic system and the greater the difference compared to the adult organism.

From birth, the baby presents with a delicate physical constitution, a deficiency of Blood (*Xue*) and *Qi*, in addition to meridians and blood vessels still forming. Their *Shen* (Mind/Spirit) is unstable, their Defensive *Qi* (*Wei Qi*) is weak, and their Essential *Qi* (*Zheng Qi*) is not completely developed.

The *Yang* energy is insufficient, and the *Yin* energy is not fully produced. *Yang* is responsible for the functions of the *Zang-Fu* organs, while *Yin* participates in the formation of bodily elements, such as essence, blood, and organic fluids. This immaturity of both types of energy results in a material basis and energetic functions that are still fragile.

Still according to the author, the aetiology of childhood diseases is related to various factors, including climatic influences, toxicity, pathogenic agents, *tai du* (foetal toxicity), diet, and lifestyle. Children exhibit greater vulnerability to climatic changes due to the immaturity of their Defensive *Qi*, which makes them more susceptible to the effects of Cold, Heat, Wind, Dampness, and Dryness. Furthermore, exposure to medications, industrialised food, maternal toxins transmitted during gestation, and repressed emotions can overload the child's organism, manifesting as colic, reflux, or respiratory problems. A disorganised diet and inadequate consumption of milk can compromise the proper functioning of the digestive system. Additionally, the excessive use of electronic devices, combined with the absence of a balance between moments of study, play, and contact with nature, can have a negative impact on children's emotional health.

2.1. The Diagnosis

The diagnosis of children in Chinese Medicine follows the same pattern as adult diagnosis (observation, palpation, auscultation, olfaction, and interrogation), but with some adaptations¹⁷. The inspection of the face and the interrogation of the parents are the most important, while hearing (due to changes in the child's speech in unfamiliar environments) and palpation (due to the difficulty in examining the pulse) are less relevant. The assessment of the index finger vein, the tongue, and crying patterns are essential tools for identifying children's imbalances and determining the most appropriate treatment¹⁷⁻¹⁹.

Child diagnosis is, paradoxically, both more difficult and easier than that of adults. On one hand, it is more difficult due to the scarcity of signs and symptoms, the children's difficulty in adequately describing them, and the parents' eagerness for a quick cure; on the other hand, it is easier because childhood diseases are, in general, simpler¹⁷⁻¹⁹.

3. Autism Spectrum Disorder and Traditional Chinese Medicine – Diagnosis and Therapeutic Approaches

In the context of ASD, diagnosis and treatment according to TCM require a holistic approach centred on rebalancing the internal organs, with special attention to the Kidneys, Spleen, and Heart, and on correcting the deficiencies of *Qi* and *Xue*, which are fundamental for the child's harmonious growth and development^{17,19}.

3.1. Diagnosis of ASD - TCM

From the perspective of TCM, the origin of developmental delays in children, including manifestations associated with ASD, may be related to different patterns of energetic imbalance in the organism.

One of the frequently cited causes is Kidney *Jing* Deficiency (先天不足, "congenital deficiency"). This condition can result from hereditary factors or complications during gestation, compromising the basis of the child's vitality and development, as the *Jing* (Essence) stored in the Kidneys is considered fundamental for growth, maturation, and the proper functioning of the body and mind²⁰⁻²³.

Another relevant cause is the insufficient *Qi* and Blood of the Spleen. The Spleen, in TCM, plays a central role in the transformation and transportation of nutrients from food, converting them into energy (*Qi*) and Blood. When this function is debilitated, the child's physical and cognitive development can be affected, manifesting, for example, as fatigue, pallor, concentration difficulties, and learning delays²³.

Finally, the presence of Heat or Phlegm clouding the Heart is also considered a possible origin of developmental disorders. In this case, the accumulation of Phlegm (a pathological by-product) or the excess of Heat in the Heart organ can compromise the child's mental clarity, communication ability, and emotional expression, directly affecting speech and social interaction¹⁷.

The Five Delays and ASD

The Syndrome of the Five Delays (五迟, *Wǔ Chí*) is mentioned in the classical literature of TCM and is intimately related to child development. The first descriptions of this syndrome emerged in ancient TCM texts, including works attributed to Bian Que (扁鹊), a famous physician of the Zhou dynasty, and Zhang Zhongjing (张仲景), a renowned clinician of the Han dynasty, author of the *Shang Han Lun* (Treatise on Febrile Diseases)^{24,25}.

However, the clear and detailed systematisation of the Five Delays is generally attributed to the Jiangsu School of Medicine of the Qing dynasty, when clinical manifestations began to be organised more precisely. The syndrome is interpreted as a disorder that reflects delays in various areas of the child's physical and mental development, such as the emergence of teething, the onset of speech, motor development, among others. This approach is based on an understanding of the deficiency of *Jing* and *Qi*^{26,27}.

According to classical TCM texts²⁸, children with ASD present:

- Delay in hair growth (发迟, *Fā Chí*) – Indicates Kidney *Jīng* Deficiency, as the Kidney governs the bones and marrow, and is also related to hair growth.
- Delay in tooth growth (齿迟, *Chǐ Chí*) – Related to the weakness of the Kidney, which governs the bones and teeth.
- Delay in motor development (行迟, *Xíng Chí*) – Associated with the insufficiency of the Kidney and Liver, which influences the strength of the tendons and bones.
- Delay in language (语迟, *Yǔ Chí*) – Connected to the Heart and Spleen, as the Heart governs the mind (*Shen*) and speech, while the Spleen is responsible for the transport and transformation of nutrients necessary for brain development.
- Delay in mental development (立迟, *Lì Chí*) – Also related to the Heart and Kidney, since the Heart houses the *Shen* and the Kidney influences general growth and development.

3.2. TCM Therapeutic Approaches and Treatment in ASD

The approach to ASD by TCM is based on a careful reading of the internal imbalances that affect *Qi*, *Xue*, bodily fluids (*Jin Ye*), *Shen*, and *Jīng*. Although diagnosis and treatment are extensively covered by Western medicine, TCM classifies ASD as a unique clinical entity, interpreting its symptoms as manifestations of distinct energetic patterns, which may be at the root of the imbalances presented by those with the pathology^{5,28}. These must be identified, differentiated, and treated individually. This holistic view dates back to classical texts like the *Huang Di Nei Jing* (黄帝内经), which already emphasised that “all diseases must be treated according to their root” (治病求本, *zhì bìng Qiú běn*)²⁹.

In this approach, symptoms are not seen in isolation, but as manifestations of imbalances in the body's energetic systems, such as the Kidney, Spleen, Heart, and Liver. The understanding of these patterns allows for a more personalised intervention, respecting the particularities of each child.

Table 1 summarises the main energetic patterns observed in children with ASD and the clinical indications associated with each, according to the principles of TCM^{16,21,27,28}.

Table 1. ASD energetic patterns and clinical indications according to TCM

Energetic Pattern	Clinical Indications
Kidney <i>Jīng</i> Deficiency (肾精不足)	Delay in physical and mental development, delay in speech and teething
Spleen <i>Qi</i> and Blood Deficiency (脾气血虚)	Fatigue, apathy, lack of concentration, poor digestion, pallor
Phlegm Clouding the Heart (痰蒙心神)	Cognitive disorders, confusion, incoherent speech, repetitive behaviour
Heart Fire Disturbing the <i>Shen</i> (心火扰神)	Agitation, insomnia, anxiety, irritability
Heart and Kidney <i>Yin</i> Deficiency (心肾阴虚)	Insomnia, nocturnal restlessness, delayed speech, hyperactivity
Liver <i>Qi</i> Stagnation (肝气郁结)	Irritability, sudden anger, digestive disorders, emotional outbursts

Based on the observation of the main energetic patterns frequently identified in children with ASD, it is possible to establish a direct correspondence between the clinical indications and the therapeutic principles of TCM.

- Kidney *Jing* Deficiency (肾精不足), expressed in delays in physical and mental development, as well as in speech and teething, justifies the application of the therapeutic principle of Tonifying the Kidney *Jing* (补肾填精), with the goal of strengthening the foundation of physical and neurological development.
- Spleen *Qi* and Blood Deficiency (脾气血虚), associated with fatigue, apathy, concentration difficulties, and poor digestion, is addressed therapeutically by Strengthening the Spleen and Nourishing *Qi* and Blood (健脾益气养血), aiming to optimise vital energy, digestive function, and cognitive capacities.
- In cases where there is the presence of Phlegm Clouding the Heart (痰蒙心神), reflected in cognitive disturbances, incoherent speech, and repetitive behaviours, the treatment focuses on Resolving Phlegm and Opening the Sensory Orifices (化痰开窍), promoting greater mental clarity and verbal expression.
- When the condition is dominated by Heart Fire Disturbing the *Shen* (心火扰神), manifesting as agitation, insomnia, anxiety, and irritability, the principle of Clearing Pathological Heat (清热解毒) becomes essential, helping to calm the spirit and stabilise emotions.
- Heart and Kidney *Yin* Deficiency (心肾阴虚), often associated with nocturnal restlessness, insomnia, hyperactivity, and speech delays, is treated through the approach of Calming the *Shen* and Stabilising the Mind (安神定志), promoting rest and emotional balance.
- Finally, in cases of Liver *Qi* Stagnation (肝气郁结), which translates into irritability, sudden anger, digestive disorders, and emotional outbursts, the therapeutic strategy involves Regulating the Liver and Unblocking *Qi* (疏肝理气), with the aim of softening the mood and restoring harmonious energetic flow.

Having identified the main energetic imbalances present in children with ASD and the respective applicable therapeutic principles, it becomes pertinent to explore the different clinical approaches of TCM that operationalise these principles in practice, namely acupuncture, herbal medicine, *Tui Na*, and cupping therapy.

Acupuncture

Acupuncture, as a central therapeutic technique of TCM, has as its main objective to restore the harmonious circulation of *Qi* and balance the functions of the organs and viscera (*Zang-Fu*), promoting the child's physical, emotional, and mental well-being. This ancient practice is based on the stimulation of specific energetic points along the meridians, being used in a personalised manner according to the identified pattern of imbalance^{13,30}.

In the case of ASD, the condition can be interpreted by TCM in light of the so-called Syndrome of the Five Delays, characterised by disturbances in motor, cognitive, speech, and teething development. This condition is associated with energetic imbalances primarily involving the Spleen-Pancreas, Kidneys, Liver, and Heart organs, which are essential for the child's harmonious growth and development.

Since children have an energetically subtle and still developing body, the acupuncture approach must be especially careful. Traditionally, in a paediatric context, needles are only placed at up to three points per session, chosen judiciously, to avoid energetic overload and respect the child's sensitivity^{17,31,32}.

The benefits of acupuncture in intervention with children with ASD include reduction of agitation and nocturnal enuresis, improvement in sleep quality, increased tolerance to noise, as well as a decrease in repetitive speech and stereotypies. Furthermore, acupuncture, by promoting a state of greater tranquillity, can, in conjunction with medical monitoring, aid in the gradual reduction of psychiatric medication, when clinically appropriate³³⁻³⁵.

Recent research has highlighted the neurobiological mechanisms underlying the therapeutic effects of acupuncture in autism, namely the activation of the hypothalamic oxytocinergic system, which triggers the release of neurotransmitters such as oxytocin,

endocannabinoids, serotonin, and dopamine. Oxytocin has been particularly studied for its prosocial, anxiolytic, and stress-regulating role, demonstrating effectiveness in reducing the social deficits characteristic of ASD ³⁶⁻³⁸.

Studies in animal models also revealed that oxytocin enhances endocannabinoid-mediated social reward processes in the nucleus accumbens, this being a promising mechanism in the modulation of social behaviour. Serotonin and dopamine also participate in the reward response associated with oxytocin, reinforcing the positive impact of acupuncture on the core symptoms of autism ³⁶.

These findings support the relevance of acupuncture as a complementary intervention in ASD, with growing evidence that the combination of acupuncture with behavioural therapies presents better clinical results in the treatment of children with autism than isolated interventions ³⁹.

Herbal Medicine

Chinese herbal medicine, as a fundamental component of TCM, constitutes a complementary therapeutic approach that acts through the administration of herbal formulas with the goal of tonifying deficiencies, eliminating pathogenic factors, and restoring the body's internal balance ⁴⁰⁻⁴². In the intervention for ASD, herbal medicine offers continuous, individualised, and systematised support, capable of enhancing the effects of other therapeutic techniques and favouring the improvement of behavioural and neurophysiological symptoms ^{43,44}. Several substances of plant origin have been investigated in experimental models and clinical contexts, with emphasis on the following compounds:

Acorus calamus (石菖蒲 – *shí chāng pú*) The *Acorus calamus* plant, traditionally used in TCM for its action on the Heart and *Shen*, has shown neuroprotective potential. A study by Ukkirapandian *et al.* ⁴⁵ used Wistar rats with valproic acid-induced autism, administering *Acorus calamus* ethanolic extract (200 mg/kg) in the postnatal period. The results indicated protection of neuronal structures in the frontal cortex and Purkinje cells in the cerebellum, with a significant reduction in neuronal degeneration compared to control groups.

Curcumin (*Curcuma longa*) (姜黄 – *jiāng huáng*) *Curcuma longa*, known in TCM for its effect of mobilising *Qi* and Blood, has been widely studied for its antioxidant and anti-inflammatory effects. Bhandari *et al.* ⁴⁶ tested curcumin (50-200 mg/kg for 28 days) in a propionic acid-induced autism model. The results revealed a restoration of social behaviours, improvement in memory and mitochondrial function, reduction of oxidative stress, and modulation of inflammatory markers such as TNF-alpha and MMP-9. Complementary studies in VPA-induced models also observed improvements in hippocampal neurogenesis and behavioural structures associated with autism, reinforcing the therapeutic potential of curcumin in modulating neuronal development ^{47,48}.

Ginkgo biloba (银杏 – *yín xìng*) in association with risperidone has been included in integrative-based studies. A randomised, double-blind clinical trial conducted by the team of Hasanzadeh *et al.* ⁴⁹ evaluated the association of *Ginkgo biloba* (80–120 mg/day) with risperidone (1–3 mg/day) in children aged 4 to 12 diagnosed with ASD. After 10 weeks of treatment, no significant differences were found between the intervention group and the control group regarding the scores on the Aberrant Behavior Checklist – Community (ABC-C), nor in the occurrence of adverse effects. A subsequent systematic review reinforced the safety of using *Ginkgo biloba*, although without conclusive evidence regarding its additional clinical efficacy.

Cupping Therapy

Cupping therapy is a traditional Chinese Medicine technique that involves the application of cups (cupping glasses) to the skin, with the objective of mobilising stagnations of *Qi* and Blood, eliminating pathological Heat, and reinforcing *Zheng Qi*, promoting a general state of balance and well-being ⁵⁰⁻⁵².

In the context of ASD, cupping therapy has been explored as a complementary approach, especially for its regulating action on the autonomic nervous system and its potential calming effect. A recent study ⁵³ investigated the effects of this technique on aggressive behaviour and sleep quality in children diagnosed with ASD. Preliminary results indicated significant improvements in these areas after the application of cupping therapy, suggesting that the technique may constitute a promising therapeutic tool in supporting behavioural and emotional regulation in children with autism.

Tui Na

Tui Na, a form of therapeutic massage in TCM, uses specific manual manipulations to stimulate the meridians and energetic points of the body, with the goal of promoting the balance of *Qi* flow, regulating the function of internal organs, and favouring the child's neurological, emotional, and motor development ^{21,54,55}.

In the context of ASD, *Tui Na* massage has shown positive effects, especially when applied as a complementary therapy to conventional care. A recent study ⁵⁶, revealed statistically significant improvements in sensory processing, particularly in auditory filtering and tactile sensitivity.

Additionally, improvements in sleep disorders were observed, with a reduction in bedtime resistance and anxiety associated with falling asleep. The study also highlighted a sharp decrease in maladaptive behaviours, such as irritability and hyperactivity. These results remained stable during the three-month follow-up period, suggesting a prolonged effect of the intervention. It is important to note that no relevant adverse effects were recorded, reinforcing the safety and applicability of *Tui Na* in children with ASD.

4. Conclusions and Future Directions

The integration of TCM offers a valuable, personalised, and holistic paradigm for understanding and treating ASD, moving beyond symptomatic management to address the underlying constitutional and energetic imbalances of the child.

4.1. Core Diagnostic Value and Personalisation

The TCM diagnostic framework, particularly the lens of the "Five Delays", provides a unique and clinically relevant method for classifying ASD symptoms based on specific energetic deficits, most notably Kidney *Jing* Deficiency, Spleen *Qi*/Blood Insufficiency, and the presence of Phlegm Clouding the Heart.

This classification enables a highly individualised therapeutic strategy (e.g., Tonifying the Kidney *Jing* vs. Resolving Phlegm) that respects the heterogeneity of ASD, directly addressing the limitations of generalised Western approaches.

4.2. Evidence-Based Efficacy of Integrated Modalities

Preclinical and clinical findings support the therapeutic potential of TCM modalities, suggesting they can actively modulate the neurobiological and behavioral symptoms of ASD:

- Acupuncture: Evidence points to its mechanism in activating the hypothalamic oxytocinergic system, suggesting a direct path for reducing social deficits and improving emotional regulation. Its combination with behavioral therapies shows synergistic benefits.
- Herbal Medicine: Specific compounds like curcumin and *Acorus calamus* demonstrate potential in modulating neuronal development by improving hippocampal neurogenesis and protecting neuronal structures in preclinical models. This reinforces herbal medicine's role as continuous, systematised support to enhance conventional treatments.

- *Tui Na* and Cupping: These techniques offer safe, non-invasive means of regulating the nervous system, showing promise in improving sensory processing, sleep disorders, and reducing maladaptive behaviours (irritability, hyperactivity).

4.3. Implications for Integrative Care

This study confirms the feasibility and necessity of developing truly integrative care models where TCM is utilised as a complementary, evidence-informed therapeutic pillar alongside conventional Western medical and behavioural interventions.

- Shifting the Narrative: TCM offers a language that views ASD not just as a deficit, but as a state of developmental imbalance, that is potentially correctable, offering families an expanded therapeutic perspective and greater sense of agency.
- Bridging the Gap: Successful integration requires:
 1. Shared Training: Developing competencies in both TCM diagnostics and neurodevelopmental science among practitioners.
 2. Standardised Protocols: Creating evidence-based, adaptable protocols for TCM interventions (e.g., specific acupuncture points, *Tui Na* sequences, and herbal formulas) tied to specific ASD energetic patterns.

4.4. Future Research Priorities

To transition from promising data to established clinical practice, future research must focus on:

1. Controlled Clinical Trials: Conducting large-scale, randomised, placebo-controlled trials specifically designed to validate the efficacy of specific TCM interventions (e.g., individualised herbal formulas, specific acupuncture protocols) against placebo and conventional care, using standardised Western outcome measures (e.g., CARS, ABC-C).
2. Neurobiological Correlates: Further investigation into the neurological and biochemical mechanisms of TCM (e.g., fMRI studies during acupuncture, serum biomarker changes post-herbal treatment) to strengthen the scientific foundation supporting its impact on neurophysiological symptoms.
3. Long-term Safety and Efficacy: Studies tracking the long-term safety, sustained effects, and optimal frequency/duration of combined TCM and Western treatments in children with ASD.

In conclusion, TCM provides a powerful framework for personalised ASD care. By prioritising rigorous research and interdisciplinary professional training, the therapeutic potential of TCM can be fully realised, leading to more humanised, comprehensive, and effective interventions that profoundly improve the quality of life for children with ASD and their families.

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Review

Menopause and Traditional Chinese Medicine: Evidence, Syndromic Perspectives, and a Self-Care Protocol Proposal.

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Abstract

Background: Menopause is a physiological transition characterised by ovarian failure and hypoeutrogenism, leading to multisystemic symptoms that affect women's physical, psychological, and social well-being. Traditional Chinese Medicine (TCM) provides a holistic framework for understanding this period through concepts such as *Yin–Yang* imbalance, *Jing* (essence) depletion, and *Zang–Fu* disharmonies. While Western medicine emphasises hormonal therapy and lifestyle modification, TCM offers complementary strategies aimed at systemic energetic regulation.

Objective: To analyse menopausal care from the perspective of TCM, compare Eastern and Western therapeutic paradigms, identify predominant TCM syndromes, review available evidence on TCM interventions, and present a structured self-care protocol for climacteric women.

Methods: A narrative review of classical TCM theory, Western biomedical literature, and 14 experimental studies on acupuncture, *Qigong*, herbal medicine, auriculotherapy, moxibustion, and diet therapy. Additionally, a self-care protocol grounded in TCM theory was systematised based on established clinical principles.

Results: TCM conceptualises menopause as a decline in Kidney *Jing* and *Yin*, leading to disharmonies involving the Heart, Liver, Spleen, and key Extraordinary Meridians (*Chong*, *Ren*, *Du*). Reviewed studies showed that interventions such as *Qigong*, acupuncture (including ACE and laser), herbal formulas, and diet therapy significantly improved vasomotor symptoms, sleep, anxiety/depression, urogenital atrophy, metabolic parameters, and overall quality of life.

A TCM-based self-care protocol was developed, integrating several relevant exercises targeting the core climacteric disharmonies by reinforcing Kidney energy, nourishing *Yin*, regulating the Heart–Kidney axis, and restoring *Qi* (vital energy) flow, supporting symptom relief and self-management. **Conclusion:** TCM offers a comprehensive and personalised approach to menopausal care, with evidence indicating effectiveness across vasomotor, psychological, urogenital, and metabolic domains. The proposed self-care protocol provides an accessible, low-risk tool for women to actively regulate symptoms and maintain energetic balance. Future research should include larger, standardised clinical trials and long-term follow-ups to validate TCM interventions and support their integration into evidence-based, integrative menopausal healthcare.

Keywords: Menopause; Climacteric; Traditional Chinese Medicine; *Qigong*; Herbal Medicine; Integrative Medicine.

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1. Background

Menopause is a milestone in a woman's reproductive life and corresponds to a physiological stage following the spontaneous cessation of menstruation, characterised by approximately one year of absence of the menstrual period, during which the menstrual and ovulatory cycles cease. In other words, it marks the end of the female sexual phases, a period in which the definitive cessation of ovarian activity in the release of follicles occurs, and therefore, the female reproductive capacity ¹. According to Duarte ², this transition can be physiological or natural and will depend on the woman's individual natural biological process. This cessation commonly occurs around 51 years of age in European countries; however, age is not the only determining factor. There are others that can contribute to this process, such as genetic predisposition or lifestyle habits (tobacco consumption, diet, physical activity, or intense mental distress) ³.

In this female condition, there is reproductive gland failure, as a reduction in oestrogen production occurs, stimulating the development of symptoms that influence the biological, physiological, and psychological aspects of her life ⁴. Numerous authors cite these manifestations: amenorrhoea (absence of menstruation), vasomotor manifestations (hot flushes, sweating/diaphoresis, and headaches), depression, emotional, mood, and sleep changes, increased risk of myocardial infarction, vulvovaginal atrophy, urinary incontinence, recurrent urinary tract infections, changes in the elasticity, thickness, and resistance of the skin, increased risk of Alzheimer's and Cerebral Vascular Accident (CVA), concentration deficits and recent memory loss, reduced salivary flow, higher frequency of dental caries and tooth loss, weight gain, changes in the hairline, joint and bone pain, reduction in vaginal lubrication and libido. Psychological health is directly influenced, thus causing a strong impact on work, social, and conjugal life, and consequently, on her quality of life ⁴⁻⁸.

Menopause is not an isolated event, but a specific point within the climacteric, the transition period between the reproductive and non-reproductive phases. Its classification varies according to aetiology and chronology, including iatrogenic types (induced by medical interventions), early (<40 years), and late (>53 years). The phase preceding it is called perimenopause, characterised by menstrual irregularity and endocrine changes, while the postmenopause encompasses the entire subsequent period.

From a therapeutic perspective, epidemiology is crucial: the age of menopause onset correlates directly with specific health risks for women. Early menopause is associated with higher overall and cardiovascular mortality due to the premature deprivation of oestrogen's cardioprotective effects, demanding an approach focused on the prevention of osteomuscular and cardiometabolic comorbidities. Conversely, late menopause, with prolonged hormonal exposure, raises the risk of hormone-dependent neoplasms (e.g., breast, endometrium), requiring specialised action in post-surgical rehabilitation and the management of sequelae such as lymphoedema ^{2,9}.

Thus, therapeutic intervention should be initiated early, personalised, and based on the patient's individual risk profile, aiming to maintain functionality and quality of life throughout the entire climacteric spectrum. The care approach for these women must be personalised, involving the individualisation of clinical factors and biomarkers necessary to stratify risk, identifying the intervention that best suits each individual ¹⁰.

Ultimately, it involves active and supportive listening to emphasise the pursuit of well-being for women during the climacteric. To achieve this, it is necessary to understand the complexity of this phase and its impact on their lives. It is the responsibility of healthcare professionals to support them through the grief of losing the capacity to conceive, or the fear of the unknown that lies ahead. It represents an opportunity to rethink life and accept that changes are natural facts in human evolution. Therapeutic assistance encompasses various practices, both in the Western and Eastern contexts ¹¹.

Western Medicine employs both medicinal and non-medicinal therapies. The former primarily focuses on Hormone Replacement Therapy (HRT) and vitamin supplementa-

tion⁶ to treat menopausal symptoms. However, the non-medicinal approach includes nutritional guidance, advocating for a suitable diet combined with physical activity, and modification of habits, such as avoiding smoking and/or excessive alcohol consumption¹², stress management, and attention to interpersonal relationships¹³. In contrast, TCM offers complementary approaches such as acupuncture, herbal medicine, and changes in diet and lifestyle to rebalance the body's energy¹⁴.

In the East, health promotion also involves practicing breathing exercises, martial arts, or other therapeutic practices like *Yoga*, *Taijiquan*, *Qigong*, and meditation, which, besides enhancing physical fitness, contribute to the ascent of these women's mental and emotional balance¹¹.

This work was developed with the aim of verifying assistance in menopause through TCM, justified by the influence of menopause and the associated bodily and mental changes, which impair several contexts of the affected women's quality of life. The objectives of this research are: To conduct a literature review on menopause and its repercussions on the human body, to draw a parallel between the TCM and traditional perspectives, to differentiate existing treatments between Western and Eastern views of menopausal care, and to identify the main TCM treatment lines and their responses.

2. Menopause

Menopause is a biological process inherent to female ageing. The average life expectancy has increased in recent years, and consequently, mortality has decreased, a factor that contributes to the global ageing of the population, resulting in an increasingly large percentage of the female population being in the postmenopause phase. Currently, in general, women will live about one-third of their life in postmenopause¹⁵⁻¹⁷.

When referring to the term menopause, it is of utmost importance to respect the internationally pre-established definitions:

- Pre-menopause – encompasses the entire reproductive phase preceding Menopause¹⁸.
- Menopause – represents the date of the last menstruation, consequently, definitive ovarian failure. The clinical diagnosis is only confirmed retrospectively after 12 consecutive months of amenorrhoea, not resulting from another pathological or physiological cause.
- Perimenopause – includes the phase preceding menopause (the preamble of the endocrinological, biological, and clinical modifications of the proximity of menopause) and the first year after menopause¹⁸.
- Postmenopause – designates the period subsequent to the last menstruation^{18,19}.

The aetiology of menopause is neither consensual nor definitive, as it is a natural and inevitable biological process. In about 74% to 90% of cases, it is classified as idiopathic, being identified by a set of symptoms²⁰.

As of the present moment, there is no independent biological marker to determine this diagnosis, thus dispensing with the serial measurement of oestradiol or Follicle-Stimulating Hormone (FSH). The common age marker is between 45 and 55 years, mostly established genetically, but there are other attributes involved, such as external factors (lifestyle). Among these, smoking is the most notorious^{15,17}, as, in smoking women, menopause tends to occur two years earlier^{15,17,19}.

Besides smoking, there are other less explicit correlated factors: nulliparity, endometriosis, manifestation of autoimmune diseases, medication, surgical intervention, exposure to toxic chemicals, chemotherapy, pelvic radiation, epilepsy, and treatment for depression¹⁵.

There are also factors that can postpone the onset of menopause, such as obesity, multiparity, and alcoholism, being classified as late when its occurrence is evidenced after

53 years of age. Due to prolonged oestrogen exposure, increased attention is warranted for the risk of breast and endometrial cancer in these cases ^{15,21}.

Menopause is a natural process, but it can be artificially induced with the total and instant loss of hormonal production, as in cases of Iatrogenic Menopause, which is defined by the cessation of menstrual flow due to surgical intervention on the ovaries (with or without hysterectomy) or after iatrogenic ablation of ovarian function (chemotherapy or radiation) ¹⁸.

After characterising the different types of menopause, it is important to highlight that the progressive decline in ovarian function, associated with the inherent hormonal changes, is not limited to the reproductive scope. This process triggers a wide range of physiological and psychosocial repercussions that, in the short, medium, and long term, can compromise a woman's quality of life. The symptomatology is multisystemic, interfering with physical health, emotional balance, and the performance of daily activities, whether in the work, relational, or affective context ¹⁹.

The intensity, duration, and combination of symptoms vary significantly among women, reflecting a complex interaction between biological, psychological, social, and cultural factors. This heterogeneity shows that the clinical manifestations of menopause constitute an individualised phenomenon, whose understanding is essential for defining appropriate therapeutic strategies ².

2.1. Manifestations in the Short and Medium Term:

- The first changes include menstrual irregularities, such as changes in flow pattern and cycle duration, resulting from ovarian dysfunction and anovulation ²².
- Vasomotor symptoms (VMS), such as hot flushes and night sweats, are the most characteristic, affecting up to 75% of women, with pathophysiology related to the dysregulation of the hypothalamic thermoregulatory centre ²³.
- Sleep disturbances, such as insomnia and recurrent awakenings, are common and often associated with VMS ²⁴.
- Genitourinary Syndrome causes vaginal and urethral atrophy, dryness, urinary urgency, dyspareunia, and recurrent urinary tract infections ²⁵.
- Skin changes include skin thinning, loss of elasticity, hirsutism, and alopecia ²⁶.
- Psychological impacts, such as emotional lability, irritability, and depression, are frequent and multifactorial, intensified by physical symptoms and psychosocial factors ²⁷.

2.2. Clinical Manifestations in the Long Term

In the postmenopausal period, oestrogen deficiency triggers a series of physiopathological changes that substantially increase the risk of developing cardiovascular diseases and osteoporosis.

- The redistribution of body fat to the abdominal compartment promotes a state of chronic inflammation and thrombogenicity (capacity to induce blood clot formation), characterised by the elevation of inflammatory markers (TNF-alpha, IL-6, CRP) and reduced adiponectin levels, while the lipid profile becomes progressively atherogenic (capable of inducing/favouring the formation of fatty plaques that accumulate on artery walls), with increased low-density lipoproteins (LDL), triglycerides, and lipoprotein(a), and decreased cardioprotective subclasses of high-density lipoproteins (HDL) ²⁸.
- Endothelial dysfunction, resulting from reduced nitric oxide availability and increased oxidative stress, exacerbates arterial hypertension and insulin resistance, fundamental components of the metabolic syndrome, whose prevalence increases significantly during the menopausal transition ²⁹.
- The risk of cardiovascular events quadruples in the first decade after menopause, with arterial hypertension affecting approximately three-quarters of women in this

phase, often aggravated by greater sensitivity to sodium and hyperactivity of the Renin-Angiotensin-Aldosterone System (RAAS) (hormonal mechanism for regulating blood pressure and fluid and electrolyte balance in the body) ^{30,31}.

Concomitantly, oestrogen deficiency potentiates osteoclast activity, accelerating the rate of bone resorption and leading to an accelerated loss of Bone Mineral Density (BMD) of 2-3% per year during the first 3-4 years of postmenopause, subsequently stabilising to 1-1.5% per year ³². This process results in the deterioration of bone microarchitecture, increasing skeletal fragility and the risk of fragility fractures. Approximately 30% of women develop osteoporosis, with vertebral and hip fractures being particularly prevalent (the latter associated with a mortality of 5-20% in the first year after the fracture and permanent disability in 25% of cases) ³³. Bone loss is especially pronounced in Caucasian and Asian women, and the combination of low BMD with changes in dermal collagen composition may constitute an indirect marker of osteoporotic risk ³⁴.

The clinical manifestations of menopause, ranging from vasomotor symptoms and genitourinary changes to cardiometabolic and osteoarticular complications, reflect the complex pathophysiology of the climacteric. This transition period, marked by the progressive decline of ovarian function and the resulting state of hypoestrogenism, is not limited solely to the end of reproductive function ³⁵.

The climacteric involves not only hormonal changes but also transformations of a biological, psychological, and social nature, requiring an integrative approach that considers the interaction between endocrine, metabolic, emotional, and contextual factors ¹⁹. Understanding this phase as a continuous set of interconnected changes is essential for developing comprehensive therapeutic strategies that seek not only to alleviate symptoms but also to prevent long-term comorbidities and promote quality of life during this inevitable stage of female ageing.

2.3. The Climacteric and its Physiology

The climacteric constitutes the transition period between the reproductive and non-reproductive phases of a woman, characterised by the progressive decline of ovarian function and follicular exhaustion, resulting in sustained hypoestrogenism ³⁵. This phase encompasses a set of signs and symptoms, designated as the "climacteric syndrome", which include menstrual irregularities, vasomotor symptoms, mood swings, and sleep disturbances, among others, with a significant impact on the woman's biopsychosocial well-being. The climacteric is divided into three non-linear phases: pre-menopause, perimenopause, and postmenopause, with menopause (permanent cessation of menstruation, confirmed after 12 months of amenorrhoea) being its central event, occurring on average at 51 years of age ^{36,37}.

Physiologically, the process begins around 35-40 years of age with the accelerated depletion of ovarian follicles and hypothalamic-pituitary dysfunction ³⁸⁻⁴⁰. In perimenopause, the endocrine compensation by the elevation of FSH and LH levels attempts to maintain folliculogenesis, leading to anovulatory cycles, menstrual irregularities, and the appearance of symptoms such as hot flushes and sleep disturbances ^{41,42}. The Menopausal Transition (MT), as defined by the STRAW system, is divided into the early phase (>7 days variation in cycle duration) and the late phase (≥ 60 days amenorrhoea and/or $\text{FSH} \geq 40$ IU/L), culminating in menopause and subsequent entry into postmenopause, marked by permanent hypoestrogenism ^{36,43}.

Hormonal Characterisation

The endocrine changes of the climacteric result from the progressive depletion of the ovarian follicular reserve and the dysfunction of the remaining oocytes and granulosa cells. This dysfunction initially manifests as a decrease in Inhibin B (a glycoprotein hormone), produced by the ovarian granulosa cells, reducing the negative feedback on the pituitary gland and leading to the early elevation of FSH levels ^{37,44}. About six years before

menopause, the acceleration of follicular depletion intensifies the drop in Inhibin B and the elevation of FSH, triggering a compensatory follicular response with shortening of the follicular phase and transient maintenance of normal or elevated oestrogen levels – a state of transient hyperoestrogenaemia characteristic of the early phase of the menopausal transition^{36,43}.

The pronounced reduction in oestradiol production begins in the late phase of the menopausal transition, deepening up to one year after menopause and continuing gradually in subsequent years. The resulting hypoestrogenism is responsible for the typical climacteric symptomatology⁴⁵. In postmenopause, a state of hypergonadotrophic hypogonadism is established, with FSH levels 10-15 times higher and LH levels 3-5 times higher than in the reproductive period, associated with low oestradiol and undetectable Inhibin B³⁷. Oestrogen production then depends exclusively on the extragonadal aromatisation of androgens into oestrone⁴⁶.

In parallel, there is a 50% reduction in androstenedione levels and a 25% reduction in total testosterone, although ovarian secretion of testosterone persists due to the stimulation of the stroma by elevated LH. The decrease in Sex Hormone-Binding Globulin (SHBG) increases the bioavailability of testosterone, which may explain the development of hirsutism and virilising symptoms in some postmenopausal women⁴⁷.

3. Traditional Chinese Medicine and Western Medicine: A Parallel on Menopausal Care

Western Medicine approaches menopause as a biological milestone resulting from ovarian failure. This perspective emphasises the loss of fertility as the central axis, attributing a determining role to hormonal changes in clinical manifestations and a woman's quality of life^{35,48}.

In contrast, TCM interprets this transition as part of a natural movement of transformation of *Jing*, *Yin*, and *Yang*, in which the cessation of menstruation is not understood as a loss, but as a reorientation of *Qi* towards the cultivation of longevity, emotional balance, and spiritual strengthening^{49,50}.

A woman's vitality is understood by the fundamental principle of *Yin* and *Yang*, where *Yin* represents the feminine essence (receptivity, internalisation, and materiality) while *Yang* symbolises an active and transformative energy. The climacteric is interpreted as a period of accentuated *Yin* depletion, resulting in energetic disharmonies that manifest physically and psycho-emotionally. Symptoms such as hot flushes, night sweats, insomnia, and mucosal dryness are understood as direct expressions of this deficiency, while agitation, emotional instability, and the tendency towards depression reflect difficulties in finding a new axis of balance⁵¹.

These manifestations arise from specific disharmony patterns, involving fundamental Organs (*Zang*) according to the Theory of the Five Energetic Movements (*Wu Xing*).

- The Kidney (Water), the root of reproductive vital energy (*Jing*), is associated with hot flushes and menopausal symptoms when deficient.
- The Liver (Wood), responsible for storing blood and the free circulation of *Qi*, manifests through menstrual irregularities and mood changes.
- The Spleen-Pancreas (Earth), central to the formation of *Qi* and Blood, can lead to dysfunctional bleeding and fluid retention when compromised^{51,52}.

In addition to the Organs, TCM attributes a crucial role to the Extraordinary Meridians in integrating reproductive functions.

- The *Chong Mai* (Sea of Blood), associated with the Earth and Water elements, nourishes the uterus with *Xue* (Blood) and *Jing*.
- The *Ren Mai* (Vessel of Conception), linked to *Yin* and Water, regulates gestation.

- The *Du Mai* (Governing Vessel), related to *Yang* and Fire, sustains reproductive vital energy.
- The *Yin Qiao Mai* and *Yin Wei Mai* meridians, associated with Water and Earth, organise menstrual cycles and stabilise *Yin* energy⁵³.

The interaction between extraordinary meridians and associated Organs of the Five Elements is fundamental for understanding the aetiopathology of gynaecological disorders, as they function as energy reservoirs that connect reproductive functions to the body's natural cycles⁵³. The most common syndromic patterns in the climacteric – such as Kidney and Liver *Yin* Deficiency, Disharmony between Heart and Kidney, and Kidney and Spleen Yang Deficiency – require distinct therapeutic approaches to restore *Yin-Yang* balance and harmony between the Organs⁵⁴.

This holistic view, which integrates body, mind, and vital energy, contrasts with the biomedical approach focused on hormonal physiology, offering distinct possibilities for care and promotion of well-being for women in the non-reproductive phase.

3.1. Female Physiology

Female reproductive ageing is a continuous and programmed physiological process, characterised by the progressive decline of ovarian reserve. In TCM, this process is conceptualised in seven-year cycles, as described in the classic *Huang Di Nei Jing*. According to this perspective, menopause occurs around 49 years of age, an age at which the decline of the Ren Mai and Chong Mai meridians is observed, resulting in the cessation of menstruation and physical changes associated with ageing⁵⁵.

Curiously, this millenary prediction aligns with modern epidemiological observations indicating the mean ages of natural menopause around 51 years in Western populations^{56,57} and 50.7 years in Malaysian women⁵⁸, suggesting a universal and relatively constant biological basis for this developmental milestone.

From a pathophysiological point of view, menopause constitutes the clinical expression of ovarian follicular exhaustion. A woman has approximately 7 million primordial follicles during foetal life, a value that decreases to about 600,000 at birth, 300,000 at menarche, and only 10,000 at the transition to menopause⁵⁹. This gradual decline, which begins *in utero*, confirms the prolonged and inexorable nature of reproductive ageing.

This process is articulated with the concept of *Jing*, understood as an innate energetic-material substrate that governs growth, development, reproduction, and ageing. *Jing*, which notably expresses itself in follicular formation and maturation, is considered a finite, non-renewable resource. Its depletion is influenced by factors such as nutrition, sleep patterns, physical activity, stress, sexual behaviours, parity, and inter-gestational intervals⁵³. Thus, the preservation of *Jing* through healthy lifestyles since childhood is considered crucial for modulating the trajectory of reproductive ageing.

However, menopause is often medicalised and culturally stigmatised as a symbol of decline, generating anxiety and negative perceptions⁵¹. A more integrative approach, such as that proposed by Campiglia⁵¹, views this transition as a natural "eventide", a phase of transformation and potential renewal, whose experience varies significantly between individuals. Acceptance of this physiological transition, rather than its pathologisation, appears to be fundamental for promoting physical and psychological well-being during this period.

In summary, the study of female physiology benefits from an integrated view that combines the ancestral knowledge of TCM (with its intuitive description of life cycles and the importance of Essence) with the quantitative precision of modern biomedicine, which details follicular dynamics and the epidemiology of menopause. Recognising menopause as a natural and universal biological process and not as a disease allows for a more holistically informed and empowering approach to this fundamental phase of a woman's life.

3.2. The Domain of Yin

The *Yin* principle represents the material and structural basis of the organism, manifesting in body fluids, blood, organic matter, and temperature maintenance. In the context of female physiology, *Yin* prevails as the dominant force, conferring a denser and less active nature compared to masculine *Yang* energy. This *Yin* predominance explains the tendency towards recollection and lower tolerance to cold temperatures in the female sex⁶⁰.

The decline of *Yin* associated with reproductive ageing directly influences the symptomatology of the climacteric. As *Yin* diminishes, an energetic imbalance occurs that tends to manifest through a relative excess of *Yang*, making the woman more vulnerable to emotional fluctuations, irritability, and restlessness. This energy transition is mediated by the Uterus Meridian (Bao Mai), which establishes a functional connection between the Heart (Fire) and the Kidneys (Water). While Water governs the ancestral matrix (genetic heritage and phenotypic expression), Fire regulates the hormonal axes, particularly the hypothalamic-pituitary-ovarian axis^{61,62}.

As described in the Yellow Emperor's Classic, women reach a critical energy transformation at 49 years of age; the *Qi* undergoes transmutation without corresponding changes in *Xue*, a process that fundamentally depends on the Kidney energy⁶³. When this transition does not occur harmoniously, imbalances manifest through specific symptoms⁶⁴:

1. Heart (*Xin*) Changes: anxiety, irritability, insomnia, fatigue, depression, reduced libido, and impaired memory.
2. Kidney (*Shèn*) Changes: hot flushes, night sweats, palpitations, headaches, and dizziness.
3. Extraordinary Meridian Imbalances: dyspareunia, vulvar pruritus, irregular bleeding, fibroids, and dysfunctional uterine haemorrhages.
4. Liver (*Gan*) and Dai Mai Changes: pain and mammary dysplasia.
5. Spleen-Pancreas (*Pi*) and Liver (*Gan*) Deficiency: joint pain, muscle pain, and osteoporosis.
6. Compromised Tissue Nutrition: atrophy and cutaneous dryness.

The primary causes of these disharmonies include: (1) aggression to *Qi* and *Xue*, (2) depletion of the Essential *Jing*, and (3) chronic processes of energy degradation that affect the Kidney, Liver, Spleen-Pancreas, and Heart⁶⁰.

The fundamental therapeutic principle is based on strengthening the *Jin Ye* (body fluids), tonifying the *Jing*, and reinforcing Kidney energy, aiming to restore the balance between *Yin* and *Yang* during this natural physiological transition⁶².

3.3. Difference Existing Between Care Perspectives

In the context of the different care perspectives on the climacteric, contemporary Western medicine predominantly emphasises evidence-based interventions, while the Eastern perspective integrates traditional holistic approaches. As Duarte² highlights, this dichotomy reflects distinct paradigms for understanding the physiological transformations inherent to this phase of a woman's life.

Western Perspective

Physical Activity

The contemporary Western approach prioritises physical activity as a fundamental pillar for healthy ageing. Regular practice is proven to improve muscle elasticity, blood circulation, and joint mobility, constituting determining factors for the comprehensive health of women in the climacteric. Evidence indicates a reduction in polypharmacy, particularly in conditions such as Alzheimer's and osteoporosis, in addition to a significant improvement in functional capacity, flexibility, balance, and motor coordination⁶⁵.

Resistance exercise assumes special relevance in the preservation of muscle mass, counteracting the basal metabolic reduction and adipose accumulation characteristic of this phase. The pathophysiological mechanism involves the secretion of hypothalamic endorphins, with direct action on thermoregulation and the attenuation of vasomotor symptoms, in addition to musculoskeletal strengthening and improved respiratory capacity ^{1,66}.

Exercise plays a crucial role in modulating anthropometric and biochemical parameters, particularly in the conversion of body composition, lipid profile, and prevention of cardiometabolic comorbidities ⁶⁷⁻⁶⁹. Additionally, the mechanical stimulus of resistance exercise promotes an increase in Bone Mineral Density through greater calcium absorption post-exercise, counteracting the 2-3% annual bone loss post-menopause ³³.

Hormonal Therapy: Conventional and Bioidentical Approaches

Conventional Western medicine has conventional Hormone Replacement Therapy (HRT) as its main pharmacological intervention ^{70,71}. However, bioidentical HRT emerges as a promising alternative, using hormones molecularly identical to endogenous ones, potentially minimising adverse effects. This approach reflects a growing trend towards more naturalised therapies, although regulatory gaps and the need for greater scientific evidence persist ^{71,72}.

Research in bioidentical HRT remains in evolution, seeking to optimise formulations and administration routes within a personalised and multidisciplinary perspective ^{73,74}. This orientation converges with the Eastern view by considering individual needs, albeit through Western scientific paradigms.

While the Western approach focuses on specific evidence-based interventions, the traditional Eastern perspective prioritises energy modulation and global organism balance ². Both perspectives, however, recognise the importance of non-pharmacological interventions, particularly physical activity, as a fundamental element in climacteric management.

The convergence between these perspectives suggests the emergence of an integrative model, where Western scientific precision dialogues with the Eastern holistic view, potentialising more comprehensive and personalised care strategies for women's health during the climacteric.

Eastern Perspective

Studies on TCM Treatments for Menopause

Our article searches on digital platforms provided 14 papers that were grouped in Table 1, allowing for a global analysis of the types of TCM approaches to menopause and the responses to symptoms.

Reference	Design	Sample Size	Method	Outcomes
⁷⁵	Randomised controlled	49 women	<i>Qigong</i>	Significantly improved genital self-image and sexual function.
⁷⁶	Randomised	125 women	<i>Qigong</i>	Significant reduction in symptoms and improvement in health-related quality of life (HRQoL) in Spanish postmenopausal women.
⁷⁷	Randomised	125 women	<i>Qigong</i>	Significant improvement in somatic, psychological, and urogenital levels, in the total MRS scores. Also showed improvements in general health, physical fitness, vitality, and mental health according to the SF-36.

78	Randomised	82 women	Acupuncture combined with <i>Ningshen</i>	The combined intervention showed improvements in clinical symptoms and sleep quality. Reduced recurrence rate and proved safer compared to conventional treatment.
79	Randomised	70 women	Auriculotherapy combined with moxibustion	The combination of therapies proved effective in improving sleep quality, anxiety, and depression in perimenopausal women with insomnia.
80	Randomised controlled	82 women	ACE Acupuncture	There was an improvement in the intestinal microbiota with increased adiponectin, resulting in weight loss.
81	Randomised controlled	30 women	Laser Acupuncture, Diet Therapy	There was a significant improvement in metabolic syndrome parameters compared to diet therapy alone.
82	Prospective, randomised, controlled, crossover without washout	32 women	Systemic and Auricular Acupuncture, Meditation (Collective + Guided Individual), Diet Therapy	- Hot Flushes (HFRDIS): Significant improvement of 56.9% ($p<0.001$). - Quality of Life (MRS): Improvement of 39.9%, but without statistical significance ($p=0.057$). - Quality of Life (WHQ): Improvement of 14.3%, no significance. - Behaviour Profile: High adherence to acupuncture (83.9%) and collective meditation (80%); reasonable adherence to diet (57.3%) and individual meditation (56.9%).
83	Randomised, double-blind, placebo-controlled	60 women	Herbal Medicine (M. Officinalis L.)	M. Officinalis L. contributes to a significant improvement across all domains of quality of life (MENQOL).
84	Randomised controlled	96 women	ACE Acupuncture	Significant reduction in body measurements, abdominal fat, appetite, and inflammation. Improvement in glucose and lipid metabolism.
85	Randomised controlled	13 women	Herbal Medicine – Tianwang Buxin Granule (TWBXG) formula	Significantly reduced PSQI scores.
86	Randomised controlled	60 women	Fire Needle combined with moxibustion	Significantly improved tear secretion, prolonged BUT. Reduced dry eye symptoms and improved systemic symptoms.
87	Cross-sectional	4595 women	Diet Therapy	Daily consumption rich in soy reduces menopausal symptoms in women in Shanghai.
88	Randomised, controlled, double-blind	70 women	Acupuncture	Improvement in sleep and comorbid depression in the short and medium term.

Table 1. Information and characteristics of TCM treatment studies for menopause

The compiled results indicate a consistent and positive effect of various TCM techniques on a wide spectrum of menopausal symptoms. Mind-body interventions, such as *Qigong*, proved particularly effective.

In the scope of instrumental therapies, acupuncture and its variations – including ACE acupuncture and laser, revealed themselves to be versatile in the management of specific comorbidities. Studies by Cai *et al.* ⁷⁸, Feng *et al.* ⁷⁹, and Zhao *et al.* ⁸⁸ demonstrated

that acupuncture, alone or combined with herbal medicine (*Ningshen*) or moxibustion, is effective in reducing sleep disturbances, anxiety, and depression.

Also notable is the evidence of its action on metabolic changes: research by Jin *et al.*⁸⁰, Kamal *et al.*⁸¹, and Yan *et al.*⁸⁴ suggests that acupuncture can induce weight loss, reduce abdominal fat, improve glucose and lipid metabolism, in addition to modulating the intestinal microbiota and inflammation, suggesting an effect that goes beyond symptomatic relief and acts on the pathophysiology of postmenopausal metabolic syndrome.

Despite the promising results, critical analysis highlights important limitations. Methodological heterogeneity is striking, with variations in designs, often small sample sizes (e.g., Yang *et al.*⁸⁵, n=13), and diverse intervention protocols, making it difficult to conduct robust meta-analyses and generalise the results. Comparison between studies is further hindered by the use of different outcome scales (MRS, SF-36, MENQOL, PSQI). Furthermore, most research lacks long-term follow-up, leaving the sustainability of the observed benefits uncertain. Thus, the results must be interpreted with caution, and new standardised and comprehensive clinical trials are essential to consolidate TCM as an evidence-based option.

In summary, the body of reviewed evidence reinforces the premise that TCM offers a multifaceted therapeutic arsenal for the comprehensive care of women during the climacteric. Interventions such as Qigong, acupuncture, herbal medicine, and diet therapy have demonstrated effectiveness in improving vasomotor, psychological, urogenital, and metabolic symptoms, in addition to favouring overall quality of life. The diversity of approaches enables personalised medicine, tailored to the needs of each patient. Future studies with larger samples, prolonged follow-up, and cost-effectiveness analyses are needed to consolidate these practices in clinical guidelines and expand access to a more humanised and holistic approach to menopausal care.

A Focus on Qigong

Qigong, a practice dating back thousands of years and integrated into TCM, represents an Eastern care paradigm focused on health promotion and disease prevention through energetic self-management. Its primary goal is to potentiate, direct, and mobilise *Qi* of the body through gentle, concise, and sequenced movements. This practice synthesises meditation, postural control, breathing techniques, and body movements, aiming at optimising physical health, treating specific pathologies based on prior diagnosis, and promoting a harmonious connection between mind and body^{89,90}.

This care perspective, which emphasises continuous care and self-regulation, is common in community spaces such as parks and gyms, estimated to be practised by over 70 million people in China^{91,92}. From an Eastern physiological standpoint, *Qigong* operates through a vegetative feedback model, unifying the autonomic nervous system and increasing the body's capacity for self-regulation⁹³. This structure is based on three essential pillars: *Qi*, *Shen* (which correlates the mental with the emotional, essential for concentration and focus), and *Jing* (which interconnects with cellular functional capacity and cellular nucleus functions)^{94,95}.

There are two main modalities of *Qigong*: internal and external. Internal *Qigong*, fostered as an autonomous practice, promotes balance and reduces energetic blockages by increasing the flow of *Qi* throughout the body. It is fundamental for health prophylaxis, improving the immune system, regeneration processes, longevity, and spiritual development, demonstrating benefits in terms of physical and emotional well-being⁹⁶. In turn, External *Qigong* constitutes an energetic treatment performed by qualified therapists, following an individualised assessment and diagnosis⁹⁶.

Scientific evidence corroborates the mechanisms underlying these benefits. Studies show that the practice promotes an increase in the flow of *Qi* in the meridians, awakening the perception of energetic flow and sensations of numbness along them. Matos *et al.*⁹² attested to these changes at the capillary level through thermography, finding a significant increase in peripheral microcirculation.

Consequently, the physiological, emotional, and energetic benefits of *Qigong* are vast, including the reduction of blood pressure, depression, and anxiety, and an improvement in balance and lower limb strength^{89,97-99}.

Given this framework, it is essential to adopt a preventive and care perspective, resorting to the regular practice of *Qigong* at the beginning of perimenopause. As Davis⁹⁶ argues, this practice is crucial for delaying hormonal decline, maintaining vitality, and sustaining a balanced emotional state during this transition. The practice should incorporate four fundamental components: gentle movement, strengthening postures, self-healing massage, and meditation. The focus resides in harmonising the body and mind, nourishing the *Yin* and the flow of *Qi*, thus offering a holistic approach to alleviating the myriad of symptoms that characterise this phase of a woman's life.

Self-care Protocol

The protocol begins with a series of light dynamic stretches, aimed at warming up the joints of the cervical region, shoulders, wrists, knees, and ankles.

Subsequently, a basic *Qigong* posture is adopted for the execution of a deep abdominal breathing exercise, called Dantian Breathing. The purpose of this technique is to establish a conscious connection and promote the accumulation of *Qi* in the Lower Dantian region, located approximately three fingers below the navel (Figure 1).

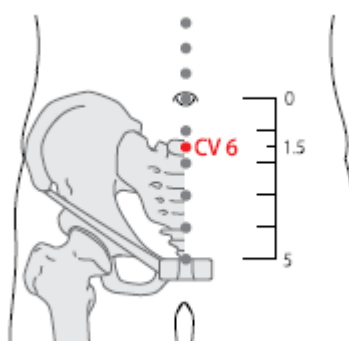


Figure 1. Dantian region location (Qihai)¹⁰⁰.

Execution:

1. In the basic posture, a mental connection is established with the aforementioned region.
2. The hands are positioned over the lower abdomen (hypogastrium), with the right hand in direct contact with the body and the left hand superimposed on the right.
3. The tip of the tongue is kept in contact with the upper palate (a posture known as "connecting the Du and Ren meridians") and the feet are firmly in contact with the ground ("rooting").
4. The respiratory cycle is performed deeply and diaphragmatically, coordinated with a gentle contraction of the perineal muscle during the exhalation phase.

Dynamic Exercise – Sipping the Essence of the Bubbling Spring

The main objective of this protocol is to tonify the Kidney energy (including the adrenal glands) and promote hormonal and body fluid regulation, mitigating fatigue. The practice is based on the stimulation of the KID-1 (*Yongquan* – "Bubbling Spring" – Figure 2) acupuncture point, located on the sole of the foot, to absorb Earth *Yin* energy.

Execution:

1. Starting Position: Adopt an erect posture with the feet approximately 90 cm (3 feet) apart and a moderate flexion of the knees.

2. Hand Placement: Position the back of the hands on the lumbar region, over the anatomical area of the kidneys.
3. Preparation and Connection: Perform a few cycles of deep inhalation and exhalation to establish a state of presence. Concentrate on visualising the KID-1 (*Yongquan*) point on both feet, conceptualising it as the portal of entry for telluric (*Yin*) energy into the organism.
4. Respiratory Cycle and Visualisation:
 - Inhalation: Visualise the Earth energy ascending from the feet, through the lower limbs and pelvis, to be stored and nourish the renal and adrenal region.
 - Exhalation: Execute a deep flexion of the knees (squat), keeping the vertebral column relatively straight (simulating sitting in a chair). Avoid lumbar hyperlordosis to prevent vertebral compression and gluteal protrusion.
5. Dynamic Movement:
 - Inhalation: Slowly return to the erect position, conceptualising the ascent of telluric energy to the renal region, under the hands. Applying gentle pressure with the back of the hands against the back can facilitate the sensation of support and energy concentration.
6. Repetitions and Auxiliary Technique: Execute the squat and lift cycle between 9 and 18 times, coordinating exhalation with the descent and inhalation with the ascent. During the inspiratory phase, gently contract the anal sphincter (perineal lift) to concentrate and retain the *Qi* in the renal region, preventing its dissipation.

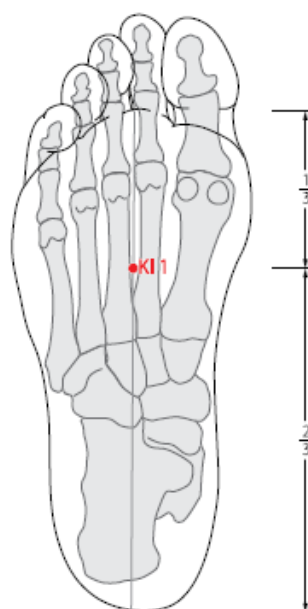


Figure 2. Kidney point number one location ¹⁰⁰.

Ovary Bridge Massage

This procedure aims to promote the nourishment of the ovaries, relieve congestion in the reproductive organs and associated energy meridians, and aid in the modulation of the hormonal decline characteristic of the climacteric.

Execution:

1. Position yourself in the supine position (on your back) with the soles of the feet in contact (adapted Baddha Konasana position).
2. Elevate the pelvis, transferring the body's weight to the upper dorsal region and the lateral faces of the feet, maintaining support.

3. Isometrically and gently contract the gluteal and pelvic floor musculature.
4. Position the palms of the hands in the lower abdominal quadrant, immediately superior to the inguinal folds.
5. Execute circular massage movements with the palms of the hands, performing approximately sixteen rotations, or until a sensation of warmth is perceived in the abdominal region.
6. Lower the pelvis in a controlled manner and conclude the protocol with a few cycles of deep breathing to promote relaxation.

Frequency Indication: For obtaining benefits, daily practice is recommended, or a minimum of three times a week.

Scalp Massage

This procedure aims to stimulate the points of the Governing Meridian (Du Mai) located on the scalp, with the intention of dissipating tension and promoting the release of negative charge, through a combined technique of massage and conscious breathing.

Execution:

1. Using the fingers, execute a massage technique similar to combing, applying gentle and uniform pressure throughout the scalp, with emphasis on the midline (the path of the Du Mai).
2. During the practice, adopt a state of mental concentration (visualisation) with the aim of dissipating accumulated tension.
3. Synchronise the ritual with a specific respiratory pattern: inhale, directing the intention and the sensation of energy flow towards the vertex (top) of the head; exhale, directing the sensation of release in a caudal direction, towards the cervical region (neck).
4. The cycle of massage and breathing should be repeated sequentially for twelve times.

Scalp massage acts as an effective somatosensory intervention in the improvement of insomnia. The mechanism is based on two main pillars: mechanical stimulation and neurophysiological modulation. The rhythmic pressure of the fingers promotes local vasodilation, increasing blood perfusion and reducing the muscle tone of the epicranial musculature, which is often tense in states of hyperarousal associated with insomnia. Simultaneously, the technique aims to activate the parasympathetic system, through synchronisation with deep diaphragmatic breathing, decreasing the activity of the Hypothalamic-Pituitary-Adrenal (HPA) axis. This modulation promotes a state of psychophysiological relaxation, facilitating the transition to sleep by lowering cortisol levels and regulating circadian rhythms. The visualisation component further aids in interrupting the flow of ruminating thoughts, a common perpetuating factor of insomnia.

Foot Massage

The procedure consists of performing acupressure on the *Yongquan* point. The stimulation of this point promotes the descent of excessive *Yang* and the afflux of *Qi* to the lower region of the body, which facilitates the state of relaxation necessary for the onset of sleep.

Additionally, the physiological relationship between the Kidney and Heart systems is explored. By supporting the Kidney, the Heart is calmed, modulating mental activity and promoting the balance between Water (Kidney) and Fire (Heart), which is fundamental for effective rest.

Heart Healing Sound

The nocturnal practice of the Six Healing Sounds, with emphasis on the Heart sound "Huuh", aims to facilitate the release of accumulated tensions and promote emotional homeostasis, preparing the organism for restful sleep. Its execution acts upon the functional sphere of the Heart (*Shen*), being indicated for disorders of anxiety, insomnia, mental agitation, and stress.

Execution:

1. In the Basic *Qigong* Posture, start with the hands positioned on the lower abdomen, palms facing upwards.
2. Inhalation: Maintain stillness.
3. Exhalation: Lift the hands to the height of the heart, keeping the arms in an oval shape.
4. Rotate the palms outwards, moving them away until they are near the temples (thumbs close to the temporal points), with the gaze directed upwards.
5. Rotate the palms inwards, directing them towards the eyes (a few centimetres away), conceptualising the projection of calming *Qi*. Close the eyes briefly to potentiate relaxation.
6. Lower the hands back to the height of the heart, reopening the eyes and maintaining a distance of one fist from the torso.
7. Inhalation: Rotate the palms downwards, with the fingers almost touching, and gently push the hands towards the abdomen, concluding the cycle.

The complete sequence should be repeated six times, after which a period of rest in *Dantian* breathing is recommended to integrate the effects. The emission of the guttural sound "huuh" (phonetics similar to "hook" without the final consonant closure) should be vibratory, felt in the throat, to maximise resonance and the regulating effect on the cardiac system.

5. Final remarks

The analysis undertaken successfully achieved the objectives of this work, evidencing the significant potential of TCM in the care and management of women during the menopausal period.

The structured review of 14 experimental studies demonstrated that a multifaceted TCM therapeutic arsenal, including Acupuncture, *Qigong*, Herbal Medicine, and Diet Therapy, offers clinically significant efficacy in addressing the core symptoms that compromise quality of life. Specifically, TCM interventions were shown to be effective in managing vasomotor symptoms (hot flushes), psychological changes (insomnia, anxiety, depression), urogenital atrophy, and, crucially, modulating cardiometabolic risk factors (weight, lipid, and glucose metabolism) associated with postmenopausal hypoestrogenism.

3.4. TCM vs. Conventional Care: A Paradigm Shift

The comparison between Eastern (TCM) and Western conventional care perspectives revealed a key point of convergence in the recognition of non-pharmacological interventions (such as physical activity/*Qigong*) as fundamental to climacteric health. However, TCM distinguishes itself through its holistic, personalised, and syndromic approach. While Western Medicine focuses on hormone replacement to address ovarian failure, TCM targets the systemic re-equilibration of *Yin-Yang* and the preservation of *Jing*, offering a strategy that is adaptable to the unique manifestation of symptoms in each patient (e.g., Kidney *Yin* Deficiency vs. Spleen/Kidney *Yang* Deficiency).

3.5. Future Directions and Clinical Integration

This study confirms the viability of TCM as a valuable complementary or alternative resource to the conventional medical model. To fully integrate these practices into mainstream clinical guidelines, future research must overcome the observed methodological limitations. Standardised clinical trials with larger sample sizes, long-term follow-up, and comprehensive analyses of cost-effectiveness are essential.

Ultimately, embracing an integrative model of care combining the quantitative precision of modern Western diagnostics with the time-tested principles of TCM's energy and essence regulation is paramount to promoting a humanised, personalised, and sustainable quality of life for women throughout the entire climacteric spectrum.

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Review

Efficacy and Feasibility of Acupuncture-Related Treatments for Anxiety and Depression in Hashimoto Thyroiditis: A Review.

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Abstract

Objective: To review the efficacy of acupuncture-related therapies in ameliorating mood disturbances, specifically depression and anxiety, associated with Hashimoto's Thyroiditis (HT).

Methods: A comprehensive electronic search was conducted across databases including PubMed, Cochrane Library, and Wan Fang to identify randomised controlled trials (RCTs) investigating acupuncture-related therapy for depression and anxiety in HT patients. The search timeframe extended from the database inception until September 2025.

Results: A total of 8 papers met the inclusion criteria. The overall findings suggest that acupuncture-related therapy may contribute to the improvement of patients' mental disorder symptoms, such as depression and anxiety. This improvement appears to be dependent on the specific technique and acupuncture meridians and points employed. However, only one study reported significant changes in Hospital Anxiety and Depression Scale Anxiety subscale (HADS-A) and Hospital Anxiety and Depression Scale Depression subscale (HADS-D) scores, focusing specifically on HT patients presenting with a Traditional Chinese Medicine (TCM) pattern of liver-qi stagnation. Other included studies reported no statistically significant changes in overall HADS scores. From the TCM perspective, liver-qi stagnation is posited to impair spleen and kidney function, contributing to mood disorders and depression. Regarding therapeutic efficiency, the aforementioned study documented statistically significant increases in the Role Emotional (RE) and Mental Health (MH) components of the SF-36 quality of life assessment ($P < 0.01$, $P < 0.001$). Furthermore, both TCM symptom scores and HADS-A scores were significantly reduced following treatment in both the treatment and control groups ($P < 0.001$, $P < 0.01$). Conversely, in the control group, these scores were observed to increase after the intervention ($P < 0.05$, $P < 0.01$, $P < 0.001$). Crucially, all reviewed papers, with a single exception, indicated a superior improvement in serum Thyroid Peroxidase Antibody (TPO-Ab) levels in the acupuncture-related therapy group compared to the Western medicine administration group.

Conclusion: Acupuncture-related therapy demonstrates potential benefit in mitigating mood disorder symptoms, such as depression and anxiety, in patients with Hashimoto's thyroiditis. Nevertheless, the robustness of these conclusions requires further validation, constrained by the current limitations in the availability of high quality, large-scale clinical studies specifically addressing depression and anxiety in HT patients.

Keywords: Hashimoto Thyroiditis; Acupuncture; Depression; Anxiety; Mood; Thyroid Antibodies.

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1. Background

HT represents the most prevalent autoimmune thyroid disease, with a global prevalence of 7.5% and a notably increasing rate of approximately 7.8% in Europe¹. The condition exhibits a marked sex disparity, with a higher prevalence in women (17.5%) compared to men (6.0%)².

First described by Japanese scientist Hakaru Hashimoto in 1912³, HT is also termed⁴. It is characterised by the immune-mediated destruction of the thyroid gland, leading to insufficient production of thyroid hormones and subsequent hypothyroidism. Common clinical manifestations include cold intolerance, dry skin, periorbital puffiness, constipation, weight gain, bradycardia, potential goitre development, musculoskeletal pain, and fatigue. Critically, patients frequently experience concomitant psychiatric comorbidities, including mood swings, cognitive impairment ("brain fog"), depression, and anxiety⁴⁻⁶.

An established association exists between Autoimmune Thyroiditis and mood disorders. Meta-analytical findings indicate that patients with HT exhibit significantly higher scores on standardised depression instruments, with a pooled odds ratio (OR) of 3.56 (95% CI, 2.14-5.94; $I^2 = 92.1\%$). For anxiety disorders, the pooled OR was 2.32 (95% CI, 1.40-3.85; $I^2 = 89.8\%$)⁷.

2. Pathogenesis of Hashimoto Thyroiditis-Associated Anxiety and Depression in Western Medicine

In the initial stages of Hashimoto's disease, damage to the thyroid gland can result in the transient release of thyroid hormones into the bloodstream, potentially causing transient hyperthyroidism. This fluctuation can acutely manifest as symptoms such as agitation, anxiety, and even psychosis. Subsequent depletion of thyroid hormone reserves often results in a state of functional hypothyroidism, which is frequently correlated with depressive symptoms, including apathy, low mood, fatigue, and cognitive dysfunction⁸. Given the critical role of thyroid hormones in the central nervous system (CNS), particularly in the production of neurotrophic factors and the regulation of mood⁹, the link between HT and psychiatric disorders is often primarily attributed to HT-induced hypothyroidism⁶. Studies have consistently confirmed the strong association between hypothyroidism and depression¹.

Furthermore, several investigations have established a correlation between mood disturbances and the presence of thyroid peroxidase (TPO) antibodies¹⁰. Elevated levels of TPO antibodies are associated with depression, general distress, obsessive-compulsive symptoms, and anxiety¹¹. Notably, the presence of TPO antibodies constitutes an early indicator of an autoimmune attack on the thyroid, sometimes preceding discernible changes in Thyroid-Stimulating Hormone (TSH) levels⁷.

Research by Churilov *et al.*¹² on Hashimoto's encephalopathy demonstrated that autoantibodies can exert significant effects on the nervous system. This finding supports the hypothesis of an independent influence of thyroid antibodies on anxiety and depression¹³. One study reported that HT patients with euthyroid TSH levels exhibited significant scores on the Beck Anxiety Inventory and Beck Depression Inventory in 81% and 89% of cases, respectively¹. Patti *et al.*¹⁴ reviewed the link between anti-thyroid antibodies and quality of life, including mental health. They found a statistically significant correlation ($P < 0.05$) between symptom distress and antibody levels in three studies, with one study specifically reporting a significant association ($P < 0.05$) between antibodies and mental health.

An additional factor implicated in mental disorders among HT patients is selenium deficiency. Like iodine deficiency, selenium deficiency may contribute to the development of HT, particularly in individuals residing in areas with low soil selenium content¹⁵. HT patients with co-morbid depression should be reasonably assessed for selenium status. Beyond its role as an essential trace element required for thyroid hormone synthesis and its antioxidant properties¹⁶, selenium possesses neuroprotective, antioxidant, and anti-inflammatory activities that safeguard the CNS and regulate mood.

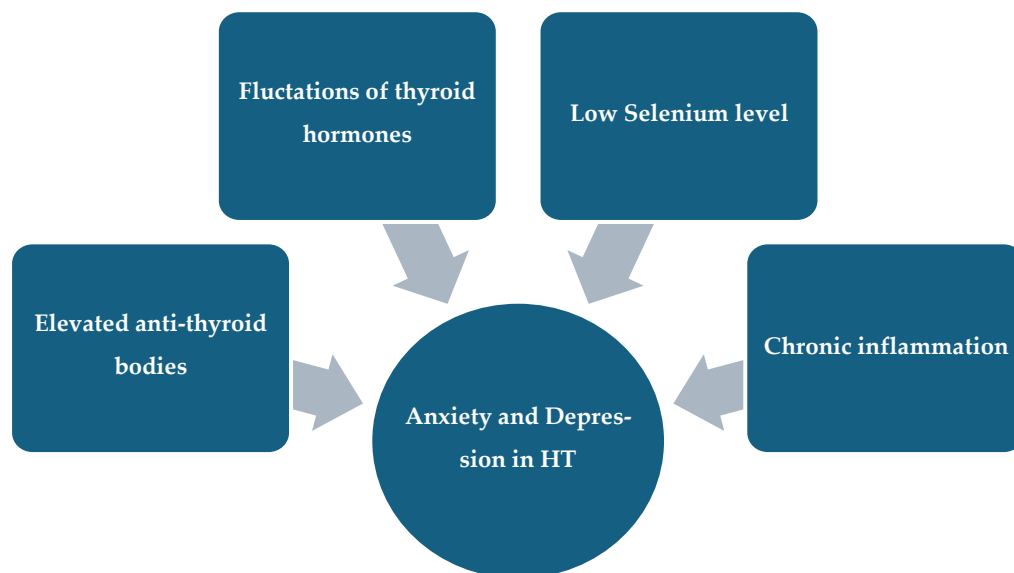


Figure 1. Hashimoto Thyroiditis-Associated Anxiety and Depression Pathogenesis.

3. Pathogenesis and TCM Patterns of Hashimoto Thyroiditis-Related Depression and Anxiety

From the perspective of TCM, Hashimoto's thyroiditis is classified under the category of "gall disease". Its pathogenesis is understood as a complex interplay of constitutional factors, emotional disorders, and improper diet, leading to the accumulation of vital energy (*Qi*) stagnation, phlegm coagulation, and blood stasis in the anterior laryngeal region. The characteristic manifestation is a swelling or mass ("gall swelling") in front of the neck¹⁷.

HT primarily affects the Liver, Spleen, and Kidney organ systems. The core pathogenesis is described as Spleen and Kidney *Yang* Deficiency alongside Liver and Spleen disorders. The disease essence is characterised as a deficiency in origin (*ben xu*) and an excess in manifestation (*biao shi*), often presenting as a mixed deficiency and excess pattern^{17,18}. HT patients frequently exhibit a chronic state of *Yang Qi* and Blood deficiency in the Spleen and Kidneys.

Autoimmune hypothyroidism is further classified into four main TCM patterns¹⁹:

1. **Spleen and Kidney *Qi* Deficiency:** This pattern is typically observed in the early stages of an underactive thyroid (Hashimoto's thyroiditis). Emotional disturbances, such as anger or depression, can cause Liver *Qi* stagnation, impeding its smooth flow, which subsequently affects the Spleen and Kidney function. This dysfunction can lead to the generation of phlegm and blood stasis, resulting in mood disorders, depression, and a sensation of neck fullness. Associated symptoms include fatigue, cold sensitivity, poor appetite, constipation, weight gain, weak bladder function, and menstrual irregularities. Physical examination reveals a pale and scalloped tongue and a weak, thready, and deep pulse²⁰. The treatment principle is to fortify and replenish Spleen and Kidney *Qi* and dissolve phlegm.
2. **Heart and Kidney *Yang* Deficiency:** This pattern also includes depression along with severe cold intolerance, periorbital and facial puffiness, weight gain, dry skin and hair, lack of sweating, poor appetite, frequent urination, constipation, a hoarse voice, and low basal body temperature. The tongue is pale, swollen, and scalloped. The pulse is weak, slow, or imperceptible. The treatment principle is to warm and supplement Kidney, Spleen, and Heart *Yang*²⁰.
3. ***Shaoyin* Pattern-*Yang* and *Qi* Deficiency:** This pattern is particularly associated with psychiatric disorders, including anxiety and depression. Common symptoms are

profound fatigue, coldness in the extremities, insomnia, and night sweats. It is a deficiency syndrome involving both *Yang* and *Qi* deficiency.

4. Deficiency and Loss of Kidney Essence

The primary organs involved are the Spleen and Kidney, with the Heart becoming affected in advanced stages ¹⁹.

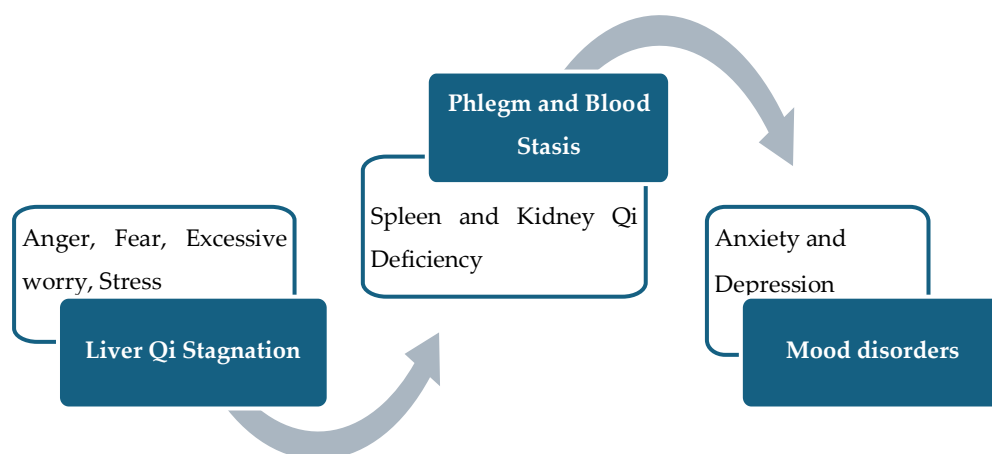


Figure 2. Pathogenesis of Hashimoto Thyroiditis-Related Depression and Anxiety according to TCM.

4. TCM Pathophysiology and Treatment Modalities for Hashimoto Thyroiditis Patients with Depression and Anxiety

Currently, there is no definitive, specific cure for HT in Western medicine. The standard treatment is oral levothyroxine sodium tablets. The therapeutic effects of supplements like selenium, as well as interventions such as surgery and low-intensity laser methods, remain unconfirmed ²¹. Furthermore, long-term use of levothyroxine may induce complications related to the cardiovascular system and bone metabolism ²².

Extensive research by Chinese scholars supports the efficacy of Traditional Chinese Medicine in modulating the endocrine system, regulating body immunity, promoting the clearance of autoantibodies, and stabilising pituitary function. The therapeutic effect of TCM in the management of thyroid diseases is considered particularly noteworthy ¹⁷. This is likely attributable to TCM's principle of individualised treatment, wherein practitioners formulate a specific protocol based on the patient's unique symptomatology and underlying imbalances.

The TCM management of autoimmune hypothyroid disease incorporates long-term acupuncture-related therapies, such as electroacupuncture, interlayer moxibustion, Peripheral Acupuncture, and acupuncture combined with *tuina* ²³, in addition to herbal medicine.

Acupuncture is utilised in HT treatment to regulate energy levels, restore hormonal balance, smooth emotions, and manage sleep, emotional, and menstrual issues ^{22,24}. Stimulation of the nervous system via needling induces specific biochemical changes within the body, thereby influencing the body's homeostatic mechanisms and promoting physical and emotional well-being ²⁴. Given that TCM identifies the fundamental cause of Hashimoto's hypothyroidism as Kidney *Yin* and *Yang* deficiency, specific acupuncture points are selected to strengthen Liver and Kidney *Yin*, clear internal heat, and restore Kidney *Yang*.

5. Methods

A computerised search was executed across Wan Fang, PubMed, Cochrane Library, and other relevant databases to identify RCTs investigating acupuncture-related therapy for depression and anxiety in the context of Hashimoto's thyroiditis. The literature review was independently performed by two researchers and included articles published in English, Chinese, and Russian. The search encompassed the period from the database's inception until September 1, 2025.

The primary efficiency indicators sought in the RCT results were the HADS-A and HADS-D scores, reflecting the focus of the paper on the improvement of depression and anxiety symptoms in HT patients. Given the established link between mood disorder and the presence of TPO antibodies, papers reporting outcomes for TPOab and TGAb levels following acupuncture-related therapy for anxiety and depression in HT patients were also included for review.

6. Acupuncture-Related Therapy Results in Hashimoto Thyroiditis Anxiety and Depression

A study²⁵ investigating the feasibility of Hand *Yangming* Meridian Penetrating Acupuncture in HT-related hypothyroidism randomised 58 subjects (ratio 1:1). After a 16-week treatment period, no statistically significant difference was observed in the change of TPOab levels between the two groups. However, the TGAb level in the acupuncture group was significantly lower than in the waiting list control group (difference: -141.97 [95% CI: -222.4 to -61.5], $P = 0.011$). There was no statistical difference noted in the HADS-D scores between the groups. The acupuncture protocol involved points such as *Sanjian* (LI3), *Hegu* (LI4), *Quchi* (LI11), *Binao* (LI14), *Jianyu* (LI15), *Renying* (ST9), and *Zusanli* (ST36). The technique employed was penetration needling with manipulation (lifting, inserting, twisting, turning) to achieve *deqi*. The researchers concluded that Hand *Yangming* Meridian Penetrating Acupuncture may reduce TGAb levels and improve symptoms.

TCM practitioners, such as Yu *et al.*²⁶ propose that not only Hand *Yangming* but also Foot *Yangming* meridians are effective in HT treatment due to their circulation paths near the neck. Thirty HT patients were treated with acupuncture points including *Quchi*, *Jianyu*, *Hegu*, *Shuitu*, *Zusanli*, *Binao*, *Renying*, *Shuitu*, and *Zhongwan*. The 12-week acupuncture course was combined with levothyroxine (Euthyrox) intake. Post-treatment analysis showed that the Visual Analog Scale (VAS) score for neck discomfort, TCM syndrome score, and TPOAb level were all significantly reduced compared to pre-treatment values.

In another study²⁷, acupoint application was reported to reduce serum levels of TgAb and TPOAb in 150 HT patients with liver-qi stagnation, concurrently alleviating thyroid enlargement, improving TCM symptoms such as anxiety, and enhancing quality of life. The patients were randomly divided into an acupoint application group and a placebo control group, treated over 4 weeks. Acupoints used in both groups included *Shenque* (CV 8), bilateral *Yongquan* (KI 1), *Yeshi*, and *Ashi* point. Post-treatment, the acupoint application group showed reduced serum levels of TgAb and TPOAb ($P < 0.05$). The Role Emotional (RE) and Mental Health (MH) components of the SF-36 were significantly increased ($P < 0.01$, $P < 0.001$). Both TCM symptom scores and HADS-A scores were lowered compared to pre-treatment in both groups ($P < 0.001$, $P < 0.01$). Conversely, these scores increased after treatment in the control group ($P < 0.05$, $P < 0.01$, $P < 0.001$).

A systematic review and meta-analysis²⁸ comparing the effectiveness of acupuncture versus levothyroxine sodium tablets in HT included 14 RCTs (1020 participants). The meta-analysis results indicated that acupuncture significantly regulated TPOAb content (mean difference [MD] = -63.18, 95% CI = -91.73 to -34.62, $P < 0.00001$) and TGAb content (MD = -68.56, 95% CI = -101.55 to -35.57, $P < 0.00001$). However, for the HADS scores, reported in 4 studies, there was no significant reduction for either the HADS-A score (MD = 0.24, 95% CI = -0.93 to 1.41, $P = 0.86$) or the HADS-D score (MD = -0.81, 95% CI = -2.02 to 0.40, $P = 0.25$). Both analyses exhibited low heterogeneity ($I^2 = 0\%$, $P = 0.69$ and $I^2 = 0.25\%$, $P = 0.19$, respectively)²⁸.

A clinical trial by Qiao *et al.*²⁷ involving 62 HT patients (predominantly female; average age 46 years old) over 3 months combined acupuncture treatment with levothyroxine sodium tablets. The trial demonstrated no significant difference between the combined therapy and levothyroxine alone in reducing the HADS-A score (MD = 0.33, 95% CI = -1.19 to 1.85, $P = 0.86$) or the HADS-D score (MD = -1.82, 95% CI = -3.92 to 0.28, $P = 0.25$), showing low heterogeneity ($I^2 = 0\%$, $P = 0.69$ and $I^2 = 25\%$, $P = 0.19$, respectively).

A case study²⁴ reported the successful treatment of a 24-year-old woman diagnosed with HT and TCM diagnosis of Kidney and Spleen *Qi* Deficiency. Treatment, administered monthly over 3 years and 8 months, involved points: DU20 (*BaiHui*), GB20 (*FengChi*), DU14 (*DaZhui*), ST9 (*RenYing*), LI4 (*HeGu*), BL15 (*XinShu*), BL20 (*PiShu*), BL23 (*ShenShu*), DU4 (*MingMen*), RN6 (*QiHai*), RN4 (*QuanYuan*), SP9 (*YinLingQuan*), ST36 (*ZuSanLi*), SP6 (*SanYinJiao*), KI3 (*TaiXi*), and LR2 (*TaiChong*). The patient's Eutirox dosage was gradually reduced until cessation, coinciding with the normalisation of her T4, TSH, and TPO levels. Concurrently, symptoms including fatigue, tiredness, and depression significantly improved.

An additional review of Chinese literature described 8 studies where acupuncture and moxibustion demonstrated superiority over Western medicine in reducing TPOAb levels in HT treatment. High heterogeneity was observed ($I^2=94\%$, $P<0.05$), with a combined effect size of SMD = -2.18 (95% CI [-3.04, -1.32]) and a test statistic $Z=4.96$ ($P<0.00001$). Improvement in TCM syndrome scores by acupuncture was reported in 2 studies, with high heterogeneity ($I^2=91\%$) and a combined effect size of SMD = -1.30 (95% CI [-2.57, -0.03]), $Z=2.01$ ($P=0.04$). Four of these studies incorporated a treatment protocol of bridge arch massage combined with acupuncture^{29,30}.

Luzina *et al.*³¹ reported that following corporal acupuncture and ear acupuncture for HT in Russia, 20% of patients discontinued hormonal medication, and 77% were able to reduce their dosage by a third. Crucially, all patients reported a decrease in the level of anxiety and depression. Key acupoints utilised, often combined with moxibustion, included *Guanyuan* (CV4), *Shenshu* (BL23), *Mingmen* (GV4), and *Qihai* (CV6).

7. Discussion

A total of 8 publications were selected for this systematic review from 33 initial papers identified regarding acupuncture-related therapy in HT. The synthesis of results suggests that acupuncture-related therapy may positively influence the amelioration of patients' mental disorder symptoms, particularly depression and anxiety.

However, a critical finding is that only a single study documented significant changes in HADS-A and HADS-D scores. This specific study focused on HT patients exhibiting the TCM pattern of liver-qi stagnation. Other reviewed papers, in contrast, showed no significant changes in overall HADS scores. This highlights a potential link between the TCM pattern (liver *Qi* stagnation affecting spleen and kidney function) and the manifestation of mood disorders. The study showing positive HADS results also reported significant increases in the RE and MH components of the SF-36 ($P<0.01$, $P<0.001$), with simultaneous reductions in TCM symptom scores and HADS-A scores in both groups post-treatment, whereas the control group showed an increase in these scores ($P<0.05$, $P<0.01$, $P<0.001$)²⁷.

Regarding objective biological indicators, all but one reviewed paper reported that the improvement in serum TPO-Ab levels was superior in the acupuncture-related therapy group compared to the Western medicine (levothyroxine sodium tablets) administration group.

The common methods employed in the acupuncture-related treatment groups included acupuncture, massage, J-type needle knife, warm acupuncture, and moxibustion, utilising various techniques. The control groups primarily received administration of levothyroxine sodium tablets.

The most frequently considered and utilised acupuncture points included: *Sanjian* (LI3), *Hegu* (LI4), *Quchi* (LI11), *Binao* (LI14), *Jianyu* (LI15), *Renying* (ST9), *Zusanli* (ST36),

Shuitu (ST10), Zhongwan (CV12), Shenque (CV 8), Yongquan (KI 1), BaiHui (DU20), FengChi (GB20), DaZhui (DU14), XinShu (BL15), PiShu (BL20), ShenShu (BL23), MingMen (DU4), QiHai (RN6), QuanYuan (RN4), YinLingQuan (SP9), SanYinJiao (SP6), TaiXi (KI3), and TaiChong (LR2).

This study is subject to several limitations. A significant constraint is the scarcity of high-quality, large-sample-sized RCTs specifically focused on the anxiety and depression symptoms in HT patients. Furthermore, the included randomised controlled clinical trials often present methodological shortcomings such as small sample sizes, incomplete reporting (e.g., details on acupuncture protocols, duration, treatment course variability), and insufficient reporting of adverse reactions. These limitations pose a considerable challenge for researchers attempting to rigorously analyse the feasibility, efficacy, and safety of acupuncture-related treatments for alleviating mental disturbance symptoms in HT.

8. Conclusion

Acupuncture-related therapy appears to be a beneficial adjunct in improving mood disorder symptoms, specifically depression and anxiety, in patients with Hashimoto's thyroiditis. There is evidence that acupuncture can contribute to lowering thyroid antibodies, which in turn may positively impact the mental disturbance symptoms and overall quality of life of HT patients. However, the final conclusions necessitate further rigorous validation due to the identified limitations in the availability of high-quality, large-scale clinical studies dedicated to depression and anxiety in the HT population.

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Review

Integrating Traditional Chinese Medicine Phytotherapy and Diet Therapy with Contemporary Endurance Nutrition: Mechanisms, Evidence, and Practical Applications.

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Abstract

Background: Traditional Chinese Medicine (TCM) is a holistic medical system emphasising energetic balance and personalised therapies, including diet therapy and phytotherapy. Its potential relevance in high-performance sport is increasingly recognised, as elite athletes face high physical and psychological demands, fatigue, injury risk, and metabolic or gastrointestinal disturbances. Contemporary endurance nutrition highlights carbohydrate periodisation, optimised protein intake, micronutrient adequacy, gut microbiota stability, and individualised dietary strategies to support performance and recovery.

Objective: To review evidence on the use of TCM diet therapy and phytotherapy in endurance sports, exploring physiological mechanisms, recovery effects, and the integration of TCM with modern nutritional strategies.

Methods: A narrative synthesis of experimental, clinical, and sports nutrition literature was conducted, including studies on macronutrient requirements, dietary periodisation, gut microbiota, and herbal interventions in athletes.

Results: Carbohydrates remain the key determinant of endurance performance, influencing time-to-exhaustion, metabolic efficiency, and gut microbial stability. Ketogenic or low-carbohydrate strategies often impair high-intensity performance. Many endurance athletes fail to meet energy and micronutrient needs, increasing the risk of deficiencies and Relative Energy Deficiency in Sport (RED-S).

TCM diet therapy focuses on strengthening Spleen Qi, nourishing Kidney Essence, and correcting imbalances, conceptually supporting metabolism, recovery, and gastrointestinal function. Constitution-based approaches (*ti zhi*) align with modern personalised nutrition. Experimental studies suggest that herbs such as ginseng and *Astragalus* may improve mitochondrial function, reduce oxidative stress, and enhance fatigue resistance, although human trials show limited and inconsistent performance effects. *Tribulus terrestris*, *Rhodiola*, and *Cordyceps* demonstrate minimal ergogenic benefits.

Conclusions: TCM diet therapy and phytotherapy may complement endurance nutrition through personalised, systemic, and recovery-focused strategies. Current evidence does not support most herbal supplements as primary ergogenic aids. Integration is most effective when TCM principles are applied alongside established nutritional practices, including adequate carbohydrate and protein intake, micronutrient sufficiency, and tailored fuelling. Further controlled human studies are required to determine efficacy and mechanisms.

Keywords: Traditional Chinese Medicine; Phytotherapy; Diet therapy; High-Performance Sport; Athletic Recovery; Herbal Medicine; Sports Nutrition.

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1. Introduction

TCM is an ancient holistic medical system deeply rooted in Chinese culture and history, with key foundational texts such as the *Huangdi Neijing* developed between 300-500 BCE¹⁻³. TCM views health as the harmonious balance of the body's energy systems (*Qi*), integrating diagnostics and treatment principles through modalities including acupuncture, herbal medicine (phytotherapy), and diet therapy⁴. In recent years, TCM modalities have gained interest as complementary approaches for managing the unique physiological and emotional demands faced by elite athletes in high-performance sports⁵⁻⁸.

Elite athletes are subject to extreme physiological and emotional demands due to high training loads, competitive pressure, and environmental variation, which can contribute to persistent fatigue, recurrent injuries, digestive disorders, and sleep disturbances beyond the reach of conventional biomedical approaches⁹⁻¹¹. In this context, TCM emerges as a complementary resource with high potential, offering both physical recovery and energetic/emotional regulation through strategies such as acupuncture, moxibustion, diet therapy, phytotherapy, and *Tuina* for injury prevention, enhanced muscular regeneration, and holistic resilience.

The primary energy source for muscle contraction is ATP, regenerated via carbohydrate, lipid, and to a lesser extent protein metabolism¹². The prevailing metabolic pathway shifted according to exercise intensity and duration, with carbohydrates dominating high-intensity efforts and lipids predominating in prolonged exercise. Energy systems include ATP-PCr for explosive activities, <10 seconds¹³, anaerobic glycolysis yielding lactate¹⁴, and aerobic metabolism using mitochondrial oxidation of glucose and fatty acids¹². Muscle and hepatic glycogen are the main carbohydrate reserves, while triglycerides store lipids¹⁵, with depletion associated with fatigue. Maximal effort relies on anaerobic pathways, while moderate/prolonged efforts depend on aerobic metabolism; the lactate threshold marks the point of significant lactate accumulation in blood¹⁶.

Skeletal muscle fibres are classified by metabolic and functional traits: Type I (slow oxidative) fibres are highly resistant to fatigue and suited for prolonged, low-intensity activities; Type IIa (fast oxidative) fibres combine aerobic and anaerobic capacities for moderate-strength and endurance; Type IIb (fast glycolytic) fibres specialise in explosive strength and speed, relying on anaerobic glycolysis and showing poor fatigue resistance¹⁷. Continuous training induces significant physiological adaptations such as increased mitochondrial density¹⁸, improved muscle capillarisation¹⁹, decreased post-exercise lactate¹⁴, and enhanced cardiovascular and neuromuscular efficiency¹². High-intensity training (>85% VO₂max) predominantly engages anaerobic pathways and accelerates lactate accumulation and muscle fatigue.

Endurance sports impose substantial physiological and metabolic demands, requiring finely tuned nutritional strategies to sustain performance, recovery, and adaptation²⁰. Diet therapy, defined as the application of individualised dietary interventions to optimise health and athletic performance, plays a central role in the management of endurance athletes²¹. Carbohydrates remain the cornerstone of endurance nutrition, as their availability directly influences time to exhaustion and work output²². Recent updates in carbohydrate research emphasise not only total daily intake but also the timing, form, and periodisation of carbohydrate availability around training sessions^{22,23}.

While some athletes adopt low-carbohydrate or ketogenic dietary approaches to enhance fat oxidation, evidence indicates that such strategies often compromise high-intensity performance and training quality^{23,24}. Periodised carbohydrate restriction, alternating between high- and low-carbohydrate availability, has been explored as a method to optimise metabolic flexibility; however, meta-analytical evidence suggests it does not consistently enhance endurance performance in trained athletes²⁵. Moreover, carbohydrate-rich diets have been shown to promote more stable gut microbiota profiles and better performance outcomes compared to high-protein or low-carbohydrate regimens²⁶.

Adequate protein intake is also essential for recovery, muscle repair, and adaptation to endurance training²⁷. Contemporary reviews emphasise the importance of protein distribution and timing across the day to maximise muscle protein synthesis and support training adaptation²⁷. Nevertheless, many endurance athletes fail to meet energy and micronutrient requirements, particularly for vitamins D, E, and folate, which may impair recovery and immune function²⁸. Additionally, inappropriate nutritional strategies can lead to adverse outcomes such as hyponatremia, dehydration, and gastrointestinal distress during competition²⁹.

Overall, diet therapy in endurance sports requires an integrative approach that considers macronutrient balance, energy availability, gastrointestinal tolerance, and individualised metabolic responses^{15,20,28}. Optimising these factors through evidence-based dietary planning may improve endurance capacity, enhance recovery, and reduce the risk of nutrition-related complications.

This review provides a bibliographic synthesis of TCM phytotherapy and diet therapy applications in sports medicine, focusing on physiological benefits, recovery, and performance optimisation.

2. Diet therapy in Endurance Sports

2.1. Carbohydrate Availability and Performance

Carbohydrates (CHO) remain the primary fuel substrate for endurance performance due to their high oxidative rate and role in maintaining muscle glycogen. Lima-Silva *et al.*³⁰ highlighted that inadequate carbohydrate availability leads to impaired time-to-exhaustion and reduced exercise economy. The recent paradigm of “fuel for the work required” proposes that carbohydrate intake should be periodised according to training load and session intensity³¹.

Carbohydrate Periodisation

A systematic review and meta-analysis by Gejl *et al.*²⁵ assessed the effects of periodised carbohydrate restriction (i.e., “train-low, compete-high”) in trained endurance athletes. Across 11 controlled trials, they found no significant improvements in VO₂max, time-trial performance, or oxidative enzyme activity compared to traditional high-CHO diets. The authors concluded that metabolic adaptations induced by low glycogen availability do not necessarily translate into improved performance outcomes.

Furber *et al.*²⁶ investigated endurance athletes undergoing dietary periodisation and found that athletes maintaining higher carbohydrate intake exhibited greater gut microbial stability and superior performance outcomes; specifically, high-CHO diets improved time-trial performance by ≈6.5%, whereas a short-term high-protein, low-CHO regimen produced a ≈23.3% decrement in performance, changes that were associated with shifts in bacterial and phage communities.

Carbohydrate Intake Recommendations

Authors³²⁻³⁴ recommend 8–12 g/kg/day of CHO for heavy training and 5–7 g/kg/day for moderate loads, emphasising multiple transportable carbohydrate sources (e.g., glucose–fructose blends) during prolonged events. Furthermore, pre-exercise CHO loading and intra-event fuelling at 60–90 g/h enhance glycogen availability and delay fatigue.

2.2. Ketogenic and Low-Carbohydrate Diets

The ketogenic diet (KD) has gained popularity as a potential strategy to increase fat oxidation and reduce dependence on glycogen. However, evidence consistently shows mixed or negative effects on performance in endurance athletes³⁵⁻³⁷. Shaw *et al.*³⁵ performed a randomised crossover study and found that while KD increases fat oxidation by 70–100%, it concurrently reduces exercise economy and high-intensity capacity. Similarly,

Burke³⁸ and Burke *et al.*³⁹ emphasised that the metabolic advantage of fat adaptation does not compensate for the reduced efficiency of ATP production from fatty acids.

Moreover, adaptation to KD often results in decreased glycogen availability, impairing performance in events involving surges or sprint finishes, common in competitive endurance sports³⁹. These findings collectively discourage the routine application of KD in endurance diet therapy.

2.3. Protein Nutrition in Endurance Athletes

Endurance athletes exhibit elevated protein requirements compared with sedentary individuals, reflecting increased amino-acid oxidation during prolonged exercise and the demands of muscle repair and mitochondrial biogenesis. Recent reviews²⁷ suggest a daily intake around ~1.8 g/kg/day is appropriate, with higher intakes (>2.0 g/kg/day) potentially warranted during periods of heavy training or carbohydrate restriction^{27,40}.

In line with recommendations from the International Society of Sports Nutrition, protein doses of ~0.25–0.3 g/kg per meal (or ~20–40 g), distributed every 3–4 h, including immediately before or within 0–2 h after exercise, may optimise muscle protein synthesis (MPS) and recovery^{41,42}.

Endurance exercise also increases oxidation of amino acids (including BCAAs) thereby increasing the need for sufficient protein to maintain nitrogen balance and support adaptation^{40,43}.

2.4. Micronutrient Adequacy and Energy Availability

The adequacy of energy and micronutrient intake in endurance athletes has been questioned. In a cross-sectional study of 95 endurance athletes, the majority (~77%) failed to meet estimated energy requirements; similarly, large percentages had intakes below recommendations for vitamins D (93.7 %), E (71.6 %), K (54.7 %), folate (54.7 %), dietary fibre (49.5 %), as well as other micronutrients⁴⁴.

As argued in a more general review on nutrition in athletes, chronic low energy availability (LEA) due to inadequate caloric intake may lead to micronutrient deficiencies, impair recovery, immune competence, and hormonal function, which are conditions associated with the clinical syndrome of Relative Energy Deficiency in Sport (RED-S)⁴⁵.

Female athletes may be particularly susceptible, because restrictive dietary practices associated with inadequate energy intake tend to be more common among women and the interplay between energy intake, micronutrient supply, and high training load may exacerbate nutritional deficits⁴⁴.

Given these findings, ensuring sufficient caloric intake, tailored to training load, is essential in nutritional planning for endurance sports (“periodised nutrition”), to avoid energy mismatch and prevent nutrient shortfalls²⁸.

When dietary intake remains inadequate (or in high-risk conditions, e.g. heavy training, restricted diet, limited sun exposure), supplementation (e.g. Vitamin D, Iron) might be considered after assessing status, particularly in athletes with documented deficiencies or physiological demands that exceed dietary supply⁴⁶.

3. Gut Microbiota and Diet therapy

Emerging evidence links gut microbial diversity and composition to endurance performance and metabolic efficiency in athletes. In a randomised dietary-periodisation trial in well-trained endurance runners, those whose gut microbial communities remained more stable during shifts between high-protein and high-carbohydrate diets exhibited better time-trial performance; by contrast, a short-term high-protein diet disrupted microbial stability, including reductions in gut phageome diversity, and was associated with a ~23.3% drop in performance, whereas a high-carbohydrate diet improved performance by ~6.5%²⁶.

Broader metagenomics also suggest that competitive athletes tend to harbour gut microbiota enriched in short-chain fatty-acid (SCFA) producing taxa (e.g., *Faecalibacterium*,

Eubacterium, *Ruminococcus*, *Blautia*) and metabolic pathways for SCFA and other beneficial microbial metabolites, features that may support metabolic efficiency, recovery and performance⁴⁷.

However, diet (especially high-protein, low-fibre intake) can perturb the microbial community, reduce SCFA-producing commensals, and alter microbial function⁴⁸⁻⁵⁰. This suggests that future nutritional interventions for endurance athletes might benefit from integrating prebiotic-rich foods or carefully selected probiotic strategies to support microbial homeostasis, gut barrier integrity, and recovery, provided that supplementation is evidence-based, strain-verified, and aligned with dietary fibre and carbohydrate intake^{47,51,52}.

Further research employing longitudinal, controlled trials and functional microbial/metabolomics readouts is warranted to elucidate the causal mechanisms linking diet-induced microbial modulation and endurance performance.

4. Nutrition-Related Adverse Outcomes

Martinez-Sanz *et al.*²⁹ reviewed nutrition-related adverse outcomes in endurance and ultra-endurance competitions and identified the most prevalent problems as exercise-associated hyponatremia (EAH), dehydration/heat illness, and gastrointestinal (GI) distress; they emphasised that misinformation about hydration and competition nutrition is a common contributor to these events²⁹.

Overhydrating with hypotonic fluids (drinking beyond thirst) is a principal cause of EAH, while excessive or poorly-tolerated carbohydrate intake during competition commonly precipitates GI symptoms such as nausea, cramping, bloating and diarrhoea^{53,54}. Implementing individualised, event-specific hydration and fuelling plans, practiced and refined under training conditions (i.e., “trial runs”), is recommended as the most effective strategy to prevent both EAH and exercise-induced GI complaints^{53,55}.

5. Principles of Chinese Diet therapy in Sports Context

Zhao *et al.*⁵⁶ defined Chinese diet therapy as the use of foods possessing specific energetic and organotrophic properties to prevent or correct imbalance. Applied to endurance training, diet therapy aims to strengthen *Spleen Qi* (associated with digestion and energy transformation), nourish *Kidney Essence* (vitality and recovery), and clear *Heat* or *Dampness* caused by prolonged physical exertion^{56,57}.

Su⁵⁸ expanded on this by developing individualised nutrition strategies grounded in TCM constitutions, such as *Qi-deficient*, *Yin-deficient*, or *Phlegm-Damp* types, suggesting that constitution-based dietary planning could improve adaptation to training load and metabolic efficiency in competitive athletes.

5.1. Experimental Evidence on Anti-Fatigue and Endurance Enhancement

Herbal Formulations

Zhao *et al.*⁵⁹ investigated the effects of a TCM dietary intervention on post-running energy metabolism. The TCM-based formula enhanced key metabolic indicators, such as aerobic enzyme activity and GLUT-4 expression, suggesting improved metabolic recovery following exercise. The authors attributed these effects to tonic components including *Astragalus membranaceus* (*Huang Qi*) and *Panax ginseng* (*Ren Shen*), which have been associated with supporting energy metabolism, mitochondrial function, and anti-fatigue activity.

Similarly, Ding *et al.*⁶⁰ evaluated a compound extract composed of multiple TCM herbs (*Ginseng*, *Lycium barbarum* (Goji berry), *Polygonatum sibiricum*, and *Dendrobium officinale*) in an in vivo fatigue model. Supplementation increased time to exhaustion and reduced malondialdehyde (MDA) concentrations, indicating lower oxidative stress and en-

hanced resistance to exercise-induced fatigue. The authors reported improvements in energy metabolism pathways, which align with TCM concepts of replenishing *Qi* and nourishing *Yin* to counteract exercise-induced depletion.

Although human evidence remains limited, Liu *et al.*⁶¹ proposed the potential ergogenic effects of *Siraitia grosvenorii* based on experimental findings showing reductions in fatigue-related biomarkers (BUN and lactate) and improvements in metabolic function. Such mechanisms may have implications for athletic performance and recovery, consistent with TCM concepts of restoring *Qi* and maintaining metabolic balance.

Integrative and Mechanistic Perspectives:

Some experimental studies have shown that certain herbal extracts (e.g., red ginseng, ginger) can activate the AMPK–PGC-1 α pathway, promote mitochondrial biogenesis and increase mitochondrial function, which, in animal models, was associated with increased exercise endurance^{62–67}. This suggests that, in principle, TCM-based diet therapy may improve endurance by optimising cellular energy production pathways. However, human data are still lacking.

5.2. Constitution-Based and Personalised Nutrition

Hsu *et al.*⁶⁸ and Zhao *et al.*⁶⁹ emphasise that effective application of dietotherapy should consider the individual constitution (*ti zhi*). Traditionally, *Qi*-deficient patients are recommended warming and supporting foods such as ginseng, yam, or jujube, whereas *Yin*-deficient individuals are advised cooling, hydrating foods such as pear or lotus root. This individualised approach parallels the principles of contemporary personalised nutrition, providing a culturally distinct yet complementary framework for tailoring endurance nutrition strategies.

6. Phytotherapy

Tribulus terrestris L. has been widely used in herbal medicine and promoted for purported ergogenic benefits, including claims of enhancing testosterone, physical recovery, and performance; however, scientific evidence regarding its efficacy remains controversial. In this context, Ardakani *et al.*⁷⁰ conducted a double-blind, randomised, placebo-controlled trial to investigate whether short-term *Tribulus terrestris* supplementation alters hormonal responses induced by a session of high-intensity resistance exercise, and found no significant differences between the supplementation and placebo groups.

The study by Antonio *et al.*⁷¹ aimed to investigate the effects of *Tribulus terrestris* supplementation on body composition and physical performance in trained male resistance athletes. Fifteen male volunteers with prior resistance training experience were randomly assigned to two groups: one group received *Tribulus terrestris* (3.21 mg/kg body weight per day) and the other received a placebo for eight weeks. Both groups followed the same training program. Results showed no statistically significant differences between groups in body composition (weight, body fat percentage, and total body water), maximal strength (1RM), or muscular endurance (maximum number of repetitions) after the supplementation period. Improvements in strength and endurance were attributed solely to the physical training performed and were similar between groups, except for bench press performance, which showed less progress in the *Tribulus*-supplemented group. Supplementation with *Tribulus terrestris* (3.21 mg/kg/day) did not promote any additional improvements in body composition, muscular strength, or muscular endurance in resistance-trained men over an 8-week period. The observed improvements were attributed to training effects regardless of supplementation intake. These results do not support the use of *Tribulus* as an ergogenic agent in trained athletes.

Moreover, the study by⁷² aimed to examine the effects of two weeks of *Tribulus terrestris* supplementation on inflammatory markers—interleukin-6 (IL-6) and high-sensitivity C-reactive protein (hs-CRP)—as well as muscle damage indicators, creatine phosphokinase (CPK) and lactate dehydrogenase (LDH), following a single session of high-intensity resistance exercise. Eighteen healthy, non-athlete males (age 22.44 ± 2.54 years; BMI

26.15 ± 1.62 kg/m²) were randomly assigned to either a *Tribulus terrestris* supplementation group or a placebo group, each comprising nine participants. Subjects consumed two 250-mg capsules per day of *Tribulus terrestris* or placebo (maltodextrin) for two weeks. After the supplementation period, participants completed six resistance exercises performed in three circuits at 80%, 85%, and 90% of 1RM. Blood samples were obtained at baseline (pre-supplementation), immediately before exercise, and immediately after exercise.

Both groups showed significant total increases in IL-6 ($p < 0.001$) and LDH ($p = 0.005$). Post hoc analysis demonstrated significant elevations in IL-6 and CPK after exercise compared with both pre-exercise and baseline values ($p < 0.001$) in the two groups. No significant within- or between-group differences were observed for hs-CRP ($p > 0.05$). Post-exercise IL-6 and CPK responses did not differ significantly between the *Tribulus terrestris* and placebo groups ($p > 0.05$). However, post-exercise LDH levels were significantly lower in the supplementation group compared with placebo ($p = 0.015$).

Overall, the findings indicate that short-term *Tribulus terrestris* supplementation does not influence IL-6 or hs-CRP responses to resistance exercise, but may contribute to reductions in certain muscle damage markers, specifically CPK and LDH, following high-intensity circuit training.

A literature review conducted by Sellami *et al.*⁷³ examined the potential benefits and risks associated with the use of herbal products by athletes, with a focus on traditional claims, available human data, and ergogenic relevance (Table 1).

Table 1. Herbal products and their evidence-based relevance according to Sellami *et al.*⁷³.

Herbal product	Relevance for athletes
Ginseng (<i>Panax</i>)	- Identified as one of the most extensively studied herbs in sports and exercise contexts. - Traditionally used for its putative anti-fatigue and vitality-enhancing effects. - Human studies show mixed results, with some reporting improvements in well-being, fatigue, and exercise tolerance, while others find no significant performance effects. - Variability in findings may be related to differences in training status, dosage, extract composition, and study design.
<i>Rhodiola rosea</i> and <i>Cordyceps sinensis</i>	- Both classified as adaptogenic herbs traditionally used to support physical and mental resilience. - Preliminary trials suggest possible benefits for fatigue and perceived exertion, but evidence for measurable improvements in endurance or aerobic performance remains inconsistent. - Findings across studies are heterogeneous, and neither herb has demonstrated consistent ergogenic effects in controlled human trials.
<i>Eurycoma longifolia</i> (Tongkat Ali) and <i>Tribulus terrestris</i>	- Commonly marketed for testosterone support, strength enhancement, or vitality. - Most controlled human studies do not show significant improvements in strength, muscle mass, power output, or anaerobic performance. - Evidence supporting performance enhancement is weak and inconsistent, and current data do not support their effectiveness as ergogenic aids.
Alkaloid-rich plants (<i>Guarana</i> , Green Tea, <i>Yerba Mate</i>)	- These plants contain bioactive compounds such as caffeine, catechins, and related alkaloids that may influence alertness, energy expenditure, and antioxidant activity. - Extracts from these plants have been associated with potential benefits on cognitive function, perceived energy, and metabolic parameters, though effects on athletic performance are variable. - Stimulant-containing products may enhance subjective alertness, but misuse or excessive intake increases the likelihood of adverse effects.

The review highlights antioxidant activity as one of the principal biological actions proposed for many herbal preparations. Although the broader scientific literature sug-

gests additional mechanisms, including modulation of stress-response systems and various metabolic pathways, Sellami *et al.*⁷³ emphasise that these hypotheses remain insufficiently substantiated in human athletic populations. Overall, the evidence supporting direct ergogenic mechanisms is limited, and many traditional claims regarding performance enhancement have not yet been validated in controlled studies.

7. Integration of Phytotherapy, Diet Therapy, and Modern Endurance Nutrition

The intersection of TCM phytotherapy, classical diet therapy principles, and contemporary endurance nutrition offers a promising yet complex framework for supporting athletic performance and recovery. Modern sports nutrition has become increasingly nuanced, emphasising periodised carbohydrate intake, optimised protein distribution, micronutrient adequacy, gut microbiota stability, and individualised fuelling strategies tailored to training load. Within this evolving landscape, TCM-based dietary and herbal strategies introduce complementary perspectives that focus on systemic balance, energetic restoration, and individualised constitution types (*ti zhi*). However, the integration of these paradigms requires careful critical appraisal.

From a modern physiological standpoint, endurance performance hinges on the capacity to sustain energy production, manage metabolic stress, control inflammation, and maintain adequate recovery. Evidence shows that macronutrient periodisation, carbohydrate availability, and protein timing significantly influence these processes. TCM diet therapy parallels this logic through its emphasis on strengthening Spleen *Qi* for metabolic transformation, nourishing Kidney Essence to support recovery and resilience, and modulating Heat, Dampness, or other imbalances that may emerge from heavy training loads. Although conceptually distinct, these frameworks converge in their shared aim of optimising metabolic efficiency, recovery quality, and adaptive capacity.

Similarly, phytotherapy offers theoretical mechanisms that could complement established nutritional strategies. Experimental studies indicate that certain herbal extracts, such as ginseng, *Astragalus membranaceus*, or polyherbal formulations, may influence mitochondrial function, reduce oxidative stress, and improve fatigue-related biomarkers. *Tribulus terrestris*, despite its popularisation in the sports domain, exemplifies the discrepancies between traditional claims and empirical evidence: controlled trials consistently show minimal effects on hormonal, performance, or inflammatory outcomes, with only modest and context-specific effects on muscle damage markers. The broader review by Sellami *et al.*⁷³ reinforces this cautious interpretation, highlighting that most phytotherapeutic agents lack consistent, reproducible ergogenic effects in well-controlled human trials.

A reflexive integration therefore requires acknowledging both the theoretical potential and the empirical limitations of phytotherapy. While many herbal preparations possess bioactive compounds capable of modulating antioxidant pathways, stress responses, or metabolic processes, current evidence remains insufficient to position them as primary ergogenic tools. Instead, their value may lie in adjunctive roles (supporting general vitality, modulating subjective fatigue, or contributing to long-term metabolic balance) particularly when used within a diet therapy framework aligned with personalised constitution-based recommendations.

The most compelling area of convergence between TCM and modern nutrition may be in the domain of individualised dietary planning. Endurance athletes exhibit considerable inter-individual differences in gastrointestinal tolerance, substrate utilisation, recovery kinetics, and gut microbiota composition. TCM's constitution-based approach offers a culturally distinct yet conceptually compatible model of personalisation. For example, *Qi*-deficient athletes may benefit from energetically warming, easily digestible foods that parallel modern guidance for optimising glycogen replenishment and digestive comfort, whereas *Yin*-deficient individuals may require hydration-supporting foods and cooling

properties that incidentally align with strategies for recovery and inflammation management. This alignment suggests that constitution-based diet therapy can serve as a complementary lens for tailoring nutrition without contradicting evidence-based principles.

Nevertheless, integration must remain grounded in methodological rigor. Herbal preparations vary widely in composition, standardisation, and bioavailability, and many claims remain untested in athletic populations. Similarly, the application of TCM principles should not replace established strategies such as carbohydrate periodisation, adequate protein intake, or evidence-supported micronutrient supplementation where appropriate. Instead, integration works best when TCM diet therapy and phytotherapy are positioned as supportive adjuncts within a broader, scientifically validated nutritional framework.

8. Conclusion

The integration of phytotherapy and TCM diet therapy with contemporary endurance nutrition presents a multidimensional approach that may enhance athlete health, recovery, and long-term resilience. While current evidence does not support the widespread use of many herbal agents as direct ergogenic aids, both TCM modalities contribute valuable paradigms of personalisation, systemic balance, and holistic recovery. Future research integrating biochemical, microbial, and performance outcomes will be essential to fully elucidate the mechanisms, applications, and limits of these complementary strategies in high-performance sport.

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Review

Paediatric *Tui Na* for Childhood Nocturnal Enuresis: A Review of Theoretical Foundations and Clinical Application.

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Abstract

Childhood nocturnal enuresis (CNE), defined as involuntary urination during sleep in children over five years of age, is a prevalent condition that can significantly affect emotional well-being, family dynamics, and quality of life. Despite numerous available treatments, both behavioural and pharmacological, many cases remain refractory or prone to relapse. Within Traditional Chinese Medicine (TCM), Paediatric *Tui Na* is a therapeutic massage designed for children. It has been described as an effective non-invasive intervention aimed at restoring energetic balance and regulating organ function.

Evidence indicates that paediatric *Tui Na* can significantly reduce the frequency of enuretic episodes by promoting the energetic regulation of the Kidney, Spleen, and Bladder systems, enhancing urinary control, and improving sleep quality. In addition to physiological regulation, improvements in emotional security and self-esteem have been consistently reported. The therapy's safety profile and its acceptance among children further support its clinical use.

Paediatric *Tui Na* represents a promising, safe, and integrative therapeutic approach for childhood nocturnal enuresis. Its combination of physiological and psychological benefits makes it a valuable adjunct or alternative to conventional treatments. Further controlled clinical studies are necessary to consolidate its evidence base and expand its integration into multidisciplinary paediatric care.

This narrative review aims to analyse the theoretical foundations, mechanisms of action, and clinical evidence supporting the use of Paediatric *Tui Na* in the treatment of childhood nocturnal enuresis.

Keywords: Childhood Nocturnal Enuresis; Paediatric *Tui Na*; Traditional Chinese Medicine; Chinese Paediatrics.

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1. Introduction

CNE is characterised by the involuntary loss of urine in children from the age of five, a stage in which urinary control should already be established, occurring at least twice a week ¹. According to the American Psychiatric Association, nocturnal enuresis is considered when a child urinates in bed at least twice a month. The ICD-10 (International Classification of Diseases, 10th version), on the other hand, defines the condition as the loss of urine at least once a month, for three consecutive months ². In the first months of life, urination is reflexive and involuntary. Around the age of one, there is an increase in bladder capacity and neural maturation of the frontal and parietal regions, which allows the child to recognise the sensation of a full bladder, although still without control over the act of urinating ^{3,4}. Voluntary control of urination, mediated by the cerebral cortex, is acquired later, allowing control according to social norms ⁵. Daytime urinary control is usually consolidated by the age of three and nocturnal control between four and five years. The absence of this control after this age characterises CNE ⁶. The disorder is common in

childhood, with a similar prevalence worldwide, affecting approximately 30% of children at 4 years, 10% at 7 years, 3% at 12 years, and 1% at 18 years, being more frequent in boys and with a family history of enuresis ^{7,8}. It is a transient condition, with a tendency for spontaneous resolution in about 15% of cases per year ⁹.

Enuresis can be classified as:

- Primary: When the child has never acquired urinary control and has no organic alterations, such as urinary tract infection, neurological dysfunction, or urological disorders.
- Secondary: Occurs after a minimum period of six months of continence and is frequently associated with emotional factors or stressful situations, such as parental separation, a change of school, or the birth of a sibling ¹⁰.
- Monosymptomatic: When the only symptom is nocturnal urine loss.
- Polysymptomatic (or complex): When it is associated with other urinary symptoms, such as urinary urgency, daytime incontinence, a weak stream, dysuria (painful urination), or pollakiuria (increased urinary frequency with decreased urinary volume) ¹¹⁻¹⁴.

Enuresis is a multifactorial disorder, involving physical, genetic, psychological, and social aspects ^{10,15}. Although some studies indicate that emotional and family factors are not the direct cause of enuresis, with psychological symptoms being a consequence of the problem ^{13,16}, other authors reinforce the association of the cause of enuresis with pre-existing behavioural or psychological disorders ^{10,11,14}.

In allopathic medicine, treatment involves behavioural and pharmacological approaches. Behavioural measures include controlling fluid intake, urinating before sleep, and treating constipation, if present. As a pharmacological approach, the use of desmopressin and imipramine can reduce nocturnal enuretic episodes, but with limitations and adverse effects ¹⁷⁻¹⁹. In addition to these approaches, the use of a nocturnal alarm is considered the most effective long-term method in cases that do not have organic causes, promoting the learning of waking up to urinate ²⁰⁻²².

In TCM, nocturnal enuresis is also defined as the involuntary loss of urine during sleep in children over five years of age, and for some authors, from three years onwards ^{23,24}. The formation and excretion of urine are related to the proper functioning of body fluid metabolism (*Jin Ye*), which depends on the harmony and proper functioning of the Kidney, Lung, and Spleen systems. From the perspective of Traditional Chinese Medicine, Nocturnal Enuresis is understood as the result of a congenital deficiency of Kidney *Qi*, a deficiency of Lung and Spleen *Qi*, or the accumulation of dampness-heat in the Liver meridian, factors that compromise the Bladder's function in controlling urination ²⁴⁻²⁷. In addition to the main patterns, the residual pathogenic factor is also considered, which may be associated with various causes, such as recurrent infections not completely resolved, inappropriate use of medications, and the administration of vaccines, as these factors can also interfere with water metabolism ²⁸. The emotional factor is also recognised as a possible cause of enuresis. During phases of childhood life in which significant changes in routine occur, such as entering a new school, parental separation, the birth of a sibling, the loss of a loved one or pet, states of mental agitation may arise. This condition favours an increase in the physiological heat of the Heart, which, in turn, consumes Kidney *Qi*. When the Kidney is weakened, its function of controlling the sphincters is compromised, resulting in the occurrence of enuresis ²⁹.

TCM distinguishes different *syndrome patterns* (energetic diagnoses) associated with CNE, according to the following signs and symptoms ^{24-27,29-31}:

1. Kidney *Qi* deficiency, characterised by weakness, cold limbs, and abundant clear urine;
2. Spleen and Lung *Qi* deficiency, often linked to fatigue, poor appetite, and loose stools and;
3. Damp-heat accumulation in the Liver meridian, manifesting as irritability, thirst, and scanty yellow urine.

While Western medicine primarily employs behavioural interventions, enuresis alarms, and pharmacotherapy (such as desmopressin and imipramine) to manage CNE, these treatments can be associated with side effects and relapse upon discontinuation^{5,13,14,17,18,23}. In contrast, TCM emphasises restoring systemic balance and addressing the root cause of the dysfunction, often integrating acupuncture, herbal medicine, moxibustion, auriculotherapy, cupping, dietary therapy, and *Tui Na*, as non-invasive, holistic interventions^{25,32,33}.

Among these, *Pediatric Tui Na* is a specialised form of Chinese therapeutic massage for children. It has gained attention for its safety, accessibility, and effectiveness³⁴⁻³⁶. By applying gentle manipulations on specific meridians and acupoints, *Tui Na* aims to harmonise *Qi* and blood (*Xue*), strengthen organ function, and promote the child's physical and emotional equilibrium. Clinical observations and controlled trials suggest that *Pediatric Tui Na* can significantly reduce the frequency of enuretic episodes, improve bladder control, and enhance sleep and emotional stability²³.

Given the increasing interest in integrative paediatric care, this review seeks to synthesise theoretical foundations and available evidence regarding the application of paediatric *Tui Na* in the treatment of childhood nocturnal enuresis. Through a narrative synthesis of classical literature and modern research, this paper aims to contextualise the role of *Tui Na* within both traditional Chinese medical theory and contemporary clinical practice.

2. Methodology

The research was carried out by analysing various sources, including specialised books on Traditional Chinese Medicine, scientific articles focused on child health, and publications available in academic databases such as SciELO, Google Scholar, PubMed, and CNKI. The following keywords were used for the search and selection of materials: *Childhood Nocturnal Enuresis*, *Traditional Chinese Medicine*, *Chinese paediatrics*, and *paediatric Tui Na*. Through this review, the intention is to deepen the understanding of the foundations and therapeutic benefits of *Tui Na* in the management of Childhood Nocturnal Enuresis, as well as to highlight the relevance of its integration with other therapeutic approaches. In this way, the study seeks to contribute to the promotion of children's health and well-being in a comprehensive and effective manner.

3. Results and Discussion

3.1. Pathophysiology of Childhood Nocturnal Enuresis from the Perspective of Conventional Medicine

CNE is a multifactorial disorder characterised by involuntary urination during sleep after the age when bladder control should normally be established. Its aetiology is complex, involving an interaction of genetic, physiological, psychological, and environmental factors^{5,9-15}. Studies suggest that delayed neurological maturation, altered circadian rhythm of antidiuretic hormone (ADH) secretion, reduced bladder capacity, and sleep arousal difficulties contribute significantly to its occurrence³⁷⁻⁴¹.

Studies indicate that most children with nocturnal enuresis have the primary and monosymptomatic type, meaning they have never acquired nocturnal urinary control and do not present other associated symptoms. A large part of these cases is related to inadequate training of urination habits, especially during the potty-training process and in controlling fluid intake.¹⁰ To a lesser extent, there are organic causes involved, more frequent

in the secondary and polysymptomatic forms, such as urological malformations, inflammation, urinary tract infection, constipation that puts pressure on the bladder, diabetes, kidney failure, and neurological and sleep disorders ²⁸.

Genetic factors play a relevant role; if one of the parents had a history of enuresis, the risk in the child is about 30%, and if both had the disorder in childhood, the possibility of the child developing it can exceed 70% ⁴²⁻⁴⁶.

Although emotional factors are not always the primary cause, they can exacerbate or perpetuate enuresis by influencing sleep patterns and arousal thresholds ⁴⁷⁻⁴⁹. Current conventional treatments include behavioural interventions, such as fluid restriction before sleep, scheduled voiding, and the use of nocturnal alarms, as well as pharmacological therapies, mainly desmopressin and imipramine. While these approaches can be effective, relapse after treatment discontinuation is frequent, and adverse effects are not uncommon ^{5,13,14,17,18,23}.

These limitations have encouraged the exploration of integrative and complementary therapies, particularly those emphasising non-invasive and holistic approaches, such as those found in TCM.

3.2. Childhood Nocturnal Enuresis According to Traditional Chinese Medicine

From the TCM perspective, urinary control depends on the proper regulation of *Qi*, *Yin-Yang* balance, and the harmonious functioning of the Kidney, Spleen, Lung, and Liver systems ^{24-27,29}. When these systems become imbalanced, water metabolism is disturbed, leading to the involuntary release of urine during sleep.

TCM classifies CNE primarily into three syndrome patterns (*zheng*):

Kidney *Qi* Deficiency

This is the most frequent pattern in CNE. The Kidney governs growth, bone development, and reproductive functions; in children, much of its energy is directed toward growth, making it prone to deficiency. When Kidney *Qi* is insufficient, the Bladder loses its ability to consolidate urine, resulting in frequent or abundant urination at night ^{24,29,50}. Clinical features include pale complexion, cold limbs, clear urine, and a deep, slow pulse. Emotional instability, especially fear and insecurity, may further weaken the Kidney's control function ^{28,29}.

Constitutional alterations of the Kidney may be present from birth, leading to subsequent deficiency of its *Qi* ^{24,29}. Kidney *Qi* deficiency is considered the primary cause of most CNE cases. This occurs because the Kidney is responsible for bone growth, marrow formation, and brain development, directing a large part of its energy toward the child's growth and maturation. This constant overload can result in energetic deficiency of the Kidney. With the onset of puberty, when growth becomes regulated mainly by hormones, a tendency toward remission of Enuresis is observed. This phenomenon is related to the physiological increase in Kidney *Yang*, characteristic of adolescence ³⁰. Children who present this syndrome generally have a weak constitution, generalised energetic deficiency, low vitality, slow digestion and growth, and greater susceptibility to colds ²⁶. They are frequently described as quiet, shy, distracted, with a tendency toward overweight, and sensitive to cold. From a clinical point of view, they present manifestations such as clear and abundant urine during the day, pale tongue with thin white coating, and deep, thin, or slow pulse, typical signs of a cold deficiency-type syndrome. In more severe cases, cold limbs and intellectual deficit may occur, as Kidney deficiency leads to insufficient marrow production and brain malnutrition, which may be associated with cognitive deficits. In certain cases, Kidney *Qi* deficiency can evolve into Kidney *Yang* deficiency, intensifying the enuresis condition. In this condition, *Yang* becomes unable to warm and sustain bodily functions, resulting in pallor, aversion to cold, and cold extremities, representing more severe stages of the syndrome. What characterises this pattern distinctively is the elimination of a large volume of urine during sleep. Kidney *Qi* deficiency compromises the

Bladder's control function, resulting in failure in water metabolism. This dysfunction explains both the act of urinating involuntarily at night and the increase in daytime urinary volume ^{24,25,50}. The Fire of Ming Men, considered the Original Fire and the vital flame of the organism, constitutes the basis of body heat and is intimately related to Kidney *Yang*. When this Fire weakens, physiological functions become slow, leading to a lack of vital impulse, developmental delay, and inability to contain urine effectively. Furthermore, children present a physiological Heart heat, which can consume Kidney *Yang*. This energetic deficiency prevents the Kidney from adequately controlling the sphincters, favouring the occurrence of enuresis. As Kidney *Yang* is consumed, there is a predominance of *Yin*, characterised by excess fluids, cold, and downward movement of energy, resulting in involuntary urinary elimination ²⁹. Children with this pattern also tend to present insecurity and recurrent fears, factors that may derive both from their constitutional nature and from external influences, such as family, school, or social environment ^{28,29}. The immature Shen contributes to alterations of the *Zhi*, the mental and emotional aspect of the Kidney, associated with courage and fear. Situations of emotional instability, especially frequent fear and stress, weaken Kidney *Qi*, compromising urinary control ²⁹.

Spleen and Lung *Qi* Deficiency

The Spleen governs transformation and transportation of fluids, while the Lung regulates water pathways through dispersing and descending functions. Recurrent respiratory illnesses, poor diet, or medication misuse can weaken these organs, impairing their fluid metabolism and leading to enuresis ^{24,28,50}. Symptoms include fatigue, poor appetite, loose stools, spontaneous sweating, and weak voice. Since the Spleen governs the muscles, its deficiency may reduce sphincter tone, exacerbating urinary. Due to the action of pathogenic factors, each episode of respiratory disturbance alters the metabolism of body fluids, compromising the functions of the Lung and Spleen. In these cases, enuresis tends to be temporary and generally disappears spontaneously after the resolution of the illness. However, there are situations in which the child presents chronic weakness of the Lung, Spleen, and Ming Men, associated with a history of recurrent digestive and respiratory disturbances ²⁸. Clinical manifestations include frequent enuresis with a small amount of urine, constitutional pallor, fatigue, lack of appetite, loose stools, poor digestion, weak chronic cough, debilitated voice, spontaneous sweating, pale tongue, and slow pulse ^{24,50}. Lung deficiency compromises its functions of dispersing and descending body fluids toward the Kidneys, impairing the passage of water and urinary control by the Bladder. Pulmonary debility interferes with the descending function of *Qi*, resulting in shortness of breath and weak cough. Furthermore, the disturbance in the mechanism of opening and closing the pores favours the occurrence of spontaneous nocturnal sweating ⁵¹. In turn, as the Spleen governs the muscles, its deficiency generates an imbalance in muscle tone, including the tone of the muscles responsible for urination control. The functional debility of the Spleen compromises the transportation and transformation of fluids, which can facilitate involuntary urination, especially during sleep, when the body is in a state of relaxation. Additionally, Spleen dysfunction can lead to the accumulation of dampness in the Middle *Jiao*, manifesting through symptoms such as lack of appetite and loose stools. Lung and Spleen *Qi* deficiency also compromises the production of *Qi* and blood, as well as the capacity to transform and transport the essence of food throughout the organism. This dysfunction results in a pale constitution, fatigue, and general decrease in vitality. Due to *Qi* insufficiency, a reduction in blood supply is observed, which manifests clinically through signs such as pale tongue and slow or deep pulse ²⁵.

Damp-Heat in the Liver Meridian

When Liver *Qi* stagnates, often due to emotional tension, diet, or infection, heat and dampness may accumulate in the Lower *Jiao*, disturbing Bladder function ^{28,29,31}. Children with this pattern exhibit irritability, restless sleep, thirst, flushed face, and yellow, strong-smelling urine. The tongue often presents a yellow coating, and the pulse is rapid and

slippery^{24,50,52}. Treatment therefore focuses on clearing heat, resolving dampness, and regulating Liver *Qi*.

These patterns underline how TCM interprets CNE as a systemic imbalance rather than a localised urological dysfunction, emphasising individualised and holistic therapeutic strategies.

The Liver is responsible for ensuring the free circulation of *Qi* throughout the organism, and any interruption in this flow can cause imbalances in other organs. The syndrome in question has as its main aetiology the stagnation of Liver *Qi*, which may result from emotional factors, inadequate diet, or the invasion of wind-cold transforming into heat in the Liver meridian. Frequently, Liver *Qi* stagnation compromises emotional flow, just as emotional imbalances, especially anger and frustration, can negatively affect the energetic function of the Liver³¹. An inadequate diet interferes with the functioning of the Spleen, which begins to perform its functions ineffectively, compromising the metabolism of fluids and favouring the accumulation of dampness-heat, also in the Lower Jiao^{28,29,50,52}.

3.3. Traditional Chinese Therapeutic Approaches for Childhood Nocturnal Enuresis

Throughout TCM history, treatment approaches have evolved according to philosophical and clinical paradigms. The Han Dynasty emphasised warming and tonifying; the Song Dynasty focused on astringency and fluid conservation; and by the Ming Dynasty, syndrome differentiation became central^{53,54}.

Core treatment principles include warming and nourishing Kidney *Yang*, strengthening the Spleen and Lung, harmonising Liver *Qi*, eliminating dampness, and calming the Shen.

Therapeutic modalities applied in Chinese paediatrics include:

- Acupuncture: Activates the Bladder and Kidney meridians, regulating urination and calming the mind. The most frequently employed points include *Zhong Ji* (CV3), *Guan Yuan* (CV4), *Qi Hai* (CV6), *Shen Shu* (BL23), *Ci Liao* (BL32), *Tai Xi* (KI3), *Zu San Li* (ST36), *San Yin Jiao* (SP6), *Tai Chong* (LR3), *Qu Quan* (LR8), *Shen Men* (HT7), *Yin Tang* (EX-HN3), and *Bai Hui* (GV20)^{23,25,27,29,53}.
- Herbal medicine: Formulas such as *Jin Suo Gu Jing Wan*, *Jin Gui Shen Qi Wan*, *Suo Quan Wan*, and *Bu Zhong Yi Qi Wan*, *Zhi Bai Di Huang Wan*, *Long Dan Xie Gan Wan*; tonify Kidney and Spleen *Qi* while regulating bladder function^{25,26}.
- Cupping: Promote *Qi* circulation, eliminate cold, and strengthen *Yang*^{25,29}.
- Auriculotherapy: Stimulates auricular points like *Shen Men*, *Kidney*, *Bladder*, *Subcortex*, and *Tension* to balance *Qi* and regulate emotions^{25,29}.
- Dietary therapy: Uses specific foods and preparation, such as such as cooked rice and pork bladder with *Poria* (Chinese fungus) and lotus seeds is recommended, these having astringent and calming properties, in addition to recipes such as boiled egg with white pepper or chicken liver with cinnamon, indicated to warm and tonify *Yang*. However, caution is necessary due to the risk of irritation in young children²⁸.

Among these, paediatric *Tui Na* is especially valued for its safety, simplicity, and adaptability, making it ideal for children and suitable for integration with other therapies^{23,28,29,51,55,56}.

3.4. Principles and Mechanisms Tui Na

The term *Tui Na* comes from the words "Tui" (to push) and "Na" (to grasp), designating a therapeutic practice that, through body manipulation, promotes energetic and physiological reactions capable of restoring organic balance, strengthening the body.

In TCM, paediatric *Tui Na* is a branch of this technique, used since the Ming and Qing Dynasties in the treatment of various childhood illnesses, in addition to contributing to the strengthening of immunity, also acting in the prevention of common childhood diseases. Unlike the application in adults, paediatric *Tui Na* uses specific points and zones of

the child's body, characterised by lighter, gentler, and more harmonious manoeuvres, yet rapid, vigorous, and stimulating, without causing pain, with an average duration of 2 minutes or 70 to 300 repetitions per point or area ^{26,29,51}. The intensity of the manoeuvres varies according to the child's age and the treated region. This approach is considered highly effective and can be applied alone or in association with other therapies. It stands out for its good acceptance among children, as it is a non-invasive and comfortable technique ^{23,28,29,51,55,56}.

By stimulating acupoints and specific areas, *Tui Na* enhances the flow of *Qi* and *Xue*, clears meridian blockages, tonifies deficiencies, disperses pathogenic factors, and harmonises internal organs. In the context of CNE, it strengthens Kidney *Qi*, regulates Bladder function, harmonises the Lower *Jiao*, and calms emotional agitation that may accompany nocturnal urination ^{25,29,51,57}.

The main manipulative techniques include ^{25,26,28,29,51}:

- *Zhi Tui Fa* (pushing) – stimulate the circulation of *Qi* and *Xue*, unblock the meridians, and reduce pain.
- *An Fa* (pressing) - Its objective is to warm the meridians, calm the mind, favor the free circulation of the collaterals, and relieve pain.
- *Rou Fa* (Kneading or Massaging) – This manoeuvre aims to move *Qi*, activate the circulation of *Xue*, clear the meridians, and favour the unblocking of the organs.
- *Cuo Fa* (Rubbing and Rolling) - promote the regulation of *Qi*, harmonise *Xue*, and relax tendons.
- *Nie Fa* (Pinching the Spine) – It seeks to favor the balance between *Yin* and *Yang*, regulate the circulation of *Qi* and *Xue*, harmonise the internal organs, and tonify deficiencies.
- *Ji Fa* (Pinching and Squeezing). – eliminates stagnation and heat;
- *Ca Fa* (Rubbing) - promotes warming, facilitating the circulation of *Qi* in the meridians, tonifying deficiency, and stimulating original *Yang*.
- *Qie Fa* or *Qia* (Marking) - It has a calming effect, contributing to the reduction of fear and mental agitation, opens passages, drains orifices, and alleviates convulsions and spasms.
- *Yun Fa* (revolving) – harmonises internal organs.

3.5. Therapeutic Points and Meridian Zones in Paediatric *Tui Na* for Childhood Nocturnal Enuresis

In the analysis of the selection of points used in paediatric *Tui Na* for the treatment of CNE ^{23,25,26,28,29,50-52,57-59}, a greater concentration was found in regions corresponding to the *Du Mai* / Governing Vessel (GV) channels, *Ren Mai* / Conception Vessel (CV), Bladder and Spleen meridians, in addition to areas and lines distributed on the hands, forearms, abdomen, and lumbosacral region. These elements are organised below according to their anatomical location (Table 1).

Basic Manipulations

Although there is no absolute consensus in the literature on the adoption of basic manipulations (Table 2) and additional manoeuvres (Table 3), selected according to the differential diagnosis of syndromes, there is a majority tendency among authors to adopt similar approaches as a therapeutic strategy in the treatment of CNE, although some present divergent approaches. All, however, have as a common objective to restore Kidney *Yang*, cultivate essence, tonify the Spleen, invigorate *Qi*, and harmonise the Liver ^{23,25,26,28,29,50-52,57-59}.

Table 1. Anatomical Location of paediatric *Tui na* Points.

Region	Point / Line	Meridian / Channel	Location / Description
Palm & Anterior Forearm	<i>Pi Jing</i>	Spleen	Distal Phalanx Of The Thumb
	<i>Shen Jing</i>	Kidney	Distal Phalanx Of The Fifth Finger
	<i>Gan Jing</i>	Liver	Distal Phalanx Of The Index Finger
	<i>Fei Jing</i>	Lung	Distal Phalanx Of The Fourth Finger
	<i>San Guan</i>	–	Anterior Forearm, Radial Side
	<i>Tian He Shui</i>	–	Anterior Forearm, Central Line
	<i>Liu Fu</i>	–	Anterior Forearm, Ulnar Side
Dorsum Of Hand & Posterior Forearm	<i>Wai Lao Gong</i>	–	Center Of Dorsum Of The Hand
	<i>Er Ma / Er Ren Shang Ma</i>	–	Depression Between 4th And 5th Mcp Joints
	<i>Bo Yang Chi</i>	–	3 <i>Cun</i> Above Center Of Wrist Extensor Crease
Abdomen	<i>Fu Yin Yang</i>	–	Line Below Costal Margins
	<i>Shen Que / Qi Zhong (Cv8)</i>	Conception Vessel	At The Navel
	<i>Qi Hai (Cv6)</i>	Conception Vessel	Anterior Midline, 1.5 <i>Cun</i> Below Navel
	<i>Dan Tian</i>	–	Pubic Region, Between Navel & Pubic Bone
	<i>Zhong Ji (Cv3)</i>	Conception Vessel	Anterior Midline, 4 <i>Cun</i> Below Navel
	<i>Qu Gu (Cv2)</i>	Conception Vessel	Upper Border Of Pubic Bone, Central
Dorsal Region	<i>Ji Zhu</i>	–	Over Spinal Column, C7 To Coccyx
	<i>Fei Shu (Bl13)</i>	Bladder	1.5 <i>Cun</i> Lateral To T3 Spinous Process
	<i>Xin Shu (Bl15)</i>	Bladder	1.5 <i>Cun</i> Lateral To T5 Spinous Process
	<i>Gan Shu (Bl18)</i>	Bladder	1.5 <i>Cun</i> Lateral To T9 Spinous Process
	<i>Pi Shu (Bl20)</i>	Bladder	1.5 <i>Cun</i> Lateral To T11 Spinous Process
	<i>Wei Shu (Bl21)</i>	Bladder	1.5 <i>Cun</i> Lateral To T12 Spinous Process
	<i>Shen Shu (Bl23)</i>	Bladder	1.5 <i>Cun</i> Lateral To L2 Spinous Process
	<i>Ming Men (GV4)</i>	Governing Vessel	Posterior Midline, Below L2 Spinous Process
	<i>Qi Jie Gu</i>	–	Line From Coccyx Tip To L4
	<i>Pang Guang Shu (Bl28)</i>	Bladder	1.5 <i>Cun</i> Lateral To S2
	<i>Ba Liao</i>	–	Sacrum, 4 Sacral Foramina Each Side
	<i>Gui Wei (GV1)</i>	Governing Vessel	Lower End Of Coccyx
Lower Limbs	<i>Zu San Li (St36)</i>	Stomach	3 <i>Cun</i> Below Patella, 1 <i>Cun</i> Lateral To Tibia
	<i>San Yin Jiao (Sp6)</i>	Spleen	Medial Leg, 3 <i>Cun</i> Above Medial Malleolus
	<i>Tai Chong (LR3)</i>	Liver	Dorsum Of Foot, Between 1st & 2nd Metatarsals
	<i>Yong Quan (KI1)</i>	Kidney	Depression On Sole, Anterior 1/3 To Middle 1/3
Head	<i>Bai Hui (GV20)</i>	Governing Vessel	Top Of Head, centre Line Connecting Ears

The clinical literature offers accumulating evidence that paediatric massage, often combined with adjunctive TCM techniques, may enhance therapeutic outcomes in childhood enuresis. For example, Lou ⁵⁵ found that children receiving paediatric massage combined with moxibustion and acupoint application achieved improved rates of continence compared to standard care, indicating a synergistic effect of manual therapy plus heat and acupoint stimulation. Wang *et al.* ⁵⁶ demonstrated that meridian-viscera massage combined with moxibustion in children with spleen- and Kidney-deficiency subtype of enuresis resulted in clinically meaningful improvements in nocturnal bed-wetting, thereby aligning treatment to TCM pattern differentiation. Su *et al.* ⁶⁰ reported short- and long-term efficacy of massage in primary enuresis in children, noting sustained benefits and low relapse rates over follow-up. Yan ⁶¹ focused on the renal-*Qi* deficiency subtype, applying *Tui Na* for “warming the Kidney and strengthening the spleen” and documented

favourable responses in enuretic children. Wang *et al.*⁶² used data-mining to analyse acupoint selection rules in massage treatments for paediatric enuresis, revealing consistent patterns in point usage (e.g., Kidney and Bladder meridian acupoints) that support protocol standardisation. Su *et al.*⁵⁹ reviewed the status of research on *Tui Na* for paediatric enuresis, highlighting methodological limitations (small sample sizes, short follow-up, heterogeneity) but nevertheless confirming clinical promise.

Table 2. Basic *Tui Na* Manipulations Used in the Treatment of paediatric Enuresis.

Point / Line	Meridian / Channel	Manipulation / Technique	Therapeutic Purpose
<i>Shen Jing</i>	Kidney	Slide With Tip Of Thumb Distal → Proximal	Tonify Kidney
<i>Pi Jing</i>	Spleen	Slide With Tip Of Thumb Distal → Proximal	Strengthen Spleen, Eliminate Dampness
<i>Wai Lao Gong</i>	–	Circular Pressing	Disperse Cold, Warm Lower <i>Jiao</i>
<i>San Guan</i>	–	Push With Index & Middle Fingers From Wrist To Elbow	Harmonise <i>Qi</i> , Strengthen <i>Yang</i> , Cultivate <i>Jing</i> , Disperse Bladder Cold
<i>Fu Yin Yang</i>	–	Slide With Thumbs From Center Outward	Strengthen Spleen
<i>Shen Que</i> (Cv8)	Conception Vessel	Circular Movements With Palm	Warm <i>Yang</i> , Strengthen Spleen, Tonify Deficiencies
<i>Dan Tian</i> (Cv4)	–	Circular Kneading With Palm Base	Tonify Kidney, Tonify Lower <i>Jiao</i>
<i>Zhong Ji</i> (Cv3)	Conception Vessel	Kneading	Strengthen Kidney, Nourish Essence
<i>Qu Gu</i> (Cv2)	Conception Vessel	Press & Rotate	Tonify Kidney, Tonify Lower <i>Jiao</i>
<i>Shen Shu</i> (Bl23)	Bladder	Circular Movements On Dorsal Shu	Tonify Kidney & <i>Jing</i>
<i>Pang Guang Shu</i> (Bl28)	Bladder	Circular Movements On Dorsal Shu	Strengthen Bladder Function
<i>Ming Men</i> (GV4)	Governing Vessel	Rub Palms & Place Over Point	Warm Region, Tonify Original <i>Qi</i> , Strengthen Kidney <i>Yang</i>
<i>Qi Jie Gu</i>	–	Push Upward	Tonify Deficiencies
<i>Gui Wei</i> (GV1)	Governing Vessel	Circular Kneading	Warm <i>Yang</i> , Calm Fear
<i>Ji Zhu</i>	–	Pinch & Roll Along Spine; Bottom → Top (Deficiency), Top → Bottom (Excess)	Harmonise <i>Zang-Fu</i> , Regulate Yin-Yang, Regulate <i>Qi</i> & <i>Xue</i>
<i>San Yin Jiao</i> (Sp6)	Spleen	Press & Rotate	Strengthen Liver, Kidney, Spleen; Disperse Dampness-Heat; Regulate Lower Burner
<i>Zu San Li</i> (St36)	Stomach	Press	Regulate & Strengthen <i>Qi</i> Of Middle Burner, Increase <i>Yang</i> , Eliminate Dampness/Cold, Strengthen Body & Immunity
<i>Bai Hui</i> (GV20)	Governing Vessel	Circular Pressing	Tonify <i>Jing</i> , Calm Mind, Soothe Fear

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Table 3. Additional paediatric Tuina Manipulations According to Syndrome Differentiation.

Syndrome / Pattern	Point / Line	Meridian / Channel	Manipulation / Technique	Therapeutic Purpose
Kidney <i>Qi</i> Insufficiency	<i>Er Ma</i> (Two Horses)	–	Circular Pressing	Recover <i>Yang</i> , Promote <i>Qi</i> Circulation, Tonify Kidney
	<i>Ba Liao</i> (Eight Sacral Orifices)	–	Rub With Palm Until Warm	Tonify, Warm, Consolidate Lower <i>Jiao</i>
	<i>Yong Quan</i> (KI1)	Kidney	Press	Tonify <i>Qi</i> & Essence, Restore Energetic Balance
Spleen and Lung <i>Qi</i> Deficiency	<i>Fei Jing Line</i>	Lung	Slide With Thumb Distal → Proximal	Strengthen Lung Function
	<i>Fei Shu</i> (BL13)	Bladder	Circular Pressing	Tonify Lung <i>Qi</i>
	<i>Xin Shu</i> (BL15)	Bladder	Circular Pressing	Regulate Heart <i>Qi</i>
	<i>Pi Shu</i> (BL20)	Bladder	Circular Pressing	Tonify Spleen, Disperse Dampness
	<i>Wei Shu</i> (BL21)	Bladder	Circular Pressing	Tonify Stomach
Dampness-Heat in Liver Meridian	<i>Gan Jing Line</i>	Liver	Slide Thumb Proximal → Distal	Harmonise Liver, Eliminate Heat, Calm Fear
	<i>Liu Fu Line</i>	–	Push With Index & Middle Fingers Elbow → Wrist	Favours Viscera Function, Cool Heat
	<i>Tian He Shui Line</i>	–	Slide Wrist → Elbow	Eliminate Heat, Dissipate Dampness, Calm Mind & Fear
	<i>Bo Yang Chi</i>	–	Circular Pressing	Disperse Heat
	<i>Yong Quan</i> (KI1)	Kidney	Press	Eliminate Heat, Decrease Irritability
	<i>Tai Chong</i> (LR3)	Liver	Press	Subdue Liver <i>Yang</i> , Move <i>Qi</i> , Eliminate Dampness
	<i>Si Heng Wen</i> (Four Transverse Creases)	–	Push, Pinch, Knead Palmar Mcp Joints 2nd–5th Fingers	Effective For Dampness-Heat Liver Type

Together, these studies corroborate the meta-analytical findings that *Tui Na* is a promising adjunctive therapy for childhood nocturnal enuresis²³ by showing: (1) integration with moxibustion and acupoint application appears to enhance efficacy^{55,56}, (2) pattern-based protocol design (renal-*Qi* deficiency, Spleen-Kidney *Yang* deficiency) improves alignment with TCM theory and likely outcomes^{61,62}, and (3) manual massage interventions may deliver sustained benefits over time⁵⁹. However, persistent limitations remain: many of the studies are not randomised controlled trials, sample sizes are modest, follow-up durations are short, and there is frequent lack of objective mechanistic data or blinding, issues also flagged by the systematic review²³.

4. Final Remarks and Conclusions

CNE remains a common paediatric condition with complex, multifactorial origins that encompass physiological, emotional, and developmental factors. Beyond its physical manifestations, the disorder significantly impacts a child's self-esteem, confidence, and family relationships. Conventional medicine provides behavioural and pharmacological strategies with variable outcomes and frequent relapse after treatment cessation. Consequently, integrative approaches that consider both physiological and psychosocial dimensions have gained increasing importance.

Within TCM, paediatric *Tui Na* emerges as a particularly valuable therapeutic tool. Based on the principles of energetic balance, it regulates the flow of *Qi* and *Xue*, strengthens the Kidney, Spleen, and Bladder functions, and harmonises *Yin* and *Yang*. The evidence summarised in this narrative review demonstrates that paediatric *Tui Na* effectively reduces the frequency of enuretic episodes, improves bladder control, enhances sleep quality, and contributes to emotional stability and self-esteem in children.

Furthermore, *Tui Na* offers practical advantages: it is non-invasive, well accepted by children, and can be taught to parents or caregivers, allowing continuity of treatment at home. This participatory approach strengthens the emotional bond between caregiver and child, promoting comfort, trust, and therapeutic adherence, elements crucial for successful outcomes.

Despite its longstanding tradition and encouraging clinical evidence, paediatric *Tui Na* remains underexplored in Western medicine. The current scarcity of large-scale, methodologically rigorous clinical trials highlights the need for further research to substantiate its mechanisms of action and optimise treatment protocols. Future studies should aim to integrate traditional diagnostic frameworks with modern evidence-based methodologies, ensuring broader acceptance and applicability within paediatric healthcare systems.

In conclusion, paediatric *Tui Na* represents a promising, safe, and effective integrative therapy for childhood nocturnal enuresis, addressing both physiological and emotional dimensions of the disorder. It exemplifies the potential of traditional therapies to complement contemporary paediatric medicine, fostering a holistic, patient-centred model of care.

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Review

Integrating Traditional Chinese Medicine into Endurance Sports: A Narrative Review of Evidence and Applications.

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Abstract

Background: Traditional Chinese Medicine (TCM) is a holistic medical system with millennia-old theoretical foundations, including the *Huangdi Neijing* and other classical texts. TCM emphasises the balance of *Qi*, blood, and organ systems, offering potential complementary strategies for athlete recovery, performance optimisation, and injury prevention.

Objective: This review evaluates the application of TCM modalities, including acupuncture, moxibustion, cupping therapy, *Tuina*, and *Qigong*, in endurance sports, focusing on physiological, neuromuscular, and psychophysiological outcomes.

Methods: Evidence was synthesised from randomised controlled trials, pilot studies, systematic reviews, and mechanistic investigations addressing the effects of TCM interventions on endurance capacity, recovery, musculoskeletal rehabilitation, immune function, hormonal modulation, and psychological resilience.

Results: TCM modalities offer complementary benefits for athletes. Acupuncture may enhance endurance, recovery, and neuromuscular function. Cupping primarily improves tissue flexibility and reduces fatigue markers. Moxibustion supports muscle recovery, immune modulation, and hormonal balance. Auricular acupuncture and vagal nerve stimulation aid cardiovascular recovery and coordination. *Qigong* promotes psychological well-being, body composition, and immune regulation. *Tuina* enhances musculoskeletal rehabilitation, particularly when combined with exercise.

Conclusion: TCM offers a multifaceted, complementary framework for supporting endurance athletes by addressing recovery, physiological stress, and holistic performance optimisation. While preliminary evidence indicates potential benefits across multiple domains, robust, high-quality randomised trials are required to standardise protocols, validate efficacy, and clarify underlying mechanisms.

Keywords: Traditional Chinese Medicine; Endurance Athletes; Acupuncture; Moxibustion; Cupping Therapy; *Tuina*; *Qigong*; Athlete Recovery; Performance Optimisation.

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1. Introduction

TCM is one of the oldest and most comprehensive medical systems in the world, deeply rooted in the philosophical and cultural traditions of China. Its foundations are described in classical medical texts such as the *Huangdi Neijing* (*Yellow Emperor's Classic of Internal Medicine*), dating from between the 3rd and 5th centuries BCE, which outlines early understandings of physiology, including blood circulation regulated by the heart. This knowledge predate Western anatomical discoveries by over a millennium ^{1,2}. Other seminal works, including *Shang Han Lun* (*Treatise on Cold Damage*) by Zhang Zhong Jing (2nd century CE), introduced the principle of disease classification based on patterns of

symptoms, and the *Shen Nong Ben Cao Jing*, an early pharmacopoeia describing 365 medicinal substances and the Eight Principles of diagnosis ^{3,4}.

These texts established the theoretical basis of an integrative and systematic medical model encompassing diagnostic and therapeutic frameworks that continue to guide clinical practice today ⁵. In TCM theory, health is understood as the dynamic balance of vital energy (*Qi*), blood (*Xue*), and organ systems (*Zang-Fu*), influenced by environmental, emotional, and lifestyle factors ⁶. This holistic understanding has increasingly drawn attention in Western sports medicine for its potential to complement biomedical approaches, especially in the context of high-performance athletics ⁷⁻⁹.

Elite athletes are routinely exposed to physiological and psychological stressors (intense training loads, competitive pressure, travel, and environmental variation) that may lead to homeostatic imbalance, overtraining, fatigue, immune suppression, sleep disturbances, and recurrent injuries ¹⁰. Conventional biomedical interventions often provide limited relief for these multifactorial syndromes, creating space for integrative approaches such as TCM to contribute to performance optimisation and recovery ^{11,12}.

TCM modalities including acupuncture, cupping therapy, moxibustion, *Tuina* (therapeutic massage), *Qigong*, and dietotherapy are increasingly employed in sports rehabilitation and prehabilitation to restore balance, improve circulation, support weakened systems, and prevent injury ¹³⁻¹⁵. For instance, acupuncture has demonstrated measurable effects on endurance, muscle recovery, and hormonal regulation, while *Qigong* and *Tai Chi* practices promote psychophysiological balance through controlled breathing, movement, and meditation ¹⁶⁻¹⁸.

According to TCM theory, physical activities such as running mobilise *Qi* and blood circulation but may also deplete the *Spleen*, *Liver*, and *Kidney* systems when performed excessively, leading to fatigue, muscle weakness, or tendon vulnerability ³. Therefore, TCM emphasises balancing active training with restorative practices, appropriate footwear, and attention to meridians originating in the feet, such as the Kidney Meridian (*Shaoyin*) beginning at point KI1 (*Yongquan*) and the Liver Meridian (*Jueyin*) starting at LV1 (*Dadun*), which are believed to play a key role in grounding energy and maintaining musculoskeletal integrity ¹⁹⁻²⁴.

Therefore, this article aims to explore the integration of TCM concepts into high-performance sports and understand if TCM techniques can enhance recovery, modulate physiological stress, and maintain energetic balance.

2. Results and Discussion

2.1. Acupuncture

Acupuncture has been investigated for potential effects on multiple aspects of athletic performance and recovery, but the existing evidence base is preliminary, heterogeneous, and in many cases inconclusive.

In endurance performance, one randomised study demonstrated that acupuncture training (8 sessions over 4 weeks) improved 3 km running performance and increased speed at the ventilatory threshold compared with baseline values in healthy recreational runners, suggesting a possible enhancement in endurance capacity after repeated acupuncture application ¹⁸. A controlled field trial also reported that runners receiving acupuncture showed greater improvements in running time and a composite “complexity factor” (running time × heart rate measures) than placebo or control groups, although interpretation is limited by study design and reporting quality ²⁵. Overall, these studies suggest *potential* benefits of acupuncture on running performance, but results should be viewed with caution due to small sample sizes and methodological limitations ²⁶.

Regarding recovery outcomes, preliminary research indicates that acupuncture at acupoints such as PC6 and ST36 may be associated with faster post-exercise heart rate and lactate recovery compared with sham or no acupuncture, particularly in trained athletes after exhaustive exercise ²⁷. A pilot case study with a small sample also reported that acupuncture applied after a cycling sprint test might enhance lactate removal at 30 and

60 minutes post-exercise, although larger controlled studies are needed ²⁸. These outcomes align with systematic review findings that some trials using PC6 and ST36 have shown reductions in lactate and heart rate versus control at later recovery time points, but the overall evidence is inconsistent ²⁶.

Evidence on strength, power, and anaerobic performance is sparse and mixed. Some small studies and observational work have reported immediate increases in measures such as explosive strength or vertical jump height following stimulation of acupuncture or acupressure points (e.g., ST36), but these findings have typically lacked appropriate control conditions or rigorous blinding, and have not been widely reproduced ^{29,30}. Systematic reviews note the limitations of the literature and the need for adequately powered randomised controlled trials before definitive conclusions can be drawn about effects on muscle performance, sprinting, or power output ²⁶.

Some research has explored neurophysiological effects of acupuncture at points such as ST36, indicating changes in motor cortical excitability, but the implications of these findings for functional athletic performance remain uncertain ³¹.

In summary, while individual trials and case studies have reported outcomes such as improved endurance times, enhanced lactate clearance, and modulations of cardiovascular recovery, the current evidence does not consistently support robust performance enhancements across diverse athletic domains. Most studies are limited by small sample sizes, inconsistent methodologies, and heterogeneous intervention protocols. Accordingly, acupuncture may hold promise as an adjunct for certain recovery or physiological responses, but further high-quality, blinded, and adequately powered trials are required to determine its true efficacy as an ergogenic aid in both endurance and resistance training contexts ²⁶.

2.2. Cupping Therapy

Recent quantitative and mechanistic information from multiple studies provides evidence for some physiological effects of cupping therapy in athletic populations. The application of cupping therapy to the dorsal *Shu* points resulted in a greater decrease in serum creatine kinase (CK) levels as compared to the control group, indicating a marked decrease in muscular fatigue and enhanced recovery following exertion ^{32,33}.

Hematologic profile information from Abdelfattah *et al.* ³⁴ reported significant increases in total white blood cell (WBC) count and increased numbers of neutrophils and lymphocytes during four weeks of wet cupping therapy in athletes. Additionally, a significant increase in red blood cell (RBC) count and haemoglobin concentration and an increase in packed cell volume (PCV) were also evident, reflecting enhanced oxygen-carrying capacity and tissue perfusion. There were no statistically significant differences in mean corpuscular volume (MCV), mean corpuscular haemoglobin (MCH) or mean corpuscular haemoglobin concentration (MCHC), indicating there was no change in erythrocyte shape or function. The platelet count and mean platelet volume (MPV) count also remain stable.

For inflammatory analysis, cupping therapy decreased monocyte-to-lymphocyte (MLR) and platelet-to-lymphocyte (PLR) ratios, both of which are recognised prognostic information for systemic inflammation. There were no changes to the neutrophil-to-lymphocyte ratio (NLR) after cupping therapy intervention.

In addition to systemic and haematological effects, cupping therapy has demonstrated meaningful impacts on flexibility and joint mobility in athletic populations. The study by Corrêa *et al.* ³⁵ evaluated lower limb chain dry cupping in male football athletes and reported significant improvements in knee extension and ankle dorsiflexion after four sessions, although no changes were observed in hip flexion or pressure pain threshold. These results suggest that cupping therapy can enhance joint range of motion even in well-trained athletes, potentially facilitating dynamic movements, reducing muscular stiffness, and supporting injury prevention.

When considered alongside other interventions, such as moving cupping therapy applied to the posterior lower limb ³⁶, which also improved hip and knee range of motion without immediate increases in muscle power, these findings support the notion that cupping therapy primarily influences tissue extensibility and joint mobility rather than immediate contractile performance. Collectively, evidence from these studies highlights the utility of cupping therapy as an adjunct for enhancing functional flexibility and recovery in athletes, while suggesting that additional modalities may be needed to directly affect strength or pain modulation.

2.3. Moxibustion

Moxibustion, a therapeutic technique used in TCM, shows some promise in the prevention and treatment of sports fatigue. Kimura *et al.* ¹⁵ reported full symptom resolution in water polo athletes following treatment with acupuncture and moxibustion on dorsal Shu points, as well as site-specific pain points.

Gao *et al.* ³⁷ examined molecular immune modulation provided by moxibustion stimulation on *Guanyuan* (CV4), *Zusanli* (ST36), and *Sanyinjiao* (SP6). In trained male runners, moxibustion was shown to modulate the balancing expression of the mRNA transcription factors T-bet (Th1) and GATA-3 (Th2), which indicated that moxibustion enhanced immune modulation compared to controls by favouring a contained Th1 immune response, while avoiding harmful Th2 rebound effects observed in controls.

Li *et al.* ³⁸ assessed the effects of moxibustion on table tennis athletes at acupoints *Shenshu* (BL23) and *Guanyuan* (CV4), reporting improved erythrocyte immune function, as indicated by enhanced RBC-C3b binding and diminished immune complex binding RBC-ICR, and evidenced a significant increase in T lymphocyte subsets (CD3, CD4) respect to control in the same group; hence, it was concluded moxibustion has an enhancing effect on both innate and adaptive immune responses in athletes undergoing a regime of intensified exercise training.

Studies indicate that moxibustion on specific acupoints significantly increases serum testosterone levels in male athletes after intensive training, compared to control groups who do not receive moxibustion. High-load exercise can cause a decline in blood testosterone, and moxibustion appears to counteract this effect.³⁹⁻⁴¹

Lastly, the effects of moxibustion on recovery from muscle fatigue showed that indirect moxibustion at the LR9 (*Yinpo*) led to a significant enhancement in the median frequency recovery of electromyographic wave patterns, and also normalised peak torque in the isokinetic knee fatigue study, showing improved recovery of muscle performance after forced exercise interruptions ⁴².

Finally, Tang *et al.* ⁴³ compared an acupuncture–moxibustion intervention with conventional physiotherapy in athletes with lateral collateral ligament injury of the ankle. After eight weeks of treatment, the acupuncture–moxibustion group demonstrated significantly greater improvements in ankle proprioceptive function, as evidenced by reduced joint repositioning error, compared with the physiotherapy group, indicating a beneficial effect on sensorimotor recovery following ligamentous injury. In summary, these studies confirm that moxibustion provides multi-faceted benefits to athletes in the context of performance and recovery by modulating the immune system, hormonal system, muscle fatigue recovery, and proprioception indicating the potential of moxibustion as a valuable adjunct therapy for athlete care and rehabilitation.

2.4. Auricular Acupuncture and AVNS

Auricular acupuncture (AA) takes advantage of the somatotopic mapping of the ear to different body regions and has experimentally been studied as a treatment to enhance recovery and performance in athletes. Lin *et al.* ⁴⁴ conducted a randomised controlled study with 24 male basketball athletes assigned to either an auricular acupuncture group (AAG) or a normal control group (NCG). The AAG received magnetic pellets applied to auricular points including *Shenmen* (vertical), heart, lung, liver, triple warmer, subcortex,

and pituitary. Following exhaustive cycling exercise, the AAG exhibited significantly lower maximal heart rate (HRmax) and blood lactate levels at 30 and 60 minutes post-exercise compared with the NCG, indicating accelerated cardiovascular and metabolic recovery. Peak oxygen consumption (VO₂max) was also significantly lower in the AAG at 30 minutes post-exercise, suggesting improved efficiency of oxygen utilisation during recovery. No significant differences were observed at 5 minutes post-exercise, indicating that the effects of auricular acupuncture became evident during later stages of post-exercise recovery.

Auricular vagal nerve stimulation (AVNS) alters the balance of the autonomic nervous system by stimulating the auricular branch of the vagus nerve. Caliota *et al.*⁴⁵ conducted an open-label randomised controlled trial to assess the acute effects of a single session of noninvasive auricular vagus nerve stimulation (AVNS) compared with sham stimulation in elite athletes. After AVNS, within-group measures showed significant reductions in heart rate and improved lower limb balance as assessed by the modified Star Excursion Balance Test, but between-group comparisons for quadriceps isometric strength and grip strength did not achieve statistical significance. These findings suggest that while a single AVNS session may acutely influence autonomic and balance parameters, it does not produce significant acute effects on key muscular performance metrics relative to sham stimulation.

Overall, AA and AVNS have the potential to improve autonomic recovery, reduce indices of fatigue, and improve neuromuscular coordination to emphasise the advantages of non-invasive neural enhancement therapies when combined into sports recovery strategies.

2.5. Qigong

TCM adopts a comprehensive method towards enhancing the performance of endurance athletes and their recovery from strenuous exercise with a focus on moving vital energy in a balanced system. One of the treatment approaches TCM provides is *Qigong*, which incorporates mind-body practice combining slow movement patterns, attentive breathing, meditation-focused thought, and relaxation for the purpose of optimum physical and emotional health⁴⁶⁻⁴⁸.

Research by Johansson *et al.*⁴⁹ has demonstrated that a single session of *Qigong* exercise can produce immediate psychological benefits, including enhanced positive mood and reduced state anxiety, with similar effects observed for both 30-minute and 60-minute practice durations. These findings suggest that even brief *Qigong* sessions may confer emotional benefits, which is particularly relevant for endurance athletes who experience prolonged physical stress and may derive support in developing psychological resilience.

In addition to psychological health, *Qigong* has been shown to provide a clinical value in many areas which are particularly relevant to endurance athletes, such as blood pressure, glycaemic regulation, chronic musculoskeletal pain and cardiac benefits^{47,50}. A systematic review by Oh *et al.*⁵¹ evaluated the effects of Tai Chi and *Qigong* on immune function and inflammatory biomarkers, reporting that these practices were associated with modest increases in overall immune cell levels compared with control conditions. Although pooled analyses did not demonstrate statistically significant changes in systemic pro-inflammatory cytokines or natural killer cell activity, trends in several markers suggest potential immunoregulatory effects. Such immunomodulatory responses may be relevant to endurance athletes, for whom training-related inflammatory processes are linked to prolonged physiological stress.

A systematic review and meta-analysis by Larkey *et al.*⁵² evaluated randomised controlled trials of Tai Chi and *Qigong* and reported that, compared with inactive control conditions, regular practice of these meditative movement modalities was associated with a small-to-medium reduction in body mass index, reflecting potential benefits for body composition. Such effects may have relevance for endurance athletes, as reduced BMI and

improved body composition are associated with enhanced endurance capacity and lower injury risk.

Together, these aspects highlight the importance of utilising *Qigong* as an approach in TCM-based practice to enhance endurance sports performance, with respect to both physiological and psychological strategies, in one model of performance. The holistic benefits of *Qigong* are also in accordance with beliefs espoused in TCM theory, which suggest the movement, practice, and incorporation of *Qigong* expands the scopes of balance and energy work, allowing for greater safety, accessibility, and multiple options, to effectively help an individual's performance in endurance sports while promoting health in any model.

2.6. Tuina

Tuina, a traditional Chinese manual therapy, has been investigated for its effects on sports-related musculoskeletal conditions and rehabilitation outcomes. A randomised controlled clinical study by Su *et al.*⁵³ involving 93 patients with grade I–II meniscal injury found that *Tuina*, functional training, and their combination all produced significant improvements in clinical symptoms and balance measures after an 8-week intervention period. The combination of *Tuina* plus functional training demonstrated greater improvement in overall Knee Injury and Osteoarthritis Outcome Score (KOOS), as well as enhanced daily living and sports/recreation subscale scores versus functional training alone. However, no statistically significant between-group differences in balance performance (Y-Balance Test) were observed at study conclusion.

Preliminary evidence suggests that *Tuina* may enhance tissue microcirculation and support neuromuscular function, which has been proposed to mitigate muscle atrophy following peripheral nerve injury and to contribute to recovery processes in various soft-tissue conditions; however, high-quality mechanistic studies in sports populations are limited.

In the context of lumbar disc herniation, multicentre randomised evidence has recently begun to emerge. A large clinical trial reported that *Tuina* combined with traditional Chinese exercises (TCEs) produced superior improvements in disability, pain, quality of life, and gait parameters compared with TCEs alone through 24 weeks of follow-up, indicating potential utility as an adjunctive rehabilitation modality for symptomatic LDH⁵⁴.

Several other LDH-related trials and protocols are currently underway, including assessor-blinded multicentre RCTs designed to further evaluate *Tuina* plus exercise versus exercise alone for functional disability and pain, which will add rigorous evidence once published⁵⁵.

For knee osteoarthritis, a recent randomised trial comparing *Tuina* therapy with manual physical therapy found that *Tuina* produced similar benefits in joint pain and function, with some outcomes favouring *Tuina* at intermediate follow-up time points, though the overall pattern was of comparable clinical effectiveness between treatments⁵⁶.

Overall, existing clinical evidence indicates that *Tuina*, whether used alone or in combination with exercise or adjunct modalities, can improve symptoms and functional outcomes in musculoskeletal conditions relevant to sports rehabilitation. However, further high-quality randomised controlled trials are needed to standardise intervention protocols, determine dose–response relationships, and elucidate underlying physiological mechanisms.

3. Conclusion

TCM provides a valuable complementary toolkit that addresses the complex demands faced by endurance athletes, to support a balanced, resilient, and optimised performance and health state. This integration into the field of sports medicine affords opportunity to decrease dependence on pharmaceutical support within the therapeutic practices, while also enhancing the whole health and performance of the athlete at a sustained

high level of functioning. More research is needed to fully understand the potential of TCM in endurance athletes.

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Review

Acupuncture and Herbal Medicine in COPD: Efficacy on Functional Performance and Systemic Inflammation.

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Abstract

Objective: To summarise the clinical efficacy of Acupuncture and Chinese Herbal Medicine as complementary therapies for stable Chronic Obstructive Pulmonary Disease (COPD), focusing on symptomatic, functional, and systemic outcomes.

Key Findings: Acupuncture - Highly effective for immediate symptomatic relief, significantly reducing dyspnoea (mMRC, Borg scale) and improving exercise capacity (6MWD gains of +67.4 m to +80.1 m). Its primary mechanism is linked to neuro-modulation and improved respiratory muscle efficiency. Herbal Medicine - Provides a sustained and systemic benefit, leading to clinically significant improvements in quality of life (SGRQ reductions > 4 points) and robust reduction in acute exacerbation frequency. Efficacy is supported by its immunomodulatory action, reducing inflammatory markers (IL-8, TNF-alpha). Pulmonary Function - Neither therapy consistently reversed structural lung damage; improvements in FEV1 and FVC were modest, suggesting their main impact is on stability and symptomatic experience, not mechanics.

Conclusion: Acupuncture and Herbal Medicine are complementary and effective adjuvant therapies for COPD. Acupuncture excels in acute functional gains and dyspnoea relief, while herbal medicine ensures systemic stability and sustained quality of life improvement. Integration of both with conventional treatment is recommended for a comprehensive approach.

Keywords: COPD; Quality of Life; Acupuncture; Herbal Medicine.

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1. Introduction

1.1. Chronic Obstructive Pulmonary Disease

COPD is a heterogeneous respiratory pathology and one of the leading causes of death worldwide. It is characterised by persistent and generally progressive obstruction of airflow, resulting from changes in the airways (bronchitis/bronchiolitis) and/or in the pulmonary alveoli (emphysema). The respiratory system, in conjunction with the circulatory system, has the main functions of exchanging oxygen and carbon dioxide, regulating body temperature, and defending against external agents. It is composed of the upper and lower airways down to the alveoli, where gas exchange (haematosmosis) occurs¹⁻³.

The development of COPD results from the interaction between genetic, individual, and environmental factors. Internal factors include premature birth, childhood respiratory diseases, premature lung ageing, gender, ethnicity, and comorbidities. Alpha-1 antitrypsin deficiency is the main associated genetic factor, especially in pulmonary emphysema, and up to 60% of individual susceptibility can be attributed to heredity^{4,5}. External

factors include smoking (responsible for around 90% of cases), atmospheric pollution, occupational and domestic exposures, in addition to socioeconomic determinants and unequal access to healthcare ^{6,7}.

Clinically, COPD manifests with progressive dyspnoea, chronic cough, persistent expectoration (sputum), wheezing, and chest tightness, often accompanied by fatigue, weight loss, muscle weakness, peripheral oedema, and cognitive changes in the most severe cases. Acute exacerbations, usually triggered by respiratory infections or pollution, are characterised by the sudden worsening of dyspnoea, cough, and expectoration. They may require hospitalisation, contributing to disease progression, increased mortality, and poorer quality of life ⁸⁻¹⁰.

Conventional treatment includes pharmacotherapy and pulmonary rehabilitation. Medications include long-acting bronchodilators – long-acting beta-agonists (LABA) and long-acting muscarinic antagonists (LAMA), inhaled corticosteroids (ICS), ensifentrine, macrolide antibiotics in selected cases, and biological therapies targeting specific inflammatory phenotypes ¹¹. Despite their effectiveness in symptomatic control, these drugs have a limited impact on reducing mortality and are associated with adverse effects ¹²⁻¹⁴. Inhaler therapy is central, but its effectiveness depends on the correct use of the devices, which are pressurized metered-dose inhalers (pMDIs), pMDIs with a spacer device, and dry powder inhalers (DPIs). However, usage errors are frequent and compromise the clinical outcome ¹⁵.

Oxygen therapy is indicated in different contexts: long-term oxygen therapy (LTOT) for severe hypoxaemia, ambulatory use during exertion, nocturnal use in cases of desaturation during sleep, acute use during exacerbations, as well as in innovative modalities such as portable oxygen concentrators (POCs) and high-flow nasal cannula (HFNC) in a hospital setting ¹⁶⁻²⁰. In cases of respiratory failure, mechanical ventilation is used, either invasive (invasive mechanical ventilation, VMI) via intubation or tracheostomy, or non-invasive (non-invasive ventilation, VNI), the latter associated with lower morbidity and mortality ²¹⁻²⁴. Pulmonary rehabilitation (PR), defined by the American Thoracic Society (ATS) and the European Respiratory Society (ERS), constitutes a comprehensive intervention that combines physical training, education, and psychological support, with a positive impact on exercise tolerance and quality of life. However, adherence is often limited due to the repetitive nature of the training and associated costs ²⁵⁻²⁹.

In more advanced cases, surgical options are used. Lung volume reduction surgery (LVRS) can improve respiratory mechanics in severe emphysema, especially heterogeneous emphysema in the upper lobes, although it involves risks such as prolonged air leak and cardiac complications ³⁰⁻³³. Bullectomy is indicated in the presence of giant bullae that compress healthy parenchyma, reducing dyspnoea and improving function, but is also associated with post-operative complications ³⁴⁻³⁷. Lung transplantation, unilateral or bilateral, remains reserved for terminal cases and can improve survival and quality of life, despite the limitation due to organ scarcity ³⁸⁻⁴¹.

From an epidemiological point of view, COPD constitutes a global public health emergency, with high direct and indirect costs ^{42,43}. In Portugal, in 2020, it was responsible for 2,600 deaths, with a mortality rate of 8.7 per 100,000 inhabitants ⁴⁴. Underdiagnosis, low adherence to pulmonary rehabilitation, and inequality in access to care continue to worsen the burden of the disease ^{45,46}.

COPD is also associated with frequent comorbidities, such as cardiovascular diseases, osteoporosis, diabetes mellitus, depression, anxiety, lung cancer, and skeletal muscle dysfunction. These conditions share pathophysiological mechanisms such as systemic inflammation, hypoxia, and oxidative stress, worsening the prognosis and requiring integrated management ⁴⁷⁻⁴⁹.

The GOLD 2023 classification stratifies the disease into four grades: Grade 1 (mild), FEV1 $\geq$ 80%; Grade 2 (moderate), FEV1 50–79%; Grade 3 (severe), FEV1 30–49%; and Grade 4 (very severe), FEV1 $<$ 30% or $<$ 50% with respiratory failure ^{50,51}. Although useful for guiding therapy, it can be complemented by multidimensional indices, such as BODE

(Body mass index, Obstruction, Dyspnea, Exercise capacity), ADO (Age, Dyspnea, Obstruction), and DOSE (Dyspnea, Obstruction, Smoking, Exacerbations), which incorporate additional factors and offer greater prognostic accuracy⁵²⁻⁵⁶.

Therefore, COPD is a common, preventable, and treatable disease, but it is still associated with high mortality, high social costs, and a significant loss of quality of life. Prevention, especially through smoking cessation, early detection, and equitable access to effective therapies, are decisive in reducing its burden nationally and globally.

1.2. TCM Syndromes at the Origin of COPD

In Traditional Chinese Medicine (TCM), COPD is viewed as a dynamic condition of energetic disharmony between the Lung, Spleen, and Kidney, rather than a static disease^{57,58}. Based on the classics *Huang Di Nei Jing* and *Shang Han Lun*, it is understood that the root of the pathology lies in the *Yin-Yang* imbalance and the interaction between external pathogenic factors and the body's defensive strength (*Zheng Qi*)^{59,60}. The syndromes can coexist and transform over time, and the diagnosis integrates signs such as tongue, pulse, and the Eight Principles (*Yin/Yang*, Cold/Heat, Deficiency/Excess, Interior/Exterior)^{61,62}. There is no direct correspondence with the Western GOLD stages, and treatment is individualised and able to address comorbidities as part of the systemic imbalance.

In the stable phase, according to Li *et al.*⁶³, four main patterns are recognised. The Lung *Qi* Deficiency syndrome is characterised by a cough or wheezing accompanied by dyspnoea aggravated by movement, mental fatigue, lack of strength or spontaneous sweating, aversion to wind, and a tendency to catch colds. The tongue appears pale, usually with a white coating, and the pulse tends to be deep and thin, or thin and weak. Diagnosis is established when three of these criteria are present, with this syndrome being observed most frequently in patients with mild or moderate pulmonary dysfunction, corresponding to GOLD stages 1 and 2.

The Lung and Spleen *Qi* Deficiency syndrome is distinguished by the association of cough or wheezing and dyspnoea aggravated by movement, with fatigue, weakness or spontaneous sweating exacerbated by exertion, aversion to wind, and ease in catching colds. Signs related to digestive function also appear, such as loss of appetite or reduced food intake, gastric and abdominal distension, fullness, or loose stools. The tongue may appear swollen or have teeth marks, accompanied by a thin and white or white and greasy coating, while the pulse manifests as deep and thin, deep and slow, or thin and weak. Diagnosis requires the presence of two criteria from the initial group, associated with two of the digestive criteria. This syndrome can be observed in all phases of pulmonary dysfunction, although it is more frequent in mild or moderate cases (GOLD 1 and 2).

The Lung and Kidney *Qi* Deficiency syndrome presents with cough or wheezing and dyspnoea that worsens with movement, associated with weakness and spontaneous sweating, also aggravated by exertion, aversion to wind, and susceptibility to colds. Low back and knee pain and weakness, tinnitus, a feeling of confusion or facial oedema, frequent urination (more during the night), and urinary leakage during coughing may coexist. The tongue is generally pale with a white coating and the pulse manifests as deep and thin, or thin and weak. Diagnosis requires the presence of two criteria from the first group, complemented by two of the additional signs. This syndrome occurs in patients with moderate, severe, or very severe pulmonary dysfunction (GOLD 2 to 4), being more common in the latter two groups.

Finally, the combined Lung and Kidney *Qi* and *Yin* Deficiency syndrome is observed in patients with greater functional severity. Clinically, it manifests as a cough or wheezing accompanied by dyspnoea aggravated by movement, spontaneous sweating or weakness intensified by exertion, and a tendency to catch colds. Low back and knee pain and weakness, tinnitus, a feeling of confusion or dizziness are frequent. The picture may include a dry cough or one with scarce sputum that is difficult to eliminate, night sweats, a sensation of heat in the palms and soles, and changes in the tongue, which may present a pale or reddish colour, a thin and scanty coating or partial peeling. The pulse generally manifests

as deep and thin, and may be weak or rapid. Diagnosis is established when two of the initial criteria, one of the signs of low back pain or tinnitus, and two of the additional symptoms are verified. This syndrome is mainly observed in patients with severe or very severe pulmonary dysfunction (GOLD 3 and 4).

Thus, in the stable phase of COPD, syndromic differentiation in TCM allows for the identification of four central clinical patterns, each associated with specific manifestations of cough, dyspnoea, fatigue, digestion, urinary changes, tinnitus, sweating, or internal heat, in addition to characteristic tongue and pulse signs. This approach enables precise diagnostic stratification, guiding therapeutic interventions adapted to the functional condition of each patient.

Acute Exacerbations

According to Li *et al.*⁶³, acute exacerbations result from the interaction between Lung and Kidney Qi Deficiency and the penetration or retention of external pathogenic factors, such as wind, cold, phlegm, and heat. The recognition of these patterns is essential to define the best therapeutic strategies.

The Wind-Cold attacking the Lung syndrome manifests as a cough or wheezing accompanied by white and fluid expectoration, fever, aversion to cold, absence of sweating, and pain in the limbs, being typical of the initial stage of exacerbations. The External Cold with Internal Fluid Retention syndrome presents with a cough or wheezing, white, thin, or frothy expectoration, whistling caused by phlegm retained in the throat, and chest tightness aggravated in the supine position, reflecting the inversion of *Qi*.

The Phlegm-Heat obstructing the Lung syndrome is characterised by a cough or wheezing with shortness of breath, viscous yellow expectoration that is difficult to cough up, fever, thirst for cold liquids, and constipation. This pattern is often observed in patients with a concomitant respiratory infection and a large volume of mucosal secretion. The Turbid Phlegm obstructing the Lung syndrome includes a cough or wheezing, white, greasy, or frothy expectoration, gastric fullness, sticky mouth, lack of appetite, a thick tongue coating, and a slippery pulse, and is also associated with the abundant presence of secretions.

In more severe situations, the Phlegm obscuring the Orifices of the Spirit syndrome may be observed, which manifests as mental changes, such as delirium, drowsiness, and unconsciousness, and may progress to spasms and convulsions, in addition to persistent wheezing and dyspnoea.

According to the study, each of these syndromes presents specific diagnostic criteria, which result from the combination of clinical manifestations, and tongue and pulse characteristics. Therefore, the TCM proposal allows for the characterisation of acute COPD exacerbation into well-defined clinical subtypes, which enables a more targeted therapeutic approach, complementing the standardised treatment of Western medicine.

There is also the possibility of Blood Stasis occurring later, which can arise in different ways, namely from phlegm or *Qi* deficiency.

“A characteristic of Blood stasis is that it can only occur after a prolonged period of time: thus, it is always a relatively serious pathogenic factor and leads to more serious diseases than *Qi* stagnation; for example, coronary heart disease, abdominal masses, tumours, arterial hypertension, stroke, etc.”

Qi deficiency can lead to Blood stasis because deficient *Qi* fails to move and transport: this leads to *Qi* stagnation and Blood stasis.” Furthermore, it also states that Phlegm is a pathological accumulation of turbid fluids, while Blood stasis is a pathological accumulation of Blood; given the interchange between Blood and Body Fluids, a pathology of Fluids such as phlegm can also lead to Blood stasis^{61,62,64}.

2. Acupuncture Treatment

Acupuncture is defined as a therapeutic intervention that consists of the insertion of extremely fine needles into specific points on the body, called acupoints or energetic

points, distributed along trajectories known as meridians^{65,66}. These points are considered areas of higher density of nerves, muscles, and connective tissue, the stimulation of which can generate local and systemic physiological effects, including the modulation of pain, circulation, and neuro-hormonal responses⁶⁷⁻⁷⁰.

2.1. Clinical Trial 1

Xu *et al.*⁷¹ conducted a randomised clinical trial with 74 patients, divided into two groups (real acupuncture and sham/placebo), with an average age of 69.6, over 36 sessions of 30 minutes, 3 times per week. The objective was to determine if, as an adjunctive therapy, acupuncture could help prevent the decay of lung function, as the results of isolated drugs are often insignificant. Both groups received conventional drugs.

The points used were: EX-B1, BL13, BL20, BL23, ST36, versus simulated acupuncture.

The groups were comparable at baseline: FEV1 was 1.16 L in the acupuncture group and 1.17 L in the sham group; the predicted FEV1% was 49.1% and 51.8%, respectively; FVC was 2.17 L and 2.10 L; and the FEV1/FVC ratio was 48.4% and 49.2%. The distance covered in the 6MWT was 390.6 m and 382.4 m, the CAT score was 13.2 and 14.3 points, and dyspnoea (mMRC) was 1.78 and 1.65 points, confirming baseline balance between the groups.

Regarding pulmonary function, the acupuncture group showed an absolute increase in FEV1 of +0.03 L, while the sham group recorded a reduction of -0.06 L, corresponding to a difference of +0.09 L between groups. FEV1 expressed as a percentage of the predicted value increased by +1.35 points in the acupuncture group, while it decreased by -2.44 points in the sham group, resulting in an absolute difference of +3.79 percentage points. In relative terms, this variation corresponded to an improvement of approximately +2.7% in the acupuncture group and a reduction of -4.7% in the sham group. The FEV1/FVC ratio also showed a more favourable behaviour, with an absolute gain of +1.44 points in the acupuncture group versus -1.42 in the sham group, a difference that totalled +2.86 percentage points.

Functional capacity, assessed by the 6-minute walk test (6MWD), followed the same trend. The real acupuncture group increased the distance covered by +4.1 m, while the sham group recorded a decrease of -5.3 m, an absolute difference of +9.4 m. Although the absolute values are modest, in relative terms this represented a gain of +1.05% compared to the baseline value in the acupuncture group and a loss of -1.39% in the sham group.

The analysis of respiratory symptoms, using the mMRC, showed a reduction of -0.65 points in the acupuncture group, compared to -0.24 in the sham group, a difference of -0.41 points. In the CAT questionnaire, which assesses COPD-related quality of life, the acupuncture group achieved an improvement of -4.68 points, superior to the reduction of -3.92 in the sham group. The absolute difference between groups was -0.76 points. However, in relative terms, this improvement corresponded to -35% in the acupuncture group, against -27% in the sham group, showing a more expressive impact on the quality of life of patients undergoing isolated acupuncture than in the placebo group.

The results suggest that acupuncture, in association with conventional treatment, contributed to the preservation and slight improvement of pulmonary function, in contrast to the decline observed in the placebo group, which only received conventional treatment, suggesting a potential beneficial effect of this intervention on the evolution of COPD, as well as an improvement in dyspnoea symptoms, compared to the control group, and it has a positive, albeit modest, impact on physical exercise tolerance.

2.2. Clinical Trial 2

The multicentre clinical trial by Li *et al.*⁷² evaluated the efficacy of acupuncture, conventional drugs, and the combination of both in 150 patients with stable COPD. The intervention lasted 12 weeks, followed by an equal follow-up period of 12 weeks. Partici-

pants were distributed into three groups, with the main outcomes being functional capacity (6MWD) and quality of life (SGRQ), and secondary outcomes being dyspnoea (mMRC), CAT, pulmonary function (FEV1, FVC, FEV1/FVC, PEF), and exacerbations.

The choice of acupuncture points was based on syndrome differentiation: for Lung *Qi* Deficiency, the points used were: BL13, DU14, BL12, LU9, ST36, and BL43; for Lung and Spleen *Qi* Deficiency, BL13, DU14, BL12, LU9, ST36, and BL20; for Lung and Kidney *Qi* Deficiency, BL13, DU14, BL12, LU9, BL23, and KI3; and for combined Lung and Kidney *Qi* and *Yin* Deficiency, BL13, DU14, BL12, LU9, BL23, and RN4.

The quantitative analysis of the results showed important differences between the groups. In the six-minute walk test (6MWD), the baseline values were similar between the groups, around 385–388 m. After 12 weeks of intervention, the group undergoing acupuncture associated with pharmacological treatment showed a significant increase, reaching 446.9 ± 78.0 m, which represented a gain of approximately 59 m compared to the start ($p < 0.001$). The group treated only with acupuncture also showed an improvement, reaching 416.3 ± 60.4 m (increase of 28 m; $p < 0.001$), while the isolated pharmacological group progressed to 393.3 ± 89.4 m, without statistical significance. In the 12-week follow-up, the gains were largely maintained, with 444.9 ± 82.8 m in the combined group, 414.2 ± 58.0 m in the acupuncture group, and 387.5 ± 87.2 m in the drug group. The results suggest that the therapeutic combination provides a synergistic effect in improving functional capacity.

The evaluation of dyspnoea, by the mMRC scale, showed similar initial scores (1.48–1.65). After 12 weeks, a more pronounced reduction was observed in the combined group (0.94 ± 0.60 ; $p < 0.001$), compared to the pharmacological group (1.04 ± 0.35 ; $p < 0.001$) and the isolated acupuncture group (1.13 ± 0.50 ; $p < 0.05$). It should be noted that the improvement in the combined group was significant as early as the fourth week, unlike the other interventions, which presented benefits later. In the follow-up, there was a slight worsening of values in all groups, but the values remained lower than baseline, a common phenomenon in short-term clinical trials.

Regarding acute exacerbations, patients had an average of 1.28–1.29 episodes per year before treatment. After 12 weeks, all groups showed a significant reduction, ranging from 0.07 ± 0.25 in the acupuncture group, 0.08 ± 0.28 in the pharmacological group, and 0.04 ± 0.20 in the combined group. This reduction was maintained in the follow-up, without statistically significant differences between the groups, although the combined group exhibited the lowest absolute values.

Pulmonary function showed slight changes. Initial FEV1 was approximately 1.31 L in the acupuncture group, 1.43 L in the pharmacological group, and 1.46 L in the combined group. After 12 weeks, the values increased slightly, reaching 1.56 L in the combined group, but without statistical significance between the groups. However, the FEV1/FVC ratio showed significant improvement only in the combined group, increasing from 53.9% to 58.4% after 12 weeks ($p < 0.001$), indicating a possible benefit of combined acupuncture on pulmonary ventilation.

Finally, the overall impact of the disease, assessed by the CAT test, presented similar baseline values (18.6–18.8 points). After 12 weeks, all groups reduced the scores, with the most expressive improvement in the combined group (13.8 ± 3.1 ; $p < 0.001$), compared to isolated acupuncture (15.6 ± 2.5 ; $p < 0.05$) and isolated pharmacological therapy (16.2 ± 2.4 ; $p < 0.05$). In the follow-up, a slight increase in scores was observed, but the values remained better than at the start.

We must then consider that what the study really proves is that all treatments work to some extent, but none dramatically distance themselves from the others. Furthermore, there is a general regression in the post-treatment period, given the reduced treatment period.

Quality of life, measured by the St. George's Respiratory Questionnaire (SGRQ), presented mean baseline scores of 43.6 ± 17.3 in the acupuncture group, 36.9 ± 16.0 in the pharmacological group, and 38.0 ± 16.8 in the combined group. After 12 weeks, all groups

showed a tendency to improve, without statistically significant differences between them. However, in the follow-up, only the acupuncture group maintained a significant reduction in scores (37.6 ± 13.8 ; $p=0.001$), which suggests a more sustained effect of this intervention on the perception of quality of life.

This observation contrasts with the performance of the combined group, which, although having achieved better objective results in parameters such as functional capacity, dyspnoea, and overall impact of the disease, did not show the same sustained effect on the subjective perception of quality of life.

This result can be interpreted in light of different dimensions. Firstly, it is important to recognise that quality of life is a multidimensional construct, which is not limited to objective clinical parameters, but also integrates subjective aspects related to emotional well-being, the perception of autonomy, and the meaning attributed to the treatment. Acupuncture, as a traditional practice widely valued in the Chinese cultural context, may have offered participants a therapeutic experience perceived as more holistic, enhancing a perception of benefit that lasted beyond the active intervention period ⁷³.

Furthermore, the literature on placebo and contextual effects shows that patients' expectations, desires, and beliefs significantly influence the perception of symptoms. The simple fact that the patient believes they are receiving effective treatment, or that they experience it in a way consistent with their personal preferences, can activate neurobiological mechanisms related to pain relief, stress reduction, and the promotion of well-being, mediated by systems such as endorphins and dopamine ^{74,75}. Thus, it is plausible to consider that, in the isolated acupuncture group, the congruence between cultural expectations and therapeutic experience amplified and prolonged the perceived effects on quality of life.

In contrast, the association of acupuncture with drugs may have shifted the participants' focus to immediate functional results, such as improved exercise tolerance and relief from dyspnoea. Although clinically relevant, these objective benefits may not have been translated by the patients into a global perception of sustained well-being. Additionally, continuous dependence on medication may cause them to focus on the chronicity of the disease, lessening the subjective value of the gains obtained ⁷⁶.

In summary, these data suggest that the way patients want, expect, or prefer to be treated can influence their perception of therapeutic efficacy and, consequently, results regarding quality of life. Drugs undeniably contribute to symptomatic control and clinical stability, but acupuncture, alone, may offer more lasting benefits in the subjective sphere of well-being.

This contrast reinforces the importance of integrating cultural and psychosocial dimensions into the interpretation of clinical results and points to the need for truly patient-centred therapeutic approaches, in which individual preferences are valued as an integral part of clinical decision-making ⁷⁷. Therefore, possibly, in the Western context, the results for quality of life would be different, depending on their preferences and expectations.

2.3. Clinical Trial 3

The clinical trial by Feng *et al.* (2016) evaluated the efficacy of acupuncture in patients with stable COPD (stages II to IV), with 72 patients randomly divided into two groups: real acupuncture and sham acupuncture, with blinding of participants and assessors. The intervention group received 30-minute sessions, three times a week, for 8 weeks, at specific points, which were LU1, LU9, LI18, ST36, GB12, BL13, BL20, BL23, without distinction of syndromes. The primary outcome was dyspnoea, assessed by the 6-minute walk test and the Borg scale, and the secondary outcomes included distance walked, minimum oxygen saturation, FEV1, and quality of life (SGRQ).

In the study by Feng *et al.* ⁷⁸, real acupuncture demonstrated significantly superior results compared to sham acupuncture. On the Borg scale, which assesses dyspnoea after the 6-minute walk test (6MWT), a reduction of -4.4 was observed in the acupuncture

group versus -0.5 in the sham group, with a difference of -3.7 ($p < 0.01$), indicating a relevant decrease in shortness of breath during exertion. The distance covered in the 6MWT increased by +67.4 m in the acupuncture group, while it reduced by -13.8 m in the control group, corresponding to a difference of +80.1 m ($p < 0.01$), considered clinically relevant for functional capacity.

Minimum oxygen saturation (SpO₂) improved by +3.4% in the treated group, contrasting with a reduction of -1.5% in the sham group, a difference of +4.9% ($p < 0.01$), reflecting better oxygenation during exercise. Quality of life, measured by the St. George's Respiratory Questionnaire (SGRQ), showed improvements in all dimensions: total (-15.3 vs. +0.5; difference -15.9, $p < 0.01$), symptoms (-25.4 vs. -2.8; difference -22.6, $p < 0.01$), activity (-13.7 vs. +1.5; difference -15.3, $p < 0.01$), and impact (-12.5 vs. +0.4; difference -12.1, $p < 0.01$), demonstrating substantial benefits in the global perception of the disease, symptoms, and social/emotional impact.

Finally, pulmonary function parameters also showed slight improvements: forced vital capacity (FVC) increased by +0.15 L in the acupuncture group versus -0.11 L in the sham group (difference +0.26 L, $p < 0.01$), and the predicted FEV₁% grew by +3.2% compared to -0.9% (difference +4.1%, $p < 0.01$).

Although statistically significant, these changes were considered small from a clinical point of view. Acupuncture, in patients with COPD, provided consistent benefits in central outcomes, reduction of dyspnoea, improvement in functional capacity, and quality of life. These gains were clinically relevant, especially in the 6MWD and the SGRQ, and accompanied by better oxygenation during exertion. The effects on pulmonary function were modest, suggesting that the impact of acupuncture manifests more in the subjective experience and functional performance than in structural changes in pulmonary mechanics.

2.4. Data Mining Study

A data mining study (research that uses computational and statistical techniques to discover patterns, relationships, or trends in large datasets), conducted by Hsieh *et al.*⁷⁹, confirmed that combinations of central acupuncture points present relevant clinical benefits in COPD patients. Among the proposed mechanisms of action, the anti-inflammatory effects, the improvement in nutritional status, the increase in respiratory muscle strength, and greater exercise tolerance stand out, all important concerns in COPD.

Another central aspect is that, in clinical practice, acupuncture is rarely applied to isolated points. However, this reasoning was corroborated when Chen *et al.*⁸⁰ and Chen *et al.*⁸¹ observed that, in cervical spondylosis, the application of multiple points resulted in greater symptomatic relief and modulation of cerebral activity compared to isolated points. Similarly, Zhang *et al.*⁸² reported that, in patients with hypertension, the combination of points LR3 and KI3 activated broader cerebral areas than the stimulation of each individual point, suggesting a synergistic effect.

Previously, Li *et al.*⁸³ demonstrated that treatment with acupuncture at BL13, BL23, and EXB1 reduced the inflammatory response, with a decrease in IL-8 and TNF- α , inflammatory mediators, through the increase in the expression of HDAC2 – an enzyme that regulates histone acetylation, a process that controls the expression of inflammatory genes – which inhibits pro-inflammatory genes and contributes to the improvement of pulmonary function. Complementarily, Suzuki *et al.*⁸⁴ observed that the application of acupuncture at multiple points (LU1, LU9, LI18, CV4, CV12, ST36, KI3, GB12, BL13, BL20, and BL23) promoted an improvement in the nutritional status of COPD patients, reflected in positive changes in body weight, respiratory muscle strength, haematological parameters, and a reduction in inflammatory biomarkers. This evidence is relevant, given that malnutrition in COPD is directly associated with muscle weakness, inefficient ventilation, exercise intolerance, and low health-related quality of life (HRQoL).

The improvement in gastrointestinal function, achieved by stimulating acupuncture points, was also described in a study by Suzuki *et al.*⁸⁵, suggesting that this mechanism

may indirectly act to improve the nutritional status in COPD patients. In turn, Maekura *et al.*⁸⁶ reported that the application of acupuncture with similar protocols resulted in an increase in maximum oxygen consumption (VO₂ peak), maximum minute ventilation (VE peak), exercise time to the limit of tolerance, and a significant improvement in HRQoL, assessed by the St. George's Respiratory Questionnaire (SGRQ).

Considering the high prevalence of COPD and the negative impact on HRQoL, dyspnoea, and exercise tolerance, the identification of effective therapeutic combinations is of great clinical importance. For this purpose, the study by Hsieh *et al.*⁷⁹ employed association rule analysis with the Apriori algorithm, based on 12 randomised clinical trials included in previous meta-analyses. 27 acupuncture points were extracted, the most frequent being BL12, BL13, BL20, BL23, BL43, CV17, EXB1, LU5, LU7, and ST36. The analysis revealed a total of 2444 association rules, among which ST36, BL12 → CV17, ST36, BL12 → EXB1, CV17, BL12 → ST36, and EXB1, BL12 → ST36 stood out.

Based on these results, two combinations with the greatest therapeutic potential were identified: ST36 + BL12 + CV17 and ST36 + BL12 + EXB1. These combinations can be considered essential as complementary acupuncture treatment.

2.5. Systematic Review with Meta-Analysis

A systematic review with meta-analysis, which consists of the search, selection, and analysis of all relevant studies on a specific question, following rigorous and pre-defined protocols, conducted by Yu *et al.*⁸⁷, analysed 23 articles, 21 of which mention the points used in the treatment of dyspnoea, the main symptom of COPD, in different pathologies (COPD, lung cancer, asthma, bronchiectasis, interstitial lung disease, chronic cor pulmonale, and bronchitis). In the included studies, a great variation in acupuncture procedures was observed, including combination with other treatments, the specific points used, the duration of stimulation, the period and frequency of treatments, as well as monitoring. Five trials combined acupuncture with other techniques, two with pulmonary rehabilitation and three with aerobic exercise. Most studies applied stimulation for 15 to 30 minutes, with only two studies reporting longer periods, one of 45 minutes and the other of 50 minutes. Most studies used between five and ten points, with only three using fewer than four. The duration of the studies varied from 7 days to 12 weeks, with treatment frequency ranging from daily to weekly, and most evaluated the results at the end of the intervention, with seven trials including follow-up periods of two weeks to six months.

Regarding acupuncture points, the most cited were ST36 (12 times) and BL13 (11 times), followed by KI3 (8 times), LU1 (7 times), CV17 and PC6 (6 times each), in addition to the points LU9, LU7, BL23, EX-B1, LI11, CV4, and CV12 (all mentioned 5 times each). SP6, LU5, ST25, ST40, and BL20 (4 times each), GB12 and ST18 (3 times each), and DU14, LI18, and ST16 (2 times each). In addition to the referred points, several other points were cited only once.

Although the variety of points cited, this study highlights the points: ST36, which appears in more than half of the studies; BL13, which appears in almost half of the studies; KI3 and LU1 are also recurrent, despite the great variety of points cited.

3. Treatment with Herbal Medicine

Chinese Herbal Medicine constitutes a primary therapeutic intervention in Traditional Chinese Medicine, used to regulate bodily imbalances, modulate the immune system, alleviate chronic symptoms, and improve quality of life, having demonstrated efficacy and safety⁸⁸⁻⁹¹.

3.1. Clinical Trial 1

A clinical trial was conducted by Wang *et al.*⁸⁸ with the aim of evaluating the efficacy and safety of two Chinese herbal formulas, *Bushen Yiqi* (BY) granules and *Bushen Fangchuan* (BF) tablets, in the treatment of moderate to severe stable COPD. The 262 participants received the treatment for 6 months, 3 times a day, as well as monitoring for a

further 12 months. Assessments were made at 5 different times. They were distributed into three parallel groups: the first received the BY granules and a placebo tablet; the second received the BF tablet and a placebo granule; and the third received only placebo treatment, all in association with conventional treatment. The primary outcomes analysed were pulmonary function, frequency of exacerbations, and quality of life, measured by the SGRQ questionnaire. Secondary outcomes assessed were physical performance via the 6-minute walk test, the BODE index, and psychological status.

In terms of pulmonary function, the results revealed discrete, but consistent, improvements in the treated groups. Vital Capacity (VC) increased from 2.38 ± 0.84 L to 2.53 ± 0.61 L in the BF group and from 2.35 ± 0.76 L to 2.42 ± 0.56 L in the BY group, in contrast to a minimal change in the placebo group (2.44 ± 0.93 L to 2.47 ± 0.76 L). FEV1 (% of predicted) showed a positive trend, especially in the BY group, which went from $48.5 \pm 15.4\%$ to $50.6 \pm 16.4\%$, while the BF group maintained virtually unchanged values ($46.7 \pm 15.6\%$ to $46.9 \pm 16.1\%$) and the placebo group remained stable ($46.3 \pm 15.1\%$ to $46.3 \pm 16.9\%$). The FEV1/FVC ratio also showed a more favourable evolution in the intervention groups, with an increase from $50.3 \pm 11.2\%$ to $52.5 \pm 12.0\%$ in the BF group and from $53.8 \pm 11.2\%$ to $55.4 \pm 13.0\%$ in the BY group, contrasting with less expressive progression in the placebo group ($50.4 \pm 10.8\%$ to $53.3 \pm 15.1\%$). After bronchodilator use, the trend was maintained: values rose to $54.5 \pm 13.1\%$ in the BF group and $57.5 \pm 15.0\%$ in the BY group, against $54.9 \pm 15.3\%$ in the placebo group.

Regarding the frequency of acute exacerbations, it was found that, throughout the six months of treatment, the proportion of patients without exacerbations remained high in the intervention groups, ranging between 84.4% and 92.8%, while in the placebo group, values ranged between 86.0% and 90.0%. Although the differences did not reach robust statistical significance at all times, the trend suggests greater clinical stability associated with the use of herbal formulas.

The analysis of inflammatory markers showed consistent reductions in the active groups. IL-6 decreased from 35.1 to 27.3 pg/mL in the BF group and from 34.6 to 25.5 pg/mL in the BY group, compared to a minimal change in the placebo group (34.3 to 33.7 pg/mL). IL-8 reduced from 20.7 to 17.2 pg/mL in the BF group and from 20.9 to 16.4 pg/mL in the BY group, while in the placebo group, it virtually did not change (21.3 to 20.9 pg/mL). Similar trends were observed for IL-17, IL-1beta, and TNF-alpha. It is important to highlight that IL-10, an anti-inflammatory cytokine, increased significantly in the treated groups (BF: 6.2 → 7.5 pg/mL; BY: 6.3 → 8.0 pg/mL), while the variation in the placebo group was minimal (6.1 → 6.3 pg/mL). Serum cortisol, a marker of the HPA axis (Hypothalamic-Pituitary-Adrenal), one of the body's regulatory systems, also increased more significantly in the intervention groups, especially in the BY group (13.9 → 15.4 µg/dL), suggesting a beneficial modulation of the systemic inflammatory response.

Regarding quality of life, assessed by the St. George's Respiratory Questionnaire (SGRQ), the BF and BY groups showed average reductions of 4.2 and 5.8 points, respectively, over 180 days, compared to only 0.9 in the placebo group. These results indicate a relevant clinical improvement, given that differences greater than 4 points are generally considered clinically significant. The BODE index improved in the BF (3.6 → 3.2) and BY (3.7 → 3.1) groups, but not in the placebo group (3.6 → 3.5).

Functional capacity, measured by the distance covered in the 6-minute walk test (6MWD), increased by +23 m in the BF group and +32 m (gains above 30 m indicate functional benefit) in the BY group, contrasting with a marginal improvement of only +5 m in the placebo group. Furthermore, in the psychological domain of the WHOQOL-BREF, a reduction in scores was observed (BF: 12.8 → 10.9; BY: 12.9 → 10.7), which suggests an attenuation of depressive and anxious symptoms associated with COPD, while the placebo group showed minimal change (12.7 → 12.2).

In summary, the study concludes that BY granules and BF tablets are effective in COPD, with BY demonstrating clinically relevant benefits in both the SGRQ and the distance covered in the 6-minute test, while BF showed clinical relevance only in the SGRQ;

the remaining effects of both formulas were mainly statistically significant, but with limited clinical impact.

3.2. Clinical Trial 2

A clinical trial was conducted by Lyu *et al.*⁹² with the aim of evaluating the efficacy and safety of the herbal formula *San-Huang Gu-Ben Zhi-Ke* (SHGBZK) in patients with stable COPD and Lung and Spleen Qi Deficiency. In total, 50 patients participated in the treatment with the formula, and 48 were included in the placebo group. The therapy lasted 24 weeks, administered three times a day, with a 28 week follow-up. The primary outcome was the frequency of acute COPD exacerbations (AECOPD), while secondary outcomes included pulmonary function, symptoms, exercise capacity, quality of life, and mortality.

In the clinical trial, the frequency of exacerbations fell from 2.04/year to 0.38 in the placebo group and from 2.00/year to 0.10 in the SHGBZK group. Although the overall difference was not statistically significant (p approx 0.10), subgroups with CAT ≥ 10 or mMRC ≥ 2 showed significant reductions. In pulmonary function, FEV1 fell slightly in the placebo group (1.69 $\rightarrow$ 1.62 L), but stabilised in the SHGBZK group (1.47 $\rightarrow$ 1.51 L), with clearer benefits in patients with frequent exacerbations. FVC also fell in the placebo group (3.19 $\rightarrow$ 3.08 L), but remained stable in the SHGBZK group (2.86 $\rightarrow$ 2.83 L), with significant improvement in subgroups ($p=0.0398$). Predicted FEV1% remained stable in both, without significant differences. PEF reduced in the placebo group (4.78 $\rightarrow$ 4.69 L/s), but increased with SHGBZK (4.11 $\rightarrow$ 4.40 L/s), with the difference being significant in the frequent exacerbations subgroup ($p=0.0262$).

As for symptoms, dyspnoea assessed by mMRC remained stable in the placebo group, but improved significantly at 24 weeks in the SHGBZK group ($p=0.0181$). CAT improved in both groups (Placebo: 10.5 $\rightarrow$ 7.5; SHGBZK: 10.4 $\rightarrow$ 6.9), with more pronounced reductions in the SHGBZK group between weeks 16 and 24 ($p<0.05$). In patients with CAT ≥ 10 , a significant reduction in exacerbations was also recorded.

In functional capacity, the placebo group reduced the distance walked in the 6MWD (405 $\rightarrow$ 395 m), while the SHGBZK group increased it (392 $\rightarrow$ 415 m), with significant differences at weeks 24, 32, and 52 ($p<0.05$). TCM symptom scores showed modest reductions in the placebo group, but continuous and significant improvement in the SHGBZK group at weeks 20 and 24 ($p<0.05$).

In terms of safety, both groups presented adverse events (21 in the placebo group and 22 in the SHGBZK group), with one severe case in the SHGBZK group unrelated to the treatment. Overall, SHGBZK proved to be safe, well-tolerated, and more effective in stabilising pulmonary function, reducing dyspnoea, improving quality of life, and increasing functional capacity, especially in patients with greater clinical severity.

Subgroup Analysis: The authors explored whether the effect of SHGBZK varied according to clinical characteristics such as sex, CAT < 10 vs. CAT ≥ 10 , mMRC < 2 vs. mMRC ≥ 2 , GOLD stages 1–2 vs. 3–4, and history of frequent exacerbations (leq 2 vs. > 2). The results show that SHGBZK exerted greater clinical benefit in more symptomatic patients and those at higher risk of progression, namely those with CAT ≥ 10 , mMRC ≥ 2 , and frequent exacerbations. In these profiles, the treatment significantly reduced the frequency of exacerbations and improved pulmonary function parameters (FVC and PEF), contrasting with the absence of relevant differences in the overall population. These results suggest that SHGBZK may have a more targeted role in high-risk patients, reinforcing the importance of clinical stratification in therapeutic choice. However, the authors emphasise that, due to the reduced sample size and the limitations inherent in subgroup analyses, the data should be interpreted with caution and confirmed in larger-scale studies.

SHGBZK showed statistically significant and clinically relevant effects in more severe patient subgroups (reduction of exacerbations, improvements in mMRC, CAT, FVC, and PEF). In the total population, the effects were partly statistically significant, but with

limited clinical relevance (e.g., 6MWD < 30 m, stabilisation of FEV1 without great gain). The real benefits seem to be concentrated in patients with CAT ≥ 10 , mMRC ≥ 2 , and frequent exacerbations. The subgroup results point to relevant benefits in higher severity profiles, suggesting that SHGBZK may have a more effective adjuvant role in these cases.

However, it must be considered that various studies indicate that patients with poorer health status and higher symptom burden may have more room to improve after interventions⁹³⁻⁹⁵.

3.3. Clinical Trial 3

The placebo-controlled clinical trial by Li *et al.*⁹⁶ evaluated the efficacy and safety of the *Yiqigubiao* (YQGB) pill in patients with stable COPD over six months (12 weeks of active treatment, administered three times a day, followed by 12 weeks of follow-up). Patients were randomly distributed into the YQGB and placebo groups, evaluated for pulmonary function (FEV1, FVC, FEV1%, % FVC, FEV1/FVC), physical capacity (6MWD), quality of life (CAT, mMRC, BODE), arterial blood gas analysis, vital signs, and safety (laboratory tests, ECG, hepatic and renal function).

At baseline, both groups presented similar profiles: FEV1 of 1.31 ± 0.52 L in the YQGB group and 1.43 ± 0.65 L in the placebo group; FVC of 2.37 ± 0.78 L and 2.43 ± 0.84 L, respectively; FEV1/FVC around 55–57%, confirming moderate ventilatory limitation and baseline comparability. CAT values (approx 15 points), 6MWD (approx 390–405 m), mMRC (approx 1.5 points), and BODE index were also similar between groups.

The results revealed that YQGB significantly reduced the proportion of patients with exacerbations (34.5% vs. 78.2%), prolonged the time to the first exacerbation (144.2 vs. 66.5 days), and shortened its duration (5.6 vs. 9.1 days). The average frequency of exacerbations per patient was also lower in the treated group (0.35 ± 0.48 vs. 1.77 ± 1.22 in six months), confirming the preventive effect. Although improvements in respiratory parameters (FEV1, FVC, FEV1%, and FEV1/FVC) did not reach statistical significance, positive trends were observed with YQGB.

In contrast, outcomes related to quality of life and functional capacity showed relevant clinical gains: CAT reduced by almost seven points in the YQGB group, while it increased in the placebo group; 6MWD improved by +41.6 m against a decrease of -37.1 m; dyspnoea (mMRC) showed a significant reduction; and the BODE index also improved (-0.5 vs. stability in the placebo group), suggesting a positive impact on the overall prognosis.

In immunological terms, YQGB demonstrated a relevant modulating effect. In T lymphocytes, a significant reduction in the proportion of CD8⁺ cells was observed ($-12.41 \pm 20.85\%$ vs. $+2.07 \pm 17.40\%$ in the placebo group; $p < 0.001$) and an increase in the CD4/CD8 ratio ($+0.32 \pm 0.82$ vs. -1.67 ± 0.80 ; $p = 0.002$), while the variation in isolated CD4⁺ cells did not reach statistical significance ($+3.83 \pm 17.80$ vs. -1.97 ± 17.63 ; $p = 0.079$). At the level of inflammatory cytokines, the treatment significantly reduced IL-8 (-1.46 ± 2.78 vs. $+1.71 \pm 10.45$; $p = 0.024$) and TNF-alpha (-1.95 ± 6.60 vs. $+5.00 \pm 7.85$; $p < 0.001$), with no relevant differences recorded for IL-6 (-0.30 ± 8.33 vs. $+0.97 \pm 11.78$; $p = 0.498$). Arterial blood gas parameters (pH, PaO₂, PaCO₂, SaO₂) remained stable in both groups, without significant differences. These results suggest that the clinical benefits of YQGB derive mainly from the modulation of the inflammatory response and immunological rebalancing, rather than from direct changes in pulmonary oxygenation.

Therefore, the trial demonstrates that YQGB, as an adjuvant, is effective in reducing exacerbations, improving quality of life, dyspnoea, and functional capacity, with clinically relevant effects (CAT, 6MWD, BODE). Gains in pulmonary function were only discreet, suggesting that the main mechanism is immunomodulatory, through the reduction of pro-inflammatory cytokines and the rebalancing of the lymphocyte profile. Thus, YQGB does not act so much on pulmonary mechanics, but rather on clinical stability and the control of chronic inflammation, crucial aspects in COPD.

3.4. Clinical Trial 4

The study by Hong *et al.*⁹⁷ was conducted with 60 patients with stable COPD, divided into two groups: *Yufeining* (YFN) associated with standard treatment (inhaled steroids and bronchodilators) and placebo associated with standard treatment. The objective was to evaluate the efficacy and safety of the Chinese herbal formula YFN in the treatment of stable COPD in combination with conventional drugs. For 8 weeks, both groups received the intervention, being evaluated immediately after treatment and again 4 months later. The primary outcome was clinical efficacy according to TCM criteria, while secondary outcomes included quality of life (CAT), dyspnoea (mMRC), and functional capacity (6MWD).

The YFN formula demonstrated consistent benefits across multiple outcomes. In pulmonary function, significant improvements were observed in both FEV1 (from 1.54 ± 0.47 L to 1.73 ± 0.52 L) and FVC (from 2.55 ± 0.63 L to 2.79 ± 0.66 L), contrasting with minimal changes in the placebo group, suggesting that YFN contributed to stabilising and optimising ventilatory mechanics in patients with stable COPD.

In terms of symptoms and quality of life, the gains were also relevant: the CAT score reduced from 16.02 ± 7.12 to 12.65 ± 5.33 in the treated group, while it remained practically unchanged in the placebo group; in the SGRQ, the improvement was about 8 points (46.12 ± 16.85 to 38.33 ± 13.51), exceeding the threshold considered clinically significant. These results indicate a real impact on the perception of the disease and the daily well-being of patients.

In the domain of functional capacity, the distance covered in the 6-minute walk test increased by an average of 35 m in the YFN group (385.71 ± 88.24 to 421.19 ± 90.12), while the placebo group showed virtually no change, confirming that the intervention improves physical performance and exercise tolerance.

Regarding exacerbations, treatment with YFN showed a robust preventive effect: the average number of exacerbations in 12 months was significantly lower (0.34 ± 0.52 vs. 0.81 ± 0.87), and the proportion of patients without any exacerbation was substantially higher (85.7% vs. 60.5%). These results translate into fewer acute episodes, less need for medical care, and better clinical stability over time.

The analysis of inflammatory biomarkers reinforces the mechanism of action of YFN. A significant reduction was observed in IL-8 ($3.12 \pm 1.45 \rightarrow 1.57 \pm 0.48$ ng/mL vs. $3.19 \pm 1.49 \rightarrow 2.03 \pm 0.89$ in the placebo group, $p < 0.05$), TNF-alpha ($162.24 \pm 83.34 \rightarrow 74.57 \pm 34.84$ pg/mL vs. $143.96 \pm 86.05 \rightarrow 109.13 \pm 65.71$, $p < 0.05$), LTB4 ($385.01 \pm 240.85 \rightarrow 268.79 \pm 191.98$ pg/mL vs. $336.26 \pm 262.56 \rightarrow 271.24 \pm 150.23$, $p < 0.05$), and C-reactive protein (CRP) ($6.02 \pm 9.12 \rightarrow 2.32 \pm 2.29$ mg/L vs. $6.60 \pm 7.94 \rightarrow 3.85 \pm 3.21$, $p < 0.05$). Only YFN promoted a significant reduction in IL-17 ($9.48 \pm 1.20 \rightarrow 8.68 \pm 0.96$ pg/mL vs. $9.41 \pm 1.00 \rightarrow 9.19 \pm 0.70$ in the placebo group, $p < 0.05$). TGF-beta 1 did not undergo relevant changes in either group ($23.17 \pm 10.15 \rightarrow 20.44 \pm 10.43$ vs. $23.55 \pm 7.84 \rightarrow 21.45 \pm 7.48$, ns). These results point to a clear immunomodulatory effect of YFN, mainly through the attenuation of active systemic inflammation, rather than on fibrotic processes or pulmonary remodelling.

Regarding safety, the placebo group recorded 3 cases of mild gastrointestinal discomfort, while the YFN group presented 1 case of change in sputum colour, without clinical relevance. Both treatments were well-tolerated and no serious adverse events occurred.

Thus, treatment with YFN, associated with conventional treatment, resulted in a higher rate of clinical efficacy (89.3% vs. 63.3%), significantly reduced CAT and mMRC scores, increased 6WD distance, and decreased inflammatory markers such as IL-8, TNF-alpha, LTB4, CRP, and IL-17A, with no serious adverse effects recorded.

Considerations on the Herbs Used

The Wang *et al.*⁸⁸ trial, with the BY and BF granules and tablets, described Lung and Kidney *Qi* Deficiency as the central pattern. Li *et al.*⁹⁶, using the YQGB formula, referred to Lung and Spleen *Qi* Deficiency, often associated with the presence of phlegm. Hong *et*

*al.*⁹⁷, with the YFN formula, included patients characterised by Lung and Kidney *Qi* Deficiency, in association with phlegm and stasis. Lyu *et al.*⁹², testing the SHGBZK formula, focused specifically on Lung and Spleen *Qi* Deficiency, which constituted the main inclusion criterion. Together, these trials reveal that, despite small variations, all were based on patterns of Lung *Qi* Deficiency, frequently associated with the Spleen or Kidney and the presence of phlegm, reinforcing the consistency of the TCM pattern framework.

4. Final Considerations

4.1. *Why did acupuncture and herbal medicine not show consistent improvements in the decline of pulmonary function?*

Despite the benefits described in several clinical trials, acupuncture and herbal medicine do not consistently show relevant improvements in spirometric parameters. This can be explained by several reasons.

In the first place, it is important to recognise that in COPD, there are irreversible structural changes⁹⁸, namely the destruction of the alveoli (emphysema), chronic inflammation, and bronchial remodelling, accompanied by a loss of pulmonary elasticity. These changes are not reversible by currently available therapies, so expressive increases in indicators such as FEV1 or FVC are unlikely.

Secondly, these interventions act predominantly at the symptomatic and inflammatory level. Acupuncture exerts effects through neurovegetative modulation⁹⁹, reducing the sensation of dyspnoea and increasing the efficiency of the respiratory musculature. Herbal medicine, in turn, presents anti-inflammatory and immunomodulatory properties⁹². Both contribute to the improvement of dyspnoea, fatigue, exercise tolerance, and quality of life, but they do not have the capacity to regenerate destroyed lung parenchyma.

Additionally, it is important to point out that pulmonary function does not constitute the only relevant clinical outcome. Several studies demonstrate that symptoms, functional capacity, and the frequency of exacerbations have a prognostic impact equivalent to or even superior to the modest variations in FEV1¹⁰⁰⁻¹⁰².

Furthermore, there are methodological limitations in the available trials, which are largely short-term and with reduced samples, making it difficult to identify statistically significant differences in parameters of a structural nature.

Thus, the reference to "improvement of pulmonary function" does not imply the reversal of irreversible injury, but rather the stabilisation or optimisation of residual function, with a reduction in the expected decline and limited functional gains.

4.2. *Does herbal medicine have a greater impact on the quality of life of patients with COPD than acupuncture?*

The available evidence in the articles suggests that herbal medicine shows greater consistency in improving the quality of life of patients with COPD, measured by scales such as the COPD Assessment Test (CAT) and the St. George's Respiratory Questionnaire (SGRQ), when compared to acupuncture. This is due to several factors. Firstly, herbal medicine exerts a systemic effect, as the bioactive compounds of the formulas are absorbed and circulate in the body, modulating inflammation at both the pulmonary and systemic levels. This effect is supported by studies that demonstrated reductions in inflammatory biomarkers such as IL-6, IL-8, TNF-alpha, IL-17, and C-reactive protein (CRP), which are directly associated with the severity of symptoms, the frequency of exacerbations, and the decline in overall health status¹⁰³.

In addition, the formulas used in Traditional Chinese Medicine have a multifactorial action, as they combine several plants with distinct properties, including anti-inflammatory, antioxidant, immunomodulatory, and tonic effects. This comprehensiveness allows herbal medicine to act simultaneously on different clinical dimensions, such as cough, expectoration, fatigue, sleep quality, and exercise tolerance, directly influencing quality of life indices. Another relevant aspect is the durability of the effect: longer-term trials, such as those by Wang *et al.*⁸⁸, Li *et al.*⁹⁶, and Lyu *et al.*⁹², demonstrated that the benefits

of herbal medicine are maintained for six to twelve months, whereas the effects of acupuncture, although relevant in controlling dyspnoea and improving exercise capacity, tend to be more immediate and dissipate after the sessions are interrupted.

Finally, quality of life is assessed through self-report questionnaires, which capture the patient's subjective perception of their health. Herbal medicine, by globally improving parameters such as appetite, energy, sleep, and resistance to infections, has a greater impact on this global perception of well-being. Acupuncture, although effective in the symptomatic relief of dyspnoea and increasing physical resistance, tends to exert less broad effects on other dimensions assessed by the CAT and the SGRQ, which explains the difference in results between the two approaches.

4.3. Does acupuncture offer a greater contribution to the relief of COPD symptoms compared to herbal medicine?

Acupuncture has demonstrated particularly robust results in the relief of dyspnoea and the improvement of functional capacity in patients with COPD. Several clinical trials^{71,72,78} evidenced significant reductions in dyspnoea scales, such as the mMRC and the Borg scale applied to the 6MWT. In the Feng *et al.*⁷⁸ study, for example, the group subjected to real acupuncture presented an average decrease of 4.4 points on the Borg scale after the 6MWT, contrasting with a reduction of only 0.5 points in the sham group. This effect also translated into objective functional gains: the same trial reported an increase of 67 m in the distance covered in the 6MWT in the acupuncture-treated group, while the control group showed a decrease of 13 m.

The pathophysiological explanation for these results lies in the capacity of acupuncture to modulate the autonomic nervous system and reduce the subjective sensation of respiratory effort. The stimulation of specific points, frequently associated with nervous and muscular pathways, can improve the coordination of the respiratory musculature and reduce the hyperactivity of the dyspnoea centres in the central nervous system. Thus, even if the spirometric parameters (FEV1, FVC) do not undergo significant changes, the patient experiences a real sensation of greater respiratory comfort¹⁰⁴⁻¹⁰⁶.

Another relevant aspect is that acupuncture promotes rapid and perceptible relief of dyspnoea, which is reflected in an immediate improvement in exercise tolerance¹⁰⁷. This characteristic distinguishes it from herbal medicine, whose impact tends to be more gradual and sustained. Consequently, acupuncture proves to be especially useful in patients who present high functional limitation and who need interventions that provide immediate symptomatic relief and greater capacity to perform daily activities.

In summary, herbal medicine and acupuncture present distinct but complementary profiles in the adjuvant approach to COPD. Herbal medicine demonstrates greater efficacy in the systemic control of inflammation, reduction of exacerbations, and sustained improvement of quality of life, while acupuncture stands out for its capacity to provide immediate relief of dyspnoea and significant gains in tolerance to physical exertion. Thus, the integration of both therapies, in association with conventional pharmacological treatment, may offer a more comprehensive and personalised strategy, capable of responding both to the needs for immediate symptomatic control and the demands of prolonged management of the chronic disease.

5. Conclusion

Acupuncture and herbal medicine are shown to be complementary approaches in COPD: acupuncture excels in the rapid relief of dyspnoea and the improvement of functional capacity/exercise tolerance, while herbal medicine offers a more sustained benefit in quality of life and exacerbation reduction through systemic inflammatory modulation. Neither therapy reverses structural lung damage, but both contribute significantly to symptomatic control and clinical stability. Integrating these approaches offers a more comprehensive treatment focused on both the immediate and long-term needs of the patient.

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Review

Effectiveness and Safety of Acupuncture and Traditional Chinese Medicine in Alzheimer's Disease: A Narrative Review.

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Abstract

Background: Alzheimer's disease (AD) is a leading cause of global dementia characterised by amyloid- β plaques and hippocampal atrophy. Current drugs offer only modest symptomatic relief without modifying disease progression. Acupuncture is being investigated as a promising, low-risk neuromodulatory alternative.

Objective: To assess the efficacy, safety, and biological mechanisms of acupuncture for AD.

Methods: A review of clinical and preclinical studies involving acupuncture, electroacupuncture, and moxibustion.

Results: Combined acupuncture and pharmacotherapy (e.g., donepezil) significantly outperformed drug monotherapy, particularly when applied ≥ 3 times weekly for two months. Preclinical models show stimulation at DU20 (*Baihui*) and BL23 (*Shenshu*) reduces A β deposition, increases hippocampal glucose metabolism, and normalises Wnt/ β -catenin signalling. fMRI and PET scans confirm enhanced hippocampal connectivity and regional blood flow following treatment. Minimal, mild adverse events were reported, indicating a favourable safety profile.

Conclusion: Acupuncture is an effective complementary therapy for AD that enhances cognitive outcomes and metabolic function. Future research should prioritise larger international trials and objective neuroimaging biomarkers to further validate these findings.

Keywords: Alzheimer's disease; Acupuncture; Traditional Chinese Medicine; Cognitive function; Electroacupuncture; Complementary therapies.

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1. Background

AD is a progressive neurodegenerative disorder characterised by cognitive decline, memory impairment, and dementia¹. It represents one of the leading causes of dementia worldwide and is among the main causes of mortality in elderly populations. Current estimates suggest that by 2030 more than 74.7 million individuals globally will be living with AD², imposing substantial social, economic, and healthcare burdens.

Age is the primary risk factor for AD, with incidence increasing significantly in individuals over 75 years old¹. Although currently available pharmacological interventions, including cholinesterase inhibitors and other agents that modulate neurotransmitter activity, may improve cognitive symptoms, communication, and behavioural outcomes, they do not modify disease progression¹. FDA-approved treatments provide only modest symptomatic benefit and are associated with adverse effects.

Recent advances in neuromodulation have suggested new potential therapeutic avenues. For example, a 2013 study conducted at the University of Toronto employed deep

brain stimulation to modulate neural activity and glucose metabolism, reporting preliminary positive outcomes; however, larger controlled trials remain ongoing³.

In the past decade, acupuncture has also been investigated as a complementary treatment for AD. Several randomised controlled trials indicate that acupuncture combined with pharmacotherapy may be more effective than pharmacotherapy alone in improving cognitive outcomes^{4,5}.

The objective of this review is to evaluate the effectiveness and safety of acupuncture interventions in the treatment of AD.

2. Alzheimer's Disease

AD is the leading cause of dementia in older adults. Although commonly associated with progressive memory decline, pathological changes develop years before the onset of clinical symptoms⁶. The disease is characterised by the accumulation of amyloid- β plaques and neurofibrillary tau tangles, leading to synaptic dysfunction, neuronal loss, and progressive cortical atrophy⁷. Early degeneration typically occurs in the hippocampus, a region essential for memory consolidation and retrieval. As neurodegeneration advances, multiple cortical regions are affected, resulting in widespread brain atrophy⁴.

Clinically, AD progression is generally categorised into three stages. In the early stage, patients may present with mild cognitive impairment, difficulty performing daily activities, impaired financial management, and subtle behavioural changes¹. In the moderate stage, impairment extends to language, executive function, sensory processing, and higher cortical functions; neuropsychiatric symptoms such as hallucinations, delusions, and impulse dysregulation may occur¹. In the severe stage, profound neuronal loss results in major functional dependence, inability to communicate, and severe cognitive decline¹.

Although most cases manifest after age 65, a smaller proportion of patients exhibit early-onset AD, often associated with genetic variants including mutations in *APP*, *PSEN1*, and *PSEN2*⁷.

Neuroimaging research highlights the vulnerability of the hippocampal–amygdaloid network in early AD⁴. Functional imaging studies report hypometabolism and structural atrophy in the hippocampal head, amygdala, and parietotemporal cortex, correlating with memory impairment and cognitive decline. Reduced cerebral glucose metabolism is strongly associated with dementia severity⁴. Preclinical research also suggests cognitive improvements with acupuncture interventions in animal models⁸.

Globally, dementia prevalence increases markedly with age. Epidemiological estimates indicate that among individuals aged 65–69, prevalence ranges from 1.25% to 1.6%, rising to approximately 25% in adults over 85¹.

3. Acupuncture

Acupuncture is a therapeutic modality rooted in Traditional Chinese Medicine (TCM) and was recognised by UNESCO in 2009 as Intangible Cultural Heritage⁹. Treatment involves diagnosis based on TCM principles and stimulation of specific acupoints (primarily located along meridian pathways) through needle insertion^{10,11}. Additional therapeutic methods may include moxibustion, auricular therapy, cupping, electroacupuncture, herbal formulations, and movement-based practices^{11–15}.

According to TCM theory, AD is associated with patterns such as kidney essence deficiency, phlegm-turbidity obstructing the orifices, blood and *Qi* deficiency, and pathogenic heat toxins^{16,17}. These imbalances are understood to contribute to progressive cognitive impairment and, ultimately, dementia¹⁶.

Experimental research indicates that electroacupuncture may modulate neurotrophic-signalling pathways, reduce amyloid plaque burden, and enhance cognitive function in animal models^{6,18}. Studies also report regulatory effects on neurotrophin expression and neural metabolism^{6,18}.

Clinical evidence suggests that acupuncture combined with pharmacotherapy, such as donepezil, may yield superior outcomes compared to monotherapy^{4,5}. Multiple randomised controlled trials report greater improvements in cognitive scores and fewer adverse events in acupuncture groups; however, further large-scale, rigorously designed clinical trials are required to validate these findings and determine generalisability^{4,5,17}.

4. Results

A systematic review by Zhou *et al.*⁵ conducted at Wuhan University analysed five clinical studies comprising 568 participants diagnosed with mild cognitive impairment (MCI), a condition frequently preceding dementia. Participants receiving acupuncture demonstrated approximately 10% greater improvement on cognitive assessments compared to those receiving pharmacological treatment alone. Combined acupuncture–drug therapy yielded superior outcomes when performed three times per week for at least two months. These findings are consistent with other published reviews.

A 2016 study at the Fujian University of Traditional Chinese Medicine⁶ investigated electroacupuncture at *Baihui* (DU20) in murine AD models. The intervention reduced amyloid- β (A β) deposition and improved cognitive performance, while modulating brain-derived neurotrophic factor (BDNF) expression toward neuroprotective isoforms. Although DU20 has historically been associated with cognitive benefits in TCM, recent research provides mechanistic evidence supporting its neurobiological effects.

Additional preclinical research suggests that electroacupuncture and moxibustion preserve hippocampal structure and modulate signalling pathways. A study by Zhou *et al.*¹⁹ demonstrated that stimulation at DU20 and BL23 reduced neuronal injury and normalised axon and β -catenin protein expression in rodent AD models.

Human neuroimaging studies support these findings. Functional MRI demonstrated enhanced hippocampal connectivity and regional cerebral blood flow following acupuncture in AD patients, particularly in frontal and temporal regions associated with memory processing²⁰.

According to the meta-analysis by Zhou *et al.*⁵ ten RCTs were identified ($n = 585$) from a pool of 1,324 publications, including three electroacupuncture and seven manual acupuncture trials, with treatment duration ranging from four to twenty-four weeks. DU20 and ST36 (*Zusanli*) were the most frequently used points; SP10 (*Xuehai*), *Sishencong* (EX-HN1), and others appeared less frequently.

Across included studies, acupuncture was associated with clinically meaningful improvements in cognitive function. Several trials found acupuncture superior to pharmacological therapy alone, while others indicated synergistic effects when combined with donepezil, piracetam, nimodipine, and related agents. Reported adverse events were mild, suggesting favourable safety profiles; however, larger rigorously designed trials are needed to confirm efficacy and long-term outcomes.

Preclinical research at Beijing University of Chinese Medicine revealed improvements in learning and spatial memory following electroacupuncture at DU20 and *Yintang*, accompanied by increased hippocampal glucose metabolism²¹. Additional studies indicate correlations between glucose hypometabolism, hippocampal atrophy, cholinergic system degeneration, and glucocorticoid regulation in AD pathology²²⁻²⁴.

In addition, Cao *et al.*²⁵ compared electroacupuncture and donepezil in APP/PS1 mice using the Morris Water Maze and micro-PET imaging. Both interventions improved cognitive performance and glucose metabolism, although electroacupuncture demonstrated greater efficacy in both measures.

5. Discussion

The reviewed findings suggest that electroacupuncture may provide potential therapeutic benefits for individuals with AD, particularly through improvements in spatial learning, memory performance, and hippocampal glucose metabolism. Preclinical studies

indicate that stimulation at DU20 exerts neuroprotective effects, including reduced β -amyloid accumulation and modulation of neurotrophic signalling pathways⁶. These results align with TCM frameworks in which Governing Vessel acupoints are associated with cognitive and neurological regulation⁴.

Despite promising outcomes, current evidence remains limited. Among RCTs included in many reviews, cognitive improvement was primarily measured through the Mini-Mental State Examination (MMSE)^{5,19,25}. Additionally, sample sizes across included trials were insufficient to support strong evidence-based conclusions.

As well, most included trials were conducted in China and published in Chinese, which may introduce language and publication bias⁵. Furthermore, a substantial portion of preclinical evidence is derived from animal studies, restricting generalisability to human populations^{6,18,26}.

Adverse events related to acupuncture were minimal, with cases described as mild and well tolerated, or no treatment-related adverse effects. These findings suggest a favourable safety profile, consistent with previous systematic reviews^{5,27}.

Another limitation is the relative scarcity of research integrating acupuncture with Chinese herbal medicine. Among the available studies, it was reported higher efficacy from combined acupuncture-herbal treatment compared with Western pharmaceuticals¹⁶, and improved MMSE scores with combined therapy^{5,28,29}.

Overall, acupuncture appears to have potential as a complementary therapy for AD, with DU20 consistently identified as a principal acupoint, and *Yintang*, ST36, SP10, BL23, and *Sishencong* commonly selected as supplementary points^{5,6,8,16,19,21}. Future research should include larger sample sizes, standardised treatment protocols, long-term follow-up, and neuroimaging biomarkers such as hippocampal volume to assess disease-modifying potential more rigorously.

6. Conclusion

Acupuncture shows significant promise as a low-risk, high-reward complementary therapy for Alzheimer's disease. While it may not replace standard pharmaceuticals, it appears to enhance their efficacy and provide neuroprotective benefits that drugs alone currently lack. To move into mainstream clinical guidelines, future studies must prioritise larger, international sample sizes and use objective neuroimaging biomarkers (like hippocampal volume) alongside traditional cognitive tests.

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Review

The Vagus Nerve and Heart Rate Variability: Physiological Markers in Naturopathic Practice.

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Abstract

This study aims to explore the role of the vagus nerve (VN) and heart rate variability (HRV) as central physiological markers for maintaining homeostasis and for naturopathic clinical practice. The literature review allowed us to understand the functional anatomy of the VN and its relevance as an integrative axis of the gut-brain and heart-brain connections, highlighting its influence on the digestive, metabolic, and immune systems, as well as emotional and behavioural regulation. HRV analysis has emerged as a non-invasive method for assessing autonomic balance, demonstrating that higher levels of vagal activity are associated with greater resilience to stress, better emotional self-regulation, and a lower risk of chronic diseases. Conversely, reduced HRV values are associated with autonomic dysfunction and greater pathological vulnerability. Within Naturopathy, practices such as conscious breathing, meditation, exercise, stress management, sleep hygiene, and a balanced diet reveal potential for stimulating vagal tone and improving HRV, reinforcing the holistic and preventive approach of this therapeutic field. The integration of HRV monitoring devices also constitutes an innovative resource for clinical assessment and intervention, promoting a more evidence-based practice.

In this way, the articulation between NV, HRV and Naturopathy constitutes a promising contribution to the promotion of integral health, although further research is required to deepen the application of these strategies in a naturopathic context, in order to consolidate their effectiveness and sustainability.

Keywords: Vagus Nerve; Heart Rate Variability; Homeostasis; Naturopathy.

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1. Introduction

The Autonomic Nervous System (ANS) is fundamental in regulating involuntary bodily functions, including heart rate, digestion, and respiration ¹. Within the ANS, the VN stands out as the main component of the parasympathetic system, responsible for promoting states of rest, recovery, and the maintenance of physiological homeostasis ². In recent years, interest in the action of the VN and Naturopathic therapeutic approaches has grown across various healthcare areas. These practices value the balance between physiological and emotional systems as a basis for promoting integral health, aligning with the principle of treating the person as a whole and with homeostatic self-regulation ³⁻⁵. Evidence from clinical trials and systematic reviews indicates that naturopathic interventions (especially when combined with techniques such as yoga and controlled breathing) can improve HRV, reduce anxiety symptoms, and promote greater well-being ^{6,7}.

HRV analysis constitutes a non-invasive method to infer the functional balance between the sympathetic and parasympathetic branches of the ANS. Evidence indicates that higher levels of vagal activity, reflected in greater HRV, are associated with better self-

regulation in cognitive, emotional, social, and health domains, as well as greater adaptive capacity and resilience to stress ^{8,9}.

Naturopathy aims to stimulate the body's natural healing mechanisms and promote integral well-being. Thus, understanding vagal function and HRV as markers of autonomic regulation becomes crucial. Recent evidence indicates that integrative interventions, including guided meditation (Heart Rhythm Meditation), breathing practices (such as Sudarshan Kriya Yoga), relaxation techniques, and aromatherapy, can increase vagal activity, reflected in an increase in HRV. These effects are associated with greater autonomic balance, resilience to stress, and better physiological well-being. Furthermore, mantra meditation practices are shown to dynamically modulate cardiac-neural interaction, reinforcing the relevance of these approaches for the maintenance of integral health ¹⁰⁻¹³.

The use of devices, such as the chest heart rate monitor, combined with mobile applications and specialised software, has been widely validated for the precise monitoring of HRV and assessment of sympato-vagal balance in clinical and research contexts ¹⁴⁻¹⁶.

Given this context, this review proposes to highlight the applicability of the VN and HRV as relevant physiological markers in naturopathic practice, emphasising their potential therapeutic application and role in promoting integral health.

2. Anatomical and Physiological Role of the Vagus Nerve in Systemic Homeostasis

2.1. Functional Anatomy of the Vagus Nerve

The VN is one of the main constituents of the parasympathetic division of the ANS. It is composed of 80% afferent sensory fibres (which send sensory information from the body to the *Nucleus Tractus Solitarius* (NTS)—located in the brainstem) and 20% efferent motor fibres, which carry information from the brain to the body, innervating important peripheral organs and regulating vital physiological functions, such as heart rate and gastrointestinal motility. All branches of the VN with visceral efferent fibres also contain afferent sensory fibres, which makes it a highly sensitive nerve. The NTS acts as an integrating centre, coordinating autonomic, neuroendocrine, and immunological responses ^{1,2,8}.

Despite vagal neurons constituting only a small proportion of the nervous system, they play an essential role in overseeing a wide range of vital functions ¹⁷, representing the main bidirectional communication pathway between the Central Nervous System (CNS) and various peripheral organs, thereby playing a crucial role in maintaining systemic homeostasis ². Also known as the “wandering nerve,” the VN is the main cranial nerve responsible for the connection between the brain and organs located in the neck, thorax, and abdomen (Figure 1).

2.2. Interconnection between Interoception, the Vagus Nerve, and Heart Rate Variability

Interoception refers to the capacity of the nervous system to perceive, integrate, and interpret signals originating from internal organs, including the heart, lungs, gastrointestinal system, and other visceral systems. This information is essential for maintaining homeostasis and for behavioural adaptation to the body's physiological needs ¹⁷. Through interoception, the brain continuously monitors the internal state of the body, adjusting autonomic, hormonal, and behavioural responses according to internal demands and the external environment ^{19,20}.

The VN plays a central role in this process, functioning as an essential communication pathway between the organs and the brain. It transports visceral signals to the NTS and, from there, to regions like the hypothalamus and the insular cortex, which modulate behaviour and physiological state ¹⁷. Vagal sensory neurons are highly specialised, detecting stimuli such as gastric distension, the chemical composition of food, and inflammatory signals, allowing the VN to function as an “internal language” of the body ²¹.

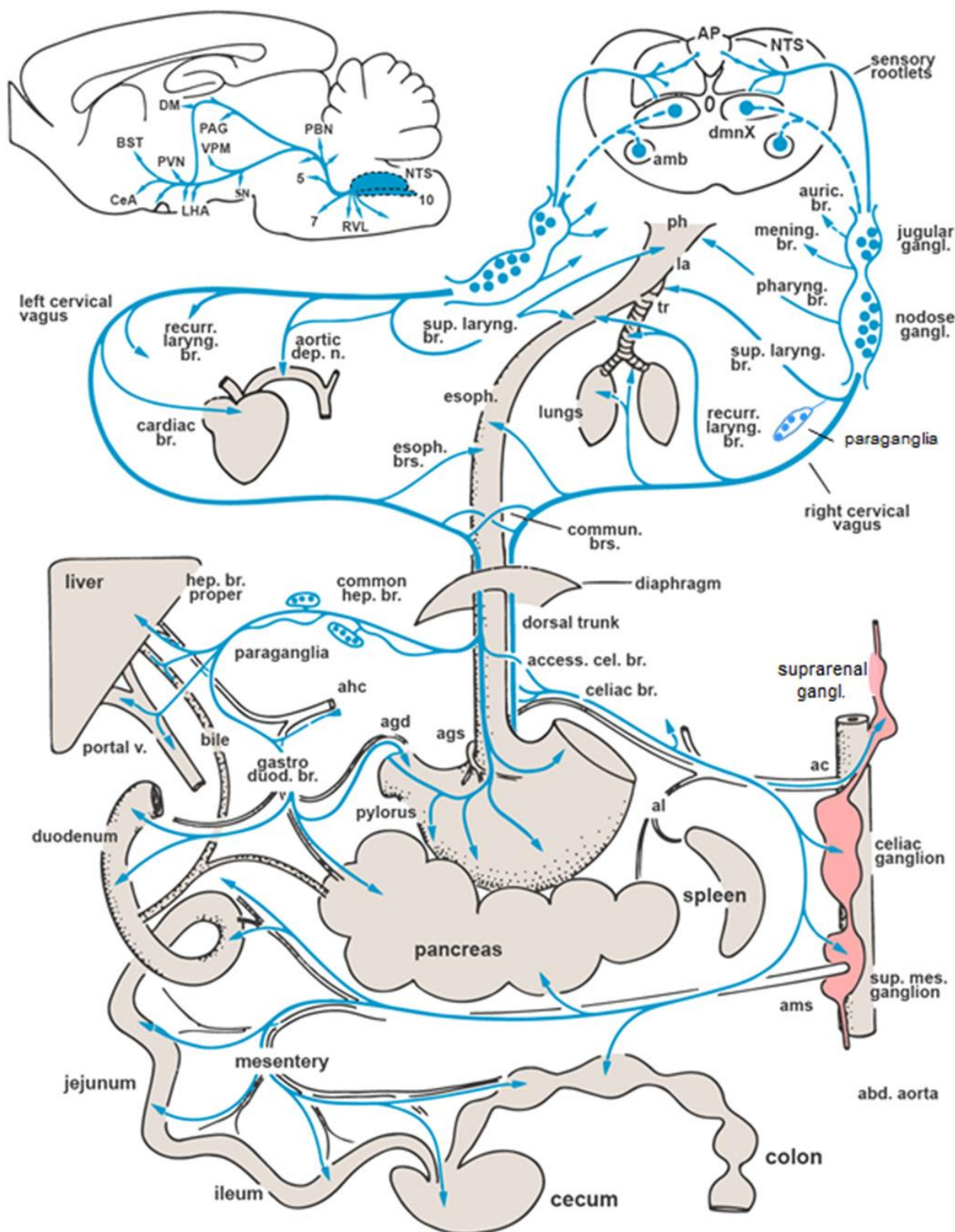


Figure 1. Vagus nerve network as illustrated by Berthoud *et al.* ¹⁸.

In the brainstem, the NTS organises these signals in a similar way to the processing of external senses. Specific maps distinguish signals from the gastrointestinal system and the respiratory tract, reinforcing the VN's role as a "sixth sense" ²². Furthermore, the VN also transmits information about immune states, detecting inflammatory molecules and

adjusting physiological and behavioural responses, such as loss of appetite or fatigue during infections ^{17,23,24}.

HRV is a central indicator of autonomic activity and reflects the heart's ability to respond flexibly to physiological and emotional changes. Vagal activity is one of the main modulators of HRV, with greater variability indicating greater resilience to stress and better autonomic adaptation ²⁵. Interoception provides precise information about the body's internal states, allowing for adjusted autonomic responses that directly influence HRV. Reciprocally, techniques that increase HRV, such as biofeedback or transcutaneous auricular VN stimulation (taVNS), can improve interoceptive perception, creating a positive feedback loop that promotes physiological balance and psychological well-being ²⁶⁻²⁸.

In summary, the VN acts as a vital bridge between the organs and the brain. It ensures the maintenance of internal balance and contributes to the perception of physiological states, influencing emotions, behaviour, and overall health. The integration between interoception, the VN, and HRV opens up new therapeutic perspectives for clinical conditions involving autonomic, cardiovascular, digestive, and immunological dysfunctions, reinforcing strategies that promote homeostasis, mental health, and general well-being ^{17,19,20}.

2.3. The Vagus Nerve as an Integrating Axis for the Gut-Brain and Heart-Brain Axes

The maintenance of homeostasis in situations of immunological challenge requires the adequate integration and transmission of signals from different body systems to the brain, allowing for the coordination of appropriate physiological and behavioural responses ²⁹. This communication is mediated by complex networks that link peripheral organs to the CNS, highlighting the gut-brain and heart-brain axes. In both, the VN assumes a central role as a bidirectional connection pathway, modulating cognitive, emotional, and autonomic functions essential for adaptive behaviour and mental health ³⁰⁻³².

In the gut-brain axis, the interaction between the brain and the gut microbiota occurs via multiple complementary pathways: neural, predominantly through the VN and spinal cord; endocrine, via the hypothalamic-pituitary-adrenal (HPA) axis; immunological, via cytokines; and metabolic, involving molecules such as short-chain fatty acids and tryptophan ³³. Neuroactive compounds produced by bacteria, such as gamma-aminobutyric acid (GABA), serotonin, dopamine, and acetylcholine (ACh), act mainly on the enteric nervous system, but some reach the brain through the bloodstream, circumventricular organs, or directly via the VN. These mediators influence not only digestive and inflammatory processes but also psychological states, affecting anxiety, mood, and stress response. Travaglini *et al.* ³⁴ highlight that the detection of bacterial metabolites and gastrointestinal hormones by vagal afferent fibres results in the integration of these signals into central neuroendocrine circuits, particularly in the hypothalamus and amygdala. Interventions such as vagal stimulation have demonstrated benefits in neural plasticity, memory, and emotional self-regulation, reinforcing the therapeutic potential of this pathway for psychophysiological conditions ³⁵. Adequate vagal regulation is essential for emotional expression, the formation of social bonds, and flexible adaptation to internal and external demands ^{36,37}.

Complementarily, the heart-brain axis represents another critical bidirectional communication pathway, equally dependent on the VN for the integration of physiological signals. Changes in cardiac activity, such as those observed in HRV, directly influence cerebral processes related to attention, stress perception, and emotional regulation ³⁸. High vagal activity is associated with the reduction of systemic inflammation, improved cardiovascular function, and stress modulation, confirming the VN's role as a mediator between emotional and cardiovascular states ³¹. Thus, more than a simple conductor of nerve impulses, the VN constitutes an integrating element that sustains physiological adaptations essential for survival and adaptive behaviour, making it a promising target for therapeutic approaches in cardiac dysfunctions, emotional disorders, and axis imbalances ³⁹.

2.4. Central Role of Vagal Pathways in the Digestive, Metabolic, and Immune Systems

The ANS, and particularly the VN, plays a central role in integrating digestive, metabolic, and immunological functions, ensuring the maintenance of homeostasis and the body's adaptive response to internal and external challenges. In the digestive context, the VN regulates satiety through afferent fibres that transmit gastric distension signals to the NTS, modulating hypothalamic nuclei responsible for appetite control and promoting the suppression of food intake ⁴⁰. Furthermore, vagal stimulation promotes gastrointestinal motility, including gastric emptying and pyloric sphincter relaxation, restoring normal slow-wave patterns in conditions of gastric rhythm disorders ^{41,42}.

Vagovagal reflexes exemplify the functional interface between the enteric nervous system and the brain, with circuits that include the NTS and the Dorsal Motor Nucleus of the Vagus (DMV), responsible for gastric relaxation and the modulation of acid and histamine secretion ^{43,44}. In addition to digestive function, the VN participates in glycaemic regulation, stimulating insulin secretion and improving metabolic control, with recent evidence pointing to the participation of FGF3, a signalling protein produced by vagal sensory neurons, in optimising insulin secretion in situations of metabolic stress ^{45,46}.

From an immune-neuroendocrine perspective, the sensory neurons of the VN can detect invading pathogens and inflammatory signals before or simultaneously with immune cells, relaying information to the CNS which modulates local and systemic immune responses ^{47,48}. The activation of vagal afferent circuits can positively modulate the HPA axis, promoting the release of CRH, ACTH, and cortisol, which contributes to the regulation of the stress response and the reduction of systemic inflammation ⁴⁹.

The cholinergic anti-inflammatory pathway, mediated by the VN, acts on $\alpha 7$ receptors on immune cells, inhibiting the release of pro-inflammatory cytokines such as TNF- α , IL-1 β , and IL-6, being crucial in controlling inflammatory responses in chronic and acute diseases ⁵⁰. The integration between enteric neurons, epithelial cells, and immune cells in the intestinal mucosa highlights the relevance of vagal pathways in neuroimmune coordination, constituting promising targets for therapeutic interventions in metabolic and inflammatory contexts ⁴⁸.

Thus, the VN functions as an integrating element that coordinates digestive, metabolic, and immunological functions, allowing for efficient adaptive responses and the maintenance of homeostasis ⁵¹. This view highlights its therapeutic potential in conditions such as digestive disorders, metabolic dysfunctions, and chronic inflammation, consolidating the central role of vagal pathways in the neurophysiological integration of the body ^{52,53}.

3. Heart Rate Variability

HRV refers to the physiological variation in heart rate caused by autonomic innervation, reflecting fluctuations in the time intervals between consecutive heartbeats (R-R intervals), measurable through electrocardiograms or equivalent devices ⁵⁴. It is considered an indirect marker of physiological and mental well-being ⁵⁵ and presents itself as an important biomarker not only of the autonomic state but also of stress and overall health, extending beyond mere cardiac function ⁵⁶. According to Shaffer *et al.* ⁹, HRV reflects the regulation of autonomic balance, blood pressure, gas exchange, and intestinal, cardiac, and vascular tone.

Polyvagal Theory, proposed by Porges ⁵⁷, emphasises the central role of the vagal pathway in regulating social behaviour and physiological state, suggesting that higher HRV (an index of vagal modulation) is associated with greater emotional self-regulation and resilience to stress. This hypothesis has been confirmed in several studies, which indicate that individuals with higher HRV values exhibit better adaptive capacity when faced with emotional and physiological challenges ^{9,58}. Vagal influences on the heart act as an attenuation mechanism for sympathetic responses to stress, promoting behavioural states of calmness and self-regulation. Vagal tone, in this sense, assumes a protective function, preventing vulnerability to states of apprehension and anxiety.

Higher HRV levels are consistently associated with better health indicators and reflect an autonomic state characterised by self-regulation, adaptability, and resilience. Conversely, reduced values are interpreted as signs of diminished adjustment capacity, reflecting a dysregulated cardiac autonomic function and predictive of worse clinical outcomes^{54,55}. This autonomic imbalance manifests as sympathetic predominance and vagal hypoactivity. Increased sympathetic tone tends to decrease HRV, while vagal predominance increases it^{9,36}.

It is also important to note that HRV is highly sensitive to contextual factors, such as posture, time of day, and psychological or physiological state, which reinforces the need for standardised measurement conditions⁵⁴. Additionally, HRV tends to decrease with age and differs according to gender^{59,60}. It is also influenced by behavioural and environmental variables, such as exercise, sleep, diet, smoking, alcohol and caffeine consumption, respiratory rate, body mass index, blood pressure, negative emotional states (stress, pain, depression), hormonal changes, medication use, and genetic or familial factors^{27,61}.

Regarding HRV measures, SDNN and RMSSD stand out clinically. SDNN represents the overall autonomic function of the heart, reflecting the joint sympathetic and parasympathetic modulation, while RMSSD predominantly reflects the vagal modulation of heart rate. It is observed that RMSSD progressively decreases from the supine position to sitting, standing, and walking, reflecting the reduction in vagal activity and the increase in sympathetic activity⁶². In 24-hour monitoring, SDNN values below 50 ms are classified as unhealthy; between 50–100 ms as compromised; and above 100 ms as healthy. In fact, individuals with an SDNN greater than 100 ms have a mortality risk 5.3 times lower compared to those exhibiting values below 50 ms³⁷. According to Rubik⁵⁶, increases in both SDNN and RMSSD reflect a reduced stress response and/or a more adjusted autonomic balance.

24-hour recordings constitute the gold standard for clinical HRV assessment, given their greater predictive power relative to short-duration measurements. However, brief recordings (60 seconds to 5 minutes), in a sitting or supine position, have been widely used and considered reliable, currently representing the most studied methodology due to its accessibility^{15,63}. These assessments can be performed using validated portable devices, such as the Polar H10 chest heart rate monitor, which has demonstrated excellent agreement with the electrocardiogram (ECG) at rest and during physical exercise. Gilgen-Ammann *et al.*⁶⁴ confirmed the validity of the Polar H10 for R-R interval detection across a wide range of intensities. More recently, Schaffarczyk *et al.*¹⁵ compared the Polar H10 with a 12-lead ECG, finding no significant differences when using the Kubios HRV software for analysis. Data can be transmitted via Bluetooth to mobile applications, such as Elite HRV, which stores the recordings and provides real-time feedback^{14,58,64}.

In addition to its value as a general physiological marker, HRV is also associated with various clinical dysfunctions. The decrease in vagal activity and sympathetic predominance can favour the development of diabetes⁶⁵. Recent evidence demonstrates that the reduction in HRV can precede the clinical manifestation of metabolic and cardiovascular diseases, functioning as an early risk marker⁶⁵⁻⁶⁷. Wang *et al.*⁶⁷ found that decreased HRV in initially healthy individuals is associated with a greater risk of type 2 diabetes, suggesting that autonomic dysfunction may precede detectable metabolic changes. Complementarily, Yu *et al.*⁶⁵ showed that high levels of plasma glucose and the presence of diabetes are negatively correlated with HRV, reinforcing its usefulness in the early detection of metabolic changes and cardiovascular risk. Also in this field, Hajdu *et al.*⁶⁶ identified determinants of HRV in individuals with type 1 diabetes, highlighting the importance of continuous monitoring of this parameter in different diabetic contexts.

The literature also evidences the association between HRV and chronic pain. Tracy *et al.*⁶⁸ showed, in a meta-analysis, that patients with persistent pain have significantly reduced HRV values, indicating autonomic dysfunction marked by a reduction in vagal activity. In parallel, Yuan *et al.*⁶⁹ demonstrated that colonic motor patterns are directly

related to autonomic activity, reflecting in HRV parameters. Such results support the relevance of HRV as an indicator of gut-brain dysfunction. Ali *et al.*⁷⁰ reinforce this evidence by demonstrating correlations between changes in colonic motility and changes in HRV. Finally, Ying-Chih *et al.*⁷¹ identified, through a systematic review, that individuals with functional somatic syndromes, such as irritable bowel syndrome, exhibit significantly lower HRV values, especially in vagal components, compared to healthy individuals. These changes in gut-brain communication can translate clinically into gastrointestinal disorders, such as hardened stools, or hyper-responsivity to environmental stress⁶⁸⁻⁷¹.

For Wareing *et al.*²⁷, although RMSSD and SDNN measures do not directly index interoception, if an individual's autonomic activity is optimal in a given context, then it may be that they are capable of detecting, integrating, and adequately responding to interoceptive afferents. Supporting this assumption, a higher resting RMSSD positively correlates with interoceptive accuracy, while lower SDNN was observed in medicated and non-medicated individuals with conditions in which interoceptive deficits have been implicated, including depression, anxiety, and post-traumatic stress disorder, which provides support for a relationship between greater interoceptive abilities and better autonomic regulation.

4. Naturopathy: An Integrative Approach to Global Health

Globally, Naturopathy is practised in at least 98 countries with representation in all regions of the world, being widely practised in Europe (54 practising countries), Latin America (51 practising countries), Africa (47 practising countries), and the Western Pacific (37 practising countries). Estimates from the World Naturopathic Federation (WNF) suggest there are between 75,000 and 100,000 naturopaths currently in clinical practice worldwide⁷². Recognised by the National Institutes of Health (NIH) and the World Health Organization (WHO) as a distinct system of complementary and integrative healthcare, it is an existing model of integral health service delivery⁷³. Naturopathy is configured as an integrative health approach that emphasises the organism's natural capacity to maintain and restore balance and well-being⁷⁴ and is taught and practised according to a globally consistent set of fundamental philosophies and principles. Holism and vitalism are the core naturopathic philosophies; Holism is founded on the recognition that "the spiritual, psychological, functional, and structural aspects of an individual act interdependently and are influenced by external, environmental, social, and other factors." Human health and the manifestations of disease are understood by naturopathic practitioners as expressions of the close and complex interactions between a series of internal systems and external factors demonstrated by the naturopathic multi-system approach⁷⁵. This holistic view of the human being recognises the intrinsic interconnection between body, mind, and spirit, highlighting the importance of treating the individual as a whole, considering their uniqueness and context⁷⁶. This holistic principle implies that treatment is not limited to resolving isolated symptoms but focuses on identifying and correcting underlying imbalances that compromise the organism's homeostasis, a central concept in VN-mediated regulation and HRV modulation⁷⁷.

The principles of Naturopathy act as a solid foundation for a patient-centred clinical practice, promoting integral health and sustainable prevention, and respecting the complexity and uniqueness of each individual (Bradley *et al.*, 2019). The incorporation of naturopathy into a primary care model could increase the focus on health promotion and disease prevention^{4,73}.

The philosophy, theory, and principles are translated into clinical practice through a variety of therapeutic modalities. The WNF identified seven main modalities: (1) clinical nutrition and diet modification/counselling; (2) applied nutrition (use of food supplements, traditional medicines, and natural health products); (3) herbal medicine; (4) lifestyle counselling; (5) hydrotherapy; (6) homeopathy; and (7) physical modalities (based on the treatment modalities taught and permitted in each jurisdiction, including yoga, naturopathic manipulation, and muscle release techniques)⁵.

According to Myers *et al.*⁵ and Steel *et al.*⁷², Naturopathy is a system of traditional medicine supported by seven principles of practice (the healing power of nature; treat the person as a whole; treat the cause; first, do no harm; naturopath as teacher; health promotion and disease prevention; and wellness). Other defining principles of naturopathic practice are patient-centeredness and individualisation, with naturopaths typically resorting to a range of therapeutic interventions to best meet the patient's health needs and preferences. In line with these principles, Naturopathy has, as one of its major cornerstones, the emphasis on prevention, which aims to anticipate and avoid the emergence of pathologies, promoting interventions that reinforce the body's natural defence mechanisms. Unlike conventional medicine, which often focuses on symptom suppression, Naturopathy prioritises long-term health promotion through the restoration of physiological and emotional balance^{78,79}. Recent studies show that naturopathic techniques, such as meditation and breathing exercises, positively influence HRV, improving autonomic regulation and resilience to stress, demonstrating the VN's modulating function in homeostasis and psychophysiological well-being^{17,80}. This preventive orientation is supported by scientific evidence that highlights the importance of early and sustained interventions for the improvement of immune and neuroendocrine response⁸¹.

However, patient education and empowerment assume a central role in the naturopathic therapeutic process. Through information and active involvement, the individual is empowered to autonomously manage their health, developing habits that support long-term physical and emotional balance⁷⁹. This partnership between therapist and patient constitutes a fundamental basis for more effective and lasting therapeutic outcomes⁸².

The recognition of lifestyle as one of the main determinants of health constitutes another fundamental pillar. Interventions that promote healthy eating, regular physical exercise, effective stress management, quality sleep, and solid social relationships demonstrate a positive impact on ANS modulation, the reduction of systemic inflammation, and the promotion of hormonal balance⁸³. These naturopathic practices optimise vagal activity, favouring interoception, gut-brain and heart-brain communication, and promoting a balanced and resilient physiological state^{20,31}. Thus, Naturopathy promotes not only the treatment of diseases but the transformation of lifestyle as a preventive and therapeutic measure, reinforcing the organism's resilience¹².

Another fundamental principle is '*primum non nocere*', or "first, do no harm". This dictates that therapeutic choices must be safe, natural, and minimally invasive, thus respecting the patient's physiological processes⁸⁴. This approach values the reinforcement of natural self-healing capacities, minimising adverse effects and promoting sustainable recovery.

Recent studies corroborate that naturopathic interventions positively influence HRV⁸⁰, because naturopathic treatments can control persistent inflammation, maintain immunological homeostasis, and reduce disease activity, thus leading to better health outcomes and better quality of life in patients with or at risk of chronic conditions, including cardiovascular diseases, type 2 diabetes/obesity, chronic pain, anxiety, multiple sclerosis, hepatitis C, and menopausal symptoms^{5,6,85,86}. Furthermore, improvements in blood glucose levels and insulin sensitivity have been observed in studies on diabetes, which may corroborate the role of naturopathy in the management of metabolic disorders⁸⁷. In this context, it becomes particularly relevant to consider the integration of VN function and HRV, as these mechanisms offer the neurophysiological support for the observed effects. Studies have demonstrated that vagal modulation is associated with reduced inflammation, autonomic balance, and better cardiovascular outcomes^{88,89}. Additionally, interventions that increase HRV show a positive impact on stress control, emotional regulation, and psychophysiological resilience⁹⁰. This perspective not only reinforces the effectiveness and durability of naturopathic interventions but also establishes a bridge between clinical practice and advances in biomedical science, highlighting the consistency and relevance of this approach for promoting integral health.

5. Conclusion

In conclusion, the evidence presented underscores the critical role of the VN as the fundamental architect of systemic homeostasis, functioning as the essential bridge between the central nervous system and the body's vital organs. Through the complex integration of the gut-brain and heart-brain axes, the VN regulates crucial metabolic, immune, and emotional processes, while HRV serves as a quantifiable and reliable biomarker of this autonomic resilience. The scientific validation of these mechanisms confirms that high vagal tone and optimal HRV are not merely indicators of cardiac function, but comprehensive markers of an individual's capacity for self-regulation, adaptability to stress, and overall physiological well-being.

Furthermore, the convergence of neurophysiology and Naturopathy offers a robust framework for promoting integral health. By recognising the VN and HRV as central targets for therapeutic intervention, Naturopathic practice gains a measurable physiological basis for its multimodal approaches, such as mind-body techniques, nutritional adjustments, and lifestyle counselling. Ultimately, bridging the gap between biomedical science and holistic principles validates the efficacy of Naturopathy in preventing chronic disease and fostering resilience, reinforcing the importance of treating the person as a whole to achieve a sustainable state of balance and health.

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