ISSN 2975-9323
ISSN 2975-9552

Journal of Complementary Therapies in Health

July 2025

Volume 3, Issue 2 - Special Number

INSTITUTO PORTUGUÊS 太極拳 氣功 TAICHI CHIKUNG

Journal of Complementary Therapies in Health

Volume 3 Issue 2 – Special Number
2025

Sponsored by:
Portuguese Institute of Taiji and Qigong – Portugal

Journal of Complementary Therapies in Health (JCTH)
ISSN 2975-9323
eISSN 2975-9552

Visit the journal at https://www.institutoptc.com/journal-complementary-therapies

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II INTERNATIONAL CONGRESS

COMPLEMENTARY THERAPIES IN HEALTH

ONLINE | JUNE 28 2025

Organized by:

Portuguese Institute of Taiji and Qigong – Portugal

In partnership with:

ABS - Atlântico Business School – Portugal

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Editorial Note: The abstracts and studies featured in this issue, pertaining to the 2nd International Congress on Complementary Therapies in Health, have been made available by the authors exclusively for the purpose of this publication. It is worth noting that certain communications presented at the aforementioned congress have not been included in this particular publication.

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Journal of Complementary Therapies in Health
ISSN 2975-9323 |eISSN 2975-9552

Editorial

The 2nd International Congress on Complementary Therapies in Health.

The 2nd International Congress on Complementary Therapies in Health, organised by the Portuguese Institute of Taiji and Qigong in collaboration with the Atlântico Business School, the Confucius Institute of the University of Coimbra, and the Centre of Biosciences in Integrative Health, has built upon the foundational success of its inaugural event. While the first congress focused on establishing a network and highlighting the potential of these therapies, the second congress took a significant step forward by displaying a deeper level of scientific inquiry and collaboration.

The keynote speakers and presentations further underscore the emphasis on evidence-based practice. The congress featured insightful contributions on topics such as "Digital Chinese Medicine and High-Tech Acupuncture" by Gerhard Litscher, which bridges traditional and modern approaches, and "Quantum Nutrition" by Rosa Vilares Santos, which explores an integrative approach to metabolic dysfunction. This blend of traditional knowledge with contemporary scientific advancements reflects the congress's mission to integrate these therapies into the modern healthcare landscape.

The breadth of topics covered in the communications and poster presentations is a testament to the growing interest and research in this field. From the efficacy of acupuncture in conditions like insomnia, Alzheimer's, and Parkinson's disease, to the role of Qigong in children's well-being and pain management, the research presented tackles a wide range of health challenges. The inclusion of studies on wet cupping for low back pain and the antimicrobial properties of medicinal herbs also demonstrates a multifaceted and comprehensive approach to complementary therapies.

The collaborative spirit that was central to the first congress continues to be a cornerstone of this second event. The partnership between the Portuguese Institute of Taiji and Qigong and its collaborators—the Atlântico Business School, the Confucius Institute of the University of Coimbra, and the newly added Centre of Biosciences in Integrative Health—is a powerful force in fostering this environment of research and knowledge exchange. The scientific committee, with members from both Portugal and China, ensures a diverse and international perspective on the presented research.

The 2nd International Congress on Complementary Therapies in Health represents a significant evolution in the field. By moving beyond networking and initial awareness to a platform for detailed, peer-reviewed research, the congress is actively contributing to the implementation of evidence-based complementary therapies in healthcare. The commitment to scientific rigour, combined with the power of multinational collaboration, lays a strong foundation for a future where these therapies are not just an alternative but also an integral part of a holistic and effective healthcare system.

Jorge Magalhães Rodrigues MSc, LAc, CMD, EP, Editor-in-Chief

Citation: Rodrigues J.M. The 2nd International Congress in Complementary Therapies on Health 10.5281/zenodo.16815918

Published: 12 August 2025

Publisher's Note: IPTC stays neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Journal of Complementary Therapies in Health
ISSN 2975-9323 | eISSN 2975-9552

Abstract

Digital Chinese Medicine and High-Tech Acupuncture: Integrating Chinese and Western Medicine.

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Abstract

This opening keynote lecture explores the integration of traditional Chinese medicine (TCM) with modern technological advancements, leading to the development of Digital Chinese Medicine (DCM) and High-Tech Acupuncture. It highlights key innovations and international collaborations between Switzerland, Austria, China, and beyond.

An introduction to DCM sets the foundation by discussing its evolution and applications in Europe and China. A short overview of high-tech acupuncture provides insights into selected content and advancements.

Key technological breakthroughs are examined, including robot-assisted acupuncture, which utilizes automation for precision treatment (cooperation with Nanjing, Taichung). Furthermore, computer-controlled laser acupuncture (cooperation with Taichung) is analyzed for its potential in non-invasive stimulation methods. The lecture also explores teleacupuncture, a cutting-edge approach enabling remote treatments across multiple locations, such as Graz, Bad Zurzach, Beijing, Wuhan, Harbin, and Shanghai.

The opening keynote concludes with an analysis of future prospects, discussing the potential for further integration of digital tools in acupuncture and traditional medicine. These advancements mark a significant step toward a more globally connected and technologically enhanced approach to integrative medicine.

Keywords: Digital Chinese Medicine; High-Tech Acupuncture; Integrative Medicine.

Citation: Litscher G. Digital Chinese Medicine and High-Tech Acupuncture: Integrating Chinese and Western Medicine. Journal of Complementary Therapies in Health. 2025;3(2) 10.5281/zenodo.16812237

Publisher's Note: IPTC stays neutral concerning jurisdictional claims in published maps and institutional affiliations.

Journal of Complementary Therapies in Health
ISSN 2975-9323 | eISSN 2975-9552

Abstract

A General View on Ageing in Chinese Medicine.

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Abstract

This keynote presentation explores the concept of aging from the perspective of Traditional Chinese Medicine (TCM), distinguishing between natural and premature aging. It introduces an ancient herbal formula, "Elderly Beaten Pill," to illustrate TCM's long-standing focus on longevity. The core argument highlights kidney deficiency as a primary cause of aging in TCM, contrasting it with the modern biomedical understanding of kidney function. Manifestations of kidney deficiency, such as hair loss, weakened senses, and decreased sexual function, are discussed, along with its two dimensions: innate kidney essence (inherited) and acquired kidney essence (influenced by lifestyle).

The speaker emphasizes that while innate essence is determined by parentage, acquired essence can be managed through reducing excessive consumption (e.g., sexual indulgence, overwork, poor sleep, emotional imbalances) and supporting spleen function to ensure proper nutrient absorption.

Beyond kidney deficiency, blood stasis is identified as another crucial factor in aging. Blood stasis, characterized by impeded flow of "*Qi*" and blood, leads to poor circulation, accumulation of harmful substances, and organ degeneration. The presentation details various causes of blood stasis, including phlegm turbidity (sticky fluids, high blood fats/sugar), *Qi* deficiency (weak heart function), liver constraint (emotional stagnation), and coldness. For each cause, it is suggested corresponding TCM herbal strategies and lifestyle adjustments.

In summary, TCM views aging largely as a result of kidney deficiency (both innate and acquired) and blood stasis. By addressing these root causes through lifestyle modifications and specific herbal interventions, individuals can aim to delay the aging process and maintain overall health.

Keywords: Aging; Traditional Chinese Medicine; Kidney Deficiency; Spleen Deficiency; Blood Stasis.

Citation: Ye X. A General View on Ageing in Chinese Medicine. Journal of Complementary Therapies in Health. 2025;3(2) 10.5281/zenodo.16812373

Publisher's Note: IPTC stays neutral concerning jurisdictional claims in published maps and institutional affiliations.

Acknowledgements: This work was presented at the 2nd International Congress on Complementary Therapies in Health, held on 28 June 2025.

Journal of Complementary Therapies in Health
ISSN 2975-9323 | eISSN 2975-9552

Review

Quantum Nutrition and Artificial Intelligence: A Bioinformational Perspective on Metabolic Health.

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Abstract
Quantum Nutrition is an emerging integrative model that aligns principles of quantum physics with nutritional science to offer a novel perspective on metabolic dysfunction. This paradigm considers the human body as a bioinformational system, responsive not only to biochemical inputs but also to vibrational and energetic signals derived from food, environment, and consciousness. Drawing analogies with Artificial Intelligence (AI), in which system learning and adaptation are driven by data quality and algorithmic feedback, the human organism is viewed as an intelligent system capable of epigenetic reprogramming in response to nutritional and emotional stimuli. Using principles such as Einstein's equation ($E = mc^2$) and Heisenberg's uncertainty principle as conceptual tools, Quantum Nutrition suggests that food acts not only as matter but as condensed energy and bioinformation capable of modulating gene expression and physiological coherence. This paper explores the potential of Quantum Nutrition as a foundational element of personalised, adaptive, and frequency-based medicine for metabolic health restoration.

Keywords: Quantum Nutrition; Einstein; Food Energy; Heisenberg; A.I.; Bioinformation; Metabolism; Integrative Practices.

Citation: Santos R.V. Quantum Nutrition and Artificial Intelligence: A Bioinformational Perspective on Metabolic Health. Journal of Complementary Therapies in Health. 2025;3(2) 10.5281/zenodo.16505940

Academic Editor: Jorge Rodrigues

Received: 29 June 2025
Reviewed: 10 July 2025
Accepted: 25 July 2025
Published: 27 July 2025

Publisher's Note: IPTC stays neutral with regard to jurisdictional claims in published maps and institutional affiliations.

1. Introduction

The 21st century has seen a growing convergence between quantum physics, systems biology, and integrative health approaches. Amid rising rates of chronic metabolic diseases such as type 2 diabetes, cardiovascular disorders, and obesity, there is increasing recognition that traditional biochemical models of nutrition may be insufficient to fully explain or reverse these multifactorial conditions [1,2]. Simultaneously, advancements in AI have transformed multiple fields by demonstrating how intelligent systems can learn, adapt, and evolve based on the quality of their inputs and feedback loops [3]. In this context, the human body can be reinterpreted as a biological system capable of processing data in the form of nutrients, emotions, and environmental signals—adapting epigenetically and energetically to internal and external stimuli [4,5]. Quantum Nutrition emerges at this intersection, proposing that food is not merely biochemical matter, but also a carrier of vibrational information capable of modulating physiological processes at the subatomic level. Inspired by foundational concepts in quantum physics—such as Einstein's mass-energy equivalence and Heisenberg's uncertainty principle—this model suggests that health outcomes depend not solely on the chemical composition of the diet, but on the frequency, coherence, and intention associated with food intake. This paper proposes an integrative framework that draws analogies between AI systems and human metabolism, incorporating quantum principles, consciousness, and bioinformation into the field of nutrition.

The implications for personalized, adaptive, and preventative medicine are profound, offering new possibilities for therapeutic intervention in metabolic dysfunction.

2. The Human Body as a Learning System: Parallels with Artificial Intelligence

AI systems are designed to process data, detect patterns, and adapt based on new information. Similarly, the human body operates as an intelligent biological network capable of interpreting biochemical and energetic inputs, integrating them into homeostatic and adaptive responses [6]. In AI, data quality is crucial—poor input leads to suboptimal or erroneous outputs. In biological systems, the nature of nutritional, emotional, and environmental inputs similarly determines physiological outcomes, including gene expression, immune response, and metabolic regulation [7].

Nutrients act as epigenetic signals capable of influencing the transcriptome. This adaptive response is like machine learning, where a system evolves through feedback loops and recalibrates based on experience. Just as AI employs algorithms to analyse and learn from data, the body relies on genetic and epigenetic coding as well as dynamic biochemical pathways to process information [8,9].

Moreover, morphogenetic fields, as proposed by Sheldrake [10], suggest that biological systems may be shaped not only by physical and chemical parameters but also by energetic patterns and memory fields. These concepts align with emerging understandings in quantum biology, where information is not limited to molecular interactions but includes vibrational and frequency-based signalling [11,12].

3. Einstein's Equation and Food as Condensed Energy

Einstein's mass-energy equivalence formula, $E = mc^2$, illustrates that matter and energy are interchangeable forms, with mass representing condensed energy. In the context of Quantum Nutrition, this concept reframes food not only as a physical substance but also as an energetic potential. The mass (m) of food, when combined with its vibrational characteristics—analogous to the squared speed of light (c^2)—represents a powerful form of stored energy that can be released and utilised by the human body [13,14].

Whole, unprocessed, and living foods retain higher vibrational coherence and therefore offer greater energetic value. When ingested, these foods may support cellular communication, coherence, and regeneration more effectively than processed, energetically 'flat' foods. This approach suggests that the quality of energy embedded in food influences not only metabolic rate but also systemic health outcomes [15,16].

Biophoton research supports this view, showing that living cells emit light and that the biophotonic quality of food can affect the electromagnetic properties of cells [17]. In essence, Quantum Nutrition invites a reinterpretation of dietary assessment: from macronutrient ratios and caloric value to bioenergetic density and coherence.

4. Heisenberg's Uncertainty and the Dynamic Nature of Nutrition

Heisenberg's uncertainty principle, a cornerstone of quantum physics, asserts that it is impossible to simultaneously know both the position and velocity of a subatomic particle with complete accuracy [18]. This principle reflects the inherent unpredictability of quantum systems and offers a useful analogy for understanding human biology and nutritional response. The human organism is not static; it is a dynamic, adaptive, and context-sensitive system influenced by internal and external variables.

In Quantum Nutrition, this translates into the recognition that the same food may elicit different physiological responses depending on the individual's emotional state, environmental context, and level of consciousness at the moment of ingestion [19]. Therefore, nutrition cannot be reduced to fixed outcomes based solely on molecular composition. Instead, it must account for the energetic and informational context in which the food is consumed.

The observer effect, another quantum concept, further reinforces this idea. Just as observation alters the state of a quantum system, the act of conscious eating—marked by intention, gratitude, and awareness—modulates digestive, hormonal, and cellular responses [20]. These principles support a more nuanced and personalised approach to nutrition, where context and consciousness are key determinants of health outcomes.

5. Vibrational Nutrition, Conscious Eating and Genetic Reprogramming

Emerging evidence in psychoneuroimmunoendocrinology and epigenetics suggests that nutritional responses are modulated not only by molecular interactions but also by emotional and cognitive states that influence hormonal, immune, and neurological pathways [21-23]. In this context, vibrational nutrition refers to the capacity of foods to transmit bioenergetic signals that interact with the body's informational and energetic fields.

Conscious eating practices—characterised by intention, presence, and gratitude—may modulate physiological functions including digestion, absorption, and gene expression [24]. These behaviours activate the parasympathetic nervous system, enhance vagal tone, and support homeostatic coherence, which are essential for optimal metabolic processing.

From a quantum nutrition perspective, food, emotion, and intention form a nutrigenomic vibrational triangle. This triad influences epigenetic pathways by sending coherent signals to the genome, potentially modulating gene expression in favour of resilience and regeneration [25]. Living and whole foods, due to their intact cellular structure and biophotonic quality, are proposed to be richer in such coherent vibrational information [26].

Moreover, environmental resonance, circadian rhythms, and emotional states also influence DNA methylation, histone modification, and RNA expression [27-29]. The integration of these variables supports a model of nutrition as a dynamic interface between matter, energy, and consciousness, opening new therapeutic possibilities for metabolic regulation and chronic disease prevention.

6. Quantum Nutrition in Practice: Implications for Metabolic Dysfunction

Metabolic dysfunction encompasses a constellation of conditions including insulin resistance, low-grade chronic inflammation, dyslipidaemia, and altered hormonal signalling — all of which contribute to the pathogenesis of type 2 diabetes, obesity, and cardiovascular disease [30,31]. While conventional approaches focus primarily on calorie restriction, glycemic control, and macronutrient balancing, Quantum Nutrition proposes a complementary strategy that integrates energetic, informational, and consciousness-based variables into clinical nutritional care.

In this model, nutritional intervention becomes a form of energy medicine: food is selected not only for its biochemical profile but also for its vibrational coherence, freshness, and alignment with the individual's biological rhythms. Priority is given to unprocessed, living foods—such as sprouted grains, fermented vegetables, and raw fruits—that maintain high levels of photonic emission and enzymatic vitality [32-34].

Furthermore, personalised timing, aligned with circadian rhythms and digestive readiness, is recommended to enhance nutrient assimilation and cellular synchronisation [35]. Practices such as silent eating, pre-prandial gratitude, and breath awareness are incorporated to shift the autonomic nervous system into a parasympathetic state, favouring metabolic recovery and coherence [36-40]. Quantum Nutrition thus offers a promising integrative strategy, particularly in patients with complex, multifactorial metabolic profiles where standard interventions show limited efficacy. Figure 1 sinthesises the concept explored in this article.

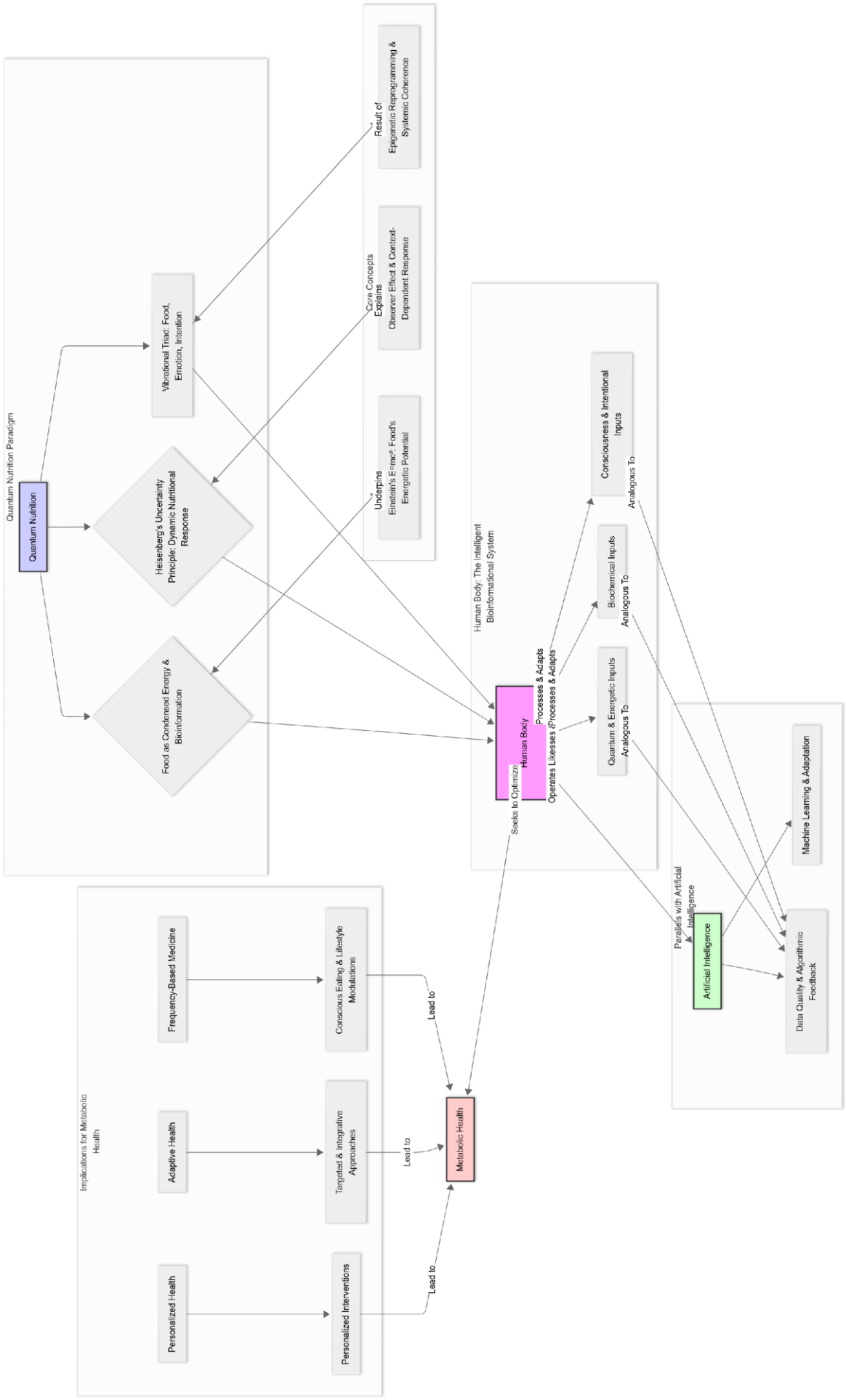

Figure 1. Concept of quantum nutrition and AI as a bioinformational perspective on metabolic health. Schematic made with mermaidchart.com.

7. Conclusion

Quantum Nutrition represents a transformative approach that transcends traditional biochemical paradigms by integrating principles of quantum physics, bioinformation, and consciousness into nutritional science. By viewing food as condensed energy carrying vibrational information and recognising the body as an adaptive intelligent system analogous to Artificial Intelligence, this model offers new insights into the complex interactions underpinning metabolic health.

Incorporating variables such as emotional state, intention, and environmental context acknowledges the dynamic and unpredictable nature of human biology, consistent with quantum uncertainty principles. The concept of conscious eating and the nutrigenomic vibrational triangle emphasizes the potential for diet and lifestyle to epigenetically modulate gene expression, promoting systemic coherence and resilience.

Quantum Nutrition's integrative framework provides a promising foundation for personalised and adaptive interventions in metabolic dysfunction, highlighting the need for further empirical research to validate and expand its clinical applications. As the future of medicine increasingly embraces complexity and holistic data, Quantum Nutrition may serve as a vital bridge connecting molecular science with energetic and informational dimensions of health.

Acknowledgements: A heartfelt thank you to Professor Jorge Magalhães Rodrigues for his unwavering support and invaluable contribution as President of the II International Congress on Complementary Therapies in Health.

Funding: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Conflict of Interest: The authors declare that there are no conflicts of interest.

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: The original contributions presented in this study are included in the article. Further inquiries can be directed to the corresponding author.

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Journal of Complementary Therapies in Health
ISSN 2975-9323 | eISSN 2975-9552

Abstract

Does Acupuncture Influence Melatonin Levels in Insomnia?

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Abstract

Introduction: Insomnia involves difficulty falling or staying asleep despite adequate rest and is linked to increased health risks. Around 10% of adults have chronic insomnia, with women, older adults, and socioeconomically disadvantaged groups being more affected. Melatonin, produced by the pineal gland, controls the body's sleep-wake cycle. Targeting melatonin may improve insomnia treatments. Traditional Chinese Medicine uses acupuncture to balance bodily systems and promote health. Studies show acupuncture can effectively treat sleep disorders, sometimes better than medication. We aim to determine if acupuncture influences melatonin levels in insomnia.

Methodology: PICO framework—patients with insomnia (population), acupuncture (intervention), any control group, melatonin levels as the primary outcome—a PubMed search was conducted. MeSH words were "Acupuncture AND insomnia AND melatonin," filtered to include randomised controlled trials (RCTs) published in the last ten years. Inclusion criteria: studies that investigated acupuncture's effects on melatonin in insomnia; Exclusion criteria: studies measuring melatonin outside insomnia. Two researchers independently screened and extracted data, resolving disagreements through a third researcher to ensure consensus.

Results: 7 met the inclusion criteria. According to our results, melatonin levels increased after acupuncture treatment in five of the seven studies. However, results are limited by factors such as small sample sizes, diverse participant populations and related conditions (including pregnant women, cancer patients, students, and older adults), varied acupuncture protocols, and inconsistent measurement methods.

Conclusion: Acupuncture is a promising treatment option for insomnia, potentially mediated by an increase in melatonin levels. However, more well-designed studies are necessary to confirm its effectiveness.

Keywords: Insomnia; Melatonin; Acupuncture; Traditional Chinese Medicine.

Acknowledgements: This work was presented at the 2nd International Congress on Complementary Therapies in Health, held on 28 June 2025. The full-text article was published as Baldaia M.J., Pinto J., Azevedo C., Ribeiro A., Rodrigues J.M. The neuroendocrine mechanisms underlying acupuncture's efficacy in insomnia: A focus on melatonin. Revista Internacional de Acupuntura. 2024;18(3-4) 10.1016/j.acu.2025.100309.

Citation: Baldaia M.J., César A., Ribeiro A., Pinto J., Rodrigues J.M. Does acupuncture influence melatonin levels in insomnia? Journal of Complementary Therapies in Health. 2025;3(2) 10.5281/zenodo.16812302

Received: 10 February 2025
Accepted: 13 February 2025

Publisher's Note: IPTC stays neutral concerning jurisdictional claims in published maps and institutional affiliations.

Journal of Complementary Therapies in Health
ISSN 2975-9323 | eISSN 2975-9552

Abstract

Efficacy of Acupuncture in Alzheimer's Disease.

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Abstract

Alzheimer's disease (AD) is a debilitating neurodegenerative disorder with limited therapeutic options. This narrative review explores acupuncture, a traditional Chinese medicine technique, as a promising complementary therapy for AD management.

Preclinical research indicates that acupuncture could enhance cognitive function by promoting neurogenesis and reducing neuroinflammation. Human studies also show some evidence of acupuncture's benefits in improving cognitive function. Furthermore, acupuncture may help manage common AD-related comorbidities such as depression, anxiety, and pain.

While preliminary evidence suggests acupuncture's potential, the current body of high-quality clinical trials is limited. To definitively establish its efficacy, optimise treatment protocols, and fully understand its mechanisms of action, larger, well-designed randomised controlled trials are essential. Acupuncture holds promise as a valuable complementary therapy that could significantly improve the quality of life for individuals with AD.

Keywords: Acupuncture; Traditional Chinese Medicine; Alzheimer's Disease; Dementia; Neurodegenerative Diseases.

Acknowledgements: This work was presented at the 2nd International Congress on Complementary Therapies in Health, held on 28 June 2025. The full-text article was published as Engler E.P., Rodrigues J.M. Exploring the Efficacy of Acupuncture in Alzheimer's Disease: A Narrative Review. Journal of Complementary Therapies in Health. 2024;2(2) 10.5281/zenodo.13308733.

Citation: Engler E.P., Rodrigues J.M. Efficacy of Acupuncture in Alzheimer's Disease. Journal of Complementary Therapies in Health. 2025;3(2) 10.5281/zenodo.16812081

Received: 18 February 2025
Accepted: 27 February 2025

Journal of Complementary Therapies in Health
ISSN 2975-9323 | eISSN 2975-9552

Abstract

Acupuncture for Managing Breast Cancer - Efficacy and Mechanisms.

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Abstract

Breast cancer is a major global cause of cancer-related deaths, profoundly affecting patients physically and psychologically. Traditional treatments often come with undesirable side effects, which underscores the importance of exploring complementary therapies. Acupuncture, a practice rooted in traditional Chinese medicine, is drawing interest for its possible advantages across a range of health issues. This review evaluates the current top-level evidence regarding the use of acupuncture in managing breast cancer. Acupuncture showed potential in alleviating stress, depression, and insomnia in individuals with breast cancer. It also proved effective in addressing side effects from treatment, such as pain, fatigue, and menopausal symptoms. However, the evidence for some outcomes is still limited. The ways in which acupuncture works are intricate and warrant further research. Acupuncture appears to be a promising complementary therapy for breast cancer patients, potentially improving both their physical and psychological well-being. While current research is encouraging, more high-quality studies are necessary to establish clear treatment guidelines.

Keywords: Acupuncture; Traditional Chinese Medicine; Breast cancer.

Acknowledgements: This work was presented at the 2nd International Congress on Complementary Therapies in Health, held on 28 June 2025. The full-text article was published as Silva H., Santos A., Monteiro A., Sousa I.R., Rodrigues J.M. Acupuncture for the management of breast cancer: A review of its efficacy and mechanisms. Revista Internacional de Acupuntura. 2024;18(3-4) 10.1016/j.acu.2025.100308.

Citation: Silva H., Santos A., Monteiro A., Sousa I.R., Rodrigues J.M. Acupuncture for Managing Breast Cancer - Efficacy and Mechanisms. Journal of Complementary Therapies in Health. 2025;3(2) 10.5281/zenodo.16812134

Received: 15 January 2025
Accepted: 23 January 2025

Journal of Complementary Therapies in Health
ISSN 2975-9323 | eISSN 2975-9552

Abstract

Effect of an Acupuncture Treatment Protocol on the Patellar Reflex in Parkinson's Disease Patients – Case Series Study.

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Abstract

Introduction: The investigation of rigidity physiology in Parkinson's Disease involves the examination of reflexes. Parkinsonian patients often demonstrate reduced sensitivity in polysynaptic reflexes within the leg extensor muscles, which is correlated with their postural instability. The compensatory mechanisms for impaired proprioceptive reflex function may involve alterations in intrinsic muscle stiffness. The interplay between gait and reflexes is intricately linked to the nervous system's functioning and motor control. Certain reflexes, such as the patellar reflex, play a pivotal role in maintaining walking and posture. Ensuring the integrity of these reflexes is essential for facilitating smooth and efficient walking. Aim: To analyse the behaviour of the patellar reflex in four Parkinson's Disease patients undergoing an acupuncture treatment protocol. Methods: This study adopts a case series design. Reflex outcomes based on amplitude and velocity were assessed at six different time moments throughout a month-long treatment protocol using the MP 36, Biopac Systems. Results: Over the long term, a tendency for an improvement in range of movement and velocity of the patellar reflex was observed. Nevertheless, in specific cases, a reduction in the amplitude during acute effects was also found. Conclusion: Our findings suggest that the acupuncture protocol used may lead to a cumulative improvement in the efficacy of the patellar reflex in patients with Parkinson's disease. However, further in-depth research, including a statistical evaluation with a larger participant pool, is necessary to validate and confirm these promising preliminary results.

Keywords: Acupuncture; Traditional Chinese Medicine; Heidelberg Model; Parkinson's Disease; Patellar Reflex; Biopac System; Amplitude.

Citation: Pereira C.R., Machado J., Criado B., Santos R., Reis A.M., Ramos B., Santos M.J., Greten H.J. Effect of an Acupuncture Treatment Protocol on the Patellar Reflex in Parkinson's Disease Patients – Case Series Study. Journal of Complementary Therapies in Health. 2025;3(2) 10.5281/zenodo.16812197

Received: 24 March 2025
Accepted: 28 March 2025

Acknowledgements: This work was presented at the 2nd International Congress on Complementary Therapies in Health, held on 28 June 2025. The full-text article was published as Pereira C.R., Machado J., Criado B., Santos R., Reis A.M., Ramos B., Santos M.J., Greten H.J. Analysis of patellar reflex in Parkinson disease patients after an acupuncture treatment protocol – Case series study. Clinical Parkinsonism & Related Disorders. 2025;12,100324 10.1016/j.prdoa.2025.100324.

Journal of Complementary Therapies in Health
ISSN 2975-9323 | eISSN 2975-9552

Abstract

Acupuncture's Role in Reproductive Health: A Look at its Potential as a Complementary Therapy.

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Abstract

Background: Infertility, characterized by the inability to conceive naturally, is a widespread health concern affecting many individuals worldwide. Traditional Chinese Medicine (TCM), particularly acupuncture, has emerged as a potential adjunctive treatment for infertility. This review investigates the effectiveness of acupuncture in addressing both female and male infertility, examining current systematic evidence and its proposed mechanisms of action.

Impact on Female Infertility: Acupuncture has shown encouraging results for various forms of female infertility, including anovulatory infertility, polycystic ovary syndrome (PCOS), endometriosis, and in enhancing endometrial receptivity. Research suggests that acupuncture, whether used alone or alongside conventional medical interventions, can lead to improved pregnancy rates, ovulation rates, and increased endometrial thickness. However, it's important to note that some findings remain inconclusive due to limitations in study methodologies. Acupuncture is believed to influence reproductive hormones, enhance ovarian function, and aid in embryo implantation, presenting a valuable therapeutic avenue for women.

Benefits for Male Infertility: For male infertility, acupuncture has demonstrated potential in improving sperm quality, balancing hormone levels, and reducing testicular damage associated with hormonal imbalances. Studies indicate that acupuncture may enhance sperm motility, concentration, and overall semen parameters by regulating endocrine functions and reducing germ cell apoptosis. While these outcomes are promising, the quality of existing studies varies, emphasizing the need for more rigorous research with robust methodologies.

Conclusion and Future Directions: This review underscores acupuncture's potential as a safe, non-invasive, and effective complementary therapy for infertility. Combining principles from Traditional Chinese Medicine with modern medical approaches could lead to more tailored and comprehensive infertility treatments, ultimately improving patient well-being and reproductive outcomes. Future research should aim to overcome current study limitations and further clarify the mechanisms by which acupuncture impacts infertility treatment..

Keywords: Acupuncture; Traditional Chinese Medicine; Reproductive Health; Infertility.

Acknowledgements: This work was presented at the 2nd International Congress on Complementary Therapies in Health, held on 28 June 2025. The full-text article was published as Engler E.P., Rodrigues J.M. Acupuncture in reproductive health: Evaluating its potential as an adjunct therapy. Revista Internacional de Acupuntura. 2024;18(2) 10.1016/j.acu.2024.100296.

Citation: Engler E.P., Rodrigues J.M. Acupuncture's Role in Reproductive Health: A Look at its Potential as a Complementary Therapy. Journal of Complementary Therapies in Health. 2025;3(2) 10.5281/zenodo.16813155

Received: 10 March 2025
Accepted: 17 March 2025

Publisher's Note: IPTC stays neutral concerning jurisdictional claims in published maps and institutional affiliations.

Journal of Complementary Therapies in Health
ISSN 2975-9323 | eISSN 2975-9552

Abstract

Scalp Acupuncture for Chemotherapy-Induced Peripheral Neuropathy: A Pilot Clinical Observation of Three Oncology Cases.

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Abstract

Background: Chemotherapy-Induced Peripheral Neuropathy (CIPN) remains a prevalent and debilitating side effect associated with taxanes and platinum-based compounds, often leading to dose reduction or treatment discontinuation. This pilot observation aimed to evaluate the potential benefits of Zhu's Scalp Acupuncture (ZSA) in improving neuropathic symptoms and quality of life in oncology patients undergoing chemotherapy.

Methods: Three patients diagnosed with breast or gastrointestinal cancer and presenting with moderate to severe CIPN were selected from an oncology department. All had received taxane or platinum-based regimens. A scalp acupuncture protocol based on the ZSA methodology was designed and applied by the same practitioner, every other day over a four-week period. Clinical outcomes were assessed using the SF-36, EORTC QLQ-C30, and the CIPN20 questionnaire at baseline and post-intervention.

Results: All three patients reported marked improvement in neuropathic symptoms, including pain, numbness, and functional mobility. Quantitative analysis of the questionnaires indicated significant enhancement in physical functioning, global health status, and neuropathy-specific items. No adverse effects related to acupuncture were observed.

Conclusion: These preliminary observations suggest that ZSA may offer a promising complementary approach in the management of CIPN. Further controlled studies are warranted to validate these findings and explore their mechanisms of action.

Keywords: Oncology; Neuropathy; Chemotherapy; Scalp acupuncture.

Acknowledgements: This work was presented at the 2nd International Congress on Complementary Therapies in Health, held on 28 June 2025.

Citation: Sousa P., Deus M, Pedrosa M., Borges H., Cruz A., Machado J., Moreira A. Scalp Acupuncture for Chemotherapy-Induced Peripheral Neuropathy: A Pilot Clinical Observation of Three Oncology Cases. Journal of Complementary Therapies in Health. 2025;3(2) 10.5281/zenodo.16812348

Received: 19 May 2025
Accepted: 21 May 2025

Publisher's Note: IPTC stays neutral concerning jurisdictional claims in published maps and institutional affiliations.

Journal of Complementary Therapies in Health
ISSN 2975-9323 | eISSN 2975-9552

Abstract

Acupuncture and Traditional Chinese Medicine: A Promising Complementary Approach for Depression.

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Abstract

Depression remains one of the most widespread mental health disorders globally and while numerous treatments exist, their effectiveness can vary. This has spurred a growing interest in alternative and complementary therapies, with acupuncture gaining significant attention.

This systematic review investigates the impact of Traditional Chinese Medicine (TCM) and acupuncture in managing depression. We analyzed 16 studies published between 2015 and 2024, retrieved from PubMed and ScienceDirect.

Our findings indicate that TCM and acupuncture can positively reduce depressive symptoms, serving as an effective therapeutic intervention. They can be used as a standalone treatment or as a complementary approach alongside conventional Western pharmacological therapy. Based on these results, we conclude that TCM and acupuncture offer a beneficial and side-effect-free option in the treatment of depression.

Keywords: Depression; Traditional Chinese Medicine; Acupuncture; Treatment.

Acknowledgements: This work was presented at the 2nd International Congress on Complementary Therapies in Health, held on 28 June 2025.

Citation: Calçada E.S., dos Santos L.S. Acupuncture and Traditional Chinese Medicine: A Promising Complementary Approach for Depression. Journal of Complementary Therapies in Health. 2025;3(2) 10.5281/zenodo.16813246

Received: 8 March 2025
Accepted: 12 March 2025

Publisher's Note: IPTC stays neutral concerning jurisdictional claims in published maps and institutional affiliations.

Journal of Complementary Therapies in Health
ISSN 2975-9323 | eISSN 2975-9552

Abstract

Five Animal Qigong (Wu Qin Xi) for Children's Wellbeing.

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Abstract

This systematic review investigates the impact of *Wu Qin Xi*, a *Qigong* practice, on the health and well-being of children. Drawing from the principles of Traditional Chinese Medicine and attributed to the ancient physician *Hua Tuo*, *Wu Qin Xi* uses movements inspired by animals to foster a connection with natural forces for therapeutic purposes. The well-being of children is influenced by a range of elements, including their physical activity, nutritional intake, and mental health. We conducted a systematic search of several databases, identifying eight studies that met our criteria for exploring the effects of *Wu Qin Xi* on children's health. The findings suggest encouraging benefits of *Wu Qin Xi* for pediatric health. Specifically, children with autism spectrum disorder showed improvements in behaviour and sensory processing, while those with asthma experienced enhanced lung function and a better quality of life. For children with lobar pneumonia, *Wu Qin Xi* was associated with improved pulmonary function and shorter hospitalisations. The technique also demonstrated benefits for children with spinal abnormalities, leading to improved mobility and posture. Furthermore, *Wu Qin Xi* appeared to reduce stress and enhance cognitive function. It is important to note, however, that the studies reviewed had some limitations, including small sample sizes and varied intervention methods. *Wu Qin Xi* shows potential as a complementary treatment for various childhood conditions. Nevertheless, more rigorous research, including studies with larger participant groups and improved designs, is needed to confirm its effectiveness thoroughly.

Keywords: *Qigong*; Five Animal *Qigong*; *Wu Qin Xi*; Wellbeing; Children.

Citation: Torres R.C., Zenha A., Cruz G., Ye X., Rodrigues J.M. Five Animal Qigong (Wu Qin Xi) for Children's Wellbeing. Journal of Complementary Therapies in Health. 2025;3(2) 10.5281/zenodo.16812024

Received: 20 February 2025
Accepted: 26 February 2025

Publisher's Note: IPTC stays neutral concerning jurisdictional claims in published maps and institutional affiliations.

Acknowledgements: This work was presented at the 2nd International Congress on Complementary Therapies in Health, held on 28 June 2025. The full-text article was published as Rodrigues J.M., Zenha A., Cruz G., Torres R.C., Ye X. The Therapeutic Potential of Five Animal Qigong (Wu Qin Xi) for the Wellbeing of Children: A Systematic Review. Integrative and Complementary Therapies. 2025;31(1) 10.1089/ict.2024.56834.rod.

Journal of Complementary Therapies in Health
ISSN 2975-9323 | eISSN 2975-9552

Abstract

Traditional Chinese Exercises for Pain Management in Patients with Knee Osteoarthritis – A Review of Meta-analyses.

Maria João Baldaia[1#*], Júlia Pinto[1#], Armanda Ribeiro[1#], César Azevedo[1#], Maria João Azevedo[1#]; Zula Munkhzul[1#], Madalena Cartaxo[1#], Andreia Zenha[1#], Carlos Grilo[1#], Susana Freitas[1#], Isabel Costa[1#], Sónia Ferreira[1#], and Regina Silva[1#].

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Abstract

Background: Knee osteoarthritis (KOA) is a chronic, incurable condition that is a leading cause of pain and functional limitations, significantly diminishing patients' quality of life. Effective management requires a personalised, multimodal approach, with exercise being a key recommended intervention.

Objective: This preliminary review aims to evaluate the existing literature on the effectiveness of Traditional Chinese Exercises (TCE) in managing pain among patients with KOA.

Methods: A comprehensive search of the PubMed database was conducted to identify relevant studies. The review focused on meta-analyses assessing the impact of TCE on pain in KOA patients.

Results: Out of 51 meta-analyses identified, 9 met the inclusion criteria, encompassing 152 randomised controlled trials (RCTs) with a combined total of 10,377 participants. The interventions included Tai Chi (100 RCTs), Baduanjin (31 RCTs), Wuqinxi (11 RCTs), Yijinjing (10 RCTs), and Qi Gong (1 RCT, broadly defined). Pain outcomes were measured using validated tools such as the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) and the Visual Analogue Scale (VAS). All nine meta-analyses reported significant improvements in pain scores associated with TCE.

Conclusion: Traditional Chinese Exercises appear to be effective in reducing pain among individuals with KOA and should be considered a viable therapeutic option. In addition to pain relief, TCE may also alleviate fatigue, improve mobility, enhance joint range of motion, and contribute to overall improvements in health and quality of life.

Keywords: Traditional Chinese exercises; Pain; Knee; Osteoarthritis.

Acknowledgements: This work was presented at the 2nd International Congress on Complementary Therapies in Health, held on 28 June 2025.

Citation: Baldaia M.J., Pinto J., Ribeiro A., Azevedo C., Azevedo M.J., Munkhzul Z., Cartaxo M., Zenha A., Grilo C., Freitas S., Costa I., Ferreira S., Silva R. Traditional Chinese Exercises for Pain Management in Patients with Knee Osteoarthritis – A Review of Meta-analyses. Journal of Complementary Therapies in Health. 2025;3(2) 10.5281/zenodo.16813005

Received: 17 March 2025
Accepted: 23 March 2025

Publisher's Note: IPTC stays neutral concerning jurisdictional claims in published maps and institutional affiliations.

Journal of Complementary Therapies in Health
ISSN 2975-9323 | eISSN 2975-9552

Abstract

The Mind-Body Connection in Health and Disease: Insights from Traditional Chinese Medicine and Naturopathy.

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Abstract

It is becoming clearer that psychological and mental health issues like chronic stress, anxiety, and depression play a major role in developing and worsening physical illnesses. Both Traditional Chinese Medicine (TCM) and Naturopathy, despite their different origins, share a core belief: emotional imbalance is often at the heart of physical problems.

This review looks at how these two healthcare systems understand the link between emotional difficulties and physical disease. TCM connects specific emotions to particular internal organs and the disruption of *Qi* (vital energy). Naturopathy, on the other hand, focuses on psychoneuroimmunological mechanisms (how the mind, nervous system, and immune system interact) and the body's natural ability to heal itself.

We examined twenty peer-reviewed articles published between 2000 and 2024 from databases like PubMed, Scopus, and ScienceDirect. These studies specifically explored the connection between emotional states and physical disorders. The research consistently shows that emotional trauma and ongoing stress are linked to conditions such as autoimmune diseases, cardiovascular problems, and gastrointestinal issues.

To address the emotional origins of illness, both TCM and Naturopathy use various treatments. These include acupuncture, herbal remedies, dietary adjustments, and mind-body practices. This evidence highlights the critical need for integrative medical approaches that consider the psychosomatic aspects of illness, ultimately aiming to restore overall health and resilience..

Keywords: Emotional Disorders; Traditional Chinese Medicine; Naturopathy; Psychosomatic Illness; Mind-body Connection.

Acknowledgements: This work was presented at the 2nd International Congress on Complementary Therapies in Health, held on 28 June 2025.

Citation: Batista S., Carrajola A., Palheira C., Ferreira I., Araújo M., Mergulhão P. The Mind-Body Connection in Health and Disease: Insights from Traditional Chinese Medicine and Naturopathy. Journal of Complementary Therapies in Health. 2025;3(2) 10.5281/zenodo.16813333

Received: 28 March 2025
Accepted: 30 March 2025

Publisher's Note: IPTC stays neutral concerning jurisdictional claims in published maps and institutional affiliations.

Journal of Complementary Therapies in Health
ISSN 2975-9323 | eISSN 2975-9552

Abstract

Prospect of Antimicrobial Activity of Three Medicinal Herbs for Superficial Infections.

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Abstract

Background: Superficial infections, including both cutaneous and mucocutaneous types, are a current public health problem with global distribution, especially in elders and diabetic patients. One of the main present/future concerns is fungal/bacterial infections by resistant microorganisms such as methicillin-resistant *Staphylococcus aureus* (MRSA). This study aimed to test if decoctions and essential oil (EO) of coptidis (*Coptis chinensis, Ranunculaceae* family), neem (Aza*dirachta indica, Meliaceae* family), as well as the EO of manuka (*Leptospermum scoparium, Myrtaceae* family) hold antimicrobial activity against prevalent species of microorganisms responsible for superficial infections. Methods: Decoction's preparation from rizhoma coptidis and neem seeds using respective dried plant parts in simmering distilled water. EOs were directly acquired from an apotheke. The antimicrobial activity was studied by determining the minimum inhibitory concentration (MIC), using broth microdilution method, and minimum lethal concentration (MLC) by subculture of MIC plates. Results and Discussion: *C. chinensis* EO and decoction demonstrated some antifungal action against the yeasts and dermatophytes tested. Greatest bactericidal effect against *P. acnes* and some action against *S. aureus* was observed. For *A. indica* only EO showed activity against dermatophytes and *P. acnes*. *L. scoparium* EO displayed the broadest antimicrobial spectrum with activity against bacteria, yeasts, and dermatophytes showing greater activity against *P. acnes* and *S. aureus*. Conclusions: *C. chinensis* (EO/decoction), EOs of *L. scoparium* and *A. indica* presented in vitro efficacy against both fungal, bacterial or even mixed agents of superficial infections, either by sensitive or resistant strains.

Keywords: Decotion; Essential Oil; Traditional Plants; Antimicrobial Activity; Superficial Infections.

Acknowledgements: This work was presented at the 2nd International Congress on Complementary Therapies in Health, held on 28 June 2025.

Citation: de Oliveira N., Noites A., Borges I., Araújo B., da Silva J.E., Machado J., Pinto E. Prospect of Antimicrobial Activity of Three Medicinal Herbs for Superficial Infections. 2025;3(2) 10.5281/zenodo.16813110

Received: 31 March 2025
Accepted: 2 April 2025

Publisher's Note: IPTC stays neutral concerning jurisdictional claims in published maps and institutional affiliations.

Journal of Complementary Therapies in Health
ISSN 2975-9323 | eISSN 2975-9552

Review

Recent Research in Acupuncture for Depression: An Overview and Methodological Analysis of Controlled Trials.

Marina Prudêncio Carvalho[1], Pedro Carvalhinha Torres[1], Carla Ferreira Cardiga[1], Patrícia Silva Soares[1], Rodolfo Costa Torres[2], and Elson Marques Serra[3]*.

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Abstract: Depression is a prevalent condition with a significant impact on affect, cognition, and daily functioning, affecting individuals globally across all demographics. While conventional treatments exist, a substantial portion of patients do not achieve adequate response or experience side effects, highlighting the need for exploring alternative therapeutic options. Acupuncture, rooted in traditional Chinese medicine, has shown potential in modulating biological pathways relevant to depression. This paper aims to synthesise findings from recent randomised controlled trials on the effectiveness of acupuncture for depression and analyse the acupuncture methodologies employed. Therefore, a literature search was conducted in PubMed and SciELO to identify randomised controlled trials published between 2020 and 2025 that evaluated acupuncture as an intervention for depression. The initial search yielded 41 records, with no duplicates. After screening, 31 articles were excluded, and 2 full-text articles could not be retrieved. Eight randomised controlled trials met the inclusion criteria and were included in the final analysis. These studies investigated the efficacy of acupuncture and electroacupuncture in diverse populations, including individuals with post-stroke depression, chronic insomnia, depression in hemodialysis patients, and fibromyalgia. The most frequently used acupuncture points were GV20 and SP6, often in combination, with electroacupuncture commonly applied between GV20 and GV29. The reviewed randomised controlled trials provide promising evidence for the effectiveness and safety of acupuncture and electroacupuncture in alleviating depressive symptoms and improving associated outcomes such as sleep quality, cognitive function, and quality of life across various conditions. Mechanistic insights from these studies and preclinical research suggest that acupuncture may exert its effects through modulation of the hypothalamic-pituitary-adrenal axis, enhancement of neuroplasticity via BDNF signalling, and regulation of neuroendocrine and metabolic pathways. The frequent use of specific acupoints like GV20 and SP6 aligns with traditional Chinese medicine patterns associated with depression. However, limitations such as methodological heterogeneity, small sample sizes, and short follow-up periods necessitate further rigorous research to optimise treatment protocols, elucidate underlying mechanisms, and identify patient-specific predictors of response for effective clinical integration.

Keywords: Depression; Acupuncture; Acupuncture Points; Traditional Chinese Medicine.

Citation: Carvalho M.P., Torres P.C., Cardiga C.F., Soares P.S., Torres R., Serra E. Recent Research in Acupuncture for Depression: An Overview and Methodological Analysis of Controlled Trials. Journal of Complementary Therapies in Health. 2025;3(2) 10.5281/zenodo.15446163

Academic Editor: Jorge Rodrigues

Received: 01 April 2025
Reviewed: 16 April 2025
Accepted: 14 May 2025
Published: 16 May 2025

Publisher's Note: IPTC stays neutral with regard to jurisdictional claims in published maps and institutional affiliations.

1. Introduction

According to the National Institute of Mental Health [1], depression can manifest with significant symptomatology impacting affect, cognition, and the capacity to execute routine daily functions, including sleep, alimentation, and occupational tasks. This condition

exhibits a universal prevalence, affecting individuals across all demographic strata, irrespective of age, ethnicity, socioeconomic status, cultural background, or educational attainment. Current research implicates a confluence of genetic, biological, environmental, and psychological determinants in the aetiology of depression [2-8].

Recent data from the World Health Organization (WHO) in 2019 estimated that around 280 million people worldwide, representing about 5% of all adults, experienced depression. In the United States, the National Institute of Mental Health (NIMH) reported that in 2021, approximately 21 million adults (8.3% of all U.S. adults) had experienced at least one major depressive episode. Depression is more common among women than men and has a higher prevalence among younger adults. The impact of depression extends beyond individual suffering, contributing to significant social and economic burdens through reduced productivity, impaired social functioning, and increased risk of suicide [1,9-11].

Conventional treatments for depression typically include pharmacological interventions, primarily with antidepressant medications, and various forms of psychotherapy, such as cognitive behavioural therapy (CBT) and interpersonal therapy (IPT). While these treatments are effective for many individuals, a significant portion of patients may not respond adequately or experience side effects [11,12]. This highlights the need for exploring and evaluating other potential treatment options to help address this gap.

The interest in acupuncture as a treatment for depression stems from its long history of use in traditional Chinese medicine for various physical and mental health conditions. From a mechanistic perspective, research suggests that acupuncture may influence several biological pathways relevant to depression. These include the regulation of neurotransmitter levels (such as serotonin, dopamine, and endorphins), modulation of the neuroendocrine axis (including the hypothalamic-pituitary-adrenal axis involved in stress response), improvement of neuroplasticity (the brain's ability to adapt and form new connections), and anti-inflammatory effects [13-16]. By acting on these systems, acupuncture may help to improve emotional state and alleviate depressive symptoms.

This paper aims to synthesise findings from recent randomised controlled trials on the effectiveness of acupuncture for depression while also detailing and analysing the acupuncture methodologies used within these studies.

2. Methods

A literature search was conducted to identify studies evaluating the effectiveness of acupuncture as a sole intervention for the treatment of depression. The search was carried out in two major electronic databases: PubMed and SciELO. The search strategy included the following terms: (acupuncture[Title/Abstract]) AND (depression[Title]) AND ((RCT[Publication Type] OR "randomized controlled trial"[Title/Abstract])) AND ((effectiveness[Title/Abstract] OR efficacy[Title/Abstract] OR outcome[Title/Abstract] OR treatment[Title/Abstract])).

To ensure the relevance of the included studies, specific inclusion criteria were applied. Only studies published within the last five years, from 2020 to 2025, were considered. Eligible articles had to be written in Portuguese, Spanish, or English. Furthermore, only studies designed as randomised controlled trials were included in the review. Finally, studies should have assessed acupuncture as a therapeutic intervention for depression.

Titles and abstracts were screened for relevance, and full texts were reviewed for eligibility based on the above criteria. Duplicate records were removed, and only studies meeting all inclusion parameters were retained for analysis.

3. Results

Figure 1 presents the articles' search and selection details.

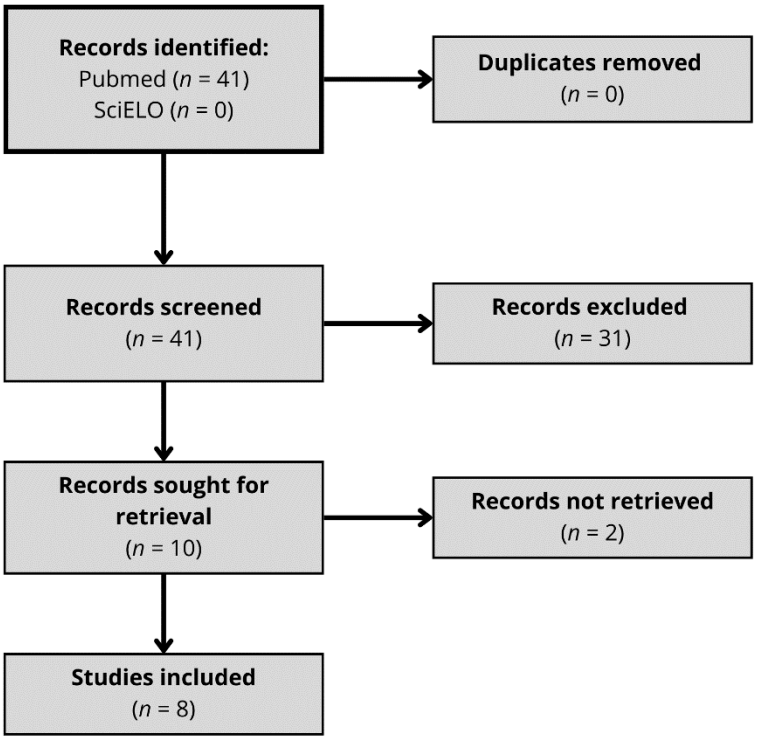

Figure 1. Flowchart of study selection.

The initial search yielded 41 records through database searches. No duplicates were found; therefore, 41 studies were screened.

Following title and abstract screening, 31 records were excluded based on relevance, leaving 10 full-text articles for detailed assessment. Of these, 2 were excluded for inability to retrieve them, resulting in 8 studies that met the inclusion criteria and were included in the analysis.

4. Discussion

4.1. Clinical efficacy and safety

This section summarises the key findings from the included studies.

Cai *et al.* [17] provided strong evidence supporting the efficacy and safety of electroacupuncture as a therapeutic option for post-stroke depression (PSD). Patients in the electroacupuncture group experienced significant improvements across various clinical outcomes, including the Hamilton Rating Scale for Depression (HRSD), Self-Rating Depression Scale (SDS), National Institutes of Health Stroke Scale (NIHSS), Barthel Index (BI), and Traditional Chinese Medicine syndrome scores (all $p < 0.001$). These findings suggest that electroacupuncture can effectively reduce depressive symptoms while also promoting neurological recovery and functional independence following stroke.

Further comparisons with a sham electroacupuncture group reinforced these results. At weeks 2, 4, and 8, HRSD scores were consistently lower in the electroacupuncture group compared to controls ($F = 31.33$, 35.58, and 25.03, respectively; all $p < 0.001$), highlighting a robust antidepressant effect. Similar significant improvements were observed in SDS, NIHSS, and BI scores, indicating that electroacupuncture also benefits motor function and activities of daily living. In terms of safety, electroacupuncture was well tolerated, with only two mild cases of local hematoma reported and no serious adverse events.

Together, these findings position electroacupuncture as a promising adjunct or alternative treatment for PSD, facilitating both psychological and functional recovery. Nonetheless, larger studies with longer follow-up periods are necessary to validate these outcomes and investigate the underlying mechanisms.

In a related context, Liu *et al.* [18] examined the efficacy of acupuncture in improving sleep quality and reducing anxiety and depression among patients with chronic insomnia. Their results demonstrated that acupuncture significantly decreased serum cortisol levels and increased serum serotonin (5-HT) concentrations compared to sham acupuncture, suggesting modulation of neuroendocrine pathways involved in stress and mood regulation. Clinically, the acupuncture group showed significantly greater and more durable improvements in Pittsburgh Sleep Quality Index (PSQI), Hamilton Anxiety Rating Scale (HAMA), and Hamilton Depression Rating Scale (HAMD) scores at treatment completion and follow-up, whereas the sham group exhibited less pronounced and less sustained effects.

These findings imply that dysregulation of the hypothalamic-pituitary-adrenal axis and serotonergic function may contribute to mood disturbances in chronic insomnia, with acupuncture potentially exerting therapeutic effects by restoring these physiological processes. The sustained benefits observed highlight acupuncture's potential as a reliable non-pharmacological intervention for mood and sleep disturbances in chronic insomnia. Further research with larger cohorts and a mechanistic focus is warranted.

Yu *et al.* [19] explored acupuncture as an adjunctive therapy for mild to moderate depression in hemodialysis patients. Treatment led to significant reductions in Hamilton Depression Rating Scale (HAMD) scores and improvements in quality of life, alongside favourable changes in biochemical markers such as serum albumin, haemoglobin, transferrin, and total protein levels. Multivariable regression analysis identified acupuncture ($P = 0.004$) and serum albumin levels ($P = 0.03$) as significant predictors of symptom improvement, with the model explaining 45% of variance (adjusted $R^2 = 0.45$). Although other biochemical markers showed modest post-treatment gains, they did not independently predict depression outcomes.

These results suggest that nutritional and metabolic status, particularly serum albumin, may influence psychological responses to acupuncture in this vulnerable population. Importantly, no serious adverse events were reported, indicating that acupuncture is a safe and well-tolerated treatment for hemodialysis patients with depression. This study supports incorporating acupuncture into multidisciplinary care plans, with further research needed to elucidate mechanisms, long-term efficacy, optimal dosing, and interactions with other therapies.

Similarly, Yin *et al.* [20] demonstrated that electroacupuncture significantly improves sleep quality in patients with depression. The electroacupuncture group showed greater reductions in Pittsburgh Sleep Quality Index (PSQI) scores compared to two control groups over the 8-week treatment period, with mean reductions of −6.64 points versus −2.23 and −2.94 points in controls (95% CI = −5.74 to −2.39 and −5.73 to −2.47, respectively). Improvements were also noted in sleep efficiency (SE) and total sleep time (TST), both showing statistically significant differences ($p < 0.01$). Additionally, reductions in depression and anxiety scores (HAMD-17, SDS, HAMA) suggested broader therapeutic effects on mood and sleep regulation.

However, no significant between-group differences were observed for sleep activity (SA) scores at treatment end ($p = 0.24$ and 0.08), indicating that while electroacupuncture improves overall sleep quality, its impact on specific sleep architecture components may be limited. These findings support electroacupuncture's clinical utility as an adjunctive insomnia treatment in depression, emphasising its multifaceted benefits. Further investigation into long-term effects and mechanisms is warranted.

Addressing cognitive impairment post-stroke, Zhang *et al.* [21] compared interactive dynamic scalp acupuncture (IDSA) with simple combination therapy (SCT) and traditional scalp acupuncture (TSA). At baseline, all groups had comparable cognitive, mood,

sleep, and functional scores. From the second month onward (M2–M4), the IDSA group showed significantly greater improvements in Mini-Mental State Examination (MMSE), Montreal Cognitive Assessment (MoCA), and Modified Barthel Index (MBI) scores, reflecting enhanced cognition and self-care ability.

Concurrently, depression, anxiety, and sleep disturbance scores (HAMD, HAMA, PSQI) were significantly reduced in the IDSA group, with a greater magnitude of change from baseline compared to SCT and TSA, except for HAMD at M4–M0. By M2, IDSA patients exhibited significantly lower severity across cognitive, emotional, sleep, and functional domains (all $p < 0.01$). No serious adverse events were reported, underscoring IDSA's safety and tolerability.

Overall, these results indicate that IDSA offers superior therapeutic benefits to conventional scalp acupuncture or combination therapies for post-stroke cognitive impairment, supporting further research into its mechanisms and potential integration into neurorehabilitation protocols.

The randomised controlled trial by Li *et al.* [22] investigated electroacupuncture combined with antidepressants versus antidepressants alone in depression treatment. Patients receiving combined therapy exhibited significantly greater reductions in Hamilton Depression Rating Scale (HAMD) scores at weeks 4, 8, and 12 (all $P < .001$), suggesting faster and more sustained antidepressant effects.

Urinary metabolomic analysis revealed significant alterations in metabolites involved in fatty acid biosynthesis (malonic acid), glutamate metabolism (cysteine, glutathione, proline), and tryptophan metabolism (tryptophan, N-acetyl-5-hydroxytryptamine). These biochemical changes implicate electroacupuncture in modulating neurotransmission, neuroinflammation, and cellular energy pathways relevant to depression pathophysiology.

Given the role of tryptophan as a serotonin precursor and glutamate in neuroplasticity, electroacupuncture's effects on these metabolic systems may underlie its synergistic action with pharmacotherapy. These findings support incorporating electroacupuncture into depression management and warrant further exploration of its metabolic mechanisms and potential biomarkers of treatment response.

Similarly, Wang *et al.* [23] assessed acupuncture at ghost points combined with fluoxetine for mild to moderate depression. While no significant differences in depression scales were seen at 4 weeks, the acupuncture group exhibited significantly lower Hamilton Depression Rating Scale (HAMD) and Self-Rating Depression Scale (SDS) scores at 8 weeks ($P < 0.05$), indicating a more pronounced and sustained symptom reduction.

Neuroimaging using fractional Amplitude of Low Frequency Fluctuations (fALFF) revealed decreased activity in the left anterior wedge leaf, posterior cingulate gyrus, and occipital gyri, alongside increased activity in the right inferior frontal gyrus, insula, and hippocampus (all $P < 0.05$). These regions are critical for emotional processing and cognitive control, suggesting that acupuncture may modulate neural circuits involved in depression.

Moreover, the effective rate was higher in the acupuncture group (51.25%) compared to controls (36.25%) after 8 weeks ($P < 0.05$), highlighting the clinical advantage of combined treatment. The delayed onset of significant effects suggests cumulative benefits with sustained acupuncture administration. These findings advocate for acupuncture as a valuable complement to pharmacotherapy, with further research needed to elucidate mechanisms and long-term outcomes.

Lastly, Garrido-Ardila *et al.* [24] compared core stability physiotherapy and acupuncture in women with fibromyalgia, focusing on quality of life, pain, joint stiffness, work-related difficulties, and depression. Both interventions yielded descriptive improvements across outcomes at weeks 6 and 13 relative to baseline; however, these changes were not statistically significant when compared to controls.

At week 6, mean Spanish Fibromyalgia Impact Questionnaire (FIQ) scores were 62.89 ± 16.91 for physiotherapy, 62.5 ± 18.09 for acupuncture, and 67.45 ± 17.07 for controls,

suggesting potential clinical relevance despite lack of significance. Notably, a minor decrease in "difficulty to work" was observed in the acupuncture group at week 13, indicating possible delayed or variable response in this domain.

Overall, these findings suggest that while both interventions may offer modest symptom relief, neither demonstrated robust efficacy within the study timeframe. This highlights the need for larger, longer-term studies and exploration of combination therapies to optimise treatment for this multifaceted condition.

Collectively, these studies provide compelling evidence supporting acupuncture and electroacupuncture as effective, safe, and well-tolerated interventions across a range of neuropsychiatric and chronic conditions, including post-stroke depression, chronic insomnia, depression in hemodialysis patients, and fibromyalgia-related symptoms. The findings consistently demonstrate improvements in mood, cognitive function, sleep quality, and functional outcomes, often accompanied by favourable biochemical and neurophysiological changes.

Electroacupuncture, in particular, shows promise in enhancing recovery post-stroke, modulating neuroendocrine and metabolic pathways implicated in depression, and augmenting the efficacy of conventional pharmacotherapy. Similarly, acupuncture appears to positively influence neurobiological substrates such as the hypothalamic-pituitary-adrenal axis and serotonergic system, contributing to sustained symptomatic relief in anxiety, depression, and sleep disturbances.

Despite these encouraging results, several studies highlight limitations such as small sample sizes, short follow-up durations, and heterogeneous methodologies. Moreover, while some interventions showed trends toward clinical benefit, statistical significance was not always achieved, underscoring the need for larger, rigorously designed randomised controlled trials.

Future research should focus on elucidating the underlying mechanisms of acupuncture's therapeutic effects, optimising treatment protocols, and exploring long-term outcomes. Integrating acupuncture into multidisciplinary care may offer a valuable adjunctive approach, particularly for patients with complex or treatment-resistant conditions.

4.2. Acupuncture methodologies analysis

Several acupuncture methodologies were employed across the included studies. Figure 2 presents the frequency of use for specific acupuncture points.

Among the 22 acupuncture points reported, GV20 and SP6 were the most frequently used (each in 5 of 8 studies), followed by GV29, HT7, and ST36 (each used in 3 studies).

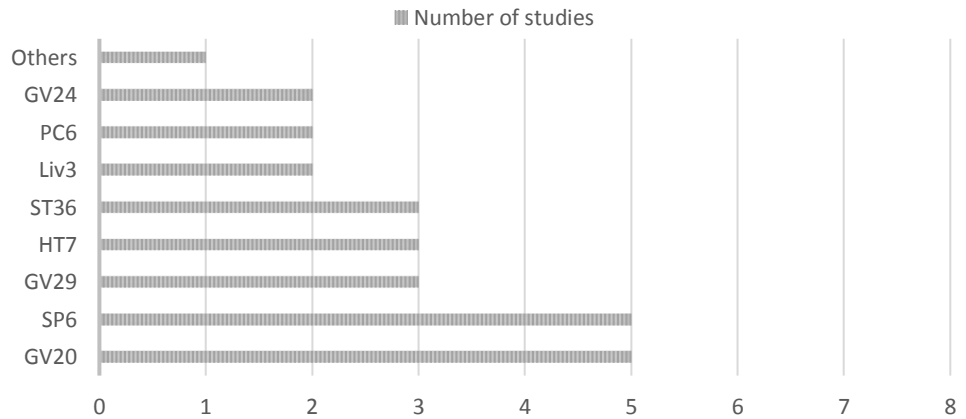

Figure 2. Frequency of acupuncture point usage across included studies.

Beyond individual point usage, we analysed concurrent point combinations and identified several recurring patterns. Specifically, the combination of GV20 and GV29 was

used in three studies, all employing electroacupuncture to connect these two points. The detailed methodologies for this electroacupuncture protocol are summarised in Table 1.

Table 1. Electroacupuncture protocols for the GV20 + GV29 combination.

GV20 + GV24 electroacupuncture		
30 minutes, 2 Hz continuous wave stimulation.	30 minutes, 30Hz continuous wave stimulation.	30 minutes, 10Hz continuous wave stimulation.
[18]	[20]	[22]

Other commonly observed 2-point combinations included GV20 + SP6 (4 studies) and SP6 + GV29 (3 studies). Of particular interest was a frequently used 3-point combination of GV20, GV29, and SP6 (3 studies), with electroacupuncture applied between GV20 and GV29.

Expanding further, a 4-point combination comprising GV20, GV29, SP6, and HT7 was observed in 3 studies, while a 5-point combination including PC6 in addition to the above was identified in 2 studies.

The following Table (Table 2) synthesises the information regarding these combinations.

Table 2. Acupuncture point combinations and frequency across studies

Combinations	**Studies**
GV20 + SP6	[22,20,18,17]
GV20 +* GV29 + SP6	[22, 20, 18]
GV20 +* GV29 + SP6 + HT7	[22, 20, 18]
GV20 +* GV29 + SP6 + HT7 + PC6	[22, 20]

*Acupuncture points connected via electroacupuncture.

4.3. Theoretical Rationale and traditional Chinese medicine Patterns

According to traditional Chinese medicine, depression has multifactorial origins. Maciocia [25] attributes its aetiology to emotional stress (anger, sadness and grief, worry, and guilt), constitutional traits, poor dietary habits, and overwork. Many of the acupuncture points used in the included studies correspond to specific depression-related traditional Chinese medicine patterns as summarised in Table 3.

Although GV29 is not directly associated with a specific pattern in Maciocia's framework, it is traditionally employed to calm the mind and improve sleep quality [26]. Since electroacupuncture requires point pairs, GV29 is a practical complement to GV20 for neuromodulatory effects.

Of note, GV20 is associated with 9 out of 13 depression-related traditional Chinese medicine patterns, underscoring its central role. SP6, HT7, and PC6 complement GV20, together covering all 13 patterns.

4.4 Mechanistic Insights from Preclinical and Clinical Studies

A preclinical study [27], showed that electroacupuncture at GV20 exerted neuroprotective effects against chronic unpredictable mild stress chronic unpredictable mild stress by enhancing BDNF expression and promoting hippocampal neurogenesis. Similarly, Gao *et al.* [28] demonstrated that stimulation of GV20, GV29, LI4, and LR3 improved depressive symptoms in chronic unpredictable mild stress models via upregulation of BDNF/mTORC1 signalling and synaptic plasticity markers such as PSD95, Synapsin I, and GluR1.

Table 3. Correspondence of acupuncture points to traditional Chinese medicine depression patterns (Maciocia [25])

Patterns	GV20	GV29	SP6	HT7	PC6
Liver-Qi stagnation	X				X
Stagnant Liver-Qi turning into heat	X				X
Phlegm-Heat harassing the mind	X		X		
Blood Stasis obstructing the mind	X		X		X
Qi Stagnation with Phlegm	X		X		X
Worry injuring the mind	X				
Heart and Spleen Deficiency	X		X		
Heart-Yang Deficiency	X		X		
Kidney-Yang Deficiency	X				
Kidney- and Heart-Yin Deficiency with empty Heat blazing			X		
Heart- and Lung-Qi stagnation				X	X
Heart and Spleen Deficiency				X	X
Diaphragm Heat					X

The complexity of depression, as recognised in both traditional Chinese medicine and Western medicine, was also reflected in a study by Zhou *et al.* [29] where electroacupuncture at ST36 and SP6 alleviated anxiety and depression-like behaviours in colitis model rats. The therapeutic effects were attributed to modulation of the gut–brain axis, including hippocampal inflammation, metabolic homeostasis, and hypothalamic-pituitary-adrenal axis regulation.

In a related domain, Liu *et al.* [30] identified GV29 and HT7 as frequently used acupressure points for managing depression, anxiety, and stress. HT7, a key point for calming the mind and nourishing the Shen, has been shown to reduce sympathetic nervous activity and regulate the hypothalamic-pituitary-adrenal axis, along with increasing BDNF expression in the brain [31-33]. GV29, likewise, has demonstrated anxiolytic properties via central nervous system modulation [34]. This pairing provides a holistic approach addressing both psychological well-being and physiological balance.

Further, Du *et al.* [35] reported that electroacupuncture at HT7 and SP6 using dilatational 5/25 Hz waveforms significantly improved sleep and consciousness regulation by lowering serum norepinephrine levels.

Supporting the inclusion of PC6, Kim *et al.* [36] demonstrated its efficacy in reversing biochemical and behavioural impairments in chronic stress models. Additionally, stimulation of PC6 attenuated symptoms of a hypoactive hypothalamic-pituitary-adrenal axis in corticosterone-induced depression models [37].

Finally, consistent with our findings, Huang [38] identified GV20 and PC6 as the most frequently used acupuncture points in the treatment of depression.

5. Conclusions

This review analysed recent randomised controlled trials investigating the efficacy and methodology of acupuncture for the treatment of depression. Across diverse patient populations (including individuals with post-stroke depression, chronic insomnia, hemodialysis-related depression, and fibromyalgia), acupuncture and electroacupuncture demonstrated promising clinical outcomes. The studies consistently reported reductions in depression and anxiety scores, improvements in sleep quality, cognitive function, and overall quality of life, with few adverse effects.

Electroacupuncture emerged as a particularly effective modality, frequently applied to acupoint combinations such as GV20 plus GV29, SP6, HT7, and PC6. These points align with multiple traditional Chinese medicine diagnostic patterns and have been supported

by mechanistic studies implicating modulation of the hypothalamic-pituitary-adrenal axis, enhancement of neuroplasticity via BDNF signalling, and neuroendocrine and metabolic regulation. Neuroimaging and biomarker analyses further reinforce acupuncture's capacity to influence central and peripheral mechanisms relevant to depression.

Nonetheless, heterogeneity in methodologies, small sample sizes, and short treatment durations limit the generalizability of findings. Variability in acupuncture point selection, stimulation parameters, and outcome measures underscores the need for greater standardisation in future trials.

In sum, acupuncture represents a safe and potentially effective therapeutic strategy for depression, either as a standalone intervention or as an adjunct to conventional treatments. Continued research should prioritise elucidating biological mechanisms, optimising treatment protocols, and exploring patient-specific predictors of response to inform clinical integration.

Credit author statement: Conceptualisation: R.T. and E.S.; Investigation: M.P.C., P.C.T., C.F.C. and P.S.S.; Project Administration: R.T. and E.S.; Supervision: R.T. and E.S.; Writing – Original Draft Preparation: M.P.C., P.C.T., C.F.C. and P.S.S.; Writing – Review & Editing: R.T. and E.S.; All authors have read and agreed to the published version of the manuscript.

Conflict of Interests: The authors declare no conflict of interests.

Funding: This research received no external funding.

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: The original contributions presented in this study are included in the article. Further inquiries can be directed to the corresponding author.

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Journal of Complementary Therapies in Health
ISSN 2975-9323 | eISSN 2975-9552

Review

The Contribution of Traditional Chinese Medicine in the Treatment of Neck Pain - A Comprehensive Review of the Literature.

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Abstract

Cervicalgia, or neck pain, is a common condition that affects a significant number of the global population and is one of the leading causes of disability. There is not a single treatment for neck pain. However, the search for alternative, less invasive methods with fewer side effects has increased the interest in complementary integrative practices, such as Traditional Chinese Medicine (TCM). This study aims to understand the contribution of TCM and its techniques in the treatment of neck pain. The methodology adopted was a narrative review of the literature. The search was carried out in two databases - PubMed and ScienceDirect - and six studies published between 2018 and 2024 were selected. The results showed that acupuncture, cupping therapy, tuina (when combined with the *yijinjing* exercise) and guidance centred on *Jin Shang* effectively relieve pain, increase functionality and improve patients' quality of life. It is concluded that TCM has a positive impact on the treatment of neck pain and can be integrated into clinical practice and the design of health policies that integrate complementary approaches in the care provided to patients with neck pain.

Keywords: Cervicalgia; Treatment; Traditional Chinese Medicine.

Citation: Calçada E.S., dos Santos L.S. The Contribution of Traditional Chinese Medicine in the Treatment of Neck Pain - A Comprehensive Review of the Literature. Journal of Complementary Therapies in Health. 2025;3(2) 10.5281/zenodo.15653018

Academic Editor: Jorge Rodrigues

Received: 02 April 2025
Reviewed: 22 April 2025
Revised: 11 May 2025
Accepted: 28 May 2025
Published: 12 June 2025

Publisher's Note: IPTC stays neutral with regard to jurisdictional claims in published maps and institutional affiliations.

1. Background

Cervicalgia, or neck pain, can be described as a common condition that affects a significant amount of the global population and has been identified as one of the leading causes of disability[1], contributing to a lower quality of life. This condition is associated with various factors being a challenge for health professionals and patients due to its complexity, which justifies that the pathophysiology of most of its conditions is still not fully understood [1]. There is not a single treatment for neck pain, which can include pharmacological therapies, physical therapies and surgical interventions. However, the search for alternative, less invasive methods with fewer side effects, especially analgesics and non-steroidal anti-inflammatory drugs [2], has increased the interest in complementary integrative practices, such as TCM. According to the International Association for the Study of Pain [1] (IASP), there is evidence in favour of multimodal rehabilitation programs (physical exercise, mobilization, manipulation) and psychological interventions, which improve function. The IASP also adds that for immediate treatment, acupuncture, low-power laser therapy, and the application of electromagnetic pulses can be beneficial, and the pharmacological approach has been effective in relieving pain [1].

In this scenario, TCM can be an alternative or complementary practice in the treatment of neck pain, and, as Santos *et al.* [3] point out, it has been much sought after by those who want a better quality of life. For this reason, this study aims to carry out a narrative literature review that allows a comprehensive analysis of existing studies, to gather the

best and most current empirical evidence that allows us to understand the contribution of TCM in the treatment of neck pain. The relevance of this study is justified by the fact that neck pain is affecting more and more people, having an impact on public health [4] and by the growing interest in non-conventional therapies (NCT).

1.1. Cervicalgia

Cervicalgia is a clinical condition characterized by discomfort or pain in the cervical segment [5], more precisely in the posterior or posterolateral region of the neck [6]. In some cases, the pain can be local or radiate to the upper limbs (shoulders, arms or upper back) in the respective dermatomes [6]. Pain is a sensory and subjective phenomenon [7] and given the nature of the caused pain, it can vary in intensity (mild, moderate and severe), but it can also be classified according to its quality and time of inception: acute neck pain or chronic neck pain. Acute neck pain is pain that starts suddenly and lasts no longer than six weeks [8] and is caused by trauma, exercise, or poor posture. Chronic neck pain, on the other hand, increases gradually and lasts for more than three months [8] and can be caused by degenerative changes, such as cervical osteoarthritis, or psychological factors, such as anxiety and stress. When neck pain persists from six weeks to three months, it is considered sub-acute pain [8].

Depending on the severity factor, this clinical condition is classified into four levels [9,10]:

1. Neck pain without signs or symptoms of structural pathology and its interference with activities of daily living (ADLs) is nil or vestigial;
2. Neck pain without signs or symptoms of structural pathology, but interference with ADLs is already very evident;
3. Neck pain without signs or symptoms of structural pathology, but there are neurological signs of nerve compression;
4. Neck pain with signs or symptoms of structural pathology.

Neck pain can also be classified according to where the pain is: upper neck pain occurs above the C4 cervical vertebra, so the pain is felt at the level of the head; lower neck pain appears below the C4 vertebra, so the pain is felt in the scapular area; suboccipital pain is felt between the occipital line and the C2 vertebra [11]. Finally, this clinical condition is also differentiated by the International Classification of Functioning, Disability and Health [9] according to the impairment of bodily functions, i.e. neck pain with: mobility deficits; associated headaches; movement coordination deficits or radiating pain.

Neck pain is one of the most prevalent musculoskeletal conditions in the world, affecting millions of people, and around 50% of adults are affected by neck pain at some point in their lives [12,13]. In this regard, David *et al.*[14] mention that 30% of the working population aged between 25 and 29 and 50% of individuals over 45 had one or more episodes of neck pain and stiffness. Haldeman and collaborators point out that neck pain is more prevalent in women [10]. It has an impact on people's quality of life, as it reduces functionality, makes it challenging to perform ADLs and interferes with physical and mental well-being, which is why cervicalgia is currently considered one of the costliest musculoskeletal problems that alter not only the health of those affected but also their quality of life [15]. Its annual prevalence is between 30 and 50% in the Western population, with consequences for health systems, but also for society, because of the financial outlay it requires: diagnosis; treatment; costs associated with a lower quality of life; and loss of work [16].

Treating neck pain requires a combination of different strategies, from physiotherapy, therapeutic exercises, relaxation techniques, pharmacological therapies [6] and in some cases, surgery may also be the most appropriate option. In recent years, integrative approaches such as TCM have been gaining prominence as a complementary alternative in the treatment of neck pain, namely acupuncture [4,6]. In fact, acupuncture has proven to be an effective non-pharmacological approach to pain treatment, being a safe, cost-effective method with low rates of side effects [17]. The study by Mendonça *et al.* [17] even shows that the various acupuncture techniques effectively treat chronic pain such as neck pain.

Cervical spine and movements

The cervical spine is made up of seven cervical vertebrae (C1 to C7) and its role is to support and move the head while protecting the neural and vascular structures (spinal cord and nerves). It is the area of the spine with the most significant mobility and, at the same time, the most prone to injury [18]. The C1 (atlas) and C2 (axis) vertebrae make up the upper cervical spine, and, it is their articulation with the occiput that allows the individual three degrees of freedom of movement [19]. The C3 to C7 vertebrae make up the lower cervical spine, allowing two movements: flexion/extension and an articulated tilt-rotation movement [19]. Although they are different, the functions performed by each part of the cervical spine complement each other, making it possible to perform pure flexion/extension, rotation and inclination movements of the head [19].

Risk factors

The causes of neck pain are very diverse, and in many cases, they are unknown [1,9]; however, they can be mechanical, inflammatory, postural or emotional. The main risk factors associated with cervicalgia are mechanical and postural, characterized by local mechanical alterations, changes in the spine and muscle contractures [20], resulting from poor posture and, for example, the continuous use of electronic devices, which can overload the cervical muscles.

According to Geertie *et al*. [21], the risk factors associated with neck pain are physical, psychosocial, individual risk and occupational. They point out that the literature on the subject shows an association between neck pain and aspects related to work, such as high professional and psychosocial demands, which causes stress, which, in turn, contributes to greater muscle tension; little control over work; poor interrelationship between employees in the workplace; low satisfaction, tension and conflicts at work; poor safety; duration of rest breaks considered to be short [21]. In addition, psychosocial demands can have a negative impact on muscle's wakeful state and the musculoskeletal disease response. Psychosocial factors and musculoskeletal pathologies can also mirror the relationship between physical risk factors and musculoskeletal changes [21].

1.2. Traditional Chinese Medicine

TCM is a complex system of healing that emerged in China over 2000 years ago to promote health and treat disease [22]. It translates into a "body of knowledge and techniques that have developed since ancient times through the sum of the experiences and clinical observations of generations of Chinese sages and healers, presenting a physiology and pathophysiology with distinct characteristics from modern biomedicine" [23]. It is considered an NCT based on an understanding of the human body and nature, aiming to re-establish the individual's energetic balance, based on their health. For this reason, the concept of health is "linked to the understanding that there is a potential for vital energy circulating in every human being, and it is by maintaining this potential, preserving it as much as possible, that health will be maintained" [23].

The principles of TCM are *Yin* and *Yang*, *Qi*, *Xue*, channels and the five movements. *Yin* and *Yang* represent the universe and the human body as a system of opposing but complementary forces, the balance between which is crucial for maintaining overall health [24]. *Qi* (read as chi) is the vital energy that flows through the body, which nourishes and maintains harmony between organs and systems, so its balance is crucial since it is *Qi* that keeps the human being physically and mentally healthy [25]. *Xue* is blood, the densest form of functional *Qi*, which nourishes and moistens the tissues [26]. The channels are a system of energy channels that run through the body with specific functions: 12 main channels; 8 extraordinary channels; 12 distinct channels; 15 collateral channels; 12 tendon-muscle channels; and 12 skin zones [27].

Santos *et al.* [6] point out that pain or illness can arise due to difficulties in the circulation of *Qi* and *Xue* through the channels, so this complex system aims to promote the

relationship between the vital substances (*Qi*, *Xue*, *Jing Ye* (organic liquids), *Jing* (essence) and *Shen* (spirit or mind)) the organs (*Zang* - heart, pericardium, lungs, liver, spleen and kidneys) and viscera (*Fu* - large and small intestines, bladder, gallbladder, stomach) [27].

The five movements form the basis of TCM and this theory assumes that the universe is made up of the movement and transformation of these movements: wood, fire, earth, metal and water [6]. These movements are associated with the organs and functions of the body, so an imbalance between them can lead to illness, as it is the interrelationships that apply to the pathophysiology of diseases when there is no balance and harmony [28].

Diagnosis in TCM

Diagnosis in TCM is characterized by a complex and detailed process based on observation of the patient and evaluation of signs and symptoms, not using medical instruments or tests [29]. For this reason, TCM is a philosophical and scientific way of thinking because it does not seek to identify diseases but rather energetic imbalances that trigger symptoms. Guided by Xiang thinking, a cognitive process based on observing the body's signs and symptoms, which include processes of association, metaphor, comparison, symbolism and analogy, to assess and analyze human pathophysiology [30].

Diagnosis in TCM is based on the four examinations of semiology and the eight principles of diagnosis [31,32], the first corresponding to: inspection, where the professional makes a general observation of the patient, taking into account appearance, skin and hair, mood, facial expression, speech, breathing, brightness of the eyes, examination of the tongue, nail bed, state of consciousness, posture and coordination of movements [33,34]; auscultation and olfaction: the former is used to listen to the patient's sound, more precisely, their voice, speech, breathing, coughing, eructation, hiccups and vomiting, and the latter allows breath, excretions and secretions (sweat, mucus, faeces and urine) [33] to be analyzed, and changes in smell can be indicative of the presence of some pathology [35]; palpation, an examination in which the therapist palpates the wrist, belly and other points on the body in order to assess local temperatures, responses to pressure, energy and the condition of the internal organs, particularly the presence and characteristics of tumors [33]; pulse, when assessed in detail, reveals important information about the individual's state of health, revealing possible energy imbalances and dysfunctions in the internal organs, determining its speed, depth, strength, character and range [29]; questionnaire, in which the patient is asked about signs and symptoms, clinical history, lifestyle and habits, complaints, treatments and/or medication [35], covering 10 aspects (sensation of cold and heat, perspiration, head and body, chest, hypochondrium, epigastrium and abdomen, eyes and ears, intake and taste, sleep, excretions, genecology and paediatrics) [33].

Classification of cervicalgia in the light of TCM

Within the scope of TCM, neck pain is considered an integral part of Cervical Spondylopathy, recognizing that degeneration, which develops at an increasingly early age, is due to the excessive use of screens and that in the neck-type, neck pain is the only symptom and treatment is the same whether there is degeneration or not [36]. In this respect, Santos *et al*. [6] explain that the aetiology of all musculoskeletal diseases can be caused by exogenous factors that influence the body's balance - external trauma, repetitive efforts and climate changes (wind, cold and humidity) - and endogenous factors, such as emotional and diet-related factors.

From a TCM perspective, pain is caused by the stagnation of *Qi* and/or *Xue* in the channels, and can be triggered by a local or systemic etiological factor or a combination of the two [37], according to *Yi Dao* - Acupuncture Center [38], cervicalgia results from imbalances in the flow of *Qi* and *Xue* in the channels that run through the neck and upper back. The stagnation of *Qi* and *Xue* is one of the main factors contributing to the onset of this clinical condition, which develops when the flow of *Qi* and *Xue* in the channels is blocked [38]. In

the same sense, Cui *et al*. [39] explain that chronic neck pain accompanied by radicular symptoms is caused by the obstruction of the flow of *Qi* and *Xue* in the neck area, resulting in symptoms such as pain, numbness and a feeling of cold.

In the light of TCM, the interruption of the flow of *Qi* can lead to pain and in cervicalgia, the channels most affected are those of the liver, gallbladder and bladder, which run through the cervical area [38]. Thus, "the Liver-Gallbladder system is of primary importance in the case of the neck. Liver syndromes such as Liver *Qi* Stagnation and Liver *Yang* hyperactivity can be associated with torticollis and shoulder contracture, and the neck area is especially susceptible to Cold Wind invasion, especially when there are predisposing factors such as Kidney *Qi* Deficiency or *Qi* Stagnation due to previous injury or emotional stress" [6]. External pathogenic factors - wind, cold and dampness - also contribute to neck pain, and the TCM approach considers that these external energies can enter the body, especially when the energy defence is low, causing pain and stiffness in the neck [38]. In addition to the above, it is also worth adding that "energy deficiency in the kidneys or liver can cause neck pain. In TCM, the kidneys govern the bones, and when there is a deficiency of *Jing* (vital essence), the bones and joints can become weak and vulnerable, resulting in pain. The liver, in turn, controls the smooth flow of *Qi* and blood; when it is stagnant, whether due to emotional stress or poor diet, circulation to the muscles and tendons of the neck is impaired, causing pain and tension" [38]. Essentially, either individually or together, when the factors described above are present, they "can cause malnutrition of the muscles, joints, soft tissues and bones, by partially or completely blocking the circulation of *Qi* and *Xue* at a superficial or deep level, disordering the functioning of the internal organs (*Zang Fu*) through a state of imbalance in the physiological energy functions" [6].

2. Research Methodology

The research protocol adopts a literature review methodology, specifically, a comprehensive narrative literature review. The narrative literature review is a type of qualitative literature review and has been carried out in various areas of knowledge [40]. Narrative literature reviews are studies characterised by comprehensive publications aiming to describe and discuss the existing literature on a given subject, from a theoretical or contextual perspective [41]. This type of review does not adopt any particular methodology and does not require a specific protocol for its preparation, standing out for its flexibility [42]. Cordeiro *et al.* [43] refer to the narrative literature review as a traditional literature review, explaining that it "presents a more open theme; it hardly starts from a well-defined specific question, and does not require a rigid protocol for its preparation; the search for sources is not predetermined and specific, and is often less comprehensive".

Although this is not compulsory for a narrative literature review and with a view to greater scientific rigour, in order to construct the research question, the question to be answered through the research, we used the PICO strategy, an acronym for: Patient, Intervention, Comparison and Outcome [42]. The description of its components is as follows: Patient - patients with neck pain; Intervention - traditional Chinese medicine; Comparison - western medicine; Outcome - therapeutic impact of TCM in the treatment of neck pain. This led to the following research question: What is the therapeutic impact of TCM in the treatment of neck pain?

2.1. Inclusion and exclusion criteria

For this review, selection criteria were defined for the studies to be considered, distinguishing between inclusion and exclusion criteria. The inclusion criteria were articles: published between 2014 and 2024; available in full; published in English and Portuguese; focusing on TCM in the treatment of neck pain. We chose articles published in the last 10

years because we wanted to present a review based on current evidence. The type of studies considered included randomized controlled trials, meta-analyses, systematic literature reviews and quantitative studies.

The exclusion criteria were articles: published before 2014; which are not openly available; published in languages other than those mentioned; and which focus on TCM in the treatment of other pathologies.

2.2. Explanation of the research method

To standardize the terms for the bibliographic search to be carried out in the next stage, the health descriptors were searched and the following were selected: neck pain; traditional Chinese medicine; and treatment outcome. Next, a Boolean phrase was constructed to be inserted into two databases (PubMed and ScienceDirect): ((neck pain) AND (traditional Chinese medicine)) AND (treatment outcome).

In PubMed, 101 results were obtained, and after inserting the inclusion criteria, four articles published between 2022 and 2024 were selected: Cheng *et al.* (2022) [45]; Lyu *et al.* (2022) [46]; Deng and Wu (2023) [47]; Yu *et al.* (2024) [48]. In ScienceDirect, 5214 results were obtained, and after applying the inclusion criteria, two articles were selected, both published in 2018: Yang *et al.* (2018) [49]; Zhang *et al.* (2018) [50].

To achieve coherence and scientific rigor, and for a better explanation of all the stages of the bibliographic research process (data sources), the PRISMA flowchart is presented below in Figure 1.

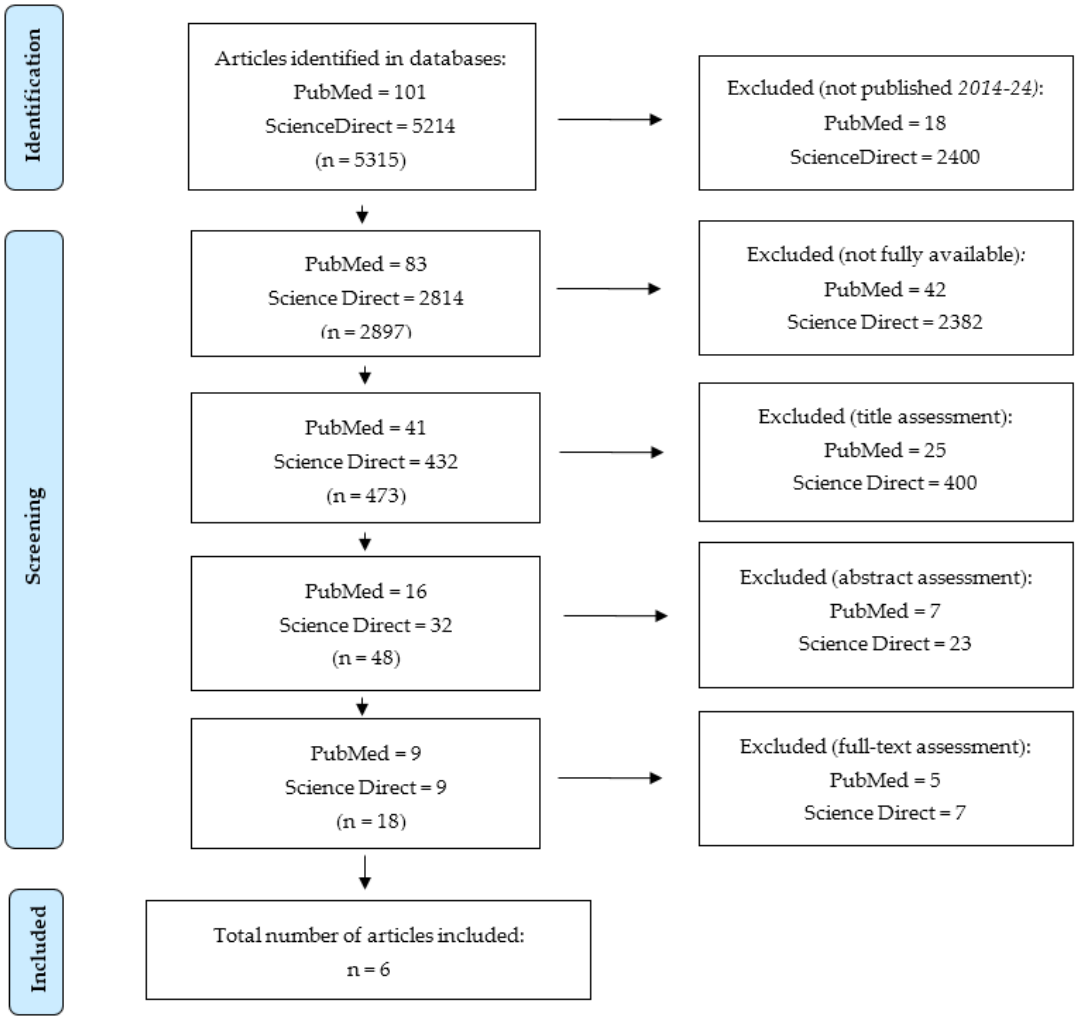

Figure 1: PRISMA flowchart

3. Results

As previously mentioned, this review includes six studies published between 2018 and 2024. Therefore, Table 1 describes each of the articles: identification of the authors, journal, objective, method, sample, results and conclusion.

Table 1: Summary of studies

Cheng *et al.* (2022) [45] - JAMA Network Open	
Objective/Sample	- To investigate the effectiveness of tuina therapy combined with *yijinjing* exercise compared to tuina therapy alone in patients with chronic nonspecific neck pain; - 102 participants with chronic nonspecific neck pain.
Method/Type of study	- Quantitative method, this was a randomized, open, blinded clinical trial lasting 12 weeks (8 weeks of intervention and 4 of observational follow-up).
Results	- The mean difference in Visual Analog Scale (VAS) scores from baseline at week 8 for the tuina group combined with *yijinjing* was -5.4. At week 8, the difference in VAS scores was -1.2 between the tuina group and the tuina combined with *yijinjing* group. The efficacy of tuina combined with *yijinjing* in the treatment of chronic nonspecific neck pain remained at the 12-week follow-up.
Conclusion	- Tuina combined with *yijinjing* was more effective than tuina therapy alone in terms of pain, functional recovery and anxiety at week 8, and the effectiveness remained at week 12.
Deng e Wu (2023) [47] - European Review for Medical and Pharmacological Sciences	
Objective/Sample	- Systematically evaluate the application of Chinese medicine in the treatment of cervical and lumbar pain; - 57 articles.
Method/Type of study	- Meta-analysis and SLR.
Results	- TCM has surpassed Western medicine in the treatment of neck pain and lower back pain and analgesic effects.
Conclusion	- TCM has better clinical efficacy and analgesic effects when compared to Western medicine in the treatment of cervical and lumbar pain, presenting a positive safety profile.
Lyu *et al.* (2022) [46] - Technology and Health Care	
Objective/Sample	- Discuss the indications for conventional acupuncture therapy (CAT) and movement style acupuncture therapy (MSAT) combined with CAT in patients with neck pain with data mining; - 76 participants with chronic neck pain were distributed into two groups: the intervention group, subjected to MSAT and CAT, and the control group, subject to CAT.
Method/Type of study	- Quantitative, as it is a randomized, blind and controlled trial.
Results	- In patients in the intervention group (MSAT and CAT) who scored between 41.70 and 68.70 in physical functioning before treatment, MSAT may improve activity restriction and have an analgesic effect. In patients in the control group who scored between 56.09 and 66.09 in general health before treatment, CAT may have a curative effect.
Conclusion	- Both MSAT and CAT can improve the quality of life of patients suffering from neck pain. However, CAT is more suitable for patients who are in good general health before treatment, and MSAT combined with CAT is more suitable for patients who have a mild to moderate decline in physiological function.
Yang *et al.* (2018) [49] - Journal of Traditional Chinese Medical Sciences	
Objective/Sample	- Compare the effects of pulsating and static cupping therapy on nonspecific neck pain and blood perfusion of local cutaneous microcirculation; - 70 participants with nonspecific neck pain were distributed into four groups: low-frequency pulsating cupping therapy, high-frequency pulsating cupping therapy, static cupping therapy, and waiting list.
Method/Type of study	- Quantitative method, as it is a controlled and randomized clinical trial.
Results	- Participants in the low-frequency and high-frequency pulsating cupping groups showed a significant reduction in VAS scores compared to participants in the static cupping group.

Conclusion	- Pulsating cupping therapy may have a greater analgesic effect on nonspecific neck pain compared to static cupping therapy, which may be associated with its more positive effect on improving local blood perfusion of the skin.
Yu *et al.* (2024) [48] - Medicine	
Objective/Sample	- Investigate the efficacy and safety of acupuncture in the treatment of neck stiffness, one of the signs of cervicalgia, comparing acupuncture with conventional treatment; - 10 randomized controlled clinical trials, including 754 patients.
Method/Type of study	- Meta-analysis and SLR.
Results	- The treatment group (subjected exclusively to acupuncture or in combination with conventional treatment) showed an improvement in the total effective rate in relation to the control group (subjected only to conventional treatment), with a decrease in VAS scores, neck disability index, enabling restoration of cervical range of motion.
Conclusion	- Acupuncture therapy is more effective than conventional treatments in relieving pain, reducing functional disabilities and increasing cervical range of motion in patients with stiff necks.
Zhang *et al.* (2018) [50] - Journal of Traditional Chinese Medical Sciences	
Objective/Sample	- To investigate the characteristics of "*Jin Shang*" in young adults with chronic neck pain and to investigate the correlation of "*Jin Shang*" with pain intensity and life disabilities, through a cross-sectional study; - 50 participants with chronic neck pain and 16 healthy participants.
Method/Type of study	- Quantitative method, as this is a cross-sectional study.
Results	- In patients with chronic neck pain, the thickness of the semispinalis capitis during isometric contraction was thinner than that of healthy participants who formed the control group. The study also showed the existence of significant relationships between the thickness of the neck extensor muscle, the VAS and the Northwick Park Questionnaire and the multiple linear regression demonstrated that the thickness of the neck extensor muscle in patients with chronic neck pain was a significant predictor of the intensity of pain and disability.
Conclusion	- There is a significant difference in neck extensor muscle thickness in young adults with chronic neck pain compared to control group participants. Changes in neck extensor muscle thickness, both at rest and during contraction, are moderately related to neck pain and life disabilities. The study also concludes that there is a correlation between "*Jin Shang*" and the symptoms of chronic neck pain, which demonstrates that the neck extensor muscle plays an important role in chronic neck pain.

4. Discussion

The results obtained highlight the positive impact of the various TCM techniques in the treatment of cervical pain, which consists of discomfort or pain in the posterior or posterolateral region of the neck [6]. This evidence is supported by the results obtained by Deng and Wu [47], who found that TCM has better clinical efficacy and analgesic effect when compared with Western medicine in the treatment of cervical and lumbar pain, presenting a positive safety profile. However, the results of Seo *et al.* [51] partially contradict these findings, as they report that acupuncture and conventional medicine for chronic neck pain are similarly effective in terms of pain and disability.

Furthermore, the literature on the subject has shown that TCM can have a positive impact on pain relief, for example, through acupuncture, by the action of endogenous neurotransmitters – endorphins and enkephalins – which are released when specific points are stimulated in the human body, the acupoints [52]. The results obtained converge with this finding: the study by Yu *et al.* [48] demonstrated that acupuncture is extremely advantageous, being particularly more effective than conventional treatments in relieving pain, reducing functional disabilities and increasing the amplitude of cervical movement in patients with neck stiffness. However, according to the findings of Seo *et al.* [51], acupuncture combined with conventional medicine contributes to even greater pain relief and electroacupuncture is even more effective. He *et al.*[53] studied the effect of acupuncture in

the treatment of chronic neck and shoulder pain in sedentary female workers. After treatment with acupuncture, applied 10 times over three to four weeks, on anti-pain acupuncture points (in the test group) or placebo points (in the control group), the authors found that the intensity and frequency of pain decreased more in the test group. In addition, although acupuncture was applied to placebo points in the control group, this group also showed improvements. However, these were more pronounced in the test group that received acupuncture at the anti-pain points. According to this study, proper treatment with acupuncture can reduce chronic neck pain, as well as shoulder and headache pain [53].

In the same sense, Lyu *et al.* [46] also demonstrated that both MSAT and CAT can improve the quality of life of patients suffering from neck pain. However, they highlighted that CAT is more suitable for patients who have a good general health status before treatment and MSAT combined with CAT is more suitable for patients who have a mild to moderate decline in physiological function [46]. In this regard, it is important to mention the systematic review and meta-analysis carried out by Fang *et al.* [54], who found that acupuncture as a complementary therapy can relieve post-treatment pain lasting at least three months for patients with chronic neck pain. They also report that although acupuncture as adjuvant therapy is not superior to sham acupuncture, it shows sustained efficacy in improving functional impairment for more than three months, with a good safety profile [54].

TCM is an ancient medical practice that offers a holistic approach and uses various techniques such as acupuncture, herbal medicine, tuina, moxibustion, cupping therapy, Chinese food therapy and energy exercises [55]. In this regard, Cheng *et al.* [45] found that tuina combined with *yijinjing* is more effective than tuina therapy alone in terms of pain, functional recovery, and anxiety. In addition to *yijinjing*, some studies found in the literature address another exercise, such as *Qi Gong*, which has positive effects in the treatment of chronic neck pain [56], namely calming and relaxing effects [57], reducing neck pain and disability [58]. Comparing these findings with those of the systematic review and meta-analysis carried out by Yuan *et al.* [59], it is clear that several TCM techniques are effective in treating neck pain. The results of the study show that acupuncture, acupressure and cupping therapy can be effective in the immediate treatment of pain and disability associated with chronic neck pain and chronic low back pain.

On the other hand, and focusing on another TCM technique, Yang *et al.* [49] concluded that pulsating cupping therapy may have a greater analgesic effect on nonspecific neck pain compared to static cupping therapy, which may be associated with its more positive effect on improving local blood perfusion of the skin. However, for Leem [60], who studied the long-term effect of cupping therapy on chronic neck pain, cupping treatments were ineffective in reducing the intensity of neck pain in the long term. On the other hand, it highlights that cupping therapy positively affected physical function and quality of life (up to two years) in patients with neck pain, namely in the body pain subscale and physical component summary [60]. This evidence is in line with that presented by Kim *et al.* [61], who found that cupping therapy reduced neck pain in patients when compared to groups that were not subjected to any intervention or as a complementary treatment, improving function and their quality of life.

Zhang *et al.* [50], when investigating the characteristics of "*Jin Shang*", tendon trauma, in young adults with chronic neck pain and its relationship with pain intensity and life disabilities, showed that the performance of "*Jin Shang*" can contribute to reducing chronic neck pain, showing a correlation between "*Jin Shang*" and chronic neck pain symptoms, i.e. the more severe the tissue alterations identified, the greater the pain intensity and limitations in daily life. These results are in line with the literature, as the Wu [62] study showed that neck pain symptoms have characteristics of TCM syndromes, with neck pain being a category of "*Jin Shang*" syndrome. The study by Zhang *et al.* [50] shows that when there is a disturbance in "*Jin Shang*", neck pain can be intensified, underlining the need to assess the neck muscles in the diagnosis and treatment of neck diseases.

5. Conclusion

It is concluded that TCM is effective in the treatment of neck pain, representing an alternative or complementary practice to conventional medicine. It has been found that within the scope of the various techniques that TCM contemplates, acupuncture, cupping therapy, tuina (when combined with the *yijinjing* exercise) and the guidelines centred on "*Jin Shang*", are effective for pain relief, increased functionality and improved quality of life for patients.

This review highlights the holistic approach of TCM, which integrates energetic and physiological concepts, enabling a more comprehensive picture of health. Given what has been said, this study is expected to contribute to a greater understanding of the effectiveness of TCM in the treatment of neck pain, providing insights for clinical practice and for the design of health policies that integrate complementary approaches in the care provided to patients with neck pain.

However, this study does have some limitations. Firstly, it is understood that the sample is small, so it would be important to include more evidence. Secondly, this review only included studies that were freely accessible, so there may have been relevant studies that may have been left out. Therefore, as a suggestion for future research, it is suggested that a literature review be carried out which includes a more representative sample of studies, and that a systematic literature review be carried out.

Credit author statement: Conceptualization: E.S.C. and L.S.S.; Investigation: E.S.C. and L.S.S.; Writing – Original Draft Preparation: E.S.C. and L.S.S.; Writing – Review & Editing: E.S.C. and L.S.S. All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest: The authors declare no conflict of interest.

Funding: This research received no external funding.

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: The original contributions presented in this study are included in the article. Further inquiries can be directed to the corresponding author.

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Journal of Complementary Therapies in Health
ISSN 2975-9323 | eISSN 2975-9552

Review

Effectiveness and Methodology of Wet-cupping for Low Back Pain – A Preliminary Systematic Review of Randomized Controlled Trials.

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Abstract

Background: Low back pain is the leading cause of disability globally, affecting more than 80% of individuals over a lifetime and incurring significant healthcare and economic burdens. European guidelines recommend non-pharmacological interventions, including traditional therapies. Wet-cupping, a practice with deep historical roots in various medical traditions, is being revisited as a potential adjunctive therapy for Low back pain management.

Objective: To evaluate the effectiveness and methodologies of wet-cupping therapy for low back pain based on current evidence from randomized controlled trials (RCTs).

Methods: A preliminary systematic literature search was conducted using PubMed, EuropePMC, and SciELO up to May 2025 for RCTs involving wet-cupping in Low back pain. Studies were included if they assessed wet-cupping as an intervention for human subjects with low back pain and reported pain outcomes. Five eligible RCTs comprising 460 participants were reviewed. Interventions included traditional *Hijamah* and traditional Chinese medicine-based wet-cupping.

Results: Both *Hijamah* and traditional Chinese medicine-based wet-cupping demonstrated significant short-term and, in some cases, long-term reductions in pain and disability scores. Studies comparing wet-cupping to standard or no treatment reported superior outcomes in the cupping groups. In addition, some studies showed a reduction in analgesic use. Treatment protocols varied, particularly in cupping technique and site selection limiting direct comparability.

Conclusions: Wet-cupping appears to be a promising complementary therapy for low back pain, with evidence supporting its effectiveness in improving pain and functional outcomes. Both traditional *Hijamah* and acupoint-based approaches yielded comparable benefits. However, methodological heterogeneity across studies calls for further high-quality, standardized research to confirm its clinical utility and long-term efficacy.

Keywords: Low Back Pain; Wet-Cupping; *Hijamah*; Traditional Chinese Medicine; Complementary Therapy; Randomized Controlled Trial; Pain Management.

Citation: de Sousa C.S., Teixeira A.T., Azevedo R.S., Nunes V.C., de Carvalho A.L., Serra E.M., Torres R.C. Effectiveness and Methodology of Wet-cupping for Low Back Pain – A Preliminary Systematic Review of Randomized Controlled Trials. Journal of Complementary Therapies in Health. 2025;3(2) 10.5281/zenodo.15657740

Academic Editor: Jorge Rodrigues

Received: 27 May 2025
Reviewed: 13 June 2025
Accepted: 13 June 2025
Published: 13 June 2025

1. Introduction

Low back pain is a significant global health issue, recognized as the leading cause of disability worldwide. At any given time, approximately 7.5% of the global population

experiences low back pain, and over a lifetime, more than 80% of individuals will be affected. The impact extends to emergency services, with low back pain accounting for 4% of all emergency department visits [1].

The prevalence of low back pain also places a substantial burden on primary care; around 20% of those experiencing low back pain consult their general practitioner annually [2]. For example, within the UK's National Health Service (NHS), back pain is a major contributor to workforce issues, responsible for a staggering 40% of all sickness absences. Economically, low back pain costs the UK economy an estimated £10 billion each year [2].

Recent European clinical practice guidelines show a strong consensus on evidence-based treatment recommendations for patients experiencing low back pain [3]. These guidelines predominantly advocate for a wide array of non-pharmacological treatment options. Therefore, it has become important to explore non-pharmacological therapies to address of complement the treatment of low back pain.

Cupping has been used differently in the traditional medicines of various civilizations [4]. However, a common objective was to promote the extraction of tocix substances from the body by producing negative pressure inside a cup or a similar hollow object [5,6]. In particular, wet-cupping is a therapeutic process involving the initiation of superficial bleeding from small vessels or their branches, primarily within the skin and muscles, to decrease congestion in the area where cups are applied and to release toxic matter accumulated close to the skin [7-9].

Its ancient practice has been recorded for thousands of years. One of the earliest mention was found in the Egyptian Ebers Papyrus (1550 B.C.) [10]. As well, with therapeutic records reaching back to the early first millennium, cupping is a long-standing practice in traditional Chinese medicine [4]. In ancient Greece, its value was similarly recognized, with Hippocrates advocating for the technique to address diverse ailments [11].

In light of wet-cupping's historical prominence and persistent clinical application, this study seeks to provide a preliminary analysis of its efficacy and methodological approaches for managing low back pain.

2. Methods

2.1. Search Strategy

A database search was performed to identify RCTs assessing the efficacy of wet cupping in the treatment of low back pain. The search strategy was implemented across several electronic databases, including PubMed, EuropePMC, and SciELO from database inception to May 2025. The search strategy employed the following operators: ("low back pain") AND (wet-cupping) AND (randomized controlled trial).

2.2. Eligibility Criteria

This review included RCTs investigating the effect of wet-cupping on low-back pain. Studies were considered for inclusion if they: (1) involved human participants with a diagnosis of low back pain; (2) were published in English, Chinese, Spanish, French, or Portuguese; (3) evaluated any form of wet-cupping as an intervention; and (4) reported pain outcomes. Studies involving animal subjects or lacking proper intervention were excluded.

3. Results

Forty-seven records were identified after the database searches. After removing 5 duplicates, 42 records were screened. Thereafter, 36 were excluded for various reasons (Figure 1). All six remaining studies were retrieved and their full-text was assessed.

Ultimately, five studies met the inclusion criteria and were included in the systematic review. Figure 1 further provides detailed information about the selection process.

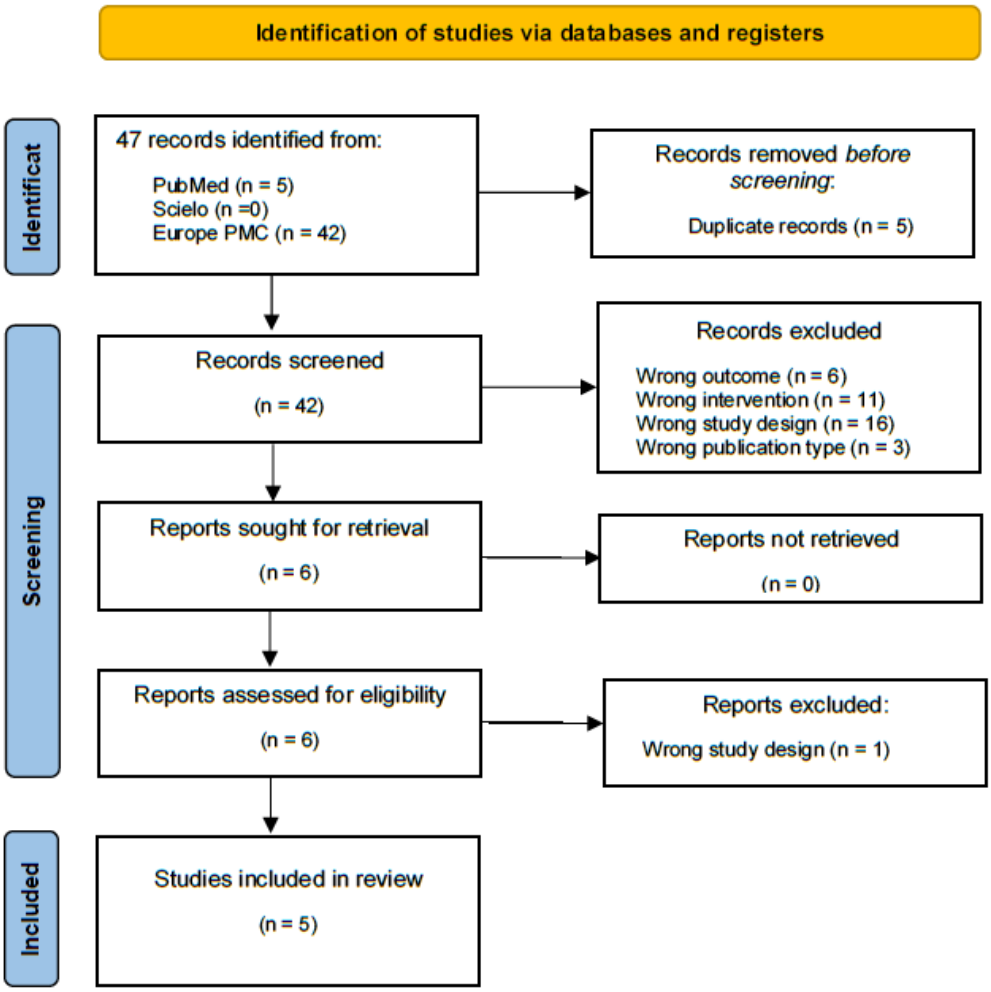


Figure 1. Flowchart of the studies selection.

Five RCTs involving 460 participants were included in this analysis. The studies evaluated the use of wet cupping for low back pain, with samples ranging from 37 to 180 participants. Mainly, two methodologies of wet cupping were studied, with 3 studies assessing the effects of traditional *Hijamah* [12-14] and 3 studies assessing traditional Chinese medicine-based cupping [12,15,16], one of which as a comparator [12].

All studies used a single-comparator methodology. Specifically, standard treatment was used in 2 studies [13,14], no treatment was used in 2 other studies [15,16] and traditional Chinese medicine-based cupping in 1 study [12].

Table 1 provides a summary of the characteristics of the included studies.

Table 1. Characteristics of the five included studies.

Study	Sample	Duration	Cupping technique	Comparator	Outcome measures
Al-Eidi *et al.* [12]	70	2 weeks	Traditional *Hijamah*	Traditional Chinese medicine-based cupping	Validated Arabic version of the NRS, PPI, and ODQ.
Mardani-Kivi *et al.* [13]	180	4 weeks	Traditional *Hijamah*	Conventional treatment	ODI and VAS

Farhadi *et al.* [14]	98	3 months	Traditional *Hijamah*	Standard treatment	PPI, ODI, and MQS.
AlBedah *et al.* [15]	80	2 weeks	Traditional Chinese medicine-based cupping	No treatment	NRS, PPI, ODQ, and Numbers of acetaminophen tablets taken
Kim *et al.* [16]	32	2 weeks	Traditional Chinese medicine-based cupping	Wait-list	NRS, PPI, ODQ, and Numbers of acetaminophen tablets taken

NRS – Numeric Rating Scale; PPI - Present Pain Intensity; ODQ - Oswestry Disability Questionnaire; ODI - Oswestry Disability Index; VAS – Visual Analogue Scale; MQS - Medication Quantification Scale

4. Effectiveness of wet-cupping for low-back pain

The reviewed studies consistently support the effectiveness of wet cupping therapy in alleviating low back pain. However, methodological differences and variations in outcome measures only allow few direct comparisons between studies.

4.1. Traditional Hijamah versus Traditional Chinese medicine-based cupping

In the study of Al-Eidi *et al.* [12], both the traditional *Hijamah* and traditional Chinese medicine-based cupping led to significant reductions in pain and disability scores (NRS, PPI, and ODQ) immediately after the intervention. These improvements were maintained at Day 7 and Day 14 post-intervention ($p < 0.001$), indicating sustained short-term benefits using either technique.

As well, there were no statistically significant differences between the two cupping techniques at any post-treatment time point (immediately, Day 7, or Day 14), suggesting that both techniques are equally effective in reducing low back pain.

4.2. Cupping versus standard treatment

The studies of Mardani-Kivi *et al.* [13] and Farhadi *et al.* [14] assessed the efficacy of cupping in comparison with usual treatment.

In study of Mardani-Kivi *et al.* [13], both the wet cupping and conventional treatment groups showed progressive improvements in pain intensity over time. However, a significant advantage in the wet-cupping group emerged at the 3-month follow-up ($P < 0.05$) and became more pronounced by 6 months ($P < 0.05$), indicating a sustained therapeutic benefit. This trend was mirrored in functional outcomes, with significantly better Oswestry Disability Index (ODI) scores observed in the wet cupping group at the final follow-up ($P < 0.05$).

Similarly, the study by Farhadi *et al.* [14] demonstrated that, at 3 months, the wet cupping group experienced significantly greater reductions in pain intensity compared to the control group (mean difference = 2.17; 95% CI: 1.72–2.60; $p < 0.01$), along with a significant improvement in disability (mean difference = 14.99; 95% CI: 11.18–18.82; $p < 0.01$). As well, this study also reported a significant reduction in medication usage (mean difference = 6.55; 95% CI: 3.60–9.50; $p < 0.01$) among participants receiving wet-cupping. Moreover, these differences remained statistically significant after adjustment for potential confounding variables, including age, gender, and duration of low back pain, reinforcing the independent therapeutic effect of the intervention ($p < 0.01$).

These findings suggest that wet cupping not only provides clinically meaningful improvements in pain and function but may also reduce reliance on pharmacological pain management. While study of Mardani-Kivi *et al.* [13] highlights the long-term benefits observed up to six months, Farhadi *et al.* [14] strengthens the evidence base through detailed effect size reporting and adjusted analyses, thereby supporting the robustness and generalizability of wet-cupping as a treatment approach.

4.3. Cupping versus no treatment

Two studies compared wet-cupping with no treatment for low back pain.

Both studies [15,16] assessed pain intensity, pain perception, and disability following wet cupping interventions. The study by AlBedah *et al.* [15] reported statistically significant improvements across all measured outcomes, including reductions in Numeric Rating Scale (NRS) scores (29.2 vs. 57.9), Present Pain Intensity (PPI) scores (1.17 vs. 2.3), and Oswestry Disability Questionnaire (ODQ) scores (19.6 vs. 35.4), with $p = 0.0001$ for all comparisons. Moreover, the benefits were sustained for at least two weeks post-intervention, suggesting a lasting therapeutic effect.

In contrast, the study by Kim *et al.* [16] found a statistically significant reduction only in PPI scores in the wet cupping group (–1.2 vs. –0.2; $p < 0.01$), while improvements in NRS (–16.0 vs. –9.1; $p = 0.52$) and ODQ scores (–5.60 vs. –1.8; $p = 0.14$) did not reach statistical significance. Both studies noted lower acetaminophen consumption in the wet-cupping groups, though this difference was not statistically significant.

Together, these findings suggest that wet cupping may exert a positive effect on both subjective pain perception and functional status, with more robust evidence demonstrated in the study of AlBedah *et al.* [15]. The trend toward reduced medication use further supports its potential as an adjunctive treatment. However, discrepancies in statistical significance across studies indicate the need for larger, well-controlled trials to confirm these outcomes and elucidate the mechanisms underpinning the therapeutic effects of wet cupping.

5. Cupping treatment methodologies

The reviewed studies demonstrated considerable heterogeneity in both the type and application protocols of cupping therapy. Broadly, two primary approaches were utilized: Traditional *Hijamah* [12-14] and wet-cupping based on acupoint selection [12,15,16].

5.1. Traditional Hijamah methodology [12-14]

The employed protocols reflect methods rooted in traditional Iranian medicine, with a focus on specific anatomical sites (e.g., interscapular area, sacral region, and calf). The procedures often involve (1) fixed anatomical locations rather than individualized acupoint selection, (2) multiple stages or sessions (as in the study of Farhadi *et al.* [14] and Table 2), (3) Use of scarification followed by bloodletting, (4) Variable cup sizes based on patient anatomy or experts' preference, and (5) retention times typically around 5 minutes with repeated cycles.

Regarding the treatment stages, some differences can be observed, For example in contrast to Farhadi *et al.* [14], Mardani-Kivi *et al.* [13] used two treatment locations (on the interscapular area and on the sacrum area) and Al-Eidi *et al.* [12] only one treatment location (low back area), which may have influenced the achieved results.

Despite the common traditional basis, procedural steps vary slightly. Table 3 presents a common *Hijamah* procedure.

Table 2. The 3 phases of treatment based on Farhadi *et al.* [14].

Wet-cupping phases	Schematic
(a) Phase 1 (day = 0): between the two scapulas, opposite to T1—T3 Scapular spine,	
(b) Phase 2 (day = 3): the sacrum area, between the lumbar vertebrae and the coccyx bone.	

(c) Phase 3 (day = 6): the calf area, in the middle surface of gastrocnemius muscle.

Note: The calf area is treated based on the experienced low back pain. If the back pain was unilateral, the ipsilateral calf should be treated. If the back pain is bilateral, both calf areas should be treated.

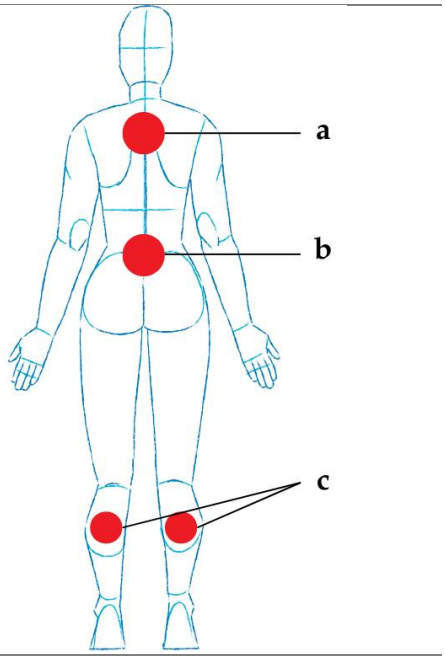


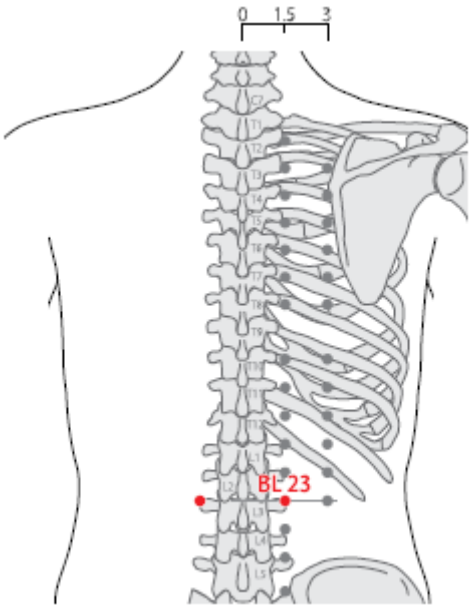
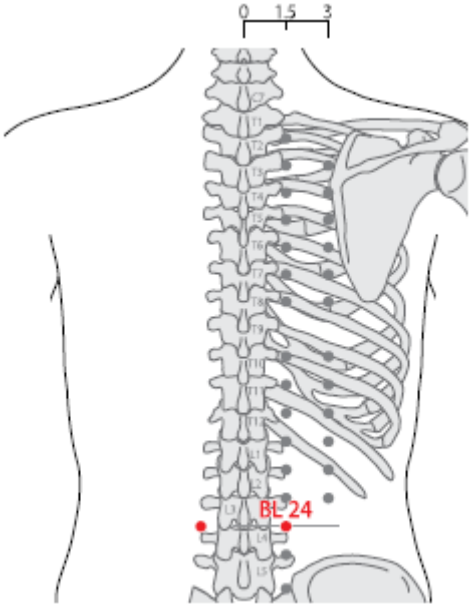
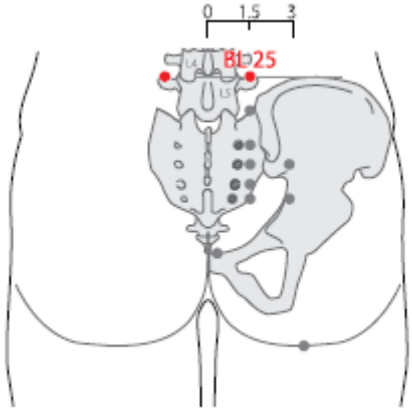
Table 3. *Hijamah* procedure steps and descriptions.

Step	Procedure Description
1	Site selection: Identify specific anatomical sites (e.g., interscapular area, sacral region, or calf) based on traditional recommendations or the patient's pain location.
2	Primary suction: Place sterile cups on the selected sites and apply negative pressure using a manual or electric pump to initiate suction. Retain cups for 3–5 minutes.
3	Cup removal: Remove the cups carefully after the initial suction phase.
4	Scarification: Perform superficial skin incisions (typically 3–6 lines per site, ~3 mm long and 0.5 mm deep) using a sterile surgical blade (e.g., size 15–21), following the "multiple superficial incisions" technique.
5	Secondary suction and bloodletting: Reapply the cups over the incised areas and re-establish suction to allow capillary blood to accumulate. Leave in place for 3–5 minutes or until sufficient blood is collected.
6	Repeat bloodletting (optional): In some protocols, the suction and bloodletting step is repeated up to two more times without re-scarification, depending on the patient's condition and blood flow.
	Cup removal: Gently remove the cups and discard used materials appropriately.
	Wound care: Clean the area with antiseptic solution and apply sterile dressing to prevent infection.
	Post-procedure advice: Advise the patient to rest, stay hydrated, avoid strenuous activity, and keep the cupped area clean for at least 24 hours.

5.2. Wet-Cupping with Acupoint Selection [12,15,16].

The included studies using traditional Chinese medicine-based wet-cupping follow a more standardized and evidence-based acupuncture framework, selecting bilateral BL23, BL24, and BL25 based on (1) pain palpation and patient-reported sensitivity, (2) WHO Guidelines for Acupuncture Point Location [17] (Table 4) and (3) practitioner experience and training [16].

Table 4. Traditional Chinese medicine-based wet-cupping points according to the World Health Organization [17].

Acupoint	Descriptive point localization	Visual point localization
BL23: Shenshu 腎俞(俞)	In the lumbar region, at the same level as the inferior border of the spinous process of the second lumbar vertebra (L2), 1.5 B-cun lateral to the posterior median line.	
BL24: Qihaishu 氣(气,気)海(海)俞(俞)	In the lumbar region, at the same level as the inferior border of the spinous process of the third lumbar vertebra (L3), 1.5 B-cun lateral to the posterior median line.	
BL25: Dachang-shu 大腸俞(俞)	In the lumbar region, at the same level as the inferior border of the spinous process of the fourth lumbar vertebra (L4), 1.5 B-cun lateral to the posterior median line.	

The treatment protocols involved 3 sessions per week for 2 weeks, with treatment points tailored to individual pain sites. While technically similar, Kim *et al.* [16] details practitioner qualifications, enhancing reproducibility and methodological rigor.

The steps used in the treatments are represented in Table 5.

Table 5. Traditional Chinese medicine-based wet-cupping treatment steps based on the included studies.

Step	Procedure Description
1	**Treatment point selection**: At each session, **2 treatment points** were selected from the **bilateral BL23, BL24, and BL25** acupoints (i.e., four possible points total). Note: The two most painful points would be identified using manual palpation and patient feedback. If no point was sensitive or painful, bilateral BL25 was used by default.
2	Scarification: Using lancet needles, shallow punctures were made at each selected point to a depth of 2 mm to enable bloodletting.
3	Cup attachment: Sterile vacuum cups were applied directly over the punctured sites.
4	Suction initiation: A manual pump was used to create maximum negative pressure within the cups, facilitating blood flow.
5	Retention phase: Cups were left in place for 5 minutes to allow for sufficient blood extraction.
6	Cup removal: The exhaust valve was opened to release pressure, and the cups were then carefully removed.

5.3. Implications for clinical practice and future research

The findings from this review provide preliminary but encouraging evidence that wet-cupping therapy may serve as an effective adjunctive treatment for patients suffering from low back pain. Across the five included RCTs, significant improvements were observed in pain intensity, functional disability, and, in some cases, reduced reliance on pharmacological agents such as acetaminophen. Notably, both traditional *Hijamah* and traditional Chinese medicine-based cupping methodologies demonstrated comparable efficacy, suggesting a level of therapeutic consistency despite procedural variation.

From a clinical standpoint, wet-cupping may offer a viable non-pharmacological option that aligns with current European guidelines recommending multimodal and conservative management of low back pain. Given the growing concerns surrounding opioid and analgesic overuse, especially in chronic pain conditions [18], wet-cupping could contribute meaningfully to reducing medication dependency and enhancing patient-reported outcomes.

Furthermore, the documented benefits in both acute and subacute settings, particularly the sustained improvements reported at 3- and 6-month follow-ups, underscore its potential for long-term symptom relief. Clinicians may consider incorporating cupping as a complementary modality, particularly for patients seeking culturally congruent or less invasive interventions. However, appropriate training, standardization of techniques, and attention to hygiene and safety protocols are essential for its integration into mainstream practice.

Despite these promising outcomes, future research remains imperative to address the current limitations. The heterogeneity observed in intervention protocols, treatment durations, and outcome measures difficult direct comparison and synthesis of results. Larger, multicenter RCTs with rigorous methodology, consistent acupoint protocols, and long-term follow-up are required to validate the effectiveness and safety of wet-cupping across diverse patient populations.

Moreover, mechanistic studies exploring the physiological basis of cupping, such as its impact on inflammatory mediators, muscle perfusion, and neuromodulation, would be valuable in elucidating how this ancient practice exerts measurable clinical effects. Finally, cost-effectiveness analyses and qualitative studies assessing patient satisfaction and cultural acceptance will further inform policy decisions and health system adoption.

6. Conclusion

In conclusion, while wet-cupping shows promise as an evidence-informed, low-cost adjunct for low back pain, its incorporation into routine care should be guided by future high-quality trials, standardized protocols, and interdisciplinary collaboration between traditional and modern healthcare practitioners.

Credit author statement: Conceptualization, E.M.S. and R.C.T.; Methodology, E.M.S. and R.C.T.; Validation, E.M.S. and R.C.T.; Formal analysis, C.S.S., A.T.T., R.S.A., V.C.N. and A.L.C.; Investigation, C.S.S., A.T.T., R.S.A., V.C.N. and A.L.C.; Resources, E.M.S. and R.C.T.; Writing - Original Draft, C.S.S., A.T.T., R.S.A., V.C.N. and A.L.C.; Writing - Review & Editing, E.M.S. and R.C.T.; Visualization, E.M.S. and R.C.T.; Project administration, C.S.S., A.T.T., R.S.A., V.C.N., and A.L.C. All authors have read and agreed to the published version of the manuscript.

Funding: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Conflict of Interest: The authors declare that there are no conflicts of interest.

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: The original contributions presented in this study are included in the article. Further inquiries can be directed to the corresponding author.

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Journal of Complementary Therapies in Health
ISSN 2975-9323 | eISSN 2975-9552

Review

Qigong as a Complementary Therapy for the Mental Health of Children and Adolescents: An Exploratory Narrative Review of the Evidence.

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Abstract: Background: Mental health issues such as anxiety, depression, and behavioural disorders are increasingly prevalent in children and adolescents. Conventional treatments like pharmacotherapy and CBT have limitations, creating a need for complementary therapies. *Qigong*, an ancient practice rooted in Traditional Chinese Medicine, has shown promise in regulating the autonomic nervous system and improving mental health.
Objective: This narrative review examines the potential of Qigong, a traditional Chinese practice, as a complementary therapy for pediatric mental health.
Methods: A comprehensive search of major databases was conducted to identify studies on *Qigong* interventions for children and adolescents. Studies were included if they focused on mental health outcomes and involved *Qigong*.
Results: Eleven studies were included, consisting of 7 experimental studies and 4 systematic reviews. Findings indicate that *Qigong* can effectively reduce symptoms of anxiety, depression, ADHD, and other behavioural disorders. It may assist in managing autism spectrum disorder, Down syndrome, anorexia nervosa, and several other conditions. Qigong was particularly noted for regulating the autonomic nervous system and improving emotional regulation. Qigong interventions were well-received and showed minimal side effects.
Conclusion: *Qigong* shows promise as a safe and feasible complementary therapy for pediatric mental health. Further longitudinal, high-quality studies are necessary to validate these findings and optimise integration into clinical and educational settings.

Keywords: *Qigong*; Mental Health; Children; Adolescents.

Citation: Zenha A., Couto R., Calado J.C., Souza T., Freitas S. Qigong as a Complementary Therapy for the Mental Health of Children and Adolescents: An Exploratory Narrative Review of the Evidence. Journal of Complementary Therapies in Health. 2025;3(2) 10.5281/zenodo.15453189

Academic Editor: Jorge Rodrigues

Received: 28 April 2025
Reviewed: 09 May 2025
Revised: 13 May 2025
Accepted: 14 May 2025
Published: 17 May 2025

1. Introduction

Children's and adolescents' psychological development is shaped by the dynamic interplay between emotional, social, and physical health. In recent years, mental health conditions such as anxiety, depression, and behavioural dysregulation have increased alarmingly among youth populations [1-5].

Conventional approaches to the treatment of mental disorders in children and adolescents predominantly include pharmacotherapy and psychotherapeutic interventions, such as cognitive-behavioural therapy (CBT). Pharmacological treatments, particularly the use of selective serotonin reuptake inhibitors (SSRIs), have demonstrated efficacy in managing symptoms of depression and anxiety; however, their use is frequently associated with adverse effects, including somatic complaints, behavioural activation, and an increased risk of suicidal ideation, especially in early stages of treatment [6,7]. Psychotherapeutic methods like CBT have shown moderate to strong evidence of effectiveness across

a range of disorders; nonetheless, limitations persist regarding accessibility, high treatment costs, variability in therapist competence, and reduced effectiveness in complex or comorbid cases [8,9]. These limitations highlight the critical need for the development and integration of complementary strategies that can address the heterogeneity of clinical presentations and improve long-term mental health outcomes in this population.

Ancient techniques with roots in Traditional Chinese Medicine, such as *Taijiquan* and *Qigong*, have become viable adjunctive therapy for mental health. Through regulated movement, breathing, and meditation, these methods, which fall under the category of Traditional Vegetative Biofeedback therapies, have been demonstrated to affect the regulation of the autonomic nervous system, promote homeostatic balance, and modify psychophysiological processes [10-15]. Through precise movements or postures, breathing methods, and meditation exercises, practitioners can alter biological functions and processes through self-directed applied psychophysiological feedback techniques [16].

According to recent research, *Qigong* and *Taijiquan* may have a variety of positive effects on mental health [11,17]. These interventions have been extensively examined in adults [18-23], but less so in pediatric populations. Nevertheless, recent evidence suggests their safety, feasibility, and possible efficacy [11].

This narrative review intends to consolidate existing research on the use of *Qigong* as an adjunct therapy for mental health in children and adolescents. Through the analysis of both experimental and systematic investigations, it aims to elucidate the therapeutic potential of these practices and recommend pathways for future interdisciplinary research and clinical incorporation.

2. Methods

2.1. Search Strategy

A comprehensive search strategy was developed to identify all relevant studies. Electronic searches were conducted in several major databases from their inception to January 2025.

The search strategy combined keywords and controlled vocabulary related to *Qigong*, Children and adolescents, and Mental Health. No language or publication date restrictions were applied initially, but limitations were noted and addressed during the screening process. We also manually searched the reference lists of included studies and relevant studies to identify additional eligible studies.

2.2. Study Selection

Two independent researchers screened the titles and abstracts of all identified records against the pre-defined inclusion and exclusion criteria. Studies deemed potentially eligible were retrieved in full text. The same two reviewers independently assessed the full-text articles for inclusion. Disagreements at both the title/abstract and full-text screening stages were resolved through discussion and consensus, or by involving a third reviewer when necessary.

2.3. Inclusion and Exclusion Criteria:

Studies were included if participants were children or adolescents, investigated the intervention of *Qigong* and reported at least one mental health-related outcome.

Studies were excluded if they investigated interventions that were not related to *Qigong* or were in combination with interventions where the effect of *Qigong* could not be isolated. Chinese traditional exercises that were related to *Qigong* (eg. *Taijiquan*) were included when in combination with specific *Qigong* exercises.

2.4. Data Extraction

Data from the included studies were extracted independently by two reviewers using a standardised data extraction table. The form collected information on study characteristics such as author, year, study design, the studied condition, intervention and comparator details, outcome measures, and main results.

Any discrepancies during data extraction were resolved through discussion and consensus, with the involvement of the third reviewer if needed. Authors of primary studies were contacted for clarification or missing data when necessary.

3. Results and Discussion

The search strategy and consecutive screenings resulted in a total of 11 studies.

The included studies demonstrated significant heterogeneity, exploring various aspects of children's and adolescents' mental health and utilising diverse intervention techniques. To better synthesise the evidence within this context, our analysis comprised 7 experimental studies and 4 systematic reviews. The reviewed studies within the initially identified systematic reviews were excluded to avoid overlap and ensure a focused synthesis of primary and high-level evidence.

3.1. Experimental Studies

In Table 1, a summary of the included experimental studies is presented.

Table 1. Experimental studies' characteristics.

Title • Journal • Citation	Intervention	Groups	Outcome Measures
Effects of taijiquan and qigong practice over behavioural disorders in school-age children: A pilot study *Journal of Bodywork and Movement Therapies* **Rodrigues *et al.*** [24]	Yang-style TJQ 8-movement form BDJ QG	Intervention group only	ADHD, CD, ODD TRF - teachers Structured Interview - children
Taijiquan and qigong as a mindfulness cognitive-behavioural based therapy in the treatment of cothymia in school-age children - A preliminary study. *Journal of Bodywork and Movement Therapies* **Rodrigues *et al.*** [25]	Shao Yin Yang style TJQ 8-movement form (routine of the five animals) Shao Yin BDJ QG	Symptomatic group Asymptomatic group	Anxiety-depression (Cothymia) TRF - teachers
Assessment of Qigong Effects on Anxiety of High-school Students: A Randomized Controlled Trial *Advances in Mind-Body Medicine* **Rodrigues *et al.*** [16]	Shao Yin QG (routine to calm and concentrate the Shen and regulate the heart)	QG group TV documentary group Typical school duties group	Anxiety STAI - students Salivary cortisol analysis - students
Xianggong (Fragrant Qigong) for the Health of School Children: A Qualitative Pilot Study of Feasibility and Effects. Journal of Chinese Medicine **Witt *et al.*** [26]	QG (Xianggong)	Only one intervention group per school	Quantitative assessments through Questionnaires for students, parents, and teachers, evaluating behaviour, school grades, absenteeism, quality of life, and health issues, alongside qualitative semi-structured interviews with teachers.
Qigong for Schoolchildren: A Pilot Study. The Journal of alternative and complementary medicine. **Witt *et al.*** [27]	QG (Xianggong	One intervention group and one control group per school	Standardised questionnaires assessing complaints, concentration, creativity, grades, QoL, and social behaviour, along with teacher assessments and medical complaints documented by parents.

Group Qigong for Adolescents inpatients with Anorexia Nervosa: Incentives and Barriers. PLOS ONE **Gueguen *et al.*** [28]	QG exercises incorporating traditional forms such as White Tiger, Wild Goose, BDJ and Jade Body.	Intervention group only	Anorexia nervosa Semi-structured interviews Qualitative assessments of participants' experiences during and after QG sessions, their perceptions of body image, adherence to the practice, and the meaning attributed to QG, were analysed through IPA.
Improved speech following parent-delivered qigong massage in young children with Down syndrome: a pilot randomized controlled trial. Early Child Development and Care **Silva *et al.*** [29]	Parent-delivered QG massage	Intervention Group Control Group	Down syndrome Bayley Scales of Infant and Toddler Development Raw scores

Abbreviations: TJQ - *Taijiquan*, QG – *Qigong*, ADHD – Attention Deficit Hyperactive Disorder, CD – Conduct Disorder, ODD – Oppositional Defiance Disorder, BDJ - Ba Duan Jin, TRF - Achenbach Teacher's Report Form, STAI - State-trait anxiety inventory, QoL - Quality of Life, IPA - Interpretive Phenomenological Analysis.

A 1-year pilot study in a school context with four children between 6 and 10 years old suggested that *Taijiquan* and *Qigong* might help regulate behavioural disorders such as attention-deficit hyperactive disorder (especially hyperactivity-impulsivity), oppositional defiant disorder, and conduct disorder [24]. The condition of positive vegetative behavioural patterns may be, in part, due to the characteristics of these techniques, acting on the nervous system and motivating a state of relaxation. Techniques such as these help address physiological symptoms of prolonged stress, regulating the mind and emotions [30]. In the study, the pathopsychophysiology of these behavioural disorders is discussed and theorised by the authors according to Chinese medicine.

Another 1-year preliminary study conducted with six school-aged children showed that these therapeutic approaches can be applied as a mindfulness cognitive-behavioural-based therapy with body movement in the treatment of anxiety-depression [25]. It demonstrated treatment capabilities in affected children, as well as preventive capabilities in children who did not display clinically relevant symptoms. In this article, the authors discuss and formulate a hypothesis about the formation of this condition based on the theory of the five internal pathologic agents of Chinese medicine. Parallelism is made between this theory and several psychological and medical formulations, such as the theory of emotions, the gut-brain axis, and the tryptophan metabolism.

Furthermore, a six-week randomised controlled trial with 104 high-school students was carried out to assess *Qigong's* effects on anxiety [16]. The *Qigong* group was the only group to achieve a statistically significant improvement in both state and trait anxiety. Improvement was mostly observed in male participants. Regarding the biochemical assessment, salivary cortisol changes were not significant, however, a higher tendency for improvement was observed in the *Qigong* group, which may result in significant changes if the intervention period was longer.

A six-month qualitative pilot study [26] conducted in four Berlin schools involving 140 children aged 10 to 17 years suggested that Xianggong (Fragrant *Qigong*), a simplified form of traditional *Qigong*, may support the psychosocial and physical well-being of schoolchildren. According to teacher reports, the practice was associated with reductions in restlessness, aggression, and social tension while promoting calmness, focus, and a sense of classroom community. Children also reported improved sleep, vitality, and fewer physical complaints such as allergies and colds. These outcomes may be partially attributed to the regulatory effects of *Qigong* on the autonomic nervous system, fostering a relaxed physiological state. In this study, the feasibility and integration of Xianggong

within regular school lessons were also explored, with findings highlighting both excessively easy exercises leading to a lack of concentration, time constraints within the school schedule and parental scepticism due to the perceived cultural or spiritual origins of *Qigong*.

Similarly, another six-month preliminary study [27] involving 90 school-aged children investigated the integration of Xianggong into regular classroom settings as a means to promote behavioural and emotional regulation. The intervention was associated with improvements in social behaviour and emotional balance, particularly in reducing restlessness and enhancing classroom harmony, as reported by teachers. Additionally, some students showed improvements in physical well-being, such as better sleep and fewer allergy-related symptoms. The study combined quantitative and qualitative methods, highlighting the utility of *Qigong* both as a preventive and supportive strategy in school health. In this article, the authors emphasise the relevance of integrating traditional mind-body techniques into modern educational settings, drawing attention to the psychosomatic and regulatory potential of *Qigong* based on Traditional Chinese Medicine theory.

A qualitative study [28] involving sixteen adolescent girls hospitalised for anorexia nervosa investigated the integration of *Qigong* as a complementary intervention within a multidisciplinary treatment program. The findings suggested that *Qigong* might support emotional regulation, enhance body awareness, and facilitate non-verbal emotional expression in this clinical population. Participants described the experience as calming and grounding, with some reporting improvements in anxiety, emotional tension, and bodily reconnection. These outcomes may be partially attributed to the physiological mechanisms of *Qigong*, which promote parasympathetic activation and support embodied awareness. Such techniques may counteract the hyperaroused stress states commonly observed in individuals with anorexia nervosa. In this article, the authors explore how *Qigong* practice aligns with Chinese medical theory, particularly the regulation of Qi and the balance of internal organ systems implicated in emotional and somatic dysregulation.

Finally, a five-month pilot randomised controlled trial [29] involving children with Down syndrome investigated the effects of parent-delivered *Qigong* massage on expressive language development. The intervention demonstrated a significant improvement in expressive language skills among children in the treatment group compared to controls. The positive outcomes may be partially attributed to the somatosensory and regulatory effects of *Qigong* massage, which targets the autonomic nervous system and promotes relaxation, sensory integration, and body awareness. These mechanisms may support neurological pathways involved in speech production and auditory processing. In this article, the authors explore the therapeutic potential of *Qigong* massage for developmental delays and hypothesise its role in enhancing communication through physiological and energetic modulation consistent with the principles of Chinese medicine.

3.2. Systematic Review Studies

Table 2 summarises the systematic reviews included in this study.

Table 2. Characteristics of the included systematic reviews.

Title • Journal • Citation	Number of included studies	Intervention(s)
Effects of Tai Chi and Qigong in Children and Adolescent: A Systematic Review of Trials. Research Reviews **Riskowski *et al.*** [31]	13	TJQ (Yang-style or Chen style) QG variations like 18-posture QG or Peace Power QG.
Qigong in the treatment of children with autism spectrum disorder: A systematic review *Journal of Integrative Medicine*	10	QG massage Nei Yang Gong

Rodrigues *et al.* [32]		
The Therapeutic Potential of Five Animal Qigong (Wu Qin Xi) for the Wellbeing of Children: A Systematic Review. Integrative and Complementary Therapies. **Rodrigues *et al.* [33]**	8	Wu Qin Xi or Five Animal QG (tiger, deer, bear, monkey, and bird)
The Effects of Tai Chi and Qigong Exercise on Psychological Status in Adolescents: A Systematic Review and Meta-Analysis. Frontiers in Psychology. **Liu *et al.* [34]**	10	TJQ (Chen-style), mindfulness-based TJQ QG: Turo Qi training, BDJ, Laughing QG, and Xianggong.

Abbreviations: QG – *Qigong*, TJQ – *Taijiquan*, BDJ – Ba Duan Jin.

A systematic review to identify *Qigong* interventions was carried out, focusing on the effects on children and adolescents with autism spectrum disorder [32]. Results demonstrated that *Qigong* seems to decrease significantly the severity of sensory, behavioural, and language impact of this neurodevelopmental disorder. *Qigong* also showed to improve self-control, sensory and cognitive awareness, healthy physical behaviour as well as sociability. Favorably, it was also observed an increase in child-to-parent bonding and a decrease in parenting stress which is important for a long-term parent-delivered treatment.

Another systematic review [33] was conducted to examine the effects of Wu Qin Xi, a traditional form of Five Animal *Qigong*, that mimics the movements and postures of the five animals, on the well-being of children. Results demonstrated that Wu Qin Xi appears to significantly improve multiple aspects of children's health, including psychological outcomes such as reduced stress and anxiety levels, as well as enhanced cognitive functions like memory and executive performance. The practice also showed benefits for physical health, particularly in improving respiratory function in children with asthma and pneumonia and promoting better posture, spinal mobility, flexibility, and body composition. Among children with autism spectrum disorder, Wu Qin Xi contributed to improvements in behaviour, sensory integration, and social interaction. Collectively, these findings suggest that Wu Qin Xi may serve as an effective complementary intervention for supporting the integrated development and well-being of children.

One more systematic review and meta-analysis was carried out to evaluate Tai Chi and *Qigong* interventions targeting adolescents, focusing on their effects on psychological outcomes such as anxiety, depression, and stress [34]. Results demonstrated that these mind-body practices appear to significantly reduce symptoms of anxiety and depression, with *Qigong* showing particularly strong effects. Additionally, *Qigong* was associated with a significant decrease in cortisol levels, indicating a potential physiological benefit in managing stress. However, the interventions showed no consistent improvements in perceived stress, mood, or self-esteem. These findings suggest that Tai Chi and especially *Qigong* may serve as effective therapeutic modalities to support adolescents' psychological well-being.

4. Final remarks

This narrative review has explored the potential role of *Qigong* as an adjunct therapy in the mental health care of children and adolescents, highlighting its growing relevance in addressing complex psychological and emotional challenges. The studies examined indicate that *Qigong*, alongside more conventional treatment modalities like pharmacotherapy and CBT, presents a promising option for enhancing mental health in young populations.

Several key findings emerged from the analysis of both experimental and systematic studies.

Across all the included studies, *Qigong* demonstrated a strong safety profile and was well-accepted by children and adolescents. This suggests that, when integrated thoughtfully into existing treatment protocols, *Qigong* can provide a low-risk intervention with minimal side effects, making it a viable option for patients, particularly those who may experience adverse effects from pharmacological treatments.

As well, *Qigong* interventions were shown to be effective in addressing a wide range of mental health symptoms, from anxiety and depression to behavioural disorders such as ADHD and conduct disorder, and a wide range of neuropsychiatric illnesses. This aligns with previous evidence in adult populations, extending its therapeutic benefits to younger demographics. In particular, *Qigong*'s ability to regulate the autonomic nervous system, foster relaxation, and promote emotional regulation makes it a valuable complementary treatment for managing stress and anxiety-related disorders.

A key mechanism through which *Qigong* operates seems to be the regulation of the autonomic nervous system, fostering a balance between sympathetic and parasympathetic activity. This has profound implications for treating conditions like anxiety, depression, and stress, as these disorders are often marked by autonomic dysregulation. Furthermore, the mind-body connection facilitated by *Qigong* encourages self-awareness and mindfulness, enhancing the child's ability to cope with emotional dysregulation and promoting resilience.

An important aspect of the reviewed studies is the incorporation of *Qigong* within school environments. These techniques have shown promise in improving classroom behaviour, focus, and emotional regulation, suggesting that *Qigong* could be an effective strategy for enhancing mental health support within schools. This integration could reduce the stigma associated with mental health treatments and promote a holistic approach to child development, focusing not just on academic achievement but also on emotional and social growth.

Despite the encouraging findings, much remains to be explored. The research so far has been largely exploratory, with few large-scale, longitudinal studies in pediatric populations. Future research should focus on the long-term efficacy of *Qigong* interventions, especially in populations with more complex or comorbid mental health conditions. Additionally, understanding the optimal dosage, frequency, and duration of *Qigong* practices in younger patients will be critical for determining best practice guidelines. Further interdisciplinary research involving child psychologists, paediatricians, and traditional medicine experts will help to fine-tune these approaches and provide more definitive recommendations for clinical use.

5. Conclusions

Qigong represents a valuable and underutilised tool in the growing toolkit for treating mental health disorders in children and adolescents. Its combination of physical movement, mindful breathing, and meditative practices not only addresses the psychological symptoms but also fosters overall well-being, aligning with holistic principles that integrate mind, body, and spirit. As research continues to uncover its therapeutic potential, *Qigong* may emerge as a cornerstone in pediatric mental health care, complementing existing treatments and offering a holistic path forward for children and adolescents facing mental health challenges.

Credit author statement: Conceptualization, R.C.; Methodology, R.C.; Validation, A.Z.; J.C.C.; S.F.; T.S. and R.C.; Formal analysis, A.Z.; J.C.C.; S.F. and T.S.; Investigation, A.Z. and R.C.; Resources, A.Z. and R.C.; Writing - Original Draft, A.Z.; T.S. and R.C.; Writing - Review & Editing, A.Z.; J.C.C.; S.F.; T.S. and R.C.; Visualization, A.Z.; J.C.C.; S.F.; T.S. and R.C.; Project administration, A.Z.; J.C.C.; S.F.; T.S. and R.C. All authors have read and agreed to the published version of the manuscript.

Funding: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Conflict of Interest: The authors declare that there are no conflicts of interest.

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: The original contributions presented in this study are included in the article. Further inquiries can be directed to the corresponding author.

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Journal of Complementary Therapies in Health
ISSN 2975-9323 | eISSN 2975-9552

Review

The Multifaceted Mechanisms of Action of Zhan Zhuang Qigong on Mental Health.

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Abstract

Mental health is crucial for individual and societal well-being, yet mental health conditions pose a significant global burden. The World Health Organization advocates a holistic view of mental health beyond the mere absence of illness. Traditional Chinese Exercises (TCE), particularly *Qigong*, offer a promising, accessible, and self-directed complementary approach. This article focuses on *Zhan Zhuang Qigong*, a low-intensity form characterised by static postures and focused mental and breathing adjustments. We explore its multifaceted mechanisms of action, highlighting its profound physiological impacts, including central nervous system regulation, hippocampal neuroplasticity, autonomic nervous system balance, HPA axis modulation, improved blood circulation, and neuromuscular benefits. Additionally, we detail its powerful psychological advantages, such as enhanced emotional regulation, mindfulness, executive function, stress tolerance, and resilience. As a safe and flexible practice with minimal side effects, *Zhan Zhuang Qigong* presents a valuable tool for promoting holistic well-being and addressing critical gaps in mental health care.

Keywords: Traditional Chinese Exercises; *Zhan Zhuang Qigong*; Chan-Chuang Chikung; Mental Health.

Citation: Fievez A.M., Azevedo H., Figueiredo M., Moreira M., Freitas S., Souza T., Grilo C. The Multifaceted Mechanisms of Action of Zhan Zhuang Qigong on Mental Health. Journal of Complementary Therapies in Health. 2025;3(2) 10.5281/zenodo.16351762

Academic Editor: Jorge Rodrigues

Received: 26 June 2025
Reviewed: 2 July 2025
Revised: 11 July 2025
Accepted: 15 July 2025
Published: 23 July 2025

Publisher's Note: IPTC stays neutral with regard to jurisdictional claims in published maps and institutional affiliations.

1. Background

Mental health encompasses a broad spectrum of mental, emotional, social, and behavioural functions essential to individual and societal well-being [1]. According to the Diagnostic and Statistical Manual of Mental Disorders – Fifth Edition (DSM-5), mental disorders are defined as clinically significant disturbances in cognition, emotion regulation, or behaviour, reflecting dysfunctions in the psychological, biological, or developmental processes underlying mental functioning [2].

The burden of mental health conditions is considerable. These disorders often involve significant physical, emotional and economic challenges, often leading to reduced work capacity and productivity [3]. Furthermore, their effects extend beyond the individual, affecting families, social networks and society at large [4]. Mental health conditions are a major cause of direct and indirect hospital admissions [5-7].

Mental health has often been considered as the absence of mental illness. However, the World Health Organization (WHO) advocates a broader view, framing mental health as "*a state of mental well-being that enables people to cope with the stresses of life, to carry out their activities, to learn and work well, and to contribute to their community*". This broader perspective argues that mental health is more than simply the absence of illness; it is a positive state inherent to an overall state of health and QOL [8].

This view also recognizes the interplay of individual, social and structural determinants across the life course. Adverse conditions, such as poverty, inequality, violence and environmental deprivation, increase vulnerability to mental health problems. Conversely, protective factors, including emotional skills, supportive social connections and access to quality care, can promote resilience and mental well-being [8].

The unmet need for mental health care remains a pressing global issue, regardless of a country's level of development. Garcia-Ceja *et al.* [4], considering that this is a fundamental human right, call on governments to treat this issue as a central priority in public policies, increasing investment in mental health, integrating it into primary health care systems and developing multisectoral policies that strengthen mental well-being, ensuring that they are equitable and accessible to all [8].

2. *Qigong*

Traditional Chinese Exercises (TCE) encompass physical and respiratory practices developed in ancient China that combine movement, breathing, mental concentration and posture, intending to promote health, prevent disease and support healing processes. Among the variety of exercises, the most common are Tai Chi and *Qigong*, which can take different forms [9-12], depending on the region of origin in China and the intended effects on a physical and mental level.

Qigong is recognised as a system of Chinese medicine and has been used for thousands of years to improve physical and psychological health in China. Some exercises are more suited to physical rehabilitation, such as the "Classic of Muscle and Tendon Transformation" (*Yijinjing*) and the "Eight Silk Brocades" (*Baduanjin*), while others are more focused on mental health, such as the "Six Healing Sounds Form" (*Liuzijue*) and the "Post Standing *Qigong*" (*ZhanZhuang gong*) [10,12].

Focusing on their therapeutic foundations, Tai Chi and *Qigong* are seen as a vegetative biofeedback therapy, contributing to homeostasis and a balanced emotional state. This effect is due to the promotion of adequate circulation of qi in the body, in a circular process of self-regulation, explained from the perspective of Western medicine, by the alternation of sympathetic and parasympathetic activity of the nervous system [13-16].

Qigong is a simple and very flexible practice that can be performed anywhere and at any time, without the need for special equipment, being simple to perform, self-directed and promoting self-healing [17]. Being a safe, accessible and viable approach [18], which can be practised at home, it reduces the burden of travel and rehabilitation costs and can be practised by the elderly and patients with chronic diseases, helping to improve both physical limitations and mental problems [15,19-22].

3. *Zhan Zhuang Qigong*

Also known as Chan-Chuang, it is a low-intensity form of *Qigong*, focused on mental adjustment and breathing, which consists of standing in a relaxed posture, with the arms in a circle as if hugging the trunk of a tree or holding a ball, breathing naturally and maintaining balance [23].

These standing exercises combine elements of rest and rehabilitation with light, healthy exercise that may include sitting, lying, and standing postures, as well as some dynamic movements. They use movement, posture, and breathing to cultivate and mobilise vital energy (*qi*) in the body. Standing postures, being the cornerstone of the system, give their name to this static practice, in which the practitioner holds a fixed position for long periods [9,24].

Characterised by simple movements and rapid effects, it is often referred to as a "mind-body" exercise that combines meditation with physical activity to improve physical and mental health [25]. It contributes to the balance of the autonomic nervous system (ANS) by stabilising sympathetic and parasympathetic activity, promoting cardiovascular

homeostasis and physical stability [15]. More than any other *Qigong* exercise, *Zhan Zhuang* is a safe, accessible, simple practice with practically no adverse effects, and is recommended even for people with cognitive deficits or in states of clinical weakness [26-28].

Zhan Zhuang includes several positions or exercises [9,17]. Based on the literature, it was possible to present in Table 1 a systematisation of the main exercises [9,10].

Table 1. *Zhan Zhuang Qigong* Types and Postures

Type	Posture	Forms/Exercises
Static	Foot	"Hold the Ball" or "Three Circles"
		"Lift the Ball"
		"Press the Ball"
		"Basic Standing Posture"
		Relaxation Form
	Sitting	Three main postures: simple, cross-legged and inclined
	Lying down	Lying down with a normal pillow under the head; variations: supine, lateral, three-way and semi-reclining

Source: Adapted by the authors.

Static posture is the core practice of *Zhan Zhuang* and, according to the literature, the main method of intervention, and is increasingly integrated into clinical medicine due to its potential therapeutic benefits [9,20]. It provides a wide range of physical and mental benefits, promotes brain synchronisation, improves cognitive and emotional states and helps in the management of stress, anxiety and emotional disorders. It also contributes to a state of tranquillity and mental clarity, increasing self-awareness, concentration, and emotional resilience. Physiologically, it stimulates the expansion of capillaries, improving systemic circulation without requiring significant physical effort, and contributes to the increase of red and white blood cells, as well as haemoglobin levels, supporting both immune function and oxygenation of the body [9,20,23].

3.1. Mechanisms of Action

Zhan Zhuang works through a multifaceted set of physiological and psychological mechanisms that contribute to the maintenance of health and therapeutic effects [9,23]. In the literature, *Zhan Zhuang* is especially recognised for its ability to regulate the ANS and improve emotional regulation, with the advantage of being well accepted and presenting minimal side effects [29].

Physiological Mechanisms

Central nervous system (CNS) regulation, or brain synchronisation, explains the effect of a mild inhibitory state in the cerebral cortex, facilitating rest, recovery and rebalancing of the nervous system, particularly through the increase in alpha waves. During practice, the brain autonomously adjusts alpha wave patterns, especially in the temporal domains of heart rate variability (HRV), promoting a transition to a calm and focused state. This process helps to interrupt cycles of overstimulation and psychological distress, supporting emotional stability, reducing symptoms of anxiety and fatigue, and also improving executive function and attention [9,20,30-32].

Long-term practice (≥12 weeks) contributes to cognitive enhancement, primarily through its effects on hippocampal neuroplasticity and neuromolecular regulation. Mech-

anistically, this is associated with the proliferation of neurons in the hippocampus, especially in the dentate gyrus, where increased neuronal growth supports memory and learning processes. Practice also influences hippocampal volume and cellular morphology, reinforcing structural integrity in areas critical to cognition. Additionally, it stimulates the expression of brain-derived neurotropic factor (BDNF), both at the protein and mRNA levels, playing a crucial role in neural survival, synaptic plasticity and long-term memory consolidation. This neurotropic effect is further supported by improved mitochondrial gene expression and activity in hippocampal cells, leading to improved energy metabolism and neuronal efficiency. As a result, practitioners may experience increased attention, improved working memory and greater cognitive resilience [9,20,30,31,33,34].

The practice of *Zhan Zhuang* has also been shown to regulate the ANS, promoting homeostatic balance and reducing stress responses [29]. Due to movement regulation, breathing techniques and meditation, *Zhan Zhuang* exerts pronounced effects on the ANS, promoting a transition from sympathetic (fight or flight) to parasympathetic (rest and digest) dominance. This is evidenced by decreased heart rate (HR), increased HRV, and reduced salivary cortisol levels—markers of reduced physiological stress and increased autonomic flexibility [9,16,20,29,33,35]. Vasodilation and increased peripheral temperature, as assessed by thermography, also reflect vascular relaxation and improved microcirculation [14,20,32,33].

Modulation of the Hypothalamic-Pituitary-Adrenal (HPA) axis is another fundamental pathway, with regular practice normalising the activity of the HPA axis, reducing chronic cortisol production and decreasing allostatic load [14,16,33]. This effect is associated with improved immunological parameters, such as increased leukocytes and haemoglobin, and reduced fatigue in clinical populations [14]. The practice also facilitates vegetative biofeedback, allowing practitioners to condition positive autonomic responses (e.g., voluntary hand warming, reduced HR), even outside formal sessions, reflecting neurovegetative plasticity [14,32].

Another relevant physiological mechanism of this practice is its effect on improving blood circulation, facilitated by maintaining relaxed but slightly activated postures that stimulate the cardiovascular system without overloading it. The resulting increase in pulse rate and vasodilation improves peripheral circulation and promotes better delivery of oxygen and nutrients, while facilitating detoxification processes [9,14,15,20,33,34].

The practice stimulates the deep core muscles, improving balance, joint coordination and muscular symmetry. Conscious relaxation of the muscles aids spinal stability and postural correction, resulting in reduced neuromuscular tension and fatigue, particularly in the chest, shoulders and abdomen, improving neuromuscular efficiency while maintaining oxygen balance and metabolism [9,20]. *Zhan Zhuang* has also been shown to improve proprioception and balance in the elderly, and reduce tremor in Parkinson's disease, enhancing neuromuscular and motor benefits [30,34,36].

Based on this, it was possible to present Table 2 as a summary of the physiological mechanisms.

Table 2. Physiological Mechanisms

Mechanisms	Description
1. Central Nervous System (CNS) Regulation	Brain synchronisation, increased alpha waves, promoting relaxation and rebalancing of the nervous system.
2. Hippocampal Neuroplasticity	Proliferation of neurons, increased neuronal growth, supporting memory and learning processes.
3. Autonomic Nervous System (ANS) Regulation	Transition from sympathetic to parasympathetic dominance, reducing stress responses and promoting homeostatic balance.

4. Hypothalamic-Pituitary-Adrenal (HPA) Axis Modulation	Normalising HPA axis activity, reducing chronic cortisol production and decreasing allostatic load.
5. Blood Circulation Improvement	Increased pulse rate and vasodilation, improving peripheral circulation and promoting better delivery of oxygen and nutrients.
6. Neuromuscular Benefits	Improved balance, joint coordination, and muscular symmetry, reducing neuromuscular tension and fatigue.

Source: Elaborated by the authors.

Psychological and Emotional Mechanisms

Zhan Zhuang plays a significant role in emotional regulation, explained by neurophysiological mechanisms. During prolonged standing meditation, the body increases the production of neurotransmitters and hormones, such as norepinephrine, epinephrine, testosterone, and BDNF. These compounds improve mood stability and increase emotional resilience. BDNF supports hippocampal function and has antidepressant-like effects, while testosterone contributes to positive mood and motivation. Additionally, *Zhan Zhuang* increases levels of gamma-aminobutyric acid (GABA), an inhibitory neurotransmitter known for its anxiolytic and mood-stabilising properties. With regular practice, the brain's ability to process and buffer emotional stimuli is increased, leading to improvements in executive function, stress tolerance, and emotional self-regulation [20,30].

On a psychological level, *Zhan Zhuang* promotes mindfulness and grounding by increasing awareness of bodily sensations and emotions. Enhanced self-awareness supports better emotional regulation, cognitive flexibility, and resilience. The practice has been shown to improve executive function, attention, and reaction time, even under conditions of academic or occupational stress [16,31,33,37]. In children with neurodevelopmental conditions, *Zhan Zhuang* practices improved sensory integration and attention [38].

Clinical studies demonstrate significant reductions in anxiety, depression, stress, and burnout symptoms in a variety of populations, including students, teachers, and healthcare professionals [16,33-35]. *Zhan Zhuang* also supports the prevention and management of emotional exhaustion (burnout) and increases stress tolerance and resilience [35,37].

Through these varied physiological and psychological mechanisms, *Zhan Zhuang* integrates body and mind to support holistic health, resilience, and well-being.

In the same way as with the physiological mechanisms, we can summarise in the following table (Table 3), the psychological pathways.

Table 3. Psychological and Emotional Mechanisms

Mechanisms	Description
1. Emotional Regulation	Increased production of neurotransmitters and hormones, improving mood stability and emotional resilience.
2. Mindfulness and Grounding	Increased awareness of bodily sensations and emotions, promoting better emotional regulation and self-awareness
3. Executive Function Improvement	Enhanced cognitive flexibility, attention, and reaction time, even under conditions of stress.
4. Stress Tolerance and Resilience	Increased ability to process and buffer emotional stimuli, reducing anxiety, depression, and burnout symptoms.
5. Emotional Self-Regulation	Improved ability to regulate emotions, leading to increased stress tolerance and resilience.

Source: Elaborated by the authors.

4. Final Remarks

This article highlights the significant burden of mental health conditions globally and emphasises the World Health Organization's broader perspective of mental well-being as

a positive state integral to overall health. In this context, TCE, specifically *Qigong*, emerge as a promising and accessible intervention. In particular, *Zhan Zhuang Qigong* is a low-intensity form characterised by static postures and focused mental and breathing adjustments, offering a complete approach to improving mental and physical health. Its mechanisms of action, spanning central nervous system regulation, hippocampal neuroplasticity, autonomic nervous system balance, HPA axis modulation, improved blood circulation, and neuromuscular benefits, underscore its profound physiological impact. Furthermore, *Zhan Zhuang*'s contributions to emotional regulation, mindfulness, executive function, stress tolerance, and resilience demonstrate its powerful psychological benefits. As a safe, flexible, and self-directed practice with minimal adverse effects, *Zhan Zhuang Qigong* presents a viable and valuable complementary approach to promoting holistic well-being and addressing the unmet needs in mental health care.

Credit author statement: All authors contributed equally. They have read and agreed to the published version of the manuscript.

Funding: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Conflict of Interest: The authors declare that there are no conflicts of interest.

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: The original contributions presented in this study are included in the article. Further inquiries can be directed to the corresponding author.

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Journal of Complementary Therapies in Health
ISSN 2975-9323 | eISSN 2975-9552

Review

Exploring Complementary Approaches: Traditional Chinese Medicine and Naturopathy in Interstitial Cystitis Management.

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Abstract

Background: Interstitial cystitis (IC) is a chronic, progressive, and recurrent urological condition characterized by pelvic pain and urinary dysfunction. The disease significantly impairs patients' physical health and psychological well-being, presenting a challenge for conventional therapeutic approaches. Objective: This narrative review aims to explore the distinct contributions of Traditional Chinese Medicine (TCM) and Naturopathy in the management of interstitial cystitis, highlighting their principles, treatment strategies, and potential benefits. Methods: A selection of relevant literature was conducted through searches in databases including PubMed, Scopus, and ScienceDirect, as well as specialized books and reference texts. Results/Conclusion: Despite the limited availability of high-quality clinical studies, the findings suggest that an integrative approach combining TCM and Naturopathy may offer promising complementary strategies for managing IC. Such approaches may contribute to safer, more personalized, and holistic care for affected individuals. Further robust and long-term studies are needed to confirm their effectiveness and cost-efficiency, particularly in light of the economic burden of IC.

Keywords: Interstitial Cystitis, Chronic Pelvic Pain, Traditional Chinese Medicine, Naturopathy.

Citation: Lopes C., Silva M.G., Silva R.P. Exploring Complementary Approaches: Traditional Chinese Medicine and Naturopathy in Interstitial Cystitis Management. Journal of Complementary Therapies in Health. 2025;3(2) 10.5281/zenodo.15545207

Academic Editor: Jorge Rodrigues

Received: 02 April 2025
Reviewed: 10 May 2025
Revised: 23 May 2025
Accepted: 27 May 2025
Published: 29 May 2025

1. Introduction

Interstitial cystitis (IC), also known as chronic pelvic pain (CPP) or bladder pain syndrome (BPS), is a long-lasting condition that mainly affects women [1,2]. In this paper, the first nomenclature will be assumed.

According to the Society for Urodynamics and Female Urology (SUFU), IC is characterized by persistent pelvic pain and urinary irritative symptoms lasting for more than six weeks, in the absence of infection or other identifiable causes [3]. It can affect women's quality of life and interfere with their physical, mental, and social well-being [4].

However, IC can affect more than the individual's health. It is not only a chronic condition, as previously mentioned, but also progressive and recurrent in nature [5]. This progression results in a "snowball effect", as the disease advances, the patient's health deteriorates, leading to an increase in treatment needs and a financial burden as a consequence [5].

In order to understand the impact of IC in women's lives the data reveal that 15% of women had to miss time from work and report reduced productivity, resulting in a loss of income of $4,216 per year [6,7].

Regarding direct costs of IC (including consultations, medication, hospitalizations, and other interventions), these are higher than those associated with diseases such as diabetes, depression, hypertension, or asthma. Also, it is estimated that a woman with IC has approximately 2.5 times the expenses when compared to a male with the same condition [6,7].

A study involving 239 women diagnosed with IC and receiving treatment estimated an annual cost of $6,614. Another study, based on 43 women with IC, reported an average annual cost of $3,631 per person according to the Medicare database. It is further estimated that, without insurance, this amount could triple [8].

Although the aetiology of the disease is still a matter of debate, it is known that factors such as dysfunction of the bladder epithelium, microvascular changes, autoimmunity, infection either by ketamine or metabolites and imbalances in the central nervous system may be involved [3,9]. Due to the multifactorial nature of IC and the difficulty of diagnosis, conventional treatment does not always offer definitive solutions, leading many patients to seek complementary therapies [10].

While TCM presents a holistic approach that aims to treat the underlying causes of disease by balancing the flow of energy (*Qi*) and restoring harmony between the body's systems [11], Naturopathy emphasizes the body's intrinsic capacity for self-healing, disease prevention, and individual responsibility in achieving health [12].

This narrative review explores the Traditional Chinese Medicine and Naturopathic views on the treatment of interstitial cystitis, looking at practices such as acupuncture, herbal medicine, Tai Chi, *Qigong* and dietary change, as well as the scientific evidence that supports them.

2. Interstitial Cystitis Pathogenesis and Aetiology

IC is more common in women aged 30-50 years with the prevalence is about 2.70% in women and almost 10 times less frequent in men. However, every year these numbers tend to rise [13,14].

Studies have indicated that IC affects 400,000 individuals in the UK (United Kingdom) and between 3 to 8 million women and 1 to 4 million men in the USA (United States of America) [15,16].

As previously mentioned, IC can be very frustrating for both patient and physician because it can be very difficult to find the causes affecting the individual. These causes can be structural, functional or even both [17].

Although no definitive pathogenic agent or mechanism has been identified as the cause of interstitial cystitis, there are some hypotheses already studied [4,18,19]. The first one, and the most common, claims that a deregulation of the bladder urothelium leads to a migration of urinary solutes across the urothelial barrier leading to symptoms [4,18–20]. This leakage may result from alterations in glycosaminoglycans, proteoglycans, cell adhesion proteins and some defense molecules which makes the bladder epithelium reactive to harmless substances and additionally causing pain [4,18–20].

Another hypothesis is the "cross-organ" theory, which proposes that the function (or dysfunction) of one organ can physiologically affect another. For example, irritable bowel syndrome can directly influence the sensory properties of bladder C-fibers [4,20].

Ultimately, autoimmune mechanisms, mast cell activation, previous diseases and infections, neuropathic changes and some environmental factors also play a role in the pathogenesis [14,19]. In these cases, we cannot say that we can achieve a cure (not having pain again). It is imperative to manage patient expectations [21].

2.1. Interstitial Cystitis – TCM diagnosis hypotheses

According to the “Guiding Principles for Clinical Research of New Chinese Medicine“, cystitis corresponds to a damp-heat-stasis syndrome [13] or damp-cold stasis syndrome if it is nonbacterial cystitis [22].

Although both syndromes are related to IC, they present different diagnostic criteria (Table 1). Damp-cold stasis syndrome is more closely associated with IC.

Table 1. Caractherístics and criteria of damp heat and cold syndrome [22].

Syndrome / Characteristics	Damp-heat-stasis syndrome	Damp-cold stasis syndrome
Urine	Dark and cloudy, sometimes with hematuria	Frequent urge to urinate, with difficulty in micturition and a sensation of heaviness in the lower abdomen
Tongue	May appear red, thick, with a yellow and sticky coating	May have a white, sticky coating at the root of the tongue
Pulse	Rapid and slippery	Slippery
Causes	Emotional burden, weakened immune system, or exposure to external damp-heat or damp-cold	Kidney *Qi* deficiency or excessive fear

The International Classification of Diseases (ICD), developed by the World Health Organization (WHO), is a widely used system for diagnosing, monitoring, and classifying diseases on a global level, including TCM [23]. The ICD-11 enhances diagnostic precision by integrating current scientific knowledge, adapting to epidemiological trends, and refining coding for chronic, rare, and mental health conditions [23]. Therefore, according to Chapter 26 of ICD-11, titled Traditional Medicine, i.e., the chapter of ICD-11 that allows for the establishment of the diagnosis according to ancient Chinese medicine, we believe that IC may be encoded with SA90, SA58, and SB07, as it is described in Table 2 [23].

Table 2. Description of IC codes according to ICD-11 [23].

Code	Description
SA90 Stony stranguria disorder (TM1)	A disorder characterized by the presence of urinary calculi, leading to painful and difficult urination due to the passage of stones. It may cause abdominal or lower back pain, and in some cases, colicky pain radiating to the perineum, or even progress to uremia. From a Traditional Chinese Medicine perspective, this condition may be attributed to the accumulation of damp-heat in the lower energizer, which steams and transforms turbid urine into retained stones in the kidneys [18].
SA58 Abdominal pain disorder (TM1)	A disorder characterized by abdominal discomfort. It may be explained by external environmental influences, parasitic infection, improper diet, formation of calculi, *Qi* and blood deficiency or stasis, or bowel obstruction due to faecal stasis [18].
SB07 Lower abdominal colic disorder (TM1)	A disorder characterized by intense, paroxysmal pain in the lower abdomen, constipation, or urinary retention. It may be explained by dysfunction of liver *Qi*, deficiency of *Qi* (particularly in infants or the elderly), herniation of the intestines into the scrotum due to increased abdominal pressure, traumatic injury, or blood stasis in the scrotum after surgery, or congenital malformation [18].

3. Treatment based on TCM

3.1. Acupuncture

Acupuncture is a TCM technique which uses needles to stimulate acupoints in order to achieve homeostasis and regulate *Qi* along the meridians [17].

Acupuncture technique allows the removal of blockage or interruption of *Qi* that occurs in the meridians [14]. This results in the relief of symptoms and pain since the insertion of the needles in these acupoints increases the synthesis of serotonin, β-Endorphin, and enkephalin (endogenous opioids) which leads to a sensation of analgesia and sedation [14,24].

Acupuncture can be used to treat IC, particularly given its lack of adverse effects [25]. There is evidence that supports a positive effect of this practice, mainly on pain relief and urinary symptoms making it a valuable option for patients with various urovaginal conditions [25,26].

This evidence highlights an opportunity for urologists to collaborate with other healthcare professionals, including acupuncturists [26].

A study enrolled 12 volunteers (female) on 10 acupuncture sessions of 25 minutes each, twice a week of the following points: SP6 (*Sanyinjiao*), SP9 *(Yinlingquan)*, ST36 (*Zusanli*), LIV3 (*Tai Chong*), LI4 (*Hegu),* KID3 (T*aixi*), BL33 (*Zhongliao*) and CV4 (*Guan Yuan*) [14]. In the first months after treatment the procedure demonstrated 100% efficacy but, after twelve months, this rate decreased to approximately 16% [14]. The authors suggest that ongoing treatment may yield more consistent results [14].

Another study demonstrated that electroacupuncture produces more favourable outcomes than minimal acupuncture, although both have positive results [27]. The authors applied a protocol once a week for six weeks that includes ST30 (*Qichong*), CV2 (*Qugu*), CV4 *(Guan Yuan*), P6 *(Neiguan*), LI4 (*Hegu*), KID3 (*Taixi),* ST36 (*Zusanli*), SP4 (G*ongsun*) and found that this protocol improved pelvic floor muscles and improved pain-related quality of life [27].

Several other studies have demonstrated the efficacy of acupuncture in IC, some have reported that it is possible to reduce pain by using only acupoints on the Kidney and Bladder meridians. However, 10 to 20 sessions are required to obtain long-term benefits [28].

3.2. Diet

According to TCM, illness is a *Qi* disharmony. Therefore, to balance it and end the disease, the first and most important measure is an appropriate diet [22]. Each country has its own dietary and nutritional patterns. However, it is possible to find similarities between regions [29].

TCM nutrition has three practical applications, namely: health preservation with food, diet therapy, and longevity promotion [29,30]. Health preservation with food is suitable for the daily diet and health care for the general population to prevent disease [29]. Diet therapy is also known as food treatment, that is, a dietary treatment used once the disease has developed [31].

The body extracts and absorbs *Gu Qi* (*Qi* derived from the food), so food acts almost like a therapeutic agent according to the properties of the food itself [22].

In TCM there are criteria by which food is classified, such as thermal nature, flavour, organ network, and direction of energy flows [31].

According to Traditional Chinese Medicine, in cases of IC, foods with a neutral and warm thermal nature should be preferred [22]. Warm foods build up the *Yang* and *Qi* and have the function of warming up the whole body and strengthening the middle burner making them suitable for treating cold symptoms and neutral foods stabilize and harmonize the body and are used to treat *Qi* vacuity [22].

Bitter and sweet flavours are preferred for removing dampness, supplementing the lower burner and Kidney *Yang*, and nourishing the spleen [22].

Sweet flavours increase the energy, build up Spleen *Qi* and nourish body fluids [22]. It also regulates inner tension, stabilizing the inner centre and helping with emotional stress [22]. Bitter flavour corresponds to the Fire phase and supports the body's excretion function [22]. It also has a calming effect when there is stress and mental strain [22].

As preparation methods, boiling and frying should be preferred [22]. Both methods enhance the *Yang* nature of food, which in TCM helps restore *Qi* or *Yin* vacuity [22].

3.3. Chinese Phytopharmacology

Phytotherapy is a form of treatment in which medicinal herbs are used [32]. In China, phytotherapy has always been the cornerstone of Traditional Chinese Medicine, therefore phytotherapy represents 70% of the TCM practice [32].

Perhaps that is why in 2007 almost 20% of adults who used complementary and alternative medicine (CAM) also used phytotherapy [33], which represents a cost of $14.8 billion in the USA, $120 per purchase [34].

Herbal medicines, also called herbal agents, are used to treat many urological diseases, including recurrent cystitis and their effectiveness has already been confirmed [35,36].

On the other hand, some authors argue that the efficacy remains controversial since the results rate varies between individuals [11].

According to the previous TCM diagnosis the *Bei Xie Fen Qing Yin* Formula (Table 3), also known as Tokoro Formula, could be used to treat genitourinary disorders such as cystitis and dysuria since it warms up Kidney *Yang*, removes dampness, and inhibits infection [32].

Table 3. Components and herb dosage of *Bei Xie Fen Qing Yin* Formula.

Scientific Name	Amount (mg)
Rhizoma Dioscoreae Tokoro	78,75
Fructus Alpinae Oxyphyllae	78,75
Rhizoma Acori Graminei	78,75
Radix Lindarae	78,75
Radix Glycyrrhizae	35,00

Rhizoma Dioscoreae Tokoro eliminates dysuria, dissolves dampness, and inhibits urinary infection; *Fructus Alpinae Oxyphyllae* warms up the Kidney and Spleen and stores the *Jing* (Vital essence); *Rhizoma Acori Graminei* dissolves mucus and dampness; *Radix Lindarae* promotes *Qi* flux and disperses cold. Also inhibits pollakiuria; *Radix Glycyrrhizae* tonifies heart *Qi* and nourishes the Spleen [32].

Another highly recommended formula for treating cystitis is *Ba Zheng Tang*, also known as the *powder of the 8 corrections* (Table 4) [37].

Table 4. Components and herb dosage of *Ba Zheng Tang*.

Scientific Name	Amount (g)
Polygoni Avicularis Herba	6
Semen Plantaginis	9
Caulis Akebiae	6
Rhizoma Rhei	9
Fructus Gardeniae Jasminoidis	6
Radix Glycyrrhizae Uralensis Praeparata	6

The first four components drain the damp-heat from the bladder and open the water pathway; *Rhizoma Rhei* clears the heat; *Fructus Gardeniae jasminoidis* drains damp-heat from tree heaters; *Radix Glycyrrhizae Uralensis Praeparata* harmonizes and ceases pain [37].

Ginseng is well known for its rich composition, including a variety of polysaccharides, proteins, and saponins, as well as its anti-inflammatory, antioxidant, anti-cancer, anti-ageing, and immune regulation properties [38]. According to a study, there are 134 gin-

seng-based formulas used for IC disease [38]. Recent studies suggest that are the anti-inflammatory and immunomodulatory properties may help improve symptoms [38] However, the specific effects vary depending on the formulation, as each preparation has different targets, active components and synergetic interactions that contribute to the treatment of IC. In summary, ginseng can help reduce inflammation and tissue damage associated with IC [38].

A study that contemplated a total of 122 eligible patients, with 61 cases in each group (antibiotic group and Chinese Medicine (CM) group). The clinical cure rate by the intention-to-treat approach was 90.2% for the Chinese Medicine group and 82.0% for the antibiotic group (P>0.05) [2]. Bacteria were eliminated from 88.5% (54/61) of patients in the CM group and 82.0% (50/61) in the antibiotic group. The recurrence rate in recovered patients at 6-month follow-up was 9.1% (5/61) and 14.0 (7/61) in the CM and antibiotic groups, respectively (P>0.05) [2]. The CM formula was derived from an ancient remedy Ba Zheng Powder (Table 5), that was officially recorded in the *Song* Dynasty and comprised 10 herbs. This formula has been proven to be effective by both clinical practice and experimental studies [39,40].

Table 5. Components and herb dosage of Bazheng Powder Formula**.**

Scientific Name	Amount (g)
Anemarrhena asphodeloides Bunge	15
Platycladus orientalis (L.) Franco	10
Angelica sinensis (Oliv.) Diels	10
Rehmannia glutinosa (Gaertn.) DC	15
Poria cocos (Schw.) Wolf	15
Salvia miltiorrhiza Bunge	10
Rheum palmatum L.	6
Polygonum aviculare L.	10
Dianthus superbus L.	10
Talcum	15

Another study used a decoction composed of *Cornus*, *Gardenia*, *Curculigo*, *Rhubarb*, *Psoralea* and *Rehmannia*, *Discoria*, *Poria*, *Morinda*, *Coscuta* and *Anemarrhea* twice a day, six days a week, for three months and then once a week [41]. After four weeks of treatment, 61% of the 25 patients reported a significant decrease in pain [41].

3.4. Qigong and Tai Chi

Qigong is an oriental practice that involves body and mind exercises (movement, respiration and meditation) whose objective is to achieve physical and psychological well-being [42].

Tai Chi, also known as Taiji, Taijiquan or Tai chi chuan, like *Qigong* is a low-intensity mind-body exercise that improves aerobic capacity, strength, balance and psychological well-being [43].

Tai Chi and *Qigong* can be framed as an energy therapy useful for maintaining health. As it was proven in a systematic review, Tai Chi and *Qigong* can improve physical function, the immunity system and quality of life [44]. Although there isn't enough scientific evidence about the influence of *Qigong* in IC, its effectiveness in managing chronic pain is well established. In fact, magnetic resonance imaging has shown that *Qigong* training can activate brain regions responsible for pain suppression [45,46]. However, efficiency varies from individual to individual according to his confidence, training and regularity [11].

Although there are no specific exercises to treat IC, some can be recommended for chronic inflammation of the urogenital system, namely the smoothing method of Five Elements Palm. These exercises nourish blood and calm the spirit [47].

The starting posture (Figure 1) consists of standing naturally with feet shoulder-width apart, parallel, standing with knees slightly bent, and the arms hanging down. Bend the wrists so the palms face upward, with fingertips pointing toward each other, and position the hands in front of the *Dantian* as if holding an object [47].

While inhaling, guide the clear *Qi* upwards along the Heart channel. While exhaling, silently pronounce "HE", focusing the mind on expelling turbid *Qi* [47].

At the same time, raise both hands as if holding an object at chest level, with legs in a horse stance (Figure 2) Then move the extended arms horizontally from left to right, in palmar flexion (Figure 3), allowing the body to move slowly to the right. At the end of the movement, turn the palms upward [47].

Then, exhale and turn the palms inwards and downwards while bending the arms and squatting, keeping the upper body straight and returning to the horse stance [47]. After repeating the process 3-9 times on the right side, switch to the right leg and perform the movements from the right to the left 3-9 times [47].

Roborant *Qigong* can also be applied to urogenital pathologies. This form of training is recognized for its ability to nourish *Qi* and strengthen Kidney energy. To achieve its therapeutic effects, it must be practised for 20 minutes, 2-3 times a day for at least three months [47].

Figure 1. Inicial Posture [64].

Figure 2. Horse Position [64].

Figure 3. Palm flexion [64].

The practice method allows flexibility in choosing the postures which may include natural cross-legs, half-lotus, full-lotus, standing or free posture. Once the posture is selected, the practitioner can choose one of three types of breathing:

- Quiet breathing – breathing naturally without focusing attention on it;
- Deep breathing - while inhaling, both the chest and the abdomen expand [47]. While exhaling, both retract [47].
- Reverse abdominal breathing- while inhaling, the chest expands and the abdomen retracts; while exhaling, the chest retracts and the abdomen distends [47].

Following this, the practitioner proceeds to mind adjustment and choosing between two techniques: guided imagination or keeping the 'mind on' [47].

In the first one, the practitioner should guide the imagination according to his condition or illness and use the suggestive power of imagination to create the ideal environment of the body, like hot, warm, cold, etc [47]. IC patients may imagine a fireball in the abdomen.

Keeping the 'mind on' consists of focusing on body areas according to the physical condition such as the *dantian*, kidneys or even acupoints [47].

4. Treatment based on Naturopathy

Naturopathy may represent an underutilized resource in advancing the understanding and management of urinary tract pathologies [48]. The therapeutic focus in interstitial cystitis is directed toward restoring the integrity of the bladder interstitium and reinforcing the urothelial lining [26]. Counselling should include guidance on identifying and avoiding personal symptom triggers [26]. Stress reduction strategies and engagement with support groups are also encouraged to help patients cope with the condition's impact on daily life [26]. Additionally, dietary modifications have been shown to contribute to symptomatic relief in many cases, as botanical medicines and other complementary treatments [26].

Patient education plays a crucial role in the management of interstitial cystitis, empowering individuals to actively participate in their treatment and symptom control [26].

4.1. Biofeedback

Biofeedback enhances voluntary control over typically involuntary physiological functions by converting internal biological signals into external sensory cues, such as visual or auditory feedback. Through training and positive reinforcement, individuals can learn to modulate these signals and develop greater control over specific bodily functions [49].

In the context of pelvic health, biofeedback therapy allows patients to visualize the activity of their pelvic floor muscles via a computer interface. This visual input facilitates awareness and conscious control over muscular contractions, effectively disrupting the spasm-pain cycle commonly observed in interstitial cystitis [41].

A study involving 48 patients diagnosed with IC implemented a 12-week pelvic floor muscle training program combined with biofeedback. The intervention focused on enhancing muscle relaxation and coordination, resulting in symptom improvement in 80% of participants and enhanced quality of life in 70%. Significant reductions in urinary frequency and pain levels were also reported [50].

Moreover, sessions lasting 30 to 60 minutes weekly over six weeks have demonstrated notable efficacy in reducing pain and alleviating muscle tenderness [26].

4.2. L-arginine

L-arginine is a key substrate in the biosynthesis of nitric oxide (NO), a process catalyzed by nitric oxide synthases (NOS). NO acts as a versatile signalling molecule with distinct roles in various physiological systems. In the central nervous system, it functions as a neurotransmitter; within the immune system, it supports host defence mechanisms; and in the cardiovascular system, it contributes to vascular homeostasis by promoting vasodilation and exerting anti-atherogenic effects on the endothelium [51].

A study observed that patients with IC exhibited decreased nitric oxide synthase (NOS) production compared to healthy controls. In a randomized, double-blind trial, 10 patients with IC were administered oral L-arginine at a dose of 1.5 grams per day for six months. The results indicated an increase in urinary NOS levels and an improvement in clinical symptoms including urinary frequency and nocturia in 8 out of the 10 patients [52].

However, evidence on the efficacy of L-arginine remains mixed. A randomized, double-blind, controlled trial found no clinically significant improvement in IC symptoms with L-arginine supplementation [50]. Conversely, another randomized, double-blind, controlled study reported a significant improvement in IC symptoms in the per-protocol analysis, though the intent-to-treat analysis showed no significant difference between the L-arginine and placebo groups [51].

4.3. Probiotics

Probiotics are live microorganisms that, when administered in adequate amounts, confer health benefits to the host [53].

A patient survey investigating probiotic use among individuals with IC revealed that 58.8% of 442 respondents reported significant symptom relief, based on self-assessment [54].

4.4. Arctostaphylos uva ursi

Although traditional use of *Arctostaphylos uva ursi* for symptomatic relief of mild recurrent lower urinary tract infections such as burning sensation during urination and/or frequent urination in women [55], there is currently no clinical evidence supporting its efficacy in IC.

4.5. Cranberry (Vaccinium macrocarpon) juice

The urothelium of the bladder is safeguarded by a dense glycosaminoglycan (GAG) layer, which serves as a critical component of the bladder's barrier function. This protective layer offers both physical and electrostatic defence against urinary irritants, pathogens, and acidic substances, thereby preventing their penetration into the underlying bladder wall [56].

Although cranberry is recognized for its rich content of polyphenols, including flavonoids and phenolic acids, which have shown beneficial effects in the prevention of urinary tract infections (UTIs) [57], its use is not recommended for individuals with interstitial cystitis (IC). This caution stems from cranberry juice's low pH (approximately 2.5) and its high concentrations of organic acids such as citric, malic, and quinic acids [57]. These compounds contribute to the juice's high titratable acidity, which may irritate the bladder mucosa and consequently worsen IC symptoms [58].

4.6. Diet

Several studies have demonstrated that specific foods and beverages may exacerbate the symptoms of interstitial cystitis. Dietary triggers often include acidic, spicy, caffeinated, or carbonated items, which can irritate the bladder mucosa and contribute to symptom flare-ups. Given this strong correlation, the American Urological Association (AUA) recommends dietary modification as a first-line intervention in the management of IC [1].

The "Events Preceding Interstitial Cystitis" case-control study revealed that 85% of individuals with IC reported symptom flare-ups following the consumption of specific foods or beverages [59]. This finding was corroborated by a secondary analysis of the Interstitial Cystitis Database cohort, which found that 77% of patients demonstrated some degree of food sensitivity [59]. Furthermore, a survey involving 598 IC patients showed that 95.8% observed a direct link between dietary intake and symptom exacerbation [60].

A growing body of evidence has established a clear association between particular dietary components and symptom modulation in IC, with certain items intensifying discomfort while others appear to provide relief [4]. Acidic foods and beverages, especially those rich in citric acid, as well as foods high in arylalkylamines, have been implicated in symptom aggravation [21].

Some studies suggest that elevated urinary potassium enhances bladder urothelial permeability, leading to increased pain due to the leaky epithelium [61]. Dietary potassium restriction is often recommended, but evidence remains inconclusive due to limited studies and inconsistent patient responses [4].

Regarding the timing of symptom onset, a study using three-day food and voiding diaries found that symptoms typically flare within two to four hours after consuming potential irritants [41]. However, more recent findings indicate considerable individual variability, with some patients experiencing symptoms within minutes, while others report delayed responses of up to 24 hours [62].

Despite ongoing uncertainty about the exact pathophysiological mechanisms involved, dietary modification is widely regarded as a first-line therapeutic strategy for IC, as endorsed by the American Urological Association [1]. Given the variability in individual food sensitivities, personalized dietary plans are essential. The standard approach involves an initial elimination of suspected irritants for a period of 2–3 months, followed by a gradual reintroduction to identify specific triggers [41]. Alternatively, some clinicians recommend that patients maintain their usual diet while tracking symptoms, subsequently focusing on the least provocative foods for a two-week period. If symptoms remain stable, additional foods can be reintroduced at three-day intervals to construct a long-term dietary plan [4].

Table 6. Foods and Beverages: Most and Least Symptom-Inducing [63].

	Most Bothersome	Least Bothersome
Vegetables	Chili peppers Pickles Sauerkraut Tomatoes and tomato products	Avocados Asparagus Beets Broccoli Brussels Sprouts Cabbage Carrots Cauliflower Celery Cucumber Eggplant Mushrooms Peas Potatoes (white potatoes, yams, sweet potatoes) Radishes Spinach Squash Turnips Zucchini
Fruits	Grapefruit and grapefruit juice Lemons Oranges and orange juice Pineapple and pineapple juice Strawberries	Apricots Bananas Blueberries Dates Melon (honeydew and watermelon) Prunes Pears Raisins
Dairy	Yoghurt	Milk (low-fat and whole) Cheeses (mild)
Protein Foods	Processed sandwich meats (salami, bologna) Soy	Beef Fish (shrimp, tuna fish and salmon) Eggs Nuts Peanut butter Pork

		Poultry (chicken and turkey) Lamb
Grains		Oats Rice
Condiments	Chili Horseradish Ketchup Salad Dressings Soy sauce Vinegar Worcester Sauce	Herbs Garlic or any herb-infused olive oil
Beverages	Alcohol Coffee (caffeinated and decaffeinated) Tea (caffeinated and decaffeinated) Carbonated drinks (cola, non-cola, diet, and caffeine-free) Cranberry juice	Grain beverages/Coffee substitutes Water
Other Foods	Chocolate Indian food Mexican food Pizza Spicy foods Thai food	Popcorn Pretzels
Additives/Artificial Sweeteners	Artificial sweeteners Monosodium glutamate (MSG)	

4.7. General Measures

Patients should be advised to maintain adequate fluid intake, consuming at least 2 litres per day [26].

Additionally, patients should be instructed to urinate after intercourse. Women who experience bladder infections following intercourse may benefit from washing the labia and urethra with a strong infusion of *Hydrangea canadensis* (2 teaspoons per cup) both before and after. If this is not effective, a dilute solution of povidone-iodine is generally helpful[26].

5. Conclusion

Despite the high prevalence of interstitial cystitis and its substantial impact on patients' quality of life, the diagnosis of this condition remains complex, primarily relying on exclusion criteria.

This is closely linked to its multifactorial pathogenesis, the existence of multiple, sometimes conflicting, etiological theories, and significant limitations in the existing literature. Even the American Urological Association (AUA) acknowledges that its clinical guidelines were developed with an awareness of these limitations.

Among the non-pharmacological strategies recommended by the AUA, lifestyle and behavioural modifications are emphasized.

However, the specific nature of these behavioural changes is not clearly defined. Within this context, TCM and Naturopathy appear to align with these recommendations by promoting holistic changes through dietary modifications, the integration of *Qigong* into daily routines, and the use of herbal medicine and supplements.

Although the current scientific evidence is limited, preliminary studies suggest that both TCM and Naturopathy may offer valuable complementary strategies in the management of IC. These findings are consistent with the core philosophies of each approach, TCM seeks to restore the balance of *Qi* to prevent and treat disease, whereas Naturopathy supports the body's intrinsic self-healing processes.

Concerning TCM, there is a notably greater investment in scientific evidence related to acupuncture, whereas the other areas receive considerably less attention. Consequently, for these remaining areas, most of the available information is derived from classical texts rather than recent scientific literature. In our research, we were unable to find studies on the effectiveness of these techniques, which highlights a significant gap in the evidence.

This review has made it possible to propose a preliminary framework for the integration of these practices into the management of IC. Notably, they are not mutually exclusive and may be used in conjunction with other approaches, promoting a more comprehensive and individualized treatment plan.

Given their low incidence of adverse effects and potential benefits, further high-quality, long-term studies are urgently needed to validate the efficacy of these interventions. Future research should also assess their cost-effectiveness compared to conventional treatments, especially considering the economic burden associated with IC.

Credit author statement: Conceptualization: C.L.; Investigation: C.L.; M.G.S..; R.P.S.; Project Administration: C.L.; Supervision: C.L.; Writing – Original Draft Preparation: C.L.; M.G.S.; R.P.S.; Writing – Review & Editing: C.L.; M.G.S.; R.P.S. All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest: The authors declare no conflict of interest.

Funding: This research received no external funding.

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: The original contributions presented in this study are included in the article. Further inquiries can be directed to the corresponding author.

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Journal of Complementary Therapies in Health
ISSN 2975-9323 | eISSN 2975-9552

Review

Naturopathy and Traditional Chinese Medicine in the Treatment of Emotional Stress as a Causal Factor of Autoimmune Diseases – A Narrative Review.

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Abstract
Emotional stress has been increasingly recognised as a significant contributing factor to the onset and worsening of autoimmune diseases. This review analyses the pathophysiological mechanisms by which stress negatively affects immune function, such as impairment of the hypothalamic-pituitary-adrenal (HPA) axis, elevated secretion of pro-inflammatory cytokines, autonomic nervous system (ANS) hyperactivity, and epigenetic alterations. In addition, the views of Traditional Chinese Medicine (TCM) and naturopathy are evaluated regarding the impact of emotional stress on the onset of these conditions. TCM views stress as a disturbance of Qi and the energy balance of the organs, while naturopathy emphasises the importance of nutrition, the gut-brain-immunity axis, and emotional health. Thus, the combined approach of these therapies may potentially create new opportunities in the prevention and treatment of stress-related autoimmune diseases.

Keywords: Emotional Stress; Autoimmune Diseases; Traditional Chinese Medicine; Naturopathy.

Citation: Batista S., Carrajola A., Palheira C., Santos C., Oliveira T., Ferreira I., Araújo M. Naturopathy and Traditional Chinese Medicine in the Treatment of Emotional Stress as a Causal Factor of Autoimmune Diseases – A Narrative Review. Journal of Complementary Therapies in Health. 2025;3(2) 10.5281/zenodo.16325671

Academic Editor: Jorge Rodrigues

Received: 30 May 2025
Reviewed: 2 July 2025
Revised: 9 July 2025
Accepted: 14 July 2025
Published: 22 July 2025

Publisher's Note: IPTC stays neutral with regard to jurisdictional claims in published maps and institutional affiliations.

1. Introduction

In recent years, there has been an increasing scientific focus on the interaction between emotional stress and autoimmune diseases. Thus, emotional stress is increasingly being recognised not only as a correlated factor, but also as a contributing element to the development of these diseases [1].

According to Aghayan *et al.* [2], the immune system is essential for the well-being and proper functioning of living organisms, being crucial for managing the body's reactions to physical injuries and infections, so that its failure can result in illness and death. In turn, dysregulation of the immune system due to stress involves cellular responses.

Furthermore, prolonged stress can induce the release of pro-inflammatory cytokines, such as interleukin-6, which can lead to the onset of several chronic diseases [3].

Although beneficial in the short term, chronic stress becomes harmful, resulting in disorders such as depression, anxiety, and heart disease. Furthermore, chronic stress elevates pro-inflammatory cytokines, disrupts immune balance, and aggravates autoimmune conditions. It also plays a detrimental role in diseases such as Alzheimer's, asthma, cancer, coronary artery disease and others [2].

Considering the potential health implications of stress, it´s essential to deepen our understanding of the complex mechanisms by which stress affects immune function and the diseases that could be caused by emotional stress. Thus, this review aims to explore

the harmful effects of emotional stress as a cause of autoimmune diseases, and the role of TCM and naturopathy.

2. Methodology

This study consists of a narrative review of the literature, which aims to study the impact of emotional stress as a potential triggering or aggravating factor of autoimmune diseases, compiling information from Traditional Chinese Medicine (TCM) and Naturopathy.

The article selection process took place through searches in the following databases: PubMed, Scielo, ScienceDirect and Google Scholar.

The criteria for inclusion of studies were: studies written in English and Portuguese; scientific articles, systematic reviews, meta-analyses and books that addressed the link between emotional stress and autoimmunity, pathophysiological mechanisms, as well as therapeutic approaches for TCM and naturopathy. Not included were: studies that didn´t specifically address the link between emotional stress and autoimmune diseases; articles with duplicate content or ambiguous data.

On the other hand, the content analysis was carried out qualitatively, collecting, comparing and integrating relevant data for the development of the work sections.

3. Emotional stress and autoimmunity

3.1. Pathophysiological mechanisms

Hypothalamic-Pituitary-Adrenal (HPA) Axis Dysfunction

The HPA axis corresponds to a neurohormonal system that integrates the secretion of corticotropin-releasing hormone in the hypothalamus, adrenocorticotropic hormone in the anterior pituitary gland and cortisol in the adrenal cortex. Therefore, the HPA axis is initiated in the hypothalamus, particularly in the parvocellular neurons of the hypothalamus, since it is in this nucleus that information from various areas of the Central Nervous System (CNS) is integrated [4].

In this sense, prolonged stress deregulates the HPA axis, leading to an uncontrolled release of cortisol, which reduces immunological tolerance. This dysfunction facilitates the production of autoantibodies and the activation of autoreactive T cells. Thus, studies indicate that emotional stress, by modifying immunological homeostasis, significantly increases the risk of systemic lupus erythematosus (SLE) [5].

There are several changes in pro-inflammatory cytokines under sustained stress. In the early phase, chronic active stress dysregulates the HPA axis, the sympathoadrenal medulla, and the vagus nerve, which in turn secrete glucocorticoids, catecholamines, and acetylcholine to disrupt inflammatory cytokines in their homeostasis and downregulate proinflammatory cytokines while upregulating anti-inflammatory cytokines. In the second phase, long-lasting exposure to stress induces HPA fatigue, glucocorticoid resistance, nuclear factor kappa-B (NF-αB) activation, and negative feedback, which in turn promote pro-inflammatory cytokines. In the third phase, continuous stress further increases pro-inflammatory cytokines and ultimately causes inflammation, which can induce various diseases [6]. On the other hand, stress promotes the release of pro-inflammatory cytokines, such as TNF-α, IFN-γ and IL-6, aggravating autoimmune diseases [6]. This is supplemented by von Drathen *et al.* [7], who provide recent evidence on cytokine dysregulation in multiple sclerosis.

Additionally, stress-induced cytokine surges accelerate relapses and disability progression in multiple sclerosis (MS) [7].

Autonomic Nervous System and Autoimmunity

The autonomic nervous system (ANS) serves to trigger acute and chronic inflammatory responses through distinct response mechanisms. In turn, the sympathetic nervous

system (SNS) is crucial in managing the mobilization of lymphocytes into the bloodstream. This regulation occurs through the direct involvement of catecholamines with β2AR, a beta-adrenergic receptor located on the surface of lymphocytes, illustrating the link between the immune system and the ANS. In this way, immune cells contribute to the production and release of substances commonly known as neurotransmitters and neuromodulators, such as acetylcholine, dopamine and other catecholamines, which are essential for local immune regulation and for more complex neuroimmunomodulatory circuits [8].

According to Lai *et al.* [9], emotional trauma causes hyperactivation of the SNS, promoting an imbalance in the lymphocyte balance in which Th17 and Treg cells direct it towards a pro-inflammatory state. This phenomenon has been particularly observed in MS and rheumatoid arthritis (RA).

Genetic and Epigenetic Modifications

Epigenetics denotes heritable modifications in gene expression that occur without changes in the DNA sequence. This links genetic influences and harmful environmental exposures to toxins, which are considered significant elements for the formation of the organism's phenotype, as they modify chromatin remodelling, DNA methylation and RNA synthesis [10].

In this context, anxiety is characterized as an unpleasant physical experience and psychological condition and is categorized as a physiological reaction to some form of threat, so that this adaptive mechanism aims to increase the individual's survival and safety. Its origin is complex and unique for each person, involving a complex interaction of genetic, environmental, social and biological elements [10].

According to Schlosser *et al.* [10], epigenetic changes induced by chronic emotional stress help explain the predisposition to autoimmune diseases. In this context, increased methylation of immune system regulatory genes has been associated with childhood trauma, predisposing individuals to diseases such as MS. For example, FOXP3 gene methylation affects regulatory T cell function, while hypermethylation of glucocorticoid receptor genes impairs HPA axis regulation, contributing to autoimmune vulnerability.

Moreover, according to Oliveira [11], the set of epigenetic alterations, known as the epigenome, is indicative of the cell type and offers mechanisms of variation and specialisation, regulating the accessibility of genetic information to the cellular machinery. Problems in the establishment or maintenance of epigenetic marks can lead to the incorrect activation or suppression of different genes and alter typical cellular physiology, resulting in the appearance of diseases.

3.2. Traditional Chinese Medicine (TCM) Perspective

Stress is a natural response that includes physical elements and/or psychological aspects, triggered by psychophysiological changes that occur when an individual is faced with situations that bother, scare, stimulate or disconcert them, or even make them happy. In this sense, stress represents a condition of mental and physical exhaustion that leads to an interruption in the general functioning of the human being [12].

In TCM, emotional stress is considered one of the main intrinsic causes of diseases, as emotional imbalance disturbs the flow of Qi (energy) and Blood, creating pathogenic conditions that aggravate autoimmune diseases [13].

Thus, TCM is based on the idea that there´s an integrated energy structure in the physical body, allowing energy to flow through pathways known as meridians. Meridians function as conductors that connect the different energy systems of the body, allowing the circulation of vital energies (Qi) or pathogenic energies (Xie), which directly affect the body and contain specific points. These points, when activated, reorganise the energy flow throughout the body [12].

Therefore, the occurrence of diseases is invariably linked to the disorganisation of the functional energy that governs and energises the meridians. This comprehensive system, which has evolved through experimentation and refinement over thousands of years, can be harmonised through acupuncture. Consequently, the Chinese realise that the general functioning of the organism and mind depends on the adequate flow of energies or the organism's vital force, our Qi [12].

Emotional Stress as a Dysfunction of Organic Systems

- Liver Qi Stagnation

Anger and continuous emotional repression affect the liver, which is responsible for the flow of Qi [12]. Additionally, stagnation can lead to movement disorders. For example, liver qi stagnation, which can originate from emotional stagnation, can cause increased liver yang activity, resulting in anxiety. Thus, stagnation of Qi can also cause the accumulation of sputum, which can hinder the free flow of the spirit, resulting in anxiety [14].

In common patterns of autoimmune diseases such as lupus and RA, liver Qi stagnation is thought to progress to blood stasis and heat [15].

- Spleen Qi Deficiency

According to Jiang [16], excessive worry and anxiety harm the spleen, compromising its ability to generate and control blood. In turn, this deficit leads to the formation of dampness and phlegm, factors often considered precursors to autoimmune inflammation.

- Kidney Yin Deficiency

Fear and chronic stress consume the kidney Yin, causing internal heat and Yin deficit. Imbalances of this type are often associated with autoimmune thyroid diseases, such as Hashimoto's thyroiditis. In turn, the main symptoms of patients with Hashimoto's thyroiditis include weakness, irritability, lack of appetite, neck discomfort and decreased memory [17].

- Heart Qi Stagnation

In TCM, stagnation of heart qi is often associated with emotional stress, particularly when feelings such as anxiety, sadness or frustration are repressed or prolonged. The heart, which contains the Shen (mind/spirit), is immediately affected by this disharmony, leading to symptoms such as tightness in the chest, palpitations, insomnia, frequent sighing and moodiness. This energetic obstruction is generally aggravated by continuous emotional tension and lack of emotional expression [12].

- Lung Qi Stagnation

In TCM, the lung is linked to feelings of sadness and grief, and when these feelings persist or are not processed properly, they can result in stagnation of Lung Qi. This emotional state affects the normal circulation of energy, complicating both energetic and physical breathing, and can manifest as tightness in the chest, short or labored breathing, weak voice, melancholy and a tendency to cry easily [18].

The TCM approach

- Phytotherapy

The Gan Mai Da Zao Tang formula consists of three primary herbs: Radix Glycyrrhiza uralensis Fisch (commonly known as Gan Cao – liquorice), Triticum aestivum Levis (Fu Xiao Mai – wheat), and Fructus Zizyphus jujubae (Da Zao – jujube). Gan Cao, characterised by its sweet flavour and neutral quality, serves to nourish the Qi of the Heart and Spleen, in addition to having antispasmodic characteristics. Fu Xiao Mai, known for its sweet and slightly salty flavour as well as its fresh quality, helps nourish heart Yin and promote mental tranquillity. Da Zao, which has a sweet taste and warm quality, nourishes Qi and blood, soothes the Liver, and moistens the internal organs (Zang). Therefore, the main therapeutic benefits of the formula include: nourishing the heart, pacifying the Shen

(Spirit), harmonizing the Middle Jiao, tonifying the spleen Qi, and relieving emotional restlessness [19].

Also, Xiao Yao San is a traditional Chinese medicine formulation that has been widely shown to effectively relieve depression in clinical studies. However, the findings are not definitive [20].

Additionally, Gui Pi Tang is a notable formula for persistent Qi and blood deficiency, as well as bleeding problems associated with these, resulting from stress and overexertion. The formula mainly focuses on spleen and heart blood, but also treats liver blood deficiency. Its use is particularly recommended for menstrual bleeding: it can be used for excessive bleeding, prolonged bleeding, painful, irregular or absent menstrual cycles [21].

- Acupuncture

Acupuncture is a traditional Chinese technique that involves stimulating specific points on the body to restore energy balance, known as Qi, and improve emotional health. Thus, acupuncture points such as Taichong (LR3) and Sanyinjiao (SP6), located on the feet and legs, are often used to manage the flow of Qi and calm the Shen (spirit), especially in stressful situations [22,23].

- Lifestyle Changes

According to Pölönen *et al.* [24], practices such as Qigong and meditation help to balance emotions. Qigong is a form of meditative movement exercise that involves conscious movement, breath control and focusing attention. Thus, meditative movement practices combine specific movement patterns, breathing techniques and mental focus to achieve cognitive and emotional changes in the human being, the understanding of which could shed new light on the interrelationship between the body and the embodied mind, especially to avoid stressful situations

3.3. The Naturopathic Approach

Naturopathy highlights the interaction between mental and physical health, emphasising the role of emotional well-being in regulating the immune system [25].

In this context, naturopathy, which is a comprehensive approach to health and well-being, highlights the body's inherent ability to heal itself when the appropriate conditions are met. Thus, preventive strategies in naturopathy provide a comprehensive framework for promoting well-being and preventing disease [26].

In naturopathy, it´s believed that health is not simply the absence of disease, but rather a state of balance that encompasses physical, mental and emotional well-being. For this reason, naturopathic practitioners focus on treating the root causes of health problems rather than just relieving the symptoms. Consequently, prevention and well-being gain importance in maintaining balance and protecting health [26].

Gut-Brain-Immunity Axis

As we look at the harmony of the gut microbiome, methods to balance microbial communities through dietary changes provide realistic solutions for addressing gastrointestinal health. In addition, there are innovative clinical methods, such as specific probiotics, faecal microbiota transplantation and neurointestinal treatments, indicating a transformative change in health care. These developments represent not only a scientific breakthrough but also pave the way for personalised and effective therapies for gastrointestinal diseases. In this collaborative relationship between science and health, intestinal microbiota actively modulates immune function and systemic health [7,27].

However, emotional stress alters the intestinal microbiota, increasing intestinal permeability, allowing bacterial endotoxins to enter the circulation and triggering autoimmune reactions. Therefore, microbiota-focused dietary changes have demonstrated benefits in both emotional well-being and autoimmune symptoms [27].

Emotional Health and Inflammatory Markers

Depressive symptoms and autoimmune activity have been associated with high levels of inflammatory markers such as C-reactive protein (CRP) and IL-6. Thus, reducing emotional distress leads to a decrease in disease severity by reducing these markers [28].

However, it´s important to highlight that the addition of pure ellagic acid leads to remarkable improvements in several factors related to depression among MS patients, observing a significant reduction in BDI-II levels along with reductions in cortisol levels, interferon-γ (IFN-δ) and indoleamine 2, 3-dioxygenase gene expression. Furthermore, ellagic acid may also influence immune response functions, leading to increased Th2 activity and decreased Th1 activity, with the upregulation of Th2 cells being particularly advantageous in the context of depression [28].

Holistic Interventions

Holistic interventions have demonstrated their effectiveness in improving physical and emotional balance, especially in the context of stress management and modulation of the inflammatory response.

Phytotherapy, for example, uses adaptogenic plants such as rhodiola and ashwagandha, which are recognised for their ability to reduce levels of pro-inflammatory cytokines and regulate cortisol, the main hormone associated with stress. These plants help the body adapt more effectively to stress and maintain homeostasis [29].

Mind-body therapies, including yoga, mindfulness meditation, and biofeedback, play a vital role in regulating the HPA axis, which is essential in the body's response to stress. These practices encourage deep relaxation and tension relief, leading to decreased SNS activation and promoting a more balanced reaction to stress [30].

Furthermore, an anti-inflammatory diet with foods rich in antioxidants and omega-3 fatty acids positively influences the reduction of chronic inflammation triggered by stress. These nutrients help fight free radicals and protect cells, contributing to reducing inflammation and improving overall well-being [31].

Therefore, integrating these methods offers an effective strategy for restoring balance to the body and mind, promoting a healthier and more resilient approach to stress.

4. Scientific Evidence Supports the Link Between Stress and Autoimmunity

As previously reported in this study, several mechanisms explain the link between stress and autoimmune diseases. Table 1 summarises the role of stress and therapeutic strategies.

Table 1. Impact of stress in autoimmune diseases and potential therapeutic approaches.

Disease	Stress Impact	Therapeutic Strategy	Reference(s)
MS	Increases relapse risk	Psychosocial treatments (CBT, mindfulness)	[7]
RA	Worsens disease activity	Stress reduction, emotional support	[15]
SLE	Associated with trauma and severity	Coping strategies, psychosocial support	[32]
T1D	Raises glucose levels via SNS activation	Stress management interventions	[33]
AS	Elevates pain and inflammation	Relaxation strategies, psychological support	Summarised from manuscript content

4.1. Multiple Sclerosis (MS)

Stress greatly increases the chances of illness and relapse. As noted by von Drathen *et al.* [7], stress constitutes a primary risk factor, and research indicates that stress management improves clinical outcomes. Psychosocial treatments, including cognitive behavioural therapy, mindfulness, and relaxation methods, have been shown to be effective in reducing the occurrence of relapses and improving patients' quality of life. Furthermore, approaches that promote emotional well-being can influence the immune response, positively affecting the progression of MS disease.

4.2. Rheumatoid Arthritis (RA)

Patients diagnosed with RA have a higher prevalence of mental health disorders when compared to the general population. Emotional distress and RA are believed to influence each other in a bidirectional manner. Longitudinal studies demonstrate that reduced stress is directly associated with decreased disease activity [15].

4.3. Systemic Lupus Erythematosus (SLE)

Traumatic life events are strongly associated with the onset and exacerbation of lupus. Strategies for coping with trauma help to reduce disease severity and autoantibody levels. Enhancing positive psychosocial factors and reducing negative psychosocial factors may alleviate perceived detrimental stress, which may improve outcomes in SLE, even in individuals with a history of prior trauma who may be more susceptible to stressful situations [32].

4.4. Type 1 Diabetes (T1D)

Stress significantly affects the control of type 1 diabetes (T1D), impacting both the physiological and emotional facets of the condition. Stress stimulates the SNS, raising cortisol and adrenaline levels, which increases glucose production by the liver and decreases the effectiveness of insulin, leading to increased blood glucose levels. Furthermore, psychological stress resulting from ongoing disease management can result in anxiety and depression, forming a harmful cycle that worsens glycemic control [33].

4.5. Ankylosing Spondylitis (AS)

Psychological stress is closely linked to the worsening of AS, affecting both the intensity of pain and the inflammatory activity of the disease. Research indicates that individuals with AS have high levels of stress, anxiety, and depression, which are positively related to clinical measures. This connection is reciprocal: stress worsens AS symptoms and, conversely, functional limitations and persistent pain increase psychological distress. Neuroimmunological processes, including activation of the hypothalamic-pituitary-adrenal axis, may shed light on this relationship, implying that stress management—through psychological interventions and relaxation strategies—may be helpful not only for emotional health but also for controlling inflammation and disease progression.

5. Discussion

The connection between emotional stress and autoimmune diseases is supported by several scientific and therapeutic means, as demonstrated in this article. Several researchers come together to analyse pathophysiological mechanisms and integrative strategies to understand and alleviate this problem.

HPA axis dysfunction, as described by Iturriaga *et al.* [4], serves as a crucial physiological basis for understanding how chronic stress affects immunity. Mismanaged cortisol secretion, highlighted by Blasbalg *et al.* [5], reinforces the argument that emotional stress can act as a catalyst for the activation of autoimmune cells, similar to what occurs in systemic lupus erythematosus (SLE).

Similarly, increased release of pro-inflammatory cytokines during periods of chronic stress, according to research by Tian *et al.* [6], illustrates a damaging cycle of inflammation that sustains and exacerbates autoimmune diseases. This mechanism has particular significance in multiple sclerosis, as demonstrated by von Drathen *et al.* [7], who relate cytokine elevations to relapses and clinical decline.

In turn, the data from Schlosser *et al.* [10] and Oliveira [11] on epigenetics are especially pertinent to elucidate how emotional stress permanently modifies immunological genetic expression, making individuals susceptible to autoimmunity — particularly those with a history of psychological trauma in childhood.

From a TCM perspective, stress is analysed as an energetic disturbance that interrupts the movement of Qi and Blood, a fundamental principle of TCM. Bastos [12], Doria *et al.* [13] and Silva [14] illustrate how dysfunctions in several organs (liver, spleen, kidneys, heart and lungs) are linked to negative emotional patterns and physical manifestations of immunity.

Chinese herbal medicine also shows significant therapeutic promise. Formulations such as Gan Mai Da Zao Tang [19], Xiao Yao San [20] and Gui Pi Tang [21] indicate efficacy in emotional and energetic modulation, being relevant in the treatment of both emotional symptoms and autoimmune manifestations.

The naturopathic perspective, as explained by Manoharan *et al.* [25] and Serpente [26], emphasises health as systemic balance. The importance of the gut-brain-immunity axis, promoted by Shang *et al.* [27], illustrates how stress-induced changes in the gut microbiota impact immune health. Furthermore, the role of systemic inflammation caused by negative emotions is supported by Hajiluian *et al.* [28], who highlight the link between inflammatory markers and emotional disorders.

Additionally, integrative and holistic therapies, including the application of adaptogenic plants [29], relaxation strategies and anti-inflammatory diets [30,31], are considered effective approaches for managing stress and autoimmunity, promoting not only symptomatic relief but also a better quality of life.

Finally, clinical evidence linking stress to autoimmune diseases—specifically MS, RA, and SLE—strengthens the need for psychosocial interventions as a vital component of treatment. As pointed out by von Drathen *et al.* [7] and Sweeney *et al.* [15], stress management directly influences immune modulation and clinical progression of autoimmune diseases.

5.1. Integrative Perspectives: Biomedical and Energetic Models

This subsection explores the potential alignment between biomedical immunological mechanisms and TCM energetic interpretations. For instance, HPA axis dysfunction and cortisol dysregulation in biomedical models are viewed in TCM as disruptions in Kidney and Liver Qi balance, leading to systemic vulnerability. Similarly, the biomedical concept of elevated pro-inflammatory cytokines, such as IL-6 and TNF-alpha, aligns with TCM interpretations of 'internal heat' or 'Yang excess', which are understood to aggravate autoimmune conditions. Furthermore, Qi stagnation as described in TCM, especially in the Liver, resonates with the biomedical recognition of autonomic nervous system imbalance and stress-induced inflammatory states.

Integrating these paradigms may provide a holistic understanding of autoimmunity, combining molecular evidence with energetic frameworks to inform prevention and treatment. Such integration could support the development of comprehensive therapies that address both the physiological and energetic disturbances underlying autoimmune diseases, offering innovative avenues for patient-centred care [23,27].

6. Conclusion

There is strong scientific evidence supporting the causal relationship between emotional imbalance and autoimmune diseases; therefore, focusing on emotional control, stress management, and holistic approaches based on TCM and Naturopathy offers promising avenues for the treatment and prevention of these conditions. However, further multidisciplinary studies are needed to integrate these approaches into clinical practice.

There remains considerable ambiguity regarding the origins of autoimmune disorders, and it´s possible that a crucial understanding lies in the interaction between these diseases and mental health. Thus, subsequent research efforts should further investigate the links between various autoimmune diseases and early mental health antecedents.

In summary, this review emphasises the importance of emotional stress as a key factor in the initiation and exacerbation of autoimmune diseases, through the disruption of physiological systems such as the HPA, the release of pro-inflammatory cytokines, the hyperactivity of the ANS, and epigenetic changes that impair the immune response. In this way, TCM and Naturopathy offer complementary points of view to the biomedical perspective, encouraging holistic methods centred on energy balance, emotional management and the promotion of a healthy lifestyle. By addressing the emotional and systemic origins of disease, these therapies may play a significant role in the prevention and treatment of stress-related autoimmune diseases. Therefore, incorporating these modalities into the clinical setting may represent a promising advancement in general health care, especially for individuals susceptible to the effects of chronic stress.

Credit author statement: Conceptualisation, S.B.; Methodology, A.C. and M.A.; Validation, A.C.; Formal analysis, C.S.; Investigation, S.B. and I.F.; Resources, C.P.; Writing - Original Draft, S.B., and I.F.; Writing - Review & Editing, A.C., C.S., T.O. and M.F.; Visualisation, C.P.; Project administration, T.O.; Supervision, T.O. All authors have read and agreed to the published version of the manuscript.

Funding: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Conflict of Interest: The authors declare that there are no conflicts of interest.

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: The original contributions presented in this study are included in the article. Further inquiries can be directed to the corresponding author.

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Journal of Complementary Therapies in Health
ISSN 2975-9323 | eISSN 2975-9552

Experimental study

Antimicrobial Properties of Plants: Uncovering the Potential of Olive Leaves from Portuguese Cultivars.

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Abstract

Background: Complementary therapies in health, such as functional nutrition and phytotherapy, have recently grown, especially under the knowledge diaspora of the Oriental herbal medicine. This shift is also driven by the emerging economic paradigm, which moves from a linear to a circular model, where plant by-products from the primary sector are upcycled into a wide range of value-added products, particularly for therapeutic applications. Different western plant parts, including olive leaves, have been consumed as extract, infusion or as a whole herbal powder with several health benefits. Objective: This study assessed the antimicrobial potential against some Gram (+) and Gram (-) bacteria by olive leaves extracts from three different Portuguese cultivars - Cobrançosa, Madural, and Verdeal - randomly mixed cultivated in an olive grove located in Vale de Salgueiros (Portugal). Methods: The antimicrobial activity of the olive tree leaf extracts was measured for Gram (+) *S. aureus*, *S. epidermidis*, *B. cereus* and Gram (-) *P. aeruginosa*, *Salmonella Enteritidis*, and *E. coli* by agar diffusion assay. Results: All cultivars displayed antimicrobial activity against Gram (-) *P. aeruginosa*, *Salmonella enteritidis* and Gram (+) *B. cereus*. Only Verdeal cultivar showed activity against Gram (+) *S. aureus*, and none presented a significant result against Gram (+) *S. epidermidis* nor Gram (-) *E. coli*. Conclusions: Overall, *O. europaea* leaves from Portuguese cultivars showed effective antimicrobial activity against prevalent bacterial strains, suggesting their applicability in therapeutic formulations for human and veterinary use, as well as a natural preservative agent in food and cosmetic products.

Keywords: Western Plants; *O. europaea L. folium*; Portuguese Cultivars; Therapeutic properties; Antimicrobial activity.

Citation: de Oliveira N., Criado M.B., Machado J., Chéu M.H., Lopes L., Barroso M.F., Silva A., Sousa S., Domingues V., Grosso C. Antimicrobial Properties of Plants: Uncovering the Potential of Olive Leaves from Portuguese Cultivars. Journal of Complementary Therapies in Health. 2025;3(2) 10.5281/zenodo.16814258

Academic Editor: Jorge Rodrigues

Received: 30 July 2025
Reviewed: 10 August 2025
Accepted: 11 August 2025
Published: 12 August 2025

Publisher's Note: IPTC stays neutral with regard to jurisdictional claims in published maps and institutional affiliations.

1. Introduction

1.1. Background

Complementary therapies in health, such as functional nutrition and phytotherapy, have recently grown, especially under the knowledge diaspora of the Oriental herbal medicine [1,2]. For this, also contributes the latest economic paradigm of transitioning from linear to circular model, wherein plant by-products generated from the primary sector are upcycled into diversified traded products, namely of therapeutic use [3,4]. Different western plant parts, including olive leaves, have been consumed as extract, infusion or as a whole

herbal powder for numerous health matters [5,6]. Several benefits and applications have been associated with the bioactive compounds found in olive leaves, and substantial compositional differences have been found amongst diverse *O. europea* L. *folium* cultivars. This differentiation regards not only qualitative and quantitative characterisation of polyphenols but also overall nutritional composition, vitamin E, fatty acids (FAs), as well as antioxidant and antimicrobial activity [4,5,7-9]. Several authors found a correlation between the composition of olive leaves and features such as air temperature and precipitation levels along seasons, type of soil, cultivation techniques and soil supplementation, as well as type of cultivar [5]. It has been consensual that the same cultivar brought up in assorted environments also displays biochemical diversity, reflecting a differential in their industrial and therapeutic applications. Mirandela (MIR) and Valpaços (VAL) in Northeast Portugal have extensive olive groves of autochthonous olive cultivars, known for their premium Protected Designation of Origin olive oil, mainly produced with Cobrançosa, Madural and Verdeal cultivars [5,7-9]. Recent leaf characterisation studies of these three cultivars confirm a biochemical diversity between plants cultivated in MIR and VAL [5,7-9]. MIR olive leaves revealed high levels of total phenolic content (TPC) and lipidic content with high levels of monounsaturated fatty acids (MUFAs) and a small *ω-6/ω-3* ratio [7-9]. These characteristics may render MIR's olive leaves as a highly beneficial antioxidant, anti-inflammatory and antimicrobial, highly renewable, natural resource. Pereira *et al.* [10] already tested the phenolic composition and the antimicrobial power of an aqueous leaf extract of *O. europaea* Cobrançosa, obtained from an olive grove in Mirandela in November 2014. The highest level of growth inhibition among all tested concentrations in that study was observed at 5 mg/mL. Although no lethal behaviour was detected, a notable inhibitory activity was recorded against *B. cereus* CECT 148, *B. subtilis* CECT 498, *S. aureus* ESA 7, *E. coli* CECT 101, *P. aeruginosa* CECT 108, *and K. pneumoniae* ESA 8. Authors also reported that the high concentration of oleuropein, followed by other phenolic compounds, such as flavonoids luteolin-7-*O*-glucoside and apigenine-7-*O*-glucoside, might contribute to this antimicrobial effect [10]. It is known that, on one hand, a higher grade of inflammation has been associated with Gram (-) rather than Gram (+) bacteria [9] raising a concern regarding the treatment of Gram (-) sepsis. On the other hand, it is known that Gram (+) bacteria contribute *circa* 76% of infections in health-compromised individuals, whereas Gram (-) microorganisms only represent 14% of these infections [9]. Moreover, multidrug-resistant (MDR) microorganisms such as *B. cereus*, *S. aureus*, and *E. coli* demand searching for alternative solutions to the overuse of antibiotics. For its broad antimicrobial activity, plant derivates such as olive leaf extracts (OLEs) have regarded as a privileged nature-based source for designing pharmacological actives.

1.2. Objective

Therefore, this study aimed to assess the polyphenolic content and antimicrobial activity of the hydroethanolic extracts of three Portuguese cultivars' leaves (Cobrançosa, Madural and Verdeal) from the MIR olive grove. In this olive grove, (coordinates in WGS84: Lat: 41.579700 and Long: -7.241642) these different varieties have been cultivated randomly mixed in the same geographical space for over 60 years, embedded in a total area of 13.5 ha, equivalently distributed: (1) 59.26% (8.0 ha) of *O. europaea* L. var *europaea* Cobrançosa, (2) 10.37% (1.4 ha) of *O. europaea* L. var *europaea* Madural, and (3) 30.37% (4.1 ha) of *O. europaea* L. var *europaea* Verdeal cultivars. The allocation of olive trees/area is around 200 items/49m^2, being even denser in topographical planes. The maintenance of this olive grove includes conventional cultivation techniques with application of (1) $CaSO_4$ (2) Sprintplus® (algae-based), and (3) organic fertiliser with soil reviver. Trees are biannually pruned after the olive harvest season.

2. Materials and Methods

2.1. Olive leaves extracts

The samples for phytochemical analysis were obtained by subjecting 0.60 g of powdered olive leaves from each cultivar to an organic extraction with 12 mL of a hydroethanolic mixture (50/50, v/v) for 60 min at 55 °C.

2.2. Phenolic and Flavonoid content assessment

Both Total Phenolic Content (TPC) and Total Flavonoid Content (TFC) values were determined via colourimetric assays based on Folin–Ciocalteu reagent according to a previous procedure [9]. Calibration curves for TPC were calculated using gallic acid (GA), and for TFC were prepared with epicatechin, and the results were expressed as milligrams of epicatechin equivalent (ECE) per gram of sample. The phenolic profile was identified through High-Performance Liquid Chromatography according to a previous protocol [9].

2.3. Antimicrobial Activity

Microorganisms and Culture Conditions

The antimicrobial activity of the olive tree leaf extracts was assessed against Gram-positive bacterial strains: *Staphylococcus aureus* (ATCC 25923), *Staphylococcus epidermidis* (NCTC 11047) and *Bacillus cereus* (ATCC 14579); and Gram-negative strains: *Pseudomonas aeruginosa* (ATCC 10145), Salmonella Enteritidis (ATCC 13076) and *Escherichia coli* (NCTC 9001). Aliquots from each culture were transferred to fresh MHB and properly diluted to an optical density of 0.09–0.11, corresponding to the 0.5 MacFarland standard, to reach 1–2 × 10^8 colony formation units (CFUs).

Agar Diffusion Assay

Assays followed the adapted protocol from the CLSI gidelines [11]: 100 µL of microbial suspensions were seeded and spread into Petri dishes containing Mueller–Hinton II agar, divided into sections - 15 µL of each tested extract (test section), DMSO (negative control section), and 40% lactic acid (positive control section) to incubate at 37°C for 24h (Figure 1). Growth inhibition was quantified, in triplicate, by diameter measurement of inhibition circular zones.

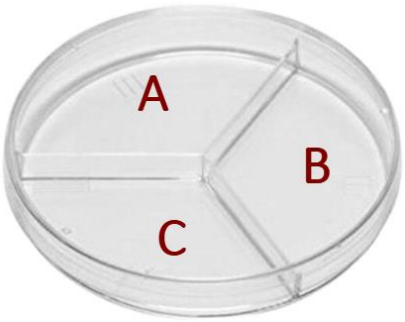

Figure 1: Petri Dish Model incubated at 37ºC for 24h. Description: A - OLE 20mg/mL. B- Negative Control (DMSO); C - Positive Control (40% Acid Lactic).

3. Results and Discussion

3.1. Phenolic Content

Literature evokes polyphenols as the main bioactives in the treatment of several health conditions, acting as anti-inflammatory, immunoprotective and antimicrobial agents [5]. Overall, MIR's OLE presented a phenolic prolife ranging from 37.90 mgGAE/g dry weight to 53.90 mgGAE/g dry weight (Figure 2).

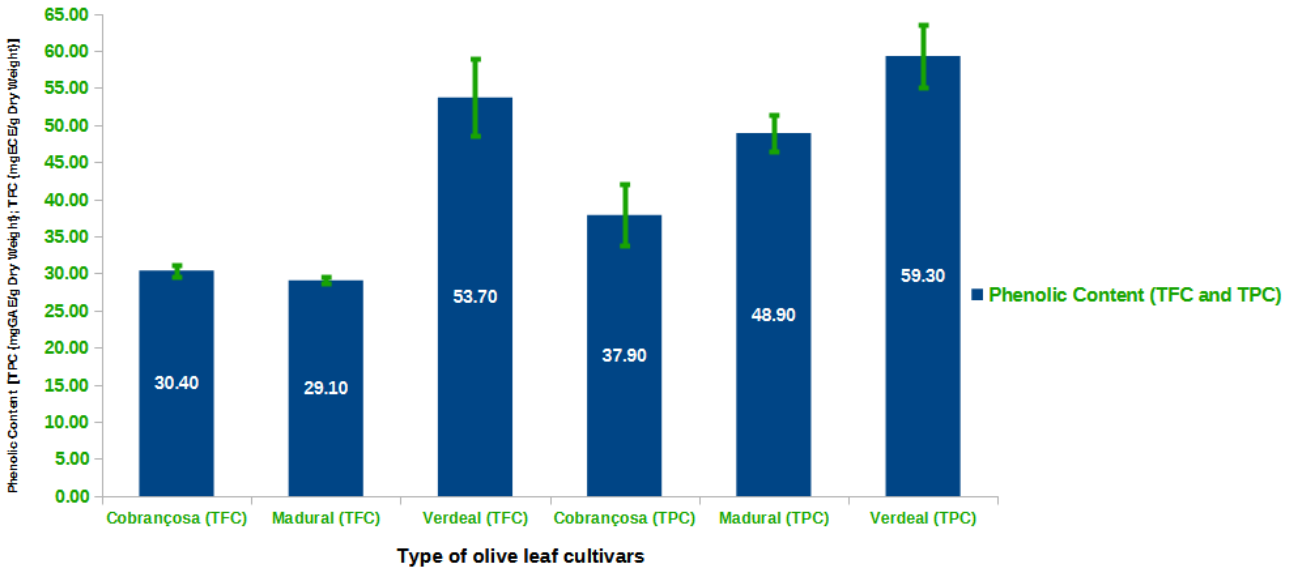

Figure 2: TPC and TFC of a fresh sample of olive leaf extracts from three Portuguese cultivars harvested in Mirandela grove.

Despite *O. europaea* L. var *europaea* Madural's extracts presenting the absolute top weight of hydroxytyrosol (HT) 10.86 mg/g of dried extract (Figure 3), each gram of *O. europaea* L. var *europaea* Verdeal's extract was relatively richer in HT (46.12%) than other compounds (Figure 4).

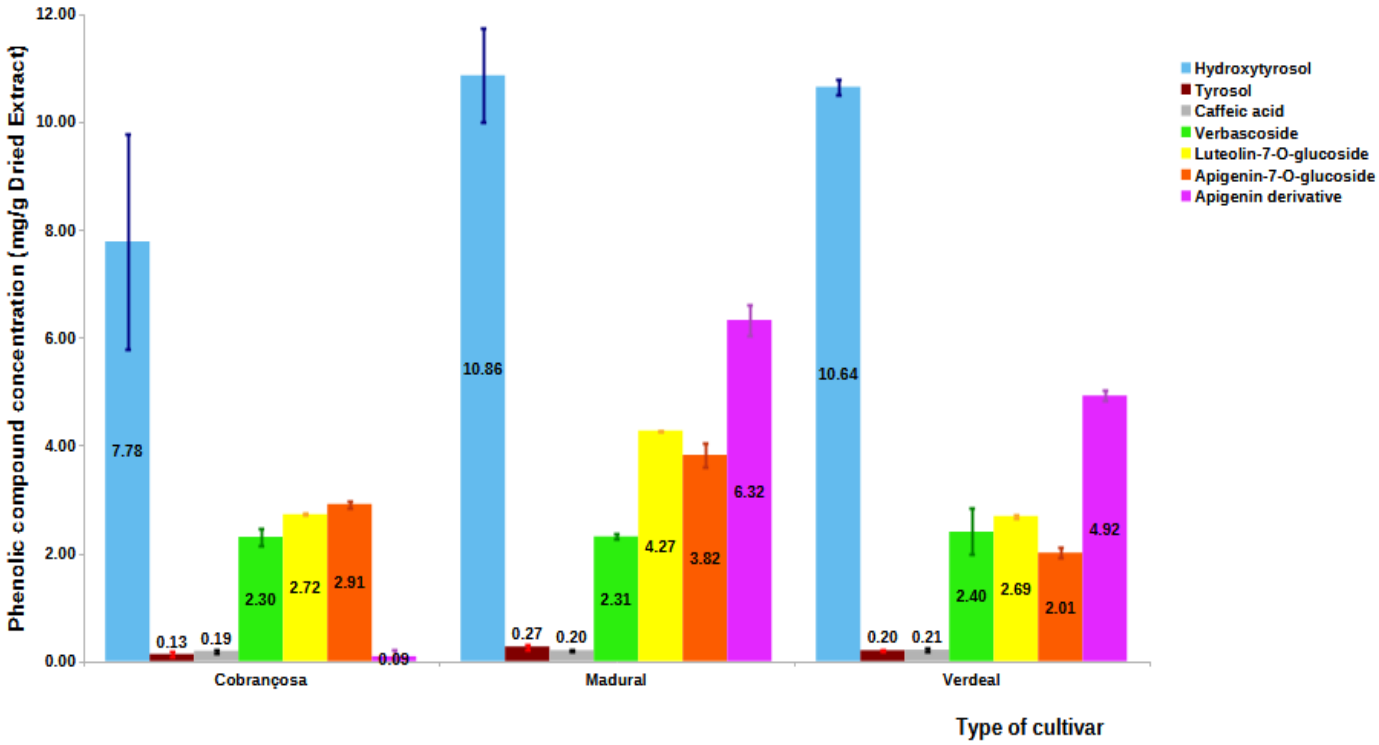

Figure 3: Absolute composition of identified phenol compounds in the hydroethanolic olive leaf extracts of three Portuguese cultivars expressed in mg/g of dried extract.

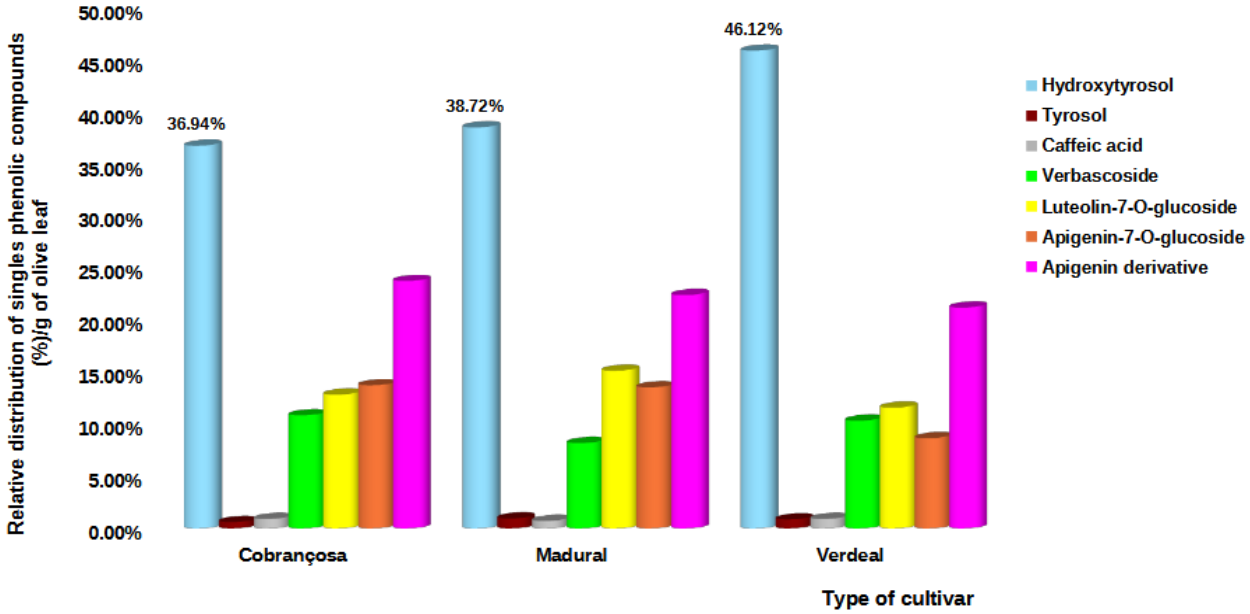

Figure 4: Relative content of identified phenolic compounds in the hydroethanolic olive leaf extracts of Portuguese cultivars expressed in percentage (%) phenolic compound/g of dried extract.

O. europaea L. var *europaea* Verdeal's leaf extract showed a relatively higher TPC level associated with a lower level of water content (data not shown), suggesting potential for obtaining high-quality polyphenols. On the other hand, *O. europaea* L. var *europaea* Verdeal's leaves also showed the lowest level of protein and the highest Arsenicum (As) content among the three selected cultivars (data not shown), which makes *O. europaea* L. var *europaea* Madural a safer substrate for polyphenols. Some studies evidenced an immunoprotection and antimicrobial action of phenolic compounds such as OLEP, TY, and HT [5,9], wherein their anti-Gram (+) and anti-Gram (-) most studied effect is membrane disruption [9]. The hydroxyl groups in phenolics steer electron delocalisation, playing as proton exchangers, inducing the cell's membrane disruption and so, bacterial death [9]. Among the several identified single phenolic compounds in the OLEs, HT was the predominant compound for all cultivars (Figures 2 and 3). HT is referred to in literature as the primary compound responsible for the bio-activity of oleuropein (OLEP), mainly because of its high antioxidant properties, but also an immuno-protective and antimicrobial action [5,7,9]. Other phenolic compounds have shown antibacterial activity *in vitro* against several bacterial strains responsible for intestinal and respiratory infections [5,9,10]. These compounds also showed promising potential as preservatives in the food industry [5,9], particularly due to their ability to inhibit the growth of *Helicobacter pylori*, a bacterium associated with peptic ulcers and gastric cancer [12]. OLE polyphenols have also revealed antiviral and antiprotozoal activities [13]. This wide antimicrobial range makes OLEs an easily available reservoir for designing pharmacological actives. In this sense, silver nanoparticles/attapulgite nanocomposites using an OLE confirmed the ability of olive leaf waste to be valorised into a biotechnological asset to target MDR bacteria, reaching inhibition at higher concentrations (100 μg/mL) [5,9]. The phenolic profile assessed in the present study showed that besides HT, flavonoids are also prominent, with an accumulated total very close for both *O. europaea* L. var *europaea* Cobrançosa and Madural, surpassing the relative percentage of HT in these OLEs (Figure 5).

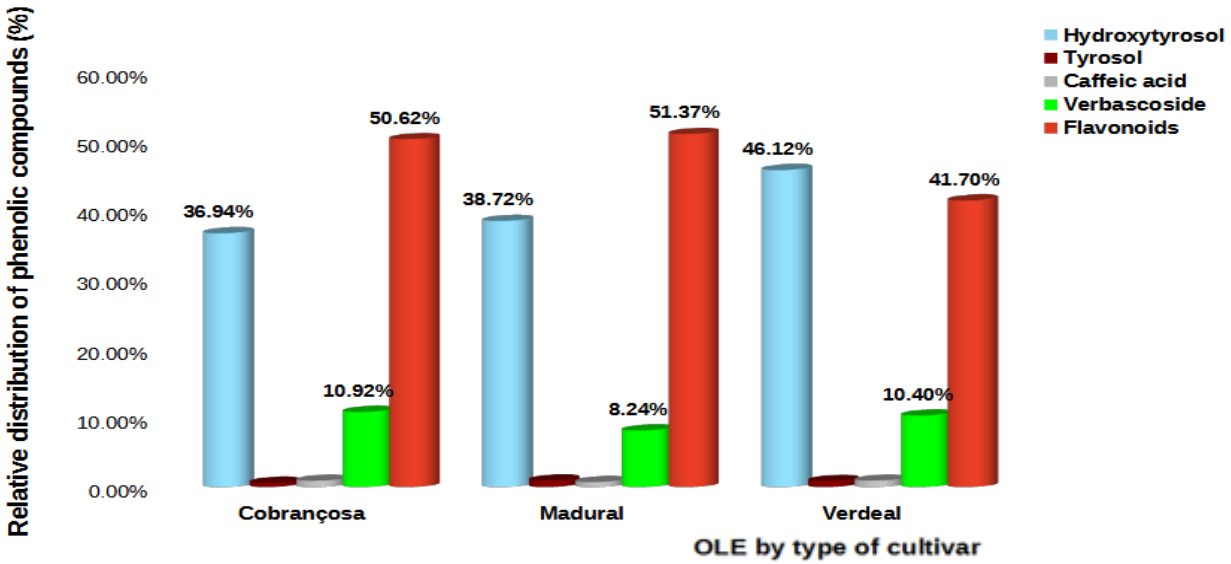

Figure 5: Phenolic relative composition (%) phenolic compound/g of OLE dried, hydroethanolic extract, with accumulated flavonoid percentual in hydroethanolic OLE of three Portuguese cultivars.

O. europaea L. var *europaea* Verdeal's extract revealed a slightly different profile compared to the other extracts, following the waning order of HT > apigenin derivative > luteolin-7-*O*-glucoside > verbascoside > apigenin-7-*O*-glucoside (Figures 3 and 4). Interestingly, it was reported that luteolin-7-*O*-glucoside and verbascoside exhibit antimicrobial activity against *S. aureus* [9], speculating a possible differential positive activity of the *O. europaea* L. var *europaea* Verdeal extract against this microbial. Also, the flavone apigenin-7-*O*-glucoside was found to be higher in both *O. europaea* L. var *europaea* Cobrançosa and Madural extracts (Figure 6).

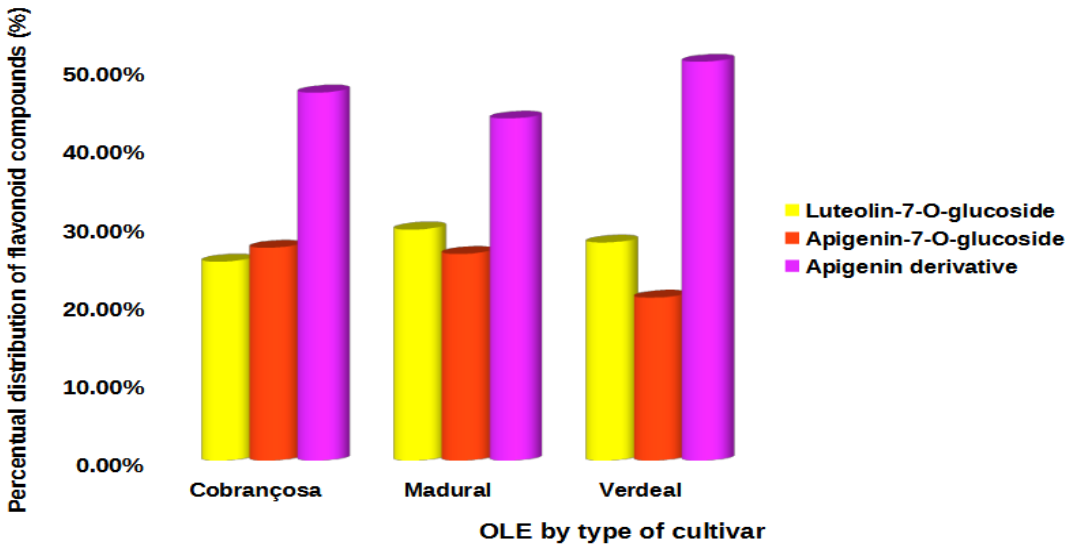

Figure 6: Relative flavonoid composition (%) of phenolic compound/g of dried hydroethanolic OLE extract of three Portuguese cultivars.

A previous work [10] reported a different phenolic profile for MIR *O. europaea* L. var *europaea* Cobrançosa leaf; however, these authors used an aqueous extract and leaves were harvested in November (Figure 7).

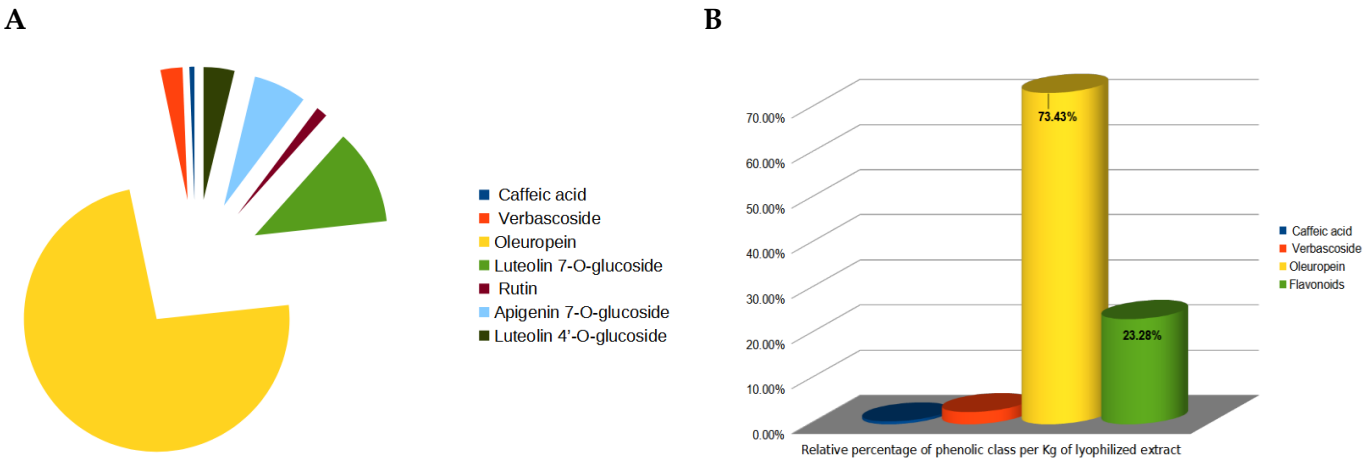

Figure 7: A. Phenolic profile of MIR *O. europaea* L. var *europaea* Cobrançosa aqueous leaf extract with harvest in November based on data of Pereira *et al.* [10] (relative% % of phenolic compound per Kg of olive leaf lyophilised extract). **B.** Discrimination of the phenolic class represented by percentage per Kg of lyophilised extract, based on data of Pereira *et al.*, 2007 [10].

This aqueous extract showed a predominance of Oleuropein> Luteolin-7-*O*-glucoside> apigenin-7-*O*-glucoside. The percentages of these flavones didn't vary much between the aqueous and our hydroethanolic extract, indicating a stronger influence of the harvesting season than the extraction solvent in the phenolic profile. Still, the aqueous extracts showed inhibitory action against most tested microorganisms at low concentrations, such as 5mg/mL [10].

3.2. Antimicrobial Activity

Diluted extracts (20mg/mL) achieved an overall wider inhibition spectrum. *O. europaea* L. var *europaea* Verdeal was the only one to show activity against *S. aureus* (ATCC 25923) (Figures 8 and 9).

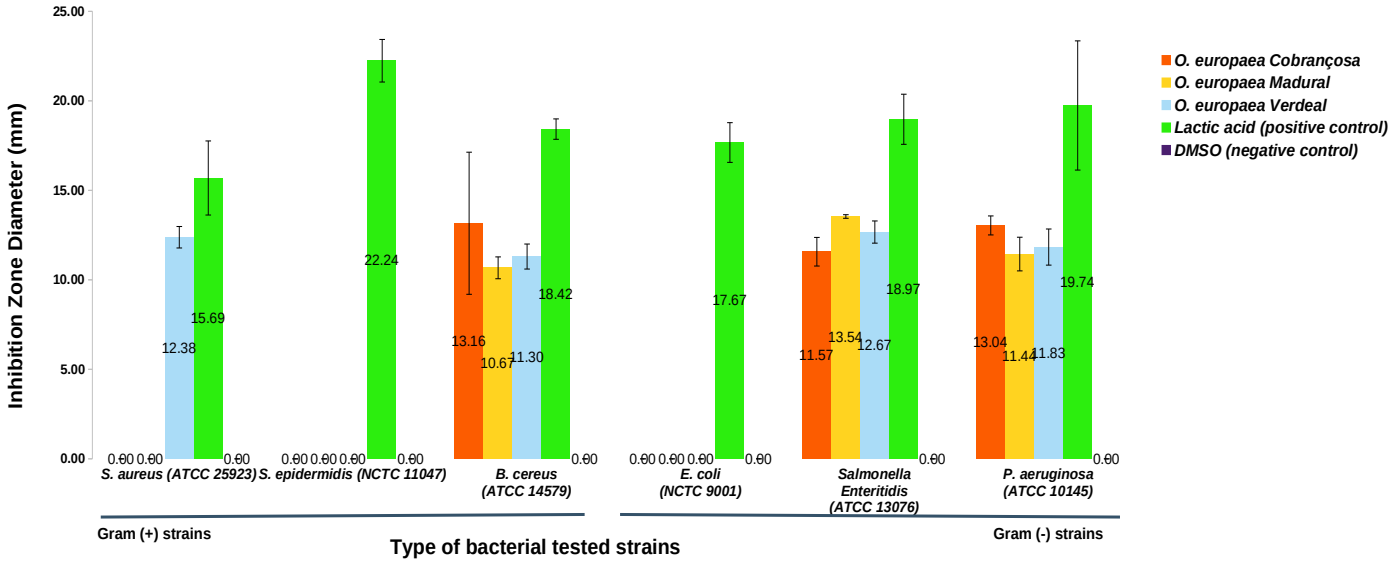

Figure 8: Antimicrobial activity of olive leaf extracts from three Portuguese cultivars against selected Gram (+) and Gram (-) bacteria, measured by diameter of growth inhibition (mm).

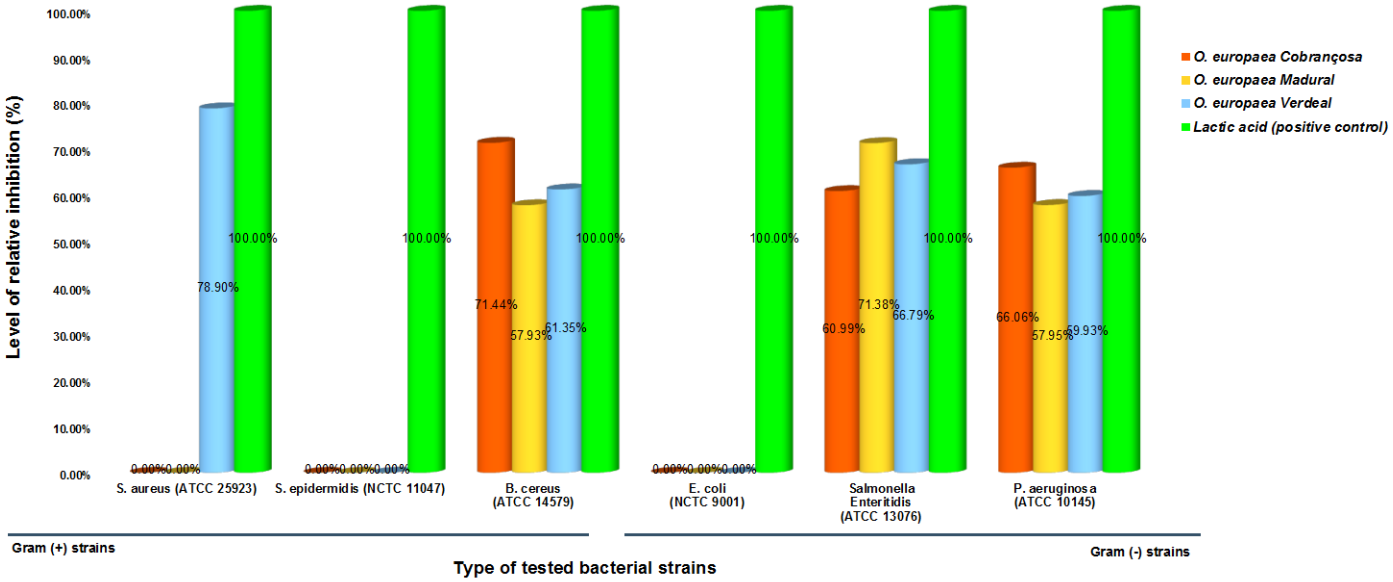

Figure 9: Relative microbial inhibition by olive leaf hydroethanolic extracts compared to the positive control expressed in percentage (%).

All extracts exhibited antimicrobial activity against Gram (+) *B. cereus* (ATCC 14579), Gram (-) Salmonella Enteritidis (ATCC 13076) and *P. aeruginosa* (ATCC 10145) (Figures 8 and 9). No trace of activity was found against Gram (+) *S. epidermidis* (NCTC 11047) and Gram (-) *E. coli* (NCTC 9001)(Figures 8 and 9). Despite an overall broader activity against Gram (-) strains, both *O. europaea* L. var *europaea* Verdeal and Cobrançosa extracts attained higher growth inhibition against two distinct Gram (+) strains. Regarding the antimicrobial effect, using as reference the positive control, we can point out:

- *O. europaea* L. var *europaea* Verdeal showed an antimicrobial efficacy against: *S. aureus* (ATCC 25923) > Salmonella Enteriditidis (ATCC 13076)> *B. cereus* (ATCC 14579)> *P. aeruginosa* (ATCC 10145), with relative inhibition values of 78.90%, 66.79%, 61.25% and 59.93%, respectively (Figures 9 and 10).
- *O. europaea* L. var *europaea* Cobrançosa acted against: *B. cereus* (ATCC 14579)> P. aeruginosa (ATCC 10145) > Salmonella Enteriditidis (ATCC 13076), with relative inhibition values of 71.44%, 66.06% and 60.99%, respectively (Figures 9 and 10).
- *O. europaea* L. var *europaea* Madural showed antimicrobial activity against: Salmonella Enteriditidis (ATCC 13076) > *P. aeruginosa* (ATCC 10145) > *B. cereus* (ATCC 14579), with relative inhibition values of 71.38%, 57.95% and 57.93%, respectively (Figures 9 and 10).

The differential behaviour found for each OLE might be intrinsically related to their specific phenolic composition, as was referred to in the literature. For that, it was developed a synthetic visual representation was developed comparing the antimicrobial behaviour of the three studied hydroethanolic OLE (Figure 10) and their respective phenolic architectural profile (Figure 11).

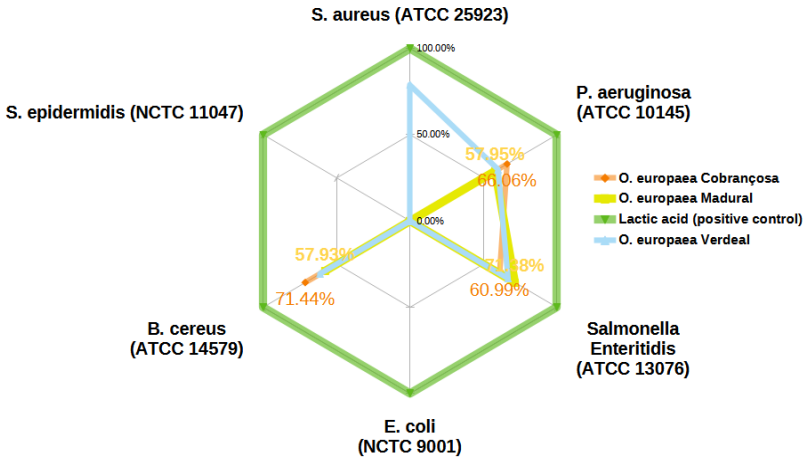

Figure 10: Spatial distribution of the overall antimicrobial activity by the hydroethanolic OLE of three Portuguese cultivars.

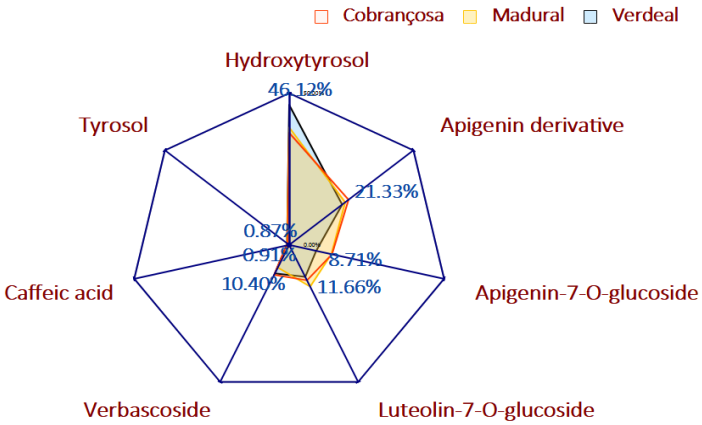

Figure 11: Spatial distribution of the overall phenolic constitution by the hydroethanolic OLE of three Portuguese cultivars.

In general, a closer profile was found between the antimicrobial action of the OLE from Cobrançosa and Madural cultivars and also for their respective phenolic composition (Figures 10 and 11). *O. europaea* L. var *europaea* Verdeal extracts were the sole to act against *S. aureus* (ATCC 25923) with an inhibition of *circa* 78.90% relative to the positive control (Figures 8, 9 and 10). The OLE from this cultivar showed the higher relative content of HT, followed by *O. europaea* L. var *europaea* Madural, whose prominent action was displayed against Salmonella Enteritidis (Figures 8, 9 and 10), but the HT content alone seems to be insufficient to explain the antimicrobial behaviour of *O. europaea* L. var *europaea* Verdeal against *S. aureus* (ATCC 25923) as well as that of *O. europaea* L. var *europaea* Madural against Salmonella Enteritidis (ATCC 13076). Furthermore, as it is shown in Figure 2, these two OLEs were identified with the highest values of TPC, and so an assorted

type of additive or synergetic effects may deliver these differential results. Literature mentions the action of flavonoids, including luteolin-7-*O*-glucoside and verbascoside against *S. aureus* [9], as well as hydroxytyrosol [14], in synergy with ampicillin [15]. Besides luteolin-7-*O*-glucoside, other OLE phenolic secondary metabolites showed additive effects against *S. aureus* and *E. coli* [15]. These results were not observed here, probably because the OLE concentration (20mg/mL) might not be enough to achieve the desired effect. Other authors referred inhibition of *E. coli* at higher concentrations, such as 62.5 mg/mL [16].

O. europaea L. var *europaea* Madural's extract achieved higher efficacy against Gram (-) Salmonella Enteritidis (ATCC 13076), with a relative inhibition of 71.38% (Figures 9 and 10), followed by very close results against Gram (-) *P. aeruginosa* (ATCC 10145) and Gram (+) *B. cereus* (ATCC 14579) with relative inhibitions of 57.95% and 57.93%, respectively (Figures 9 and 10). On the other hand, *O. europaea* L. var *europaea* Cobrançosa's cultivar inhibited mostly Gram (+) *B. cereus* (ATCC 14579), showing about 71.44% relative inhibition, followed by Gram (-) *P. aeruginosa* and *Salmonella Enteritidis* with relative microbial growth inhibition of 66.06% and 60.99%, respectively (Figures 9 and 10). Despite their closer phenolic profile (Figure 11), flavones apigenin-7-*O*-glucoside, apigenin derivatives and verbascoside were found in higher concentration in *O. europaea* L. var *europaea* Cobrançosa extract (Figures 3, 4 and 11), whereas HT and luteolin-7-*O*-glucoside were found at slightly higher values in *O. europaea* L. var *europaea* Madural (Figures 3, 4 and 11), which could explain their differential antimicrobial properties. On the other hand, the OLE from *O. europaea* L. var *europaea* Cobrançosa also displayed a differential antimicrobial activity compared to the aqueous leaf extract from this cultivar harvested in MIR in 2004 by Pereira *et al.* [10]. These authors found inhibition of all the tested bacteria and fungi, suggesting a broad antimicrobial activity of olive leaf extracts in a concentration-dependent manner [10], with an inhibition of growth against: *B. cereus* ~ *C. albicans* > *E. coli* > *S. aureus* > *C. neoformans* ~ *K. pneumoniae* ~ *P. aeruginosa* > *B. subtilis* [10]. In the study of Pereira *et al.*, it was also found IC_{25} values of 0.63mg/mL, 1.81 mg/mL, 2.68 mg/mL and 3.22 mg/mL for *B. cereus, E. coli, S. aureus* and *P. aeruginosa,* respectively. This behavioural difference between these two leaf extracts of the same cultivar might derive from a diversified biochemical architecture influenced by: harvest in another season, varied agricultural practice (including genetic variation by crossed pollination due to other cultivars' vicinity), but also by different extraction solvent polarity.

Knowing that polyphenols are responsible for antioxidant action, which is also linked to antimicrobial behaviour, we compared the antioxidant activity of the three cultivars' extracts analysed *in this study.* Alike their phenolic and antimicrobial action profiles, these extracts also displayed a distinguished antioxidant behaviour among three different tests - DPPH, FRAP and NO inhibition: *O. europaea* L. var *europaea* Cobrançosa displayed higher DPPH radical scavenging activity (around 1.3 x more than *O. europaea* L. var *europaea* Madural and 3.1 x more than *O. europaea* L. var *europaea* Verdeal, data not shown); *O. europaea* L. var *europaea* Madural, exhibited reduced antioxidant power (around 1.1 x more than *O. europaea* L. var *europaea* Verdeal and Cobrançosa, data not shown); *O. europaea* L. var *europaea* Verdeal displayed a slightly higher NO scavenging activity (1.5x more than *O. europaea* L. var *europaea* Cobrançosa and 1.9 more than *O. europaea* L. var *europaea* Madural, data not shown). This divergence in the antioxidant behaviour might indicate that the phenolic profile *per se* isn't enough to justify the OLE antimicrobial behaviour. Literature also refers to the antimicrobial action of FAs, though disruption of the electron transport chain, cell lysis, inhibition of nutrient uptake, and cell deactivation [9], disrupting quorum sensing, horizontal gene transfer, metabolic routes and nucleic acid reproduction [17], stating that FA unsaturation and carbon-length chain affect FA's antimicrobial activity [17]. In this sense, our extracts from *O. europaea* L. var *europaea* Cobrançosa and Verdeal showed higher ΣMUFAs (data not shown), which could mean some additive/synergetic action with phenolic content against *B cereus*, for example, and *O. europaea* L. var *europaea* Madu-

ral and Verdeal extracts had higher ΣPUFAs, which could mark a differential against Salmonella Enteritidis. Overall, our results bring forward a panoply of compounds that might be acting in an additive/synergetic mode to deliver a valuable differentiated antimicrobial behaviour by the studied OLEs. To better understand which specific compounds and molecular mechanisms could be associated with the displayed behaviour, further multivariate statistical procedures, such as Principal Component Analysis, should be performed upon the experimental results.

4. Conclusions

All tested extracts (Cobrançosa, Madural, and Verdeal) from Mirandela showed antimicrobial activity against Gram-positive *B.cereus* (ATCC 14579) and Gram-negative *P. aeruginosa* (ATCC 10145) and *Salmonella Enteritidis*. Only the Verdeal cultivar extract was effective against *S. aureus* (ATCC 25923), and none of the extracts were effective against *S. epidermidis* or *E. coli*. Each cultivar demonstrated a specific antimicrobial inhibition profile: Verdeal - highest efficacy against *S. aureus*; Cobrançosa - strongest inhibition of *B. cereus* (ATCC 14579); and Madural: best performance against *Salmonella Enteritidis* (ATCC 13076). These differences can be associated with variations in phenolic composition. However, the data suggest that synergistic effects between phenolic compounds better explain the antimicrobial activity differences. Unsaturated fatty acid composition and antioxidant activity may also play a role. From the results obtained, we can conclude that the Portuguese olive leaf extracts studied show significant potential for therapeutic use, including: human and veterinary phytotherapeutic formulations, natural preservatives for the food and cosmetics industries and development of green nanocomposites, such as silver nanoparticles (AgNPs), for targeted antimicrobial applications. *O. europaea* L. var *europaea* Verdeal's leaf extracts presented the most adequate matrix for producing green AgNPs against Gram (+) *S. aureus*. The leaf extracts of *Olea europaea* L. var. *europaea* Cobrançosa demonstrated greater potential for incorporation into green nanocomposites targeting Gram (+) *B. cereus* and Gram (-) *P. aeruginosa*. In contrast, the extracts from *Olea europaea* L. var. *europaea* Madural appeared more suitable for the development of NCs aimed at combating Gram (-) *Salmonella Enteritidis*. Further studies are needed to test higher extract concentrations, different extraction methods, and perform advanced statistical analysis (e.g., Principal Component Analysis) to better understand the underlying mechanisms. Additional research should also explore the synergistic potential of combining extracts from different cultivars and assess effects against more resistant strains. This study highlights the therapeutic and economic potential of olive leaf extracts from Portuguese cultivars and represents a scientific and practical valorisation of a natural resource with promising cross-sectoral applications. Olive leaves could symbolize hope embodied in nature for their diversified array of successful applications whether in pharmaceutical, cosmetic or food industry mirroring a model of sustainable circular economy inspired in the natural cycles themselves where it is possible to apply the words of the chemist Antoine-Laurent de Lavoisier (1743 -1794): nothing is lost, nothing is created, everything is transformed.

Acknowledgements: This work was presented at the 2nd International Congress on Complementary Therapies in Health, held on 28 June 2025.

The authors show their gratitude to the farm owners from Vale de Salgueiros, Mirandela region, who made it possible to access samples of three Portuguese variants of olive leaf for analysis in the present study. Also, a word of gratitude to ICBAS, in particular to Professor Jorge Machado, for supporting the research and revival of homeland plant varieties as a push for local and sustainable economic development.

Funding: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Conflict of Interest: The authors declare that there are no conflicts of interest.

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: The original contributions presented in this study are included in the article. Further inquiries can be directed to the corresponding author.

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2025