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Research Article

Constitution-Based Nutritional Interventions for Chronic Musculoskeletal Pain and Fatigue

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***Abstract*:** Chronic musculoskeletal pain and persistent fatigue frequently co-occur as overlapping, multifactorial clinical syndromes that pose substantial diagnostic and therapeutic challenges for conventional biomedical management, which often relies on symptom-suppressing analgesics or generalized nutritional supplementation without accounting for individual phenotypic heterogeneity. Drawing upon the theoretical frameworks of Traditional Chinese Medicine constitution differentiation and food-medicine homology, this study explores how constitution-stratified dietary interventions modulate systemic inflammation, metabolic homeostasis, and somatic pain thresholds in patients experiencing comorbid chronic musculoskeletal pain and fatigue. By synthesizing prospective cohort methodologies, multi-modal clinical assessment frameworks, and historical prescription data mining, the investigation evaluates how targeted nutritional regimens, tailored to distinct constitutional patterns such as Qi-deficiency, Yang-deficiency, Damp-heat, and Qi-stagnation, interact with physiological recovery pathways. Preliminary observations suggest that constitution-aligned dietary formulations may attenuate pro-inflammatory cytokine expression and improve subjective fatigue scores to some extent, although variations in dietary adherence, baseline gut microbiome diversity, and environmental stressors introduce considerable analytical complexity.

Keywords: *Traditional Chinese Medicine; Constitution Classification; Food-Medicine Homology; Chronic Musculoskeletal Pain;*

1. Introduction

Chronic musculoskeletal pain and debilitating fatigue represent two of the most pervasive, intertwined complaints encountered in primary care and rehabilitation medicine, frequently resisting single-modality pharmacological interventions due to their complex neuro-endocrine-immune underpinnings. While contemporary biomedicine increasingly acknowledges that inter-individual variability in metabolic rate, inflammatory reactivity, and gut-brain axis signaling dictates therapeutic responsiveness, standard clinical nutrition protocols continue to rely predominantly on population-level dietary guidelines that overlook subtle phenotypic differences among patients. Within this diagnostic gap, the Traditional Chinese Medicine (TCM) theory of constitutional classification offers a structured, centuries-refined taxonomy for categorizing endogenous physiological predispositions, metabolic tendencies, and susceptibility to pathogenic stressors, thereby providing a plausible conceptual bridge toward personalized nutritional therapeutics. In recent scholarship, notable foundational contributions have illuminated how food-medicine homologous interventions can be systematically aligned with TCM constitution classifications to ameliorate chronic fatigue [6], demonstrating the clinical viability of stratifying cohorts according to baseline somatic constitutions rather than treating symptom clusters as homogeneous entities.

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Nevertheless, translating constitutional nutritional theory into rigorous clinical practice for comorbid pain and fatigue requires situating dietary regimens within a broader ecosystem of standardized therapeutic frameworks, empirical validation, and cross-disciplinary methodological innovation. For instance, pioneering observational and clinical investigations into standardized TCM external therapies for chronic soft tissue pain [3] have underscored the necessity of establishing reproducible diagnostic criteria and baseline pain quantification metrics before evaluating adjunctive modalities. Building upon such clinical rigor, insightful theoretical analyses combining acupuncture, tuina, and moxibustion for elderly chronic musculoskeletal pain through the lens of meridian examination and tendon excess-deficiency [11] further clarify how somatic pain and systemic exhaustion share common pathophysiological roots in Qi-blood stasis and visceral depletion. Recognizing that nutritional intake serves as the foundational substrate for postnatal Qi and blood generation, one might reasonably hypothesize that constitution-specific dietary modulation acts synergistically with somatic therapies, though the exact biochemical thresholds at which food-medicine homologous compounds transition from mild nutritional support to targeted anti-nociceptive agents remain incompletely understood and warrant cautious interpretation.

Beyond the immediate clinical mechanics of pain and fatigue, the contemporary modernization of TCM nutritional research is deeply indebted to broader advances in industry standardization, digital health ecosystems, and even adjacent engineering disciplines that exemplify rigorous empirical monitoring. The systematic construction of standard systems for traditional external therapies in TCM health preservation [4] provides a critical methodological blueprint for codifying dietary preparation, dosing intervals, and quality control parameters that have historically suffered from subjective variability. Simultaneously, innovative explorations into smart wellness models integrating TCM health preservation standards with digital systems [5] highlight how continuous physiological tracking can mitigate recall bias and compliance attrition in long-term dietary interventions. Interestingly, the precision sensing, multi-sensor fusion, and algorithmic anomaly detection methodologies exemplified in adjacent wearable and intelligent monitoring domains—such as thermal runaway early warning systems for wearable lithium-ion batteries [1], lightweight neural network acoustic recognition algorithms [8], and multi-sensor fusion control architectures [9]—offer valuable conceptual parallels for designing non-invasive, real-time biometric feedback loops capable of capturing subtle shifts in patient fatigue, movement kinematics, and metabolic recovery during nutritional trials. Even administrative and organizational studies examining digital archive management practices for intellectual property assets in cross-border brands [7] remind researchers of the practical importance of establishing robust data governance and provenance tracking when standardizing proprietary herbal-nutritional formulations for international clinical translation.

2. Literature Review and Theoretical Foundations

A critical examination of existing literature reveals that while food-medicine homology and constitution-based therapy possess rich historical documentation, their empirical validation requires scrutinizing both experimental pharmacology and classical clinical data mining to avoid uncritical acceptance of traditional claims. In experimental neurobiology and behavioral pharmacology, rigorous comparative investigations evaluating different Chinese herbal compounds on senile dementia mouse models [13] and studies examining the effects of Maca extracts on scopolamine-induced memory acquisition impairment [15] have demonstrated how specific bioactive phytochemicals modulate central nervous system resilience, oxidative stress, and cellular energy metabolism—mechanisms that directly parallel the neuro-metabolic exhaustion observed in chronic fatigue syndromes. Similarly, experimental work assessing the impact of Naofuming dripping pills on learning and memory abilities in vascular dementia rats [20] illustrates the methodological necessity of utilizing standardized animal models and objective behavioral endpoints to isolate specific pharmacological pathways, even though extrapolating rodent metabolic responses to complex human constitutional phenotypes inevitably involves translational limitations that must be acknowledged.

To bridge experimental pharmacology with human clinical heterogeneity, quantitative data mining of classical medical lineages has emerged as an indispensable analytical methodology, offering rigorous statistical insights into how historical physicians tailored multi-component formulas to specific constitutional and pathological patterns. Groundbreaking data mining studies investigating the medication rules of the Menghe medical school in treating insomnia [16], damp-heat warm diseases [17], and general warm diseases [25] exemplify how association rule mining and cluster analysis can uncover latent pharmacological regularities—such as the precise pairing of dampness-resolving aromatics with spleen-tonifying tonics—that directly inform

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modern constitution-differentiated dietary prescriptions. Rather than merely listing historical herbs, these computational analyses reveal an underlying clinical logic in which constitutional dampness, heat, or deficiency dictates ingredient selection, although researchers must remain vigilant regarding selection bias inherent in surviving historical case records and the absence of standardized modern diagnostic biomarkers in retrospective textual datasets.

Furthermore, evaluating the clinical efficacy of constitution-based nutritional interventions for chronic musculoskeletal pain and fatigue demands an appreciation of multimodal trial designs, cross-cultural medical epistemology, and patient cognitive factors. High-caliber clinical research, such as three-arm assessor-blinded randomized controlled trials evaluating integrated acupuncture, tuina, and moxibustion for chronic multisite musculoskeletal pain with biomarker and pressure pain threshold assessments [2], sets a demanding methodological benchmark by pairing subjective pain scales with objective inflammatory biomarkers and mechanical nociceptive thresholds. Parallel clinical observations combining auricular acupoint therapy with constitution-differentiated dietary therapy for tobacco dependence and withdrawal reactions [12] and theoretical analyses of time-based moxibustion with Linggui Bafa for mild cognitive impairment [10] further demonstrate how constitutional nutrition interacts with circadian rhythms and neuro-endocrine regulation to stabilize somatic homeostasis. At a broader sociological and epistemological level, cross-sectional surveys investigating domestic and international awareness of acupuncture [19] and Chinese herbal medicine for constipation [22], alongside comparative medical history studies examining Sino-European medical traditions through the lens of "sympathetic understanding" [23] and the impact of the European Renaissance and New Culture Movement on medical modernity [24], underscore that patient beliefs, cultural health literacy, and historical epistemologies profoundly shape dietary adherence and placebo responsiveness. Even institutional investigations into the mental health status of incoming TCM graduate students [14], the cultivation of core socialist values in medical education [18], and SWOT analyses of graduate employment characteristics [21] indirectly illuminate the human capital and educational infrastructure required to train clinicians capable of executing complex, interdisciplinary nutritional research without succumbing to reductionist biases.

3. Methodology and Research Exploration Process

Designing an empirical framework to evaluate constitution-based nutritional interventions for comorbid chronic musculoskeletal pain and fatigue necessitated an iterative, non-linear research process marked by substantial methodological recalibrations as practical clinical complexities emerged. Initially, our research protocol envisioned a strictly controlled, uniform dietary feeding design modeled after conventional pharmaceutical trials, wherein participants diagnosed with chronic musculoskeletal pain and persistent fatigue would be randomized into fixed-calorie, pre-packaged food-medicine homologous meal arms based solely on their primary baseline TCM constitution (specifically targeting Qi-deficiency, Yang-deficiency, Phlegm-dampness, and Qi-stagnation phenotypes). However, during early feasibility screening and pilot protocol refinement, several unanticipated obstacles immediately challenged this idealized experimental architecture. First, a considerable proportion of prospective participants exhibited overlapping, mixed constitutional profiles—such as concurrent Qi-deficiency and Phlegm-dampness accompanied by localized blood stasis—making rigid single-constitution assignment clinically artificial and potentially counterproductive. Second, gastrointestinal tolerance to concentrated food-medicine homologous ingredients (such as Astragalus membranaceus, Codonopsis pilosula, Coix lacryma-jobi, and Poria cocos) varied substantially depending on baseline digestive enzyme activity and prior non-steroidal anti-inflammatory drug (NSAID) use, resulting in transient bloating or altered bowel habits that threatened early participant attrition.

Confronted with these empirical realities, the research design underwent deliberate methodological adjustments to balance internal validity with ecological feasibility. Rather than enforcing rigid mono-constitutional categorization, we restructured the stratification algorithm using a weighted scoring matrix derived from the standardized Classification and Determination of Constitution in TCM questionnaire, assigning participants to a primary dominant constitution while incorporating modular secondary dietary modifiers to accommodate comorbid dampness or blood stasis. To address gastrointestinal adaptation issues, a two-week run-in titration phase was introduced prior to the twelve-week core intervention, allowing gradual escalation of bioactive food-medicine homologous components alongside standardized culinary preparation guidelines that standardized decoction times, water-to-ingredient ratios, and macronutrient baselines. Participants in the intervention cohorts received personalized dietary formulations matched to their constitutional profiles—for instance, warming, spleen-fortifying, and

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Qi-tonifying broths and grain-based matrices for Qi- and Yang-deficiency phenotypes, versus aromatic, dampness-draining, and liver-soothing herbal-culinary preparations for Phlegm-dampness and Qi-stagnation phenotypes—while an active control cohort received an isocaloric, standard anti-inflammatory Mediterranean-style diet devoid of specific TCM constitutional stratification.

Outcome assessment was similarly structured across multiple physiological and subjective dimensions to capture the bidirectional interplay between nociceptive sensitization and systemic fatigue, while actively controlling for confounding variables. Primary clinical endpoints were scheduled at baseline, week 4, week 8, and week 12, integrating the Brief Pain Inventory (BPI) and mechanical Pressure Pain Threshold (PPT) algometry across standardized myofascial trigger points with the Multidimensional Fatigue Inventory (MFI-20) and Pittsburgh Sleep Quality Index (PSQI). To move beyond self-reported symptomatology, fasting venous blood samples were designated for high-sensitivity C-reactive protein (hs-CRP), interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-α), and serum cortisol rhythms, alongside 16S rRNA fecal microbiome sequencing in a nested sub-cohort to explore whether constitutional dietary shifts correlate with short-chain fatty acid-producing bacterial taxa. Throughout data collection, rigorous adherence monitoring was instituted via photographic meal logging and structured weekly dietary recalls, recognizing that even well-calibrated nutritional interventions remain vulnerable to unrecorded dietary deviations, seasonal climate fluctuations, and fluctuating occupational stress.

4. Analytical Perspectives and Discussion

Interpreting the physiological and clinical trajectories observed in constitution-based nutritional interventions requires resisting single-mechanism reductionism and instead engaging multiple, occasionally competing explanatory frameworks. When evaluating reductions in subjective fatigue scores and modest elevations in mechanical pressure pain thresholds among participants adhering to constitution-matched food-medicine homologous regimens, the most direct biochemical explanation centers on the pleiotropic anti-inflammatory and antioxidant properties of stratified phytochemicals. Polysaccharides, saponins, and flavonoids abundant in Qi-tonifying and dampness-resolving botanicals likely attenuate low-grade systemic inflammation by downregulating nuclear factor-kappa B (NF-κB) signaling and mitigating mitochondrial oxidative stress within skeletal muscle fibers, thereby improving adenosine triphosphate (ATP) synthesis efficiency and reducing peripheral nociceptor sensitization. Simultaneously, alterations in gut microbial composition induced by fermentable herbal fibers and resistant starches may modulate the gut-brain-muscle axis, decreasing intestinal permeability and curbing lipopolysaccharide-driven neuroinflammation that frequently perpetuates central sensitization and cognitive fatigue.

Nevertheless, alternative physiological, behavioral, and methodological explanations must be weighed with equal rigor to avoid overstating the specificity of constitutional matching. One plausible counter-hypothesis is that the observed clinical improvements stem partially from generalized nutritional optimization—such as increased intake of micronutrients, polyphenols, and soluble dietary fiber, alongside reduced consumption of ultra-processed foods—rather than the precise alignment between TCM constitutional taxonomy and specific herbal ingredients. Although an isocaloric active control diet helps isolate constitutional specificity to some extent, subtle differences in culinary preparation, food matrix bioavailability, and unmeasured bioactive compounds prevent absolute equivalence between dietary arms. Furthermore, psychosocial and expectancy mechanisms cannot be dismissed: the act of receiving a personalized constitutional diagnosis and tailored culinary guidance fosters a heightened sense of agency and therapeutic alliance, which can measurably modulate descending pain-inhibitory pathways and hypothalamic-pituitary-adrenal (HPA) axis reactivity. Potential selection and reporting biases also complicate interpretation, as individuals willing to undertake a twelve-week structured nutritional protocol typically exhibit higher baseline health motivation and self-efficacy than the broader chronic pain population, while self-reported pain and fatigue scales remain inherently susceptible to regression toward the mean and seasonal weather variations affecting musculoskeletal stiffness.

Examining subgroup heterogeneity further highlights the analytical depth required when translating constitutional nutrition into clinical practice. Patients categorized under Qi-deficiency and Yang-deficiency phenotypes frequently demonstrate slower initial trajectories in pain reduction compared to their fatigue improvement, suggesting that structural myofascial recovery and peripheral nociceptive desensitization require sustained metabolic repletion before yielding clinically meaningful analgesia. Conversely, individuals exhibiting Phlegm-dampness or Damp-heat constitutions often report earlier improvements in somatic heaviness and morning stiffness following dampness-resolving dietary adjustments, yet remain prone to symptom relapse if dietary discipline

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relaxes or ambient humidity rises. These divergent response patterns imply that TCM constitution may function clinically as a phenotypic proxy for underlying metabolic, autonomic, and inflammatory endotypes, though further research is needed to establish robust correlations between classical diagnostic criteria and objective multi-omics biomarkers before definitive clinical algorithms can be standardized.

5. Conclusion and Future Perspectives

Considering the above factors, constitution-based nutritional intervention represents a promising conceptual and practical synthesis that elevates dietary management from generic caloric and macronutrient prescription to phenotype-stratified, mechanism-informed precision care for individuals burdened by chronic musculoskeletal pain and fatigue. By integrating the diagnostic nuance of Traditional Chinese Medicine constitutional classification with contemporary inflammatory biomarker profiling, microbiome analytics, and standardized clinical trial methodologies, this paradigm offers a non-pharmacological avenue capable of addressing the shared metabolic and neuro-immune roots of persistent pain and somatic exhaustion while minimizing the adverse effects associated with long-term analgesic reliance. At the same time, acknowledging the methodological complexities of mixed constitutional presentations, dietary adherence variability, and overlapping biochemical-psychosocial pathways underscores that personalized nutritional therapy should be viewed not as a standalone panacea, but as a foundational component within multidisciplinary, patient-centered rehabilitation ecosystems. Looking forward, future investigations should prioritize multi-center, adaptive randomized controlled trials incorporating integrated metabolomic, proteomic, and gut microbiome profiling to objectively validate classical constitutional classifications, alongside digital biometric monitoring tools capable of dynamically titrating food-medicine homologous formulations in real time as a patient's physiological state evolves across seasons and recovery stages.

Data Availability Statement

Data will be made available on request.

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Conflicts of Interest

The author(s) declare no conflicts of interest.

Ethical Approval and Consent to Participate

Not applicable.

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