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Research Progress on Traditional Chinese Medicine Treatment for Cancer-Related Fatigue

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Abstract: ***Cancer-related fatigue is one of the most common and profoundly impactful symptoms among cancer patients, significantly impairing their quality of life and prognosis. Conventional Western pharmaceutical treatments yield generally limited efficacy, whereas Traditional Chinese Medicine, leveraging its holistic perspective and unique strengths in syndrome differentiation and treatment, demonstrates considerable potential in managing Cancer-related fatigue. Therefore, this review systematically examines the pathogenesis and syndrome differentiation of Cancer-related fatigue, focusing on Traditional Chinese Medicine treatment strategies. Various Traditional Chinese Medicine therapies—including single herbs and their active components, herbal formulas, acupuncture, massage, acupressure, and progressive muscle relaxation training—are widely applied. The current research landscape and its limitations are analyzed to provide novel insights for clinical prevention and treatment.***

Keywords: Cancer-related Fatigue, Traditional Chinese Medicine Treatment, Research Progress.

1. Introduction

Cancer-related fatigue (CRF) is one of the most common and distressing symptoms experienced by cancer patients [1]. The National Comprehensive Cancer Network (NCCN) defines CRF as a persistent, subjective feeling of tiredness associated with cancer or its treatment. This fatigue is often accompanied by decreased physical, emotional, and cognitive function. Importantly, it cannot be alleviated by rest and significantly impacts patients' quality of life [2, 3]. With advances in cancer treatment and prolonged survival, improving quality of life has become a key goal in cancer care. This shift has led to an increased focus on the prevention and management of CRF. Epidemiological studies indicate that CRF affects over 60% of cancer patients [4, 5], with particularly high prevalence among those with breast cancer, lung cancer, and colorectal cancer [6-8]. Its occurrence is closely linked to tumor stage and treatment intensity, often persisting long after the completion.

Currently, Western medicine faces significant limitations in treating CRF: there is a lack of specific drugs, existing psychostimulant medications have limited efficacy, and they are accompanied by side effects such as insomnia and palpitations. Additionally, non-pharmacological interventions like exercise therapy, while showing some effectiveness, are constrained by patients' physical conditions [9]. Therefore, there is an urgent clinical need for safe and effective complementary and alternative therapies. Traditional Chinese Medicine (TCM), which emphasizes holistic concepts, syndrome differentiation and treatment, and integrated mind-body regulation, possesses profound accumulated experience and unique potential in addressing CRF [4]. In recent years, preliminary evidence has emerged demonstrating the efficacy of TCM methods—including herbal medicine, acupuncture, and traditional exercise—in alleviating fatigue and improving quality of life, reflecting their multi-targeted, holistic regulatory characteristics [10]. For instance, ginseng can alleviate CRF and enhance patients' quality of life [11], while acupuncture improves fatigue symptoms in lung cancer patients [12]. This paper aims to systematically review the progress of TCM treatment for CRF, providing a reference for clinical practice.

2. Theoretical Framework of Cancer-Related Fatigue in Traditional Chinese Medicine

2.1 Etiology and Pathogenesis

Within the framework of TCM, there is no direct equivalent to the modern diagnosis of "Cancer-Related Fatigue." Based on its core symptoms—fatigue, limb heaviness, mental lethargy, hypersomnia or insomnia, and poor appetite—it is classified under the category of "consumptive disease." The fundamental pathogenesis involves "underlying deficiency with superficial excess, a mixture of deficiency and excess." This condition often arises from the interplay of multiple factors—including constitutional predisposition, tumor invasion, treatment-related damage, emotional distress, and dietary imbalances—leading to a deficiency of vital energy, organ dysfunction, and the internal generation of pathogenic toxins, thereby creating a vicious cycle.

At the etiological level, it can be categorized into three types: The primary internal etiologies include congenital deficiency and progressive depletion resulting from the development of a tumor. In TCM, the kidneys are considered the foundation of innate constitution, responsible for storing essence and producing marrow. Therefore, congenital deficiency weakens the root of healthy qi. Tumors belong to the category of "abdominal masses and accumulations" (zheng jia ji ju), the formation and progression of which continuously consume qi,

blood, body fluids, and essence, leading to malnutrition of the zang-fu organs and meridians. This pathological process is consistent with the classical doctrine stated in the Su Wen (Plain Questions): "When essence and qi are depleted, deficiency ensues." The external etiology involves the invasion of the six pathogenic factors. Tumor patients typically present with an inherently deficient constitution. As noted in The Spiritual Pivot (Ling Shu), in the chapter "The Root of a Hundred Diseases," "When deficiency exists both in the body and in the pathogenic factor, the evil is able to enter and lodge." Wind, cold, heat, dampness, dryness, and fire readily take advantage of this deficiency to invade the body, thereby further exacerbating the underlying deficiency. Other contributing factors include iatrogenic damage, emotional disturbances, and irregular dietary or lifestyle habits. These factors can directly impair the internal organs, particularly by depleting the qi and blood of the spleen and stomach. This depletion ultimately compromises the physiological sources of qi and blood production.

Core Pathogenesis: "Deficiency in Root, Excess in Manifestation." The "deficiency in root" refers to an insufficiency of vital energy, encompassing patterns such as qi deficiency, blood deficiency, yin deficiency, and yang deficiency. Clinically, qi deficiency is the most common, followed by blood deficiency. The "excess in manifestation" refers to pathogenic factors—such as toxins, blood stasis, and phlegm-dampness—that arise from prolonged dysfunction of the organs. These pathogenic factors obstruct the circulation of qi and blood, and constitute the tangible, often excess-type manifestations of the disease.

2.2 Differentiation of Syndrome Patterns

TCM management of CRF is guided by the principles of "pattern differentiation and treatment" and a "holistic approach." The therapeutic strategy follows the method of "tonifying deficiency and draining excess," focusing on the regulation of qi, blood, yin, and yang, with an emphasis on deficiency patterns of the five zang organs, while also addressing mixed deficiency-excess presentations. Although clinical pattern classifications are not yet fully standardized, deficiency patterns are most commonly observed. Based on TCM pattern differentiation, CRF is primarily categorized into the following six patterns: Spleen Qi Deficiency Pattern, Spleen-Kidney Deficiency Pattern, Heart-Spleen Deficiency Pattern, Liver Qi Stagnation with Spleen Deficienc, Lung-Kidney Deficiency Pattern, Spleen Deficiency with Dampness Obstruction [13].

Therapy focuses on reinforcing healthy qi and addressing the root cause. For patterns of qi deficiency, blood deficiency, yin deficiency, and yang deficiency, the corresponding methods applied are tonifying qi and strengthening the spleen, tonifying qi and nourishing blood, tonifying qi and nourishing yin, and tonifying qi and warming yang, respectively. Among these approaches, the method of tonifying qi and fortifying the spleen is consistently applied throughout treatment [14]. Herbs such as Astragalus root (Huangqi) and Chinese yam (Shanyao) are primarily used to regulate the lung, spleen, and kidney systems. Supplemented by the approach of dispelling pathogenic excess to address symptoms, methods such as resolving phlegm, activating blood circulation, strengthening healthy qi, and detoxification are employed for conditions involving intermingled phlegm and stasis or internally accumulated cancerous toxins, in order to dissipate phlegm-stasis and clear heat toxins. At the same time, emphasis is placed on the connection between emotional states and organ functions. For liver qi stagnation, methods to soothe the liver and regulate qi are integrated; for spleen deficiency with dampness accumulation, approaches to strengthen the spleen and resolve dampness are incorporated. Clinical practice demonstrates that formulas such as Bu Zhong Yi Qi Tang (Center-Supplementing Qi-Boosting Decoction) and Shuyu Wan (Dioscorea Pill), along with prepared medicines like Jian Pi Sheng Mai Gao (Spleen-Fortifying Pulse-Generating Paste) and Yi Qi Wen Yang Granules (Qi-Boosting Yang-Warming Granules), effectively alleviate CRF symptoms while enhancing patients' immune function and quality of life.

3. Primary Traditional Chinese Medicine Interventions for Cancer-related Fatigue

3.1 Single Herbal Medicines and Active Components

Single herbs and active compounds from TCM constitute the fundamental material basis for treating CRF. Centered around the core therapeutic principle of "fortifying the root and nourishing essence, supporting vital qi and dispelling pathogens," they regulate physiological functions through multi-target and multi-pathway mechanisms. These mechanisms primarily involve immunomodulation, anti-inflammatory effects, and the improvement of energy metabolism. Substantial progress has been made in both clinical application and mechanistic research in this field.

Central to monotherapy approaches are herbs such as ginseng and astragalus, both of which serve as fundamental components in various formulas for CRF [15-18]. They play key roles in regulating and reinforcing the spleen and stomach, thereby replenishing vital qi. Ginseng and American ginseng have been shown to significantly alleviate CRF through downregulation of inflammatory pathways and modulation of hypothalamic-pituitary-adrenal (HPA) axis function and cortisol levels [19,20]. Astragalus polysaccharide (PG2), the primary active constituent of astragalus, has been widely applied in clinical settings. Approved in Taiwan for treating CRF in patients with advanced cancer, its efficacy is supported by Phase IV clinical trials, which confirm its role in alleviating CRF symptoms—particularly in breast cancer patients following chemotherapy. An eight-week course of treatment provided sustained symptomatic relief to 71% of patients. Its mechanism of action also involves regulating gut microbiota composition, increasing short-chain fatty acid levels, and promoting the proliferation of anti-inflammatory bacterial species [21-23]. Furthermore, various active components in TCM demonstrate potential for precision therapy in CRF. The flavonoid quercetin alleviates cisplatin-induced CRF by inhibiting muscle atrophy, regulating the hypothalamic-pituitary-adrenal (HPA) axis, and modulating the monocyte chemoattractant protein-1 (MCP-1) signaling pathway [24]. When combined with leucine, it synergistically improves muscle grip strength [25]. The triterpenoid ganoderic acid reduces chemotherapy-related fatigue by enhancing mitochondrial function in skeletal muscle, promoting energy metabolism, and suppressing the expression

of inflammatory factors [26]. Among polysaccharide constituents, Dioscorea polysaccharides alleviate skeletal muscle inflammation and oxidative stress while also inhibiting tumor growth [27]. Rhodiola polysaccharides exert anti-fatigue effects through antioxidant and immunomodulatory mechanisms. Astragaloside IV suppresses the expression of prolyl hydroxylase 2 (PHD2), activates the mitophagy pathway, clears dysfunctional mitochondria, and improves overall metabolic function [28]. Resveratrol enhances exercise endurance [29], while fenugreek alkaloids optimize mitochondrial activity and increase muscle strength [30]. Curcumin, derived from turmeric, contributes to the amelioration of CRF through its triple actions of anti-inflammation, antioxidant activity, and antitumor effects [31]. Additionally, the proprietary formulation Nuvastatic (containing 6% rosmarinic acid) has been demonstrated in Phase II clinical trials to reduce levels of the urinary inflammatory marker F2-IsoP, alleviate fatigue symptoms in patients undergoing chemotherapy, and improve quality of life [32].

These single herbs and active components primarily function by modulating immune responses, inflammatory pathways, energy metabolism, oxidative stress, and the neuroendocrine system, offering a substantial pharmacological foundation for the precision treatment of CRF. Future research should focus on conducting large-scale randomized controlled trials to validate the efficacy and safety of additional candidate compounds, thereby promoting their clinical translation and standardized application.

3.2 Traditional Chinese Medicine Formulas

Compound formulas represent the cornerstone of TCM treatment for CRF, guided by the principle of "syndrome differentiation and treatment" and closely aligned with the pathogenesis of "deficiency at the root and excess at the branch." Core formulas include Bu Zhong Yi Qi Tang (Tonify the Middle and Augment Qi Decoction), Si Jun Zi Tang (Four Gentlemen Decoction), and Shi Quan Da Bu Tang (Ten-Ingredient Major Tonifying Decoction). These formulas address specific syndrome patterns such as spleen qi deficiency, qi and blood deficiency, and spleen-kidney yang deficiency. Their therapeutic effects are achieved through strategies such as tonifying qi and fortifying the spleen, nourishing blood and supplementing yin, and warming yang and reinforcing the kidneys. By modulating immune function, reducing inflammatory responses, and improving qi and blood metabolism, they effectively alleviate fatigue with clinically validated efficacy.

Compound formulas aimed at tonifying qi and fortifying the spleen are frequently utilized in the treatment of CRF. Among these, Astragalus and Four Gentlemen Decoction (Huangqi Si Jun Zi Tang) and Bu Zhong Yi Qi Tang (Tonify the Middle and Augment Qi Decoction) are the most widely employed [33]. Studies indicate that Astragalus and Four Gentlemen Decoction can alleviate CRF symptoms in breast cancer patients through multiple signaling pathways, including PI3K-Akt, significantly improving Piper Fatigue Scale scores [34]. Bu Zhong Yi Qi Tang represents the standard therapeutic formula for CRF with spleen qi deficiency pattern. It has been shown to significantly improve fatigue scores within two weeks of administration. The primary active components of its core herbs exert positive effects on CRF by targeting key molecules such as AKT1 and IL-6, as well as signaling pathways like TNF and NF-κB. Adjusting dosages or combining these agents with other medications can further enhance therapeutic efficacy [35-37]. The Four Gentlemen Decoction (Si Jun Zi Tang) addresses the core pathogenesis of spleen deficiency by tonifying qi and strengthening the spleen, thereby nourishing the foundation of the acquired constitution and effectively alleviating chronic fatigue associated with this pattern [38]. Both Renshen Yangrong Decoction (Ginseng Nourishing Decoction) and Shiquan Dabu Decoction (Ten-Ingredient Grand Tonifying Decoction) emphasize the simultaneous treatment of the spleen and kidneys. In non-anemia-related CRF, the former significantly reduces fatigue levels within six weeks, with therapy eliciting statistically and clinically meaningful improvements in fatigue severity and daily functioning [39]. The latter activates natural killer cells and modulates regulatory T cells, markedly alleviating fatigue in lung and breast cancer patients after chemotherapy, thus achieving integrated support of both acquired and innate vital qi [40, 41]. Jianpi Huayu Decoction improves immune balance in murine models by upregulating pro-inflammatory cytokines such as IFN-γ and IL-2 while downregulating anti-inflammatory cytokines including IL-4 and IL-10. It inhibits the expression of the tumor proliferation marker Ki-67 and alleviates CRF by modulating the Th1/Th2 immune equilibrium via the IL-27/STAT1 signaling pathway [42]. Shenqi Fuzheng Injection, centered on ginseng and astragalus, reverses T-cell dysfunction, regulates immune checkpoint molecule expression, and suppresses the production of pro-inflammatory cytokines [4]. It enhances patients' Karnofsky Performance Status scores and quality of life, alleviates fatigue, and simultaneously inhibits tumor progression and mitigates depressive-like behaviors [43-45]. Compound Ejiao Syrup, by virtue of its actions of tonifying qi and nourishing blood, ameliorates anemia and bone marrow suppression in patients with qi deficiency and blood stasis syndrome, thereby relieving CRF and improving overall quality of life [46]. For CRF presenting with a liver qi stagnation pattern, Shu Gan Jian Pi granules can alleviate symptoms by soothing the liver and promoting qi circulation while strengthening the spleen, thereby regulating qi flow [47]. Shengmai San, a synergistic formula composed of ginseng, ophiopogon, and schisandra, is the preferred treatment for CRF with qi and yin deficiency, and its efficacy has been confirmed through randomized controlled trials [48].

Current evidence supporting the application of TCM compound formulas in treating CRF is largely derived from small-scale studies, with the underlying mechanisms still lacking robust experimental substantiation. Future research should prioritize high-quality, large-scale clinical trials that integrate approaches such as network pharmacology and molecular biology to systematically elucidate the mechanisms of action. This will help advance the development of standardized and individualized diagnostic-therapeutic frameworks that effectively integrate TCM with Western medicine.

3.3 Acupuncture

Acupuncture, as a cornerstone of external therapies in TCM

for managing CRF, is based on the theoretical principles of unblocking meridians, harmonizing qi and blood, and balancing yin and yang [49]. By targeting specific acupoints, it addresses the pathogenesis of CRF, which is characterized by 'deficiency at the root and excess at the branch.' This approach regulates organ function, reinforces healthy qi, and dispels pathogenic factors. Recognized in the National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines for CRF, acupuncture provides an important intervention for patients experiencing CRF during or after active cancer treatment. Research on its clinical efficacy and mechanisms has become increasingly systematic. Its therapeutic strengths lie in its safety, minimal invasiveness, low rate of adverse reactions, and holistic regulation of body and mind. Acupuncture effectively alleviates multidimensional fatigue symptoms spanning physical, emotional, and cognitive domains.

Research by Vickers et al. on acupuncture for cancer-related CRF reported an average improvement rate of 31.1% following treatment, indicating that acupuncture merits further investigation as an intervention for chemotherapy-related fatigue [50]. Key components of acupuncture therapy include acupoint selection principles, needling techniques, and adaptation based on syndrome differentiation. Point selection follows the principle of tonifying deficiency and reinforcing the root, while regulating qi and blood circulation. Core acupoints frequently used include Zusanli (ST36), Sanyinjiao (SP6), Guanyuan (CV4), Qihai (CV6), and Baihui (GV20) [51,52]. These are supplemented with pattern-specific points to formulate individualized treatment plans. Zusanli (ST36), often referred to as the "longevity point," fortifies the spleen, boosts qi, and nourishes blood, making it a fundamental point in the treatment of CRF. Sanyinjiao (SP6) harmonizes the liver and kidneys and tonifies the spleen and kidney systems; when combined with Zusanli (ST36), it reinforces the effect of strengthening the body's foundation. Guanyuan (CV4) and Qihai (CV6) work together to warm yang, augment qi, and nourish the original qi. Baihui (GV20) elevates yang, clears the mind, and alleviates mental fatigue [53,54]. For specific syndrome patterns: CRF with Liver Qi Stagnation and Spleen Deficiency: Combine the "Fatigue-Relieving Three Needles" (Sishenzhen, Neiguan PC6, Zusanli ST36) with Taichong (LR3) and Ligou (LR5). CRF with Lung-Spleen Qi Deficiency: Add Feishu (BL13) and Pishu (BL20). CRF with Qi and Blood Deficiency: Include Xuehai (SP10) and Shenmen (HT7). This methodology embodies the principle of "selecting points based on pattern differentiation to achieve targeted treatment." The techniques applied in acupuncture treatment are diverse, including traditional manual acupuncture, electroacupuncture, and moxibustion, each offering distinct therapeutic advantages. Manual acupuncture employs methods such as twisting, lifting, and thrusting to regulate deficiency or excess of qi and blood, making it adaptable to various syndrome patterns. Electroacupuncture enhances acupoint stimulation through low-frequency electrical pulses, which are particularly beneficial for patients with severe fatigue. Moxibustion combines needling with thermal stimulation, providing marked warming and meridian-unblocking effects, and is especially suitable for CRF presenting with yang deficiency patterns. Furthermore, specialized techniques such as the Burning Mountain Fire Needling method and the Ten Ancient Needles approach have shown notable clinical efficacy. These techniques effectively alleviate depressive symptoms and improve cognitive function in patients with CRF. Clinical studies have demonstrated that an acupuncture treatment cycle of 6 weeks (with 2–5 sessions per week) yields optimal outcomes, significantly reducing scores on the Brief Fatigue Inventory (BFI) and Piper Fatigue Scale, while also alleviating anxiety and depressive symptoms and enhancing quality of life [55-58]. Regarding its mechanisms of action, acupuncture regulates bodily functions through multiple pathways: modulation of inflammatory response—it reduces plasma levels of pro-inflammatory cytokines such as TNF-α, IL-1, and IL-6, thereby attenuating systemic inflammation [59]; regulation of neuroendocrine function—it modulates the HPA axis and helps normalize hormone levels, including 17-hydroxycorticosteroids [60]; enhancement of immune function—it increases the proportion of $CD3^+$ and $CD4^+$ T cells and elevates the $CD4^+/CD8^+$ ratio, thereby strengthening anti-tumor immunity [61]; and regulation of gastrointestinal hormones—it adjusts the secretion of hormones such as ghrelin and leptin, contributing to improved nutritional metabolism and sleep quality [62].

Current clinical evidence supporting acupuncture for CRF continues to grow, yet limitations remain, including small sample sizes, inconsistent methodological quality, and significant heterogeneity among studies. Some trials have reported minor adverse events, such as hematoma or localized bleeding at needling sites. Future research should prioritize large-scale, multicenter, high-quality randomized controlled trials. Incorporating molecular biology and related technologies will help clarify the underlying mechanisms of acupuncture. Standardizing acupoint selection protocols and operational procedures will further promote the internationalization and personalized application of acupuncture in CRF management.

3.4 Other Traditional Chinese Medicine Interventions

Other TCM therapies follow the core principle of regulating qi and blood and strengthening the root foundation, closely corresponding to the pathogenesis of CRF, which is characterized by deficiency at the root with excess at the branch. These include various non-pharmacological modalities such as moxibustion, therapeutic massage, acupressure, and progressive muscle relaxation training [63-66]. Known for their safety, minimal invasiveness, ease of implementation, and low rate of adverse reactions, these approaches not only alleviate fatigue specifically but also improve related symptoms such as mood disturbances and sleep disorders. As an integral part of the comprehensive CRF treatment system, they are particularly suitable for patients who are intolerant to medication or acupuncture [64, 67].

Moxibustion is a core modality in TCM, primarily functioning to warm yang, tonify deficiency, unblock meridians, and activate collaterals. Its clinical applications are diverse, each with distinct characteristics. Zhao's Thunder-Fire Moxibustion, specifically indicated for CRF with qi deficiency, targets key spinal segments such as Pishu (BL20) to Qihaishu (BL24) and Weishu (BL21) to Guanyuanshu (BL26). This method significantly improves patients' Brief Fatigue Inventory (BFI) scores, TCM syndrome scores, and

leukocyte counts, effectively enhancing treatment response rates [51]. Infrared laser moxibustion represents a modern adaptation of traditional moxibustion, overcoming drawbacks such as smoke and odor. By stimulating tonifying acupoints like Guanyuan (CV4), Qihai (CV6), and Zusanli (ST36) with a 10.6-μm infrared laser, it notably reduces fatigue levels after six weeks of treatment. Follow-up at 18 weeks demonstrates sustained efficacy, which remains significantly superior to sham treatment, indicating durable therapeutic effects [68]. Acupoint selection in moxibustion consistently follows the principle of "centering on the Ren and Du meridians while integrating zang-fu organ points." As Li Shizhen remarked in A Study of the Eight Extraordinary Vessels: "The Ren and Du vessels are the guiding channels of the human meridian system, the very source from which primordial qi arises." By warming and unblocking the Ren and Du meridians while nourishing the zang-fu organs, this approach achieves the therapeutic aim of strengthening the root and alleviating deficiency-type fatigue.

Tuina massage emphasizes both physiological and psychological regulation, tailored to the profiles of CRF patients, who often present with both physical discomfort and emotional distress. Common techniques such as kneading, acupressure, and meridian massage are applied primarily to acupoints along the spleen, stomach, and kidney meridians. These methods effectively improve blood circulation, increase muscle blood flow and oxygen partial pressure, relieve muscle tension, and modulate autonomic nervous system function. For breast cancer patients with CRF, guided by the physiological principle that "the liver governs women's physiology," massage can precisely alleviate symptoms such as belching, fatigue, and anxiety caused by liver constraint and spleen deficiency [69]. In colorectal cancer patients, this therapy significantly reduces the incidence of CRF while improving sleep quality, achieving the dual benefit of "alleviating fatigue and tranquilizing the mind [70]."

Acupressure and progressive muscle relaxation training provide accessible and practical options for managing CRF. Clinical studies indicate that pressing relaxation-oriented acupoints such as Yintang (GV24.5), Anmian (EX-HN1), Shenmen (HT7), Sanyinjiao (SP6), and Taichong (LR3) is significantly more effective than stimulating points like Baihui (GV20) and Qihai (CV6) in alleviating chronic fatigue and improving sleep quality [71]. A meta-analysis of 12 randomized controlled trials involving 1,047 cancer patients demonstrated that progressive muscle relaxation training produces measurable therapeutic benefits over usual care in improving CRF and reducing anxiety and depressive symptoms [36]. These non-pharmacological therapies exemplify the holistic approach of TCM. Some methods not only relieve fatigue but also concurrently improve comorbid conditions such as depression and sleep disturbances, thereby significantly enhancing patients' overall quality of life [62].

Currently, these therapies still face challenges such as limited sample sizes, inconsistent methodological quality across studies, and an incomplete understanding of their mechanisms of action. Future efforts should prioritize large-scale, multicenter, high-quality randomized controlled trials. These studies should integrate modern techniques—such as circulating inflammatory biomarker profiling—to deepen mechanistic insight. Furthermore, standardizing operational protocols and establishing evidence-based application criteria will promote the standardization and global integration of non-pharmacological TCM approaches for CRF.

4. Summary and Outlook

Traditional Chinese Medicine offers multidimensional and individualized therapeutic benefits for CRF. Single-herb preparations and active components—centered on ginseng and astragalus—exert their effects through constituents such as ginsenosides and astragalus polysaccharides, which modulate inflammatory pathways and enhance energy metabolism. Compounds like quercetin and ganoderic acids specifically regulate key processes, including mitochondrial function and immune responses. Compound formulas follow the principle of pattern differentiation and treatment. Classic prescriptions, such as Bu Zhong Yi Qi Tang (Tonify the Middle and Augment Qi Decoction) and Shi Quan Da Bu Tang (Ten-Ingredient Major Tonifying Decoction), are tailored to distinct syndrome patterns. Through strategies such as tonifying qi and strengthening the spleen, nourishing blood and replenishing yin, and warming yang and reinforcing the kidneys, these formulas address both symptoms and root causes. External therapies, including acupuncture and massage, are widely valued for their safety and minimal invasiveness. Acupuncture focuses on key acupoints such as Zusanli (ST36) and Sanyinjiao (SP6). Moxibustion — including modern adaptations like infrared laser moxibustion — warms and activates yang qi. Tuina massage and acupressure alleviate symptoms by regulating qi and blood flow in the meridians and relieving muscular tension. Non-pharmacological approaches, such as progressive muscle relaxation training, also simultaneously improve fatigue and emotional distress. These therapeutic modalities work through multiple pathways, including immune regulation, inflammatory balance, neuroendocrine modulation, and optimization of energy metabolism. Together, they illustrate the distinctive strengths of TCM in achieving holistic systemic regulation.

Although current research supports the efficacy of TCM in alleviating CRF and improving patients' quality of life, significant limitations remain: there is a lack of unified diagnostic classification and outcome assessment criteria; clinical studies are mostly small-scale, single-center trials with inconsistent methodological quality; mechanistic research is still largely limited to animal experiments or preliminary studies, with insufficient depth in elucidating molecular targets and signaling pathways, and the active material basis of TCM formulas remains unclear; operational protocols for certain external therapies and individualized adaptation strategies require further refinement, while international promotion faces the dual challenges of theoretical translation and evidence accumulation.

Future research should prioritize three key directions: standardization, precision, and internationalization. This includes establishing a unified diagnostic and efficacy evaluation system; conducting large-scale, multicenter randomized controlled trials to strengthen the clinical evidence base; integrating modern technologies such as network pharmacology and molecular biology to deeply

analyze the mechanisms of TCM formulas and their active components, and to identify core targets and signaling pathways; standardizing external treatment protocols and exploring personalized strategies that combine pattern differentiation with disease diagnosis; and enhancing integrative Chinese–Western medicine research and international collaboration to promote the global dissemination of TCM theory and practice. Through these efforts, TCM can make a substantial contribution to the worldwide prevention and treatment of CRF, while offering patients safer and more effective therapeutic options.

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