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Integrative Management of CKD-Related Sarcopenia: Mechanisms and Clinical Efficacy of She Ethnic Medicine (Jianpi Yishen Tea) Combined with Resistance Training

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Abstract: *Objective:* This study systematically elucidates the clinical efficacy, molecular mechanisms, and translational value of *Jianpi Yishen Tea*—a characteristic formula of She ethnic medicine—combined with resistance exercise in the management of sarcopenia associated with chronic kidney disease (CKD). *Methods:* Guided by the *2024 Expert Consensus on the Diagnosis, Treatment, and Prevention of Sarcopenia in Chronic Kidney Disease,* we conducted a comprehensive review of domestic and international literature from the past five years. Moving beyond a reductionist perspective, this study performs a panoramic analysis of the pathological network underpinning CKD-related sarcopenia, covering pharmacokinetics of uremic toxins, micro-inflammatory cascades, mitochondrial quality control (MQC) homeostasis, and the "Gut-Kidney-Muscle" axis. Subsequently, an evidence-based evaluation of the combined intervention was performed. *Results:* Current evidence identifies the pathological core of CKD-related sarcopenia as systemic metabolic and immune dysregulation, clinically manifesting as "Spleen-Kidney deficiency combined with damp-turbidity and stasis." Modern pharmacological research confirms a synergistic "drug-exercise coupling" effect between *Jianpi Yishen Tea* (containing *Chimonanthus nitens*, *Astragalus membranaceus*, etc.) and resistance training. This combined protocol specifically inhibits the NF-κB signaling pathway—thereby blocking inflammatory storm-mediated muscle protein degradation—and significantly upregulates PGC-1α expression. Consequently, this restores mitochondrial function across three dimensions: biogenesis, fusion-fission dynamics, and mitophagy. Furthermore, the therapy remodels the gut microbiota, reducing the accumulation of gut-derived toxins such as indoxyl sulfate. Clinical data demonstrate that compared to monotherapy, this integrated regimen yields superior outcomes in reversing skeletal muscle atrophy, ameliorating the decline in estimated glomerular filtration rate (eGFR), and reducing all-cause mortality. *Conclusion:* The integration of She medicine (*Jianpi Yishen Tea*) with resistance exercise establishes a precision-based, multi-targeted intervention model. This strategy leverages the unique wisdom of ethnic medicine to disrupt the vicious cycle of sarcopenia in CKD, offering a novel, evidence-based therapeutic paradigm.

Keywords: She ethnic medicine; *Jianpi Yishen Tea*; Chronic Kidney Disease; Sarcopenia; Resistance Exercise; Mitochondrial Quality Control; NF-κB Pathway; Gut-Kidney-Muscle Axis

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1. Introduction

Amidst global demographic aging and shifting metabolic disease profiles, chronic kidney disease (CKD) has emerged as a significant public health challenge. During the progressive trajectory of CKD, the depletion of skeletal muscle mass and function—termed CKD-related sarcopenia—represents a critical complication rather than a mere comorbidity. Epidemiological evidence correlates declining estimated glomerular filtration rates (eGFR) with a stepwise increase in sarcopenia prevalence, exceeding 50% in patients with end-stage renal disease (ESRD) [1]. This pathological alteration, characterized by anatomical muscle loss and functional deterioration, serves as an independent predictor for falls, fractures, cardiovascular events, and all-cause mortality [2-3].

While the European Working Group on Sarcopenia in Older People (EWGSOP) and the Asian Working Group for Sarcopenia (AWGS) advocate for early intervention, conventional Western medical approaches face clinical paradoxes. Strict low-protein diets may compromise substrate availability for muscle synthesis, whereas isolated exercise therapies are often hampered by poor patient tolerance and exercise-induced oxidative stress within a uremic environment [4].

Consequently, integrating traditional medical wisdom becomes imperative. Traditional Chinese Medicine (TCM) categorizes this condition under “Wei Zheng” (flaccidity syndrome) or “Xu Lao” (consumptive fatigue), attributing the etiology to “root deficiency of the Spleen and Kidney, manifesting as dampness, turbidity, and stasis” [5]. She ethnic medicine, a distinct branch of traditional healing, offers a unique theoretical framework emphasizing “tonifying deficiency and draining turbidity.” This review transcends conventional enumerative summaries to systematically elucidate the scientific basis of combining the She formula *Jianpi Yishen Tea* with resistance exercise.

By adopting a multi-target perspective, we aim to provide a translatable, integrated diagnostic and therapeutic strategy for clinical practice.

2. Pathophysiological basis: systemic dysregulation in a multidimensional network

The pathogenesis of CKD-related sarcopenia is not linear but represents a systemic biological dysregulation involving metabolic toxicity, immune-inflammation, organelle homeostasis, and microecological shifts.

2.1. Uremic toxin accumulation and protein metabolic collapse

With nephron loss, the retention of metabolic waste is inevitable. Protein-bound uremic toxins (PBUTs), specifically indoxyl sulfate (IS) and p-cresyl sulfate (PCS), act as potent myotoxins. These compounds penetrate skeletal muscle cells via organic anion transporters (OATs), inducing a surge in reactive oxygen species (ROS) [6]. This oxidative stress disrupts myofibrillar structural integrity and activates the ubiquitin-proteasome system (UPS). Specifically, IS upregulates muscle-specific E3 ubiquitin ligases—Atrogin-1 and MuRF-1—tagging proteins for degradation. Concurrently, toxin accumulation suppresses the anabolic IGF-1/Akt/mTOR pathway. Compounded by metabolic acidosis, which further primes the ATP-dependent UPS and promotes branched-chain amino acid (BCAA) catabolism, muscle tissue succumbs to a state of “suppressed synthesis and accelerated degradation” [6-7].

2.2. The Micro-inflammatory cascade and nf-κb switching

CKD is characterized by a persistent micro-inflammatory state. Circulating pro-inflammatory cytokines (TNF-α, IL-6, IL-1β) stimulate muscle receptors, activating the nuclear factor-κB (NF-κB) pathway[8]. NF-κB serves as a molecular switch for muscle wasting; phosphorylation and nuclear translocation of its p65 subunit initiate the transcription of MuRF-1, leading to the rapid degradation of myosin heavy chain (MHC). This inflammation-driven atrophy creates a self-amplifying cycle. Interventions blocking the TNF-α/NF-κB axis (e.g., resveratrol) have shown efficacy in mitigating

atrophy, validating the central role of this inflammatory cascade [8].

2.3. Collapse of the mitochondrial quality control (mqc) network

Skeletal muscle function relies heavily on mitochondrial homeostasis, which is severely compromised in CKD. The expression of PGC-1α, the master regulator of mitochondrial biogenesis, is downregulated, inhibiting downstream transcription factors NRF-1 and TFAM, thus stalling mitochondrial renewal[9]. Simultaneously, mitochondrial dynamics are disrupted: the fission protein Drp-1 is upregulated while the fusion protein Mfn-2 is suppressed, causing excessive fragmentation and energetic inefficiency. Crucially, mitophagy—the clearance mechanism for defective mitochondria—is impaired, leading to the accumulation of dysfunctional organelles that release ROS and cytochrome c, triggering apoptosis [9,12].

2.4. Dysbiosis of the "gut-kidney-muscle axis"

The "Gut-Kidney-Muscle Axis" offers a novel pathogenic perspective. CKD-induced intestinal barrier compromise and urea accumulation drive gut dysbiosis, favoring proteolytic bacteria (e.g., *Escherichia coli*, *Bacteroides*) over saccharolytic species (*Bifidobacterium*, *Lactobacillus*). This shift increases the production of gut-derived toxins (IS, PCS) and facilitates endotoxin (LPS) translocation, fueling systemic inflammation[10]. These circulating factors further inhibit muscle mitochondrial function, establishing a vicious cycle where enteropathy aggravates renal failure, which in turn accelerates muscle wasting [14].

3. She ethnic medicine jianpi yishen tea: ethnobotanical theory and formula analysis

She ethnic medicine emphasizes "conforming to natural laws" and the homology of food and medicine. *Jianpi Yishen Tea* is refined from the folk formula "Shiliang Cha," integrated with the TCM principle of "simultaneous treatment of Spleen and Kidney." According to She medical theory, CKD-related sarcopenia follows a pathogenesis of "deficiency leading to excess," where early stages are dominated by Qi deficiency of the Spleen and Kidney, while advanced stages involve the accumulation of turbid toxins and stasis.

Reflecting this theoretical framework, the pharmacological architecture of the formula follows a rigorous hierarchy. The Minister herb, *Chimonanthus nitens* (She name: "Shiliang Cha"), is traditionally prized for clearing heat and dampness; phytochemical analyses reveal it is rich in volatile oils, quercetin, and kaempferol, exhibiting broad-spectrum anti-inflammatory properties that regulate immune homeostasis[11]. The Sovereign herb, *Astragalus membranaceus*, is employed in high doses to tonify Qi. Its primary bioactive compound, Astragaloside IV, has been shown to downregulate TGF-β1 to inhibit renal fibrosis and specifically upregulate skeletal muscle PGC-1α, promoting mitochondrial biogenesis[12]. Supporting this core pair, *Codonopsis pilosula* and *Polygonatum sibiricum* nourish the vital source, while *Poria cocos* and *Lycium barbarum* balance fluid metabolism, and *Crataegus pinnatifida* enhances circulation and lipid metabolism. This intricate combination targets the "root deficiency" while simultaneously clearing the "branch excess" of stasis and toxins.

4. Pharmaco-exercise coupling: clinical implementation and evidence

4.1. Protocol precision: beyond general recommendations

Adhering to the 2024 expert consensus, this combined therapy emphasizes precision in "timing" and "intensity" rather than arbitrary exercise recommendations[4]. The protocol strictly follows FITT-VP principles, prioritizing resistance training supplemented by moderate aerobic activity, with a frequency of 3–4 sessions per week on alternate days. Intensity progresses from 40–50% of 1RM (One-Repetition Maximum) to 60–70%, guided by the Borg RPE scale. Uniquely,

the pharmacological intervention is synchronized with the physical regimen: *Jianpi Yishen Tea* is administered daily to leverage its sustained anti-inflammatory effects, effectively counteracting exercise-induced oxidative stress and optimizing the microenvironment for anabolism.

4.2. Clinical evidence

Meta-analyses of Randomized Controlled Trials (RCTs) substantiate the clinical superiority of this integrated regimen over monotherapy[13]. Patients undergoing the combined therapy exhibited profound phenotypic reversal, evidenced by significantly greater increases in Appendicular Skeletal Muscle Mass Index (ASMI). These structural gains translated directly into functional restoration, with marked improvements in grip strength and gait speed signaling reduced fall risk and enhanced autonomy. Crucially, addressing clinical concerns regarding potential renal load from high-intensity interventions, the regimen demonstrated a robust safety profile; serum creatinine (Scr) levels improved and the decline in eGFR slope was attenuated, likely attributable to muscle-mediated enhancements in insulin sensitivity and renal microcirculation. Moreover, serological analysis confirmed the subsidence of the systemic inflammatory storm, with significant reductions in hs-CRP, IL-6, and TNF-α levels, indicating that the therapy successfully disrupted the "inflammation-atrophy" cycle.

5. Mechanistic insight: multi-target molecular regulation

The synergy of *Jianpi Yishen Tea* and resistance exercise addresses the core pathology of CKD sarcopenia via distinct, yet complementary, molecular pathways.

5.1. Restoring mitochondrial quality control (MQC)

Research utilizing adenine-induced CKD models demonstrates that bioactive components like Astragaloside IV work synergistically with mechanical signaling from resistance exercise to activate the AMPK/PGC-1α axis[14]. This activation acts as a master switch, restarting mitochondrial biogenesis through the upregulation of NRF-1 and TFAM, effectively restoring mtDNA copy numbers. In parallel, the intervention rebalances mitochondrial dynamics by inhibiting the fission protein Drp-1 and upregulating the fusion protein Mfn-2, while concurrently restoring Pink1/Parkin-mediated mitophagy to clear damaged organelles[12].

5.2. Blockade of the NF-κB inflammatory cascade

Beyond mitochondrial repair, the formula specifically inhibits the IKK/IκB/NF-κB signaling axis in both renal and muscle tissues[14-15]. By preventing the phosphorylation and degradation of IκB, the intervention sequesters the NF-κB p65 subunit in the cytoplasm, blocking its nuclear translocation. This transcriptional silencing downregulates pro-inflammatory cytokines (IL-1β, MCP-1) and, most critically, suppresses the expression of the E3 ubiquitin ligase MuRF-1. This effectively turns off the genetic "switch" for muscle protein degradation, preserving muscle mass.

5.3. Remodeling the "Gut-Kidney-Muscle Axis"

Finally, metabolomic studies reveal that the *Jianpi Yishen* formula exerts profound effects on the gut-kidney-muscle axis. It optimizes gut microecology by increasing beneficial genera such as *Lactobacillus* and *Akkermansia* while strengthening the mucosal barrier. Furthermore, it modulates tryptophan metabolism to activate the Aryl Hydrocarbon Receptor (AhR) pathway, reducing systemic levels of indoxyl sulfate. This reduction in circulating toxins improves skeletal muscle insulin sensitivity via remote organ crosstalk, facilitating systemic metabolic recovery [15].

6. Conclusion and future perspectives

CKD-related sarcopenia is a complex metabolic syndrome resistant to single-target interventions. The integration of She ethnic medicine (*Jianpi Yishen Tea*) with resistance exercise represents a paradigm shift, aligning with the "Spleen-Kidney" theory while addressing modern molecular pathologies. This therapy delivers a "triple benefit" of muscle hypertrophy, renal protection, and anti-inflammation by repairing the MQC network, blocking NF-κB signaling, and remodeling the gut microbiota.

Future research should prioritize large-scale, multi-center RCTs focusing on hard endpoints such as mortality and rehospitalization rates. Concurrently, employing single-cell sequencing and spatial transcriptomics will further elucidate how She medicinal components regulate skeletal muscle satellite cell fate, advancing the modernization of ethnic medicine.

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Disclosure statement

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