DOI: 10.53469/jcmp.2026.08(01).42

Shaoyao Gancao Decoction in Orthopedics and Traumatology: Advances in Clinical Application and Experimental Research

Panxin Ma[1], Feixiang Feng[1], Fuchao Ding[1], Puwei Yuan[2,*]

[1]First Clinical Medical College, Shaanxi University of Chinese Medicine, Xianyang 712046, Shaanxi, China
[2]Key Laboratory of Integrated Traditional Chinese and Western Medicine for Prevention and Treatment of Bone Degenerative Diseases, College of Integrated Chinese and Western Medicine, Shaanxi University of Chinese Medicine, Xianyang 712046, Shaanxi, China
**Correspondence Author*

Abstract: ***The rising prevalence of orthopedic and traumatological conditions, driven by population aging and increased sports-related injuries, significantly compromises patients' quality of life and represents a growing public health burden. Contemporary research supports Shaoyao Gancao Decoction (SGD) as a therapeutic formulation with distinctive advantages in this field, making its clinical applications and mechanistic studies a key focus in traditional Chinese medicine (TCM) research. Originating from the "Treatise on Cold Damage Diseases" ("Shang Han Lun"), this classical formula combines Paeoniae Radix Alba (Bai Shao) and Glycyrrhizae Radix et Rhizoma (Gan Cao). Historically used for limb spasms and abdominal pain, it is known to soothe the liver, relieve spasms, and harmonize the "ying" and "wei" systems. Clinically, SGD demonstrates broad utility in managing post-fracture pain and spasms, cervical spondylosis, lumbar disc herniation, osteoarthritis (OA), and rheumatoid arthritis (RA). Experimental studies confirm its ability to: 1) Attenuate local inflammatory damage by modulating cytokines and suppressing inflammatory cascades, 2) Counteract oxidative stress through free radical scavenging, thereby protecting articular cartilage and periarticular tissues, 3) Regulate apoptosis-related gene expression to inhibit excessive cell death and maintain tissue homeostasis. This review systematically synthesizes current evidence on the clinical and experimental progress of SGD in orthopedics, aiming to establish a theoretical foundation for its evidence-based application and to guide future mechanistic research.***

Keywords: Shaoyao Gancao Decoction, Orthopedics and Traumatology, Clinical Application, Experimental Research, Review.

1. Introduction

In recent years, due to factors such as population aging, sports injuries, and occupational strain, the incidence and disability rates of orthopedic and traumatological diseases in China have risen significantly [1][2], posing serious challenges to patients' quality of life and adding to the societal healthcare burden [3]. Epidemiological studies indicate that the prevalence of knee osteoarthritis (OA) among individuals over 50 years old is approximately 22.1%, while osteoporosis affects about 19.2% of this population. Orthopedic and traumatological conditions are among the leading contributors to the disease burden in middle-aged and elderly individuals [4][5]. Key risk factors include aging, prior trauma, prolonged poor posture, osteoporosis, and weak muscle strength. Conventional treatments primarily involve non-steroidal anti-inflammatory drugs (NSAIDs) for pain relief, physical therapy, surgical intervention, and functional rehabilitation. However, long-term use of NSAIDs is associated with gastrointestinal side effects, hepatorenal toxicity, and cardiovascular risks. Moreover, some patients continue to experience recurrent pain, incomplete functional recovery, and postoperative adhesions [6]. The main influencing factors include aging, history of trauma, long-term poor posture, osteoporosis and weak muscle strength, etc. Modern medicine mainly employs non-steroidal anti-inflammatory drugs (NSAIDs) for pain relief, physical therapy, surgical repair and functional rehabilitation. Long-term use of Western medicine can easily lead to gastrointestinal reactions, liver and kidney toxicity, and cardiovascular risks. Some patients still face problems such as recurrent pain, incomplete functional recovery, and postoperative adhesions.

2. Origin and Background

SGD was first documented in Article 29 of Zhang Zhongjing's Treatise on Cold Damage Disorders: Differentiation and Treatment of Taiyang Diseases" from the Eastern Han Dynasty: "In cases of febrile disease with floating pulse, spontaneous sweating, frequent urination, restlessness, mild aversion to cold, and foot cramps… if the feet later become warm, add Peony and Licorice Decoction, and the feet will promptly extend." The formula consists of peony root and honey-fried licorice. Peony root is sour and cold in nature, softening and moistening, nourishing "yin", and effective in enriching blood and regulating menstruation. Honey-fried licorice is sweet and warm, boosting "qi", tonifying deficiency, and alleviating urgency. It excels in harmonizing other herbs. When combined in equal proportions, the two ingredients work together to produce the effects of transforming "yin" through sour and sweet flavors, relieving urgency and pain. Hence, it has been praised by later generations as the "Leg-Stretching Decoction" [7]. In TCM theory, most orthopedic and traumatological conditions fall under the categories of "bi syndrome" (painful obstruction), "wei syndrome" (atrophy), and "tendon injury." The primary etiology and pathogenesis involve liver and kidney deficiency, insufficiency of "qi" and blood leading to malnourishment of tendons and bones, combined with external trauma, overexertion, or invasion by wind, cold, and dampness. These factors lead to pathological changes such as "blood stasis," "deficiency," and "obstruction," often presenting as a root deficiency with superficial excess, or a mixed deficiency - excess pattern [8]. The ability of SGD to transform "yin" and relieve cramps and pain through its sour and sweet properties

aligns well with the clinical features of pain and spasms caused by poor nourishment of tendons and meridians and impaired circulation of "qi" and blood in orthopedic and traumatological disorders. Therefore, SGD has long been applied in this field, and its scope of use has continued to expand with accumulated clinical experience. Numerous studies indicate that SGD possesses anti-inflammatory and analgesic effects, promotes fracture healing, improves local blood circulation, and relieves muscle spasms [9][10], demonstrating unique advantages in treating orthopedic and traumatological diseases.

3. Clinical Application of SGD in Orthopedic and Traumatological Diseases

3.1 Post-Fracture Pain and Spasms

Following a fracture, local pain, swelling, and muscle spasms commonly occur, significantly hindering patient recovery [11][12]. SGD has shown favorable effects in alleviating post-fracture symptoms and promoting rehabilitation. Cheng Hui et al. [10] treated osteoporotic vertebral compression fractures of the liver-kidney insufficiency and "yin"-blood deficiency type using modified SGD combined with acupuncture. Results indicated that this combination therapy significantly relieved postoperative pain, improved bone density and bone metabolism, effectively promoted thoracolumbar functional recovery, enabled earlier initiation of rehabilitation training, and enhanced overall therapeutic outcomes, underscoring its clinical value. Shi et al. [13] conducted a systematic review of the efficacy and safety of SGD in treating limb dysfunction following periarticular fractures of the knee. Through analysis of randomized controlled trials based on indicators such as pain, edema, stiffness, and dysfunction, they provided new evidence supporting the effectiveness and safety of SGD. In summary, SGD offers an effective TCM approach for promoting functional recovery by addressing post-fracture pain and spasms through multiple pathways.

3.2 Cervical Spondylosis

Cervical Spondylosis (CS) is characterized by degeneration of cervical intervertebral discs, often resulting from long-term strain, osteophyte formation, or disc protrusion, which irritate or compress cervical nerve roots, the spinal cord, or vertebral arteries. This leads to symptoms such as neck and back pain, stiffness, limb numbness and weakness, dizziness, and nausea, seriously affecting quality of life [14]. SGD demonstrates notable efficacy in treating CS by relieving neck muscle spasms, inhibiting nerve root inflammation, improving symptoms, and enhancing quality of life. Zhang Le et al. [15] conducted a clinical observation involving 130 patients with nerve-root-type CS attributed to "qi" and blood deficiency with blood stasis. They found that SGD significantly alleviated pain, improved clinical symptoms, and reduced cervical dysfunction scores, possibly through anti-inflammatory mechanisms. Additionally, patients' sleep quality and daily living abilities improved markedly. Chen Jincheng et al. [16] performed a retrospective study on 30 CS patients and found that oral administration of modified SGD combined with massage was more effective than massage alone, significantly reducing neck pain and lowering cervical dysfunction index scores. These studies suggest that SGD not only effectively alleviates pain and dysfunction in nerve-root-type cervical spondylosis but also improves patients' quality of life via anti-inflammatory mechanisms, reflecting its holistic regulatory benefits.

3.3 Lumbar Disc Herniation

Lumbar Disc Herniation (LDH) is a prevalent spinal disorder, where symptoms such as low back pain, leg pain, and numbness arise from disc degeneration, annulus fibrosus rupture, and herniation of the nucleus pulposus compressing neural structures [17]. Recent studies have substantiated the significant therapeutic efficacy of SGD in managing LDH. Utilizing network pharmacology, Zhong Yuanming et al. [18] identified the primary active components of SGD and constructed a compound-target network, elucidating its potential mechanism for alleviating early-stage LDH pain. Their research suggests that SGD may suppress the production of inflammatory mediators and mitigate inflammatory and immune responses by modulating key targets including Interleukin-6 (IL-6), Matrix Metalloproteinase-9 (MMP-9), Interleukin-1β (IL-1β), Protein Kinase B (AKT1), and Vascular Endothelial Growth Factor A (VEGF-A). In a clinical trial involving 80 LDH patients, Su Meiyi et al. [19] investigated a treatment regimen combining floating acupuncture with a modified SGD formula. The results demonstrated significant post-treatment improvements in both the Visual Analogue Scale (VAS) and Japanese Orthopaedic Association (JOA) scores for all participants ($P<0.05$). Notably, the total effective rate was significantly higher in the treatment group (97.5%) compared to the control group (87.5%), with a statistically significant difference also observed in the marked effectiveness rate ($P < 0.01$). This indicates the superior efficacy of the combined therapy in reducing pain and improving lumbar mobility limitations. In conclusion, by inhibiting inflammatory cascades and demonstrating synergy with adjunctive therapies like floating acupuncture, SGD offers a significantly optimized, effective, and safe non-surgical strategy for LDH pain management.

3.4 Osteoarthritis

Osteoarthritis (OA) is a prevalent degenerative joint disease characterized by progressive destruction of articular cartilage, subchondral bone sclerosis, osteophyte formation, and synovial inflammation, often leading to joint pain, stiffness, and functional impairment [20]. Research indicates that SGD exerts multi-target protective effects in OA treatment, with its efficacy supported by basic research, clinical trials, and network pharmacology. Studies by Hou et al. [21] and Song Qinghui et al. [22] demonstrate that SGD can significantly inhibit the release of key pro-inflammatory cytokines such as IL-1β, IL-6, and tumor necrosis factor-α (TNF-α). It promotes extracellular matrix (ECM) synthesis by upregulating the expression of collagen type II alpha 1 chain (COL2A1), while mitigating excessive ECM degradation by downregulating matrix metalloproteinase-13 (MMP-13) and inhibiting the overall expression of MMPs, thereby maintaining cartilage metabolic homeostasis. Furthermore, SGD reduces interleukin-17 receptor B (IL-17RB) in articular cartilage, promotes chondrocyte proliferation, and inhibits chondrocyte

apoptosis, collectively slowing cartilage degeneration. Wang Zhiyuan [23] conducted a randomized controlled trial involving 240 OA patients. The control group underwent arthroscopic debridement, while the observation group received additional SGD treatment. Results showed the total effective rate was significantly higher in the observation group (95.83%) than in the control group (88.83%). Post-treatment clinical symptom scores and IL-1β levels were also significantly lower in the observation group. Zhu et al. [24] utilized network pharmacology to construct networks, predict targets, and perform module analysis, identifying crucial signaling pathways for SGD intervention in OA. They identified 23 bioactive compounds corresponding to 226 SGD targets, of which 187 were related to OA and 161 were overlapping targets. Functional enrichment analysis suggested that SGD exerts its pharmacological effects by regulating pathways involved in the cell cycle, apoptosis, drug metabolism, inflammation, and immunity. These studies collectively indicate that SGD, by modulating the network of inflammatory-oxidative-metabolic imbalance, delays the cartilage degeneration process through multiple targets, positioning it as a potential key agent in OA treatment.

3.5 Rheumatoid Arthritis

Rheumatoid Arthritis (RA) is a chronic systemic autoimmune disease characterized pathologically by synovial hyperplasia and inflammation, leading to destruction of articular cartilage and bone [25]. Its core mechanism involves abnormal activation of the immune system, producing autoantibodies that result in symmetrical polyarticular swelling, morning stiffness, and progressive deformity [26]. esearch indicates that SGD intervenes in RA progression through multi-target mechanisms. Zhu et al. [27] combined network pharmacology with cellular experiments to explore SGD's mechanism in treating RA, finding that it may exert anti-RA effects by regulating the nuclear factor-kappa B (NF-κB) and mitogen-activated protein kinase (MAPK) signaling pathways, intervening in processes such as protein phosphorylation and negative regulation of drug response. Chu Guike [28] conducted a clinical observation involving 60 RA patients, finding that treatment with a modified SGD formula combined with methotrexate significantly improved symptoms, signs, and specific laboratory markers (erythrocyte sedimentation rate/ESR, C-reactive protein/CRP, rheumatoid factor/RF). Post-treatment, patients' immunoglobulin levels (IgG, IgA, IgM) decreased while complement C3 levels increased, indicating immunomodulatory effects. The efficacy of the combined traditional Chinese and Western medicine treatment group was significantly superior to that of the Western medicine-alone group, without side effects such as stomach pain, bloating, fatigue, or weight loss. These results suggest that SGD combined with conventional Western medicine can synergistically regulate immune dysregulation in RA, enhancing therapeutic efficacy while reducing adverse drug reactions, highlighting the value of integrative medicine.

3.6 Tenosynovitis

Tenosynovitis (TS) is a non-infectious inflammation of the tendon sheath, pathologically characterized by congestion, edema, fibrin exudation, and abnormal synovial fluid secretion within the sheath. It is often caused by overuse, trauma, or infection, manifesting as local pain, triggering (trigger finger), and limited joint movement [29]. Basic and clinical studies indicate a significant interventional effect of SGD on this condition. Lin et al. [30] found that SGD improved mechanical pain threshold and thermal pain latency in rats with chronic inflammatory pain (CIP). The mechanism involved upregulating the expression of semaphorin 3G (Sema3G) protein in dorsal root ganglia and inhibiting the mRNA expression levels of IL-6 and CCL2. Zhang Kezhuang [31] treated over 30 TS patients using a modified SGD formula via fumigation, oral decoction, and soaking. Results showed pain relief and restored limb flexion/extension after 3 doses, with pain disappearance and normal finger movement after one week and no recurrence upon follow-up. Both basic and clinical evidence confirms that SGD can target and regulate pain-related signaling pathways, rapidly alleviate TS symptoms, and reduce recurrence rates, demonstrating potential for clinical application.

3.7 Frozen Shoulder

Frozen Shoulder (FS), also known as adhesive capsulitis, is characterized by severe shoulder pain and markedly restricted range of motion, often worsening at night and significantly affecting sleep. It may be related to inflammation and adhesion of periarticular soft tissues and contracture of the joint capsule [32]. Several studies have explored the role of traditional Chinese medicine in its treatment. Song Weiping [33] selected 80 FS patients of the stagnation type. The control group received bloodletting acupuncture, while the observation group received additional SGD. After two treatment courses, both groups showed decreased VAS scores and increased Constant-Murley scores, with more significant improvement in the observation group, indicating better efficacy for the combined therapy. Wu Xiao [34] used a self-modified SGD formula to treat 180 FS patients, achieving a cure in 104 cases and a total effective rate of 93.8%. Wen Guirong [35] reported treating FS with a modified combination of SGD and Guizhi Tang (Cinnamon Twig Decoction). Pain and limited mobility decreased after 3 doses, with symptoms disappearing completely after half a month. Consistent clinical observations indicate that SGD, through its actions of nourishing blood, freeing the collaterals, and harmonizing "ying" and "wei", can effectively break the vicious cycle of pain and restricted movement in FS, restoring shoulder joint function.

3.8 Restless Legs Syndrome

Restless Legs Syndrome (RLS) is a sensorimotor neurological disorder whose core symptoms involve uncomfortable sensations in the lower limbs and an irresistible urge to move them during periods of rest [36]. Recent research confirms that acupuncture combined with SGD can synergistically improve the inflammatory state, sleep architecture, and quality of life in RLS patients. Huang Xin et al. [37] studied the effects of acupuncture combined with SGD on RLS patients, randomizing 85 cases into groups. Results showed that the combined therapy group had greater reductions in CRP and greater increases in ferritin and albumin compared to monotherapy groups ($P<0.05$). Reductions in motor evoked potential (MEP), micro-arousal index (AI), and Pittsburgh

Sleep Quality Index (PSQI) scores, as well as the increase in slow-wave sleep (SWS) percentage, were also greater in the combined group ($P<0.05$). Furthermore, the combined group showed greater reductions in International Restless Legs Syndrome Scale (IRLS) and Depression Anxiety Stress Scales-21 (DASS-21) scores, and a greater increase in the Restless Legs Syndrome Quality of Life questionnaire (RLS-QLI) score ($P<0.05$). The total effective rate was higher in the combined group (97.67%) than in the monotherapy group (80.95%) ($P<0.05$). The results indicate that acupuncture combined with SGD can inhibit inflammation, improve serum protein levels, enhance sleep quality and clinical efficacy, alleviate symptoms and negative emotions, and improve quality of life. Zhou et al. [38] conducted a controlled clinical study on 80 RLS patients. The control group received tramadol, while the observation group received an additional self-prescribed decoction (Ye'an Zhentong Tang) combined with a modified SGD formula. Results showed more significant improvements in the observation group regarding TCM symptom scores, IRLS, RLS-QLI, PSQI, and clinical efficacy. Research demonstrates that the synergistic effect of acupuncture and SGD deeply regulates the neuro-immune-sleep axis in RLS, opening a new therapeutic avenue for this intractable condition.

3.9 Bone Marrow Edema Syndrome

Bone Marrow Edema Syndrome (BMES) is a transient bone and joint disorder pathologically characterized by fluid accumulation within the bone marrow. Its essence involves abnormally increased vascular permeability in the marrow cavity, leading to plasma exudation into the trabecular spaces, which causes local edema, microcirculatory disturbance, and elevated intraosseous pressure [39][40], It is a significant cause of non-traumatic ankle joint pain. Yan Xiaoguang [41] randomly divided 100 ankle BMES patients into groups. The control group received oral diclofenac sodium combined with ice therapy, while the observation group received oral SGD combined with ice therapy, both groups performed ankle functional exercises. After 14 days, the total effective rate was significantly higher in the observation group ($P<0.05$). At 3 and 6 months post-treatment, the American Orthopaedic Foot & Ankle Society (AOFAS) ankle-hindfoot scores were higher in the observation group ($P<0.05$), and the incidence of adverse reactions was significantly lower ($P<0.05$). Zhao Xinyou's [42] study on 90 ankle BMES patients showed that the observation group, which received SGD in addition to diclofenac sodium and ice therapy, had significantly better outcomes than the control group in terms of total effective rate, time to ankle function improvement, time to bone marrow edema resolution, and hospitalization duration ($P<0.05$). This indicates that the regimen is effective in relieving discomfort, improving ankle function and quality of life, accelerating recovery, shortening hospital stays, and has a favorable safety profile. Compared to Western medicine alone, SGD more effectively promotes edema resolution and functional reconstruction in BMES with higher safety, highlighting its therapeutic advantage in bone and joint edematous diseases.

4. Mechanisms of Action of SGD

4.1 Antispasmodic and Analgesic Effects

The antispasmodic and analgesic effects of SGD stem from synergistic multi-target mechanisms. Its high-content active components, such as albiflorin, paeoniflorin, liquiritin, and glycyrrhizic acid, inhibit abnormal muscle contraction through dual pathways: Paeoniflorin directly modulates calcium channels to inhibit Ca^{2+} influx, reducing the excitability of smooth and skeletal muscles, components like glycyrrhizic acid competitively block acetylcholine (ACh) receptors at the neuromuscular junction and inhibit ACh release, thereby relieving spasms [43]. SGD exerts efficacy through coordinated central and peripheral pathways: the central pathway enhances gamma-aminobutyric acid (GABA) ergic signaling to inhibit neuronal hyperexcitability, the peripheral pathway downregulates the expression of the pain-related neuropeptide substance P (SP) and the inflammatory mediator prostaglandin E_2 (PGE_2), significantly inhibiting the overactivation of key pain sensitization targets such as transient receptor potential vanilloid 1 (TRPV1) and the Toll-like receptor 4–myeloid differentiation factor 88 (TLR4–MyD88) signaling pathway. This forms a three-tiered regulatory network spanning muscle relaxation, blockade of pain signal transmission, and suppression of neurogenic inflammation [44].

4.2 Anti-inflammatory and Immunomodulatory Effects

SGD achieves anti-inflammatory and immunomodulation via a multi-level signaling network. Its active components (e.g., glabridin, paeoniflorin) target and regulate key pathways including NF-κB, MAPK, and JAK-STAT, significantly inhibiting the release of pro-inflammatory mediators such as TNF-α, IL-1β, IL-6, and cyclooxygenase-2 (COX-2). Molecular mechanisms include direct blockade of the nerve growth factor (NGF)/TRPV1/COX-2 signaling axis activation and suppression of TLR4/NF-κB signaling by remodeling the gut microbiota and protecting the intestinal barrier, thereby truncating systemic inflammatory cascades [45][46]. At the level of immune balance, SGD synchronously modulates adaptive and innate immunity: on one hand, it promotes Th2 anti-inflammatory responses and inhibits excessive Th1 activation, improving T-lymphocyte subset imbalance by regulating the PI3K-AKT-mTOR pathway [47], on the other hand, it drives macrophage polarization from the pro-inflammatory M1 phenotype toward the reparative M2 phenotype. A core mechanism involves the upregulation of NDUFS1 protein expression to inhibit the production of M1 polarization markers, facilitating immune homeostasis restoration [48]. This two-dimensional regulation, from blocking inflammatory signals to remodeling immune cell phenotypes, constitutes the pharmacological basis for SGD's efficacy in treating immune-inflammatory diseases such as RA [27].

4.3 Antioxidant and Cytoprotective Effects

SGD mediates antioxidant and cytoprotective effects through multi-level synergy. In countering oxidative stress, it directly enhances the activity of superoxide dismutase (SOD) and glutathione peroxidase (GSH-Px), reduces reactive oxygen species (ROS) levels, and strengthens cellular antioxidant capacity. It activates the nuclear factor erythroid 2–related factor 2/antioxidant response element (Nrf2/ARE) pathway, inducing the expression of phase II detoxifying enzymes such

as heme oxygenase-1 (HO-1), thereby re-establishing redox homeostasis. This mechanism simultaneously inhibits key processes of ferroptosis, manifested as reduced intracellular iron overload, alleviated glutathione depletion, and decreased malondialdehyde (MDA) production [49]. Regarding cytoprotection, SGD regulates apoptotic cascades and mitochondrial homeostasis: it upregulates Bcl-2 expression while downregulating Bax and Caspase-3 activity to inhibit apoptosis, it prevents apoptosome formation by stabilizing mitochondrial membrane potential and reducing cytochrome c (Cyt-c) release. Active components such as glabrone, liquiritin, and paeoniflorin sulfonate enhance mitophagy to clear damaged mitochondria, mitigating inflammation and cell necrosis [50], this constitutes a protective mechanism ranging from combating oxidative stress and inhibiting ferroptosis to regulating apoptosis and repairing mitochondria.

4.4 Neuroendocrine Regulation

The neuroendocrine regulatory effects primarily stem from glycyrrhizic acid mimicking glucocorticoid effects to modulate the hypothalamic–pituitary–adrenal (HPA) axis, reducing stress responses and maintaining homeostasis. SGD significantly promotes serotonergic (5-HT) and GABAergic neurotransmission, improving anxiety and insomnia. Animal experiments confirm this mechanism can ameliorate post-stroke spasticity: electron microscopy revealed enhanced synaptic structural integrity, increased vesicles, and prolonged synaptic contact areas in rats treated with electroacupuncture combined with SGD, alongside significantly upregulated protein expression of neurotrophin-3 (NT3) and brain-derived neurotrophic factor (BDNF) ($P < 0.001$), indicating improved motor function via enhanced synaptic plasticity [51]. Furthermore, SGD reduces visceral hyperalgesia in a rat model of irritable bowel syndrome by inhibiting TRPV1 expression and function, downregulating tryptophan hydroxylase (TPH) levels, and decreasing 5-HT content and enterochromaffin cell (EC) counts. In regulating intestinal motility, SGD improves slow-transit constipation by remodeling gut microbiota structure and affecting GABA and 5-HT levels in intestinal contents [52]. It should be noted that while its active components (flavonoids and monoterpenes) possess neuroprotective and gastrointestinal regulatory effects, glycyrrhizic acid derivatives may induce pseudo aldosteronism [53].

4.5 Synergistic Enhancement Mechanism

The anti-inflammatory and antispasmodic effects of paeoniflorin complement the immunomodulatory and antioxidant activities of glycyrrhizin, achieving multi-target intervention through pharmacodynamic synergy. Pharmacokinetic studies indicate that licorice components significantly enhance the oral bioavailability of paeoniflorin by inhibiting its first-pass metabolism mediated by cytochrome P450 3A4 (CYP3A4), increasing the area under the plasma concentration–time curve (AUC) by 30–50% and prolonging its half-life [54][55]. Based on TCM compatibility theory, Paeoniae Radix Alba (Bai Shao) soothes the liver and restrains “yin” to relieve cramping, while Glycyrrhizae Radix et Rhizoma (Gan Cao) fortifies the center and boosts “qi” to harmonize other herbs. The “Bai Shao–Gan Cao” herb pair achieves the effect of soothing the liver and alleviating urgency, simultaneously improving spastic pain caused by liver “qi” stagnation and gastrointestinal dysfunction related to liver constraint and spleen deficiency [56].

5. Discussion

SGD demonstrates advantages of holistic, multi-target, and multi-pathway regulation in the treatment of orthopedic and traumatological diseases. Its clinical value is reflected not only in significant efficacy against conditions such as post-fracture pain and spasms, cervical spondylosis, and lumbar disc herniation but also in the synergy of its mechanisms: paeoniflorin alleviates muscle spasms by inhibiting Ca^{2+} influx, while glycyrrhizic acid blocks acetylcholine receptors, complementing each other pharmacodynamically. Concurrently, licorice components enhance paeoniflorin’s bioavailability by 30–50% through CYP3A4 inhibition, forming a pharmacokinetic synergy. Compared to the gastrointestinal and hepatorenal toxicities associated with NSAIDs, SGD exhibits a superior safety profile. However, current research has limitations, such as relatively small sample sizes in clinical trials and the need for deeper validation of mechanisms like microecological regulation. Future efforts should focus on developing nano-formulations to enhance targeting, exploring precision medicine biomarkers by integrating genomics, and promoting the transformation of SGD application from “multi-target intervention” toward “personalized application,” thereby providing new perspectives for TCM in the prevention and treatment of orthopedic diseases.

6. Summary

SGD can be widely applied in various orthopedic and traumatological diseases, including post-fracture pain and spasms, cervical spondylosis, lumbar disc herniation, and osteoarthritis, significantly improving clinical symptoms. Its core mechanisms encompass antispasmodic and analgesic, anti-inflammatory and immunomodulatory, antioxidant and cytoprotective, and neuroendocrine regulatory effects. The combination of Paeoniae Radix Alba and Glycyrrhizae Radix et Rhizoma follows the TCM theory of “sour and sweet flavors transforming ‘yin’,” soothing the liver and alleviating urgency to harmonize spastic pain, while pharmacokinetic synergy enhances therapeutic efficacy. In summary, SGD embodies the TCM holistic concept through its integrated multi-target actions, providing a safe and effective solution for the prevention and treatment of orthopedic diseases and holding significant importance for integrative medicine approaches in this field.

Fund Project

The 2018 National Famous Traditional Chinese Medicine Experts Inheritance Studio Construction Project of the National Administration of Traditional Chinese Medicine (Guo Zhong Yao Ren Jiao Han [2018] No. 134) The Construction Project of the “Double-Chain Integration” Middle-aged and Young Scientific Research and Innovation Team of Traditional Chinese Medicine in Shaanxi Province by the Administration of Traditional Chinese Medicine

(Project No. :2022-SLRH-LJ-001) Discipline Construction Innovation Team Project of Shaanxi University of Chinese Medicine (Project No. :2019YL-02) Xianyang Key Laboratory Project for Integrated Traditional Chinese and Western Medicine Prevention and Treatment of Osteodegenerative Diseases (Project No. :2019K01-53).

References

[1] Long H, Zeng X, Liu Q, et al. Burden of osteoarthritis in China, 1990–2017: findings from the Global Burden of Disease Study 2017[J]. The Lancet Rheumatology, 2020, 2(3):e164-e172.

[2] Wei J. High prevalence and burden of osteoarthritis in China[J]. The Lancet Rheumatology, 2020, 2(3):e127-e128.

[3] Wang Y, Chen B, Liu X, Temporal trends in the burden of musculoskeletal diseases in China from 1990 to 2021 and predictions for 2021 to 2030[J]. Bone, 2025, 191:117332.

[4] Chinese Society of Osteoporosis and Bone Mineral Research, ZHANG Zhenlin. Guidelines for the Diagnosis and Treatment of Primary Osteoporosis (2022) [J]. Chinese General Practice, 2023, 26(14):1671-1691.

[5] XIN Liwei. Epidemiological Investigation of Osteoarthritis of Knee Joint in China [J]. Biped and Health, 2018, 27(20):73-74.

[6] QIU Guixing, PEI Fuxing, TANG Peifu, et al. A guideline for the management of common pain in orthopaedic clinical practice in China [J]. Chinese Journal of Bone and Joint Surgery, 2019, 12(03): 161-167.

[7] Zhu Guangwei, Zhang Guijun, , Wang Meng, et al. Research situation about origin, active components alignment and phramacological actions of Shaoyao Gancao Decoction [J]. China Journal of Traditional Chinese Medicine and Pharmacy, 2015, 30(08): 2865-2869.

[8] LIU Yong-sheng. Research progress of rheumatism arthralgia treated by traditional Chinese medicine [J]. Chinese Journal of Urban and Rural Enterprise Hygiene, 2020, 35(12):56-58.

[9] Li Hailei. Key Points of the Modified Peony and Glycyrrhiza Decoction for the Treatment of Acute Pain [J]. Forum On Traditional Chinese Medicine, 2021, 36(01):13-14.

[10] CHENG Hui, BAI Yu, ZHENG Wei, et al. Effect of Modified Shaoyao Gancao Decoction Combined with Acupuncture on Oswestry Dysfunction Index of Patients After Surgery for Osteoporotic Vertebral Compression Fracture [J]. Journal of Guangzhou University of Traditional Chinese Medicine, 2024, 41(05):1167-1174.

[11] LIU Zhong. Multimodal analgesia is used to relieve the pain after operation of fracture patients [J]. Journal of Taishan Medical College, 2018, 39(10):1132-1134.

[12] ZHANG Jing. Discussion on Nursing Care of Patients with Joint Stiffness after Limb Fracture [J]. China & Foreign Medical Treatment, 2021, 40(03):118-120.

[13] Shi X, Bai Y, He X, et al. Shaoyao Gancao Decoction for limb dysfunction after fractures around the knee: A protocol for systematic review[J]. Medicine (Baltimore), 2022, 101(11).

[14] Theodore N. Degenerative Cervical Spondylosis[J]. N Engl J Med, 2020, 383(2):159-168.

[15] ZHANG Le, YANG Jia, HUANG Chengjun. Efficacy Analysis of Acupuncture Pressure-Sensitive Points Combined with Shaoyao Gancao Decoction on the Treatment of Cervical Spondylotic Radiculopathy of Qi and Blood Deficiency and Blood Stasis Type [J]. Chinese Journal of Traditional Medical Traumatology & Orthopedics, 2022, 30(09):31-35.

[16] CHEN Jincheng, CHEN Shuijin, LIN Zhigang. Modified Shaoyao Gancao Decoction Combined with Massage in Treatment of Cervical Spondylosis in 30 Cases [J]. Fujian Journal of Traditional Chinese Medicine, 2021, 52(08):17-18.

[17] Jin Q, Chen L, Wu K, et al. Buttock pain in lumbar disc herniation: clinical characteristics, risk factors, and surgical outcomes[J]. J Neurosurg Spine, 2025, 42(5):572-578.

[18] Zhong Yuanming, He Bingkun, Wu Zhuotan, Wu Sixian, Wan Tong, Zhong Xifeng. An exploration on the mechanism of Shaoyao Gancao Decoction in treating early pain of lumbar disc herniation based on network pharmacology [J]. Chinese Journal of Tissue Engineering Research, 2021, 25(20):3194-3201.

[19] Su Meiyi, Fan Dehui, Zhang Zhenning, et al. Observation on the clinical efficacy of floating needle combined with modified Shao Yao Gan Cao Decoction in the treatment of Lumbar Intervertebral disc Protrusion [J]. Journal of Qiqihar Medical University, 2020, 41(14): 1756-1758.

[20] Perruccio A V, Young J J, Wilfong J M, et al. Osteoarthritis year in review 2023: Epidemiology & therapy [J]. Osteoarthritis Cartilage, 2024, 32(2): 159-165.

[21] Hou C, Yu Z, Song Q, et al. Identification of the key role of IL-17RB in the treatment of osteoarthritis with Shaoyao Gancao decoction: Verification based on RNA-seq and bioinformatics analysis[J]. PLoS One, 2025, 20(2): e315913.

[22] SONG Qinghui, LI Qiuyue, YANG Liping, et al. Validation of Key Targets and Pathways of Shaoyao Gancao Decoction in the Treatment of Osteoarthritis Based on Western Blot Experiments [J]. Journal of Liaoning University of Traditional Chinese Medicine, 2022, 24(09):10-13.

[23] WANG Zhiyuan. Evaluation on Analgesic Effect of Shaoyao Gancao Decoction and Preparation in the Treatment of Osteoarthritis [J]. Systems Medicine, 2018, 3(14):146-148.

[24] Zhu N, Hou J, Ma G, et al. Network Pharmacology Identifies the Mechanisms of Action of Shaoyao Gancao Decoction in the Treatment of Osteoarthritis[J]. Med Sci Monit, 2019, 25:6051-6073.

[25] Konzett V, Aletaha D. Management strategies in rheumatoid arthritis[J]. Nat Rev Rheumatol, 2024, 20(12):760-769.

[26] Brown P, Pratt A G, Hyrich K L. Therapeutic advances in rheumatoid arthritis[J]. BMJ, 2024, 384:e70856.

[27] Zhu M, Guo H, Dai L, et al. [Mechanisms of Shaoyao Gancao Decoction in treatment of rheumatoid arthritis based on UPLC-Orbitrap-MS~2, network pharmacology, and cellular experiment verification] [J]. Zhongguo Zhong Yao Za Zhi, 2024, 49(22):6149-6164.

[28] Chu Guike, Shao Yao Gan Cao Decoction was used to treat 60 cases of rheumatoid arthritis [J]. Chinese Medicine Modern Distance Education of China, 2012, 10(01):72-73.
[29] Challoumas D, Ramasubbu R, Rooney E, et al. Management of de Quervain Tenosynovitis: A Systematic Review and Network Meta-Analysis[J]. JAMA Netw Open, 2023, 6(10):e2337001.
[30] Lin R, Gu J, Wang Z, et al. Mechanism of action of Shaoyao-Gancao decoction in relieving chronic inflammatory pain via Sema3G protein regulation in the dorsal root ganglion[J]. Heliyon, 2024, 10(1):e23617.
[31] Zhang Kezhuang. Analysis of Modified Shaoyao Gancao Decoction in Treating Tenosynovitis of Hand Flexor Tendons [J]. GUANGMING JOURNAL OF CHINESE MEDICINE, 2015, 30(10):2150-2151.
[32] Berner J E, Nicolaides M, Ali S, et al. Pharmacological interventions for early-stage frozen shoulder: a systematic review and network meta-analysis[J]. Rheumatology (Oxford), 2024, 63(12):3221-3233.
[33] Song Weiping Observation on the Therapeutic Effect of Modified Shao Yao Gan Gan Decoction Combined with Meridian Pricking and Bloodletting Therapy in the Treatment of Stasis Type Periarthritis of the Shoulder [J]. Hubei Journal of Traditional Chinese Medicine, 2020, 42(01):56-58.
[34] Wu Xiao, Zhang Xude, Han Qisuo, et al. 180 cases of periarthritis of the shoulder were treated with modified Shao Yao Gan Gan Decoction [J]. Shaanxi Journal of Traditional Chinese Medicine, 2000(11):491.
[35] Wen Guirong. New Use of Peony and Licorice Decoction [J]. Hubei Journal of Traditional Chinese Medicine, 2005(03):40.
[36] Castillo-Alvarez F, Marzo-Sola M E. Restless legs syndrome. Pathophysiology, diagnosis and treatment[J]. Med Clin (Barc), 2025, 164(2):84-90.
[37] HUANG Xin, LI Yan. Effects of Acupuncture Combined with Shaoyao Gancao Decoction on Improvement of Motor Dysfunction, Sleep Quality and Serum Protein in Patients with Restless Leg Syndrome [J]. Chinese Journal of Medicinal Guide, 2023, 25(11):1186-1190.
[38] Zhou B, Li W, Li Y, et al. Effect of Self-developed Ye”an Analgetic Decoction/Jiawei Shaoyao Gancao Decoction Combined with Tramadol on TCM Symptom Scores and RLS Severity of patients with Restless Legs Syndrome[J]. Pak J Med Sci, 2024, 40(5):1017-1021.
[39] Li S, Yu H, Long S, et al. Research Advances in the Treatment of Bone Marrow Edema Syndrome[J]. J Clin Densitom, 2023, 26(2):101367.
[40] Evola F R, Compagnoni R, Pieroni A, et al. The Efficacy of Conservative Treatment of Bone Marrow Edema Syndrome: A Scoping Review of the Last Ten Years of Literature[J]. J Clin Densitom, 2022, 25(4):506-517.
[41] YAN Xiaoguang. Analysis on the Curative Effect of Peony and Licorice Decoction in the Treatment of Ankle Marrow Edema Syndrome [J]. Clinical Medicine & Engineering, 2019, 26(01):75-76.
[42] Liu Xiaobo, Ma Yingcun, Yang Bin. Effect of Shaoyao Gancao decoction on the treatment of ankle bone marrow edema syndrome[J]. Clinical Journal Of Chinese Medicine, 2018, 10(36):142-144.
[43] Xu Y, Li C, Chen T, et al. Quantitative Analysis of the Multicomponent and Spectrum-Effect Correlation of the Antispasmodic Activity of Shaoyao-Gancao Decoction [J]. J Anal Methods Chem, 2022, 2022:2279404.
[44] Chen Y, Lu R, Wang Y, et al. Shaoyao Gancao Decoction Ameliorates Paclitaxel-Induced Peripheral Neuropathy via Suppressing TRPV1 and TLR4 Signaling Expression in Rats[J]. Drug Des Devel Ther, 2022, 16:2067-2081.
[45] Luo Y, Qiu Y, Zhou R, et al. Shaoyao Gancao decoction alleviates the central hyperalgesia of recurrent NTG-induced migraine in rats by regulating the NGF/TRPV1/COX-2 signal pathway[J]. J Ethnopharmacol, 2023, 317:116781.
[46] Chang Z, Deng G, Shao Y, et al. Shaoyao-Gancao Decoction Ameliorates the Inflammation State in Polycystic Ovary Syndrome Rats via Remodeling Gut Microbiota and Suppressing the TLR4/NF-kappaB Pathway[J]. Front Pharmacol, 2021, 12:670054.
[47] Liu Xiaobo, Ma Yingcun, Yang Bin. The effect of modified Peony and Glycyrrhiza Decoction combined with auricular point pressing on beans in the treatment of postherpetic neuralgia [J]. Chinese Journal of Gerontology, 2025, 45(05):1117-1121.
[48] XIAHOU Zhi-Kai, XIAO Hong, SONG Ya-Feng, et al. Shakuyakukanzoto Relieves Ulcerative Colitis in Mice by Regulating The Expression of NDUFS1 and Inhibiting The Polarization of Macrophages to M1 [J]. Progress In Biochemistry and Biophysics, 2024, 51(05):1174-1190.
[49] Hu S, Luo Y, Yang X, et al. Shaoyao Gancao Decoction protects against dextran sulfate sodium-induced ulcerative colitis by down-regulating ferroptosis[J]. J Pharm Pharmacol, 2023, 75(8):1111-1118.
[50] Wu Y, Li W, Zhang J, et al. Shaoyao-Gancao Decoction, a famous Chinese medicine formula, protects against APAP-induced liver injury by promoting autophagy / mitophagy[J]. Phytomedicine, 2024, 135:156053.
[51] Shao Y, Guo Y, Gao J, et al. Shaoyao-Gancao Decoction Relieves Visceral Hyperalgesia in TNBS-Induced Postinflammatory Irritable Bowel Syndrome via Inactivating Transient Receptor Potential Vanilloid Type 1 and Reducing Serotonin Synthesis[J]. Evid Based Complement Alternat Med, 2020, 2020:7830280.
[52] ZHANG Ziqi, ZHOU Hongyun, ZHAO Qiong, et al. Effects of Modified shaoyao gancao decoction on intestinal transit function, intestinal flora and metabolite content in slow transit constipation rat [J]. China Pharmacy, 2025, 36(02):154-159.
[53] Facheng Z, Rongli Q, Li Z, et al. Shaoyao Gancao decoction, an Ancient Classical Prescription: a review on its chemical composition, pharmacology, pharmacokinetics, clinical applications, and toxicology [J]. J Pharm Pharmacol, 2025.
[54] Bi X, Gong M, Di L. Review on prescription compatibility of shaoyao gancao decoction and reflection on pharmacokinetic compatibility mechanism of traditional chinese medicine prescription based on in vivo drug interaction of main efficacious components[J]. Evid Based Complement Alternat Med, 2014, 2014: 208129.
[55] CUI Enze, FANG Jingjing, WANG Jie, et al. Mechanism of Classical Famous Formula Shaoyao

Gancaotang in Alleviating Spasm and Pain:A Review [J]. Chinese Journal of Experimental Traditional Medical Formulae, 2025, 31(14):267-278.

[56] Gao Cuixia, huang Lingling, Cao wenxuan. Research Progress on the Combination of Peony and Licorice [J]. Traditional Chinese Medicinal Research, 2023, 36(08): 92-96.