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REVIEW

Comprehensive Treatment of Gout with Traditional Chinese Medicine: A Modern Pathophysiological Perspective

Jiamin Yang[1], Rui Xu[2], Kaiqing Li[1], Jiachen Han[1], Ying Tong[2]

[1]Department of Graduate School, Heilongjiang University of Chinese Medicine, Harbin, Heilongjiang, 150006, People's Republic of China; [2]Department of Rheumatology, First Affiliated Hospital, Heilongjiang University of Chinese Medicine, Harbin, Heilongjiang, 150040, People's Republic of China

Correspondence: Ying Tong, Department of Rheumatology, First Affiliated Hospital, Heilongjiang University of Chinese Medicine, Harbin, Heilongjiang, 150040, People's Republic of China, Email tongying@hljucm.edu.cn

Abstract: Gout, a prevalent metabolic disorder characterized by elevated uric acid levels, has numerous adverse health implications. Current medical therapies can control symptoms and lower uric acid, yet they are often limited by adverse effects and incomplete long-term efficacy. Traditional Chinese Medicine (TCM) has a long history of application in gout and is reported to provide advantages in both prevention and management. To evaluate its role from a modern biomedical perspective, this review systematically examined literature retrieved from PubMed, CNKI, and Web of Science up to 2024, covering randomized controlled trials, observational studies, and mechanistic investigations. The reviewed evidence indicates that TCM interventions, including classical herbal formulations and acupuncture, have been associated with improvements in inflammatory regulation, uric acid metabolism, symptom relief, and recurrence prevention. Moreover, experimental studies suggest potential protective effects on renal function and joint structures. By integrating clinical data with mechanistic insights, this review aims to provide a comprehensive overview of the therapeutic potential of TCM in gout and to outline directions for future translational and clinical research.

Keywords: gout, gout attack, MSU, inflammatory reaction, TCM

Introduction

Gout is the most common form of inflammatory arthritis and arises from persistent hyperuricemia, which promotes deposition of monosodium urate (MSU) crystals in joints and surrounding tissues,[1] and globally, approximately 4% of adults are affected, with prevalence continuing to rise in many developed countries.[2] Acute gout attacks are characterized by sudden onset of severe pain, swelling, and erythema, often in the first metatarsophalangeal joint, and can progress to chronic tophaceous gout with joint deformity and functional impairment.[3] Beyond articular manifestations, gout is increasingly recognized as a systemic disease associated with metabolic syndrome, cardiovascular disease, chronic kidney disease, and reduced life expectancy.

Conventional medical management relies on acute anti-inflammatory therapy and long-term urate-lowering treatment to reduce serum uric acid and prevent crystal formation.[4] Although effective, these strategies face important limitations. Many patients experience treatment-related adverse effects, poor adherence, and suboptimal control of symptoms.[4] Furthermore, these pharmacological approaches focus mainly on biochemical reduction of uric acid rather than on the broader metabolic and immunological processes underlying gout. Recent studies also highlight that the pathogenesis of gout involves complex interactions between genetic predisposition, inflammatory signaling, gut microbiota, and metabolic dysfunction, suggesting that single-target therapies may not provide sufficient long-term benefit.

Traditional Chinese Medicine (TCM) has been used for centuries to prevent and treat gout within a holistic framework that emphasizes syndrome differentiation and individualized care.[5] From the TCM perspective, gout is associated with patterns such as damp-heat accumulation, phlegm-blood stasis, and liver-kidney deficiency. Therapeutic approaches

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are directed toward restoring systemic balance rather than focusing solely on urate levels. Modern pharmacological studies provide increasing evidence that TCM interventions exert multitarget effects, including inhibition of xanthine oxidase, regulation of renal and intestinal urate transporters, suppression of NLRP3 inflammasome activation, and modulation of inflammatory cytokine networks.[5–7] These findings suggest potential advantages of TCM as either an alternative or an adjunct to conventional therapies.

Despite these advances, several research gaps remain unresolved. First, although many studies have examined TCM therapies for gout, there has been no comprehensive integration of TCM principles with the modern pathophysiological framework, limiting their translation into evidence-based guidelines. Second, the mechanistic basis for TCM's multi-target effects is incompletely understood, particularly the relationship between traditional syndrome classification and contemporary biomarkers of inflammation and metabolism. Third, strategies for combining TCM with Western medicine remain poorly defined, leaving uncertainty about how to optimize integrative approaches to improve outcomes and minimize adverse effects.

The purpose of this review is to address these gaps by synthesizing evidence from both traditional and modern perspectives. Specifically, we aim to: (1) examine current understanding of gout pathophysiology, including epidemiological, genetic, and mechanistic aspects; (2) analyze TCM theoretical frameworks and their correlations with pathophysiological processes; (3) evaluate clinical and experimental evidence for TCM therapies such as herbal formulations and acupuncture; and (4) propose strategies for integrating TCM with conventional medicine to enhance treatment effectiveness. The methodological search strategy for this study is provided in the Supplementary Material. (See Supplementary Material: Table 1).

Epidemiology

Accurately comparing the prevalence and incidence of gout across nations is complicated by variability in study methodologies. Many surveillance-based studies rely on self-reported diagnoses, which are subject to recall bias, and as a result, no single estimate can capture the global prevalence of the disease. Reported rates vary considerably by region, and substantial data gaps remain in numerous countries. The highest prevalence has been documented in Oceania, particularly among certain ethnic groups such as the Taiwanese Aborigines[8] and the Māori,[9] where estimates exceed 10%.[8,10] In contrast, prevalence rates in North America and Western Europe generally range from 1% to 4%,[11] while gout is relatively infrequent in regions such as the former Soviet Union,[12] Guatemala,[13] Iran,[14,15] Malaysia,[16] the Philippines,[12] Saudi Arabia,[17] rural Turkey,[18] and several African countries.[19,20] Discrepancies among studies can be attributed to differences in participant age distribution,[21] sex, geographic setting, sampling methodology, diagnostic definitions, ethnic composition, and the survey year.

In many developed nations, particularly North America and Europe, gout prevalence exceeds 1%. In the United States, the 2007–2008 National Health and Nutrition Examination Survey (NHANES), which employed stratified multi-stage sampling, reported a self-reported prevalence of 3.9% among adults.[1] Within Europe, the highest prevalence has been observed in Greece (4.75%).[22] In the United Kingdom, data from the Clinical Practice Research Datalink (CPRD) estimated a prevalence of 3.22%,[23] with similar findings in Spain[24] and the Netherlands.[25] A German study reported a prevalence of 1.4%.[26] Lower prevalence rates have been observed in France and Italy, with a telephone survey of over 10,000 French adults identifying a prevalence of 0.9%,[27] while Italian national primary care data indicated a prevalence of 0.91% in 2009.[28] The lowest prevalence rates in Europe have been reported in Portugal[29] and the Czech Republic,[30] at 0.3%.

In Asia, gout prevalence varies considerably. Japan and South Korea report some of the lowest rates globally. In Osaka, Japan, a survey estimated an all-age prevalence of 0.51%,[31] while in South Korea only 0.4% of adults were affected in 2008.[32] By contrast, higher rates have been reported in Taiwan, Hong Kong, and Singapore. For example, a 2001 survey in Hong Kong found prevalence rates of 5.1% in individuals aged 45–59 years and 6.1% in those aged 60 years or older.[33]

Epidemiological data from developing countries remain sparse, but the incidence of gout in these regions appears lower than in more affluent nations. The Community Oriented Program for the Control of Rheumatic Diseases (COPCORD) has been the principal framework for collecting gout prevalence data in developing regions, employing

a standardized and validated questionnaire to screen for rheumatic diseases.[34] To date, COPCORD has provided data for 15 countries. Additional regional studies have been conducted in China. In Shandong Province, a coastal area of northern China, the prevalence of gout among adults was estimated at 1.14%,[35] higher than in most other parts of mainland China but lower than in Hong Kong.[33,36–40]

In summary, the global prevalence of gout is highly variable, with the highest rates observed in Oceania and certain parts of North America and Europe, and lower rates in Asia, Africa, and developing regions. Methodological heterogeneity, ethnic variation, and regional dietary and lifestyle factors contribute to these discrepancies. While robust data exist for developed nations, further standardized epidemiological research is needed in underrepresented regions to fully understand the global burden of gout.

Clinical Signs and Diagnosis

The earliest clinical manifestation of gout usually appears as an acute inflammatory arthritis predominantly affecting the joints of the lower extremities, most characteristically the first metatarsophalangeal joint, and is accompanied by intense pain.[41] In untreated cases, acute attacks are typically self-limiting, lasting between 7 and 14 days, after which patients enter an asymptomatic phase referred to as intercritical gout until the onset of the next attack. Over time, individuals with persistent hyperuricemia may progress to tophus formation, chronic gouty arthritis, and structural joint damage.

During acute attacks, gout can involve joints as well as periarticular soft tissues, producing pain commonly described as stinging, gnawing, burning, or throbbing.[42] The pain often escalates rapidly, reaching peak intensity within 12 hours.[41] Acute flares are frequently accompanied by swelling, erythema, and varying degrees of fever.[43] The severity of these symptoms can significantly compromise mobility, such that even minimal physical contact with the affected area becomes intolerable.[41]

The distribution of joint involvement is an important diagnostic feature. Although gout predominantly affects the lower extremities, particularly the first metatarsophalangeal joint,[44] other sites such as the elbows, wrists, and hands may be involved in patients with long-standing or poorly controlled disease. Axial joint involvement is rare but has been reported.[43] While attacks are usually monoarticular, oligoarticular or polyarticular presentations may occur, especially in hospitalized patients or those with uncontrolled hyperuricemia. Polyarticular flares are more likely to produce systemic manifestations, including fever, chills, and occasionally delirium.[45]

The recurrence of gout attacks is variable and difficult to predict, though their frequency correlates with the severity of hyperuricemia.[46] Common triggers include consumption of purine-rich foods, alcohol intake, joint trauma, and acute illness.[47–49] Some individuals may experience a single attack without recurrence,[50] but most develop repeated flares.[41] With continued exposure to elevated serum uric acid and accumulation of monosodium urate (MSU) crystals, attacks may increase in duration, overlap with one another, and shorten or eliminate the intercritical phase. Although chronic gouty arthritis and tophaceous gout may occasionally manifest early,[51] they most often indicate long-standing disease and inadequate uric acid control.[52] Subcutaneous tophi appear as chalky nodules beneath translucent skin, sometimes accompanied by dilated overlying blood vessels, and are typically found in joints, ears, the olecranon bursa, finger pads, and tendons.[44]

The gold standard for diagnosis is arthrocentesis with identification of MSU crystals in synovial fluid under polarized light microscopy. However, due to its non-invasive nature, imaging has become increasingly important in supporting the diagnosis. The American College of Rheumatology (ACR) and the European League Against Rheumatism (EULAR) have established classification criteria that integrate clinical, laboratory, and imaging findings.[53] Among available imaging techniques, musculoskeletal ultrasound (US) is the most widely applied for detecting urate deposition. Typical findings include the double contour sign, the "blizzard" sign, heterogeneous soft tissue collections, and intratendinous tophi.[54] Despite its utility, ultrasound interpretation is influenced by operator experience and equipment quality, leading to variability in diagnostic reliability. To address these challenges, recent work has applied artificial intelligence–based convolutional neural networks to recognize tophi in ultrasound images with high accuracy.[55] In addition to imaging, omics technologies have been explored to identify potential biomarkers in biological fluids. These approaches have provided valuable insights into the pathophysiological mechanisms of hyperuricemia and gout; however, no specific diagnostic biomarker has yet been validated for clinical use.[56]

Gout is clinically defined by acute arthritis characterized by severe pain, swelling, and erythema, most often affecting the first metatarsophalangeal joint. Diagnosis is confirmed by the presence of MSU crystals on arthrocentesis, while imaging modalities, particularly ultrasound, provide valuable non-invasive support. Emerging tools such as artificial intelligence and omics approaches are enhancing diagnostic accuracy, although a definitive biomarker for gout has not yet been established.

Genetics

Gout is influenced by both genetic and lifestyle factors. Mutations in genes encoding renal transporters are recognized as important contributors to disease susceptibility. Bardin et al[57] identified mutations in the lactate dehydrogenase D (LDHD) gene that correlate with gout, potentially elevating d-lactate levels in blood or urine and exacerbating gouty arthritis. Other studies have established associations between inflammatory regulators such as free fatty acid receptor 2 (FFAR2) and suppressor of cytokine signaling 3 (SOCS3) and the occurrence of gout flares, highlighting their involvement in both initiation and resolution phases of inflammation.[58] Genetic variants located near the major histocompatibility complex class 1 (MHC-1) region, as well as region-specific copy number variants (CNVs), have been linked to increased serum urate concentrations and greater risk of gout across multiple populations.[59,60]

Genetic correlations between goutand other conditions have also been identified. A candidate gene linking gout to attention-deficit/hyperactivity disorder suggests shared biological pathways.[61] Furthermore, genetic determinants of body mass index overlap with those of gout, and adherence to a healthy diet has been associated with reduced disease risk, even among genetically predisposed individuals.[62,63]

Epigenetic mechanisms play an additional role in the pathogenesis of gout. MicroRNAs (miRNAs) regulate gene expression relevant to inflammation and uric acid metabolism.[64] An epigenome-wide association study identified specific CpG DNA methylation sites associated with serum uric acid (SUA) levels, particularly within genes related to small molecule transport and cardiometabolic regulation, emphasizing the contribution of epigenetic modification to disease susceptibility.[65]

Insights from post-genome-wide association study (GWAS) research have further refined the genetic understanding of gout. The ATP-binding cassette subfamily G member 2 (ABCG2) transporter has been identified as a key factor in hyperuricemia and gout, with implications for pediatric diagnosis and for guiding allopurinol therapy.[66] Genetic variation in ABCG2 has also been shown to influence allopurinol pharmacokinetics and treatment response.[67] Polygenic risk scores (PRSs) derived from GWAS data are being evaluated as predictive tools; for instance, a PRS including 19 European genetic variants has been associated with earlier onset of gout, with stratification by sex offering further refinement of risk prediction.[68,69]

GWAS have also contributed to therapeutic discovery. Computational screening has identified candidate compounds targeting IL-4 and IL-3 signaling pathways as potential treatments.[70] A multi-omics approach analyzing serum and urine from patients with hyperuricemia identified metabolites and gene networks, including those related to caffeine metabolism, as possible therapeutic targets.[71] In parallel, the integration of artificial intelligence (AI) and machine learning (ML) has enhanced biomarker discovery and clinical prediction. ML models have been developed to predict renal dysfunction phenotypes in gout using genetic and clinical variables,[72] and to distinguish between frequent and infrequent gout attacks based on metabolomic signatures.[73] AI-based imaging tools have also demonstrated high accuracy in detecting MSU crystal deposits on ultrasound, providing a potential method for automated diagnosis and monitoring of gout and related rheumatic diseases.[74]

In summary, advances in genetics, epigenetics, and computational approaches have expanded understanding of gout by clarifying the contribution of transporters and regulatory pathways, identifying new therapeutic targets, and supporting the development of predictive and diagnostic tools.

Pathophysiology (See Figure 1)

Hyperuricemia

Hyperuricemia represents the primary precursor to the development of gout. Urate, the final product of purine nucleotide catabolism, is strongly influenced by dietary intake, particularly purine-rich foods, which elevate serum urate levels and

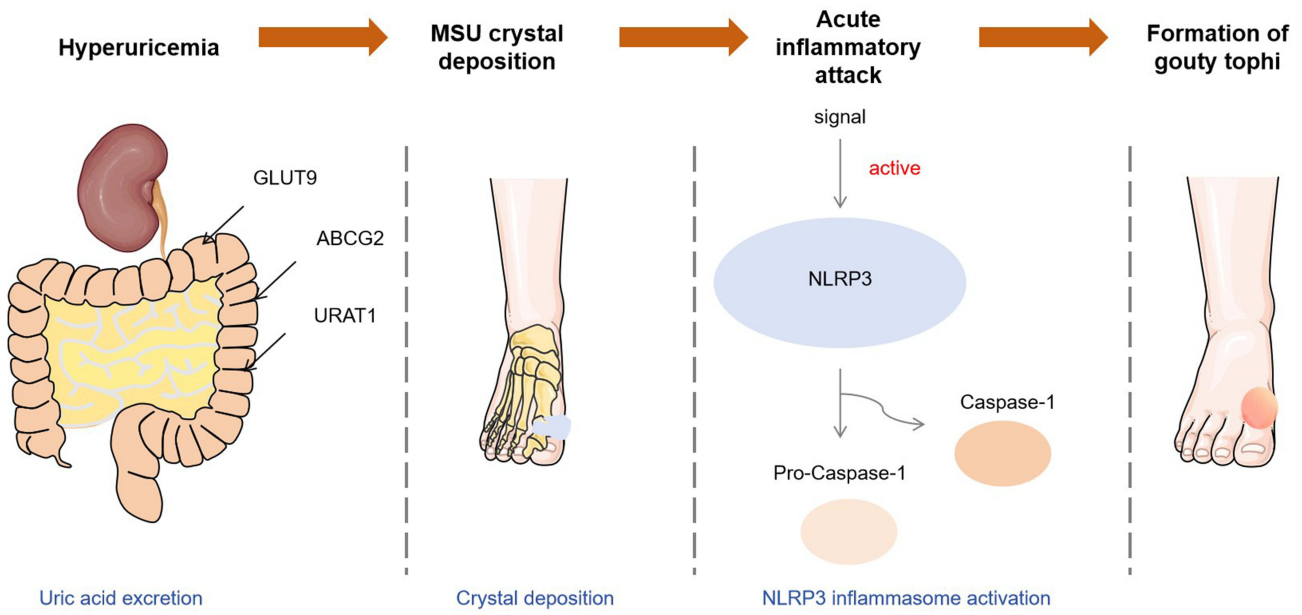

Figure 1 Clinical course of gout and integrative treatment strategies. The diagram illustrates therapeutic approaches across the acute, relief, and stable phases. In the acute phase, Western medications such as NSAIDs and colchicine are combined with TCM herbs for clearing heat and draining dampness. During the relief period, TCM therapies that regulate metabolism and immunity complement urate-lowering agents (allopurinol, febuxostat). In the stable phase, individualized TCM prescriptions and lifestyle interventions are applied for prevention. The lower panel compares uric acid control, pain relief, and recurrence rates between Western medicine alone and combined TCM–Western therapy, based on clinical studies discussed in Medical Practice of TCM Comprehensive Treatment of Gout (See Figure 4).[78–86]

increase the risk of gout flares.[75–77] In addition, medical conditions characterized by heightened cellular turnover, such as psoriasis and myeloproliferative disorders, also contribute to hyperuricemia by driving excessive urate production.

The regulation of urate homeostasis relies predominantly on renal and intestinal excretion, with impaired renal clearance playing the most significant role in elevating serum urate. The close correlation between serum creatinine and uric acid levels underscores the importance of renal excretory function in maintaining urate balance.[87] Within the kidney, urate is filtered at the glomerulus and handled by a complex network of transporters located in the proximal tubule. Key reabsorptive transporters include URAT1 (SLC22A12), OAT4 (SLC22A11), OAT10 (SLC22A13), and GLUT9 (SLC2A9), which facilitate movement of urate from the tubular lumen into epithelial cells.[88–91] Conversely, secretory transporters such as ABCG2, ABCC4, and NPT1 (SLC17A1) promote urate excretion.[92–94] On the basolateral membrane of proximal tubule cells, additional transporters including OAT1 (SLC22A6), OAT2 (SLC22A7), OAT3 (SLC22A8), and GLUT9 further contribute to urate flux into the circulation.[95–97]

Although renal handling of urate is more efficient than intestinal excretion, the gastrointestinal tract also plays a critical role. The transporter ABCG2 is strongly implicated in intestinal urate excretion, and genetic variants of this transporter are associated with extrarenal urate underexcretion and hyperuricemia.[98] Other intestinal urate transporters likely exist but have yet to be fully identified.[99]

The significance of renal and intestinal transporters is further highlighted by the association of genetic polymorphisms in SLC2A9 (GLUT9), ABCG2, and SLC22A12 (URAT1), which exhibit the strongest correlations with serum urate concentrations and gout risk across populations worldwide.[100,101]

Overall, hyperuricemia arises from increased urate production or impaired renal and intestinal excretion, with renal transporters playing a pivotal role. Genetic polymorphisms affecting transporter function further influence individual susceptibility to elevated urate and gout.

MSU Crystal Deposition

Deposition of monosodium urate (MSU) crystals is a defining pathological feature of gout. Microscopically, these crystals are needle-shaped, negatively birefringent, and composed of closely packed purine rings.[102] Imaging modalities such as ultrasound and dual-energy computed tomography (DECT) have revealed that approximately 25% of

hyperuricemic individuals already harbor MSU deposits, highlighting that hyperuricemia alone is insufficient to trigger crystal deposition.[103,104] Deposition typically occurs at specific anatomical sites, most notably the first metatarsophalangeal joint, midfoot, MSU crystallization progresses through three sequential stages: low solubility, nucleation, and crystal growth. Elevated urate concentrations play a central role in all phases.[105] Experimental assays demonstrate that MSU crystallization occurs when urate concentrations exceed 0.41 mmol/L at 37 °C and pH 7.0, or 0.36 mmol/L at 35 °C.[106] Solubility is further reduced at lower temperatures, in the pH range of 7–8, and in the presence of elevated sodium concentrations.[105] Other biological factors, including connective tissue components, bovine cartilage homogenates, human synovial fluid, and urate-binding antibodies, also facilitate MSU nucleation and growth.[105]

Together, MSU crystal deposition occurs preferentially at certain anatomical sites and results from a combination of elevated serum urate and local physicochemical and biological factors, which together drive nucleation and growth.

Acute Inflammatory Response to MSU Crystals

MSU crystallization triggers tissue injury and activates innate immune pathways. Engagement of the NLRP3 inflammasome within macrophages and monocytes is strongly implicated in the initiation of gout flares.[107] Inflammasome activation follows a tightly regulated two-signal process. The first signal involves activation of NF-κB via Toll-like receptors (TLR4 and TLR2), leading to transcription of pro-IL-1β and inflammasome components.[108,109] The second signal is provided by MSU crystals, which drive inflammasome assembly and activate caspase-1. Activated caspase-1 cleaves pro-IL-1β into its mature form, IL-1β, which binds to its receptor and initiates downstream cytokine and chemokine release, thereby recruiting neutrophils and other immune cells to the site of deposition.[110]

Importantly, this two-step mechanism explains why MSU crystals may exist in joints without causing overt inflammation, as additional priming factors are required to initiate flares.[104,111] Triggers such as free fatty acids, microbial components, and alterations in gut microbiota can provide the initial signal, while anti-inflammatory pathways mediated by AMP-activated protein kinase (AMPK) act as a brake on inflammasome activation.[112–115]

Neutrophils play a dual role: they release pro-inflammatory mediators that drive acute attacks, but they also facilitate resolution through the formation of neutrophil extracellular traps (NETs), which sequester and degrade inflammatory molecules.[116] Resolution is further promoted by endogenous anti-inflammatory mediators, including interleukin-1 receptor antagonist (IL-1ra), interleukin-10 (IL-10), transforming growth factor-beta (TGF-β), and interleukin-37 (IL-37), which together contribute to the self-limiting nature of gout flares.[117,118]

In summary, MSU crystals activate the NLRP3 inflammasome via a two-step process, leading to IL-1β release and acute inflammation. However, regulatory mechanisms such as AMPK, NETs, and anti-inflammatory cytokines promote resolution, explaining the episodic course of gout.

Advanced Gout

Advanced gout is characterized by tophi, chronic gouty synovitis, and irreversible structural joint damage. Tophi represent organized granulomatous structures containing a dense MSU crystal core, a surrounding cellular crown, and an outer fibrovascular zone.[119] These structures are infiltrated by both innate and adaptive immune cells, including multinucleated giant cells, which maintain persistent inflammation.[120]

Joint structural damage in advanced gout is marked by bone erosion and cartilage degradation, frequently occurring at sites of tophus deposition. At these locations, direct interactions between osteoclasts, tophi, and bone surfaces promote bone resorption.[121] Experimental studies further demonstrate that MSU crystals impair osteoblast viability and function[122] while shifting osteoblast activity toward bone resorption, thereby perpetuating both inflammation and structural injury.[123]

In summary, advanced gout reflects the culmination of unresolved inflammatory processes and MSU-driven alterations in bone and cartilage metabolism, leading to progressive joint deformity and functional impairment.

Pathophysiological Mechanisms of TCM in the Treatment of Gout (See Figure 2)

Gout-related inflammation is a central driver of disease morbidity, and TCM regulates this process through a network of interrelated mechanisms. Many classical formulations and their active compounds have been shown to modulate

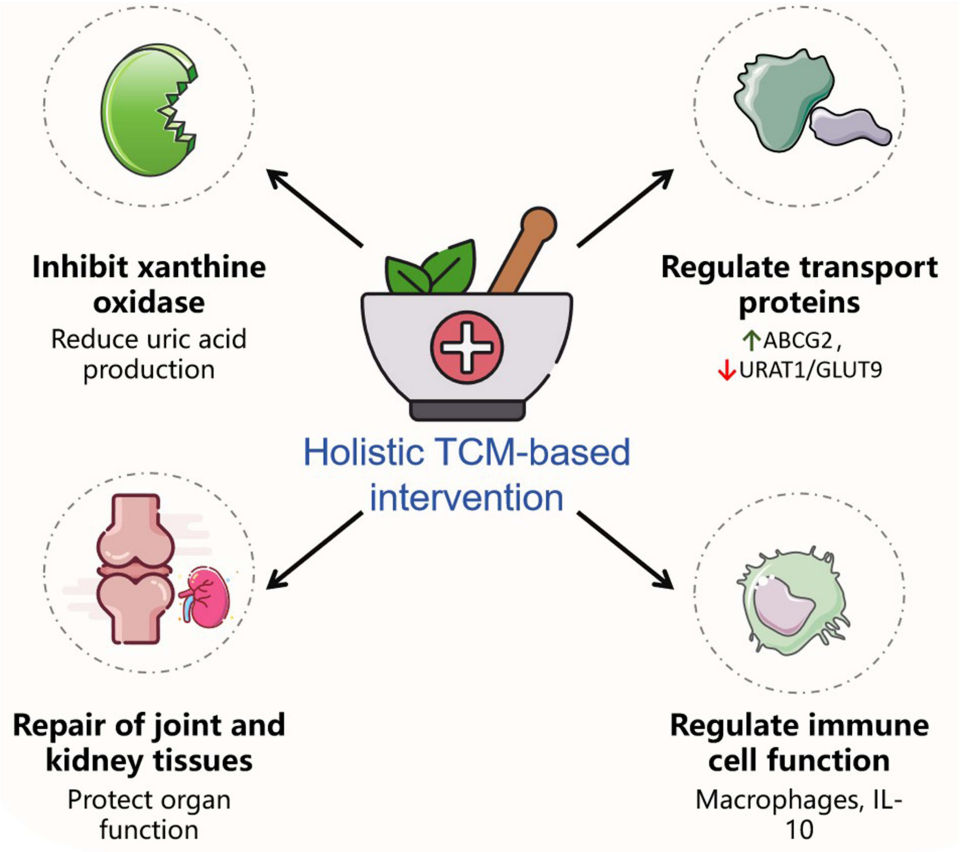

Figure 2 Pathogenetic cascade from hyperuricemia to gouty tophi. Impaired renal and intestinal urate transport (URAT1, GLUT9, ABCG2) leads to hyperuricemia and monosodium urate (MSU) crystal deposition in joints. MSU crystals activate the NLRP3 inflammasome, promoting caspase-1 activation and release of pro-inflammatory cytokines, which drive acute inflammatory attacks. Persistent inflammation results in tophus formation. Adapted from mechanistic evidence summarized in Pathophysiology (See Figure 1).[75–77,87–125] The green arrow indicates an increase, and the red arrow indicates a decrease.

inflammatory signaling. Extracts from prescriptions such as Guizhi Shaoyao Zhimu Decoction and Simiao Powder suppress activation of the nuclear factor kappa B (NF-κB) pathway and the NLRP3 inflammasome, thereby attenuating inflammation initiated by monosodium urate (MSU) crystals. Inhibition of NF-κB phosphorylation and blockade of its nuclear translocation reduce the transcription of pro-inflammatory cytokines, including tumor necrosis factor-alpha (TNF-α) and interleukin-1 beta (IL-1β), while direct inhibition of NLRP3 disrupts the downstream release of inflammatory mediators. These effects collectively dampen the acute inflammatory cascade.

Beyond signaling pathways, TCM influences the functional behavior of immune cells involved in gouty inflammation. Activated macrophages and neutrophils contribute substantially to cytokine production during acute attacks. TCM formulations can inhibit excessive macrophage activation, decrease secretion of pro-inflammatory mediators, and promote the release of anti-inflammatory cytokines such as interleukin-10 (IL-10). Clinical and experimental studies have confirmed that patients treated with TCM exhibit changes in macrophage phenotype and downregulation of inflammation-related gene expression, leading to a more balanced immune response.[126]

TCM also exerts marked effects on uric acid metabolism. Several herbal compounds inhibit xanthine oxidase (XOD), thereby reducing uric acid synthesis. For instance, extracts from Smilax glabra and Phellodendron chinense have been shown to directly bind to XOD and suppress its enzymatic activity in a dose-dependent manner, leading to reduced uric acid production.[126]

In addition, TCM promotes uric acid excretion by regulating urate transporters. Upregulation of ABCG2 enhances intestinal urate clearance, while downregulation of URAT1 and GLUT9 decreases renal tubular reabsorption, collectively lowering serum uric acid concentrations. These effects have been demonstrated both in vitro and in vivo, providing mechanistic support for clinical outcomes.

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The therapeutic scope of TCM extends beyond controlling inflammation and uric acid levels to influencing joint tissue damage and repair. During gout attacks, deposition of MSU crystals damages articular cartilage and synovium, while chronic inflammation accelerates degeneration. TCM formulations have been reported to stimulate proliferation of chondrocytes and enhance extracellular matrix synthesis, while simultaneously suppressing synovial hyperplasia and inflammatory infiltration. These dual actions promote cartilage repair and improve joint function.[127]

Chronic hyperuricemia also contributes to renal injury and gouty nephropathy. Certain TCM agents, including Tongfengshu Decoction and patent medicines such as Jingulian capsule and Hulisan, alleviate renal injury by suppressing NF-κB pathway activation in renal tissues, reducing expression of pro-inflammatory mediators, and attenuating fibrotic changes. Furthermore, TCM enhances metabolic function of renal tubular cells, promotes repair and regeneration, and protects overall renal function.[128] In addition to prescriptions and patent medicines, modern pharmacological research has identified numerous bioactive compounds from TCM, including flavonoids, alkaloids, and saponins, with clear urate-lowering and anti-inflammatory activity. These compounds act through diverse mechanisms such as xanthine oxidase inhibition, transporter regulation, and blockade of NLRP3 and NF-κB signaling, illustrating the molecular basis for the multitarget effects of TCM.

In summary, TCM intervenes at multiple levels of gout pathophysiology: it reduces uric acid production, promotes uric acid excretion, modulates inflammatory signaling pathways, regulates immune cell activity, protects cartilage and synovium, and preserves renal function. The combined effects of classical prescriptions, modern patent medicines, and isolated compounds reflect the multitarget and integrative nature of TCM, underscoring its potential in the modern management of gout.

Basic Theory of TCM in the Treatment of Gout

Study on Etiology and Pathogenesis of Gout in TCM

In TCM, gout is primarily classified under "arthralgia syndrome" and "Lijie disease". Its etiology and pathogenesis are considered multifactorial, involving both endogenous deficiencies and exogenous pathogenic influences. From a holistic perspective, insufficiency of healthy qi represents the internal basis for disease onset. When healthy qi is weakened, the body becomes vulnerable to the invasion of external pathogens, thereby precipitating the development of gout.[126]

Exogenous pathogens such as wind, cold, dampness, and heat can penetrate the body, obstructing the circulation of qi and blood in the meridians and joints. This obstruction manifests clinically as joint pain, swelling, and functional impairment. Dietary factors also contribute significantly; long-term consumption of rich, greasy foods and alcohol disrupts the transportation and transformation functions of the spleen and stomach, leading to the accumulation of damp-heat and phlegm, which may infiltrate the joints and aggravate gout symptoms.

Additional risk factors include emotional disturbances, excessive fatigue, and organ dysfunction, all of which impair the metabolism of qi, blood, and body fluids. These disruptions promote the generation of pathological substances—phlegm, dampness, and blood stasis—that obstruct meridians and joints, further driving disease progression. Recent evidence highlights a correlation between gout and alterations in intestinal flora.

Herbs commonly used in TCM contain fiber, polyphenols, polysaccharides, and other bioactive compounds that modulate gut microbiota following oral administration. Such interventions increase beneficial bacteria, including Bifidobacterium and Lactobacillus, while reducing harmful genera such as Proteus. These microbial changes influence key metabolites, including short-chain fatty acids and lipopolysaccharides, which in turn affect uric acid metabolism and systemic inflammatory responses.[126]

From a constitutional standpoint, several TCM constitution types are frequently observed in gout patients, most notably the phlegm-dampness type. This constitution is typically associated with obesity and impaired spleen and stomach function, factors that predispose to both the onset and chronicity of gout. Other common constitutions include qi deficiency, damp-heat, and Yang deficiency. Recognition of these constitutional characteristics not only provides insight into individual variation in clinical manifestations and prognosis but also establishes the foundation for syndrome differentiation and individualized treatment in TCM.[129]

The Historical Use of TCM in the Treatment of Gout

The application of TCM in gout management has a long history, with references traceable to classical medical texts. These sources describe the symptoms, causes, and therapeutic strategies for gout, laying the theoretical and practical foundation for subsequent clinical practice. Ancient physicians emphasized syndrome differentiation and individualized treatment, prescribing specific therapies according to each patient's constellation of symptoms, signs, and constitution. Common modalities included internal and external herbal formulations as well as adjunctive interventions such as acupuncture and massage. Numerous classical prescriptions remain influential in contemporary practice. For example, Guizhi Shaoyao Zhimu Decoction, first recorded in the Synopsis of Prescriptions of the Golden Chamber, is widely recognized for its ability to dispel wind, eliminate dampness, clear heat, and unblock collaterals. It has been frequently applied to gouty arthritis, historically categorized as rheumatic heat arthralgia. Clinical studies confirm that this prescription alleviates joint pain and swelling and improves functional outcomes, thereby enhancing patients' quality of life.[130] Over successive generations, experiential knowledge of TCM in gout has been systematically refined and transmitted. Building upon these classical foundations, modern research has sought to clarify the underlying mechanisms of TCM therapies. Investigations reveal that many traditional medicinal substances contribute to gout management by regulating uric acid metabolism and suppressing inflammatory responses. Furthermore, increasing attention has been directed toward TCM compounds and multi-herb formulations, which exert multitarget effects and offer distinct advantages over single-agent therapies. Certain compounds not only lower serum uric acid but also attenuate joint inflammation, thereby providing effective treatment with relatively few adverse effects. These characteristics highlight the potential of TCM as a safer and more comprehensive therapeutic approach for gout.[131]

TCM Theory of Syndrome Differentiation and Treatment of Gout (See Figure 3)

In TCM, the treatment of gout is fundamentally guided by syndrome differentiation, which relies on a comprehensive evaluation of symptoms, physical signs, tongue characteristics, and pulse patterns to establish a precise syndrome type and corresponding therapeutic plan. The major syndromes associated with gout include damp-heat accumulation, phlegm

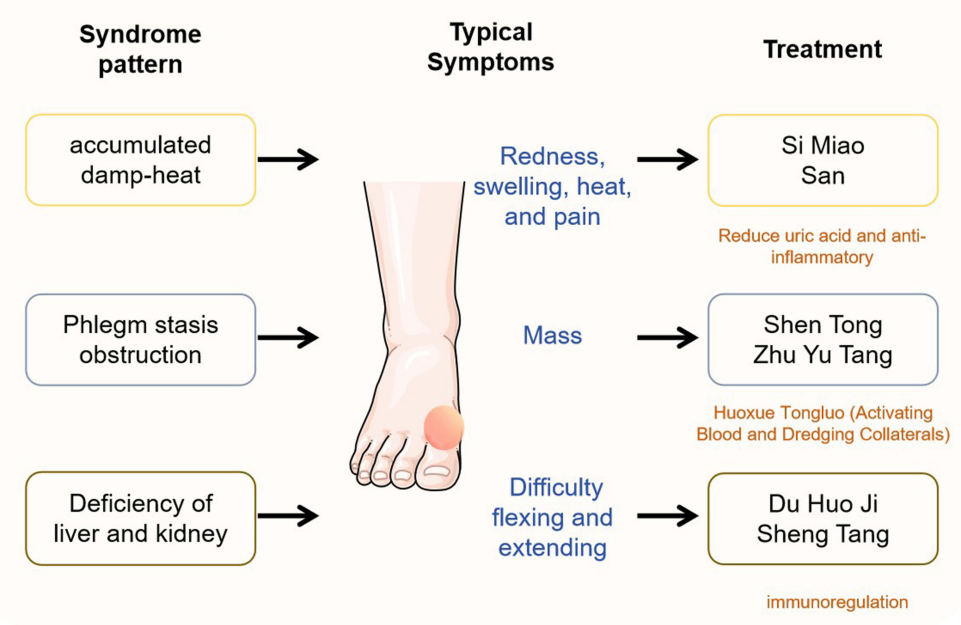

Figure 3 Multitarget mechanisms of TCM interventions in gout. TCM therapies inhibit xanthine oxidase to reduce uric acid production, regulate urate transport proteins (↑ABCG2, ↓URAT1/GLUT9) to enhance excretion, modulate immune responses including macrophage activity and IL-10 expression, and promote repair of joint and renal tissues. These multitarget effects demonstrate the systemic regulatory role of TCM, as described in Pathophysiological Mechanisms of TCM in the Treatment of Gout (See Figure 2).[126–128]

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and blood stasis, and liver–kidney deficiency, each reflecting distinct pathological processes and requiring tailored treatment strategies.

Damp-heat accumulation syndrome is the most frequently observed pattern, typically presenting with acute joint swelling, redness, severe pain, fever, and thirst. Therapeutic principles emphasize clearing heat, promoting diuresis, unblocking collaterals, and alleviating pain. A representative prescription is Simiao Powder, which has been shown to significantly lower serum uric acid levels, reduce joint inflammation, and improve clinical symptoms in patients with acute gout.[127]

Phlegm and blood stasis syndrome often occurs in patients with a longer disease course and is characterized by persistent joint pain and swelling, deformities, and subcutaneous nodules. Treatment focuses on resolving phlegm, eliminating blood stasis, unblocking collaterals, and relieving pain. Shentong Zhuyu Decoction is commonly used in this context, and clinical observations demonstrate that it can improve joint function while lowering serum uric acid and inflammatory markers.[130]

Liver and kidney deficiency syndrome is more prevalent among patients with chronic or recurrent gout, manifesting as joint pain, limited mobility, weakness of the lower back and knees, and general debility. The therapeutic approach aims to tonify the liver and kidneys, nourish deficiency, unblock collaterals, and relieve pain. Duhuo Jisheng Decoction is widely employed, and modern pharmacological studies suggest that it not only modulates immune function but also mitigates cartilage and joint tissue damage, thereby exerting long-term protective effects in chronic gout management.[130] In addition to syndrome-specific prescriptions, TCM adopts a holistic perspective that integrates syndrome differentiation with an individualized assessment of constitution, lifestyle, and environmental influences. Treatment often incorporates dietary regulation, emotional guidance, and preventive measures to enhance therapeutic outcomes and reduce the risk of recurrence. This emphasis on systemic balance and patient-specific tailoring underscores the comprehensive and dynamic nature of TCM in the management of gout.

Medical Practice of TCM Comprehensive Treatment of Gout (See Figure 4)

The clinical application of TCM in gout has been increasingly investigated through RCTs, with growing evidence supporting its efficacy in alleviating inflammation, reducing serum uric acid, and improving syndrome-specific manifestations. TCM interventions range from classical decoctions to empirical prescriptions, often administered alongside

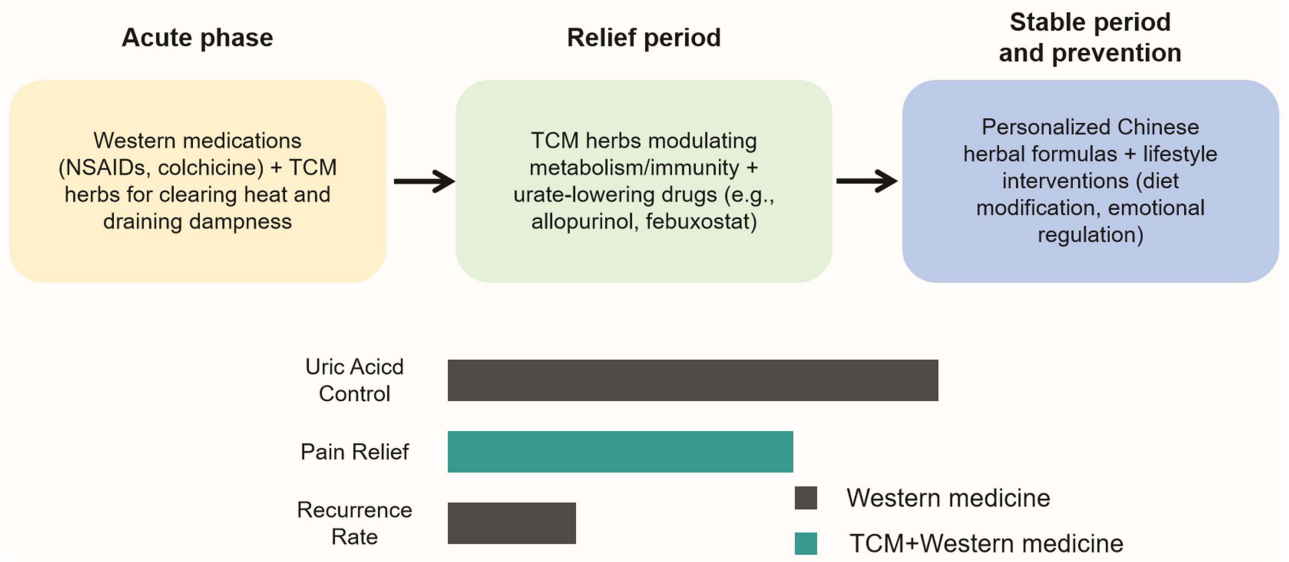

Figure 4 Syndrome differentiation and representative TCM prescriptions in gout. The figure presents three common TCM syndrome patterns: accumulated damp-heat, phlegm stasis obstruction, and liver-kidney deficiency. Each pattern is associated with characteristic clinical features and corresponding herbal prescriptions (Si Miao San, Shen Tong Zhu Yu Tang, Du Huo Ji Sheng Tang), which exert effects on uric acid metabolism, inflammation, and immune regulation. Content corresponds to TCM Theory of Syndrome Differentiation and Treatment of Gout (See Figure 3).[127,130]

conventional Western medications. The following studies highlight how specific formulas have demonstrated both symptomatic relief and systemic regulation in acute and persistent gout.

TCM Treats Gout

Sun Pengyuan et al[78] conducted an RCT to evaluate the efficacy and safety of Qingrelishifang for acute gout characterized by damp-heat accumulation. Sixty patients were randomly assigned to a treatment group or an observation group, with 30 participants in each cohort. Both groups received non-steroidal anti-inflammatory drugs (NSAIDs), while the treatment group was additionally given Qingrelishifang for five days. Clinical efficacy was assessed by changes in TCM symptom scores, syndrome scores, arthralgia scores, white blood cell (WBC) counts, and the neutrophil-to-lymphocyte ratio (NLR), alongside inflammatory markers such as C-reactive protein (CRP), cytokine levels, serum uric acid (SUA), urinary uric acid (UUA), and adverse events. The findings demonstrated that the addition of Qingrelishifang significantly alleviated inflammatory responses, improved syndrome-related manifestations, and enhanced overall efficacy while maintaining a favorable safety profile in patients with acute gout of the damp-heat accumulation type.

Ji Junjie et al[79] designed an RCT to investigate the therapeutic effect of Guizhi Shaoyao Zhimu Decoction in patients with persistent gout. A total of 89 participants were randomized into an observation group, which received Guizhi Shaoyao Zhimu Decoction combined with sodium bicarbonate and etoricoxib tablets, and a control group, which received only sodium bicarbonate and etoricoxib. The primary outcomes included rest pain, pressure pain, swelling, and overall clinical efficacy. The results indicated that Guizhi Shaoyao Zhimu Decoction provided significant improvements in pain reduction and swelling relief compared with the control group, confirming its beneficial role in the treatment of persistent gouty arthritis.

Yuan et al[80] evaluated the clinical efficacy of Tongfeng Shujie Decoction, an empirical prescription developed by Guo Jianhua, in an RCT involving 60 patients with acute gout. Participants were randomized into two groups: one receiving Tongfeng Shujie Decoction in addition to basic treatment, and the other receiving etoricoxib with basic treatment. Clinical assessments included syndrome scores, pain scores, laboratory parameters, and the incidence of adverse reactions before and after therapy. The trial demonstrated that Tongfeng Shujie Decoction effectively improved syndrome scores, alleviated pain, reduced inflammatory responses, lowered serum uric acid, and improved joint-related symptoms such as local tenderness, swelling, skin changes, and systemic discomfort. Importantly, the decoction also showed fewer adverse reactions, highlighting its distinctive advantages in the management of acute gout.

Acupuncture Treatment of Gout

Lixian et al[81] conducted a randomized controlled trial (RCT) involving 126 patients with acute gout to evaluate the clinical efficacy of Tongyuan acupuncture. Participants were randomly assigned into an observation group or a control group, each comprising 63 patients. The control group received health education and standard therapy, whereas the observation group was additionally treated with Tongyuan acupuncture. Clinical outcomes were assessed by evaluating symptoms and pain intensity with the visual analogue scale (VAS), while musculoskeletal ultrasound was employed to measure synovial hyperplasia, blood flow signals, and joint effusion. Laboratory assessments included serum uric acid (UA), erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), tumor necrosis factor-alpha (TNF-α), and interleukin-1 (IL-1) levels before and after treatment. The results demonstrated that the addition of Tongyuan acupuncture produced significant improvements in clinical signs and symptoms, while also reducing serum uric acid and inflammatory markers in patients with acute gout.

In another RCT, Huang et al[82] investigated the effects of direct bee acupuncture on acute gouty arthritis using serum proteomic analysis. The study applied an antibody array to detect differential expression of 50 serum proteins between patients with acute gout and healthy volunteers, followed by Gene Ontology (GO) enrichment analysis to clarify their biological functions. Enzyme-linked immunosorbent assays (ELISA) were used to validate protein expression and inflammatory markers before and after bee acupuncture, and receiver operating characteristic (ROC) curve analysis was performed to assess the diagnostic potential of four differentially expressed proteins. The intervention was shown to

modulate the expression of GM-CSF, IL-8, MIP-1β, and TNF-RII, thereby improving the inflammatory status of patients with acute gout and enhancing their anti-inflammatory responses.

Zhang et al[83] further examined the efficacy of acupuncture-based therapies by conducting an RCT on 66 patients with acute gout, who were randomly assigned to receive either celecoxib capsules or a combination treatment using Yuanluo and Back-shu acupoints with blood-letting and cupping. Pain relief and joint swelling were assessed using VAS and joint swelling scores at multiple time points (baseline, one hour, three days, five days, and after completion of treatment), while CRP levels were measured before and after therapy. In addition, recurrence rates and adverse reactions were monitored to evaluate long-term outcomes and safety. Compared with celecoxib, the acupuncture-based intervention produced greater reductions in pain and swelling, lowered serum CRP and uric acid levels, and demonstrated a more durable therapeutic effect with fewer adverse events.

Taken together, these trials provide converging evidence that acupuncture, whether applied through Tongyuan techniques, direct bee acupuncture, or acupoint-based interventions with adjunctive blood-letting and cupping, can significantly improve both clinical symptoms and inflammatory indices in acute gout. These findings highlight the capacity of acupuncture to complement conventional treatments, offering effective and safe therapeutic options within a comprehensive management framework.

TCM Comprehensive Treatment of Gout

Qiaoli et al[84] conducted a randomized controlled trial to evaluate the effects of acupoint catgut embedding in combination with the modern Chinese patent medicine Jingulian capsule and electroacupuncture in elderly patients with gouty arthritis characterized by damp-heat stagnation. A total of 120 elderly participants with damp-heat arthralgia were enrolled and randomly assigned into a study group and a control group, with 60 patients in each cohort. The control group received Jingulian capsule and electroacupuncture, whereas the study group was additionally treated with acupoint catgut embedding. Clinical efficacy was assessed by comparing changes in TCM syndrome scores, blood β2-microglobulin (β2-MG) levels, and numeric rating scale (NRS) scores before and after treatment. The results demonstrated that the combined regimen produced superior outcomes, with significant improvements in clinical signs and symptoms, more pronounced pain relief, and reductions in β2-MG, indicating alleviation of renal function impairment. These findings suggest that the integration of acupuncture-based therapies with standardized Chinese patent medicines enhances the therapeutic effect in elderly gout patients, addressing both symptomatic relief and systemic metabolic burden.

Huang et al[85] designed a randomized controlled trial to examine the efficacy of Tongfengshu Decoction, a classical herbal prescription, combined with Hulisan, a modern Chinese patent medicine, in patients with acute gout of the damp-heat accumulation type. Ninety patients were randomized into three groups: control group 1, which received basic treatment alone; control group 2, which received basic treatment combined with Tongfengshu Decoction; and the observation group, which received basic treatment combined with both Tongfengshu Decoction and external application of Hulisan. Clinical outcomes were evaluated by measuring joint swelling and pain as well as laboratory parameters, including serum uric acid, erythrocyte sedimentation rate (ESR), white blood cell count, and C-reactive protein (CRP), before and one week after treatment. The combination of Tongfengshu Decoction with Hulisan achieved the most significant improvements, producing marked reductions in joint swelling, pain severity, and uric acid levels, while also demonstrating a stronger anti-inflammatory effect than either intervention alone. This trial illustrates the complementary roles of classical prescriptions and patent medicines in contemporary gout therapy, where integration enhances both local and systemic disease control.

In another randomized controlled trial, Qiaoli et al[86] assessed the clinical efficacy of acupuncture combined with the external application of Sihuang powder for the treatment of acute gout. Sixty patients were randomly divided into a treatment group and a control group, each consisting of 30 patients. The treatment group received acupuncture in conjunction with external application of Sihuang powder, whereas the control group was treated with oral diclofenac sodium sustained-release capsules. Comparative evaluation showed that the integrated TCM regimen achieved greater reductions in visual analogue scale (VAS) scores, ESR, blood uric acid (BUA), and hypersensitive C-reactive protein (hs-CRP) compared with the control regimen. Furthermore, the incidence of adverse reactions was lower in the TCM group,

confirming not only superior efficacy but also better safety. These results highlight the therapeutic value of combining traditional acupuncture with external herbal preparations, offering a well-tolerated alternative to conventional pharmacological agents in acute gout management.

Taken together, these clinical studies demonstrate the advantages of comprehensive TCM treatments that combine classical decoctions, modern patent medicines, acupuncture, and external therapies. Such multimodal strategies provide synergistic effects in reducing uric acid, suppressing inflammation, alleviating pain, and protecting organ function. By linking traditional prescriptions with standardized patent formulations and integrative techniques, TCM offers a practical pathway for modernizing its role in gout management and aligning traditional practices with contemporary clinical standards.

Current Limitations and Prospects

Although research on the application of Traditional Chinese Medicine (TCM) in gout has expanded considerably, important limitations remain in the available evidence. A substantial proportion of clinical studies, including randomized controlled trials of classical prescriptions such as Guizhi Shaoyao Zhimu Decoction, Qingrelishifang, Tongyuan acupuncture, and Jingulian capsule, have been conducted as single-center investigations with relatively small sample sizes.[78–86] These factors reduce the generalizability of their findings and limit the strength of clinical recommendations. Methodological inconsistencies are also evident, as different studies apply varying diagnostic criteria, syndrome differentiation standards, treatment protocols, and outcome measures, leading to heterogeneous results and restricting direct comparison across trials.[130,131] In addition, the possibility of publication bias cannot be ignored, as studies reporting positive therapeutic outcomes are more frequently disseminated than those with neutral or negative results.[127]

These limitations reflect the urgent need for high-quality evidence to advance the field. Future research should prioritize well-designed, multicenter randomized controlled trials with larger sample sizes to confirm the efficacy and safety of TCM interventions. Also, the standardization of diagnostic frameworks, therapeutic protocols, and outcome assessment tools is also required to reduce heterogeneity and facilitate evidence synthesis. At the same time, mechanistic studies that link traditional syndrome differentiation with contemporary biomarkers and molecular pathways could be essential to bridge traditional and modern perspectives. By addressing these gaps, future research can provide a stronger scientific foundation for integrative strategies that combine TCM with modern medicine, ultimately enhancing the comprehensive management of gout.[84–86]

Summary

Potential Research Directions of TCM in Gout Treatment

Future research on TCM for the management of gout should continue to advance mechanistic, pharmacological, and clinical understanding. Although substantial progress has been made, further elucidation of the regulatory mechanisms by which active constituents of TCM influence uric acid metabolism and modulate inflammatory signaling pathways remains necessary. In particular, investigations should address how these effects differ across patients with varying constitutions, comorbidities, and stages of disease. An additional priority is to clarify the role of TCM in regulating the gut microbiota and its metabolites, which may uncover novel therapeutic targets for the prevention and treatment of gout.

In drug development, modern scientific and technological methodologies should be fully integrated with traditional knowledge. High-throughput screening technologies can be employed to identify bioactive compounds with urate-lowering or anti-inflammatory activity from the extensive resources of TCM. Synthetic biology offers opportunities to optimize and modify active components, thereby enhancing efficacy and safety. Furthermore, secondary development of classical prescriptions is warranted, including systematic investigation of their mechanisms of action, refinement of dosage forms and administration routes, and improvement of therapeutic efficiency.[131]

From a clinical research perspective, the implementation of well-designed, multi-center, large-sample randomized controlled trials is urgently required to establish robust evidence regarding the efficacy and safety of TCM. Complementary real-world studies should also be conducted to assess long-term outcomes and practical application in diverse clinical contexts. Precision medicine approaches should be prioritized by integrating genetic polymorphisms,

constitution types, and individual physical characteristics into therapeutic strategies, thereby advancing personalized TCM-based interventions for gout. In summary, future research should integrate modern methodologies with classical TCM principles to elucidate mechanisms, optimize formulations, and conduct rigorous clinical trials, ultimately aiming to advance the evidence base and improve patient-centered care.

The Prospect of TCM Combined with Modern Medicine in the Treatment of Gout

The integration of TCM with modern medicine provides a promising avenue for comprehensive gout management. In the acute phase, Western pharmacotherapy remains essential for rapid control of inflammation and pain, whereas TCM contributes to metabolic regulation and prevention of recurrence during the remission phase. A synergistic model can therefore be established, in which colchicine and other Western agents alleviate acute inflammation while TCM interventions such as heat-clearing and diuresis-promoting therapies enhance efficacy, reduce drug dosage, and minimize adverse effects. Evidence indicates that combined regimens achieve superior outcomes compared to Western medicine alone in lowering serum uric acid, relieving pain, and reducing attack frequency.

Diagnostic practices may also benefit from integration. Advanced imaging and laboratory tools from modern medicine, when combined with TCM syndrome differentiation, enable more comprehensive assessments. For example, incorporating biochemical indices such as uric acid and inflammatory markers with TCM diagnostic methods, observation, auscultation, olfaction, inquiry, and palpation, can provide a holistic evaluation of both disease status and patient constitution. This integrated approach supports the development of individualized treatment strategies. Patients with hyperuricemia and damp-heat accumulation identified by TCM syndrome differentiation, for instance, may benefit from combined therapeutic approaches that target both urate metabolism and inflammatory clearance. Moreover, mechanistic research on how TCM complements modern pharmacology will further enhance its acceptance and application within contemporary medical frameworks.

In summary, the integration of TCM and Western medicine offers synergistic benefits for both treatment and diagnosis, fostering a more individualized and mechanistically informed approach to the management of gout.

International Development Trend of TCM in the Treatment of Gout

The global development of TCM in gout management shows considerable potential. Rising international interest in natural remedies has created opportunities for TCM to gain wider recognition for its distinctive theoretical foundations and therapeutic effectiveness. To achieve this, cross-border collaborations should be strengthened through multinational and multicenter clinical trials designed to validate efficacy and safety under internationally recognized standards. Partnerships between Chinese and international research teams, such as those in Europe and the United States, demonstrate how integration of TCM syndrome differentiation with established diagnostic and therapeutic evaluation criteria can accelerate global acceptance of TCM. Cultural and academic exchange also play a vital role. International conferences on TCM, along with dissemination of TCM culture, can enhance understanding of its theoretical framework and clinical methodologies across diverse regions. Training initiatives are equally important: TCM professionals should be educated in both classical theory and modern scientific standards, as well as proficient in international languages and regulatory practices, to promote broader dissemination. Additionally, aligning TCM product quality with global pharmaceutical standards is essential for ensuring credibility and fostering global application.

In summary, by strengthening multinational research collaborations, promoting cultural and academic exchange, enhancing professional training, and standardizing product quality, TCM is poised to play an increasingly important role in the international management of gout.

Abbreviations

SUA, serum uric acid; MSU, monosodium urate; TCM, Traditional Chinese Medicine; NHANES, National Health and Nutrition Examination Survey; CPRD, Clinical Practice Research Datalink; COPCORD, Control of Rheumatic Diseases; ACR, American College of Rheumatology; EULAR, European League Against Rheumatism; US, ultrasound; LDHD, lactate dehydrogenase D; FFAR2, free fatty acid receptor 2; suppressor of cytokine signaling 3, SOCS3; MHC-1, major histocompatibility complex class 1; CNVs, copy number variants; GWAS, genome-wide association studies; PRS,

polygenic risk score; AI, artificial intelligence; ML, machine learning; DECT, dual-energy computed tomography; AMPK, AMP-activated protein kinase; NETs, neutrophil extracellular traps; IL-1ra, interleukin-1 receptor antagonist; TGF-β, transforming growth factor-beta; NF-Kb, nuclear factor kappa B; TNF-α, tumor necrosis factor-alpha; RCT, randomized controlled trial; NSAIDs, non-steroidal anti-inflammatory drugs; WBC, white blood cell; MLR, neutrophil to lymphocyte ratio; NLR, neutrophil to lymphocyte ratio; CRP, C-reactive protein; UUA, urine uric acid; UA, uric acid; ESR, erythrocyte sedimentation rate; GO, Gene Ontology; ELISA, enzyme-linked immunosorbent assay; ROC, receiver operating characteristic; VAS, visual analog scale; β2-MG, β2-microglobulin; NRS, numeric rating scale; BUA, blood uric acid; hs-CRP, hypersensitive C-reactive protein.

Disclosure

The authors declare that they have no affiliations with or involvement in any organization or entity with any financial interest in the subject matter or materials discussed in this manuscript.

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