Journal of Applied Pharmaceutical Science 2025. Article in Press
Available online at http://www.japsonline.com
DOI: 10.7324/JAPS.2026.254687
ISSN 2231-3354

Traditional Vietnamese herbal remedies treatments for Gout: A comprehensive review of mechanisms, practical applications, and therapeutic potential

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ARTICLE HISTORY

Received on: 27/04/2025
Accepted on: 27/07/2025
Available Online: XX

Key words:
Gout, arthritis, traditional Vietnamese medicine, Bi pattern.

ABSTRACT

Gout represents a significant health challenge in Vietnam, where conventional urate-lowering drugs are frequently complemented with traditional herbal medicine. The clinical presentation and progression of Gout vary based on the patient's physiology, comorbidities, and treatment response. Despite breakthroughs in modern healthcare, Gout management remains suboptimal worldwide, contributing to increased morbidity, disability, and reduced quality of life. This review synthesizes recent evidence on traditional Vietnamese medicine (TVM) formulations used in both experimental models and clinical settings for the treatment of Gout. We examine the pathophysiology of Gout from the perspective of Bi pattern disorders, analyze the clinical applications of single herbs and compound formulations, and elucidate their pharmacological mechanisms and bioactive constituents. This research compiled scholarly articles focused on the research of anti-Gouty arthritis conducted from 2010 to 2024. Data were collected from diverse academic journals and online resources, including PubMed, Web of Science, Elsevier, and Google Scholar. The process of sourcing and reviewing literature was based on search terms such as "acute Gouty arthritis and Vietnam herbal medicine," "acute arthritis and treatment," and "acute arthritis herbal extract." Our analysis reveals that Vietnamese herbal medicines demonstrate multiple therapeutic actions, including xanthine oxidase inhibition, anti-inflammatory effects, antioxidant properties, and enhanced uric acid excretion. The review highlights both single herbs (such as *Caesalpinia sappan*, *Blumea balsamifera*, and *Gnetum montanum*) and complex formulations (including *Hoa U Hoan* and *Chi Thong Nhu Than Thang*) with documented efficacy. While promising, current research has limitations in terms of standardization, sample size, and mechanistic understanding. This comprehensive review provides a foundation for integrating TVM into modern Gout management and developing novel therapeutic approaches with enhanced efficacy and reduced adverse effects.

1. BACKGROUND

Gout is a disorder associated with metabolic abnormalities characterized by a disturbance in the metabolism of purines, resulting in increased uric acid concentrations and the abnormal accumulation of monosodium urate crystals in joints and surrounding tissues [1–3]. This condition is intricately linked to hyperuricemia and related to numerous comorbid heart and renal conditions, including hypertension, heart attack, stroke, obesity, dyslipidemia, type 2 diabetes, and chronic kidney disease Figure 3 [4]. The clinical features of Gout vary based on the pattern of urate crystal accumulation, with manifestations ranging from acute and/or chronic arthritis of joints and extremities, commonly referred to as Gouty arthritis [3,5]. Patients typically experience acute episodes of intense joint pain, burning sensations, and swelling [6]. The rapid flare of arthritis, joint inflammation, the formation of renal calculi, and

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chronic joint injuries reduce life quality and result in disability [7]. Gout in Vietnamese patients may lead to complications, including chronic arthritis, renal impairment, kidney stones, and cardiovascular disease. Furthermore, healthcare disparities between urban and rural regions limit access to early diagnosis and effective long-term management. Patients in Vietnam are commonly treated with non-steroidal anti-inflammatory drugs (NSAIDs) and traditional herbal medicines, which often include uncontrolled corticosteroids. This limited approach often leads to poor treatment results and poor outcomes [8]. Global epidemiological data indicate that Gout affected approximately 41.22 million people (0.54% of the world's population) in 2017, with prevalence steadily increasing over the past 25 years [9]. Gout also significantly increases health care costs related to medications, hospitalizations, reduced mobility, impact on work and daily living, and disability [10,11]. The prevalence of musculoskeletal pain in adults in an urban population in Vietnam was estimated at 14.5%, in which osteoarthritis was the most commonly found arthritis Table 2 [12].

Despite established treatment guidelines, Gout management remains suboptimal globally, with fewer than half of diagnosed patients receiving definitive urate-lowering therapy as recommended by medical societies, including the ACR 2020 guideline [13]. Currently, the management rests on two methods: nonpharmacological and drug-based treatments [14,15]. Nonpharmacological therapy consists of life education for patients, dietary recommendations, and weight management. At the same time, pharmacological treatment aims to achieve treatment targets, reducing inflammation-related pain as rapidly as possible in the acute phase, controlling Gout progression and subsequent Gout flares, eliminating urate crystal deposits, and tophus formation in the chronic phase [14,15]. The medication treatments include colchicine, corticosteroids, nonsteroidal anti-inflammatory drugs, and interleukin-1 antagonists with suitable guideline treatment [14–16]. Although scientists have made significant efforts in up-to-date therapy with specific goals, they have difficulty maintaining long-term treatment effects, and even some of these drugs have serious adverse effects [6]. Furthermore, these conventional treatments typically do not prevent, halt, or reverse the progression of this complex condition.

Traditional Vietnamese medicine (TVM) offers a complementary approach to Gout management. Within the TVM framework, Gout is identified as a Bi disorder, attributed primarily to stagnation of Qi in the channels and collaterals. Guided by pattern differentiation principles, classical TVM formulations and herbal compounds have been employed to treat Gout with promising results. Several bioactive constituents isolated from Vietnamese medicinal herbs demonstrate multi-target effects and relatively low toxicity, suggesting potential benefits in both the preventive and treatment strategy of Gout. Vietnamese practitioners have historically utilized ancient TVM prescriptions to address metabolic disorders, including Gout, through multi-target mechanisms. This review intends to provide a comprehensive synthesis of available knowledge regarding herbal interventions for Gout management, including evidence of their efficacy and safety profiles, with specific emphasis on the application and clinical utility of Vietnamese herbal medicines for Gout treatment.

2. OVERVIEW

2.1. Gout and Bi syndrome

The first symptom of Gout, which patients complain about the most, is severe pain and localized swelling in the big toe [17,18]. Clinical manifestations of Gout may also affect other joints, including the knees and ankles [5,17,18]. Gout tends to affect a localized joint at a time; however, if left untreated properly, the condition can cause many serious complications [17,19]. Extremely increased uric acid concentrations in the blood, under the skin, and joint spaces can lead to the formation of tophi or kidney stones [19,20]. Gout has also been related to other severe medical problems such as hypertension, diabetes mellitus, and chronic kidney disease [21]. Based on the severity, the clinical manifestation of Gout is classified into three stages: asymptomatic hyperuricemia, acute Gouty arthritis, intercritical period, and chronic tophaceous Gout [22].

In traditional therapies, Gout relates to the classification of Bi pattern or "Bi-impediment" of "Bi zheng" disorders [9]. In Chinese history, Gout was first described by Tao Hong-Jing during the Liang dynasty (the name in Chinese is "tong-feng") in his document, Ming-Yi-Bie-Lu. The Bi syndrome is typically characterized by soreness, numbness, and restricted mobility in the muscles and joints, believed to be caused by the invasion of external pathogenic factors such as cold, wind, dampness, or heat [23]. The main causes are the shortage of healthy Qi and the direct effect of these other factors, such as high or low temperature and wind. The curative fundamentals in traditional Vietnamese and Chinese medicine aim to eliminate these disease-causing factors from the body [24]. In cases where patients experience the Bi symptom during a period of weak constitution, not only therapy for the elimination of pathogenic factors, but also strengthening organs such as the liver, spleen, and kidneys, and fortifying blood should be implemented. In addition to complications such as sputum, blood congestion, clearing congestion, expelling phlegm, and stimulating blood circulation, other measures should also be implemented [25,26].

2.2. The practical application of the TVM prescription in the Gout management regimen of Gout

Modern medicine's strategies for treating hyperuricemia and Gout primarily target uric acid metabolism; medicinal agents aim to reduce urate production, enhance excretion, or inhibit inflammation associated with crystal deposition [14–16]. According to modern medicine, pharmacological agents, such as corticosteroids, NSAIDs, and colchicine, are prioritized for use in acute Gout because of their effect in reducing pain and inflammation (Fig. 1) [27]. Additionally, biologic agents targeting IL-1β signaling, including anakinra and canakinumab, modulate inflammatory cascades by suppressing caspase-1 and IL-1β secretion in macrophages [28,29]. However, these agents also display severe side effects and drug interactions. Significant side effects include gastrointestinal discomfort, emesis, watery stools, hyperglycemia, rebound flares, and severe hypersensitivity skin reaction [6,29].

Herbalism products are broadly distributed from growing to developed countries. A valuable herbal resource is studied for new drugs to treat different diseases, including

Gout. Herbal medicine is available in various forms of drug preparations, such as decoctions, powders, tinctures, teas, and capsules [30,31].

2.2.1. Gout treatment with single herbal medicine

The single plants included in the overview study are commonly used ingredients from traditional Vietnamese herbal medicine formulas, with a long-term record of safe conventional use and a known low toxicological profile. These herbs have long-standing traditional use, are generally considered safe, and have been shown to exert anti-inflammatory, antioxidant, and urate-lowering actions through multiple molecular pathways supported by pharmacological studies (*in vitro, in vivo*, or clinical) that target multiple molecular pathways (e.g., cytokines, enzymes, oxidative stress). The mechanisms of action in many kinds of Vietnamese herbal regimens to treat Gout are different. Both the properties and effects of many herbs have been mentioned in the research in Vietnam and other countries worldwide.

Artemisia vulgaris (mugwort) contains a range of flavonoids (e.g., apigenin, eriodictyol, kaempferol, luteolin) [32,33] Table 1. Flavonoids are known to be not only potent antioxidants and potential therapeutic agents for free radical-related diseases but also inhibitors of enzymes, including xanthine oxidase (XO), cyclooxygenase (COX), and lipoxygenase (LOX), which play essential roles in the pathogenesis of Gout. Therefore, *A. vulgaris* has the potential therapeutic effects in Gout by XO inhibitory activity of its flavonoid components.

Vietnamese *Caesalpinia sappan*, a novel biogenetically native plant widely distributed in tropical Asia, exhibits strong anti-inflammatory and antioxidant characteristics. Some biologically active substances have been extracted from *C. sappan*: homoisoflavonoids, episappanol, caesappin A and B, protosappanin B and C, sappanone A, B… showed significant XO inhibitory activity. According to the documentation, fractionated extracts (e.g., methanol-ethyl acetate) were found to act as competitive XO inhibitors, reinforcing their potential therapeutic relevance [34]. The pharmacokinetic experiments of these inhibitors show them as competitive inhibitors, such as allopurinol [35].

Blumea balsamifera (L.) DC. *(Asteraceae*), commonly known as Sambong, is widely used across Southeast Asia countries, such as China, Thailand, Vietnam. Nguyen *et al.* [35] described the methanol derivative from *B. balsamifera* (planted in Lam Dong province, Vietnam), which has the ability to inhibit XO with a detailed IC_{50} value equal to 6.0 µg/ml.

Isolated flavonoids from *B. balsamifera*, such as luteolin and quercetin, also contribute to anti-inflammatory and antioxidant effects. In addition to its urate-lowering capacity, this herb exhibits a broad pharmacological profile, including antimicrobial, hepatoprotective, anti-obesity, and wound-healing activities.

The amount of biological activities extracted from Sambong includes scavenging of superoxide radicals, tumor inhibition, hepatoprotective, antioxidative effects, antimicrobial, anti-inflammatory activity, anti-plasmodial, suppression of tyrosinase activity, platelet aggregation, promotion of transdermal absorption ion, wound healing, anti-obesity effects, and disease and insect-resistant activities. There are seven substances of *B. balsamifera* methanol essence in Vietnam that showed considerable XO inhibitory activity [36].

Gomphrena celosioides treatment of Gout is an herbal medicine that has been widely circulated recently. Vietnam research on this plant indicates that *G. celosioides* contains steroids, glycosides, alkaloids, and flavones with known anti-inflammatory, detoxifying, and antipyretic effects [37] Table 1. In addition to Brazil, one of the genera, *Gomphrena,* is targeted for rheumatism treatment. The research of Macorini *et al.* [38] shows that ethanol extracts of *G. celosioides* have demonstrated analgesic effects in animal studies of both short-term (acute) and long-term (chronic) arthritis, supporting its traditional application [38]. Additionally, *Piper sarmentosum* is a popular remedy for Gout, not only in Eastern medicine but also in Vietnam, due to its analgesic, antibacterial, and anti-inflammatory properties [37]. In traditional medicine, *P. sarmentosum* leaves have been used as a natural antioxidant by decoction with water for the treatment of rheumatism. To date, decoctions from the leaves have traditionally been used in the management of rheumatism and Gout, with phytochemical investigations identifying over 140 bioactive compounds, including alkaloids, flavonoids, essential oils, and lignans [39,40].

The treatment of green beans (also termed *Vigna radiata*) for reducing Gout joint pain helps inhibit the rapid uptake of protein and decrease the breakdown of protein metabolism for energy generation. These processes lead to a reduction in the synthesis of uric acid, which is the leading cause of Gout. Bioactive constituents extracted from its seeds and sprouts—such as phenolic acids, lipids, and flavonoids—have been isolated from mung bean seeds and sprouts have particular activities such as oxidative stress reduction, antimicrobial, suppression of inflammatory, controlling blood sugar level as blood, along with effects on lipid metabolism and tumor inhibition effects, etc., so they become prevalent choice for suppression inflammation in management of Gout [41].

Increasing uric acid elimination from the body is one practical approach to controlling blood uric acid levels. *Brassica juncea* is one of the chosen plants due to its very diuretic feature. *Brassica juncea* contains various types of vitamins, including vitamin A, C, B, and K, as well as nicotinic acid, albumin, and carotene, which contribute to its preventive capabilities when used daily. Its pharmacological roles include free radical scavenging, inflammation suppression, and bacterial growth inhibition [42].

Betel leaves have been used for Gout control in Vietnam for many years [43]. Recent studies have shown that betel leaves have a slow analgesic effect and can safely decrease blood uric acid levels. Essential oils, such as eugenol, estragole, chavibetol, and chavicol, have functions in the recovery of compromised joints, improvement in metabolic disorders, and the clearing of toxins from the body [43]. The antioxidant extracts were assessed through two *in vitro* methods: xanthine/XO, 1,2-diphenyl-2-picrylhydrazyl (DPPH) free radical scavenging assay, and superoxide scavenging assay. In terms of the anti-inflammatory properties, hyaluronidase, XO, and

LOX inhibition assays were chosen, which described the most significant inhibitor effects [43].

The floral part of *Chrysanthemum sinense* is a well-known traditional Vietnamese medicinal herb that has been extracted with many known substances, including flavonoids, caffeoylquinic acid derivatives, phenolics, and a monoterpenoid glucoside. The majority of the *Chrysanthemum* spp. flowers are rich in compounds, including anthocyanins, cyanidin 3-(3-malonoyl) glucoside, cyanidin 3-glucoside and cyanidin 3-(3-malonoyl) glucoside as well as carotenoids substance such as lutein, β-cryptoxanthin, zeaxanthin, 13-cis-β-carotene, trans-β-carotene α-carotene, and 9-cis-β-carotene, which described potent XO inhibitory activity in a concentration-dependent manner, and the inhibitor activity of compounds is more powerful than that of a allopurinol drug (IC_{50} = 2.50 µM), with IC_{50} values ranging from 0.13 to 2.31 µM *Chrysanthemum spp*. has many bioactive properties, such as antimicrobial properties, antioxidants, and functional roles in skin cancer, various bone diseases [44].

Other components of the *Tetracera scandens* have been applied to manage diverse diseases, including rheumatism and inflammation. It originates in some regions of South and Southeast Asian (Vietnam, India, Southern China, etc.). According to Nguyen *et al.* [35], *T. scandens* reported XO inhibitory activity. A triterpene, identified as 28-O-β-D-glucopyranosyl ester of platanic acid, isolated from the MeOH extract of the stem of *T. scandens L,* with six other compounds. Compounds 1-6 show strong XO inhibitory activity in a concentration-dependent manner, and the inhibitor activity of compound 4 is more potent than that of the allopurinol drug (IC_{50} = 2.50 µM), with IC_{50} values of 1.9 µM [35,45].

The plant *Gnetum montanum* Markgr. (family Gnetaceae) is a type of vine distributed in Vietnam that is culturally applied for the management of Gout by affecting XO enzyme. Phytochemical research on the extract isolated from the trunks of *G. montanum* Markgr resulted in the isolation of a new stilbene-related compound, (E)-2′-methoxy-3,5,5′-trihydroxystilbene, and six known compounds, lehmbachol, gnetulin trans-shegansu B, cis-shegansu B, (+)-hannokinol, and gnetol. The functions of the trunks of this plant are toxic cleansing, suppressing inflammation, disinfection, stimulating the blood system, eliminating rheumatism, preventing leprosy, and losing weight. Notably, in Vietnamese natural medicine, the trunks and leaves are aimed at relieving joint pain, Gout, and poisoning [46,47].

These single-herb interventions, though varied in composition and mechanism, share common pathways of action, including XO inhibition, anti-inflammatory modulation, and antioxidant defense. Their historical usage, coupled with modern pharmacological validation, supports further investigation into their standardization and clinical application in integrative Gout therapy.

2.2.2. Gout treatment with compound herbal medicine

In recent years, traditional medicine regimens have emerged as a promising treatment option due to their fewer side effects compared to modern treatments. TVM is a concerned choice for Gout management due to not only being highly effective but also having limited side effects. In terms of Gout management, "Hoa U Hoan" capsules are composed of herbal medicines. Paeonia *lactiflora* Pall and *Angelica sinensis* (Oliv) Diels increase uric acid excretion through diuretic effects—*Polygonum multiflorum* Thunb, Pleomele cochinchinensis Merr, which exhibited significant XO inhibitory activity. The therapeutic effects of "Hoa U Hoan" have been evaluated in experimental animal models [12]. The studies have reported *in vivo* anti-inflammatory and inhibitory activity on XO of "Hoa u hoan", suggesting the potential for preventing Gout and serving as supportive therapy. This review evaluated the analgesic, anti-inflammatory, and hypouricemic impact of "Hoa u hoan" at the oral doses of 3.6 and 7.2 g/kg in mice. The analgesic effect was observed in the hot plate and pain threshold models. The anti-inflammatory effect was determined in mice with induced edema by 1% carrageenan and peritonitis, and the reduced serum uric acid in the potassium oxonate-induced hyperuricemic model in mice. The results show that both doses of 3.2 and 7.6 g/kg decreased acid uric level by 73.8% and 57.25% in comparison to the control group, respectively, and reduced both the volume and protein levels in the inflammation fluid of the peritonitis model, increasing the pressure and reaction time compared to the control group and pre-administration.

The hypouricemic effects in hyperuricemic mice induced by "HV Thong Tieu Ky" capsules, which have been studied clinically and showed a significant reduction in symptoms after 30 days of treatment for the model group with p <0.05 [48]. The appropriate weight loss mechanism of the drug is explained by combining herbal medicine with effects such as anti-inflammatory and pain relief from the plant. Weight loss is commonly recommended for Gout. Furthermore, weight loss from bariatric surgery is related to decreased incidence of hyperuricemia and Gout [49]. Some of these drugs work to reduce inflammatory risk biomarkers, including IL-1β, TNF-α, and PGE2, supporting efficient weight loss. Herbal plants such as *G. montanum* and *Lactuca indica L.* have a diuretic effect, promoting the excretion of uric acid from the system, thereby reducing the corresponding amount. In addition, *G. montanum* Mgf. and *Eleutherine bulbosa* contained in the remedy have the effect of increasing blood circulation, helping to bring nutrients and oxygen to organs better, and at the same time, helping to remove waste products from the body.

The remedy ***Chi Thong Nhu Than Thang*** is a combination of many herbs with different mechanisms related to pain relief in Gout [50]. Herbal ingredients with inflammation-reducing effects, such as oroxylin A and baicalein in *Phellodendron chinensis* Schneid, inhibit the NF-KB, resulting in inhibition of the release of PGE2, IL6, IL-1ß [51]. The substance ß-eudesmol in *Atractylodes chinensis (DS)* Loidz inhibits IL6 and NF-KB, then has a substantial impact on the anti-inflammatory ability, thereby reducing symptoms of swelling, heat, and especially pain [52]; Radix Gentianae Qinjiao, Spina Gleditsiae, Radix *A. sinensis,* and *Semen perricae* have also been shown to have effective anti-inflammatory effects [53–56]; The ethylacetate component of *Ledebouriella seseloides* Wolff has significantly reduced the redness caused by IL-6 in the serum [57]. The gentiopicrodide in Radix Gentianae Qinjiao

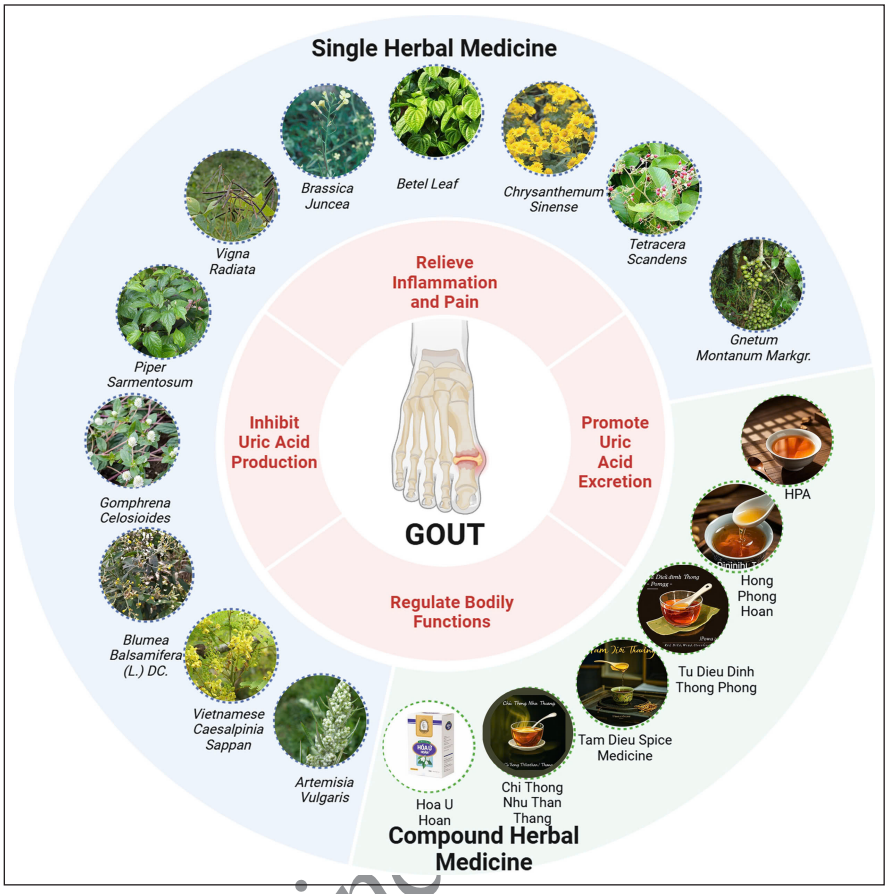

Figure 1. The single and compound herbal medicines used in traditional Vietnamese therapy for Gout, along with their therapeutic functions, include relieving inflammation and pain, inhibiting uric acid production, promoting uric acid excretion, and regulating bodily functions.

has also been shown to have a strong anti-inflammatory effect that helps affect the pituitary gland and adrenal cortex [58]. In addition, some ingredients in the remedy can affect the central nervous system, helping to reduce pain signals transmitted to the brain and enhancing the production of endorphins, an endogenous hormone that has natural pain-relieving effects. The remedy can help improve blood circulation to the joints and protect cells from damage caused by free radicals, thanks to the antioxidants in the remedy, thereby helping to reduce pain and promote recovery. In this study, 60 patients were divided into two groups: the control group (administered colchicine only) and the research group (receiving ***Chi Thong Nhu Than Thang*** combined with colchicine) Table 2 [59]. After 14 days, it was shown that in the treatment group, the number of painful joints and a significant reduction in Visual Analog Scale (VAS) pain scores were shown, with p <0.05. The proportion of patients assessed to be completely cured and effective is >90%. Some other studies also show the effectiveness of the remedy in reducing pain in different areas, such as back pain, headaches, and pain caused by injuries.

The role of traditional herbal medicine in the clinical management of chronic Gout is through mechanisms that reduce blood uric acid, inhibiting acute and chronic inflammatory reactions, thereby contributing to improving acute symptoms, especially chronic ones, of the disease. An animal study and clinical experiment of ***Tam Dieu Gia Vi*** remedy (TDGV) (prepared from the ancient remedy ***Tam Dieu Thang***, adding some herbs: *Cinnamomum cassia* Presl, *Tinospora sinensis* Merr, *Homalomena occulta* Schott, *Zea mays* L.) has shown potential in the treatment of chronic Gout through lowering blood uric acid and improving clinical symptoms [60,61]. Hypouricemia is explained through mechanisms such as inhibiting the XO enzyme, increasing uric acid excretion through urine, and adjusting purine metabolism to limit uric acid production. Specifically, blood uric acid levels in experimental animals decreased significantly ($p < 0.01$), and uric acid levels excreted in urine elevated considerably ($p < 0.01$) relative to the control group that did not receive TDGV. The significance of TDGV capsules in chronic Gout is demonstrated by their ability to maintain serum uric acid concentrations after a course of treatment. If, after a course of treatment, blood uric acid concentrations remain stable upon stopping the drug, it will help patients avoid prolonged use of the drug, minimize unwanted effects, and reduce the costs of treatment. In this study, after 6 weeks of treatment, patients whose blood uric acid results were within normal limits will stop treatment and be monitored for the next 4 weeks. Results show that 17 patients (80.95%) still maintained uric acid index within normal limits, demonstrating

the ability to maintain very good uric acid contents in the patient population responding to treatment. Clinically, it indicates that serum uric acid levels, as well as the number of acute pain attacks due to Gout within 6 months, decreased with statistical significance (p <0.01) when the disease group was treated with this capsule. In addition to its pain-relieving effect on Gout patients, TDGV capsules also show positive effects in pain relief in many other diseases with mechanisms such as anti-inflammation via downregulation of inflammatory substances such as TNF-α, IL-1β, IL-17A, VEGF-α, and phospholipase A(2), COX-1, COX-2, 5-LO and lead to reduced release of inflammatory factors including TNF-α, IgE, IL-4, and nitric oxide (NO) act on the central nervous system to reduce pain signals transmitted to the brain, increasing the production of endogenous endorphins to reduce pain naturally. There is an apparent effect in reducing inflammation in model studies, as shown by reducing vascular permeability, leading to a decline in inflammatory exudate volume, a decrease in the number of white blood cells, and a decline in protein content in the inflammatory exudate in experiments causes peritonitis in mice (a significant statistical difference from the control group, p < 0.05). The study also showed that the peripheral analgesic effect was equivalent to the drug aspirin when performed on animal research models by causing cramping pain with acetic acid and causing pain by mechanical means.

Vietnam has a diverse medicinal herb. In TVM, there are many effective remedies to treat Gout. ***Tu Dieu tan*** remedy is one of them Table 2 [60]. The remedy ingredients include *Coix lachryma* Jobi, *Achyranthes bidentata* Blume, *P. chinensis* Schneid, *A. chinensis* (DS) Loidz. Research has proven that polysaccharides in *A. chinensis* (DS), Loidz, and baicalein, oroxylin A in *P. chinensis* Schneid have an anti-inflammatory effect, stigmasterol and acid p-coumaric in *C. lachryma*-Jobi L. participate in the process of excretion of urinary uric acid, and achyranthine in *A. bidentata* Blume helps to increase the urine volume on the diuretic assessment model [62–64]. In the model, *in vitro* and *in vivo*, stigmasterol and p-coumaric acid participate in the uric acid excretion process, inhibit the nucleation and growth stage, and combine with calcium oxalate, which inhibits the attachment of urate crystals to renal tubular epithelial cells [65]. ***Tu Dieu tan*** granule helps anti-inflammation, relieves pain, and lowers uric acid concentration in the blood of chronic Gout patients. After the treatment period, the total number of painful joints decreased compared with before. Improvement in pain relief with the VAS1 scale compared to before treatment is 4.71 ± 1.26, the average of motor function according to the Health Assessment Questionnaire (HAQ) score after treatment is 0.96 ± 0.32, and the reduction of blood uric acid concentration compared to before treatment is 200.42 ± 100.14 µmol/l. The indexes improved more; statistical analysis revealed a significant difference, p < 0.05 [61,66].

Thong Phong Hoan has an anti-hypouricemic effect in Gout patients. After 30 days of using the medicine on the group of subjects with simple hyperuricemia, the results showed that it was quite effective in 76.3%, averagely effective in 18.3%, and ineffective in 5.4% of the patients Table 2 [67].

Our research on the treatment effect of chronic Gout of **HPA** medicine to help relieve pain, reduce blood stasis, and reduce blood uric acid levels showed that the medicine has good clinical effects (p < 0.01) with overall treatment efficacy of 94.0% Table 2 [68]. According to the research, HPA medicine reduces the uric acid level through four pathways: inhibits the intravascular coagulation, increasing the volume and quality of blood to the tissue; helps activate the enzyme that decreases the uric acid level; increases the blood volume to the kidneys, hence increasing the elimination of uric acid; and increases the activity of intestinal bacteria that decomposes uric acid [68]. This activity is one of the main concerns of TVM.

3. DISCUSSION

In this comprehensive review, we have explored the application and mechanisms of traditional Vietnamese herbs in Gout treatment. Through systematic analysis of existing research, several key findings and insights emerge.

3.1. Efficacy of TVM in Gout treatment

The body of research examined demonstrates the significant therapeutic potential of Vietnamese traditional herbs in Gout management. Various single herbs, including *C. sappan*, *A. vulgaris*, and *B. balsamifera*, have shown a remarkable ability to inhibit XO activity through their flavonoid constituents and other bioactive compounds, thereby effectively reducing uric acid production. Supporting data from *in vitro* assays, animal models, and clinical studies collectively affirm the relevance of these herbal agents in Gout treatment.

Previous studies have illustrated that extracts of *A. vulgaris* significantly reduce paw edema in mice subjected to carrageenan-induced inflammation. The extract revealed notable antioxidant properties, as evidenced by multiple assays, including the DPPH, ABTS, reducing power, and hydrogen peroxide scavenging assays. Moreover, it showed potent inhibitory effects on XO activity, suggesting a potential mechanism for reducing uric acid production in the body. These findings provide scientific support for the prospective use of *A. vulgaris* (mugwort) as a therapeutic drug for controlling Gout among Vietnamese patients [32,33].

Preliminary investigations of methanolic extracts from *C. sappan* heartwood revealed notable XO inhibitory activity, with an IC_{50} of 14.2 mg/ml. Isolated compounds from *C. sappan* were further evaluated for their XO inhibitory effects using assays conducted at five different concentrations ranging from 0.2 to 100 mM. Among these, some agents demonstrated significant, dose-dependent inhibition of XO activity. Notably, their inhibitory effects were comparable to those of allopurinol, a practically established XO enzyme inhibitor used in the management of Gout [35].

In Nguyen et al.'s research, three among seven compounds isolated from *B. balsamifera* quercetin, ethyldihydroquercetin, and quercetin-3,3′,4′—exhibited notable XO inhibition with IC_{50} values between 0.23 and 1.91 mmol/l. Complementary studies reported that the methanolic extract demonstrated superior XO inhibitory activity (IC_{50} = 0.111 mg/ml) relative to chloroform (0.138 mg/ml) and petroleum ether extracts (0.516 mg/ml). In addition, six novel diterpenoid structures were characterized using spectroscopic and computational techniques extracted from the methanolic extract

of *B. balsamifera*. These diterpenoids demonstrated dose-dependent inhibition of inflammatory mediator production. A combination of Western blotting, ELISA, and quantitative reverse transcription monitoring amplification in real-time (qRT-PCR) analyses revealed that they suppressed several steps of the mediators of inflammation in the RAW 264.7 macrophages, involving the production of NO, transcription and translation of IL-6, TNF-α, iNOS, and COX-2, as well as phosphorylation events in the NF-κB pathway. *In vivo*, the model of paw edema induced by carrageenan, the compounds significantly alleviated carrageenan-induced paw edema in both phases of inflammation. Molecular docking research further showed that the major constituents interacted with and inhibited key targets in the process of inflammation, such as the acid arachidonic metabolism, MAPK, and NF-Kb signaling pathways. Collectively, these findings confirm the potent anti-inflammatory properties of the isolated compounds, experimental (*in vitro* and *in vivo*) and computational (*in silico*) models approaches, and highlight their potential as candidates to support the discovery of novel anti-inflammatory compounds for Gout treatment [36,69].

The ethanolic extract of *G. celosioides* exhibits antihyperalgesic and antiarthritic effects in various acute and chronic models. A study assessed the effect of *G. celosioides* on mice, showing that *G. celosioides* at doses of 300, 700, and 1,000 mg/kg significantly decreased edema formation, with reduced mechanical hyperalgesia observed 3 hours post carrageenan injection At 1,000 mg/kg, leukocyte counts diminished, and 300 mg/kg notably suppressed leukocyte migration in zymosan-induced arthralgia [38].

According to the models of animal and cell-based *in vitro* assays, *P. sarmentosum* extracts have demonstrated promising anti-inflammatory pharmacological activities. In the rat paw edema model induced by carrageenan, *P. sarmentosum,* administered at three doses of 50–200 mg/kg, strongly inhibited the acute inflammatory response in a manner dependent on dosage, with 300 mg/kg reducing swelling by 47.41% at 1 hour and 24.78% at 3 hours. Furthermore, a rat granuloma formation model showed significant decreases in dry weights following 1,200 mg/kg dosing, measuring 78.59 ± 5.21 mg and 309.92 ± 23.67 mg, respectively. *In vitro*, the ethanol extract at concentrations dose-dependently inhibited TNF-α release, with corresponding inhibition percentages and an IC_{50} of 25.65 ± 1.99 µg/ml. Clinically, *P. sarmentosum* is a key constituent of the traditional Chinese medicine Zhonghua Dieda pill, as listed in the Chinese Pharmacopoeia, and is widely used for its efficacy in reducing swelling and alleviating pain [40].

Assessed the potential anti-inflammatory effects of *mung bean* ethanol extracts in lipopolysaccharide-activated macrophages. Polyphenols in *mung bean* extract at a dose of 3.7 mg/ml were dramatically downregulated in cells treated with inflammation-promoting cytokines, including TNF-α, IL-1β, IL-12β, IL-6, and iNOS receptors in lipopolysaccharide-stimulated macrophages, indicating potential benefits in inflammatory conditions, including Gout [41]

Mustard extract has also been shown to have positive effects on reducing inflammation. Ethanol extracts of *B. juncea* on acute and chronic inflammation by croton oil in mice demonstrate that they substantially lowered the thickness of the ear tissue and activity of myeloperoxidase in the inflammatory model and also inhibited the mRNA and protein concentrations of cytokines (TNF-α and IL-6). The ethyl acetate and n-butanol fractions of *Mustard* significantly suppressed the production of NO and nitrite synthesis in lipopolysaccharide-stimulated peritoneal macrophages. Among the two, the ethyl acetate fraction of *Mustard* leaf significantly protects cells exposed to lipopolysaccharide and shows stronger inhibition of nitrite synthesis than n-butanol fractions of *Mustard* leaf. This NO and nitrite inhibition may support explain some of the anti-inflammatory effects of Mustard [42].

The phenolic agents in *Betel* leaves ethyl acetate fractions demonstrated potent scavenging activities against ABTS, DPPH radicals, and NO with IC_{50} values of 45.60 ± 0.56, 41.52 ± 1.02, and 51.42 ± 1.25 µg/ml, respectively. Besides, *Betel* leaf extracts demonstrated potent tyrosinase inhibition activity in mice, mushrooms, and humans (IC_{50} = 20.59 ± 0.83, 7.72 ± 0.98, and 24.78 ± 0.56 µg/ml, respectively) [43,70].

The flower of *C. sinense* MeOH extract (IC_{50}, 5.1 mg/ml), traditionally used for the treatment of inflammatory and rheumatism conditions. Six active fractions of the extract were analyzed for their ability to inhibit XO. Of these compounds, luteolin exhibited stronger potent inhibitory activity (IC_{50} = 1.3 mM) compared to the standard control allopurinol (IC_{50} = 2.5 mM) [30].

The trunks of *G. montanum* methanol extract have some stilbene derivatives that showed XO inhibition with IC_{50} values ranging from 13.6 to 47.7 µM, in comparison to the positive control, allopurinol (IC_{50} = 2.9 µM) [47].

Compared to studies on well-known herbal medicine, a similar mechanism has been observed. Curcumin, an alternative treatment for Gout disease, non-clinical experiments have illustrated that curcumin plays an anti-inflammatory role, inhibits XO, exhibits uric acid-lowering characteristics, and possesses antioxidant effects [71,72]. It exhibits an anti-inflammatory activity by blocking the expression of NF-κB, cytokines (IL-6 and TNF-α). *In vivo*, assessment of the anti-inflammatory effects of curcumin in monosodium urate-induced acute Gouty arthritis in mice shows that the severity of joint inflammation gradually decreased in comparison to the control group.

On the other hand, *Colchicum autumnale*, an ancient medicinal treatment for Gout, demonstrates the modulation of multiple pro- and anti-inflammatory pathways linked to Gouty arthritis in multiple mechanisms. As a primary outcome in the mechanism of treatment, colchicine functions by blocking the release of IL-1β, expression of IL-1–induced L-selectin, modulating the secretion of inflammatory cytokines, and reducing neutrophil chemotaxis to cytokines, serving [73].

Besides preventing Gout by controlling inflammation, TVM showed strongly significant XO inhibitory activity, such as *A. vulgaris* and *C. sappan*. Notably, 188 extracts were prepared from 96 Vietnamese medicinal plants that exhibited XO inhibitory activity, reducing acid uric in blood and stimulating urate elimination. In addition, TCM also shows that the active ingredients in medicinal herbs have pain-relieving effects, helping to improve the symptoms of Gout [32]. We believe that

controlling inflammation, uric acid concentrations, and other symptoms will help prevent Gout and limit complications.

These findings substantiate their capacity to lower serum uric acid contents and alleviate Gouty arthritis symptoms. However, further basic studies are required to fully characterize the active constituents in medicinal herbs and elucidate their precise mechanisms of action in Gout treatment. Moreover, complex herbal formulations such as ***Hoa U Hoan*** and ***Chi Thong Nhu Than Thang*** have demonstrated not only significant uric acid reduction and anti-inflammatory effects in experimental models but have also shown clinical efficacy in trials. These compound formulations provide comprehensive therapeutic approaches through multi-faceted mechanisms of action, addressing various pathophysiological aspects of Gout simultaneously.

3.2. Therapeutic advantages of TVM

Gout, characterized by uric acid crystal deposition in joints and tissues, significantly impacts quality of life. Scientific investigations have demonstrated that traditional medicine, particularly when integrated with conventional approaches, offers enhanced efficacy in pain relief and functional improvement compared to conventional monotherapy.

As illustrated in Figure 2, experimental studies reveal that TVM possesses significant advantages in Gout treatment, with numerous herbal constituents targeting multiple pathways involved in Gout pathogenesis. These include enhanced uric acid excretion, XO inhibition, and anti-inflammatory effects. Beyond the mechanism mentioned above, new emerging targets have also been identified in recent studies. Some treatments from traditional medicine, along with their active agents, have shown efficacy in the treatment of Gout, reducing serum uric acid concentrations and mitigating the development of inflammation. Active compounds derived from traditional remedies have been shown to modulate key signaling pathways, such as MAPK, NF-κB, and JAK/STAT, which are crucial in the pathophysiology of Gout. Furthermore, it affects acid urate transporters, such as urate transporter 1 (URAT1), which is key in balancing urate levels. Given its vital role in reabsorbing urate, URAT1 has become a primary focus for drug development in Gout therapy. Inhibitors of URAT1 are a direct strategy to promote urate excretion by preventing its reabsorption in the renal tubules. However, inherent instability and low expression of the human URAT1 hinder a complete understanding of the drug's action mechanisms and selectivity [74]. Besides, recent studies have shown that the NLRP3 inflammasome has emerged as a pivotal regulator of the inflammatory cascade in Gout. Although the precise biochemical mechanisms of NLRP3 activation remain incompletely elucidated, natural products targeting NLRP3-mediated inflammation have shown promise and represent a potential novel therapeutic strategy [75].

In summary, to address Gout-specific mechanisms, traditional herbs have contributed to overall physical regulation and improved quality of life. Furthermore, compared to conventional pharmaceuticals, traditional herbal medicines generally exhibit lower toxicity profiles, making them more suitable for long-term management.

3.3. Limitations and future directions

Despite the promising therapeutic potential of TVM in Gout management, numerous significant limitations exist in the current research frameworks. The studies reviewed typically feature small sample sizes (including limited participant numbers), limiting statistical power and external validity of findings. Many investigations lack standardized methodologies for herbal preparation and administration, creating challenges for reproducibility and clinical translation. Moreover, most research has focused predominantly on animal models, with fewer well-designed human clinical trials, particularly those with rigorous randomized controlled designs.

The biological mechanisms constituting the process of the therapeutic effects of Vietnamese herbal medicines remain

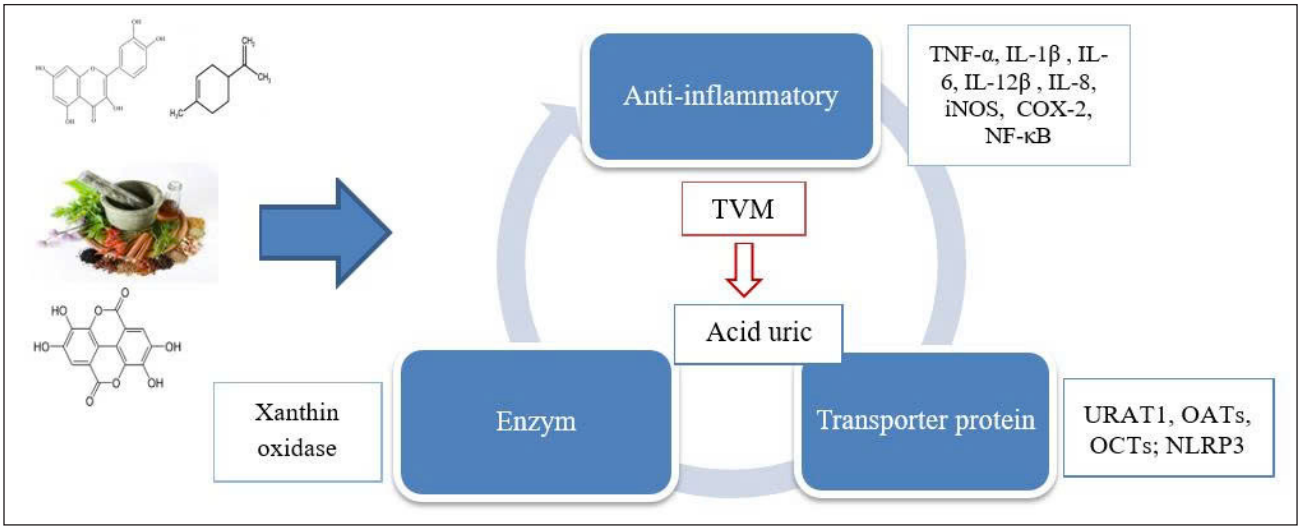

Figure 2. The multi-target role of TVM in the treatment of Gout. Urate transporter 1 (URAT1); Organic anion transporters (OATs); organic cation transporters (OCTs); TNF-α: tumor necrosis factor alpha; NF-κB: nuclear factor-kappa B; IL-1β: interleukin 1β; IL-12β: interleukin 12β; IL-8: interleukin 8; IL-6: interleukin 6 NLRP3: nucleotide-binding and oligomerization domain; Inducible nitric oxide synthase (iNOS); Cyclooxygenase-2 (COX-2).

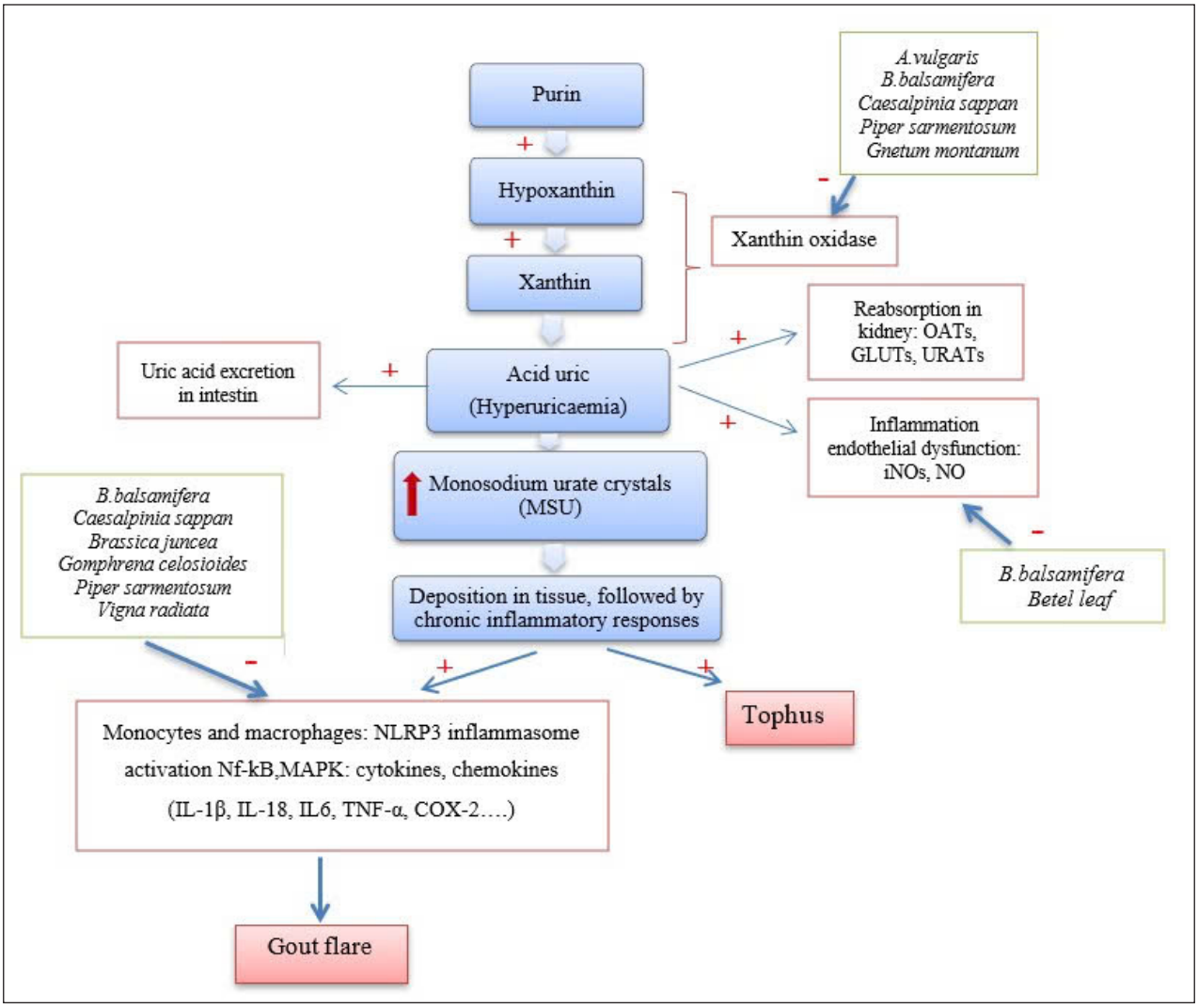

Figure 3. Multi-target interactions TVM in the treatment of Gout.

incompletely characterized at the molecular mechanisms. While many studies have investigated the effects of individual medicinal components, there is insufficient research examining potential synergistic or antagonistic interactions when these herbs are combined in traditional formulations. Such interactions may significantly influence therapeutic outcomes but remain largely unexplored. Furthermore, the current research disproportionately emphasizes XO inhibition, potentially overlooking other valuable therapeutic targets and pathways relevant to Gout pathophysiology. These findings highlight a broader trend observed in current Vietnamese research on herbal medicine for Gout treatment, which remains largely preliminary. Most studies to date have focused primarily on phytochemical screening and the identification of basic pharmacological activities, such as anti-inflammatory effects (e.g., through cytokine modulation), analgesic properties, antioxidant activity, and XO inhibition. As noted earlier, several plant extracts commonly used in Vietnam have demonstrated both potent XO inhibition activity and multi-target actions relevant to Gout pathophysiology. This observation points to an important gap in the literature: the lack of comprehensive studies that integrate mechanistic, pharmacokinetic, and comparative efficacy data for these herbal remedies.

Nowadays, laboratories in Vietnam are investing in scientific infrastructure and biomedical research. Future studies should aim to elucidate the molecular mechanisms of action, explore synergistic effects among herbal compounds, and conduct comparative evaluations with established anti-Gout therapies. Such efforts are essential to substantiate the clinical relevance of traditional medicinal plants and facilitate their integration into evidence-based Gout management strategies. Advanced molecular and cellular studies are necessary to carry out the experiment to elucidate the precise modes of action beyond XO inhibition. Particular attention should be directed toward anti-inflammatory pathways, immunomodulatory effects, and the influence of herbal compounds on crystal-induced inflammasome activation. Recent developments in targeted therapy for acute Gouty arthritis, including interleukin-1β inhibitors and biological agents targeting NLRP3, highlight promising new directions for investigation [76].

Table 1. Single Vietnamese herbal medicine therapies.

Scientific name	Medicinal parts	Model	Positive control	Effective constituent	Pathways and targets for the treatment of Gout	References
Artemisia vulgaris	Leaf	*In vitro*	Allopurinol (IC_{50} 2.5 µM)	Apigenin, rutin, eriodictyol, kaempferol, quercetin, luteolin, myricetin	XO inhibitory activity; *Artemisia vulgaris* $IC_{50,}$ 14.7 µg/ml Quercetin IC_{50} 2.22 µM),; Luteolin IC_{50} 3.34 µM), Apigenin IC_{50} 3.89 µM),	[32,33,77]
Vietnamese *Caesalpinia sappan*	Wood	*In vitro*	Allopurinol (IC_{50} 2.5 µM)	Homoisoflavonoid, sappanol, episappanol, protosappanin B and C, caesappin A and B, sappanone A, B…	XO inhibitory activity (IC_{50} 14.2 µg/ml)	[32,34,35]
Blumea balsamifera	Whole plant	*In vitro*	Allopurinol (IC_{50} 2.5 µM)	Flavonoids: Flavon, flavonols, flavanones, chalcones, steroids, triterpenes, lignans…; umbelliferon, hydranngetin.	XO inhibitory activity (IC_{50} 6.0 µg/ml)	[32,36,69,78]
Gomphrena celosioides	Aerial parts	*In vivo*	Dexamethasone 1 mg/kg	Steroids, glycosides, alkaloids, and flavones	Anti-inflammatory, antipyretic, and detoxifying (the doses of *G. celosioides* (300, 700, and 1,000 mg/kg)	[37,38]
Piper sarmentosum	Leave, root, stem	*In vivo, In vitro*	-	Essential oil, alkaloids, flavonoids, lignans, and steroids.	Antioxidant analgesic, antibacterial and anti-inflammatory properties. (Water extract (30, 100 and 300 mg/kg) could strongly inhibit acute inflammation and nociceptive in a dose-dependent manner, ethanol extract (1, 10, 50 and 100 mg/ml) could inhibit TNF-a release (%) from RAW 264.7 cells (IC_{50} = 25.65 ± 1.99, 37.22 ± 2.5, 55.02 ± 2.04 and 81.90 ± 0.89 µg/ml, respectively) *Piper sarmentosum*at 250 µg/ml show high superoxide scavenging assay.	[37,39,40]
Vigna radiata	The seeds and sprouts	*In vitro*	-	Flavonoids, phenolic acids, organic acids, amino acids, lipids, and carbohydrates.	Antioxidant, antimicrobial, anti-inflammatory, lipid metabolism, antidiabetic, antihypertensive, and antitumor effects. (Polyphenols at 3.7 µg/ml show the anti-inflammatory effects)	[41]
Brassica juncea	Seed	*In vivo*	Indomethacin 10 mgkg	Vitamins, minerals, dietary fiber, chlorophylls, glucosinolates, polyphenols and volatile components	Anti-oxidation, anti-inflammation, and bacteriostatic and antiviral activity. (anti-inflammation effect at both doses of 125 and 250 mg/kg)	[42,79]
Betel leaf	Leaf	*In vitro*	-	Eugenol, chavibetol, chavicol, and estragole	Antioxidant and anti-inflammatory (DPPH, ABTS radicals, and NO scavenging activity with an IC_{50} value of 41.52 ± 1.02 µg/ml, 45.60 ± 0.56 µg/ml, and 51.42 ± 1.25 µg/ml), respectively)	[43]
Chrysanthemum sinense	Flower	*In vitro*	Allopurinol (IC_{50} 2.5 µM)	Lutein, zeaxanthin, β-cryptoxanthin, 13-cis-β-carotene, α-carotene, trans-β-carotene, and 9-cis-β-carotene	XO inhibitory activity, antioxidant (IC_{50} value of 5.1 µg/ml)	[32,44]
Tetracera scandens	Root, stem	*In vitro*	Allopurinol (IC_{50} 2.5 µM)	The MeOH extract of the stem of *Tetracera scandens* triterpene, 28-O-β-D-glucopyranosyl ester.	XO inhibitory activity ($IC_{50,}$ 15.6 µg/ml)	[32,35,45]
Gnetum montanum	Root, stem	*In vitro*	Allopurinol (IC_{50} 2.9 µM)	(E)-2′-methoxy-3,5,5′trihydroxystilbene and six known compounds, lehmbachol, gnetulin trans-shegansu B cis-shegansu B, (+)-hannokinol, and gnetol	XO inhibitory activity (IC_{50} values of (E)-2-methoxy-3,5,5-trihydroxystilben, lehmbachol, gnetulin, trans-shegansu B, cis-shegansu B, 13.6, 35.2, 38.7, 43.4, and 47.7 µM)	[46,47]

"-": No positive control

Table 2. Compound Vietnamese herbal medicine therapies.

Remedy	Drug composition	Active ingredient	Model	Positive control	Pharmacological mechanism	References
Hoa U Hoan	*Paeonia lactiflora*, *Angelica sinensis (Oliv), Polygonum multiflorum, Pleomele cochine chinensis, Gnetum montanum, Lactuca indica L., Eleutherine bulbosa*	Paeoniflorin lactone glycoside, paeoniflorin, hydroxy paeoniflorin, ferulic acid, angelica polysaccharide, emodin methyl ether, rhein, emodin, dracohodin, dracoresene, nor-dracohodin, etc.	*In vivo*	Allopurinol	Promote uric acid excretion and regulate the level of uric acid in the body. Inhibit XO and reduce the generation of uric acid.	[12]
Chi Thong Nhu Than Thang	*Phellodendron chinensis Schneid, Atractylodes chinensis, Radix Gentianae Qinjiao*, *Spina Gleditsiae, Radix Angelicae sinensis, Semen perricae, Ledebouriella seseloides, Radix Gentianae Qinjiao*	Berberine, phellodendrine, atractylol, atractynonnatractylodin, gentiopicroside, swertiamarin, ferulic acid, ligustilide, amygdalin, ethyl acetate etc.	Clinical	Colchicin	Inhibit the release of inflammatory factors and exert anti-inflammatory effects. Improve local blood circulation and promote tissue repair. Anti-oxidize and reduce the damage of free radicals to cells.	[59]
Tam Dieu Spice medicine	*Phellodendron amurense Rupr., Atractylodes lancea Thunb., Achyranthes bidentata Blume, Stigmata Maydis, Tinospora sinensis Merr, Homalomena aromatica (Roxb), Boehmeria nivea (L) Gaud, Cinnamomum cassia Blume*	Cinnamaldehyde, cinnamic acid, coumarin, chondrofoline, isochondrofoline, linalool, α-pinene, β-pinene, flavonoids, etc.	*In vivo*	Allopurinol	Reduce the concentration of blood uric acid and maintain uric acid homeostasis. Alleviate inflammatory reactions and relieve symptoms.	[60]
Tu dieu dinhthong phong	*Coix lachryma Jobi. Achyranthes bidentata Blume, Phellodendron chinensis Schneid, Atractylodes chinensis (DS) Loidz*	Coixenolide, coix polysaccharide, achyranthoside, ecdysterone, berberine, phellodendrine, atractylol, atractynon, atractylodin, β-eudesmol, etc.	Clinical	-	Inhibit inflammation and relieve the inflammatory state of joints. Reduce the generation of uric acid and promote the excretion of uric acid.	[80]
Thong Phong Hoan	*Rehmannia glutinosa Libosch., Paeonia lactiflora Pall., Angelia sinensis Oliv, Ligusticum wallichii Franch, Prunus persica Stokes, Carthamus tictorius L.*	Catalpol, rehmannioside, rehmannin, paeoniflorin, paeoniflorin lactone glycoside, ferulic acid, ligustilide, angelica polysaccharide, ligustrazine, amygdalin, safflower yellow, carthamin, etc.	Clinical	Allopurinol	Regulate uric acid metabolism and improve the condition of hypouricemia.	[67]
HPA	*Astragalus membranaceus Bge, Atractylodes lancea (Thunb.), Homalomena occulta, Polygonum multiforum Thunb, Spatholobus suberectus Dunn, Citrus reticulata, Achyranthes bidentata Blume , Typhonium trilobatum Schott, Dioscorea tokoro Makino., Smilax glabra Roxb, Talcum, Psoralea corylifolia L., Leonurus heterophyllus Sw.*	Astragalus polysaccharides, astragalosides, atractylol, atractynon, linalool, α-pinene, β-pinene, emodin, chrysophanol, spatholobus alcohol, limonene, hesperidin, achyranthes saponin, ecdysterone, dioscin, astilbin, engeletin, magnesium silicate, etc.	Clinical	-	Relieve the feeling of pain and alleviate the suffering of patients. Improve blood flow and prevent the formation of blood stasis. Regulate the intestinal flora and promote the decomposition of uric acid.	[68]

Future research should prioritize larger-scale, methodologically rigorous clinical trials with diverse patient populations to establish definitive evidence for efficacy and safety. These studies should incorporate standardized preparation methods and dosing regimens to enhance reproducibility and facilitate clinical implementation. Pharmacokinetic data of herbal medicine are limited. Comprehensive pharmacokinetic and pharmacodynamic investigations are needed to understand the absorption, distribution, metabolism, and excretion profiles of key bioactive compounds, along with potential herb–drug interactions with conventional Gout medications.

Research exploring how Vietnamese herbal medicines might modulate these pathways could reveal novel therapeutic mechanisms and applications. The success rate for understanding the mechanism of the new TVM is limited when the new herbal medicine has many other constituents. *In silico* studies, particularly molecular docking and network pharmacology, are increasingly being used to investigate the binding potential of traditional treatments for Gout. These findings may facilitate the development of potent anti-inflammatory drugs with minimal side effects in the future. Long-term safety monitoring is another critical area requiring attention, as chronic Gout management often necessitates extended treatment periods. While traditional herbs generally demonstrate favorable safety profiles in short-term use, comprehensive data on long-term effects, particularly regarding hepatic and renal function, are lacking. Additionally, standardization of herbal extracts and quality control measures should be established to ensure consistent therapeutic effects and minimize batch-to-batch variability in clinical applications.

Nowadays, the advancement of people's material living conditions and a rise in purin-heavy food have led many in the global populace to grapple with Gout. The intermittent flaring condition often brings painful discomfort; the acute flare-up of Gout has been treated by administering corticosteroids, colchicine, and NSAID medications. Even so, these readily available treatment options merely mitigate symptoms or postpone the onset of Gout, and even entail significant side effects, including gastrointestinal disturbances, skin rashes, systemic imbalances, and the potential risk for renal dysfunction.

Integrative approaches combining TVM with conventional treatments represent a particularly promising direction for future research. Studies examining optimal combination strategies, potential synergistic effects, and protocols for reducing conventional medication requirements while maintaining therapeutic efficacy could significantly advance Gout management. Such integrative approaches may help mitigate side effects associated with conventional pharmaceuticals while enhancing overall treatment outcomes.

Addressing these research gaps will be essential for improving and extending the efficacy of TVM treatment regimens, reducing relapse rates, and enhancing the living standards of patients with Gout. The development of evidence-based clinical guidelines incorporating TVMs into contemporary Gout management represents an important goal that could benefit patients worldwide, particularly in regions where access to conventional pharmaceuticals may be limited or where traditional medicine remains an integral component of healthcare systems.

CONCLUSION

Gout significantly impairs both the physical and mental well-being of patients, leading to a substantial decline in quality of life. The global prevalence of Gout is rapidly increasing, driven by environmental and lifestyle factors, thereby heightening its clinical importance. Although no definitive cure currently exists, various therapeutic strategies aim to manage symptoms and prevent disease progression. There is no cure for the disease, yet several treatment approaches have been used to manage and prevent the progression of the disease. This presents a considerable challenge to the management of uric acid, as well as the prevention and treatment strategies for Gout. Medicines or herbal extracts focus on interfering with disease mechanisms, such as inhibiting the XO enzyme, reducing purine metabolism, a process that creates acid uric, increasing the renal excretion pathway of acid uric, enhancing cell protection and resilience against oxidants that are products of the inflammatory process. Combining Western medicine drugs brings many improvements in managing both acute and chronic Gout. limiting side effects associated with conventional drugs, and leading to increased treatment and increased recovery ability, improving the quality of life for patients. However, several challenges persist in the application of TVM for Gout treatment: there is a pressing need for larger studies to carry out more high-quality randomized controlled trials, and the herbal plants focus only on XO inhibitors, which limits the diversity in choosing treatment approaches. Improving and extending the clinical benefits of the TVM treatment approach, reducing the rate of recurrence, and enhancing overall patient outcomes in Gout management.

Future efforts by the medical and scientific community should prioritize these objectives to fully harness the benefits of traditional medicine in combating this increasingly prevalent disease.

4. LIST OF ABBREVIATIONS

DPPH, 1,2-diphenyl-2-picrylhydrazyl; IC50, Half-maximal inhibitory concentration; TVM, Traditional Vietnamese medicine; SOD, Superoxide dismutase; XO, Xanthine oxidase.

5. ACKNOWLEDGMENTS

The authors are thankful to the authorities of Chengdu University of Traditional Chinese Medicine for providing support to the study and other necessary facilities like internet surfing, library, and other technical support to write a review article.

6. AUTHORS' CONTRIBUTIONS

All authors made substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data; took part in drafting the article or revising it critically for important intellectual content; agreed to submit to the current journal; gave final approval of the version to be published; and agree to be accountable for all aspects of the work. All the authors are eligible to be authors as per the International Committee of Medical Journal Editors (ICMJE) requirements/guidelines.

7. FINANCIAL SUPPORT

This work was supported by a grant from the National Natural Science Foundation of China, 82274247.

8. CONFLICT OF INTERESTS

The authors have no conflict of interest in this study. The authors alone are responsible for the content and writing of the paper. The present study has been conducted as an MD thesis at Chengdu University of Traditional Chinese Medicine.

9. ETHICAL APPROVALS

This study does not involve experiments on animals or human subjects.

10. DATA AVAILABILITY

All data generated and analyzed are included in this research article.

11. PUBLISHER'S NOTE

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12. USE OF ARTIFICIAL INTELLIGENCE (AI)-ASSISTED TECHNOLOGY

The authors declare that they have not used artificial intelligence (AI) tools for writing and editing the manuscript, and no images were manipulated using AI.

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How to cite this article:
Hoang HM, Yong LY, Au KH, Pham TM, Pham VAT, Dang THT, Gao YX. Traditional Vietnamese herbal remedies treatments for Gout: A comprehensive review of mechanisms, practical applications, and therapeutic potential. J Appl Pharm Sci. 2025. Article in Press. http://doi.org/10.7324/JAPS.2026.254687