

# Gout Arthritis Progression in Treatment with Herbal Therapy: A Systematic Review

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## Abstract

**Introduction:** Gout is a common arthritis condition due to deposition of monosodium urate (MSU), and is closely related to hyperuricemia. The goal of gout treatment in the acute stage of gouty arthritis mainly focuses on relieving pain while slowing down or stopping progression and further gout flares in the chronic stage, ultimately improving joint function, and increasing the quality of life.

**Material and Methods:** A literature search was carried out to determine potential studies for this review up to November 2022. The search was performed using the PubMed/MEDLINE, Cochrane Library, and Google Scholar databases including keywords that matched the MeSH rule and the term used for herbal therapy and gout arthritis.

**Results:** The search strategy generated several diverse literatures presenting a variety of randomized control trial of herbal therapy in gout arthritis patient. A total of 8 eight studies were included in the review. Satisfactory pain relieve and decreasing of serum uric acid level were found in most of the studies. Decreasing of serum uric acid level statistically significantly found in 6 six of the 8 eight studies studied. Also Furthermore, significant fewer incident of adverse event found in 4 four studies.

**Conclusion:** Herbal therapy or medication are potentially more effective than western medications or placebos at slowing the progression of pain, lowering blood uric acid levels, and preventing some adverse events in gout patients.

**Keywords:** Arthritis, gout, herbal therapy, progression, uric acid level.

## Introduction

Gout is a common arthritis condition due to deposition of monosodium urate (MSU), and is closely related to hyperuricemia. Because of Due to disorders of purine metabolism or impaired renal excretion, serum uric acid levels rise to be abnormally high, and finally, there would be the deposition of uric acid and acute persistent inflammatory reactions in the joints. [1]. Gout affects a significant portion of the population worldwide annually, and according to the estimates of the World Health Organization (WHO), 3.9% of

people worldwide are suffering from gout. The high incidence of gout is no longer limited to the elderly, and there is a tendency for the early onset in younger populations. [2]. The most common clinical manifestations of gout are acute burning sensation and swelling of the joints including tophi deposition, characteristic recurrent acute arthritis, and deformed joints in chronic case. [1]. In addition, this disease often affects the kidneys, causing chronic interstitial nephritis and the formation of urinary tract stones composed of uric acid. In severe cases, gout can lead to damaged or

mained joints and renal insufficiency. [3].

The goal of gout treatment in the acute stage of gouty arthritis mainly focuses on relieving pain while slowing down or stopping progression and further gout flares in the chronic stage, ultimately improving joint function, and increasing the quality of life. [4]. Conventional medicine treatments for gout focus primarily on the treatment of high uric acid. Drugs such as colchicine, corticosteroids, and non-steroidal anti-inflammatory drugs (NSAIDs) have been used to treat the acute onset of gout.

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**Table 1: Characteristic of the included studies**

No.	Author, Year	Age (Mean)		Sample size		Intervention		Duration
		EG	CG	EG	CG	EG	CG	
1	Yihua Fan, 2022 [5]	41.68	31.5	45	44	Qinpi Tongfeng Formula (QPTFF) granule	Diclofenac sodium sustained-release tablets	7 days
2	Estee Chan, 2014 [6]	59	59	54	182	Complementary and Alternative Medicine (CAM)	Non-CAM use	1 year
3	Hongbo LI, 2020 [7]	43.56	42.82	47	47	Turbidity-elimination gout soup and external application of TCM	Colchicine tablets	21 days
4	Wang Shasha, 2020 [8]	46.4	46.6	82	83	Chinese formula granules (CFG)	Chinese herbal tablets (CHT)	7 days
5	Wang Y, 2014 [9]	51.76	53.82	88	88	Chuanhu anti-gout mixture	Colchicine with placebo agent	10 days
6	Xiao Ning Yu, 2018 [10]	45.33	49.21	24	24	Yellow-dragon Wonderful-seed Formula (YWF)	Allopurinol	28 days
7	Zhijun Xie, 2017 [11]	46	49	139	71	Compound Tufuling Oral Liquid (CoTOL)	Placebo CoTOL	12 weeks
8	Bantar Suntuko, 2019 [12]	46.8	49.5	23	21	Herbal extracts ( <i>Eugenia polyantha</i> , <i>Apium graveolens</i> , <i>Nigella sativa</i> )	Allopurinol	4 weeks

TCM: Traditional Chinese Medicine, EG: Experimental Group, CG: Control Group

These drugs show good short-term effects, but long-term use can lead to gastrointestinal reactions, rashes, systemic vacuities, and even renal failure. In addition, such drugs cannot prevent, halt, or reverse the progression of this complicated disease. [2]. The current international guidelines recommend the use of xanthine oxidase inhibitors (such as allopurinol and febuxostat) as first-line treatment and uricosuric agents (such as

benzbromarone) as second-line treatment for chronic gout. [4]. Although several studies have been conducted on gout, the current treatment drugs are not satisfactory since all urate-lowering drugs have potential side effects and drug interactions.

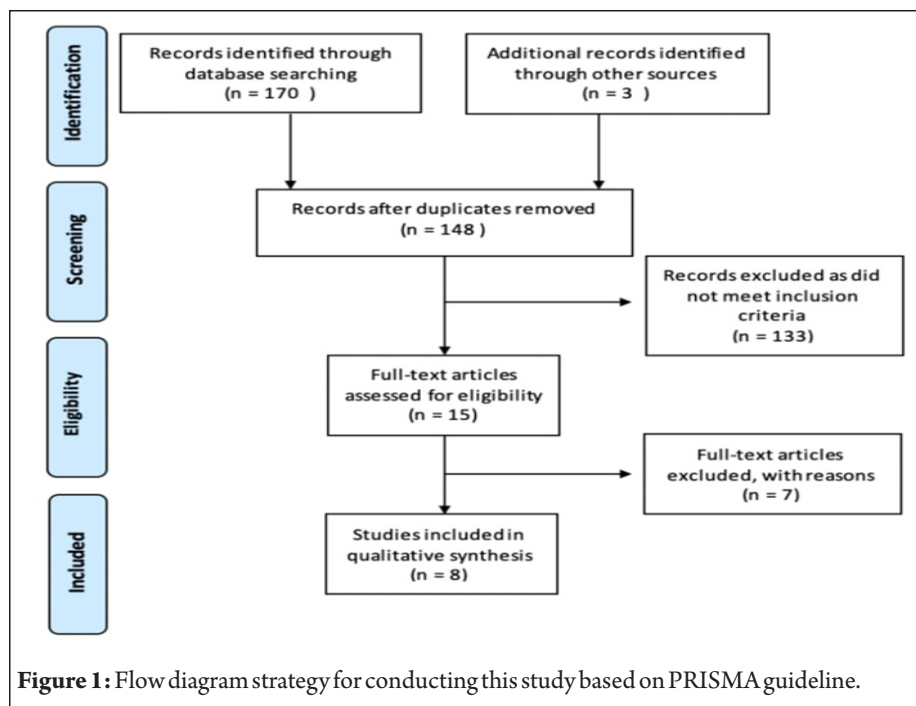
Therefore, more attention should be paid to complementary and alternative medicine (CAM) of herbal therapy to prevent the occurrence and progression

of gout. [2,4]. This systematic review aims to critically evaluate the evidence use for herbal therapy in progression and complication among gout arthritis.

## Materials and Methods

### Database and search strategy

This study was a systematic review of prospective randomized studies. The systematic research was carried out in November 2022 by identifying relevant studies through Google Scholar and Pubmed PubMed database. The systematic review was done using PRISMA Guideline in databases including keywords that matched the MeSH rule and the term used for gout arthritis (“gout arthritis” OR “gouty arthritis” OR “Gouty”) and the term used for herbal therapy (“herbal therapy” OR “herb therapy” OR “herbal medicine”). Gout arthritis is defined as a disease in which the metabolic condition hyperuricemia leads to the formation of monosodium urate crystals, which provoke acute and chronic inflammatory responses in the joint through activation of the innate immune system. Herbal therapy is a type of medicine that uses roots, stems, leaves, flowers, or seeds of plants to improve health, prevent disease,



**Figure 1:** Flow diagram strategy for conducting this study based on PRISMA guideline.

and treat illness.

The selection and review process were done manually by two independent reviewers. The references of the selected studies that eligible to the inclusion and exclusion criteria of this review were also additionally reviewed, including the studies that were not present in the initial search. The main focus of this review is to analyze the use of herbal therapy in response to progressiveness and complication in gout arthritis cases.

**Inclusion and exclusion criteria**

Inclusion criteria include any research investigating gout arthritis treated with the herbal therapy within the past ten 10 years, that is, published in English language, has an abstract, and involves humans as the subject in the study. Given the limited number of studies, there was no restriction in terms of patient’s demographics. Exclusion criteria include

any single case reports, review articles, and any research of out arthritis treated by conventional medicine or surgical treatment.

**Ethics and dissemination**

As the study will review the published literature, no ethical approval is required, as there will be no patient recruitment and no personal data collection. The results of this systematic review will be disseminated by publishing a manuscript in a peer-reviewed journal or presenting it at a related conference. Clinical practice guidelines (CPGs) were prepared and disseminated, including this study.

**Results**

The systematic search resulted in 173 records from Google Scholar, PubMed, and other sources database were found. Twenty-five studies were removed due to duplication. One hundred forty-eight

records were screened based on titles and abstracts, 15 records were included. Full-text articles were reviewed by the author and screened using inclusion and exclusion criteria. Through this selection process, 8 eight final articles are included in the systematic review (Fig. 1). The data was were collected based on progression of pain, serum uric acid, and adverse effect of herbal therapy in gout arthritis patient reported by the studies. Studies included in this review are characterizecharacterized in Table 1.

**Discussion**

A variety of different herbal therapy have been suggested based on several studies. Most of the study compare both of herbal therapy (in some study mention as TCM) and Western Medication or placebo in gout arthritis patient. Each intervention presented its own results based on its progression of pain in gout

**Table 2: Comparison outcome of therapy in pain, serum uric acid and adverse effect**

No.	Author, Year	Pain				Serum uric acid changes (Mean)				Adverse effect		P	
		EG		CG		EG		CG		EG	CG		
		Initial	After	Initial	After								
1	Yihua Fan, 2022 [5]	6	1	5	1	↓ 42.64 μmol/L			↓ 9.81 μmol/L		Vomit (n=2)	Abnormal liver function (n=4), Abnormal renal function (n=2), Nausea (n=2), Acid reflux (n=1), Diarrhea (n=3), Stomachache (n=2), Dizzy (n=1)	0.012
		P (0.798)				P (0.004)		P (0.419)		Diarrhea (n=2)			
2	Estee Chan, 2014 [6]	N/A	N/A	N/A	N/A	↑ 20.00 μmol/L			↓ 20.00 μmol/L		Higher cost related	None	N/A
						P (0.44)		P (0.45)					
3	Hongbo LI, 2020 [7]	6.5	1.2	6.7	3.8	↓ 119.30 μmol/L			↓ 78.93 μmol/L		Redness and swelling (1.19)	Redness and swelling (1.84)	0.001
										Aggravation on heat (0.71)		Aggravation on heat (1.19)	
										Adverse joint flexion & extension (0.76)		Adverse joint flexion and extension (1.34)	
										Scanty dark urine (0.68)		Scanty dark urine (1.04)	
		P (0.001)				P (0.001)				Constipation (0.57)		Constipation (1.15)	
4	Wang Shasha, 2020 [8]	4	1	4	1	N/A	N/A	N/A	N/A		Erythema (1)	Abdominal distension (1)	>0.05
		P < 0.01								Diarrhea (1)		Nausea (1)	
										Nausea (1)			
5	Wang Y, 2014 [9]	↓ 97.44 points		↓ 79.56 points		↓ 63.17 μmol/L			↓ 29.00 μmol/L		Diarrhea (1)	Diarrhea (21)	<0.001
		P (0.013)				P (<0.001)				Nausea (1)		Nausea (3)	
												Vomiting (1)	
6	Xiao Ning Yu, 2018 [10]	N/A	N/A	N/A	N/A	↓ 36.00 μmol/L			↓ 137.17 μmol/L		No adverse events reported.	No adverse events reported.	N/A
						P > 0.05		P < 0.05					
7	Zhijun Xie, 2017 [11]	38.53% recurren		63.16%		↓ 74.28 μmol/L			↓ 28.81 μmol/L		Leukopenia (3)	Leukopenia (7)	0.033
		recurren paint				P (0.004)							
		P (0.003)											
8	Bantar Suntutko, 2019 [12]	N/A	N/A	N/A	N/A	↓ 27.36 μmol/L			↓ 66.62 μmol/L		No adverse events reported	No adverse events reported	N/A
						P (0.016)							

patient, changes in serum uric acid level, and present of adverse effect from the therapy (Table 2).

### Progression of pain

Pain intensity assessed by scoring systems and time to meaningful pain relieve. Five trials reported pain relieve progression of targeting joint immediately after treatment by using herbal therapy. Four trials found herbal medicine significantly effective in relieving joint pain after treatment [7, 9, 11, 14, 13], two of them mention pain scale relieve as effective as the control group and two other found more effective in the treatment group than the control group. Significant change in progression of pain as same as the control group in intervention of Turbidity-elimination gout soup and external application of TCM compared to Colchicine tablet (n = 94 patients; pP = 0.001) [7] also compared Chinese formula granule with Chinese herbal tablet (n = 165 patients; pP < 0.01) [13, 14]. Other trial comparing of Chuanhu anti-gout mixture with colchicine and placebo agent found more significant relieving of pain in treatment group (n = 176, pP = 0.013), and more effective in prevention of recurrent pain in treatment group Compound Tufuling Oral Liquid (CoTOL) than placebo CoTOL [11]. Different result found in meta-analysis from two trials, comparing herbal medicine with colchicine and allopurinol, showed that there is no statistical difference between groups in pain relief. On average time (day) to meaning pain relieve, one study found that NASID and allopurinol group was significantly more effective than herbal medicine group. [13, 14].

### Serum uric acid

Seven study comparing herbal medicine with other therapy to gout arthritis patient in changes of uric acid serum. Six out of seven trials found a significant difference between herbal medicine than

western medicine and other placebo in lowering blood uric acid level after treatment (n = 420 vs. 477 patients), in favor to experimental group. [4, 5, 7, 9, 11, 12]. However, one study comparing the use of complementary and alternative medicine (CAM) to non-CAM showed no correlation between the intervention and serum uric acid level and that the correlation was insignificant. [6].

Some studies discovered a statistically significant difference between the groups in lowering the blood uric acid level, according to a meta-analysis of two trials that compared herbal therapy with colchicines during a 7-day treatment. In four trials that examined Chinese herbal medication with allopurinol, only two discovered a significant difference between the groups. [16]. The analysis of the mechanisms that Chinese herbal medicine acts further to lower sUA makes it clearly evident that most Chinese herbal medicines act on several targets or many pathways to lower sUA. The primary components of the study's analysis of the therapeutic mechanism of Chinese herbal medicine were UA synthesis, UA transport, inflammation, renal fibrosis, and oxidative stress. [13, 14].

### Adverse event

Regarding adverse event, conventional Western medications like such as colchicine, probenecid, allopurinol, and non-steroidal anti-inflammatory pharmaceuticals can have analgesic and anti-inflammatory effects by lowering the accumulation of uric acid and the corresponding inflammatory response. The aforementioned drugs do not lower blood uric acid levels because they have no effect on the synthesis, breakdown, or excretion of uric acid salts. These drugs can, however, have a number of negative adverse event events, including gastrointestinal problems such nausea, vomiting, diarrhea, and appetite loss. These unfavorable effects, which include bone marrow suppression, liver damage,

and kidney damage, can somewhat impair patient compliance [13, 14].

In this study, five trials mention adverse effect in some of treatment group compare to the control group. Four study studies show a statistically significant in the presence of adverse event (Table 2). Regarding to gastrointestinal adverse event, two trials mention the use herbal therapy such as Qinpi Tongfeng Formula (QPTFF) granule compared with diclofenac sodium sustained-release and Chuanhu anti-gout mixture compared with colchicine with placebo agent thus found fewer incidence of gastrointestinal event in the experimental group. Other study with turbidity-elimination gout soup and external application of TCM compared with colchicine tablets also show fewer incidence incidences of redness and swelling, aggravation on heat, adverse joint flexion & extension, scanty dark urine, and constipation in the experimental group. Adverse event of laboratory changes of leukopenia found 3 three patients in experimental group and 7 seven patients in control group of compound tufuling oral liquid (CoTOL) compared to placebo CoTOL. Three other study studies did not observe of adverse event in the use of herbal therapy; however, a study by Estee Chan found the use of CAM related with higher cost of treatment in gout arthritis patients.

Two systematic reviews were found, one for gout and the other for acute gouty arthritis. Chinese herbal medicine is effective, according to the earlier systematic review, which included 14 randomized controlled trials with 1,179 patients. The later systematic review, which included 25 randomized control trials with 1,750 patients, claimed that traditional Chinese medicine had a better therapeutic effect and a lower incidence of adverse reactions for gout [13, 14]. Due to the heterogeneity of comparisons and treatment durations, our data did not

support a potential meta-analysis for all included studies. Our research's findings regarding safety are in line with these earlier reviews, and our paper's methodological quality evaluation is consistent with that of the other two systematic reviews. One of the strengths of our study is that it identified a relevant evidence, and we included comprehensive outcomes of gout arthritis in progression of pain, changes in serum uric acid and its relation to adverse event.

There are limitations on this review. We disqualified randomized controlled trials that did not disclose the diagnostic standards, therapeutic results, or the use

of non-human intervention during the second full-text review for eligibility. As a result, a comprehensive and all-encompassing summary of the evidence was not possible. Due to a lack of data, quantitative subgroup analyses examining the impacts of age, intervention type, comorbidity, or treatment course could not be carried out. In addition, we were unable to locate any proof of herbal medicine therapies long-term effectiveness, which was primarily due to the lack of follow-up results.

### Conclusion

The findings of the comprehensive

review show that herbal therapy or medication are potentially more effective than western medications or placebos at slowing the progression of pain, lowering blood uric acid levels, and preventing some adverse events in gout patients. The effectiveness and safety of these herbal medications in the treatment of gout arthritis patients can be further demonstrated by additional studies with sophisticated research designs. The clinical translation and application of these components can be aided by the identification of the active compounds and the clarification of the underlying mechanisms of action.

**Declaration of patient consent:** The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given his/her consent for his/her images and other clinical information to be reported in the Journal. The patient understands that his/her name and initials will not be published, and due efforts will be made to conceal his identity, but anonymity cannot be guaranteed.

**Conflict of Interest:** NIL; **Source of Support:** NIL

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