

Short Review

Simiao Powder as an Effective Remedy for Gout

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Abstract

Gout is an increasing metabolic disease due to the buildup of uric acid. The buildup of uric acid due to inadequate excretion leads to uric acid crystal formation. Treatment for gout aims to eliminate the uric acid crystal formation so that inflammation decreases. Traditional gout medication is usually allopurinol, but increasing studies have proven that herbal remedies may be promising. Over the past few years, studies have demonstrated that Simiao powder, a traditional Chinese medicine (TCM), is more effective than allopurinol in reducing elevated uric acid. The four main herbs in Simiao powder, Cyathulae Radix, Coicis Semen, Atractoylodes Lancea, and Phellodendri Chinrnsis Cortex combined, possess anti-inflammatory properties that can effectively reduce uric acid. Simiao powder also has properties that can treat metabolic syndrome, which often coexists with gout. Though TCM can be more effective in some ways, combining TCM with Western medicine proves that the two can overlap effectively. The success of Simiao powder opens the door to further explorations of TCM in treating modern chronic conditions.



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Keywords

Hyperuricemia; gout; Simiao powder; TCM; herbal remedy

1. Introduction

Gout is an ancient disease dating back to 2640 BC when the Egyptians identified it as a distinct disorder [1]. In recent years, the prevalence of gout has been increasing due to several factors. Obesity, sedentary lifestyles, high blood pressure, and the lack of nutritious diets are just a few reasons for the rise in gout. The modern treatment for gout includes medications like allopurinol, which has been widely prescribed since its invention in 1963 [1]. Before allopurinol and other medications developed, the typical treatment for gout was herbal medicine. One of the earliest herbal remedies was colchicum, also known as meadow saffron. Colchicum, first prescribed by Alexander of Tralles in the sixth century BC, was proven effective [1]. Therefore, using herbal medicine as a cure is not a new concept. The use of Traditional Chinese Medicine (TCM) includes a plethora of herbs that have been used for thousands of years.

This paper will focus on the studies of Simiao powder, a form of TCM, as an effective remedy for gout. This review aims to explore the question of whether TCM can be used as an effective remedy for gout compared to traditional medication. The significance of Simiao powder as a treatment of gout is that it may be an alternative treatment with reduced side effects and perhaps more effectiveness. Given that TCM may be a promising treatment, metabolic disease may, in turn, be mitigated since it is often comorbid with gout. Gout and metabolic disease are becoming a greater health concern, which is why it is important to consider alternative treatments if traditional ones pose additional risks. Though there are many promising studies on Simiao powder, there is still room for more research to be conducted in the future. TCM is slowly becoming more accepted since many have concerns about the quality of the herbs since the government does not regulate it. Financial costs may also be another factor to consider.

2. Definition of Gout

To fully understand why Simiao powder is effective, it is necessary to understand what gout is. Gout is a disease characterized by an accumulation of uric acid crystals in the joints due to decreased uric acid output [2]. This mechanism is commonly called hyperuricemia. These crystals produce an inflammatory effect, resulting in arthritis. Hyperuricemia is the inability of the kidneys to regulate uric acid and completely excrete it. In this condition, the kidneys lack the proper enzymes needed for purine metabolism [2]. Chronic inflammation in the joints leads to erosions and bone destruction from the osteoblasts that release pro-inflammatory cytokines [2]. The dissolving of the bone tissue allows for uric acid crystal formation. Therefore, the main goal for treating gout is reducing the accumulation of uric acid crystals and inducing an anti-inflammatory effect.

3. The Potent Properties of Simiao Powder Ingredients

The promising results of Simiao powder as a treatment for gout were primarily due to the potent properties of its ingredients. The four main Simiao powder herbs include *Cyathulae Radix*, *Coicis Semen*, *Atractoylodes Lancea*, and *Phellodendri Chinensis Cortex* [3].

Cyathulae Radix is a powerful Chinese herb that has been used to treat a variety of conditions, one of them being gout. *Cyathulae radix* (CR) constituents include tannins, alkaloids, flavonoids, fatty acids, and triterpenes [4]. These properties all contribute to the anti-inflammatory and antioxidant effects. Many inflammatory responses are related to the activation of gene pathways. NF- κ B is a gene pathway that regulates many biological processes, such as immunity, cell growth, apoptosis, and inflammation [3]. *Cyathulae radix*'s powerful properties downregulate the gene expression of NF- κ B 65 and inhibit the activity, reducing inflammation [4]. Thus, this explains why CR is a potent component of Simiao powder for gout treatment. It is efficient, and its prolonged use has proven it a safe form of TCM [5].

Coicis semen is another potent Chinese herb used to treat gout and several conditions. *Coicis semen* is a polyphenolic compound derived from coix, usually in the form of coix lacryma-jobi. Unsaturated fatty acids, esters, polysaccharides, and triterpenoids being the main active components [6]. In one specific study of coicis semen, its properties were particularly successful in treating ischemic stroke. An ischemic stroke is a blockage in one of the blood vessels that supplies the brain. When ischemic stroke transpires, a large amount of ROS (reactive oxygen species) is produced, and oxidative stress is activated [6]. The authors found that coicis semen could exceptionally decrease the number of ROS cells, reflecting its anti-oxidative properties [6]. *Coicis semen* could, therefore, also be taken as a preventative measure for ischemic stroke, which is triggered by inflammation and free radicals.

Atractoylodes Lancea (AL) is an additional component in Simiao Powder and gout treatment. AL is particularly effective due to its powerful constituents. sesquiterpenoids (β -eudesmol, hinesol and atractylon) and polyacetylene (atractylodin) are the major active components in AL; A few ingredients that display anti-inflammatory effects include Atractylenolide I, Atractylenolide II, Atractylone, Hinesol, and B-Eudesmol [7]. One extraction of AL called petroleum ether (PE) could induce apoptosis, thus producing an anti-cancer effect [7]. Apoptosis kills many of the abnormal cells that cause cancer. Another extraction named Atractylenolide III can reduce the release of pro-inflammatory cytokines [7]. As mentioned, pro-inflammatory cytokines are released due to the chronic inflammation present in gout. Therefore, this proves that AL is a crucial component of Simiao powder used to treat gout.

Lastly, *Phellodendri Chinensis Cortex*, or *Cortex Phellodendri Chinesis* (CPC), is the last main ingredient used in Simiao powder. *Cortex phellodendri chinesis* comes from the dried bark of *Phellodendron chinensis Schneid.* or *Phellodendron amurense Rupr.* (Family Rutaceae). The rough bark mainly contains alkaloids, isoquinoline alkaloids, limonoids, phenolic acids, etc. [8]. Sun et al. [8] conducted a study to identify the chemical markers of CPC and cortex phellodendri amurense (CPA) and thus compared their effects. Though CPC and CPA are often used interchangeably due to their overlapping properties, in CPC, the antidiarrheal, antibacterial, and anti-inflammatory effects are linked to its chemical markers berberine and 3-o-feruloylquinic acid [8]. These chemical markers heavily contribute to the overall anti-inflammatory properties of CPC when utilized in Simiao powder.

Therefore, the four herbs in Simiao powder display several qualities that contribute to promising results in the treatment of gout. Each of the four herbs contains similar characteristics that are further enhanced when combined into one concoction. The common denominator between the four appears to be that each herb possesses anti-inflammatory effects, which explains why Simiao powder is especially effective in treating gout. Furthermore, the biological manner that explains why Simiao powder is able to reduce inflammation can be explained by its ability to hinder the NLRP3 inflammasome [9]. Therefore, NLRP3 is an immune receptor that is targeted by the constituents of Simiao powder.

4. The Effect of Simiao Powder on Lowering Uric Acid Levels

In earlier years, some studies have investigated the effect of the chemicals in Simiao powder on lowering uric acid. In subsequent studies, the experimenter also demonstrated the specific principle of the impact of Simiao powder on lowering uric acid. In addition, this review further investigated the role and effect of various remedies modified by Simiao powder in reducing UA function.

In 2008, Shi et al. demonstrated that Simiao powder can effectively reduce blood uric acid levels in patients as a treatment for gout symptoms by comparing clinical efficacy [10]. However, they did not further investigate the specific substance in Simiao powder with a mechanism of action for lowering uric acid and its related pharmacology.

In 2008, Qiu Renbin et al. explored the efficacy of the traditional Chinese medicine prescription Modified Simiao Decoction in the treatment of gouty arthritis and its impact on uric acid and C-reactive protein levels [11]. The study included 120 patients with gouty arthritis, divided into the treatment group treated with Modified Simiao Tang (MST) and the control group treated with allopurinol. The results showed that the total effective rate of the MST group was significantly higher than that of the allopurinol group. Moreover, MST was more effective in reducing uric acid and C-reactive protein levels, indicating that it can significantly improve signs and symptoms of gouty arthritis [11].

In 2014, Hu et al. studied the effect of the Simiao pill, which has the same composition as Simiao powder, on uric acid levels [12]. Using a mouse model of hyperuricemia, they found that the Simiao pill lowered blood uric acid levels [12]. Hyperuricemia is a disease manifested by high serum uric acid levels, making it a precursor of gout [13]. The Simiao pill enhances uric acid excretion in hyperuricemic mice by downregulating renal mURAT1 and mGLUT9, which upregulates renal mOAT1 to reduce their uric acid levels [12].

In 2017, Liu et al. and his collaborators conducted a meta-analysis of Modified Simiao Decoction (MSD) in the treatment of gouty arthritis. The analysis chose 24 RCTs that showed the effects of MSD on serum uric acid levels. The MSD groups were more beneficial than anti-inflammation medication, urate-lowering therapies, and combined therapies [14]. Furthermore, there was no statistical heterogeneity for AEs reported in 11 trials, indicating that MSD is safe when used correctly [14].

In a 2022 study, Ling Cao et al. analyzed the composition of Simiao powder and found that it contained a phytohormone called estrone [15]. Estrone, a type of estrogen, has the effect of increasing uric acid excretion [16]. Therefore, when women are in the reproductive stage, the high production of estrogen allows women to rarely develop hyperuricemia or gout [17]. In this study, the researchers found that because Simiao powder is rich in estrone, SUA levels in hyperuricemic

mice were significantly reduced after treatment [15]. This study shows that women with gout may have reduced symptoms during the reproductive stage.

Meanwhile, in 2022, Huachong Xu et al. used a network pharmacology approach combining a multi-component target pathway model consisting of a network of drug component targets and biological targets [3]. By using allopurinol and Simiao powder separately to treat mice with high uric acid levels, he found that Simiao powder was able to reduce serum uric acid levels to normal levels while allopurinol was able to reduce them further below normal levels [3].

Research by Yue Qian and Yan Shen in 2023 paid special attention to the impact of Simiao powder on intestinal flora. This study conducted experiments on a rat model of potassium oxonate-induced hyperuricemia [18]. The results of the study showed that Simiao powder intervention significantly reduced serum uric acid, blood urea nitrogen, and creatinine levels, while increasing uric acid levels. In addition, Simiao powder can also reduce pathological damage to the kidneys of hyperuricemic rats and exhibit a dose-dependent decrease in xanthine oxidase activity in serum and liver tissue [18]. Notably, Simiao powder improved the diversity of intestinal microbiota in hyperuricemic rats, reducing the abundance of specific bacterial species such as *Parabacteroides johnsonii*, *Corynebacterium urealyticum*, and *Burkholderiales bacterium* [18]. These results suggest that Simiao powder can alleviate hyperuricemia by modulating the composition of intestinal microbiota.

5. Metabolic Properties of Gout

Gout is exacerbated by poor metabolic and endocrine regulation, which makes it a metabolic disorder [3]. Tottham and his colleagues [19] explored the relationship between metabolic syndrome and gout. Metabolic syndrome has many risk factors that result in repercussions, including insulin resistance and diabetes, obesity, hyperlipidemia, hypertension, and cardiovascular disease [19]. Tottham, et al. [19] used data from WHO to find that half of the participants with gout also had metabolic syndrome. There is a significant link between gout and metabolic syndrome, with one worsening the other. Using Simiao powder as a treatment for gout may also reduce symptoms of metabolic syndrome since Simiao powder can attach to two of the targets related to metabolism and endocrine: PTGS1 and PPARG [3]. Xu, et al. [3] explains that when binding PTGS1 and PPARG with Simiao powder, reactions to inflammatory stress are mediated. This binding action is referred to as molecular docking. Simiao powder possesses a powerful ability to dock molecularly and reduce inflammation from gout. This molecular docking with PTGS1 and PPARG that reduces inflammation from gout reveals the mechanism of action for Simiao powder.

The success of Simiao powder as a remedy for gout opens the door to further explorations in TCM. Though TCM has existed for thousands of years, many still question its safety and effectiveness. Xu & Xia [20] explain that randomized control trials rarely validate TCM. TCM has proven to be hard to back up since some concepts are subjective. Most Chinese people have concluded that TCM is more effective for chronic diseases, while modern medicine is more effective for minor ailments [12]. This conclusion explains why Simiao powder is more effective in treating gout since it is a chronic condition. The herbs used in Simiao powder can even be a preventative measure for gout. An advantage of TCM is that there may be fewer side effects [12], so it can be used preventatively or over an extended period of time.

6. The Overlap between Simiao Powder and Western Medicine

In 2024, Qu, Pengda et al. found that compared with conventional treatment, traditional Chinese medicine decoction can effectively reduce adverse events and laboratory indicators such as blood uric acid and inflammatory markers [21]. Network pharmacology identified active ingredients and target genes, highlighting underlying mechanisms and signaling pathways such as IL-17 and PI3K-AKT [21]. This suggests that traditional Chinese medicine treatment may be an effective complementary therapy for gouty arthritis.

Long-term experiments have proven that conventional Western medical gout treatment often has some side effects. Colchicine, non-steroidal anti-inflammatory drugs, and glucocorticoids are the traditional treatments in Western medicine. They can achieve efficacy in the short term, improve patients' pain symptoms, and control the disease [22]. Yet, even when these drugs are used as prescribed, they may cause serious side effects, such as liver and kidney function damage due to overdosing. There may also be gut discomfort, so physicians often limit the clinical use of these drugs [22].

Furthermore, allopurinol is more effective in reducing serum UA, but Simiao powder is more effective in lowering serum urea nitrogen (BUN) levels and serum creatinine (Cr) levels [3]. However, allopurinol can only treat the linear stage of gout, whereas Simiao powder can treat gout at any stage of the disease due to its properties [3]. Therefore, the implication is that Simiao powder is more effective and versatile in alleviating gout than the conventional drug allopurinol.

Under the premise of using Simiao powder as the base drug, researchers have also invented many remedies to enhance the efficacy of Simiao powder. In 2019, Wu found that the gout formula made up by adding the ingredients of the original Simiao powder, such as Cichorium, Ginseng, Poria, Zelenia, Plantago, and Lonicera [23], was taken together with Celecoxib capsules to achieve a combination of Chinese and Western medicine treatment. This combination can effectively reduce the acute inflammatory index in the patient's blood, inhibit the body's inflammatory response, and induce a hypouric acid effect [23]. Therefore, an overlap between TCM and Western medicine proves the ability of the two to work together.

7. Implications and Limitations

While TCM is an effective remedy for gout, there are still implications to address. TCM, along with vitamins, supplements, and herbs are not regulated by the government. There may be a difference in two of the same products where the quality of herbs may be uneven [24]. Furthermore, the process of acquiring materials for TCM may also be cumbersome since it may involve harvesting and cultivating products [24]. Another point to address is that TCM is usually not covered by insurance. Traditional medication for gout, like allopurinol, are commonly covered by insurance, whereas Simiao powder would not be. This may lead to increased financial costs if it is being used as the main form of treatment.

8. Conclusion

In conclusion, Simiao powder is an effective form of TCM used to treat gout. Gout has been around for thousands of years and has recently increased. Obesity, lack of nutritious diets, sedentary lifestyles, high sodium, and processed foods are just a few things that have contributed

to this rise. Gout is characterized by uric acid buildup, or hyperuricemia, in the joints, leading to inflammation. Many studies have established that Simiao powder is an effective treatment for gout because of its potent properties. The four herbs in Simiao powder all possess powerful constituents that are anti-inflammatory. The analysis that Xu, et al. [3] and his team conducted revealed that 95% of the ingredients in Simiao powder tackled the targets of gout. Simiao powder also possesses many metabolic properties that can concurrently treat metabolic syndrome. Nonetheless, many may still question the effectiveness and safety of TCM treatments like Simiao powder. Table 1 below provides a summary of the information reviewed as it relates to whether Simiao powder is an effective remedy for gout. The benefits of Simiao powder to treat gout is still worth further exploring, particularly if the benefits surpass modern medicine.

Table 1 Summary of reviewed literature and relation to Simiao powder for gout.

Classification	Significance	Year	Authors	Research Method	Results/Target
[1]	Gout history	2006	Schwartz		n/a
[2]	Gout mechanism	2017	Ragab, et al.		hyperuricemia
[3]	Simiao powder tackles gout targets	2022	Xu, et al.	Network pharmacology and in vivo experiments	95% of ingredients in Simiao powder tackled gout
[4]	Cyuthae radix	2019	Huang, et al.	In vivo and in vitro	Alkaloids and flavanoids reduce inflammation
[5]	CR safety	2006	Nanjing University		CR is a safe form of TCM
[6]	Coicis semen	2020	Du, et al.	In vivo and in vitro	Decreased ROS cells
[7]	Atractylenolide I and Atractylenolide II	2017	Jun, et al.	In vivo and in vitro	↓PI3K/Akt/mTOR ↓p-STAT3/p-Src
[8]	Cortex Phellodendri Chinesis (CPC)	2016	Sun, et al.		berberine and 3-o-feruloylquinic acid lead to antibacterial, antidiarrheal, and antiinflammatory effects
[9]	Simiao powder mechanism of action	2011	Kingsbury, et al.		NLRP3 is targeted by Simiao powder constituents
[10]	Simiao powder	2008	Shi, et al.	Clinical trial	Reduced blood uric acid levels

[11]	Simiao Decoction	2008	Qiu Renbin et al.	Clinical trial	Reduce uric acid and C-reactive protein levels
[12]	Simiao pill vs allopurinol	2010	Hu, et al.	Hyperuricemic mice	Simiao pill decreased serum uric acid and creatinine levels
[13]	Hyperuricemia in gout	2020	Skoczyńska, et al.		Elevated serum uric acid
[14]	Simiao Deconcotion	2017	Liu et al		Reduce serum uric acid levels
[15]	Si-miao-san (SMS) powder	2022	Cao, et al.	In vivo	phytohormone estrone reduces SUA levels
[16]	Estrone	2015	Gautam, et al.		Estrone increases uric acid excretion
[17]	Women in reproductive stage	2011	Nakayama, et al.		Higher estrone leading to reduced gout
[18]	Simiao powder	2023	Yue Qian and Yan Shen	Hyperuricemic mice	Modulate the composition of intestinal flora to alleviate hyperuricemia.
[19]	Metabolic syndrome in gout	2017	Thottham, et al.		Half of participants with gout also have metabolic syndrome
[20]	TCM effectiveness	2019	Xu, J., & Xia, Z	Randomized control trials	Randomized controlled trials (RCTs) rarely validate TCM
[21]	traditional Chinese medicine decoction	2024	Qu, Pengda et al.		Compared with conventional treatment, traditional Chinese medicine decoction can effectively reduce adverse events
[22]	Western medication side effects	2017	Huang F, Ma WF		Liver and kidney function damage and gut discomfort
[23]	Simiao powder ingredients (TCM) combined with celecoxib capsules (western medication)	2019	Wu, et al.		Reduced inflammatory response and induce hypouric effect

[24]	TCM safety	2018	Tang, et al.	SWOT analysis	Quality of herbs may be uneven and the process is cumbersome
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Author Contributions

Author Anna Koczwara drafted the original manuscript, including collecting and analyzing the data to formulate the review. Author Lingfan Jiang reviewed the manuscript and added substantial material. Both authors contributed to revisions. Author Shasha Zhang provided oversight during the drafting process, including the original topic idea. All authors reviewed the final manuscript.

Competing Interests

The authors have declared that no competing interests exist.

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