

## THE MULTIFUNCTIONAL ROLE OF HERBAL PRODUCTS IN THE MANAGEMENT OF GOUT (VATARAKTA): A COMPREHENSIVE REVIEW

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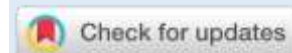
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## ABSTRACT

**Introduction:** *Vatarakta* is a *Vata Vyadhi* that occurs due to exacerbated *Vata* and *Rakta Dosha* by their causative factors. It can occur in the whole body but since joints of the hand and foot are more affected it resembles gouty arthritis as described in allopathic science. Gout is a disease described in conventional medicine that has similarities to the *Vatarakta*. It is a type of inflammatory arthritis that is triggered by the crystallization of uric acid within the joints and is often associated with hyperuricemia. Hyperuricemia can be caused by overproduction of uric acid, or, more commonly by inefficient excretion by the kidneys. The clinical presentation of gout ranges from the typical episodic acute inflammation of the joint to chronic tophaceous gout, chronic polyarticular arthritis, urate nephrolithiasis, and interstitial nephropathies. Several herbal drugs are well known for their therapeutic effects and lower toxicity and are important substances for new drug development.

**Objective:** The objective of this systematic review was to explore and validate the efficacy of herbal medicines in the management of gout. This review aims to update some research findings regarding the biological activities of the herbal ingredients of *Ayurvedic* medicines used in gout and also to collect an adequate basis for the optimal integration of *Ayurvedic* medicines into the conventional health system (Allopath).

**Materials & Methods:** Systematic literature searches were carried out and the available information on *Vatarakta* and gout was collected via electronic search and a library search for articles published in peer-reviewed journals and locally available books. Literature searches were also carried out to find the biochemical effects of various herbs mentioned in the management of hyperuricemia and gout.

**Conclusion:** It has been demonstrated that plant-derived biochemicals have a potential effect on gout. These effects comprise XOD inhibitory action, uricosuric, anti-inflammatory, anti-oxidant effects, etc. During the analysis of the literature available in *Ayurveda*, Allopathy, and related other branches of health science it was found that integrative medicine would be the optimal strategy to develop more effective agents in the treatment of gout (*Vatarakta*) and a combination of therapies may be very effective in reducing both the effect and frequency of disease.

**Key words:** *Vatarakta*, *Ayurveda*, *Vata Dosha*, *Rakta Dosha*

## INTRODUCTION

*Vatarakta* is a *Vata Vyadhi* that occurs due to exacerbated *Vata* and *Rakta Dosha* by their causative factors.

[1] It is a clinical condition that induces severe pain in the joints of the whole body especially of foot and hand. [2] People with a sedentary lifestyle and excessive eating are more likely to develop *Vatarakta*. [3] It can occur in the whole body but since joints of the hand and foot are more affected it resembles gouty arthritis as described in allopathic science.

Gout is one of the most prevalent diseases among crystal arthritis that is a consequence of disturbed uric acid metabolism. It is a type of inflammatory arthritis that is triggered by the crystallization of uric acid (UA) to monosodium urate (MSU) crystal and its deposition within the joints. Most of the time it is associated with high blood serum uric acid (hyperuricemia). [4]

Uric acid is produced during the metabolism of both endogenous and exogenous (dietary) purines. It is a type of weak acid and the normal solubility at physiological level is 6.8mg/dl. In humans, a large part of it is excreted through the kidney (approximately 2/3 part) and a small amount through the gastrointestinal tract (1/3 part). The normal level of uric acid in male blood is 3.5 to 7.2 mg/dL and 2.6 to 6.0 mg/dL in females. [5]

The prevalence of hyperuricemia has impetuously grown in the whole world. It is 1–4% of the general population. In Western countries, it occurs more in men than women. [6]

The goals of treatment provided by modern science are to end the pain of acute flares, prevent future attacks, and slow or prevent the formation of tophi and kidney stones [7] New emergent drugs are effective in the management of gout and hyperuricemia, but long-term

clinical trials are needed to validate their efficacy and safety profile. [8]

Medicinal plants are used in alternative medicine systems in the treatment of various diseases and health maintenance. Plants secrete many organic compounds known as bioactive compounds that have some biological activity with medicinal potential. Bioactive compounds mainly include three main groups, terpenes, phenolics, and nitrogen-containing compounds such as alkaloids. The anti-inflammatory and anti-analgesic can be attributed to their high steroids, tannins, terpenoids, and saponins while anti-oxidant can be due to polyphenolic compounds, flavonoids, carotenoids, etc. This unique anti-oxidant, anti-inflammatory, and other cellular effects help in various chronic and metabolic disorders. [9]

In this context, the causative factors of the disease were assessed, a treatment guideline based on the texts of *Ayurveda* and modern science was explored, and the optimal way to integrate the medical materials available in both the systems of *Ayurveda* and modern science was evaluated.

## MATERIAL AND METHODS:

Various aspects of *Vatarakta* as per *Ayurveda* such as the description of the disease, causative factors, involvement of *Dosha & Dushya*, development of disease, and management were reviewed in the *Samhitas* and other *Ayurvedic* literature. Available information on gout was collected via electronic search, articles published in peer-reviewed journals, and also locally available books. Literature on the biochemical effects of various herbs in the management of hyperuricemia and gout was also searched.

### Literature on gouty arthritis:

#### Physiology of purines and pathophysiology of Gout:

Uric acid is a metabolic waste product from purines which are involved in the enzymatic processes of nucleic acid synthesis. Purines are a group of nucleotides present in all body tissues and in many foods so purines can be synthesized endogenously or be derived from dietary sources. The dietary intake of purines contributes substantially to the blood uric acid.<sup>[10]</sup>

UA is the end-product of the breakdown of dietary and endogenous purines. Hyperuricemia arises from overproduction (from increased breakdown of exogenous or endogenous purines) or renal under-excretion of UA. Renal under-excretion accounts for 70% of urate load. Hyperuricemia is central to the development of gout. It reduces urate solubility and promotes MSU crystal nucleation and growth. Gout results from sustained hyperuricemia (serum uric acid (SUA)  $\geq 360$   $\mu\text{mol/L}$ ), which leads to intra- and/or peri-articular monosodium urate (MSU) crystal deposition.

MSU triggers the inflammatory process by being engulfed by synovial phagocytic cells leading to the release of lysosomal enzymes and the production of inflammatory chemokines. The presence of urate crystals on synovial fluid analysis is a gold standard method of definitive diagnosis but gout can be clinically diagnosed by both EULAR recommendations and ACR criteria.<sup>[11]</sup>

#### Different modalities of clinical management in modern science:

Asymptotic hyperuricemia, acute attacks, inter-critical gout, and chronic tophaceous gout are the four stages that evolved during the condition if not treated.<sup>[12]</sup>

The management of patients with gout implies the control of risk factors related to hyperuricemia, the effective and rapid control of acute attacks, and the persistent reduction of serum uric acid levels.<sup>[13]</sup> The goals of treatment are to end the pain of acute flares and intense inflammation with the help of Nonsteroidal anti-inflammatory drugs (NSAIDs) and colchicine, prevent future attacks and slow or prevent formation of tophi and kidney stones with the help of long-term management of hyperuricemia with drugs inhibits Xanthine

Oxidase activity namely Xanthine Oxidase Inhibitors (XOIs) and drugs inhibits the reabsorption of uric acid namely Uricosurics drugs.<sup>[14]</sup>

#### Literature on Vatarakta:

Vatarakta is a *Vata Dosha-dominated* disease that occurs due to aggravation of etiological factors of *Vata* and *Rakta Dosha*. Vitiating *Vata* and *Rakta Dosha* contribute to the induction and evolution of disease; hence its name is *Vatarakta*. *Adhya Vata*, *Kudha Vata*, and *Vata Balasa* are some common names used in the text for *Vatarakta*.<sup>[15]</sup> Obstruction of *Vata Dosha* by vitiating *Rakta Dosha* and worsening of *Rakta Dosha* by vitiating *Vata Dosha* are the main pathological developments in the origin and progression of the disease. This continues until the disease appears in the body.

Due to the *Sukshmatwa* & *Saratwa* properties of *Vayu* and *Dravatwa* & *Saratwa* of *Rakta*, *Rakta* & *Vayu* spread throughout the body and their channels. The angular anatomical structure of the joint hinders the movement of *Rakta* and *Vayu Dosha*.<sup>[16]</sup> As per involvement of body parts, it is of two types i.e., *Uthana* and *Gambhira*.<sup>[17]</sup> When symptoms are found in the whole body, it is known as *Ubhayashrita Vatarakta*.

#### Different modalities of clinical management in Ayurveda:

Specifically, excess *Vata Dosha*, excess *Rakta Dosha*, and *Shroto-avarodha* are the three cornerstone conditions that cause the development of the disease. Drugs comprising *Vatahara*, *Raktahara*, and *Shroto-Sodhak* properties are beneficial in this disease. Various single herbs or compound formulations in various dosage forms have been described in *Ayurvedic* literature for the amelioration and restoration of *Doshas* in general and the treatment of *Vatarakta* disease in particular. Bioactive compounds of herbal ingredients of these drugs have various beneficial therapeutic effects that help in alleviation of disease. (Table No. 1) *Ayurveda* drugs such as *Mahamanjisthadi Kashaya*, *Punarnava Guggulu*, *Amrita Guggulu*, *Kaishore Guggulu*, *Balaguduchyadi Taila*, *Pinda Taila*, *Guda Haritaki*, *Guduchi*, *Nimbadi Churna* *Sukumara Taila*, *Madhuka Taila*, *Satapaka Madhuka Taila*, etc., provide beneficial effects in the management of *Vatarakta*.

**Table No.: 1 Medicinal and therapeutic properties of various drugs described in Ayurveda for arthritic conditions:**

S. No.	Name of drugs	Therapeutic properties
1.	Mahamanjsthadi Kashaya <sup>[18], [19]</sup>	Many ingredients have Anti-oxidant and Anti-analgesic properties.
2.	Punarnava Guggulu <sup>[20]</sup>	Many ingredients have Anti-oxidant and Anti-analgesic properties.
3.	Amrita Guggulu <sup>[21]</sup>	Many ingredients have Anti-oxidant and Anti-analgesic properties.
4.	Kaishore Guggulu <sup>[22]</sup>	Many ingredients have Anti-oxidant and Anti-analgesic properties.
5.	Balaguduchyadi Taila <sup>[23]</sup>	Many ingredients have Anti-analgesic properties.
6.	Pinda Taila <sup>[24]</sup>	Many ingredients have Anti-analgesic properties.
7.	Triphala	Anti-oxidant, Anti-inflammatory, and Anti-hyperuricemia effects (Xanthine Oxidase Inhibitor (XOI) effect
8.	Tinospora cordifolia	Anti-hyperuricemia effects (Uricosuric action)
9.	Apium graveolens (Ajmoda)	Xanthine Oxidase Inhibitor (XOI) effect
10.	Azadirachta indica (Nimba)	Xanthine Oxidase Inhibitor (XOI) effect
11.	Catharanthus roseus (Sadabahar)	Xanthine Oxidase Inhibitor (XOI) effect
12.	Citrus limon (Nimbu)	Xanthine Oxidase Inhibitor (XOI) effect
13.	Cymbopogon citratus (Nimbu Bheda)	Xanthine Oxidase Inhibitor (XOI) effect
14.	Nyctanthus arbour-tristis (Parijata)	Xanthine Oxidase Inhibitor (XOI) effect
15.	Trigonella foenum-graecum (Meethi)	Xanthine Oxidase Inhibitor (XOI) effect
16.	Guggulu	Anti-inflammatory, Anti-oxidant activities, and Anti-arthritic properties

## DISCUSSION

*Ayurveda* is one of the oldest, complete and most scientific healthcare systems of AYUSH worldwide. It provides a comprehensive management of any disease conditions. The priority of this system is always to ensure an effective treatment program for the patient so that a complete cure is achieved. *Ayurvedic* medicines keep the organs healthy and strong during diseases and provide relief to the body by fighting diseases.

Increased *Vata Dosha*, *Rakta Dosha*, and obstruction in channels are the principal causes of the manifestation of *Vatarakta* disease. *Vatahara Drugs*, *Raktahara Drugs*, and *Sroto-Sodhak* drugs are essential in alleviating the symptoms. *Raktamokshan* and *Basti* are the most recommended procedures described in the literature.<sup>[25]</sup> The cumulative effect of all these regimes restores the movement in channels, pacifies the *Doshas*, and later improves the disease condition.

Herbal medicines not only provide safe and effective options for their goals but being multifunctional, they also work simultaneously on different aspects of the

body's disturbed internal environment. Herbal plants contain several bioactive chemicals (phytochemicals) whose comprehensive therapeutic efficacy is beneficial in the prevention and management of many diseases. Alkaloids, terpenes, flavonoids, lignans, plant steroids, curcumines, saponins, phenolics, and glucosides are some common phytochemicals extracted from plants that have therapeutic efficacy for the prevention and management of many disorders. There is ample evidence of anti-hyperuricemia potential, XOD inhibitory action, uricosuric, anti-inflammatory effects, and anti-oxidants in naturally occurring bioactive compounds from various medicinal plants that can protect the body from various insults and maintain its integrity and functions.

*Mahamanjsthadi Kashaya* is a very known *Kashaya* used in the *Vatarakta*. It contains more than forty herbal drugs including *Rubia cordifolia* (*Manjistha*), *Cyperus rotundus* (*Musta*), *Holarrhena antidysenterica* (*Kutaja*), *Tinospora cordifolia* (*Guduchi*), *Saussurea lappa* (*Kustha*) etc. It ameliorates the *Rakta Dosha* and strengthens nerves. It works on all three *Doshas* viz

*Kaphahar*, *Pittahara*, and *Vatahara*. The phenolic compounds of drugs have anti-oxidant properties which give it protective power in case of inflammation. Many studies show the anti-oxidant properties of its ingredients such as *Rubia cordifolia*, *Tinospora cordifolia*, *Cedrus deodar* etc.

*Punarnava Guggulu* is a polyherbal formulation including *Boerhavia diffusa* Linn (*Punarnava*), *Ricinus communis* Linn. (*Erandamula*), *Sesame indicum* (*Tila*) *Taila*, *Zingiber officinale* Roxb (*Sunthi*), *Commiphora mukul* (*Guggulu*), etc. is used in mainly for the treatment of *Vatarakta*. It is also indicated for the treatment of *Gridhrasi*. Most of the ingredients of *Punarnava Guggulu* are *Laghu*, *Ushna* and *Ruksha Guna*, *Katu*, *Tikta*, *Kashaya Rasa*, *Ushna Virya*, and *Katu Vipaka*. It pacifies *Kapha* and *Vata Dosha*.

*Amrita Guggulu* a polyherbal formulation that is mentioned in the management of *Vatarakta* contains *Tinospora cordifolia* (*Guduchi*), *Commiphora mukul* (*Guggulu*), *Terminalia chebula*, *Emblica officinalis* and *Terminalia bellerica* (*Triphala*), *Baliospermum montanum* (*Danti*), *Zingiber officinale* (*Sunthi*) *Piper nigrum* (*Marica*), *Piper longum* (*Pippali*), *Embelia ribes* (*Vidanga*), *Operculina turpethum* (*Trivrtta*) and *Cinnamomum zeylanicum* (*Dalchini*). Most of the ingredients are *Laghu*, *Ushna* and *Ruksha Guna*, *Tikta*, *Kashaya*, *Katu Rasa*, *Ushna Virya*, and *Katu*, *Vipaka*. It has *Tridoshahara* property but mainly alleviates *Kapha* and *Vata Dosha*.

*Kaishore Guggulu* is a medicine mainly used in *Vatarakta* (Gout). It is a polyherbal medicine containing *Terminalia chebula* (*Haritaki*), *Terminalia bellirica* (*Vibhitaki*), *Emblica officinalis* (*Amlaki*), *Tinospora cordifolia* (*Guduchi*), *Piper longum* (*Pippali*), *Piper nigrum* (*Marich*), *Zingiber officinalis* (*Sunthi*), *Embelia ribes* (*Vidang*), *Operculina turpethum* (*Nishoth*), *Baliospermum montanum* (*Danti*) and *Commiphora mukul* (*Guggulu*). Most of the ingredients are *Laghu*, *Ruksha Guna*, *Tikta*, *Katu Rasa*, *Ushna Virya*, and *Katu Vipaka*. It pacifies vitiated *Vata & Rakta Dosha* and clears the channels to make the normal movement of *Vata & Rakta Dosha*.

*Pinda Taila*, a unique oil preparation contains Beeswax (*Madhucchishta*), *Rubia cordifolia* (*Manjistha*),

Oleo-gum resin of *Shorea robusta* (*Sarja rasa*), and *Hemidesmus indicus* (*Sariva*), *Jala* (water) and *Sesame indicum* (*Tila*) *Taila*. These drugs are *Rakta-sodhaka*, *Daha-hara*, *Sula-hara* in nature. It alleviates the symptoms of *Vatarakta* like *Ruk*, *Daha*, *Toda*, and *Sotha*.

*Balaguduchyadi Taila* contains *Sida cordifolia* (*Bala*), *Tinospora cordifolia* (*Guduchi*), *Cedrus deodara* (*Surdaru*), *Nardostachys jatamansi* (*Jatamansi*), *Saussurea costus* (*Kushtha*), *Pterocarpus santalinus* (*Rakta-chandana*), *Boswellia serrata* (*Kundururu*), *Valerina wallichii* (*Nata*), *Withania somnifera* (*Ashwagandha*), *Pinus roxburghii* (*Sarala*), *Pluchea lanceolata* (*Rasna*), *Sesame indicum* (*Tila*), and it has *Vataraktahara*, *Dahaghna*, *Vedanasthapana*, *Shophaghna* action. Most of the ingredients are *Tikta*, *Madhura Pradhana Rasa*, *Laghu*, *Snighdha guna*, *Ushna Virya*, *Katu Vipaka*.

*Triphala* is a famous herbal medicine that comprises equal parts of three medicinal myrobalans; *Terminalia chebula* Retzr. (*Haritaki*), *Terminalia bellerica* Linn. (*Vibhitaki*) and *Emblica officinalis* Gaerth (*Amalki*). It contains several phytochemical compounds such as ellagic acid, gallic acid, chebulinic acid, bellericanin,  $\beta$ -sitosterol, and flavonoids in high concentration. The anti-oxidant, anti-inflammatory, and other effects of *Triphala* have been studied through various studies. A study explored the anti-hyperuricemia effect of *Triphala*, in potassium oxonate-induced hyperuricemic mice in vivo, and examined its inhibitory effects on xanthine oxidase (XOD), inflammatory mediators and DPPH radicals in vitro. In another similar study free radical scavenger and uric acid formation inhibition indicative of xanthine oxidase enzyme inhibitory activity was explored.<sup>[26]</sup>

*Tinospora cordifolia* commonly called *Guduchi* is one of the extensively used herbs in *Ayurvedic* medicine. A variety of bioactive chemicals derived like alkaloids, steroids, diterpenoid lactones, and glycosides from different parts of the plant body which include the stem, root, and whole plant. The starch obtained from their stem known as "*Guduchi-satva*" is very useful in many diseases. The compounds possess various medicinal properties and make it possible to have wide applications in multiple disease conditions. A study on

extracts of *T. cordifolia* shows potent uricosuric action. Polysaccharides in aqueous extract and *Galo satwa* may be responsible for uricosuric action.<sup>[27]</sup>

In vitro Xanthine Oxidase Inhibitory (XOI) effect of some medicinal plants namely *Apium graveolens* (*Ajmoda*), *Azadirachta indica* (*Nimba*), *Catharanthus roseus* (*Sadabahar*), *Citrus limon* (*Nimbu*), *Cymbopogon citratus* (*Nimbu Bheda*), *Nyctanthus arbour-tristis* (*Parijata*), *Psidium guajava* (*Amrooda*), *Salvia hispanica* (*Chia*), *Tinospora cordifolia* (*Guduchi*) and *Trigonella foenum-graecum* (*Meethi*), was measured spectrophotometrically. Allopurinol has been used as a positive control in this study. The plant parts used are leaves and seeds. Plant extracts are extracted in two different solvents: water and methanol. The study was undertaken to examine the potential of these plants for their inhibitory activity against the enzyme called XOD.<sup>[28]</sup>

*Guggulu* is purified Oleo-gum resin, and it has been very effective in chronic arthritic conditions such as gout, rheumatoid arthritis etc. It has very potent anti-inflammatory and anti-oxidant activities due to its bioactive compound. *Guggulu* contains diterpenoids, triterpenoids, steroids, long-chain aliphatic tetrols, aliphatic esters, ferulates, lignans, carbohydrates, and a variety of inorganic ions besides minor amounts of sesamin and other unidentified constituents. *Guggulu* is defined as an excipient capable of increasing the bioavailability and efficacy of the drug in the tissues with which it is co-administered. It helps in the reduction of pain, redness, and inflammation by its anti-inflammatory and anti-arthritic properties.<sup>[29]</sup>

## CONCLUSION

This review provides a comprehensive summary of *Ayurvedic* medicines based on plants described in ancient literature for the treatment of gout. Many herbo-mineral preparations as well as single herbal and mineral drugs are mentioned in *Ayurvedic* literature for their anti-gout effect and their scientific evidence is also being evaluated through various scientific procedures. Still, only a few have scientific validation. The plant contains a mixture of complexes of various categories of bioactive compounds having biological

properties such as anti-oxidants, detoxification enzymes, and stimulation of the immune system. Further, the preclinical and clinical studies on these active constituents should be performed to explore their anti-gout and anti-hyperuricemia effects. Plant-derived biochemicals have a potential effect on gout comprising XOD inhibitory action, uricosuric, anti-inflammatory effects, anti-oxidants, etc. Based on these it can be submitted that combination therapy may also be used to develop more effective agents in the treatment of gout due to their synergistic effect.

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