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Medicinal Plants Used in Hyperuricemia and Gout - A Review

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Abstract: ***Hyperuricemia is a clinical condition characterized with excess of uric acid in the blood. It develops either by overproduction of uric acid caused by a metabolic disorder or due to under excretion of blood uric acid due to abnormal renal urate transport activity. Gout is a chronic progressive rheumatic disease in which elevated serum urate levels lead to the precipitation of monosodium urate crystals within the joints and other tissues. Medicinal plants have been used to treat various ailments since ancient times; hence, ethnobotanical investigations play an important role in pharmacological studies. This article provide a comprehensive review ofsome Evidence based In - silico, In - vitro, In - vivo and Clinical studies to support the scientific use of Ayurveda herbal medicine for hyperuricemia and and Gout. Ayurvedic Medicinal plants with Anti - inflammatory, Analgesic, Anti - hyperuricemic, Anti - oxidant property along with Mūtrarōgahara, Śōthahara, Vātahara, Āmavātahara properties are expected to have effect in Hyperuricemia and Gout. The purpose of this review is to collect and document information of the Ayurveda herbal medicine with anti - hyperuricemic and anti - gout potential.***

Keywords: Hyperuricemia, Gout, Uric Acid

1. Introduction

Hyperuricemia is a clinical condition characterized with excess of uric acid in the blood It develops either by overproduction of uric acid caused by a metabolic disorder or due to under excretion of blood uric acid due to abnormal renal urate transport activity. [1] Kidney is the main regulator of serum uric acid levels where renal urate excretion is determined by the balance of the reabsorption and secretion of urate. Renal urate reabsorption is mainly mediated by two urate transporters—urate transpoter 1 (URAT1) and glucose transporter 9 (GLUT9) [2]

Uric acid is the end product of purine metabolism. Purines are derived from diet and partly from endogenous metabolism [3]. Xanthine oxidoreductase (XOR) is a highly versatile enzyme that is widely distributed among various species. It is a member of the group of enzymes known as molybdenum - iron - sulfur - flavin hydroxylases. XOR has two interconvertible forms, In human, xantine oxidase (XO) and xanthine dehydrogenase (XDH), Both the enzymes catalyze the oxidation of hypoxanthine to xanthine and then further forms uric acid final reactions in the metabolism of purine bases [4]. Uricase is an enzyme that further catalyzes the conversion of uric acid to the highly soluble allantoin that is excreted in the urine Unfortunately, uricase is not a functional human enzyme and, as a result, humans can develop hyperuricemia [5]. Hyperuricemia occurs when serum uric acid levels are >0.42 mmol/L [6]. Therefore, reducing uric acid is the main approach for the treatment of gout, with target levels of serum uric acid of less than 0.36 mmol/L [7]. Several risk factors have been established for the development of gout, including hyperuricemia, age, genetic factors, dietary factors, alcohol consumption, metabolic syndrome, hypertension and chronic renal disease [8].

Gout is a chronic progressive rheumatic disease in which elevated serum urate levels lead to the precipitation of monosodium urate crystals within the joints and other tissues [9]. Men are believed to have increased the risk of developing gout than women; however post menopausal women have more chance of developing gout, as the uricosuric action of estrogenis lost [10].

Prevalence of gout and hyperuricemia has increased in recent years. Despite major advances in treatment modalities 90% of patients with gout are poorly and improperly managed and their hyperuricemia continue [11]. Several drugs are approved for the treatment of Hyperuricemia and gout, like colchicine, steroids, non - steroidal anti – inflammatory drugs (aspirin, ibuprofen, naproxen) and allopurinol. Although these are effective, they cause severe side effects, such as skin allergies, fever, rash, renal dysfunction, and hepatic dysfunction [12]. Allopurinol, which isthe most commonly used xanthine oxidase inhibitor for gout causes nephrolithiasis, hypersensitivity reaction, Stevens - Johnson syndrome, renal toxicity, allergic reactions, and fatal liver necrosis. [13]

Recently, treating disease using medicinal plants is gaining new interest and research on medicinal plantshas increased worldwide due to fewer side effects. As per data available three quarters of worldwide population depend upon traditional herbal medicines for their primary health care in some aspect of their life. Recently there is a worldwide trend to go back to traditional and indigenous medicinal plants and research on such plants has increased worldwide. [14]

Ayurveda, the traditional Indian medicinal system remains the most ancient yet living traditions with sound philosophical and experimental basis. The ancient wisdom in this traditional system of medicine is still not extensively explored. Ayurvedic herbal medicine has been refined by

thousands of years of experience and practical application. According to *Ācārya caraka*, there exist no single *dravya* without medicinal value and which cannot be utilized as medicine [15]. India is a country that has more than 8, 000 species of medicinal plants and traditional medicines are being practiced for the treatment of gout and other rheumatic disorders from ancient time. However, in the present world we need Evidence based researches to prove the efficacy of a medicinal plant [16].

The aim of the present article is to provide a comprehensive review of some evidence – based *In - silico, In - vitro, In - vivo* and Clinical study data to support the scientific use of some plants which are mentioned in classics and also some Ethnobotanically useful plants in hyperuricemia and Gout. This article also includes the experimental methodologies, active compounds and mechanism against gout. Ayurvedic Medicinal plants with Anti - inflammatory, Analgesic, Anti - hyperuricemic, Anti - oxidant property along with Mūtrarōgahara, Śōthahara, Vātahara, Āmavātahara action are expected to have effect against Hyperuricemia and Gout.

2. Materials & Methods

The *In - silico, In - vivo, In - vitro*, Clinical study data of some Ayurvedic plants were collected and reviewed from journal articles and publications from internet. Publications with available abstracts were also reviewed.

A. In - Silico & In - Vitro Study

1) *Jalapippalī* (*Phyla nodiflora* (L.) Greene)
Useful Part: Leaf, Whole plant
Ayurvedic properties: *Asrajit, Artinut*
Pharmacological properties: The plant *Phylanodiflora* had traditionally used in the Ayurvedic, Sidha systems, for the treatment of urinary disorder, joint pain andswelling. The anti - hyperuricemic mechanism of the plant were studied by performing xanthine oxidase inhibitory, uricosuric, and liver xanthine oxidase/xanthine dehydrogenase (XOD/XDH) inhibitory studies in potassium oxonate - and hypoxanthine - induced hyperuricemic rats. The molecular docking of the active compound to the xanthine oxidase was simulated using computer aided molecular modeling analysis. The anti - hyperuricemic effect possessed by Plant was contributed by liver XOD/XDH inhibitory activities and also by uricosuric effect in both in - vivo and in - silico study. Flavonoids of the plant were also found to possess uric acid lowering action mainly through the inhibition of XOD/XDH activities. [17]The methanolic extract of leaves of the plant were tested for its anti - inflammatory and antinociceptive activities. The extract showed a significant antinociceptive activity comparable to diclofenac sodium in acetic acid induced writhing in white albino mice and a significant anti - inflammatory activity comparable to phenylbutazone against carrageenin - induced paw edema in rats. [18]

2) *Aśyuka (Morinda citrifolia*. L)
Useful Part: Fruit, leaf, root
Ayurvedic properties: *Tridoṣagna*
Pharmacological properties: In silico docking was performed in plant *Morinda citrifolia*commonly known as Noni, for 23 compounds which include 19 phytoconstituents which are reported in for the treatment of gout. The protein was obtained from protein data bank and the ligands were obtained from PubChem compound database. Flexible docking was performed using Molegro virtual docker. MolDock score, Re rank score and H bond interactions were used as parameters for evaluation of the protein - ligand complexes. In vitro activity was performed using xanthine oxidase isolated from bovine milk. The plant extract was compared with the standard drug allopurinol and it showed least inhibition as compared to that of the standard drug. The extract of *Morinda citrifolia* was found to possess Good hypouricemic activity where one or more of the phytoconstituents present in the extract may be responsible for the activity [19]. The noni plant wereused in painful inflammatory conditions like arthritis. The analgesic activity of plant juice on Mice was investigated using the hot plate test and it reduced pain sensitivity compared to standard. Alcohol extract of plant caused inhibition of MMP - 9 release from human monocytes. This anti - inflammatory effect was comparable to hydrocortisone. The plant showed excellent Anti - inflammatory activity [20].

B. In vivo Study

1) *Gudūci* (*Tinosporia cordifolia* (Wild.) Hook. f. &Thomson)
Useful Part: Fruit, leaf, root
Ayurvedic properties: Tridoṣagna, Raktaśōdaka
Pharmacological properties: The plant*Tinospora cordifolia* was studied to assessUricosuric activity of its different extracts in hyperuricemia induced in albino Wistar rat models using potassium oxonate. The uric acid level in serum and urine were measured. Uricosuric activity was evaluated using phenol red dye excretion model also. In potassium oxonate induced hyperuricemia - aqueous, hydro - alcoholic, dichloromethane extract of plant and giloy satwa significantly lowered the serum uric acid levels. All the extracts increased uric acid excretion and decreased the elevated serum uric acid levels induced due to potassium oxonate. aqueous extract and galo satwa significantly increased fractional excretion of uric acid and phenol red levels in blood indicating uricosuric property of the plant. Polysaccharides in aqueous extract and giloy satwa may be responsible for uricosuric action showed by the plant [21]. Comparitive study between proprietary and classical samples of *Gudūci* Ghana were evaluated for anti - inflammatory activity using carrageenan induced paw edema model in rats. Group A received test drug, Group B received market sample at a dose of 50 mg/kg orally, Group C (control group) received tap water. Decrease in edema was observed in Group A and B at 3 h interval by 33.06% and 11.71% respectively. Group A showed significant effects in comparison to control group. These experimental results were showed anti - inflammatory activity of *Gudūci* Ghana [22].

2) *Eraṇḍakarkaṭī (Carica papaya* L.)
Useful Part: Fruit, leaf, Latex, Seed
Pharmacological properties: A Study has been Conducted on the Protective influence of *Carica papaya* L. aqueous leaf extract against experimental hyperuricemia and acute renal injury in animal model. In this study it was found that alkaloids, flavonoids, 2 - deoxysugars and tannins were

present in the papaya leaf extract. Groups treated with papaya leaf extract had significantly lowered post induction blood uric acid levels but the effects were not dose dependent. Aqueous extract of *Carica papaya* leaf extract have shown potential Xanthine oxidase inhibitory activity. Papaya treated group showed less severe acute kidney injury. It showed significantly less areas of focal tubular granulovascular epithelial cell degeneration and glanular debris in tubular lumens and renal tissue was almost preserved [23]. In vitro and in vivo studies have shown that papaya extracts and papaya - associated phytochemicals possess anti - inflammatory and immunomodulatory properties [24].

3) *Palāṇḍu (Allium cepa* L.)
Useful Part: Fruit, leaf, root
Ayurvedic properties: Pramehajit, Agnidīptikara
Pharmacological properties: Onion is a well known traditional medicinal plant that has been consumed for its nutritional and health benefits for centuries. Freshly prepared Red onion juice were given by oral lavagein 3.5 g/kg.5 g/kg, 7 g/kg for hyeruricemic rats for 7 days. The study suggests that The serum uric acid level of the hyperuricemic groups treated with the highest dose of onion juice was similar to the allopurinol treatment, it revealed that in the treatment of gout 10.5 g/kg/day of Onion juice can be potentially used as a substitution of allopurinol. onion was found to increase the total antioxidant status in hyperuricemic rats more than that treated with allopurinol [25]. A study was reported that red onion appeared to contain highest anti - oxidant activity in methanol extracts compared to garlic, green peppers, white cabbage and white and yellow [26]. Astudy was carried out to determine the possible analgesic and anti - inflammatory effects of fresh onion juice in experimental animals. Hot plate and formalin tests were used to study the analgesic effect of drug in mice during acute and chronic pain stages respectively. The anti - inflammatory effect of fresh onion juice was assessed by applying carrageenan sub plantar injection to Sprague - Dawley rats. The obtained results were revealed that a significant analgesic property for fresh onion juice in both pain phases were found and the effects were similar to that of morphine (5 mg/kg) as the standard treatment. In anti - inflammation study, fresh onion juice was able to decrease the hind paw thickness significantly in comparison with control group and standard diclofenac group with a 10 mg/kg dosage. It can be concluded that fresh juice of onion is capable of inhibiting both acute and chronic pain as well as inflammation, with a stronger effect towards inflammation [27].

4) *Pāribhadra* (*Erythrina stricta* Roxb.)
Useful Part: Fruit, leaf, root
Ayurvedic properties: Śōthahara
Pharmacological properties: In a study it is revealed thatthe pet ether, chloroform and ethyl acetate fractions of plant extract when administered to hyperuricemic mice at a dose of 200mg/kg BWwas showed a significant reduction in urate levels in animal model. These fractions were elicited significant inhibitory actionon the Xanthine oxidase (29.88%, 35.75%, 15.97%) and xanthine de hydrogenase (29.88%, 35.75%, 15.97%) respectively. Phytochemical screening of the leaves of Erythrina stricta were revealed the presence of tannins, flavonoids, alkaloids and terpenoids . These results suggest that the leaves of the plant might be used as a potential source to treat gout and other inflammatory disorders [28]. In a study the extract of the plant was exhibited its anti - inflammatory action by means of inhibiting the synthesis, release of inflammatory mediators like serotonin, histamine and prostaglandin. From these results, it was revealed that anti oedematogenic effect of the plant on carrageenan and formalin induced oedema might be related to inhibition of inflammation mediator formation. So, study results were strongly suggested that the extract of plant leaves showed anti - inflammatory activity in albino rats [29].

5) *Āmalakī (Phyllanthus embilica* Gaertn.)
Useful Part: Fruit, leaf, root
Ayurvedic properties: Tridōṣagna, Rasāyana
Pharmacological properties: Antigout activity of aqueous and alcoholic extracts of Phyllanthus emblica fruits was evaluated on potassium oxonate - induced gout rat model following its 28 days repeated oral administration. The study was conducted in seven groups having six rats in each group. Groups 1, 2, and 3 were served as vehicle control group, gout control group, and standard treatment control group, respectively. Rats of all the groups except vehicle control group were administered potassium oxonate at 250 mg/kg (IP). For 28 days Groups 4 and 5 group orally received aqueous extract of P. emblica at 200 and 400 mg/kg, and alcoholic extract of P. emblica at 200 and 400 mg/kg. In the study it is revealed that, in gouty rats which were treated with aqueous and alcoholic extracts of P. emblica at 200 and 400 mg/kg body weight and standard treatment allopurinol at 5 mg/kg body weight showed reduction in serum creatinine, uric acid, BUN, and XO enzyme level along with significant improvements in histological structure of kidney. This suggested that Oral administration of aqueous and alcoholic extracts of P. emblica fruits for 28 days had shown protection against gout in dose - dependent manner in rats [30]. Anti - inflammatory activity was found in the water fraction of methanol extract of the plant leaves of Phyllanthus emblica [31] .

6) *Varānga* (*Cinnamomum cassia* (L.) J. Presl)
Useful Part: Bark, Leaf
Ayurvedic properties: Vātahara, Vastirōgahara, Āmahara
Pharmacological properties: Cinnamomum cassia plant bark is mainly used as a spice**.** Cassia oil from the plant at 600 mg/kg was found to be as potent as allopurinol, which reduced hepatic urate levels. In normal mice, urate levels in liver, were altered with dose - dependent decrease after cassia oil treatment. Also the ratio between liver uric acid and serum uric acid, was determined after cassia oil administration with time - and dose - dependent were found to show decreases in hyperuricemic mice. The positive dose - dependent decrease ratio was also observed after cassia oil treatment in the normal animals. In addition, cassia oil significantly showed marked reductions in liver XDH/XOD activities, with dose - dependence in the normal and hyperuricemic mice. The onset of inhibition in enzyme activities elicited by allopurinol was much higher than that elicited by cassia oil. These results were suggested the hypouricemic actions of cassia oil [32]. Cinnamon and its

components like cinnamic aldehyde wereuseful in the treatment of age - related inflammatory conditions [33].

7) *Āmra* (*Mangifera indica* L.)
Useful Part: Fruit, Leaf, Bark
Ayurvedic properties: Tridōṣagna
Pharmacological properties: The leaves of Mangifera indica were used as a medicinal material in traditional herb medicine for a long time in India, China, and other Asian countries. The study wereconducted to investigated the therapeutic effects of the ethanol extract of Mangifera indica in rat with monosodium urate (MSU) crystals - induced gouty arthritis. Effects of plant extract (50, 100, and 200 mg/kg) administrated for 9 days on the ankle swelling, synovial tumor necrosis factor - alpha (TNF - α), and interleukin - 1beta (IL - 1β) levels were assessed in MSU crystal rat. Oral administration of 100 and 200 mg/kg plant extract for 9 days reversed the abnormalities in ankle swelling, synovial TNF - α, IL - 1β mRNA, and protein levels. The results indicated the antigouty arthritis effect of plant extract may be mediated, at least in part, by inhibiting TNF - α and IL - 1β expression in the synovial tissues. The study suggested that Mangifera indica and its extract have a considerable potential for development as an anti - gouty arthritis agent for clinical application [34]. The aqueous extract of the plant were able to produce a dose - dependent and significant inhibition of the acute inflammation induced by the carrageen in rats when compared with controls. The percentage inhibition of oedema formation produced by plant was similar to that elicited by acetylsalicylic acid. The results were suggested that the plant contains active compounds with an anti - inflammatory activity [35].

C. In vitro & In vivo Study

1) *Bhūmyāmalakī (Phyllanthus niruri*L.)
Useful Part: Whole plant
Ayurvedic properties: Śōthahara, Mūtrajanana, Mūtrarōgartisamani
Pharmacological properties: Phyllanthus niruri is used as folk medicine in South America to treat excess uric acid. The study showed that the methanol extract of Phyllanthus niruri and its lignans were able to reverse the plasma uric acid of hyperuricemic animals. The mechanisms were investigated using uricosuric studies and xanthine oxidase assay in potassium oxonate - and uric acid - induced hyperuricemic rats. Plant methanol extract exhibited Good in - vitro xanthine oxidase inhibition with an IC50 of 39.39 microg/mL and a moderate in - vivo xanthine oxidase inhibitory activity. However, the lignans displayed poor xanthine oxidase inhibition in vitro and a relatively weak in vivo inhibitory activity at 10mg/kg. The intraperitoneal treatment with Phyllanthus niruri methanol extract showed 1.69 folds increase in urinary uric acid excretion when compared to the hyperuricemic control animals. Likewise, the lignans, phyllanthin, hypophyllanthin and phyltetralin exhibited up to 2.51 and 11.0 folds higher in urinary uric acid excretion and clearance, respectively. The pyrazinamide with phyllanthin co - administration exhibited a significant suppression of phyllanthin's uricosuric activity resembling that of pyrazinamide with benzbromarone. The study showed that the antihyperuricemic effect of Phyllanthus niruri methanol extract may be mainly due to its uricosuric action and partly through xanthine oxidase inhibition, whereas the antihyperuricemic effect of the lignans was attributed to their uricosuric action [36]. In Anti - inflammatory study showed Significant reduction of egg albumin - induced inflammation was observed only at a dose of 100 mg PNF1/kg bw, which was comparable with the effect produced by aspirin (100 mg/kg bw). At 50 and 100 mg/kg bw, PNF1 significantly increased pain threshold of inflamed tissue in the Randall - Selitto test but did not increase response to thermally induced pain in the hot - plate test. It was concluded that Phyllanthus niruri possesses antipyretic, anti - inflammatory, and antinociceptive effects that are peripherally mediated [37].

2) *Karkaṭaśṛṅgī* (*Pistacia integrima* J. L. Stewart)
Useful Part: Galls
Ayurvedic properties: Kaphavātahara
Pharmacological properties: Radical scavenging activity of the plant was determined by 1, 1 - diphenyl - 2 - picrylhydrazyl (DPPH) and xanthine oxidase (XO) inhibitory activity assay in vitro. Serum uric acid lowering effect was assessed by Fructose induced hyperuricemic animal model in various extracts of the plants. Ethyl acetate and n - BuOH fractions had the highest DPPH radical scavenging activity. The antioxidant activity as well as the inhibitory activity towards the enzyme XO by quercetin - 3 - O - beta - d - glucopyranoside, kaempferol - 3 - O - beta - d - glucopyranoside, quercetin - 3 - O - (6" - O - syringyl) - beta - d - glucopyranoside, kaempferol - 3 - O - (4" - O - galloyl) - alpha - l - arabinopyranoside, rutin together with aglycons, quercetin, kaempferol and apigenin was promising to continue in vivo hypouricemic studies. Ethyl acetate extract of leaf had dose dependent Uric acid lowering effect in hyperuricemic mice. This effect was comparable with quercetin but less than the standard drug allopurinol [38]. The plant Pistacia integrima had modest activity against hind paw acute and chronic inflammation induced by formalin and also showed significant analgesic activity against diclofinac [39].

3) *Nirguṇḍī (Vitex nigundo* L.)
Useful Part: Leaf, root, seeds
Ayurvedic properties: Rucāpaha, Śōthahara, Āmahara
Pharmacological properties: Hypouricaemic and antioxidant activity study of the various fractions of the hydromethanolic extract of the leaves of *V. negundo*, were conducted in hyperuriceamic mice model. Hyperuricaemia was induced by the uricase inhibitor, potassium oxonate. The antioxidant activity was assayed by in vitro methods such as DPPH assay, hydrogen peroxide and hydroxyl radical scavenging assays. Pyrocatehol and quercetin equivalents respectively were used to estimate the total phenolic and flavonoid contents of the fractions. All the fractions of the plant produced a significant reduction in serum urate levels and inhibited xanthine oxidase/xanthine dehydrogenase enzyme activities. All the fractions possessed hydrogen donor ability and free radical scavenging activity. The ethyl acetate and petroleum ether fractions were showed highest phenolic and flavonoid contents. The leaves of V. negundo exhibited as a potential source of antioxidant to treat gout and related inflammatory disorders [40]. The fresh leaves of Vitex negundo have anti - inflammatory and pain suppressing activities by mediating Prostaglandin synthesis

inhibition, antihistamine, membrane stabilising and antioxidant activities [41].

4) *Bimbī* (*Coccinia grandis* (L.) Voigt)
Useful Part: Leaf, root
Ayurvedic properties: Śōthahara, Kaphapithahara
Pharmacological properties: The Various fraction of plant were used to assess its anti - hyperuricemic effect. The degree of xanthine oxidase inhibition of Leaf extract of *Coccinia grandis* was determined in vitro by measuring the increase in absorbance at 295 nm associated with uric acid formation. Among the all fractions tested, the chloroform fraction exhibited highest potency. This was followed by the pet - ether, ethyl acetate, and residual fractions. The IC_{50} value of allopurinol was 6.1µg/ml. The hypouricemic and hepatic xanthine oxidase (XO) /xanthine dehydrogenase (XDH) inhibitory activities of the fractions were examined in - vivo using oxonate (280 mg/kg, i. p.) induced hyperuricemic mice. At a dose of 200 mg/kg orally for 7 days, the pet - ether, chloroform and ethyl acetate fractions produced a significant reduction in serum urate level and also inhibited hepatic XO/XDH activities when compared to hyperuricemic mice [42]. In a study it is revealed that the plant possess anti – inflammatory action. Treatment of the cells with the extract of plants significantly down regulated the expression and release of pro - inflammatory cytokines (IL - 6, IL - 1β, CCL2, CCL22, CXCL10/IP - 10, CX3CL1 and CXCL8/IL - 8), proteins (ERK5, BAX, BCL2, Cyclin D, ERK1, NF - κB, P - IκBα, P - NF - κB and P - p38) and molecular signaling pathways (NF - κB, p38 MAPK, ERK1/2 and IL - 6/JAK/STAT3 signaling cascades), which confirmed the action of the plant against inflammation [43].

Clinical Study

1) *Harītaki* (*Terminalia chebula.* Retz.), *Vibītaki* (*Terminalia bellerica* (Gaertn.) Roxb.)
Pharmacological properties: Clinical trial betweenStandardized aqueous extracts of Terminalia chebula and Terminalia bellerica versus febuxostat and placebo were done on reduction in serum uric acid levels in subjects with hyperuricemia. A total of 110 eligible subjects with hyperuricemia were assighned and randomized to either of the five treatment groups – T. chebula 500 mg twice a day (BID), T. bellerica 250 mg BID, T. bellerica 500 mg BID, placebo BID, and febuxostat 40 mg once daily plus an identical placebo – for a duration of 24 weeks. Serum uric acid levels were measured initially and at the end of 4, 8, 12, 16, 20, and 24 weeks. Statistical analysis was done using GraphPad Prism Software 4. All active treatment groups showed a reduction in serum uric acid levels compared to baseline and placebo. Significant reduction in mean serum uric acid levels started as early as 4 weeks following treatment, compared to baseline, with T. bellerica (500 and 250 mg), febuxostat, and T. chebula 500 mg; an increase in serum uric acid levels was seen with placebo. The serum uric acid levels became steady after 16 weeks of treatment and remained the same until the end of 24 weeks. The reduction of serum uric acid levels in the T. bellerica 500 mg group was nearly twice that of the T. chebula 500 mg group as well as T. bellerica 250 mg group at all time points. T. bellerica 500 mg reduced serum uric acid levels from 8.07±0.87 to 5.78±0.25 compared to febuxostat, which reduced serum uric acid levels from 8.53±0.97 to 4.28±0.67 at the end of 24 weeks. The efficacy of T. bellerica appeared to be dose dependent. All the formulations were well tolerated. The study concluded thatT. bellerica has the potential for treating hyperuricemia as it was devoid of any serious adverse effects in the study [44].

3. Discussion & Conclusion

Gout and Hyperuricemia are major health problems in worldwide population in recent years. Significant advances in treatment have been made. Current available treatment options are not completely satisfactory and have many side effects. To eliminate this problem, cost effective, safe and non - toxic drugs are required. In this paper, there is compiled In - silico, In - vitro, In - vivoandClinical study data of *Jalapippali, Aśyuka***,** *Gudūci, Erandakarkati, Palāndu, Pāribhadra, Āmalaki, Varānga, Āmra***,** *Bhumyāmalaki, Karkatakaṣrngi, Nirgundi Bimbi, Harītak andVibītaki* which are widely used ayurveda herbal medicines. These plants can be used in the treatment of gout and hyperuricemia. These plants exhibit anti - gout action by different mechanisms, such as uricosuric activity, XO inhibition, anti - inflammatory activity, and antioxidant activity. Plant extracts and isolated constituents which showed promising XO inhibition are also considered. Most of the isolated constituents were found to be flavonoids and phenolic glycosides. This review provides a comprehensive summary of medicinal plants described in ancient literature for the treatment of gout. Of these, in majority of plants only preclinical studies were done. Furthur clinical trials are required for promoting their therapeutic usage. Beside this, studies in combination therapy also can be used to develop more effective agents in the treatment of gout due to their synergistic effect.

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5. Conflict of Interest

The authors declare no conflict of interest.

6. Abbreviations

XO - xanthine oxidase
XDH - xanthine dehydrogenase
BW - Body weight

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