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Herbal Plants for the Treatment of Gout-A Review

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ABSTRACT: Gout is a common type of inflammatory arthritis caused by MSU formed in particular tissues, joints, and bones as a result of hyperuricemia. Gout is treated with different mechanisms Including Xanthine oxidase inhibitors, breakdown of uric acid, excretion of uric acid, and reducing inflammation. While medications offer therapeutic benefits, they can also have harmful side effects. The use of herbal medicine becoming popular due to the toxicity and side effects of allopathic medicines.Since ancient times, herbal and natural remedies have been used around the world to treat gouty arthritis with various mechanisms. This study presents some plants that are used for gout management with Xanthine oxidation inhibition. Xanthine and hypoxanthine levels in individuals with gout are higher than in healthy individuals. xanthine and hypoxanthine can be used as alternative indicators of uric acid for the diagnosis of gout in clinical practice. In this paper, we annexed the list of herbal plants and their chemical constituents used in the treatment of gout. The main substances that inhibit xanthine oxidase are flavonoids, Tannins, Chalcones, Xanthone and coumarin, Isoflavones, Saponins, Terpenoids, Stibenes, Alkaloids, Phenylethanoid glycosides.

KEYWORD: Gout, Herbal plants, Xanthine oxidase inhibitor, chemical constituent

I. INTRODUCTION

Herbal medicine, also known as botanical medicine or phytomedicine, involves using a plant's seeds, berries, roots, leaves, bark, or flowers for medical purposes. Herbalism has a longer history of use than Western medicine. Herbal medicine is gaining popularity due to advancements in clinical research, analysis, and quality control, demonstrating its effectiveness in illness prevention and treatment. With the advent of chemical analysis in the early 19th century, scientists began extracting and modifying plant active components.Later, chemists develop account for nearly one-fourth of all pharmaceutical medications. [1,2]

According to the World Health Organization, herbal medicines are used by 80% of the global population for primary healthcare. In Germany, 70% of physicians prescribe plant-based medicines, which range from 600 to 700. Over the last 20 years, the US has seen an increase in herbal medicine use due to public unhappiness with prescription pharmaceutical costs and a desire for natural or organic cures. [3,4]
Herbal medicine has been used for centuries to treat illnesses and maintain health. It has been used by all nations and civilizations. Herbal medications are widely regarded as "the people's medicines" due to their accessibility, safety, and ease of preparation. Herbal medicine is becoming more popular in many countries due to advancements in analysis, quality control, and clinical research, highlighting its efficacy and safety for disease prevention and treatment.In some Asian and African nations, 80% of people rely on traditional herbal treatments for primary healthcare. In affluent countries, 70-80% of the population uses complementary or alternative treatments (CAM), mostly herbal. Herbal medications are generally recognized for their safety and effectiveness in medicinal applications. Herbal medications are widely utilized in underdeveloped nations, and nearly all current prescription drugs contain active ingredients sourced from plants, either through extracts or synthetic compounds.

Many of the medications available to physicians today have a lengthy history of use as herbal treatments. According to the World Health Organization (WHO), about 25% of current medications used in the United States are derived from plants. More than 120 active chemicals extracted from higher plants are now widely employed in modern allopathic medicine, with 80% demonstrating a favorable correlation between their current therapeutic use and thetraditional usage of the plants from which they are derived.

The current pharmacopoeia of pharmaceuticals contains at least 7,000 therapeutic chemicals originating from plants, which are the constituents of herbal medicine Because of the present trend of increased usage of herbal medicines and their growing popularity around the world, the quest for plant-derived pharmaceuticals and dietary supplements

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has quickened in recent years. Pharmacologists, pharmacognosists, microbiologists, botanists, and natural-products chemists are combing the earth for phytochemicals and leads from herbs and plants that could be created to cure various diseases.[5]

II. GOUT

During the COVID-19 pandemic, gout is a comorbid condition that enhances the likelihood of infection with the SARS-Cov-2 virus.[6] Gout is an inflammatory joint disease caused by monosodium urate crystals formed in periarticular tissues, joints, and bones. [7,8] Gout is caused by hyperuricemia, when blood uric acid levels surpass the usual limit (7.0 mg/dL for men and 6.5 mg/dL for women). [9] Consuming too many purines from animal protein, alcohol, and diuretics can lead to higher serum uric acid levels. Without proper treatment, this disorder can progress to chronic gout, affecting kidney function, coronary heart disease, and stroke.[10]

Gout is an arthritic condition that causes joint pain, exhaustion, and, in certain cases, a high temperature. It is a condition caused by an excess of uric acid in the tissues, which is a byproduct of purine metabolism. It is caused by the precipitation of monosodium urate crystals from supersaturated fluids in the body into tissues. Deposition of these crystals causes an inflammatory reaction in tissues by forming tophi.[11] Gout manifests as acute episodic arthritis, chronic tophaceous gout, or visceral gout, with different molecular and cellular mechanisms underlying each presentation.[12] Though there are various treatments available on the market, these treatments only provide brief relief by reducing symptomatic symptoms. However, there is no medication that can totally cure the condition.

Gout is treated using a variety of ways. Various medication types, including Xanthine oxidase inhibitors, corticosteroids, and NSAIDs, are routinely utilized in the treatment. The most successful and preferable treatment is to block xanthine oxidase, which eventually reduces uric acid production. However, using these medications has certain undesirable effects, such as:

- Multi-organ hypersensitivity, serious skin reactions, heart attack, stroke
- Osteoporosis, cataract
- Peptic ulcer and acute renal failure respectively.

Besides that, these drugs possess some lacunas, like

- They exhibit only either local effect or systemic effect.
- To obtain multifactorial effect polypharmacy is required

Due to the potential negative effects of modern treatments, many people prefer traditional medicine. Herbal medications derived from plant extracts are safer and more effective when used in accordance with laws[13-14]. According to the World Health Organization (WHO), 88% of the global population uses traditional medicine. [13,14,15]

III. GLOBAL EPIDEMIOLOGY OF GOUT

The disease's prevalence is believed to be around 2%. It is commonly seen in adults over the age of 40 who have metabolic syndrome. Typically, the male population is more affected. The rise in the number of gout cases is projected to result in rising social expenses, including direct medical treatment expenditures as well as indirect costs. Gout is the most prevalent inflammatory arthritis, affecting people of all ages, genders, and races. It is caused by elevated levels of uric acid in the blood, which form crystals in the joints and other tissues, resulting in severe inflammation and swelling. Gout can be treated by reducing uric acidlevels with drugs, but many people do not get or follow the recommended treatment.

Gout's prevalence and incidence varies greatly over the world, depending on the population and monitoring methodologies. A recent study found that the global prevalence of gout ranged from less than 1% to 6.8%, with an incidence of 0.58-2.89 per 1,000 person-years.[16] Many countries have seen increases in prevalence and incidence throughout time.

Some countries have greater rates of gout than others. In 2017, the nations with the highest age-standardized point prevalence estimates for gout were New Zealand (1,394.0), Australia (1,171.4), and the United States (996.0) per 100,000. The nations wit[17] According to current studies, the prevalence of gout in India is predicted to be 0.6% among urban people and 0.1% among rural adults in 2015-16. The study also discovered that gout was more prevalent in men than in women, and in older age groups than in younger age groups.[18]

The likelihood and frequency of gout are influenced by sex and age. Men are more likely than women to get gout until the age of 60. After that age, the risk and occurrence of gout are comparable between sexes. According to a comprehensive assessment, the incidence of gout, defined as the number of new cases per year, ranges from 0.8 to 12.6 per 1000 males and 0.1 to 6.4 per 1000 women across age categories. The prevalence of gout ranges from 0.2% to 12.7% in men and 0.1% to 6.4% in women throughout age groups.[19]

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IV. PATHOPHYSIOLOGY &CLINICAL FEATURES OF GOUT

Gout is generally triggered by MSU crystals which result from uric acid supersaturation as a systemic uric acid overload. MSU crystal formation increased during metabolism from massive cellular release, or from weakened renal clearance [20]. Tophaceous and visceral gout, on the other hand, are marked by the appearance of tophi, which are abscess-like creamy masses made up of MSU crystals and dead immune cells.

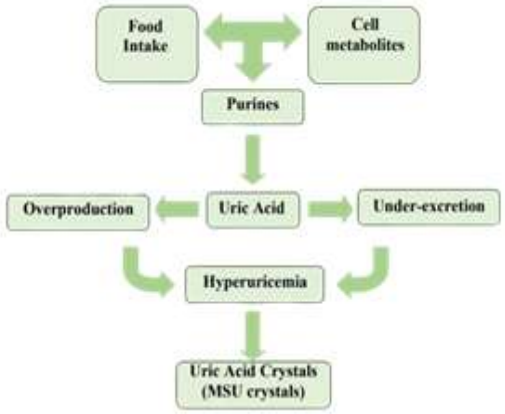
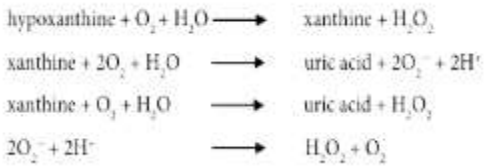


Fig 1. Pathogenesis of Hyperuricemia result in MSU crystals

V. CONVENTIONAL TREATMENT STRATEGIES WITH LIMITATIONS:



Gout treatment involves either reducing uric acid synthesis (XO inhibitors) or boosting excretion (uricosuric medications).[21] New treatments for gout include uricase equivalents and biological cytokine inhibitors [22,23]. Allopurinol, a regularly used XO inhibitor, can cause hypersensitivity syndrome, Stevens Johnson syndrome, renal toxicity, and potentially death from liver necrosis. [24-25] Long-term usage of anti-inflammatory drugs can lead to gastric and renal side effects. Selective COX-2 inhibitors are less hazardous than non-selective NSAIDs, but have similar renal side effects as conventional NSAIDs. [26] Urate-lowering medications, including XO inhibitors and uricosuric agents, have been linked to fatal hypersensitivity syndrome, gastrointestinal problems, and nephrotic damage. Colchicine often causes nausea, vomiting, severe diarrhea, and renal damage.

Although cytokine inhibitors are highly successful and have minimal adverse effects, they are significantly more expensive than standard treatments. [27-28]

Some herbs have been screened individually and their dose is identified and well defined against gout. These plants have been reported to show anti-gout effect which is like allopurinol (xanthine oxidase inhibitor) without any undesired effects obtained as that allopurionl.Mono-combinational extract of multiple drugs will overcome various lacunas occurring with usage of synthetic drugs mentioned above

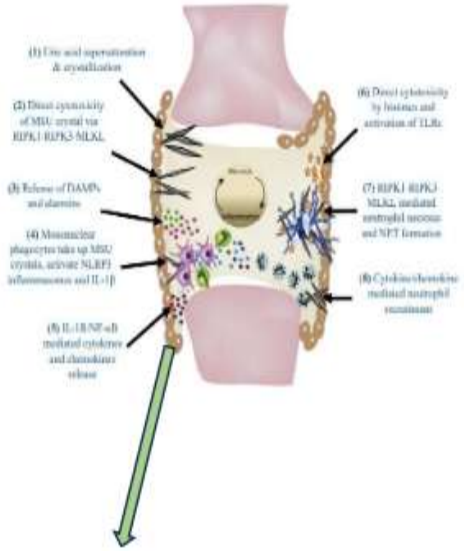


Fig SEQ Figure * ARABIC 1. Pathogenesis of Hyperuricemia result in MSU crystals

VI. XANTHINE OXIDASE

In 1902, Schardinger discovered an enzyme in milk that converts aldehydes to acids and reduces methylene blue, which led to the name "Schardinger enzyme" for the enzyme. Morgan et al. discovered in 1922 that milk includes an enzyme called xanthine oxidase (XO), which can oxidize xanthine and hypoxanthine and reduce O_2 to H_2O_2. According to Hass & Hill and Hass & Lee, milk contains a chemical termed "itate" that can convert nitrite to nitrate when exposed to an aldehyde and O_2. Under some conditions, milk can turn nitrate to nitrite. In 1938, Booth provided substantial evidence that the Schardinger enzyme is an XO. [29]

International Journal of Pharmaceutical Research and Applications
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XO is a dimeric protein with a molecular mass of 300 kDa. Each monomeric unit contains three groups. The first group contains the active site of iron-sulphur [2Fe-2S], with a molecular mass of 20 kDa. The intermediate flavin adenine dinucleotide (FAD) has a molecular mass of 40 kDa. The molybdenum-pterin (Mo-Pt) core has a molecular mass of 85 kDa. [30]

XO plays a role in uric acid production. XO catalyzes the conversion of hypoxanthine to xanthine and uric acid, producing superoxide anion, H_2O_2, and reactive oxygen species (ROS) as shown below: [29-30]

Medicinal plants include active substances in all plant parts, including roots, stems, leaves, fruit, seeds, flowers, and bark. Active substances can have therapeutic effects, either directly or indirectly, when used as medicines. Medicinal plants, often known as herbal plants, are commonly utilized in traditional medicine. [31]

VII. MECHANISM OF XANTHINE OXIDASE:

Fig 2.Mechanism of treatment

Xanthine oxidase (XO) is one of the main enzymatic sources that create reactive oxygen species (ROS) in the living system. It is a dehydrogenase enzyme that performs electron transfer to nicotinamide adenine dinucleotide (NAD+), while oxidizing hypoxanthine, which is an intermediate compound in purine catabolism, first to xanthine and then to uric acid. XO turns into an oxidant enzyme that oxidizes thiol groups under certain stress conditions in the tissue. The last metabolic step of conversion of hypoxanthine into uric acid is catalysed by XO. Uric acid, when present in higher concentrations, is considered as waste product, get crystallized and can cause kidney stones and gouty arthritis. Thus, XO inhibitors are one of the drug classes used against gout, a purine metabolism disease that causes urate crystal storage in the joint and its surroundings caused by hyperuricemia.

Urate - lowering therapy includes XO inhibitors that reduce uric acid production as well as uricosuric drugs that increase urea excretion. Current drugs that obstruct uric acid synthesis through XO inhibition are allopurinol, febuxostat, and uricase. However, since the side effects, safety and tolerability problems of some current gout medications still exist; intensive research is ongoing to look for new, effective, and safer XO inhibitors of natural or synthetic origins for the treatment of the disease.

In the present review, we aimed to assess in detail XO inhibitory capacities of pure natural compounds along with the extracts from plants and other natural sources. The data pointed out to the fact that functional groups of herbal plants, particularly phenolics such as enlisted below have a great potential for new XO inhibitors capable of use against gout disease [32]

1. flavonoids (quercetin, apigenin, and scutellarin)
2. tannins (agrimoniin and ellagitannin)
3. chalcones (melanoxethin)
4. Xanthone and coumarin
5. Isoflavones
6. Saponins
7. Terpenoids
8. Stibenes
9. Phenylethanoid glycosides
10. alkaloids (berberine and palmatin)

According to the literature [21], Xanthine oxidase inhibitory activity was assayed from 6 species belonging to different families traditionally used for the treatment of gout and related symptoms. The aqueous methanol - water mixture and methanolic extract of Acalypha indica (Euphorbiaceae), Adhatodavasica (Acanthhaceae), Coccinea Grandis (Cucurbitaceae), Datura metel (Solanaceae), Strychnos nux-vomica (Loganiaceae) and Vitex negundo (Lamiaceae) plants were used for the experiment.

VIII. CHEMICAL CONSTITEUNTS SHOWING XO INHIBITOR:

[1] FLAVONOIDS:

Flavonoids are secondary metabolites produced in plants via the shikimate and phenylpropanoid pathways. These bioactive substances are found in various plant parts, including

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roots, rhizomes, wood, bark, stem bark, seeds, leaves, and flowers. Flavonoids can be found in several parts of plants, including epidermal cells, guard cells, subepidermal cells, aerial areas, vascular parenchyma cells, flowers, cell walls, and cortical parenchyma cells.[33]

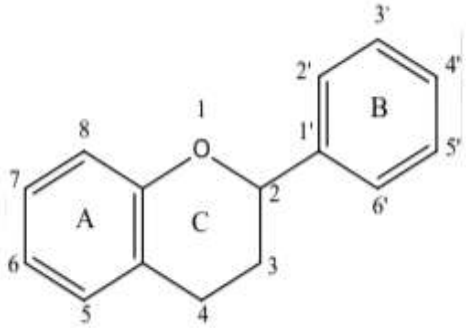

Fig 3.Flavonoid basic structure

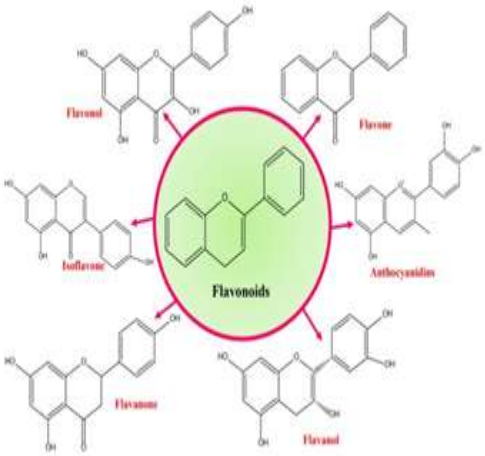

Fig 5.Derivatives of Flavonoid for the anti-gout

Flavonoids are the third most abundant natural product group, following alkaloids (12,000) and terpenoids (30,000).[34] Flavonoids are phenolic chemicals having a C6-C3-C6 basic framework made up of two benzene rings (A and B) connected by a heterocyclic pyran ring (C).[35] Flavonoids have a conjugated aromatic structure that absorbs UV-Vis light.[36] Band II (240-285 nm) corresponds to the benzoyl system in ring A, while band I (300-400 nm) represents the cinnamoyl system in ring B.[34] Flavonoids are classified as aglycone derivatives, glycosides, methylation, acetylated, and sulfate.[37] These chemicals have multiple biological effects, including antioxidant, anticarcinogenic, antimicrobial, antiallergic, anti-inflammatory, anti-aging, anticancer, and antiviral.[33,35,38]Flavonol, Flavone, Anthocyanidins, Flavanol, Flavanone, Isoflavone derivates of Flavonoids also found as the Xanthine oxidation inhibitor.

[2] TANNINS:

Tannins are also known as proanthocyanidins possessing useful properties such as an antioxidant,anti-apoptosis,anti-aging, anti-carcinogenic and as well as anti-inflammatory. Tannins are a significant component found in herbal plants that is widely being used for anti-gout activities.Tannins are commonly found in the barks, seeds, and fruit skins of many vegetable species. A tannin-rich tree extract safely decreases uric acid, lowering the need for gout medications.[39]

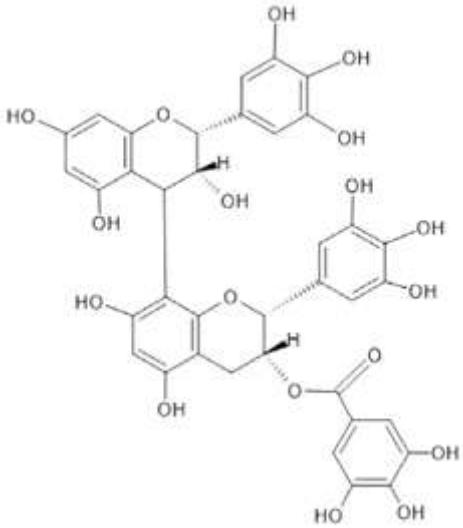

Fig 4. Tannin Structure

The tannins serve as a radical scavenger and an inhibitor of xanthine oxidase. Tannin molecules such as geraniin, corilagin, and gallic acid have uricosuric properties, while ellagic acid is an XO inhibitor. [40]Tannins can work as xanthine oxidase inhibitors if taken in moderation and with minimal negative effects.

[3] CHALCONES:

Chalcones, which are intermediates in flavonoid production but do not accumulate in most plants, have been linked to numerous health benefits. Both natural and synthesized chalcones have been identified as possible XO inhibitors. The hydroxylation of chalcones, specifically the catechol groups, promotes XO inhibition. Methoxylation of hydroxyl groups decreases activity on the first ring but increases activity on the second. An additional caffeoyl substitution significantly improves the XO inhibitory activity of the corresponding chalcone derivative. [41]

International Journal of Pharmaceutical Research and Applications
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Chalcones can form heterodimers with themselves or other flavonoids. Termipaniculatone A, a chalcone-flavanone heterodimer derived from Terminthia paniculata, has been shown to reduce blood uric acid levels and decrease XO activity in both serum and liver. [42]

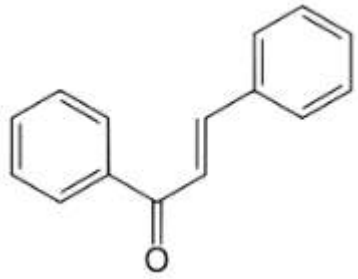

Fig 6. ChalconesStructure

[4] XANTHONE AND COUMARIN:

The XO inhibitory properties of xanthones have previously been investigated, and the presence of a cyano group at the para position of the benzyl moiety was the preferable substitution pattern.[43] Norathyriol, a natural xanthone, was recently shown to exhibit dual hypouricemic properties, suppressing XO in an uncompetitive way while also increasing uric acid excretion. Thongchai et al. studied the impact of allylic substitutions on the XO inhibitory activity of xanthone.2,4-diallyl-1,3-dihydroxythioxanthone had the strongest inhibitory action on XO.[44]

28 coumarin are evaluated for their Xanthine oxidase inhibitory activities and coumarin had sevenfold higher inhibition effect on xanthine oxidase than allopurinol. These compounds appeared to bind to residues different from the catalytic site of the enzyme, indicating an uncompetitive inhibition method.[45]

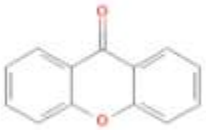

Fig 9. Coumarin Structure

[5] ISOFLAVONES:

A study found that formononetin, genistein, and sophoricoside have mild inhibitory effects on XOD. Another study found that daidzein and genistein reduce XOD activity.Still, the inhibition rate was not very high. [46] Genistein inhibits XOD by forming an XOD-genistein complex through hydrophobic interactions. This alters the secondary structure of XOD and prevents substrate (xanthine or hypoxanthine) linkage. [47]

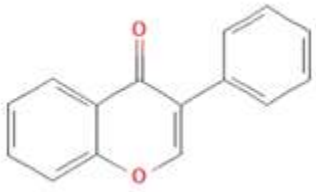

Fig 2. Isoflavones Structure

[6] SAPONINS:

Four saponins from ethanolic (50 and 75%) root extracts of Ilex pubescens (Aquifoliaceae) were tested for XOD inhibitory activity.[48] In which ilexsaponin C, ilexsaponin B1, ilexsaponin B1 were isolated. The substance ilexsaponin C demonstrated stronger XOD inhibitory effects than other compounds. The sugar component of their structure is crucial for inhibiting XOD due to its unique properties. Compared to other saponins, ilexsaponin C had stronger XOD inhibitory activity. In another study, A saponin glycoside Pallidifloside D is effective against XOD from Smilax riparia roots and rhizomes.[49]Additionally, they extracted riparoside B and timosaponin J from Smilax riparia. These two drugs demonstrated XOD inhibitory activity.[50]

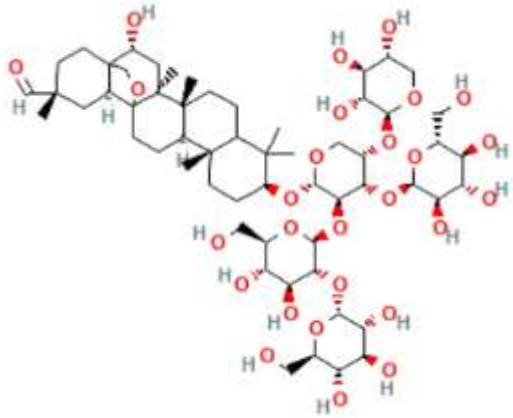

Fig 10. Saponins Structure

[7] TERPENOIDS:

Terpenoids are one of the largest classes of natural substances, with about 40,000 compounds.[51] Researchers have found that terpenoids from diverse plant species can aid in the treatment of HUA. Three monoterpene glycosides were isolated and screen for

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XOD inhibitory activities. Albiflorin and paeoniflorin, two isolated chemicals, inhibited XOD.[52]

Stauntoniabrachyanthera leaves and fruits contain nor-oleanane triterpenoids, which have been shown to suppress XOD.11 nor-oleanane triterpenoids were extracted from Stauntoniabrachyanthera leaves and tested for their anti-HUA activity in vitro. [53] Triterpenoids from Garcinia subelliptica did not suppress XOD, except in a dose-dependent manner. [54]

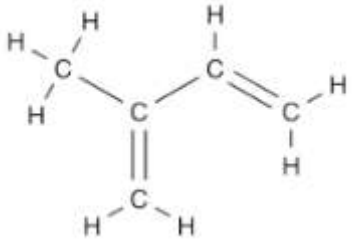


Fig 11. Terpenoids Structure

[8] STIBENES:

Stilbenes are polyphenolic chemicals found frequently in plants. These chemicals had a wide range of therapeutic properties against various diseases. (anti-inflammatory, anti-tumor, antioxidant) [55]Cajaninstilbene acid from Cajanus cajan (L.) Millsap leaves effectively inhibit XOD activity.[56] Binding with the XOD enzyme in which electrostatic interaction playcrucial role. An oligostilbene from Vaticamangachapoi was found to inhibit XOD.[57]

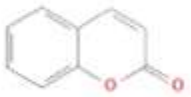
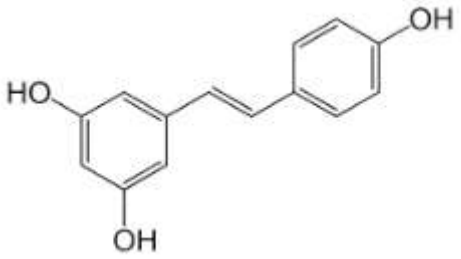


Fig 12. StibenesStructure

[9]PHENYLETHANOIDGLYCOSID:

Phenylethanoid glycosides, a water-soluble chemical found in plants, provide significant health benefits.Verbascoside, a phenylethanoid glycoside isolated from Plantago asiatica L seed, was tested for XOD inhibition. [58] Verbascoside inhibits XOD enzyme and binds to it through its phenyl rings, according to a study. [59]



PHENYLETHANOIDGLYCOSID

[10] ALKALOIDS:

Eurycoma longifolia Jack roots contain 37 chemicals, primarily quassinoid triterpenoids and β-carboline alkaloids.In a rat model of MSU-induced acute gout arthritis, EL extracts at medium and high doses effectively reduced joint swelling. Instudy researchers isolated six oxindole alkaloids compounds (costinones A, costinones B, isaltinones A, isaltinones B, indirubin, trisindoline). In which Costinones A showed stronger XOD inhibitory efficacy compared to other compounds. [60] The study's pharmacological activity indicates the use of indirubin and other alkaloids to treat HUA. [61] Another recently published study found that alkaloids from Nelumbinis folium have the potential to treat hyperuricemia. The crude extract of Nelumbinis folium has significant XOD inhibitory action. [61]

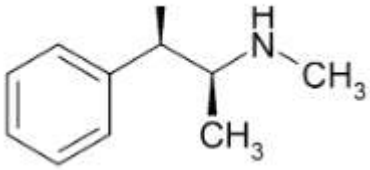


Fig 14. Alkaloid Structure

Table 1. SOME BIOACTIVE COMPOUNDS OF DIFFERENT CHEMICAL CONSTITUENTS ARE LISTED BELOW IN TABLE: 1 THAT MODRATES HYPER URICEMIA ACTIVITY BY INHIBITORY XATHINE OXIHIBITORY ENZYME

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Volume 9, Issue 2 Mar-Apr 2024, pp: 960-974 www.ijprajournal.com ISSN: 2249-7781

Class	Bioactive compounds
Flavonoids	Quercetin, isoquercitrin, quercetin - 3 - O - - D -glucopyranoside, (2R,3S) -(_) - 4 ′ - O - methyldihydroquercetin, (2R,3R) -(+) - 4 ′ -Omethyldihydroquercetin, (2R,3R) -(+) - 4 ′,7 -di -O methyldihydroquercetin, (2R,3R) -(+) - 7 - O - methyldihydroquercetin, 5,7,3 ′,5 ′ -tetrahydroxy flavanone, quercetin -3,7,3 ′ - trimethyl ether, quercetin -3,3 ′,4 ′ -trimethyl ether, kaemferol, kaempferol 3 - O -isorhamninoside, rhamnocitrin - 3 - O -isorhamninoside, rhamnetin - 3 - O - isorhamninoside, amentoflavone, lonicerin, vitexin, isovitexin, acacetin, acacetin - 3 - O - - L - rhamnopyranosyl -(1 →6) - - D -glucopyranoside, acacetin 7 - O -(3 - O -acetyl - - D -glucopyranoside, isorhamnetin, isorhamnetin - 3 - O -rutinoside, isorhamnetin - 3 - O -robinobioside, isorhamnetin - 3 - O - glucoside, isorhamnetin - 3 - O - - L -rhamnopyranosyl -(1 →6) - - D - glucopyranoside, isoliquiritigenin, liquiritigenin, eupatilin, luteolin, luteolin 7 - O -glucuronide, luteolin 7 - O -rutinoside, luteolin 7 - Oneohesperidoside, luteolin 7 - O -glucoside, luteolin 40 - O -glucoside, 5 -Hydroxy -6,7,3',4' - tetramethoxyflavone, saponarin, carallidin, mahuannin A, 3 - O -caffeoylquinic acid, melanoxetin, 7,8,3`,4` -tetrahydroxyflavone, chrysin, apigenin, baicalein, baicalin, galangin, morin, myricetin, diosmetin, hyperin, rutin, genistein, naringenin , epiphyllocoumarin - 3 - O - - d -allopyranoside, tetrahydroamentoflavone and silybin.
Hydroxycinnamic acids	dihydrocaffeic acid, chlorogenic acid, cynarin, 4 -hydroxycinnamic acid, 4 - O - - D - glucopyranosyltrans -cinnamic acid, 1,4 -di - O -caffeoylquinic acid, 1,5 - di - O -caffeoylquinic acid, methyl 3,4 -di - O -caffeoylquinate, 4 - O - caffeoylquinic acid, 3 - O -caffeoylquinic acid, methyl 3,5 -di - O - caffeoylquinate, chlorogenic acid methyl ester and 3,4 -di - O - caffeoylquini
Chalconoid	Okanin, isosalipurposide, aspalathin
Terpenoids	Albiflorin, paeoniflorin, brachyantheraoside B4, brachyantheraoside A3, 3 - O - a - L - rhamnopyranosyl -(1 →2) - a - L -arabinopyranosyl -30 - norolean - 12,20(29) -dien -28 -oic acid, brachyantheraoside A1, brachyantheraoside D1, 5β,19 β -epoxycucurbita -6,22,24 -trien -3 α –ol, cucurbita -1(10),5,22, 24 - tetraen -3α -ol), 3 β -hydroxymultiflora - 8 -en -17 -oic acid, garcinielliptones A, 24 -methylenelanost - 8 -en -3β -ol and tanshinone
Saponin	Pallidifloside D, ilexsaponin C, prosapogenin, riparoside B, timosaponin J, smilaxchinoside A and smilaxchinoside C
Tannins	Valoneic acid dilactone, llagic acid, geraniin, corilagin and gallic acid
Alkaloids	Roemerine, costinones A, costinones B, isatinones A, isatinones B, indirubin, trisindoline and berberine
Stilbenes	Cajaninstilbene acid, vaticanol A and resveratrol

Table 2. UPTILL NOW MANY PLANTS HAS REPORTED WITH DIFFERENT ACTIVE COMPONTENTS DISCUSS HERE WITH XANTHINE OXIDATION INHIBITORY ACTIVITY WHICH ARE LISTED IN TABLE 2.

International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 2 Mar-Apr 2024, pp: 960-974 www.ijprajournal.com ISSN: 2249-7781

Plant name	Plant part and solvent used	Active components	XOD activity (%/IC_{50}/EC_{50})	References
Bulnea balsamifera L.	Aerial part, methanolic extract	**Dihydroflavonol, (2R,3R)-(+)-4′-Omethyldihydroquercetin, (2R,3R)-(+)-4′,7-di-O-methyldihydroquercetin, (2R,3R)-(+)-7-Omethyldihydroquercetin, 5,7,3′,5′-tetrahydroxy flavanone, quercetin, quercetin-3,7,3′-trimethyl ether, quercetin-3,3′,4′-trimethyl ether.	**0.23+0.01 µM	[62]
Gnaphalium affine	Petroleum ether, ethyl acetate, water	*Eupatilin, apigenin, luteolin and 5-hydroxy-6,7,3',4'- tetramethoxyflavone	0.37 Ki	[63]
Phyllanthus niruvi	Leaves, methanol	Phyllanthin, *hypophyllanthin, phyltetralin, niranthin	*20.83 ± 7.74%	[64]
Piper nudibaccatum	Aerial parts methanol	Neolignan, ellagic acid analog, *neotaiwanensol B, sarmentosumols A and B, (2E,4E)-N-isobutylhexadeca-2,4-dienamide, (2E,4E)- Nisobutyl-2,4-decadienamide, 1-[7-(1,3- benzodioxol-5-yl)-1-oxo-2,4-heptadienyl]piperidine, retrofractamide A, dehydropipernonaline, (2E,4E)-N-isobutyl- 7-(3,4-methylenedioxyphenyl)hepta-2,4-dienamide, (2E,8E)-N-[9-(3,4-methylenedioxyphenyl)-2,8-nonadienoyl] piperidine, retrofractamide C, piperolein B, 5,6- dihydropiperlonguminine, pressafonin A, trans-phytol, ergosta4,6,8(14),22-tetraen-3-one, quinone, tocopherylquinone, a phenylpropanoid, 4- allyl-1,2-phenylene diacetate, monomethyl olivetol	*0.28 µM	[65]
P. belte	Leafs	Hydroxychavicol	77.7%	[66]
Semecarpus anacardium	Seeds, methanol	Tetrahydroamentoflavone	50 ± 3 µg/ml	[67]
Pistacia integerrima	n-Butanol, leaves	Quercetin, kaempferol, apigenin, rutin, quercetin-3-O-β-dglucopyranoside, kaempferol-3-O-β-d-glucopyranoside, quercetin-3- O-(6__-O-syringyl)-_β-d-glucopyranoside and kaempferol-3-O-(4``- O-galloyl)-α-l-arabinopyranoside	19 µg/ml	[68]
Momordica charantis	Stem and fruit methanol	*Taiwacin A, 23,24,25,26,27-pentanorcucurbitane, momordicoside K, 3-O-(b-D-glucopyranosyl)-A. 24b-ethyl-5a-chalesta-7,22,25(27)-trien-3b-ol	*24.1 ± 3.4 µM	[69]
Momordica charantis	Stem, methanol	3b-hydroxymultiflora-8- en-17-oic acid, cucurbita1(10),5,22,24-tetraen-3a-ol, 5b,19b-epoxycucurbita-6, 22,24-trien-3a-ol	36.8 ± 20.5 µM	[70]

International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 2 Mar-Apr 2024, pp: 960-974 www.ijprajournal.com ISSN: 2249-7781

Artocarpus communis	Cortex of root chloroform	**Cyclogeracommunin, artoflavone A, artomunoisoxanthone, artocommunol CC, artochamin D, artochamin B, dihydroartomunoxanthone	**73.3 ± 19.1 µM	[71]
Artocarpus elaticus	Root	Cycloartelastoxanthone, artelastoheterol, cycloartobiloxanthone, **artonol A	43.3 ± 8.1 µM	[71]
Rhamnus alaternus L.	Leaves petroleum ether, chloroform, ethyl acetate, and methanol	*Kaempferol 3-O-isorhamninoside, rhamnocitrin3-O-isorhamninoside (2) and rhamnetin-3-O-isorhamninoside	*18 µg/ml	[72]
Teucrium polium L	Aerial parts methanol	Poliumoside B, poliumoside, 8-O-acetylharpagide, teucardoside, luteolin 7-O-rutinoside, luteolin 7-O-neohesperidoside, luteolin 7-Oglucoside, **luteolin 40-O-glucosid	**6.7 µM	[73]
Salvia nemorosa L.	Aerial parts nhexane, dichlorometha ne, and methanol	2E-Hexenal, a-Thujene, Sabinene, a-Terpinene, o-Cymene, gterpinene, terpinene-4-ol, Carvacrol, E-Caryophyllene, a-Humulene, b-Ionene,,Bicyclogermacrene, Spathulenol, Caryophyllene oxide, aCadinol, Humulene epoxide, Leden oxide, 14-hydroxy a-Humulene, 2E,6E-Farnesol, Hexahydrofarnesyl acetone, Phytol, Monoterpene hydrocarbons, Oxygenated monoterpenes, Sesquiterpene hydrocarbons, Oxygenated sesquiterpenes	207.2 ± 6.9 µg/ml	[74]
Pogostemoncabl inbenth	Aerial part, aqueous	Rosmarinic acid	8.53±0.91 µg/ml	[75]
Salvia miltiorrhiza	Roots	magnesium lithospermate B	4.06 mg/mL	[76]
Rabdosia japonica hara	Dired leaves	Pedalitin, quercetin, rutin, isoquercitrin, rosmarinic acid, ursolic acid, kojic acid, α-tocopherol, 3-hydroxyphenyl acetic acid, homovallic acid, *3,4-hihydroxy phenylacetic acid	*3.5 ±0.5 µM	[77]
Radix saviaeMiltiorrhizae	Ethanol 60%	Salvianolic acid B, tanshinone II B, tanshindiol B, tanshindiol A, 15,16-dihydrotanshinone I, 1,2-dihydrotanshinone I, *danshenxinkun B, cryptotanshinone, tanshinone I, 3-hydroxy methylene tanshinquinone, methylene tanshinquinone, tanshinone II A	*17.45 ± 2.1 µM	[78]
Garcinia subeliptica	Seed, chloroform	Garcinielliptone Q, garcinielliptone R, garcinielliptone S, garcinielliptone FC, **garcinielliptones, A, garsubelline A, garcinielliptones, F	**53.8 ± 11.5 µM	[79]

International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 2 Mar-Apr 2024, pp: 960-974 www.ijprajournal.com ISSN: 2249-7781

Lagerstroemia speciosa	Leaves, methanol, butanol, water, ethyl acetate	*Valoneic acid dilactone, ellagic acid	* 2.5µM	[80]
Ilex pubescens	Root, ethanol	*ilexsaponin C, ilexsaponin B1, ilexsaponin B2, prosapogenin	9.18±0.12 mmol/L	[48]
Sinofrachetia chinensis	Air-dried plant, methano	Liquiritigenin	49.3 mM	[81]
Plumula nelumbinis	Methanol	Quercetin	8.2 µg/ml	[82]
Balanophoralaxifora	Ethyl acetate	1-O-(E)-caffeoyl-4,6-(S)-hexahydroxydiphenoyl-β-d-glucopyranose ,1-O-(E)- caffeoyl-β-d-glucopyranose, 1,3-di-O-galloyl-4,6-(S)-hexahydroxydiphenoylβ-d-glucopyranose, and 1-O-(E)-p-coumaroyl-β-d-glucopyranose	73.8 ±2.4%	[83]
Caralliabrachiata	Bark, hexane, dichloromethane, ethanol and methanol	*Carallidin, mahuannin A, p-hydroxy benzoic acid	*12.9 µM	[84]

CONCLUSION:

In conclusion, herbal plant are gaining popularity as an alternative treatment for gout due to limited or no side effect as compare to synthetic drugs. The study highlights the use of various plants with Xanthine oxidation inhibitory properties in managing gout, emphasizing the Mechanism action that contributes in termination of pathogenesis of disease.

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