

Ethnopharmacological comparison of anti-gout remedies: A review of ginger (*Zingiber officinale*), onion (*Allium cepa*), and lotus seed (*Nelumbo nucifera*) in Ethiopian and Indian traditional medicine

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Abstract

Gout is a chronic inflammatory arthropathy whose increasing global burden has intensified interest in safer, accessible, plant-based therapeutic alternatives. This comparative review examines the ethnopharmacological evidence, phytochemical composition, and mechanisms underlying the potential anti-gout effects of ginger (*Zingiber officinale*), onion (*Allium cepa*), and lotus seed (*Nelumbo nucifera*) within Ethiopian and Indian traditional medicine. Literature from PubMed, Scopus, Web of Science, and ethnobotanical repositories was systematically evaluated. The findings reveal substantial differences in the concordance between traditional knowledge and pharmacological evidence. Onion shows the strongest alignment, with documented traditional use and convincing preclinical evidence supporting xanthine oxidase inhibition (IC₅₀ 17.36 µg/mL) and serum urate reduction. Ginger demonstrates moderate alignment, as its established anti-inflammatory activity, including NLRP3 inflammasome inhibition, supports potential management of acute gout inflammation, although direct urate-lowering evidence remains limited. Lotus seed exhibits the weakest ethnopharmacological alignment because, despite promising nuciferine-mediated urate-lowering effects, traditional use for gout is undocumented in both contexts. Their distinct phytochemicals, including gingerols, flavonoids and organosulfur compounds, and proanthocyanidins and alkaloids, may explain these differences. Overall, onion emerges as the strongest candidate for further clinical investigation, while ginger and lotus seed require additional context-specific validation.

Keywords: Allium cepa, Comparative analysis, Ethiopia, Ethnopharmacology, Gout management, India, Nelumbo nucifera, Traditional medicine, Xanthine oxidase inhibition, Zingiber officinale.

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Contribution of this paper to the literature

This review provides a novel cross-cultural ethnopharmacological comparison of ginger, onion, and lotus seed as potential anti-gout remedies in Ethiopian and Indian traditional medicine. It integrates traditional knowledge with phytochemical and pharmacological evidence, identifies onion as the strongest candidate, and highlights critical evidence gaps, thereby guiding culturally grounded research and future clinical development.

1. Introduction

1.1. Background and Rationale

Gout is a chronic inflammatory arthropathy caused by monosodium urate crystal deposition in joints and tissues secondary to sustained hyperuricemia [1]. It constitutes a growing global health burden. The Global Burden of Disease Study 2021 reported a rise in prevalence from 22.3 million cases in 1990 to 56.5 million in 2021, with the age-standardized rate increasing from 536.54 to 653.82 per 100,000 population. Incidence rose 136.1 % over this period, accompanied by a 21.3 % increase in age-standardized death rates and a substantial rise in disability-adjusted life years [1]. In 2021, 37.2 million cases occurred among individuals aged ≥55 years (age-standardized prevalence 2505.4 per 100,000). Males are disproportionately affected (sex ratio 3–4:1). Incidence has increased 63.44 % over two decades, with the highest rates in high-sociodemographic-index regions [2]. Hyperuricemia and gout are also rising in pediatric populations (e.g., 16.6 % prevalence in the United States) [3]. Projections indicate continued growth, underscoring the need for improved management [2].

Pathogenesis centers on hyperuricemia from uric acid overproduction or underexcretion. Xanthine oxidase (XO) catalyzes the final steps of purine catabolism and is a primary therapeutic target. Crystal deposition activates the NLRP3 inflammasome, releasing interleukin-1β and driving acute inflammatory flares.

Conventional therapy relies on XO inhibitors (Allopurinol, febuxostat) and anti-inflammatory agents (NSAIDs, colchicine, corticosteroids). Allopurinol can cause severe, potentially fatal hypersensitivity reactions, especially in HLA-B*5801 carriers. Febuxostat carries a black-box warning for increased cardiovascular mortality. NSAIDs risk gastrointestinal bleeding and cardiovascular events; colchicine has a narrow therapeutic index; prolonged corticosteroids produce metabolic and immunosuppressive toxicity. These limitations drive interest in safer alternatives.

Plant-derived natural products offer multi-target anti-gout activity with favorable safety profiles. Analyses of 282 studies identified 164 plant extracts and 148 bioactive compounds, chiefly terpenoids, polyphenols, and flavonoids that lower uric acid, inhibit XO, reduce inflammation, and protect joint tissues, supporting further development of natural therapeutics.

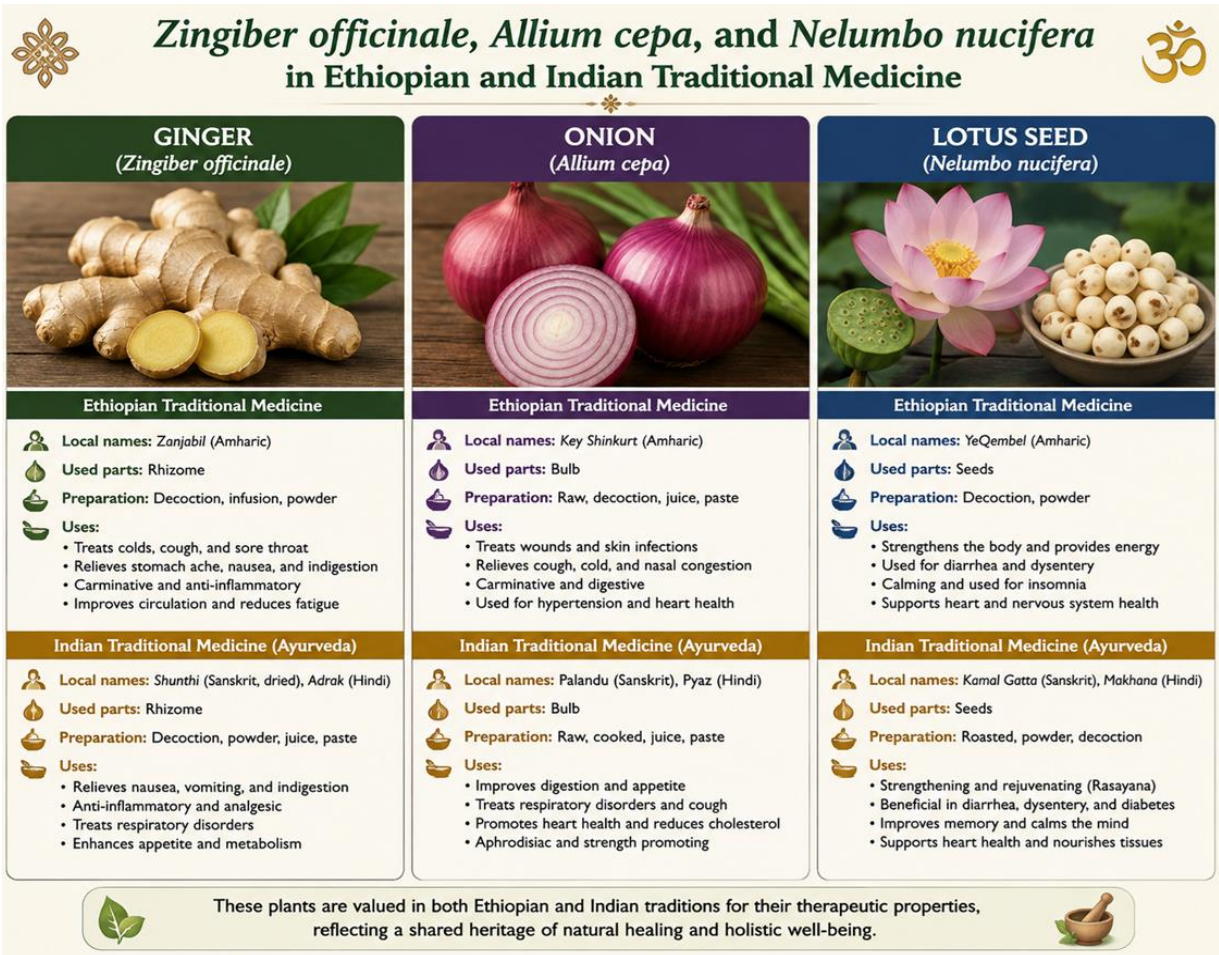


Figure 1. Comparative ethnomedicinal uses, preparation methods, and therapeutic applications of ginger, onion, and lotus seed in Ethiopian and Indian traditions.

Figure 1 illustrates the shared therapeutic importance of Zingiber officinale, Allium cepa, and Nelumbo nucifera in Ethiopian and Indian traditional medicine. Although cultural practices and preparation methods differ, all three species are consistently employed to manage gastrointestinal disorders, inflammation, respiratory ailments, and metabolic dysfunctions. The comparison highlights substantial ethnopharmacological convergence, suggesting common bioactive constituents and complementary therapeutic knowledge that provide a valuable foundation for phytochemical investigation, pharmacological validation, and evidence-based drug discovery (Figure 1).

Among the vast array of medicinal plants with documented anti-gout potential, three species: ginger (*Zingiber officinale*), onion (*Allium cepa*), and lotus seed (*Nelumbo nucifera*), present a compelling basis for comparative investigation. These plants are particularly noteworthy because they occupy distinct positions within the traditional medicine systems of Ethiopia and India, two countries with rich and well-documented ethnopharmacological traditions. Ginger (*Zingiber officinale*) is widely used in both Ethiopian and Indian traditional medicine, though its specific indications differ: in Ethiopia, it is primarily employed for tonsillitis, febrile illnesses, and digestive complaints, while in Ayurveda, it is extensively documented for joint pain, inflammation, and cervical spondylitis [4, 5]. Onion (*Allium cepa*) has been explicitly documented in Ethiopian ethnobotanical surveys for the treatment of gout, with traditional preparation methods including crushing seeds and immersing in water, or boiling the corm in milk with honey [6]. In Ayurveda, onion (*Palandu*) is recognized for its medicinal properties and has been used for rheumatism and joint pain. Lotus seed (*Nelumbo nucifera*), while not traditionally used for gout in Ethiopia, has been extensively studied in recent pharmacological research, particularly from East Asian traditional medicine contexts for its anti-inflammatory, antioxidant, and xanthine oxidase inhibitory activities [7]. Each of these plants possesses distinct phytochemical profiles: gingerols and shogaols in ginger, flavonoids and sulfur compounds in onion, and alkaloids (nuciferine) and proanthocyanidins in lotus seed, which are purported to mediate their anti-gout effects through different mechanistic pathways. The comparative evaluation of these three plants within the specific cultural and geographical contexts of Ethiopian and Indian traditional medicine offers a unique opportunity to assess the convergence and divergence between traditional knowledge and pharmacological evidence, and to identify promising candidates for further clinical development.

1.2. Objectives of the Review

The present review is designed with the following specific objectives.

- To systematically compare the ethnopharmacological evidence for ginger (*Zingiber officinale*), onion (*Allium cepa*), and lotus seed (*Nelumbo nucifera*) in the management of gout within the Ethiopian and Indian traditional medicine contexts, critically evaluating the documented traditional uses, preparation methods, and cultural significance of each plant in both regions.
- To evaluate the phytochemical basis and mechanistic pathways underlying the anti-gout activities of these three plants, including their effects on xanthine oxidase inhibition, uric acid reduction, anti-inflammatory activity, antioxidant properties, and renal protection, drawing upon *in vitro*, *in vivo*, and *in silico* evidence.
- To identify gaps in the current evidence base—including the absence of head-to-head comparative studies, limited human clinical trials, lack of standardized extracts, and insufficient ethnobotanical documentation in certain regions—and to propose evidence-based directions for future research.
- To provide a balanced, culturally grounded perspective that respects the specificities of each traditional medical system (Ethiopian traditional medicine, Ayurveda, Siddha, and Unani), acknowledging that therapeutic knowledge is place-based and that the transferability of plant-based remedies across cultures must be critically examined rather than assumed.

1.3. Scope and Methodology

This review was conducted through a systematic literature search of PubMed, Scopus, Web of Science, Google Scholar, and specialized ethnobotanical repositories covering Ethiopian and Indian traditional medicine. Keyword combinations included “gout,” “hyperuricemia,” “*Zingiber officinale*,” “ginger,” “*Allium cepa*,” “onion,” “*Nelumbo nucifera*,” “lotus seed,” “xanthine oxidase inhibitor,” “ethnopharmacology,” “traditional medicine,” “Ethiopia,” “India,” “Ayurveda,” and “ethnobotany.” Reference lists of retrieved articles were manually screened for additional relevant studies.

Inclusion criteria comprised: (1) ethnobotanical or ethnopharmacological documentation of traditional uses of ginger, onion, or lotus seed for gout or related conditions in Ethiopian or Indian contexts; (2) pharmacological studies (*in vitro*, *in vivo*, or *in silico*) investigating anti-gout mechanisms, including xanthine oxidase inhibition, uric-acid reduction, anti-inflammatory, or antioxidant effects; (3) clinical or observational evaluations of efficacy or safety; and (4) systematic or narrative reviews of the evidence base. Studies were excluded if unavailable in English, unrelated to gout or hyperuricemia, or focused on other plant species.

Ethiopia and India were selected as the dual geographical focus because both maintain living traditions of plant-based medicine (used by up to 80 % of Ethiopians and codified in India’s Ayurvedic, Siddha, and Unani systems), possess rich phytodiversity, and have documented the three target plants in distinct cultural contexts. The contrast between Ethiopian oral and Indian textual traditions further enables comparative insight.

The analytical framework examines three domains: ethnopharmacological context (traditional uses, preparations, and cultural significance), phytochemical composition, and mechanisms of action. Within each domain, the plants are compared systematically, highlighting convergences and divergences between traditional knowledge and experimental evidence.

2. Ethnopharmacological Context – Traditional Uses in Ethiopia and India

2.1. Overview of Traditional Medicine Systems

2.1.1. Ethiopian Traditional Medicine

Ethiopia maintains a rich, ancient tradition of plant-based medicine that remains central to its healthcare system. Over 80 % of the population continues to rely on medicinal plants, driven by cultural acceptance of traditional healers, lower cost relative to modern pharmaceuticals, and limited access to formal health facilities, especially in rural areas [8, 9]. Even in urban settings where allopathic services are available, traditional remedies account for roughly 30–50 % of total medicinal consumption [9].

The system encompasses diverse practitioners. Prominent among them are the *debtera*, un-ordained clergy of the Ethiopian Orthodox Tewahedo Church who combine scribal, liturgical, and therapeutic roles. They have long employed amulets, protective scrolls, and sacred texts, addressing ailments perceived to have spiritual dimensions [10]. Other healers include *tenquay* (diviners), bone-setters, birth attendants, herbalists, and spiritual specialists

such as weqaby and kalicha. Healing extends beyond disease cure to the protection of physical, spiritual, social, mental, and material well-being [8, 9].

This practice is underpinned by exceptional phytodiversity. Ethiopia harbors more than 6,500 plant species, approximately 12 % of which are endemic. Of the 213 flowering-plant families present, 92 contain medicinal species, with Lamiaceae, Asteraceae, Fabaceae, and Euphorbiaceae contributing the largest numbers [9, 11]. Ethnobotanical surveys have documented roughly 206 species used for various ailments. Preparations are administered orally (decoctions, with food), topically (fresh leaves, powders, oils), by rubbing, or by squeezing. This orally transmitted knowledge base constitutes a valuable resource for evidence-based phytotherapy and drug discovery [9].

2.1.2. Indian Traditional Medicine

India's classical medical systems, Ayurveda, Siddha, and Unani rank among the world's oldest codified traditions. Ayurveda is the most comprehensive and widely practiced, with foundational texts spanning more than two millennia [12].

The principal works are the Charaka Samhita and Sushruta Samhita, which, together with Vagbhata's Astanga Hridaya, constitute the Brhatrayi ("Great Three") [13]. The Charaka Samhita focuses on internal medicine, etiology, diagnosis, and therapeutics, while the Sushruta Samhita emphasizes surgical techniques and pharmacology [12].

Ayurvedic physiology centers on the three doshas, Vata, Pitta, and Kapha, biological principles derived from the five great elements. Vata (air + ether) governs movement; Pitta (fire + water) governs metabolism; Kapha (earth + water) governs structure and cohesion. Health is equilibrium among the doshas; disease arises from their vitiation [12, 13].

Gout-like disorders are classified as Vatarakta (or vatashonita), produced by concurrent vitiation of Vata and Rakta dhatu (blood tissue). The condition is managed according to the principles of Vatavyadhi Chikitsa. Clinical features, severe joint pain, tenderness, inflammation, and burning, resemble modern gout, inflammatory polyarthritis, and vasculitis. The Sati and Deole [14] provide detailed etiology, classification, and treatment protocols, including oleation (snehana), purification (panchakarma), and herbal formulations that pacify Vata and purify the blood [14]. Pathogenesis is linked to sedentary habits and unsuitable diet [15].

2.2. Ginger (*Zingiber Officinale*)

2.2.1. In Ethiopian Traditional Medicine

Ginger (*Zingiber officinale* Roscoe) is one of the most highly regarded medicinal plants in Ethiopia. It is widely available in local markets and is considered a multipurpose nutraceutical species used by local people for a variety of health conditions [9]. Ethnobotanical studies consistently rank ginger among the top species with high preference scores. In the Goba District of Bale Zone, Southeast Ethiopia, *Zingiber officinale* scored the highest mark and ranked first in preference ranking, indicating that it was perceived as the most effective treatment for tonsillitis [16]. The plant is also among the top-cited species used in the treatment of respiratory tract infections in Ethiopia.

Documented traditional applications of ginger in Ethiopia include the treatment of common cold, abdominal cramp, and nausea/vomiting, where it is administered as an aqueous decoction, maceration, or by drinking crushed root with water or tea [9]. It is also used for respiratory problems, with dried ginger powder macerated in warm milk to create a soothing tea for colds and coughs [9]. Ethiopian farmers brew a decoction of fresh ginger root with water and a pinch of salt to treat stomach aches and fevers [9]. Additionally, ginger is chewed or masticated with feto (*Lepidium sativum*) for stomach disorders [9]. In ethnoveterinary practice, ginger is top-ranked for treating diarrhea in livestock [9]. *Zingiber officinale* has also demonstrated high fidelity level values for treating bloat in ethnoveterinary medicine [17].

Critically, despite ginger's prominence in Ethiopian traditional medicine, no documented traditional use for gout specifically has been identified in the available ethnobotanical literature [9, 16]. Ethiopian traditional knowledge associates ginger primarily with tonsillitis, febrile illnesses, colds, and digestive complaints, rather than with gout or hyperuricemia [9, 16].

2.2.2. In Indian Traditional Medicine (Ayurveda)

In stark contrast to the Ethiopian context, ginger occupies a central and extensively documented position in Ayurvedic medicine for conditions related to joint inflammation and pain. In Ayurveda, *Zingiber officinale* is known as Ardraka (fresh ginger) and Shunthi (dry ginger), and is regarded as a "universal medicine" (Viswabhesaja). Descriptions of the drug appear in almost all pharmacopeias of Ayurveda, including the Nighantu (lexicons), Samhita (treatises), Chikitsasagrantha (compendia), and Rasa grantha (pharmacopeias) [18]. Dry ginger is one of the ingredients of Trikatu (a group of three pungent spices), a famous Ayurvedic formulation for the treatment of digestive and other disorders [18].

Ayurvedic texts describe extensive therapeutic applications for both fresh and dry ginger. Fresh ginger (Ardraka), alone or in combination with other drugs, is used for fever, coryza, bronchial asthma, cough, digestive disorders, diarrhea, anorexia, piles, edema, abdominal disorders, fainting, urticaria, earache, and rheumatoid arthritis. Dry ginger (Shunthi) is used for fever, diarrhea, loss of appetite, indigestion, malabsorption syndrome, piles, hyperacidity, abdominal pain, heart diseases, abdominal lump, edema, hiccough, bronchial asthma, cough, alcoholism, rheumatoid arthritis, filarial diseases, diseases of the mouth, ear, eye, and head, for purifying breast milk, jaundice, and scorpion poisoning. Ginger is recognized as a Vata and Kapha pacifying herb, making it particularly valuable in conditions characterized by Vata vitiation, including joint pain and inflammation [19]. It is described as shothahara (anti-inflammatory) and Vata-kaphahara (pacifying Vata and Kapha) and is used in various diseases including shula (colic), amavata (rheumatoid arthritis), atisara (diarrhea), shotha (edema), kasa (cough), shwasa (asthma), hridroga (heart disease), and jvara (fever) [19]. It exerts anti-inflammatory effects by inhibiting the activity of prostaglandins and plays an important role in reducing joint inflammation. The rhizome is rich in volatile oils containing active compounds such as [6]-gingerol, [6]-shogaols, zingiberol, zingiberone, and α -zingiberene, which are responsible for its medicinal uses, including anti-arthritis and anti-inflammatory properties. The classical

Ayurvedic texts explicitly document the use of ginger in hyperuricemia and gout (Vatarakta), establishing it as a foundational anti-gout remedy within the Indian traditional medicine system.

2.2.3. Cross-Cultural Comparison

Ginger demonstrates high cultural familiarity in both Ethiopia and India, yet the two traditions exhibit divergent traditional indications. In Ethiopia, ginger is primarily valued for tonsillitis, respiratory ailments, and digestive complaints, with no documented traditional use for gout [9, 16]. In India, ginger is extensively documented in Ayurvedic texts for joint inflammation, rheumatoid arthritis, and Vatarakta (gouty arthritis) [19]. This divergence reflects the differing historical development of ethnobotanical knowledge in the two regions and underscores the importance of context-specific evaluation rather than assuming cross-cultural transferability of therapeutic indications.

2.3. Onion (*Allium Cepa*)

2.3.1. In Ethiopian Traditional Medicine

Onion (*Allium cepa* L.) is widely used in Ethiopian traditional medicine, where it is known locally as Qeyi-shinkurt (Amharic, literally "red onion") or Qullubbii diimaa (Oromo) [20, 21]. Ethnobotanical surveys have documented its use for various conditions, including hypertension, where the bulb is chopped, macerated in water, filtered, and drunk [20]. For skin infections, the bulb of *Allium cepa* is crushed along with the root of *Rumex abyssinicus* and combined with the juice of *Citrus aurantifolia* and salt [9]. For diarrhea, a mixture of chopped onion with egg and oil is roasted without adding water and then eaten with injera (Ethiopian flatbread) [9].

Critically, Ethiopian ethnobotanical surveys have explicitly documented onion for the treatment of gout [22]. Traditional preparation methods include crushing the seeds and immersing them in water, filtering through a clean cloth, and drinking the infusion before food, or cutting the corm, boiling it in milk, adding honey, and administering the preparation orally [20]. In a review of medicinal plants for gout management, *Allium cepa* was identified among 14 plants and nine phytochemicals with anti-gout properties [22]. The documented use of onion for gout in Ethiopian traditional medicine represents a significant convergence between indigenous knowledge and modern pharmacological evidence, as onion has subsequently been identified as a potent xanthine oxidase inhibitor [22].

2.3.2. In Indian Traditional Medicine (Ayurveda)

In Ayurveda, onion is known as Palandu (Sanskrit) and is recognized for its medicinal properties. It is described as a herb that aggravates Kapha and alleviates Vata, though it is noted not to alleviate Pitta. It is considered heavy, aphrodisiac, strength-promoting (Balya), and appetizing.

Ayurvedic texts document the use of onion (Palandu) for rheumatism, headache, and hemorrhoids. Due to its anti-inflammatory and analgesic properties, Palandu is specifically used to treat joint pain, arthritis, and gout, helping to reduce swelling and inflammation in the joints and providing relief from pain and stiffness [23]. The most common preparation is fresh onion juice (Palandu Swarasa), typically 5–10 ml for adults, taken on an empty stomach for digestive and reproductive issues, though raw onion may exacerbate acid reflux or gastritis in Pitta-dominant individuals [23].

2.3.3. Cross-Cultural Comparison

Onion demonstrates documented anti-gout use in both Ethiopian and Indian traditional medicine systems. Ethiopia provides particularly strong ethnobotanical evidence, with explicit documentation of onion's use for gout in multiple surveys, alongside detailed preparation methods [20, 22]. India's Ayurvedic tradition similarly recognizes onion (Palandu) for gout, arthritis, and rheumatism, grounded in the theoretical framework of Vata alleviation and anti-inflammatory action [23]. This convergence between two geographically and culturally distinct traditional medicine systems both identifying onion as a remedy for gout, strengthens the credibility of its anti-gout potential and provides a compelling rationale for pharmacological investigation.

2.4. Lotus Seed (*Nelumbo Nucifera*)

2.4.1. In Ethiopian Traditional Medicine

No documented traditional use of lotus seed (*Nelumbo nucifera*) for gout exists in Ethiopian traditional medicine [9]. The plant is not indigenous to Ethiopia and does not feature in the Ethiopian ethnopharmacopoeia. Comprehensive reviews of Ethiopian medicinal plants, which have documented hundreds of species across diverse regions, do not list *Nelumbo nucifera* among the flora used in traditional healthcare [9, 11].

A related species, *Ziziphus lotus*, has been the subject of recent pharmacological research for its xanthine oxidase inhibitory activity [24]. However, *Ziziphus lotus* is not part of Ethiopian traditional practice and has not been documented in Ethiopian ethnobotanical surveys for gout or any other condition [9]. The conflation of *Nelumbo nucifera* (sacred lotus, native to Asia) with *Ziziphus lotus* (a different species) reflects a common source of confusion in the literature but does not alter the fundamental observation: lotus seed, in any form, is not a traditional Ethiopian remedy for gout.

2.4.2. In Indian Traditional Medicine (Ayurveda)

The sacred lotus (*Nelumbo nucifera* Gaertn.) is a well-known medicinal plant in India, where it is recognized for its diverse therapeutic applications. Various parts of the plant, including leaves, seeds, flowers, and rhizomes, have been reported to possess beneficial effects in the treatment of pharyngopathy, pectoralgia, spermatorrhoea, leucoderma, smallpox, dysentery, cough, haematemesis, epistaxis, haemoptysis, haematuria, metrorrhagia, hyperlipidaemia, fever, cholera, hepatopathy, and hyperdipsia [25, 26]. The whole plant has been traditionally used as an astringent, emollient, and diuretic, and for the treatment of diarrhea, tissue inflammation, and homeostasis [25]. In Ayurvedic texts, lotus seeds are ground into a paste and applied as a poultice to reduce inflammation and promote wound healing; this practice is referenced in the Charaka Samhita [26, 27].

However, specific traditional use of lotus seed (*Nelumbo nucifera*) for gout is not prominently documented in classical Ayurvedic texts [25]. While the plant is recognized for its anti-inflammatory and diuretic activities, the classical indications focus primarily on gastrointestinal, respiratory, and dermatological conditions, as well as fever and bleeding disorders [25]. The anti-gout potential of *Nelumbo nucifera* has emerged predominantly from recent pharmacological research, particularly studies on its alkaloid nuciferine, which has been shown to decrease serum urate levels and improve kidney function in hyperuricemic animal models [28].

2.4.3. Critical Observation

The anti-gout potential of lotus seed is largely a product of recent pharmacological research, particularly from Chinese traditional medicine contexts, rather than a traditional indication in either Ethiopia or India [25]. In traditional Chinese medicine, the embryo of lotus seeds (*Lian Zi Xin*) is used primarily for nervous disorders, insomnia, and cardiovascular diseases [25]. The identification of lotus seed as an anti-gout agent is a contemporary development driven by phytochemical screening and mechanistic studies, not by centuries of traditional use in the regions under consideration [24]. This distinction is critical: while lotus seed may possess genuine pharmacological activity against gout, its inclusion in a review of Ethiopian and Indian traditional medicine must be accompanied by this caveat, as it does not represent indigenous knowledge from either region.

2.5. Summary Table: Traditional Use Documentation

The comparative analysis presented in Table 1 reveals a striking divergence in the traditional use documentation of the three selected plants across Ethiopian and Indian medicine systems. Onion (*Allium cepa*) emerges as the only species with convergent traditional use for gout in both regions, with explicit documentation in Ethiopian ethnobotanical surveys and Ayurvedic texts. This cross-cultural convergence substantially strengthens the credibility of onion's anti-gout potential and provides a robust ethnopharmacological rationale for mechanistic investigation. Ginger (*Zingiber officinale*) presents a paradoxical profile: although highly valued in both traditional systems, its anti-gout indication is documented exclusively in Ayurveda, while Ethiopian traditional knowledge associates it with respiratory and digestive complaints. Lotus seed (*Nelumbo nucifera*) exhibits the weakest traditional evidence, with no documented use for gout in either region, suggesting its anti-gout potential is largely a product of contemporary pharmacological research rather than traditional knowledge. The level of evidence for each plant, strong for onion, moderate for ginger, and weak for lotus seed, correlates with the strength of its traditional documentation in the two cultural contexts examined.

Table 1. Comparative documentation of traditional anti-gout use for ginger, onion, and lotus seed in Ethiopian and Indian medicine systems.

Plant	Ethiopian Traditional Use for Gout	Indian Traditional Use for Gout	Level of Evidence
Ginger (<i>Zingiber officinale</i>)	Not documented; used for tonsillitis, colds, fever, digestive complaints [9, 16]	Documented in Ayurveda (<i>Ardraka</i> / <i>Shunthi</i>) for joint pain, rheumatoid arthritis, and <i>Vatarakta</i> (gouty arthritis) [19]	Moderate
Onion (<i>Allium cepa</i>)	Documented in Ethiopian ethnobotanical surveys for gout; preparation: crushed seeds in water, or corm boiled in milk with honey [20, 22]	Documented in Ayurveda (<i>Palandu</i>) for rheumatism, arthritis, and gout; used for its anti-inflammatory and <i>Vata</i> -alleviating properties [23]	Strong
Lotus Seed (<i>Nelumbo nucifera</i>)	Not documented; plant not indigenous to Ethiopia; <i>Ziziphus lotus</i> (a different species) studied pharmacologically but not used traditionally [9]	Not prominently documented for gout in classical Ayurvedic texts; used for pharyngopathy, diarrhea, fever, and hepatopathy [25]	Weak

3. Phytochemical Composition and Bioactive Compounds

3.1. Ginger (*Zingiber Officinale*)

The rhizome of *Zingiber officinale* (family *Zingiberaceae*) contains a complex array of bioactive constituents that underpin its diverse therapeutic properties. The characteristic odor and flavor of ginger are attributable to a combination of volatile oils and pungent phenolic compounds. The rhizome contains 4–10% oleoresin, composed of nonvolatile, pungent constituents (phenols such as gingerols and their related dehydration products, shogaols), alongside nonpungent fats and waxes, and 1.0–3.3% volatile oils, of which 30–70% are sesquiterpenes. At least 115 different bioactive compounds have been identified in ginger through various analytical processes [29].

The gingerols, a group of volatile phenolic compounds that are pungent in nature are the primary bioactive constituents responsible for ginger's pharmacological effects. Among these, 6-gingerol (1-[4'-hydroxy-3'-methoxyphenyl]-5-hydroxy-3-decanone) is the major pharmacologically active component and is characteristic of fresh rhizomes, responsible for their taste and aroma. Other gingerol homologues, including 8-, 10-, and 12-gingerols, are present in lesser concentrations. Shogaols, particularly 6-shogaol, are dehydration products of gingerols that typically occur in aged or processed material rather than in fresh rhizomes. During processing, 6-gingerol undergoes dehydration to form 6-shogaol, which exhibits enhanced bioactivity [30]. Zingerone is another important bioactive phenolic compound. The volatile oil fraction contains numerous compounds, with major components including camphene, sabinene, α -curcumene, zingiberene, α -farnesene, β -sesquiphellandrene, neral, and geranial.

In Ayurvedic practice, a critical distinction is made between fresh ginger (*Ardraka*) and dried ginger (*Shunthi*), each possessing different therapeutic properties and phytochemical profiles. Fresh ginger is rich in gingerols, while the drying process converts gingerols to shogaols through dehydration, altering the pharmacological properties. Concentrations of gingerols in fresh ginger have been found to be more than those in dry ginger, whereas the concentrations of shogaols, which are the major gingerol dehydration products, are more abundant in dry than in fresh ginger [29]. *Shunthi* has been found to contain more pungent compounds than *Ardraka*, with the presence of

shogaols; 6-shogaol is more pungent than 6- and 8-gingerol. This transformation has implications for anti-inflammatory and antioxidant activities, as shogaols exhibit different potency and bioavailability profiles compared to gingerols. Comparative studies have demonstrated that 6-shogaol exhibits the most potent antioxidant and anti-inflammatory properties among ginger constituents, which can be attributed to the presence of an α,β -unsaturated ketone moiety [31]. Gingerols and shogaols demonstrate a wide range of properties, including antioxidant, anti-inflammatory, antidiabetic, and anticancer effects, which operate through various mechanisms including inhibition of pro-inflammatory cytokines and disruption of NF- κ B signalling pathways.

3.2. Onion (*Allium Cepa*)

Onion (*Allium cepa* L., family Amaryllidaceae) is renowned for its rich and diverse phytochemical composition, which includes organosulfur compounds, flavonols, ascorbic acids, and carbohydrate prebiotics. The plant is one of the richest sources of flavonoids and organosulphur compounds, possessing a high level of antioxidant activity [32-35].

The flavonoid profile of onion is particularly noteworthy. Quercetin and its glycosides are the most studied and abundant bioactive constituents. Major flavonol glycosides identified in onion solid waste include quercetin-4'-O-monoglucoside (QMG), quercetin-3,4'-O-diglucoside (QDG), quercetin (Q), and isorhamnetin-3-glucoside (IMG). Other flavonoids present include kaempferol, anthocyanins (concentrated in the outer scales of red onions), and luteolin. Total phenol and flavonoid content in onion varieties ranges from 5.94 to 11.22 mg gallic acid equivalent/g dry weight and 0.67 to 1.52 mg quercetin equivalent/g dry weight, respectively.

The organosulfur compounds in onion are equally important bioactive constituents. Major organosulfur compounds include diallyl monosulfide, diallyl disulfide, diallyl trisulfide, and diallyl tetrasulfide. Additional sulfur-containing compounds include thiosulfates, thiosulfonates, cepaenes, S-oxides, S, S-dioxides, mono-, di-, and trisulfides, and sulfoxides. These compounds contribute to the onion's characteristic pungency and its diverse pharmacological activities.

Importantly, synergistic effects have been observed in whole onion compared to isolated quercetin. The whole onion demonstrates higher potential than isolated quercetin alone to inhibit oxidative stress, possibly due to the enhanced bioavailability of quercetin glycosides compared to quercetin aglycone. Onion and its flavonol glycosides have demonstrated significant xanthine oxidase inhibitory activity. Studies have reported IC₅₀ values ranging from 15.2 ± 0.8 to 35.8 ± 0.2 μ g/mL for onion solid waste extracts and 10.5 ± 0.06 to 20.8 ± 0.05 μ g/mL for flavonol glycosides. These findings position onion and its flavonol glycosides as potential antioxidant and antigout agents.

3.3. Lotus Seed (*Nelumbo Nucifera*)

The sacred lotus (*Nelumbo nucifera* Gaertn., family Nelumbonaceae) seeds possess a remarkably diverse phytochemical profile that has attracted significant research interest. Hot water extracts of *Nelumbo nucifera* have been reported to possess up to 14.8% total phenolic acids and 56.1% total flavonoids by weight, a concentration much higher than many other herbs.

The proanthocyanidins (also known as condensed tannins) are among the most abundant bioactive compounds in lotus seeds. Using ultrahigh-performance liquid chromatography–photodiode array detection–high-resolution tandem mass spectrometry, researchers have identified 16 dimeric, 18 trimeric, and 4 tetrameric proanthocyanidins in lotus seeds. Proanthocyanidins and flavonoids were found to be prevalent in lotus seed coats, with proanthocyanidins present at a concentration of $8,226.19 \pm 249.96$ μ g/g (dry weight) in green–brown stage seed coats. Oligomeric procyanidins from the seedpod of *Nelumbo nucifera* have been extensively characterized, with main molecular weight distribution ranging from 291 to 1155. Specific oligomeric proanthocyanidins identified include dimeric procyanidin B1 (PB1), procyanidin B2, and procyanidin B4.

The flavonoid content of lotus seeds is equally impressive. Dihydrokaempferol and dihydromyricetin have been detected in lotus seeds. Flavonoids in lotus seed pod are hypothesized to possess superior anti-gout activity, and quercetin glucuronide has been identified from the seedpod. The seedpod is particularly rich in phytochemicals categorized as proanthocyanidins, oligomeric procyanidins, flavonoids, alkaloids, and terpenoids.

The alkaloids represent another major class of bioactive compounds in lotus seeds. Alkaloids including dauricine, lotusine, nuciferine, pronuciferine, liensinine, isoliensinine, roemerine, neferine, and arnepavine are the main secondary metabolites found in the seeds. Glycosylated alkaloids were detected in seed cotyledons. Among these, nuciferine, a major aporphine alkaloid has been most extensively studied for its anti-gout potential. Nuciferine decreases serum urate levels, improves kidney function, and inhibits systemic and renal interleukin-1 β (IL-1 β) secretion in potassium oxonate-induced hyperuricemic mice. It achieves these effects by regulating renal organic ion transporters, including urate transporter 1 (URAT1, SLC22A12) and glucose transporter 9 (GLUT9, SLC2A9), to promote uric acid excretion, and by suppressing TLR4/MyD88/NF- κ B signaling and NLRP3 inflammasome activation. Network pharmacology studies have revealed that the mechanism of action of *Nelumbo nucifera* leaf alkaloids in treating hyperuricemia involves multiple target genes, including GAPDH, STAT3, JUN, CASP3, PTGS2, XDH, and MAPK1.

Additionally, lotus seeds contain amino acids, terpenoids, and other secondary metabolites that contribute to their therapeutic profile. The phytochemical composition varies throughout seed maturation, with levels of proanthocyanidins, flavonoids, and amino acids decreasing during maturation.

3.4. Comparative Phytochemical Analysis

The three plants under investigation; ginger, onion, and lotus seed, possess distinct and largely non-overlapping chemical classes that mediate their respective anti-gout activities (Table 2).

Ginger is characterized by gingerols and shogaols, phenolic compounds unique to the Zingiberaceae family, along with volatile terpenes. These compounds exert their effects primarily through anti-inflammatory and antioxidant mechanisms.

Onion is distinguished by its flavonoid-rich profile, particularly quercetin and its glycosides, alongside organosulfur compounds. The xanthine oxidase inhibitory activity of onion is attributed to its flavonol glycosides, positioning onion as a direct urate-lowering agent mechanistically similar to allopurinol.

Lotus seed presents the most diverse phytochemical profile, encompassing proanthocyanidins, flavonoids, and alkaloids (notably nuciferine). This broad chemical diversity enables multi-targeted actions, including xanthine oxidase inhibition, anti-inflammatory effects, and renal protection.

The implications of these distinct phytochemical profiles for mechanisms of action and pharmacokinetics are profound. Ginger's gingerols and shogaols are relatively lipophilic and undergo extensive first-pass metabolism, affecting their bioavailability. Onion's quercetin glycosides have enhanced bioavailability compared to quercetin aglycone, explaining the superior activity of whole onion. Lotus seed's alkaloids and proanthocyanidins exhibit varying degrees of absorption and metabolism, with nuciferine demonstrating good oral bioavailability and tissue distribution.

Table 2. Comparative phytochemical profiles of ginger, onion, and lotus seed.

Feature	Ginger (<i>Zingiber officinale</i>)	Onion (<i>Allium cepa</i>)	Lotus Seed (<i>Nelumbo nucifera</i>)
Major chemical classes	Gingerols, shogaols, volatile oils (sesquiterpenes)	Flavonoids (Quercetin, kaempferol), organosulfur compounds	Proanthocyanidins, flavonoids, alkaloids (Nuciferine)
Primary bioactive compounds	6-Gingerol, 6-shogaol, zingerone	Quercetin, quercetin glycosides, diallyl sulfides	Nuciferine, oligomeric procyanidins, dihydroflavonols
Key functional groups	Phenolic ketones, dehydration products	Flavonol glycosides, thiosulfinates	Aporphine alkaloids, condensed tannins
Primary mechanisms	Anti-inflammatory, antioxidant	Xanthine oxidase inhibition, antioxidant	Xanthine oxidase inhibition, anti-inflammatory, renal protection
Bioavailability considerations	Extensive first-pass metabolism; shogaols more bioavailable than gingerols	Glycosides more bioavailable than aglycone	Nuciferine shows good oral bioavailability

The comparative phytochemical analysis presented in Table 2 reveals that ginger, onion, and lotus seed possess distinct and non-overlapping chemical profiles that determine their respective anti-gout mechanisms. Ginger is characterized by gingerols and shogaols, phenolic compounds with potent anti-inflammatory and antioxidant activities, making it suitable for acute flare management. Onion contains flavonoids (quercetin glycosides) and organosulfur compounds that directly inhibit xanthine oxidase, positioning it as a urate-lowering agent [32, 34]. Lotus seed exhibits the most diverse profile, encompassing proanthocyanidins, flavonoids, and alkaloids (notably nuciferine), enabling multi-targeted actions including xanthine oxidase inhibition, anti-inflammatory effects, and renal protection [28, 36]. These distinct profiles have significant implications for bioavailability, with onion glycosides showing enhanced absorption compared to aglycones, while ginger's shogaols demonstrate superior bioactivity to gingerols [31].

4. Mechanisms of Anti-Gout Action

4.1. Xanthine Oxidase Inhibition

Xanthine oxidase (XO) is a critical enzyme in purine catabolism, catalyzing the oxidation of hypoxanthine to xanthine and subsequently to uric acid, and represents a primary therapeutic target for gout management [37]. The three plants under investigation exhibit markedly different capacities for XO inhibition.

Onion (*Allium cepa*) demonstrates the strongest evidence for XO inhibition among the three plants. In a landmark study, Haidari, et al. [38] demonstrated that oral administration of *Allium cepa* L. (5 g/kg) and its major flavonoid quercetin (5 mg/kg) for 14 days significantly reduced serum uric acid levels in potassium oxonate-induced hyperuricemic rats in a time-dependent manner (p = 0.000). Both treatments significantly inhibited hepatic xanthine oxidase/xanthine dehydrogenase (XDH/XO) activity. The hypouricemic property of onion and quercetin is explained at least partly by their inhibitory effects on XO/XDH activity, as flavonoids are structurally similar to XO/XDH substrates and can competitively inhibit the enzyme. Total onion polyphenols demonstrated significant XO inhibitory activity with an IC₅₀ of 17.36 µg/mL in a xanthine/xanthine oxidase system. Onion and its flavonol glycosides have demonstrated IC₅₀ values ranging from 15.2 ± 0.8 to 35.8 ± 0.2 µg/mL. Notably, the extent of reduction in XDH/XO activity elicited by allopurinol was much higher than that observed with onion and quercetin administration, indicating that while onion is effective, its potency is lower than the standard pharmaceutical agent. However, onion offers advantages in terms of safety and additional antioxidant benefits that allopurinol does not provide.

Lotus seed (*Nelumbo nucifera*) has demonstrated XO inhibitory activity through its diverse phytochemical constituents. Studies have identified that combinations of *Scutellaria baicalensis* and *Nelumbo nucifera* extract (SNE) exhibit potent inhibitory effects on XOD activity. In hyperuricemic mice, SNE decreased serum uric acid by downregulating XOD activity. Additionally, roemerine, an alkaloid found in *Nelumbo nucifera* has been identified as a potential active XO inhibitor with an IC₅₀ value of 3.313 µg/mL. Flavonoids in the lotus seed pod are hypothesized to possess superior anti-gout activity through XO inhibition.

Ginger (*Zingiber officinale*) exhibits limited direct evidence for XO inhibition, though some studies suggest activity. In vitro inhibitory enzyme tests have shown that ginger extract, ferulic acid, and p-coumaric acid (phenylpropanoid components in dried ginger) exhibit XO inhibitory activity. 6-Gingerol has been reported to significantly inhibit XO activity (85%). More recently, three gingerols (6-, 8-, and 10-gingerol) were found to reversibly inhibit XOD activity in a mixed manner with IC₅₀ values of 13.16 ± 0.41, 10.18 ± 0.22, and 6.88 ± 0.11 µM, respectively. Ginger extract has been reported to inhibit XO activity with an IC₅₀ of 188.5 µg/mL. However,

the primary mechanism of ginger in gout management is not XO inhibition but rather its potent anti-inflammatory effects.

4.2. Anti-Inflammatory Mechanisms

Gouty arthritis is characterized by intense inflammation triggered by monosodium urate (MSU) crystal deposition, which activates the NLRP3 inflammasome and leads to the release of pro-inflammatory cytokines, particularly interleukin-1 β (IL-1 β). All three plants exhibit anti-inflammatory properties, though through distinct mechanisms.

Ginger demonstrates strong anti-inflammatory effects primarily through its gingerol and shogaol constituents. Ginger phytochemicals, particularly 6-shogaol, have been shown to inhibit the canonical NLRP3 inflammasome-mediated IL-1 β secretion. At 20 μ M, 10-gingerol and all shogaols significantly inhibited canonical IL-1 β secretion, with shogaols exhibiting more potent inhibitory capacity than corresponding gingerols. These effective ginger phytochemicals not only inhibited the LPS-primed expression of pro-IL-1 β and NLRP3 but also decreased ATP-activated caspase-1. The anti-inflammatory effects are achieved through inhibition of prostaglandin activity and suppression of various inflammatory mediators. Red ginger extract, rich in gingerol, reduces uric acid through anti-inflammatory effects.

Onion exhibits anti-inflammatory, analgesic, and antioxidant properties. Quercetin, the major flavonoid in onion, has been extensively studied for its anti-inflammatory effects in hyperuricemia and gouty arthritis. Quercetin reduces synovitis in particular joints induced by gouty arthritis in a naloxone-sensitive manner and inhibits MSU-induced synovitis by decreasing inflammatory infiltrate cells. Quercetin inhibits nephroinflammatory factors such as TNF- α , IL-6, and TGF- β 1, cytokines associated with tissue damage and renal fibrosis. The anti-inflammatory mechanisms include inhibition of XO, reduction of pro-inflammatory cytokines, and enhancement of antioxidant defense systems.

Lotus seed demonstrates anti-inflammatory effects primarily through its alkaloid nuciferine. Nuciferine reduces the production of NO, PGE2, TNF- α , IL-1 β , and IL-6, depicting potent anti-inflammatory effects. In potassium oxonate-induced hyperuricemic mice, nuciferine inhibited systemic and renal IL-1 β secretion. The anti-inflammatory mechanism involves suppression of renal activation of TLR4/MyD88/NF- κ B signaling and NLRP3 inflammasome activation. Lotus seed protein isolate has also demonstrated anti-inflammatory effects in LPS-stimulated RAW264.7 macrophages.

4.3. Antioxidant Mechanisms

All three plants exhibit significant antioxidant properties through their phenolic and flavonoid content, though onion and lotus seed show particularly strong antioxidant profiles.

Ginger possesses substantial antioxidant activity attributed to its phenolic compounds. Ginger extracts have demonstrated significant antioxidant capacity, with red ginger showing the highest antioxidant activity (79.83%) by the infusion process. The total phenolic content of ginger rhizome extract has been reported as 1.716 mg GAE/g. 6-Gingerol revealed high FRAP-reducing activity (IC₅₀: 5 $\pm$ 0.4 μ M). Ferulic acid, p-coumaric acid, and ginger extract have demonstrated good antioxidant and XO inhibition in vitro.

Onion exhibits strong antioxidant properties through its rich polyphenol and flavonoid content. Total onion polyphenols showed significant antioxidant activity in DPPH, FRAP, and OH-assays (IC₅₀ values of 43.24, 560.61, and 12.97 μ g/mL, respectively). Onion demonstrates higher potential than quercetin alone to inhibit oxidative stress, possibly due to the enhanced bioavailability of quercetin glycosides compared to quercetin aglycone. The antioxidant activity of onion is attributed to sulfur and phenolic-containing compounds, particularly flavonoids. Studies have reported total phenolic content in onion ranging from 4.6 to 74.1 mg/g GAE.

Lotus seed exhibits exceptionally strong antioxidant properties due to its high phenolic and flavonoid content. Hot water extracts of *Nelumbo nucifera* possess up to 14.8% total phenolic acids and 56.1% total flavonoids by weight. The total phenolic content in lotus leaves has been reported as 165 mg tannic acid equivalent/g of dried extract, with another study reporting 282.84 $\pm$ 9.03 GAE μ g/mg of extract. Lotus seeds are rich in alkaloids, flavonoids, phenolic compounds, tannins, and glycosides, exhibiting antioxidant, anti-inflammatory, and other properties. Polyphenol extract from lotus seedpod has demonstrated significant antioxidant activities.

4.4. Uric Acid Excretion and Renal Protection

Beyond XO inhibition, the regulation of renal urate transporters represents a critical mechanism for uric acid reduction.

Lotus seed demonstrates the strongest evidence for renal protection and enhanced uric acid excretion through nuciferine. Nuciferine, a major aporphine alkaloid of *Nelumbo nucifera* leaves, decreases serum urate levels and improves kidney function in potassium oxonate-induced hyperuricemic mice. Mechanistically, nuciferine reverses the expression alteration of renal urate transporter 1 (URAT1), glucose transporter 9 (GLUT9), ATP-binding cassette subfamily G member 2 (ABCG2), organic anion transporter 1 (OAT1), organic cation transporter 1 (OCT1), and organic cation/carnitine transporters 1/2 (OCTN1/2). Nuciferine also suppresses renal activation of TLR4/MyD88/NF- κ B signaling and NLRP3 inflammasome activation to reduce serum and renal IL-1 β levels. These findings suggest that a dietary supplement of nuciferine-rich lotus leaf may have potential for the prevention and treatment of hyperuricemia with kidney inflammation.

Onion reduces serum uric acid in hyperuricemic models without significantly affecting normal levels. However, the involvement of enhanced uric acid clearance or actions on other purine metabolizing enzymes beyond XO inhibition cannot be ruled out. Quercetin has been reported to regulate renal urate transporters, contributing to increased uric acid excretion.

Ginger may contribute to uric acid reduction indirectly through its anti-inflammatory actions rather than through direct effects on uric acid excretion or renal transporters. Ginger consumption has been reported to help decrease uric acid levels, likely through its anti-inflammatory and antioxidant properties.

4.5. Summary Table: Mechanistic Comparison

The mechanistic comparison presented in Table 3 reveals a clear differentiation in the anti-gout action profiles of the three plants. Onion demonstrates the strongest xanthine oxidase inhibition, with confirmed hepatic XDH/XO inhibition and an IC₅₀ of 17.36 µg/mL [6], positioning it as a direct urate-lowering agent. Lotus seed exhibits a multi-targeted profile, combining moderate XO inhibition (Roemerine IC₅₀ 3.313 µg/mL) with strong anti-inflammatory effects and unique renal protection through regulation of urate transporters (URAT1, GLUT9, ABCG2) and suppression of TLR4/NF-κB signaling [28]. Ginger demonstrates exceptional anti-inflammatory potency through NLRP3 inflammasome inhibition [39] but shows limited direct XO inhibition, making it most suitable for acute flare management. These distinct mechanistic profiles suggest that the three plants may serve complementary roles in gout management rather than being interchangeable alternatives.

Table 3. Comparative mechanistic profiles of ginger, onion, and lotus seed in anti-gout action.

Mechanism	Ginger (Zingiber officinale)	Onion (Allium cepa)	Lotus Seed (Nelumbo nucifera)
Xanthine oxidase inhibition	Limited/Indirect; IC ₅₀ 188.5 µg/mL (extract); 6-gingerol inhibits 85% [38, 40]	Strong; hepatic XDH/XO inhibition confirmed; IC ₅₀ 17.36 µg/mL (total polyphenols) [38]	Moderate; flavonoid-mediated; roemerine IC ₅₀ 3.313 µg/mL [28]
Uric acid reduction	Indirect (anti-inflammatory) [41]	Direct (enzyme inhibition) [38]	Direct (nuciferine, flavonoids) [28]
Anti-inflammatory	Strong; NLRP3 inflammasome inhibition; 6-shogaol most potent [39]	Moderate; quercetin reduces synovitis; inhibits TNF-α, IL-6 [42]	Strong; cytokine reduction (IL-1β, TNF-α); TLR4/NF-κB inhibition [28]
Antioxidant	Moderate; FRAP IC ₅₀ 5 µM (6-gingerol) [43]	Strong; DPPH IC ₅₀ 43.24 µg/mL; higher than quercetin alone [38]	Strong; high phenolic/Flavonoid content; up to 56.1% flavonoids [44]
Renal protection	Limited evidence [9]	Limited evidence; some renal parameter restoration [45]	Demonstrated; regulates URAT1, GLUT9, ABCG2; suppresses TLR4/NF-κB [28]

5. Comparative Analysis and Discussion

5.1. Alignment between Traditional Knowledge and Pharmacological Evidence

The comparative analysis reveals a striking gradient in the alignment between traditional knowledge and pharmacological evidence across the three plants, ranging from strong convergence to significant disconnect (Table 4).

Onion (*Allium cepa*) exhibits the strongest convergence between traditional use and pharmacological validation. Ethiopian ethnobotanical surveys have explicitly documented onion for gout treatment, with preparation methods including crushed seeds immersed in water or corms boiled in milk with honey [9]. Similarly, Ayurvedic texts recognize onion (*Palandu*) for rheumatism, arthritis, and gout, attributing its effects to anti-inflammatory and Vata-alleviating properties [23]. These traditional indications align robustly with preclinical evidence demonstrating that onion and its flavonol glycosides exhibit significant xanthine oxidase inhibitory activity, with *Allium cepa* ranking among plants with the highest xanthine oxidase inhibitory activity in systematic reviews [22]. The convergence extends to mechanistic specificity: traditional use for gout, a condition characterized by urate crystal deposition is supported by pharmacological evidence of direct enzyme inhibition and urate reduction [38]. This alignment between two geographically and culturally distinct traditional systems, Ethiopian and Indian, substantially strengthens the credibility of onion's anti-gout potential and provides a robust ethnopharmacological rationale for further clinical development.

Ginger (*Zingiber officinale*) presents a more complex and regionally differentiated pattern of alignment. In Ethiopia, ginger is highly valued in traditional medicine but is documented primarily for tonsillitis, febrile illnesses, colds, and digestive complaints, with no documented traditional use for gout specifically [9, 16]. This represents a disconnect between Ethiopian traditional knowledge and the plant's potential anti-gout applications. In contrast, Indian Ayurvedic tradition extensively documents ginger (*Ardraka/Shunthi*) for joint pain, rheumatoid arthritis, and Vatarakta (gouty arthritis) [18, 19]. Pharmacological evidence strongly supports ginger's anti-inflammatory effects through inhibition of prostaglandin activity and suppression of inflammatory mediators, with 6-shogaol exhibiting the most potent inhibition of NLRP3 inflammasome-mediated IL-1β secretion [39]. However, evidence for direct urate lowering is limited; ginger extract has been reported to inhibit xanthine oxidase with an IC₅₀ of 188.5 µg/mL, but this is not its primary mechanism [46]. Ginger consumption has been associated with reduced uric acid levels, but this effect is likely attributable to its anti-inflammatory properties rather than direct enzyme inhibition [47]. Thus, ginger demonstrates partial alignment—strong pharmacological support for its anti-inflammatory effects (consistent with Ayurvedic use for joint inflammation) but limited evidence for direct urate-lowering mechanisms that would justify its use as a primary gout therapy.

Lotus seed (*Nelumbo nucifera*) exhibits the most significant disconnect between traditional knowledge and recent pharmacological interest. In Ethiopian traditional medicine, lotus seed has no documented traditional use for gout; the plant is not indigenous to Ethiopia and does not feature in the Ethiopian ethnopharmacopoeia [9]. In Indian Ayurvedic tradition, while *Nelumbo nucifera* is well-known and various parts are used for pharyngopathy, inflammation, cough, fever, and hepatopathy, specific traditional use for gout is not prominently documented in classical Ayurvedic texts [25]. The anti-gout potential of lotus seed has emerged predominantly from recent pharmacological research, particularly studies from Chinese traditional medicine contexts rather than from traditional use in Ethiopia or India. Lotus seedpods have been found to be rich in proanthocyanidins, oligomeric procyanidins, flavonoids, alkaloids, and terpenoids, with nuciferine demonstrating urate-lowering effects through regulation of renal organic ion transporters and suppression of TLR4/MyD88/NF-κB signaling [28, 48]. However,

this pharmacological activity represents a contemporary discovery rather than validation of traditional knowledge in the Ethiopian or Indian contexts.

5.2. Cultural and Geographical Considerations

The comparative analysis underscores the fundamental importance of place-based traditional knowledge in ethnopharmacological research. A plant's therapeutic value cannot be assumed to translate across cultures simply because it has been studied elsewhere or used in one traditional system.

Ethiopia's distinct phytogeography and traditional medical practices shape its unique pharmacopeia. Ethiopia is home to more than 6,500 plant species, of which approximately 12% are endemic, with approximately 206 medicinal plant species documented for the treatment of various diseases [9]. Traditional knowledge in Ethiopia is transmitted orally across generations and is closely tied to the country's diverse ecological zones, from the highlands to the Rift Valley. The Ethiopian traditional medicine system encompasses a range of healing practitioners, including the debtera (scribes and therapeutic experts within the Ethiopian Orthodox Tewahedo Church tradition) and tenquay (diviners and spiritual healers), whose knowledge is deeply embedded in local cultural and spiritual contexts [10]. This oral tradition, while rich and extensive, differs fundamentally from the codified textual traditions of India.

India's sophisticated textual traditions, particularly Ayurveda, provide systematic documentation of plant uses that has been preserved and transmitted through written texts for over two millennia. The Charaka Samhita, Sushruta Samhita, and Astanga Hridaya provide detailed descriptions of disease etiology, diagnosis, and treatment, including the conceptual framework of Vatarakta (gouty arthritis) [13, 14]. This textual tradition enables precise identification of traditional indications, dosages, and preparation methods, facilitating systematic comparison with pharmacological evidence. The Ayurvedic understanding of gout as a condition involving vitiated Vata and Rakta provides a theoretical framework that has guided the selection and use of specific herbs, including ginger and onion, for centuries.

The risk of imposing external traditional knowledge onto Ethiopian and Indian contexts is a critical methodological concern. The recent pharmacological interest in lotus seed for gout has been driven largely by research from Chinese traditional medicine contexts, where different plant parts and indications may apply. In traditional Chinese medicine, the embryo of lotus seeds (Lian Zi Xin) is used primarily for nervous disorders, insomnia, and cardiovascular diseases, not gout [25]. Extrapolating this interest to Ethiopian and Indian contexts without acknowledging the absence of traditional use risks misrepresenting local medical realities and potentially misleading practitioners and patients.

5.3. Strengths and Limitations of the Evidence Base

5.3.1. Strengths

The evidence base for the three plants exhibits several notable strengths. First, well-established preclinical evidence for onion provides a solid foundation for its anti-gout potential. Systematic reviews have identified *Allium cepa* among plants with the highest xanthine oxidase inhibitory activity, attributed to its unique natural bioactive compounds including phenolics, flavonoids, and organosulfur compounds [22]. Animal studies have confirmed that oral administration of onion reduces serum uric acid in hyperuricemic rats through significant inhibition of hepatic xanthine dehydrogenase/xanthine oxidase activities [6]. Second, a growing body of research on lotus seed phytochemistry has revealed a remarkably diverse profile of bioactive compounds, including proanthocyanidins, oligomeric procyanidins, flavonoids, and alkaloids, with demonstrated antioxidant, anti-inflammatory, and urate-lowering activities [28, 48, 49]. Third, some clinical evidence exists for ginger in pain management, with ginger compresses noted as a complementary therapy for gouty arthritis, potentially improving pain and inflammation [4]. Ginger's safety profile is well-established, with the FDA classifying it as generally recognized as Safe (GRAS) [47].

5.3.2. Limitations

However, significant limitations constrain the evidence base. The absence of head-to-head comparative studies is a major gap; no studies have simultaneously evaluated ginger, onion, and lotus seed under controlled conditions, preventing direct comparison of their relative efficacy. Limited human clinical trials exist for all three plants; most evidence derives from in vitro and animal studies, with few randomized controlled trials in human gout patients. The lack of standardized extracts and dosage protocols complicates comparison and clinical application; variability in extraction methods, bioactive compound concentrations, and administration routes makes it difficult to generalize findings. The scarcity of rigorous ethnopharmacological validation in Ethiopian contexts represents a particular gap; while Ethiopian ethnobotanical surveys have documented traditional uses, systematic pharmacological validation of these claims remains limited. Furthermore, the absence of documented traditional use for lotus seed in both Ethiopia and India raises questions about the relevance of this plant to these specific cultural contexts.

5.4. Research Gaps

Several Critical Research Gaps Emerge from this Comparative Analysis.

No direct comparative studies have simultaneously evaluated ginger, onion, and lotus seed under controlled conditions. Such studies are essential to establish relative efficacy, optimal dosing, and comparative safety profiles. Given the distinct mechanisms of action, onion as a direct xanthine oxidase inhibitor, ginger as an anti-inflammatory agent, and lotus seed as a multi-targeted compound, head-to-head comparisons would provide valuable guidance for clinical decision-making.

Synergistic effects of combined use remain unexplored. Traditional medicine systems frequently employ polyherbal formulations, and the combination of these three plants may produce additive or synergistic effects that exceed those of individual agents. Given that ginger and onion are commonly used together in culinary and medicinal contexts, investigation of their combined anti-gout activity is warranted.

Human clinical trials are urgently needed across all three plants. While preclinical evidence is promising, the translation to human subjects requires rigorous randomized controlled trials evaluating efficacy, safety, optimal

dosing, and long-term outcomes. Such trials should include standardized extracts with quantified bioactive compound concentrations to enable reproducibility.

Standardization of extracts and bioactive compound quantification is essential for both research and clinical application. Variability in plant material, extraction methods, and bioactive compound content complicates comparison and limits the generalizability of findings. Development of validated analytical methods and quality control standards would facilitate progress.

Most critically, there is an urgent need for more comprehensive ethnobotanical surveys in Ethiopia documenting anti-gout remedies. While some surveys have identified onion for gout treatment, the full range of Ethiopian traditional anti-gout remedies remains inadequately documented. Given that up to 80% of the Ethiopian population relies on traditional medicine [9], systematic documentation and pharmacological validation of these remedies represent a priority for public health and drug discovery.

5.5. Practical and Clinical Implications

The comparative analysis yields several practical and clinical implications for gout management.

Onion emerges as the most credible traditional remedy with the strongest evidence base. The convergence of Ethiopian and Indian traditional use with robust preclinical evidence of xanthine oxidase inhibition and urate lowering positions onion as a promising candidate for clinical development. Its widespread availability, cultural acceptability, and favorable safety profile make it particularly suitable for integration into gout management protocols, especially in resource-limited settings where access to conventional pharmacotherapy is limited. The documented traditional preparation methods, crushed seeds in water or corms boiled in milk with honey, provide culturally grounded administration routes that may enhance patient acceptability and adherence.

Ginger's value lies primarily in its anti-inflammatory and analgesic effects, making it suitable for acute flare management rather than chronic urate lowering. The strong evidence for ginger's anti-inflammatory properties, including inhibition of NLRP3 inflammasome-mediated IL-1β secretion [39], supports its use as an adjunctive therapy during acute gout flares. Ginger compresses have been noted as a complementary therapy for gouty arthritis, potentially improving pain and inflammation [4]. However, patients should not rely on ginger as a sole therapy for chronic urate management, given the limited evidence for direct urate-lowering effects.

Lotus seed shows promise as a source of novel xanthine oxidase inhibitors but requires further validation, particularly in the Ethiopian and Indian contexts where it lacks traditional grounding. The identification of nuciferine and other bioactive compounds with urate-lowering and anti-inflammatory activities warrants continued pharmacological investigation. However, the absence of traditional use in Ethiopia and India means that clinical development should be approached with caution, and the plant should not be promoted as a traditional remedy in these contexts without appropriate cultural contextualization.

Table 4. Alignment between traditional knowledge and pharmacological evidence for ginger, onion, and lotus seed.

Plant	Ethiopian traditional use	Indian traditional use	Pharmacological evidence	Alignment
Ginger (Zingiber officinale)	Not documented for gout; used for tonsillitis, colds, fever [9, 16]	Documented for joint pain, rheumatoid arthritis, Vatarakta [19]	Strong anti-inflammatory; limited XO inhibition [39, 46]	Partial
Onion (Allium cepa)	Documented for gout; crushed seeds in water or corm in milk with honey [9]	Documented for rheumatism, arthritis, gout [23]	Strong XO inhibition; urate reduction confirmed [22, 38]	Strong
Lotus Seed (Nelumbo nucifera)	Not documented; plant not indigenous to Ethiopia [9]	Not prominently documented for gout [25]	XO inhibition; nuciferine-mediated urate reduction [28, 48]	Weak

The alignment analysis presented in Table 4 reveals a clear gradient in the convergence between traditional knowledge and pharmacological evidence across the three plants. Onion demonstrates the strongest alignment, with documented traditional use for gout in both Ethiopian and Indian medicine systems [9, 23] robustly supported by preclinical evidence of xanthine oxidase inhibition and urate reduction [22, 38]. This cross-cultural convergence substantially strengthens the credibility of onion's anti-gout potential. Ginger exhibits partial alignment; strong pharmacological support for anti-inflammatory effects [39] aligns with Ayurvedic use for joint inflammation, but the disconnect in Ethiopian traditional use and limited evidence for direct urate lowering [46] temper its overall alignment. Lotus seed shows weak alignment; despite promising pharmacological activity [28], the absence of traditional use documentation in both Ethiopia and India [9, 25] indicates its anti-gout potential is a contemporary discovery rather than validated traditional knowledge. This gradient has important implications for clinical development priorities and the interpretation of each plant's relevance to Ethiopian and Indian traditional medicine contexts.

6. Conclusion and Future Perspectives

This comparative review evaluated the ethnopharmacological evidence, phytochemistry, and anti-gout mechanisms of ginger (Zingiber officinale), onion (Allium cepa), and lotus seed (Nelumbo nucifera) in Ethiopian and Indian traditional contexts. A clear gradient of alignment between traditional knowledge and pharmacological data emerged.

Onion shows the strongest concordance. Traditional use for gout is documented in both Ethiopian surveys and Ayurvedic texts and is supported by robust preclinical evidence of xanthine-oxidase inhibition and urate reduction, mediated chiefly by quercetin and its glycosides. Ginger exhibits partial alignment: Ayurveda extensively records it for joint pain and Vatarakta, yet Ethiopian practice associates it mainly with respiratory and digestive ailments. Its primary benefit is anti-inflammatory (notably 6-shogaol's suppression of NLRP3-mediated IL-1β), making it more

suitable for acute flares than chronic urate lowering. Lotus seed displays the weakest alignment; anti-gout activity is largely a product of recent pharmacological studies rather than traditional use in either region.

Future research priorities include systematic ethnobotanical documentation in Ethiopia, head-to-head comparative pharmacological assays, randomized clinical trials, investigation of polyherbal synergy, and development of standardized, quality-controlled phytotherapeutic preparations.

These findings support culturally sensitive integration of evidence-based traditional remedies, particularly onion, into gout management, especially in resource-limited settings. Collaborative partnerships between traditional practitioners and biomedical researchers, grounded in mutual respect and equitable benefit-sharing, offer the most promising path toward safe, accessible, and contextually appropriate therapies.

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