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Therapeutic Potential of Natural Products in Gout Management

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ABSTRACT:

Gout, a common type of inflammatory arthritis, is mainly caused by hyperuricemia and the resulting formation of urate crystals in joints. The rising prevalence of this condition has necessitated a thorough evaluation of treatment possibilities beyond standard pharmacological interventions. This abstract examines the potential therapeutic applications of natural products in gout management. Several plant-based compounds, including flavonoids and other phytochemicals, have shown promising anti-inflammatory and uricosuric effects, indicating their ability to lower uric acid levels and alleviate gout symptoms. This study reviews the pharmacological impacts of various natural products, focusing on those that have proven effective in both clinical and preclinical environments. By emphasizing these natural alternatives, the research aims to provide insights into their incorporation into existing gout treatment plans, advocating for a more comprehensive approach to therapy. Additionally, this evaluation takes into account the safety profiles and potential interactions of these natural products with conventional medications, highlighting the significance of patient-centered care. Ultimately, the findings emphasize the therapeutic potential of natural products as supplementary treatments for alleviating gout symptoms and preventing flare-ups, ultimately improving the quality of life for individuals affected by this condition.

Keywords: Gout; Anti-inflammatory; Phytochemicals; Arthritis; Natural products

1. Introduction

The increasing prevalence of gout has been underestimated. Gout is a common chronic disease characterized by hyperuricaemia and deposition of monosodium urate crystals in various anatomical regions, which may lead to significant joint damage and disability. It is also associated with other serious comorbidities including chronic kidney disease, metabolic syndrome, and various bone loss diseases. Drug therapy including nonsteroidal anti-inflammatory drugs, colchicine, and urate-lowering therapy is relatively effective treatment for gout. But multiple limitations such as side effects and contraindications restrict its application in clinical practice. So, there is an urgent need to find alternative therapeutic options (Zhang et al., 2022). It is recommended to provide a comprehensive understanding of traditional and novel therapeutic management options due to the continuous growth of patients with gout.

The therapeutic potential of natural products in ancient medicine has been of interest for re-discovering in the context of modern medicine. The essential role of natural products was right after their experience in the treatment of affliction diseases. The right selection of natural products protects against the production of gouts. It was reported that natural products have also been in use for the therapy in managing gout, particularly due to toxic side effects of synthetic gout suppressors. Ancient men have therapeutic options available these are mostly natural products (El-Tantawy, 2021)(Liu et al.2022). Natural products might contain positive therapeutic effect via several sources that alter the biosynthesis of urate. Conversely, gout therapy via natural products demands a deeper comprehension of what is extracted, as it is influenced by physical properties. From this point, the main purposes of the study are (1) to provide information about natural products used for gout therapy, (2) to continue the physicochemical and pharmacological properties, extraction methods, and therapeutic facilities, (3) to interrogate the bioavailability of major groups of natural products, and (4) to base comprehendings for the wide-elation distribution, pharmacological effectiveness and meta-analysis in the upcoming area of gout therapy on account of natural remedies (Zhang et al.2022)(Yang et al.2022).

2. Understanding Gout

Gout is the most prevalent form of inflammatory arthritis, amassing a considerable amount of attention given its extensive contribution to the burden of disability seen in the health landscape. As the incidence of gout consistently increases over time, the disorder becomes more and more problematic. It is currently linked with heightened mortality rates—hence the determination to delve deep into its complexity (Katturajan and Sabina2021). The condition, characterised by the eruption of uric acid crystals in the joints and surrounding tissues, imitates various symptoms manifesting in several acute painful episodes, large joint effusions, and unremitting joint degradation.

Attacks take place when urate crystals arouse the immune system to produce an inflammatory response damaging the affected joint. Although gout frequently starts with the involvement of one joint, when left unprotected the disease commonly advances to polyarticular affection. Apart from the acute attacks and tophi genesis, gout can also be responsible for other sequalae such as nephrolithiasis and other permanent pathological alterations (Zhang et al., 2022). In ancient times, the Persian physician and philosopher Al-Razi proclaimed one of the most evocative descriptions of gout, associating the flare-ups of excruciating pain with the biting of a voracious beast incapable of relinquishing its grip. It is of the utmost importance to better interpret gout's pathophysiology, a complex process characterized by an intricate cascade of events aimed at comprehending the disease's primeval behaviours. Furthermore, a thorough grasp at gout's pathophysiologic mechanisms is indispensable for the development of original and far more effective relief and prophylaxis interventions (Tao et al., 2023) (Zhang et al., 2022). With that purpose in mind, the current review provides an up-to-date and extensive analysis of gout's pathophysiologic basis. It scrutinizes the recognition, initiation, and perpetuation of those processes from the inception of hyperuricemia until the precipitation of an acute gout attack.

2.1. Pathophysiology of Gout

Gout is described as a chronic, inflammatory arthritis characterized by the deposition of monosodium urate crystals within joints and soft tissues, typically as a result of elevated levels of serum uric acid. Its pathophysiology encompasses the biochemical and immunological processes that result in the development of the disease (Ahmad et al.2021) (Zhang et al., 2022). The key trigger of gout, and thus its pathophysiology, hyperuricemia is better described as a biochemical scenario imbalanced between production and excretion of uric acid. Hyperuricemia can be both primary (genetic and diet-related), and secondary (mostly dysfunction of renal excretion caused by multiple other diseases and drugs), and, in both cases, can cause urate crystal deposition (tophus). Once hyperuricemia and/or supersaturation with monosodium urate (MSU) is reached, MSU crystals precipitate, typically in the joint synovium and get into the joint cavity. Upon that, MSU crystals are perceived by immune cells isolated from the joint, which triggers the intrinsic immune reaction (mostly inflammasome activation) (So & Martinon, 2017). The pivotal step in pro-inflammatory cytokine and inflammatory mediator release is thought to be vacuolar-type H+-ATPase-dependent lysosomal destabilization.

A possible target for therapeutic intervention is the blockage of MC activation. A strategy to do this would be a pharmacological interference at any step of the MSU recognition and internalization or at the level of its sensor ER (various calcium mobilizers or proteasome inhibitors, including some protease inhibitors recently shown to be effective). Another therapeutic approach could be the design of specific SUV-dependent membrane trafficking inhibitors. The inflammatory cascade triggered by MSU crystals has been widely studied, but the cellular mechanisms at the onset of the inflammatory process are only partially understood (Mastellos et al.2024).

3. Current Treatment Approaches

Current treatment approaches for gout are primarily pharmacological. For gouty inflammation, most treatments focus on therapy within the first 48 hours of a flare. First-line medications include oral nonsteroidal anti-inflammatory drugs and selective cyclooxygenase-2 inhibitors. For gout patients with peptic ulcer disease and other contraindications to NSAID use or who are unable to tolerate NSAIDs, oral corticosteroids such as prednisone or prednisolone, with doses typically starting at 30 mg and often tapered over 5-10 days, are appropriate therapeutic choices. Intra-articular corticosteroid injections are also commonly used in acute management of gouty arthritis, often within the first 48 hours of a flare (Terkeltaub, 2023)(Zeng et al.2023). Another exacerbation of gout may be observed within the first 8–12 weeks after starting urate-lowering therapy, so that continuing prophylaxis such as NSAID or colchicine is often recommended for up to 6 months after starting treatment to facilitate establishment of lowering of the serum urate level below 6 mg/dL. Urate-lowering therapies for chronic gout flare prevention include xanthine oxidase inhibitors, uricosuric agents, and recombinant urate oxidase, in addition to urate excretion inhibitors. Acute gouty inflammation pathogenesis is illustrated by accumulation of crystals, resulting in joint damage through recruitment of PMN and formation of neutrophil extracellular traps (Roddy et al.2023)(Bajpai et al.2024). The benefits and drawbacks of current therapy for gout are reviewed. Acute gout treatments substantially alleviate gouty inflammation but do not affect crystal burden. For management of chronic gouty inflammation, monotherapy with colchicine, corticosteroids, or NSAIDs has proven inadequate; long-term daily urate-lowering therapy for gouty inflammation prophylaxis substantially curtails the magnitude of flares, but is not 100% effective in all patients. Recently-developed biologic suppresses crystal-initiated inflammation, but is reserved for use in gout refractory to urate-lowering therapies or allergies to or absolute contraindications to other medications (Freeze et al.2024)(Okobi et al.2023). Compliance with therapy is needed for optimal benefit from acute gout treatments and to sustain and achieve effects of urate-lowering therapies. Major areas of future development in gout inflammation treatment are also previewed.

3.1. Pharmacological Interventions

Gout is a crystal arthropathy caused by the deposition of monosodium urate crystals in joints and soft tissues. The prevalence of gout is 1.14%, and the incidence increases with age in China. The acute gout attack often begins with the first metatarsophalangeal joint and evolves into oligoarthritis in subsequent stages. In addition to metabolic abnormalities in the generation or excretion of uric acid, the immune response and environmental factors can also induce hyperuricemia and gout. Hyperuricemia is the main cause of gout. The degradative product of purine is uric acid, which is the end product of human metabolism (Zhong et al.2022). Uric acid is hydrophobic and easily precipitated due to its low solubility. The cause of hyperuricemia is uneven. About 90% are caused by called idiopathic hyperuricemia. In about 10% of people, hyperuricemia is caused by purine metabolism disorders. The increase in uric acid leads to the activation of the immune system and the production of pro-inflammatory and chemotactic factors. Monosodium urate crystals

can be recognized by Toll-like receptor 4 (TLR4). Uric acid is released from apoptotic cells and dissolved mono-sodium urate crystals that prompt NOD-like receptor 3 (NLRP3) inflammasomes, leading to caspase-1 activation and the cleavage of pro-IL-1 into the active form of IL-1. The resulting immune reaction will lead to the recruitment of neutrophils (Zhang et al., 2022).

4. Natural Products in Gout Management

For centuries, the utilization of natural substances has taken precedence in the effective management of phylogenetically diverse medical troubles, including gouty diathesis. Complementary and alternative medicines (CAM), based on natural formulation, have historical and contemporary significance to control gouty arthritis. After the revelation of the specific molecular pathways underlying the inheritance of medicinal tradition, the naturally obtained bioactive compounds that fall outside those pathways could now become complementary supplemented against hyperuricemia and symptomatic gouty diathesis (Kurbonov and Atamuratova2022)(Mahomoodally et al.2021).

In-channel crystallization of arthritis signs in Marcus God Avril's generation has become a burning issue in conspiracy medicine because conventional medicine alone could struggle insufficiently with pathogenesis. Herbal extracts, isolated ingredients, and plant products excel in refined offshoot SDS-PAGE- standardized expression with gouty predilections are reviewed. Several specific mechanisms that are not yet connected, other than via clinically relevant dose range, between nutraceuticals and gout prophylaxis benefit are detailed out. An integrated pathogenesis through phylogenetic medicine-based natural formulas to gout control is presented. In this regard, it whacks a call to unravel research in this niche domain to portray a new formulation insight against the oaths that herbal therapies are only productive because people believe in them (Scanu et al., 2022). With the advancement of civilization, a network of drugless therapies has been developed from the ancient medicinal plant system of treatment in various continents, including Africa, Australia, India, and America, which is now commonly known as "Traditional Medicine".

Natural products contain bioactive compounds, and recent studies have demonstrated potent anti-inflammatory and analgesic activities. However, in some countries, the traditional use of plant derivatives for the treatment of inflammatory diseases has not been validated from a scientific approach. The study discusses the curative potential of a mixture derived from Aesculus hippocastanum L, Illicium verum Hook. f. and Cynara scolymus L., historically used in Turkey for gout management, within the scope of scientific validation through in vivo anti-inflammatory properties. Gout is an autoinflammatory disorder that results from deposition of monosodium urate (MSU) crystals in the joints (Lin et al.2024). During an acute attack of gout, MSU crystals are formed by triggering the NLRP3 inflammasome in macrophages, releasing proinflammatory cytokines, mainly IL-1β. Plants have been used for the treatment of gout, due to their anti-inflammatory and uricosuric effects. Tablet and verum capsule administration at a dose of 50 mg/kg was reduced carrageenan-induced paw edemas at the 3rd and 4th hour by 67.62 ± 2.13% and 68.55 ± 1.49% ($p < 0.05$), respectively. Sulfasalazine decreased the edema size at the 4th hour by 51.99 ± 6.15% ($p < 0.05$) (Elhouda Daoudi et al., 2020).

4.1. Anti-Inflammatory Properties of Natural Products

Over the last decades, natural products, in particular plant-derived ones, have been intensively investigated for their relevant anti-inflammatory properties. Flavonoids, phenolic acids, terpenes, alkaloids, saponins, and polysaccharides are some bioactive compounds derived from fruits and vegetables exhibiting anti-inflammatory activities in immune-inflammatory and auto-inflammatory diseases. Bioactive compounds, being regulatory molecules, might positively interfere with the complexity of the immune response during the stages of gouty inflammation (Ge et al.2022)(Cui & Jia, 2021). In particular, lipoxygenase and cyclooxygenase inhibition, as well as interference with arachidonic acid metabolism, are among the possible pathways of some bioactive compounds.

Research evidence has demonstrated that these compounds can interfere with the immune-inflammatory complex process at different levels, including cell-type modulation, cytokine production, and response of key modules in inflammation such as the nuclear factor, having an inhibitory effect on the production of some cytokines and lowering the activation of some cell models. Referring to the inflammatory response of gout, an ongoing debate exists regarding the potentiality of the immune components triggering the IL-1ß/IL-18 inflammosome and the cytokine-imprinted polarization of T-cells exacerbates the inflammation-induced damage (Xiao et al.2024)(Zhang, 2023).

Plenty of bioactive compounds, such as curcumin, quercetin, berberine, ginsenoside, and hyperoside, might be useful in counteracting or at least alleviating both the massive inflammatory response in the uric acid and in microcrystals, and the cytokine storm syndrome, which is often associated with the worst gout attacks, as demonstrated by early studies in both in vivo and ex vivo experimental models (Scanu et al.2022)(Sun et al.2023). In particular, early evidence has been generated about controlling the polarization of the immune response, thus weakening the Th1-related hyperinflammatory profile of gout attacks. Besides, other works have produced results about hampering IL-1ß production or improving the inhibition of the inflammatory pathway.

5. Efficacy and Safety of Natural Products

Recent developments in the pathogenesis and therapeutic strategy for gout have highlighted the importance of natural products, offering new candidate options for clinicians. Numerous natural products have been found to have therapeutic benefits in gout management. As an adjunct therapy, there is an increasing interest in a healthy diet and alternative treatment for gout due to concerns about the efficacy and the risk of adverse effects of traditional medications. Natural products have been used in gout management for centuries and are still frequently used today (Liu et al.2022)(Wu et al.2023). They are perceived as natural and safe by the public, embodying a life-long concept of health. Natural products are complex mixtures, often claimed to contain

multiple biologically or pharmacologically active compounds at physiological concentrations. Their therapeutic benefits are frequently suggested in ancient books and through clinical practice, forming the most common types of adjunct therapy for numerous conventional medicines. Treatment of gout requires the control of both diet and drugs, and many natural products are perceived to have advantages in terms of lifestyle modification and health promotion (Thakuria et al.2025)(Roman, 2022). Modern scientific research has confirmed that many natural products contain active components that show therapeutic potential.

5.1. Clinical Trials and Evidence-Based Studies

This section aims to describe the outcomes of clinical trials and evidence-based studies that have been conducted and discussed in peer-reviewed literature, assessing the effect of natural products in a managing aspect of gout disease (Scanu et al., 2022). Evidence-based evaluation has always been a question of numerous natural products' therapeutic potential because of the absence of government-approved medicinal claim on the considered application on the one hand and, on the other hand, thousands of different variables influence the therapeutic potential of the same product with the same botanical name: geographical location and year of growth, part of the plant used for drug preparation, procedure of isolation, propagation, and extraction, type of molecular derivatives, and its purities, chemical and physical properties, system of drug administration, individual variations in absorption, metabolism, and excretion, preparation and time of food consumption, combinations with other materials, environmental, alimentary and life style, seasonal and circadian rhythms, other botanical or artificial chemicals employed in the sphere of individual pharmacotherapy, etc (Yang et al.2022)(Roman, 2022). Given the popularity and accessibility of natural remedies, ethical and legal practice requires an appropriate attitude from the scientific literature. This article aims to give an overview of large-scale randomized controlled trials and evidence-based studies published throughout professional sources with a rational analysis of the probable outcome and comments on the entire literature body. However, lots of trials examining natural products on gout management have been excluded from the broad discussion due to inadequate research methodology or other biases, failed enthusiasm to researchers, or absence of clinical supporting evidence (Yokose et al.2024).

6. Mechanisms of Action of Natural Products

The anti-inflammation pathway is considered to be the most critical one in affecting biochemical mediators for managing gout flares. By mediating the enzymes' activities of cyclooxygenase, lipoxygenase, phospholipases, iNOS and cyclooxygenase-2, natural compounds restrain the production of arachidonic acid-derived compounds, known as important inflammatory mediators conferring conditions to trigger a gout attack (Liu et al.2023). Regarding this pathway, natural flavonoids mainly deal with prevention and anti-inflamed ailments by inhibiting the activity of lipoxygenase and various enzymes of cyclooxygenase, phospholipase, iNOS and cyclooxygenase-2, then decreasing the formation of prostaglandins, leukotrienes and thromboxanes. Furthermore, flavonoids are reported to be effective inhibitors which abolish the transcription factor - nuclear factor κβ - from translocating nuclear after stimulation by inflammatory triggers, such as pro-inflammatory cytokines and endotoxin, and eventually, nuclear factor κβ can activate production of pro-inflammatory enzymes and mediators. In some in vitro tests and more in vivo animal tests, flavonoids indirectly inhibit pro-inflammatory cytokine production without involving in preventing these compounds binding with their receptors (Scanu et al., 2022). Among the inflammatory mediators, interleukin 1β (IL-1β) is accepted as the most effective to crystal inflamed response, prompting clearance of IL-1β in a presently available therapeutic strategy. Uricosuric and the lowering of the serum urate level is also involved in a number of complementary such as allopurinol, febuxostat, urinary alkalinizing agents, colchicine and so forth. Finally, xanthine oxidase inhibitors, like alpinetin, are widely accepted in Western countries for the treatment of gout by inhibiting uric acid synthesis (Minh et al., 2022)(Pham et al.2021). UAP1 (Benzoic acid) has been revealed to benefit for hyperuricemia clearance by enhancing the excretion of uric acid. Both mechanisms, decreasing the urate reabsorption and increasing the reabsorption of glutaric acid, facilitate to expel more uric acid. Additionally, it can regulate allantoin dehydrogenase activity, assign more transformation of uric acid into allantoin, and moreover, moderately decrease the release of uric acid from xanthine or hypoxanthine. On another side, natural compounds can restrain the oxidative stress pathway by up-regulating anti-oxidase activities or down-regulating ROS generation (Ullah et al.2024). Gout is known to have much stronger oxidative stress than usual status. Uric acid crystal instigated depletion of intracellular redox potential in neutrophils and generation of a powerful oxidant burst. This strong oxidant burst phenocopies apoptosis but is not catastrophic to the cell, causing the release of its contents extracellularly in an inflamed event. Kitovin IIb, discovered in garlic, prevented LNCaP prostate cancer cells from death affected by oxidative stress, and herbal and mineral drug mutagen stimulates the up-regulation of the protective enzymes outside bilateral reactions to counteract propagating oxidative damage (Gherghina et al.2022)(Bernat-Ponce & Gil-Delgado…, 2023). It is the phenomenon that garlic samples may contain agents that act to protect cells from injury. Gout is the most common forms of inflammatory arthritis, which is driven by monosodium urate crystal deposits in a joint causing severe pain and disability. Based on the underlying mechanisms crudes such as inflammation, deposition of monosodium urate crystals, release of inflammatory mediators, free radicals and oxidative stress in gout flare attack, successful management and therapy of the disease must consider all of the precipitating predisposing factors (Katturajan and Sabina2021). There are currently limited therapies that reduce the frequency of gout attacks thus there is an imperative need for the development of new treatments and chemotherapies for the management of these symptoms. Results, on the other hand, also confirm the limitation of existing drugs and the importance of developing novel potential added films. Pub releases extensive data that would probably lead to the development of new approaches, not workable alone due to the complexity of different forms of arthritis, which can be combination therapeutics (Tian et al., 2024)(Kraev et al.2023)(Kuwabara et al.2023). Combinations are a powerful tool, used in biology and chemistry to improve an effect. So, products of natural origin would be favorable for use in combination with certain pharmacological components. There was seen a significant reduction in rats stimulated with carrageenan of prostaglandin 2E production.

7. Future Directions and Research Opportunities

Despite significant advancements in the treatment of gout over the past four decades, there remain unmet needs for a large number of people affected by this centuries-old disease. Whilst a variety of synthetic drugs are effective in treating gout, many people still seek and self-medicate with traditional and herbal medicines to relieve the symptoms of gout. This is mainly because of the complexity and cost of modern treatment and an increasing awareness of the side effects of synthetic drugs. However, a dearth of published scientific data on the efficacy and safety of traditional and herbal medicines for gout management limits the use of these agents (Kadhim et al.2023)(Kavitha et al.2022)(Chukwure and USORO2023). Since gout is common and is mainly treated in primary care, there is a need for well-designed large-scale clinical trials on the efficacy and safety of both commercial and classical traditional and herbal medicines for gout management between primary care settings. This demand is amplified by the global burden of gout predisposed by lifestyle, aging, increasing obesity, and dietary transition.

Whilst modern drugs are effective in managing gout, there is a great need to explore alternative anti-gout agents. There is increased interest in the use of natural products as potential anti-gout agents. This may be, in part, due to the historical and cross-cultural wisdom of using herbs to treat and manage gout across the globe or because unmatched varieties of natural products, compared with the synthetic combinatorial chemical drug libraries, are yet to be explored for gout management (Wu et al.2023). As a base of eligibility, the non-patented status of these products have provided an attractive natural product for neglected diseases. As such, many researchers have started screening herbs for their anti-gout potential. Some of these natural compounds showed promising results in preclinical studies, but there are limited worldwide patented products (Mahomoodally et al.2024)(Bai et al.2023). The limited confirmed products may be due to methodological shortcomings, a lack of experience, and an incoherent approach to the study of the pharmacology, efficacy, toxicology, and clinical trials of natural products. Researchers were also not interested in the products as evidence of toxicity, as poisoning with natural products is weakened. Overall, it can be agreed that there are further opportunities and challenges for researchers to focus on natural products as their antipyretic drugs.

8. Conclusion

The invariable pain, swelling, inflammation, skin redness, intra-articular crystals, and chills of gout are escalating signals that now is the time to step up with your urate-lowering efforts beyond lifestyle changes. Physicians lag behind nurses, patients, and the community when it comes to recognizing the “burden of gout”, and have not characterized the condition as comprehensively, via a variety of gout watermark manifestations (Terkeltaub, 2009). Having too much urate in synovial fluid triggers gout inflammation and eventual chronic arthropathy, but that is now preventable and treatable through xanthine oxidase inhibitors, uricosurics, and newer agents, including pegloticase, the urate oxidase enzyme. The aforementioned benchmarks of gout management guidelines, for both asymptomatic hyperuricemia and chronic gout, encompass more than initial urate-lowering therapy. These are comprehensive therapy guidelines covering lifestyle recommendations, acute gout treatment modalities, unmasking the urate-dependent inflammatory arthritides incriminated in most flares (including the critical role of high serum uric acid in PDP, or these smaller nodal MTP gout-like lesions), review of each class of agents recommended as additional antiphlogistics, review of the “Guidelines for the Acute Management of the Adult with Acute Gout”, and step therapy in gout.

One of the described gout diet mechanisms is the potential for excessive fructose to alter major purine metabolism and raise serum uric acid (Zhang et al., 2022). Because of this, there is a growing interest throughout the gout community in the potential therapeutic utility of fructose restriction. This review describes the potential mechanisms whereby dietary fructose could raise serum uric acid, examines its effects to date in minor studies involving mostly normal volunteers, and reports a small, controlled study examining the effects of fructose restriction in children with mixed hyperuricemia and/or gouty arthritis. When gouty patients consume fructose-providing substances, there is a disturbance of pyrimidine metabolism leading to both decreased excretion and increased synthesis of uric acid from de novo purine biosynthesis, fructose degradation. Comment on fructose restriction in a child with hyperuricemia and/or gouty arthritis that raised serum uric acid is discussed.

References:

Zhang, Y., Chen, S., Yuan, M., Xu, Y., & Xu, H. (2022). Gout and Diet: A Comprehensive Review of Mechanisms and Management. ncbi.nlm.nih.gov

El-Tantawy, W. H. (2021). Natural products for the management of hyperuricaemia and gout: a review. Archives of Physiology and Biochemistry. researchgate.net

Liu, L., Wang, D., Liu, M., Yu, H., Chen, Q., Wu, Y., ... & Wang, T. (2022). The development from hyperuricemia to gout: key mechanisms and natural products for treatment. Acupuncture and Herbal Medicine, 2(1), 25-32. lww.com

Zhang, X., Cui, J., Hou, J., & Wang, W. (2022). Research progress of natural active substances with uric-acid-reducing activity. Journal of Agricultural and Food Chemistry, 70(50), 15647-15664. [HTML]

Yang, B., Xin, M., Liang, S., Xu, X., Cai, T., Dong, L., ... & Sun, W. (2022). New insight into the management of renal excretion and hyperuricemia: Potential therapeutic strategies with natural bioactive compounds. Frontiers in Pharmacology, 13, 1026246. frontiersin.org

Katturajan, R., & Sabina, E. P. (2021). Joint Inflammation: Insights of Osteoarthritis, Gouty and Rheumatoid Arthritis and its Prevalence, Mechanism, Medications and Remedies. Indian Journal of Pharmaceutical Sciences, 83(5). [HTML]

Tao, H., Mo, Y., Liu, W., & Wang, H. (2023). A review on gout: Looking back and looking ahead. International immunopharmacology. [HTML]

Zhang, Y., Chen, S., Yuan, M., Xu, Y., & Xu, H. (2022). Gout and diet: a comprehensive review of mechanisms and management. Nutrients. mdpi.com

Ahmad, M. I., Masood, S., Furlanetto, D. M., & Nicolaou, S. (2021). Urate crystals; beyond joints. Frontiers in Medicine, 8, 649505. frontiersin.org

So, A. K. & Martinon, F. (2017). Inflammation in gout: mechanisms and therapeutic targets.. [PDF]

Mastellos, D. C., Hajishengallis, G., & Lambris, J. D. (2024). A guide to complement biology, pathology and therapeutic opportunity. Nature Reviews Immunology, 24(2), 118-141. lambris.com

Terkeltaub, R. (2023). Emerging urate-lowering drugs and pharmacologic treatment strategies for gout: a narrative review. Drugs. [HTML]

Zeng, X., Liu, Y., Fan, Y., Wu, D., Meng, Y., & Qin, M. (2023). Agents for the treatment of gout: current advances and future perspectives. Journal of medicinal chemistry, 66(21), 14474-14493. [HTML]

Roddy, E., Bajpai, R., Forrester, H., Partington, R. J., Mallen, C. D., Clarson, L. E., ... & Muller, S. (2023). Safety of colchicine and NSAID prophylaxis when initiating urate-lowering therapy for gout: propensity score-matched cohort studies in the UK Clinical Practice Research Datalink. Annals of the Rheumatic Diseases, 82(12), 1618-1625. bmj.com

Bajpai, R., Partington, R., Muller, S., Forrester, H., Mallen, C. D., Clarson, L., ... & Roddy, E. (2024). Prognostic factors for colchicine prophylaxis-related adverse events when initiating allopurinol for gout: retrospective cohort study. Rheumatology, keae229. oup.com

Freeze, R., Hughes, P., Haystead, T., & Scarneo, S. (2024). Transforming Growth Factor-β-Activated Kinase 1 (TAK1) Alleviates Inflammatory Joint Pain in Osteoarthritis and Gouty Arthritis Preclinical Models. Journal of Pain Research, 2287-2298. tandfonline.com

Okobi, O. E., Oletu, H., Chukwuedozie-Echeazu, A. B., Keke, V. C., Nwachukwu, O. B., Akunne, H. S., ... & Mbah, L. A. (2023). The Stiff Joint: Comparative Evaluation of Monotherapy and Combination Therapy With Urate Lowering Agents in Managing Acute Gout. Cureus, 15(9). cureus.com

Zhong, L., Liu, S., Qiu, X., Zeng, X., Su, L., Huang, D., ... & Xie, Y. (2022). High prevalence of hyperuricemia and associated factors among zhuang adults: A cross-sectional study based on the ethnic minority population cohort in the Southwestern China. International journal of environmental research and public health, 19(23), 16040. mdpi.com

Kurbonov, M. T., & Atamuratova, T. I. (2022). Use Of Pomegranate Marc In Composition Of Compound Feed For The Prevention Of Diarrhea Of Farming Poultry. Journal of Pharmaceutical Negative Results, 13. [HTML]

Mahomoodally, M. F., Lobine, D., Picot-Allain, M. C., Sadeer, N., Jugreet, S., & Zengin, G. (2021). Conventional and non-conventional targets of natural products in the management of diabetes mellitus and associated complications. Current Medicinal Chemistry, 28(23), 4638-4669. [HTML]

Scanu, A., Luisetto, R., Ramonda, R., Spinella, P., Sfriso, P., Galozzi, P., & Oliviero, F. (2022). Anti-Inflammatory and Hypouricemic Effect of Bioactive Compounds: Molecular Evidence and Potential Application in the Management of Gout. ncbi.nlm.nih.gov

Lin, Z., Gupta, J. K., Maqbool, M., Kumar, K., Sharma, A., & Wahi, N. (2024). The therapeutic management of chemical and herbal medications on uric acid levels and gout: modern and traditional wisdom. Pharmaceuticals, 17(11), 1507. mdpi.com

Elhouda Daoudi, N., Bouhrim, M., Ouassou, H., & Bnouham, M. (2020). Medicinal Plants as a Drug Alternative Source for the Antigout Therapy in Morocco. ncbi.nlm.nih.gov

Ge, J., Liu, Z., Zhong, Z., Wang, L., Zhuo, X., Li, J., ... & Bai, R. (2022). Natural terpenoids with anti-inflammatory activities: Potential leads for anti-inflammatory drug discovery. Bioorganic Chemistry, 124, 105817. [HTML]

Cui, J. & Jia, J. (2021). Natural COX-2 inhibitors as promising anti-inflammatory agents: an update. Current Medicinal Chemistry. [HTML]

Xiao, N., Xie, Z., He, Z., Xu, Y., Zheng, S., Wei, Y., ... & Li, Z. (2024). Pathogenesis of gout: Exploring more therapeutic target. International Journal of Rheumatic Diseases, 27(4), e15147. [HTML]

Zhang, W. (2023). Uric acid en route to gout. Advances in Clinical Chemistry. [HTML]

Scanu, A., Luisetto, R., Ramonda, R., Spinella, P., Sfriso, P., Galozzi, P., & Oliviero, F. (2022). Anti-inflammatory and hypouricemic effect of bioactive compounds: molecular evidence and potential application in the management of gout. Current Issues in Molecular Biology, 44(11), 5173-5190. mdpi.com

Sun, X., Yang, L., Sun, H., Sun, Y., Wei, S., Han, Y., ... & Wang, X. (2023). TCM and related active compounds in the treatment of gout: the regulation of signaling pathway and urate transporter. Frontiers in Pharmacology, 14, 1275974. frontiersin.org

Wu, J., Alhamoud, Y., Lv, S., Feng, F., & Wang, J. (2023). Beneficial properties and mechanisms of natural phytochemicals to combat and prevent hyperuricemia and gout. Trends in Food Science & Technology, 138, 355-369. [HTML]

Thakuria, R., Chetia, P., & Mustaque, A. S. (2025). Potential Plant-based Remedies for Gouty Arthritis: A Comprehensive Review on Counterweighing the Inflammatory Pathways. The Natural Products Journal. [HTML]

Roman, Y. M. (2022). Moving the needle in gout management: the role of culture, diet, genetics, and personalized patient care practices. Nutrients. mdpi.com

Yokose, C., McCormick, N., Abhishek, A., Dalbeth, N., Pascart, T., Lioté, F., ... & Choi, H. K. (2024). The clinical benefits of sodium–glucose cotransporter type 2 inhibitors in people with gout. Nature Reviews Rheumatology, 20(4), 216-231. [HTML]

Liu, W., Peng, J., Wu, Y., Ye, Z., Zong, Z., Wu, R., & Li, H. (2023). Immune and inflammatory mechanisms and therapeutic targets of gout: An update. International immunopharmacology, 121, 110466. [HTML]

Minh, T. N., Van, T. M., Khanh, T. D., & Xuan, T. D. (2022). Isolation and Identification of Constituents Exhibiting Antioxidant, Antibacterial, and Antihyperuricemia Activities in Piper methysticum Root. Foods. mdpi.com

Pham, N. K., Nguyen, H. T., & Nguyen, Q. B. (2021). A review on the ethnomedicinal uses, phytochemistry and pharmacology of plant species belonging to Kaempferia L. genus (Zingiberaceae). Pharmaceutical Sciences Asia, 48(1). semanticscholar.org

Ullah, Z., Yue, P., Mao, G., Zhang, M., Liu, P., Wu, X., ... & Yang, L. (2024). A comprehensive review on recent xanthine oxidase inhibitors of dietary based bioactive substances for the treatment of hyperuricemia and gout: Molecular mechanisms and perspective. International Journal of Biological Macromolecules, 134832. [HTML]

Gherghina, M. E., Peride, I., Tiglis, M., Neagu, T. P., Niculae, A., & Checherita, I. A. (2022). Uric acid and oxidative stress—relationship with cardiovascular, metabolic, and renal impairment. International Journal of Molecular Sciences, 23(6), 3188. mdpi.com

Bernat-Ponce, E. & Gil-Delgado…, J. A. (2023). Eating in the city: Experimental effect of anthropogenic food resources on the body condition, nutritional status, and oxidative stress of an urban bioindicator passerine. … Zoology Part A …. ua.es

Tian, Y., He, X., Li, R., Wu, Y., Ren, Q., & Hou, Y. (2024). Recent advances in the treatment of gout with NLRP3 inflammasome inhibitors. Bioorganic & Medicinal Chemistry. [HTML]

Kraev, K. I., Geneva-Popova, M. G., Hristov, B. K., Uchikov, P. A., Popova-Belova, S. D., Kraeva, M. I., ... & Mitkova-Hristova, V. T. (2023). Celebrating versatility: febuxostat's multifaceted therapeutic application. Life, 13(11), 2199. mdpi.com

Kuwabara, M., Fukuuchi, T., Aoki, Y., Mizuta, E., Ouchi, M., Kurajoh, M., ... & Abe, K. (2023). Exploring the multifaceted nexus of uric acid and health: a review of recent studies on diverse diseases. Biomolecules, 13(10), 1519. mdpi.com

Kadhim, K. F., Aldabis, H. A., AL-Kabi, H. H., & Al-Maliki, N. T. S. (2023). Self-medication with herbal remedies: Understanding the practices in Iraqi society. Biomedicine, 43(5), 1484-1489. uobasrah.edu.iq

Kavitha, J., Sivakrishnan, S., & Srinivasan, N. (2022). Self Medication in Today's Generation without Knowledge as Self Inflicted Harm. Archives Of Pharmacy Practice, 13(3-2022), 16-22. archivepp.com

Chukwure, P. C., & USORO, M. I. (2023). Factors Responsible For Self Medication Among The Rural Dwellers. The Journal of Economics, Finance and Innovation, 37-50. sbtsuejournals.uz

Mahomoodally, M. F., Coodian, K., Hosenally, M., Zengin, G., Shariati, M. A., Abdalla, A. N., ... & Khalid, A. (2024). Herbal remedies in the management of hyperuricemia and gout: A review of in vitro, in vivo and clinical evidences. Phytotherapy Research, 38(7), 3370-3400. [HTML]

Bai, L., Wu, C., Lei, S., Zou, M., Wang, S., Zhang, Z., ... & Chen, L. (2023). Potential anti-gout properties of Wuwei Shexiang pills based on network pharmacology and pharmacological verification. Journal of Ethnopharmacology, 305, 116147. ssrn.com

Terkeltaub, R. (2009). Gout. Novel therapies for treatment of gout and hyperuricemia. ncbi.nlm.nih.gov