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ANTI-GOUT AND ANTI-ARTHRITIC ACTIVITY OF MEDICINAL PLANTS: A SCIENTIFIC REVIEW

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ABSTRACT: Gout and arthritis are prevalent and debilitating inflammatory disorders that primarily affect the joints, leading to intense pain, swelling, stiffness, and restricted mobility. These conditions significantly impair the quality of life and often require long-term management. While conventional pharmacological treatments such as non-steroidal anti-inflammatory drugs (NSAIDs), corticosteroids, and urate-lowering agents offer symptomatic relief, they are often associated with adverse effects, high costs, and limited efficacy in certain patient populations. Consequently, there is increasing interest in the potential of medicinal plants with anti-gout and anti-arthritic properties as alternative or complementary treatments. This review aims to provide a comprehensive and critical evaluation of a wide range of medicinal plants that have shown potential in mitigating the symptoms of gout and arthritis. The review focuses on identifying key phytochemicals and understanding their mechanisms of action, which include anti-inflammatory, antioxidant, analgesic, immunomodulatory, and uric acid-lowering effects. By synthesizing contemporary scientific findings, this review emphasizes the therapeutic relevance, safety profile, and clinical applicability of medicinal plants, thereby presenting them as promising adjuncts or alternatives in the management of gout and arthritis.

INTRODUCTION: Gout and arthritis are two prevalent forms of joint inflammation that significantly impact the quality of life of millions worldwide. Gout is characterized by the deposition of monosodium urate crystals in joints, leading to intense pain and swelling, while arthritis encompasses a broader range of joint disorders, including rheumatoid arthritis and osteoarthritis, marked by inflammation and degeneration of joint tissues.

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Conventional treatments, including non-steroidal anti-inflammatory drugs (NSAIDs), corticosteroids, and urate-lowering therapies, often have undesirable side effects and limitations, prompting the search for alternative therapies. Medicinal plants have long been used in traditional medicine for their anti-inflammatory and analgesic properties, offering a potential complementary approach to managing gout and arthritis.

Role of Medicinal Plant in Primary Healthcare: About 3 billion people, or 65–80% of the world's population, still depend on herbal remedies to address their health requirements. Due to the practice's advantages in medicine and its enduring status in many cultures worldwide, it is being carried out today.

Ayurveda, Unani, and homoeopathy are three examples of the respectable healthcare systems developed in India that cover the whole gamut of human health and promote good individual health. However, over time, some unfavourable interferences with these systems have led to the need to codify and unify the entire system. Establishing guidelines for Ayurvedic medications is crucial in this regard. This is especially true now that the business is supplying more and more ayurvedic medications instead of ayurvedic doctors making them on the spot.

Additionally, commercially available Ayurvedic medications may debut in global markets that are searching for complementary therapies to treat illnesses for which the current medical system is unable to provide a remedy. These conditions include degenerative or metabolic diseases such as arthritis, cardiac difficulties brought on by lifestyle choices, diabetes, cancer, dementia, age-related illnesses, immunological issues, and gynaecological issues.

While debating the acceptability of the role of traditional medicine and its practitioners in primary healthcare, it is crucial to formulate key rules defining the type and scope of our participation. While some of the conventional medical system's procedures have previously been studied, others need further care. The following criteria might be taken into consideration in this regard. Humanity has advanced so quickly in its history that information derived from science is now used to the study of natural origin drugs. The ultimate goal of researching natural products is to help establish a logical connection between the chemical makeup of naturally occurring drugs and the biological or therapeutic effects they produce. Natural remedies are becoming more and more popular in the current global environment since they are affordable, widely accessible, and generally devoid of adverse effects. In an effort to identify a single physiologically active chemical, scientists are now placing a strong emphasis on studying traditional plant remedies. According to WHO estimates, 80% of people in underdeveloped nations get their main medical treatment from traditional medicines, which are mostly made of plant-based pharmaceuticals [1]. Many traditional health care systems now rely heavily on medicinal plants, and a considerable portion of the global population, particularly in affluent nations, relies on traditional medicine to satisfy their everyday health needs. Many industrialised nations also have a broad use of plant-based medicines, and many drugs are produced from or based on plants. Likewise, plants with therapeutic or medicinal properties may find their way into cosmetics and other home items. India is home to an abundance of herbal plants that are said to be priceless in the treatment of dread diseases including diabetes, jaundice, asthma, malaria, *etc*. Approximately 2,500 plant species are employed in India alone in the Ayurvedic, Unani, and Siddha systems of traditional medicine, while the pharmaceutical business uses approximately 500 plant species [2]. The growing market for herbal medications in industrialised nations has led to a rise in the use of medicinal plants in recent decades [3]. Medicinal plants are an inexpensive source of raw materials since their components may be chemically modified to boost their potency and function as model ingredients for medication development. The human body is capable of breaking them down, which makes biogenic medication generally more tolerable than synthetic ones. The complex and potent pharmacological activity of crude plant extracts explains their superiority over pure separated products, as shown by the observed synergistic impact of several components.

GOUT: Over the last 50 years, gout has become more common, particularly in developing nations.[4] Gout is a kind of inflammatory arthritis that is brought on by interactions between tissue and monosodium urate (MSU) crystals during purine breakdown by the xanthine oxidase enzyme [5]. Inflammation that is excruciating is caused by the oxidative hydroxylation of hypoxanthine to xanthine by xanthine oxidase. The extremely soluble allantoin that is expelled in the urine is produced by the subsequent catalysis of uric acid by the enzyme uricase **Fig. 1.**

Regrettably, humans are not equipped with the enzyme uricase, which may lead to hyperuricemia. Kidney stones, joint abnormalities, and tophi have also been linked to gout [6]. One of the main etiological factors of gout, hyperuricemia, arises from either an excess of uric acid produced by a metabolic disease or an insufficient elimination of

uric acid in the blood owing to aberrant renal urate transport activity. The balance between urate production and reabsorption controls renal urate excretion, with the kidney serving as the primary regulator of blood uric acid levels. Two urate transporters urate transporter are primarily responsible for mediating renal urate reabsorption. For instance, the most often prescribed xanthine oxidase inhibitor for gout, allopurinol, increases the toxicity of 6-mercaptopurin and induces nephrolithiasis, hypersensitivity response, Stevens-Johnson syndrome, renal toxicity, and allergic reactions [7]. Because they have fewer side effects and are less expensive, medicinal plants are becoming more and more popular as a means of treating illness [8]. As a result, research on medicinal plants has expanded globally.

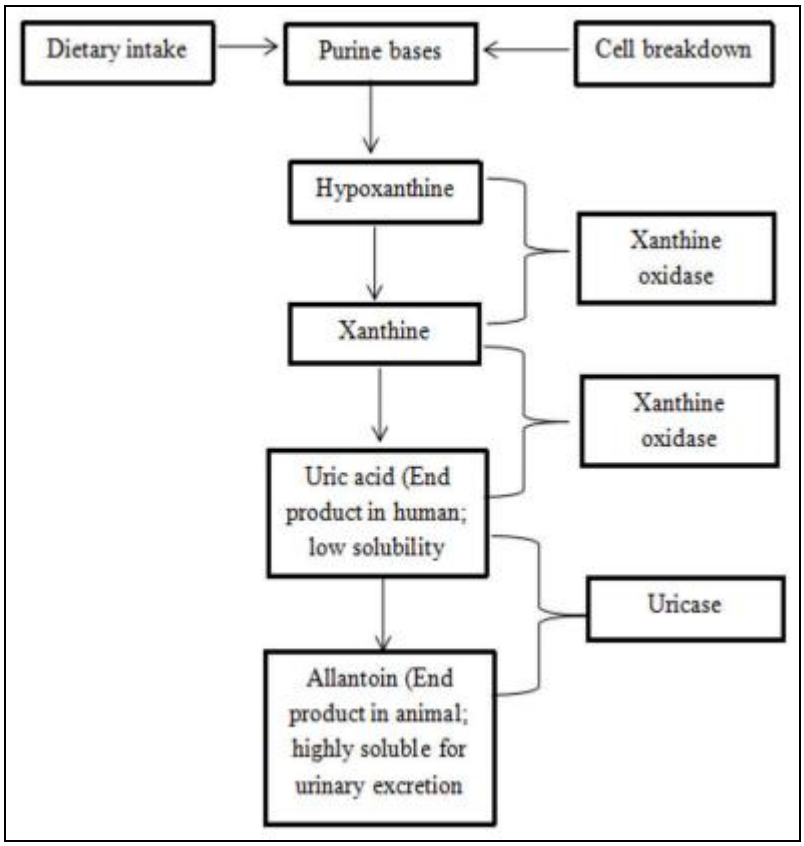

FIG. 1: PURINE CATABOLISM MECHANISM

Rheumatoid Arthritis (RA): Rheumatoid arthritis (RA) is associated with inflammation, the development of pannus, damaged bone and cartilage, and synovial destruction. Diagnostic classifications of RA include seropositive, seronegative, rheumatoid factor, and juvenile rheumatoid arthritis, which are used to determine the appropriate drugs for therapy. Because RA affects the joints, their ability to function correctly is compromised. The autoimmune parameters control how the illness progresses. Utilising radiological analysis as a supplementary method may help differentiate RA from other autoimmune diseases. Joint deterioration is seldom visible in the early stages and develops progressively over time. Taking into mind cytokines such as IL-1, TNF α, and TNF γ causes the inflammatory responses in RA. Intraosteumin-17 (IL-17) induces synovitis, which results in inflammation and alterations to the structural makeup of bones. Rheumatoid arthritis causes bone destruction, which results in oedema and discomfort. Inflammation in several bodily areas is exacerbated by this illness. Generally speaking, RA is a condition where the body's immune system becomes accidentally targeted. This will cause swelling in the region around the hands, elbows, knees, feet, and ankles due to inflammation of the synovium, the tissue that surrounds the joints. The illness is thought to be symmetrical and systemic, meaning that it affects all bodily systems simultaneously, such as the

respiratory or circulatory systems, as well as each joint in turn.

Rheumatoid Arthritis Burden: As an example, rheumatoid arthritis was predicted to rank 40th in the world in 1990 for nonfatal saddle injuries [9]. As seen in **Fig. 2.**

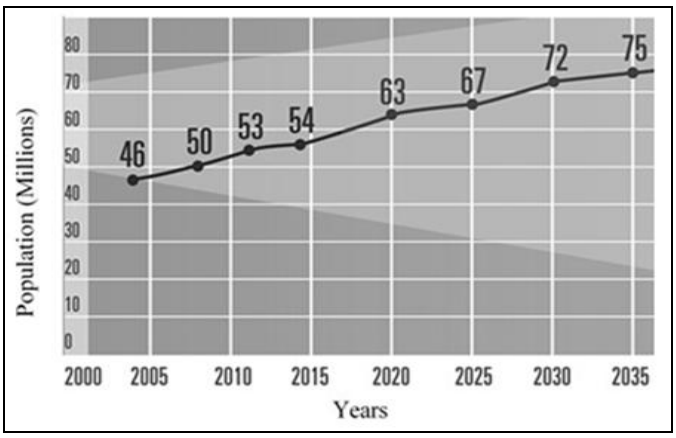

FIG. 2: RHEUMATOID ARTHRITIS EPIDEMOLOGY

India is projected to become the arthritis capital by 2035, with over 75 million people afflicted due to increased obesity and longer lifespans. In developing and industrialized nations, the prevalence of RA is around 0.6% and 0.5-1%, respectively. Globally, the frequency of RA is 0.8%, and in women over the age of 70, it gradually rises to 5%. Women are two to three times more likely than males to have RA. It was anticipated that the frequency in India would be 0.7%. Depending on their wealth distribution, which in turn affects the financial elements of society, both rural and urban regions have greater incidences of arthritis. Many nations acquire statistics on the prevalence of arthritic illnesses because financial data collection information is vital and significant. The burden of RA is increased in developing nations due to the spread of different infectious illnesses among the populace. In India, the majority of those suffering from arthritic illness were not employed. Due to their lack of awareness on the prevalence of illnesses linked to arthritis, many people find it difficult to evaluate their financial burden. The well-being and stability of its members will be crucial to the society's progress. The state of each person's finances will determine the society's financial standing. The burden of rheumatoid arthritis illness varies since every family offers protection and assistance to those who are afflicted with arthritis. People with arthritis behave differently in society, which contributes to the prevalence of RA in that population.

Pathophysiology: Rheumatoid arthritis develops due to both ecological and genetic factors. As seen in **Fig. 3.**

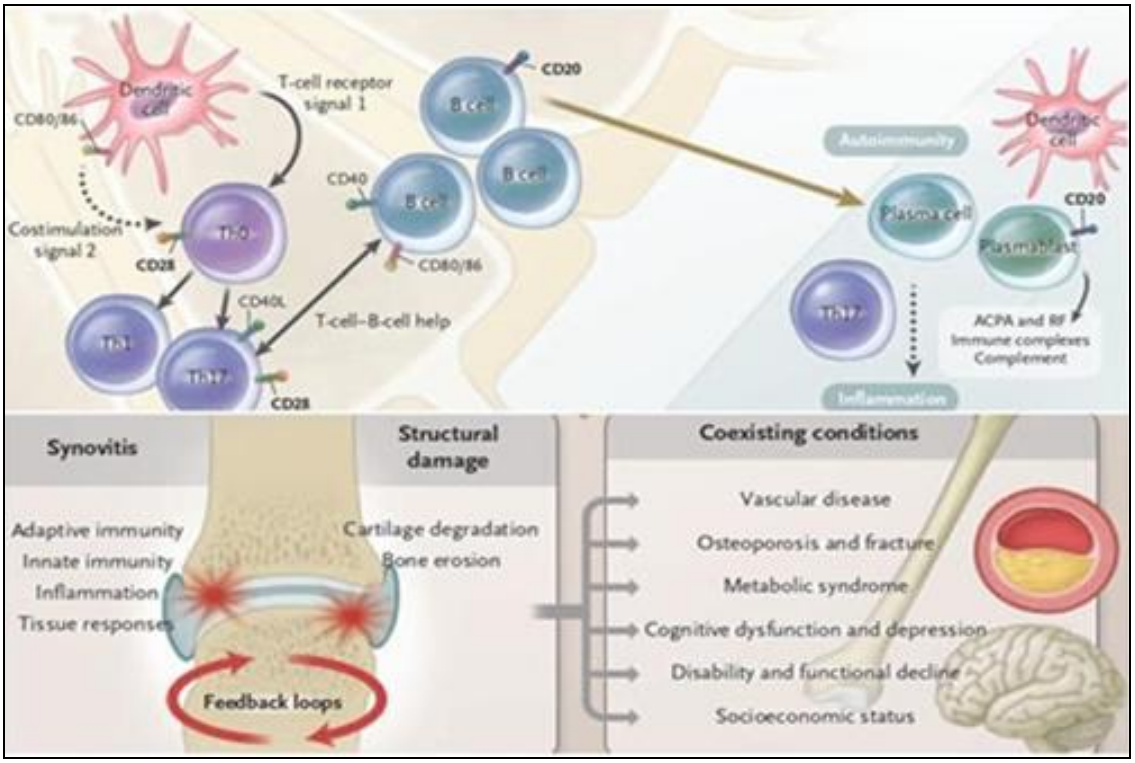

FIG. 3: PATHOLOGICAL CONSIDERATION IN RHEUMATOID ARTHRITIS

The coordinated interaction of immune system cells and cytokines controls the pathogenesis of RA. Th 17 cells are produced by the proliferation of immune cells (T cells), which controls the release of potent cytokines like IL-17. The release of TNF-α and interleukins triggers the infiltration of IL-6 and IL-1, as well as the activation of cells that cause synovitis. The presence of pannus in the synovial membrane causes bone degradation, while the enzymes released by inflammatory synovium cells damage cartilage. To provide some explanation for the disease's start even when genetics isn't enough. The predominant characteristic is hyperplastic synovial inflammation. Dendritic, plasma, and macrophage cells are among the inflammatory and immunological cells that infiltrate RA. Unrelenting conscription, inappropriate preservation, and poor apoptosis may be the cause of the persistently provocative response and joint obliteration regardless of the drugs utilised. Obesity and smoking may function as triggers for RA, increasing the release of growth factors that damage the lining of joints and tendons [10].

Manifestation: Tenderness, redness, swelling, and discomfort are signs of inflammation (synovitis), which is brought on by white blood cells in the synovium. The disease sometimes presents as an inflammatory reaction to cartilage thinning and degradation. Rheumatoid arthritis symptoms are associated with a generalised deficiency in bone function. The extra-articular and non-articular complications of RA affect muscles and organs that are unique to different regions, as shown in **Fig. 4.**

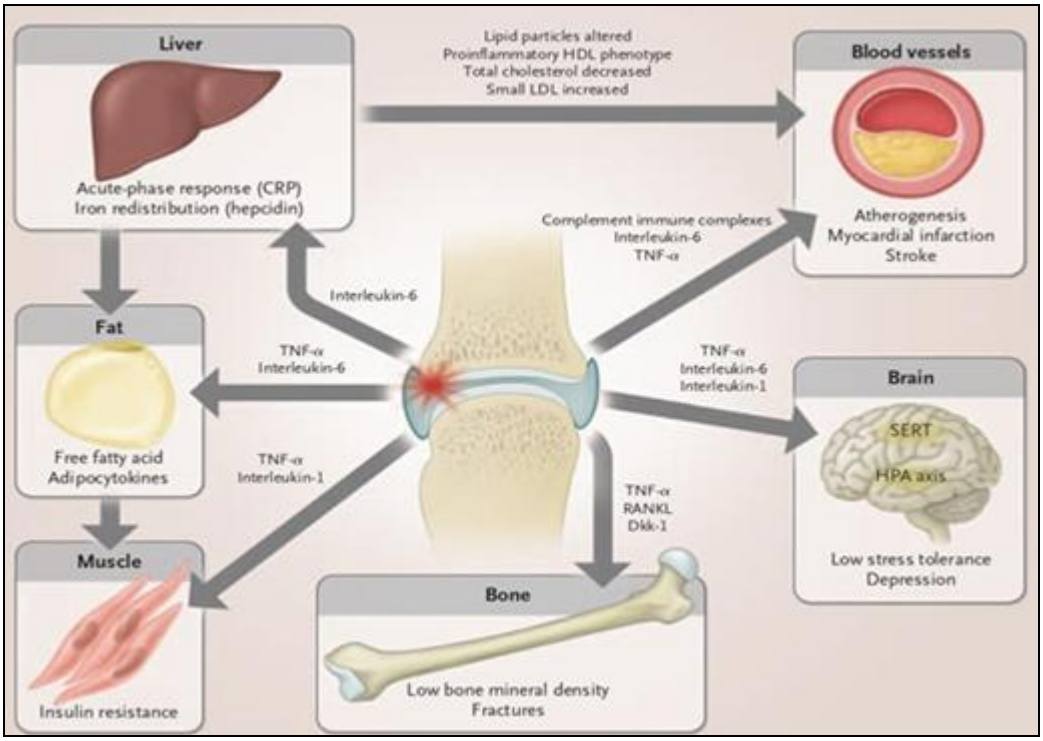

FIG. 4: FACTORS CONTRIBUTE EXTENDED IMPEDIMENT IN RA

Sclera, the salivary gland (Sjogren's disease), the lungs (pulmonary fibrosis), and the heart (pericarditis) are among the many organs that fail. Demyelinisation and pulmonary neuropathy, which affect people with severe rheumatoid arthritis, are additional symptoms. In individuals with arthritis, haematological irregularities were the main cause of concern. Among the cancers identified in arthritic individuals are anaemia and thrombocytopenias.

RA medicine causes gastrointestinal issues. Arthritic symptoms are brought on by a chronic arthritic condition. Compared to males, women are more affected by these symptoms.

Treatment and Management: The issue pertaining to RA may be resolved using nonpharmacologic means of therapy. Among the methods used to treat the RA illness were yoga, consistent exercise, and surgery. Medication such

as biologics and non-biologic disease-modifying anti-rheumatic medicines (DMARDs), methotrexate, and corticosteroids, as previously mentioned, are used in the treatment of RA. Individuals who get early therapy with glucocorticosteroids in addition to DMARDs have a decreased risk of irreversible bone and cartilage impairment. A multidisciplinary approach is used in the care of RA to lessen pain, inflammation, and restore joint function. In practical terms, the goal of intensive treatment is to decrease inflammation. According to a previous scientific study [11], aspirin may inhibit the cyclooxygenase enzyme and limit prostaglandin levels, which would reduce arthritis-related pain and inflammation. Several of the systems listed above may be targeted by non-herbal conventional disease-modifying antirheumatic medications like methotrexate to lessen inflammation.

Similar to this, a number of herbal medicinal compounds may function at the molecular level as multicomponent medications that operate on many therapeutic targets at once. For instance, "leigongteng" has been used for centuries in Chinese medicine to treat inflammatory tissue swelling. In Europe, herbal remedies such as *Harpagophytum procumbens* and *Urtica dioica* were well-liked for treating rheumatism, and *Zingiber officinalis, Capsicum frutescens, Mentha piperita*, and *Curcuma longa* have been documented as effective treatments for a variety of joint pains.

These plants' active ingredient either increases or inhibits the release of cytokines, which inactivate enzymes like metalloproteinase. The mechanism of action of topical capsaicin differs in that it stimulates vanilloid receptors, which disrupt the production, storage, transport, and release of *P. neuropeptide* substance. It also inhibits lipoxygenase and causes the irreversible destruction of fine nerve endings. Similar to how *Uncaria tomentosa* acts on 5-HT2 receptors to demonstrate anti-inflammatory activity, it seems that herbal medicine has a mode of action related to the rheumatoid arthritis aetiology. According to this theory, varieties of herbs used in traditional medicine have been shown to have anti-arthritic properties and are even sold as anti-arthritic medications.

Herbal Therapy for the Treatment of Arthritis: The use of herbal remedies for medical conditions dates back to ancient times; in fact, it would not be an exaggeration to claim that this practice predates human history. Traditional herbal remedies have their origins in the healing practices of ancestors who practiced this ancient medical method for hundreds of years. Researchers are increasingly interested in plant-based therapeutic compounds due to the fact that existing pharmaceuticals are either prohibitively costly or come with unwanted side effects. A vast variety of medicinal herbs have been bestowed to humanity by Mother Nature, and these plants are dispersed over the globe, serving as a source of natural remedies for a broad range of illnesses. The World Health Organisation reports that herbal medicines are used by 80% of the world's population as their main source of healthcare. Part of human society's arsenal against illness from the beginning of civilization has been herbal remedies.[12] Chemical components of these herbal plants are what give them their therapeutic value by eliciting a certain physiological effect in the body.

Ayurveda, Unani, Sidha, Homoeopathy, and Naturopathy are some of India's legally recognised alternative medical systems that have relied on herbal remedies for centuries. The Indian subcontinent is home to about 2500 kinds of plants that have traditional medicinal uses. Both as an independent kind of folk medicine and an ingredient in more modern medications, herbal remedies have a history stretching back more than three thousand years. As a result, it is possible to learn about traditional herbs and their uses in order to find new, less expensive medications. We have done our best in this review article to discuss all of the ayurvedic approaches to RA therapy that aim to eliminate adverse effects. Researchers hope that RA treatments in the future will be more successful [13].

Medicinal Plants with Anti-Gout Activity:

Boswellia Serrate: Known for its anti-inflammatory properties, *Boswellia serrata*, or Indian frankincense, contains boswellic acids that inhibit pro-inflammatory enzymes such as 5-lipoxygenase. Clinical studies have shown that Boswellia extracts can reduce joint pain and improve mobility in gout patients.

***Curcuma longa*:** Commonly known as turmeric, *Curcuma longa* contains curcumin, a compound with potent anti-inflammatory and antioxidant properties. Curcumin has been shown to lower uric acid levels and reduce inflammation, making it beneficial for gout management.

***Zingiber officinale*:** Ginger, or *Zingiber officinale*, is widely recognized for its anti-inflammatory effects. Gingerols and shogaols, the active components in ginger, have demonstrated the ability to reduce pain and inflammation in gout by inhibiting the production of inflammatory cytokines.

Medicinal Plants with Anti-Arthritic Activity:

***Withania somnifera*:** Also known as ashwagandha, *Withania somnifera* has been used in Ayurvedic medicine for its anti-inflammatory and immunomodulatory effects.

Studies have indicated that ashwagandha can reduce the severity of rheumatoid arthritis symptoms by modulating immune responses.

***Camellia sinensis*:** The leaves of *Camellia sinensis*, or green tea, are rich in polyphenols, particularly epigallocatechin gallate (EGCG), which has strong anti-inflammatory and antioxidant properties. EGCG has been shown to inhibit inflammatory pathways and reduce cartilage degradation in arthritis.

***Harpagophytum procumbens*:** Known as devil's claw, *Harpagophytum procumbens* contains harpagoside, which exhibits significant anti-inflammatory and analgesic effects. Clinical trials have reported reductions in pain and improvement in physical function in patients with osteoarthritis.

Mechanisms of Action: The therapeutic effects of these medicinal plants can be attributed to various bioactive compounds that target key pathways involved in gout and arthritis:

Anti-inflammatory Action: Many of these plants inhibit pro-inflammatory enzymes (e.g., COX-2, 5-LOX) and reduce the production of inflammatory cytokines (e.g., TNF-α, IL-1β).

Antioxidant Effects: Compounds such as curcumin and EGCG neutralize free radicals, reducing oxidative stress and subsequent inflammation in joint tissues.

Uric Acid Lowering: Certain plants, like *Curcuma longa*, help in reducing uric acid levels, preventing crystal deposition in joints.

Clinical Evidence and Safety: Numerous clinical trials have demonstrated the efficacy of these medicinal plants in managing symptoms of gout and arthritis. For instance, *Boswellia serrata* has shown improvements in pain and joint function in osteoarthritis patients, while curcumin has been effective in reducing inflammation and pain in rheumatoid arthritis. However, the quality of evidence varies, and more rigorous, large-scale trials are needed to establish definitive efficacy and safety profiles [14].

Challenges and Future Directions: Despite the promising potential of medicinal plants, several challenges need to be addressed to fully integrate them into clinical practice:

Standardization: Ensuring consistent quality and concentration of active compounds in herbal preparations is crucial.

Regulatory Oversight: Establishing regulatory frameworks to oversee the safety and efficacy of herbal medicines.

Research and Development: Conducting more extensive clinical trials to confirm therapeutic benefits and optimal dosing regimens.

CONCLUSION: Medicinal plants offer a promising complementary approach to the management of gout and arthritis, providing anti-inflammatory, antioxidant, and uric acid-lowering effects. While plants such as *Boswellia serrata*, *Curcuma longa*, and *Zingiber officinale* have shown significant potential, further research and standardization are essential to fully harness their therapeutic benefits. With continued exploration and rigorous clinical validation, these natural remedies could be integrated into evidence-based medical practice, offering safer and effective alternatives to conventional treatments for gout and arthritis.

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