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Review article

Novel Herbal formulations and their application in Arthritis

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ABSTRACT

Interest in herbal remedies for arthritis is developing, necessitating a scientific evaluate of their safety and effectiveness primarily based on randomized clinical trials (RCTs). Many natural treatments are claimed to benefit arthritis; however, studies are vital to assess their effectiveness, safety, and capability drug interactions. Traditional arthritis remedies often contain medicines with frequent dosing and adverse outcomes, prompting sufferers to are looking for herbal alternatives. This work highlights, a well-known plant sources used in arthritis remedy lacking powerful formulations, highlighting the want for numerous dosage paperwork past oils. Innovative strategies like liposome technology and transdermal drug delivery structures may want to enhance herbal compound transport.

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1. Introduction

Arthritis, together with osteoarthritis (OA) and rheumatoid arthritis (RA), offers significant problems, causing severe joint pain and affecting a universal pleasant lifestyle. While nonpharmacologic agents are often the first line of defense, pharmacologic treatments, while vital, can be expensive and have serious side effects. As a result, there is a growing interest in alternative treatments, especially natural medicine, for its ability to accurately and effectively manage arthritis [1]. The aim of this review is to summarize the mechanisms, safety profiles and efficacy of herbal treatments for OA and RA and highlight their positive outcomes on symptoms, pain and inflammation. These natural preparations exhibit effective anti-inflammatory and antioxidant properties that contribute to the reduction of inflammation and tissue damage. Some herbs even introduce new mechanisms for treating OA and RA. Despite the encouraging effects, further research and scientific trials are needed to confirm their protection, efficacy, biological activity and maximum bioavailability [1].

There are over 100 known types of arthritis, with OA and RA being among the most prevalent [1-3]. Both conditions result in structural and functional joint impairment, although they differ in symptoms, underlying causes, and treatment strategies [1]. OA, the most common form, is characterized by biomechanical and inflammatory processes influenced by factors such as mechanical stress, oxidative stress, injury, age, obesity, and metabolic disorders [4, 5]. Osteoarthritis (OA) includes the degeneration of joint cartilage, changes in the underlying bone, and synovitis, with irritation brought on by way of seasoned-inflammatory mediators and hydrolytic enzymes. OA normally develops slowly, frequently taking place later in existence and leading to incapacity. Its symptoms consist of localized joint ache, tenderness, and morning stiffness. As a commonplace musculoskeletal degenerative ailment, osteoarthritis imposes a large socioeconomic burden. Current treatment options intention to relieve symptoms rather than regulate the disorder, with surgical intervention in superior stages. The complex mechanisms of osteoarthritis onset and progression have led to the exploration of novel therapeutics, consisting of small molecules of herbal foundation. These molecules show promise for osteoarthritis treatment because of their anti-inflammatory, anti-catabolic, and anabolic outcomes [1, 6].

Rheumatoid arthritis (RA) is a systemic disorder characterised with the aid of immune disorder and inflammation, typically affecting multiple joints. Risk factors for this condition encompass woman gender, genetic predisposition, and smoking [8]. The type of rheumatoid arthritis into seropositive or seronegative kinds, primarily based on the presence of antibodies, is important for assessing the severity and development of the sickness. Patients with seropositive RA commonly enjoy more intense irritation and joint harm, that may result in irreversible deformities and disabilities. It is expected that around 60% of individuals with rheumatoid arthritis end up not being able to paint within a decade of analysis. Common signs and symptoms of RA consist of smooth, warm, and swollen joints, as well as stiffness in the morning and after intervals of inaction [9-11].

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Table 1. Current treatment of arthritis [1].

Disease	Major Risk Factors	Pathology	Clinical Manifestations	Available Therapies
Osteoarthritis	Age, Gender, Obesity, Joint trauma, Genetics, Metabolic disease	Joint cartilage degeneration, synovitis, increased oxidative stress, diminished chondrocyte proliferation, MMPs-induced cartilage degradation	Pain, Joint stiffness, Loss of flexibility	NSAIDs, Tramadol, Duloxetine, Corticosteroids, Hyaluronic acid
Rheumatoid arthritis	Genetics, Smoking, Gender, Microbiome	Synovial inflammation, autoantibody production, cartilage and bone destruction, chronic inflammation leading to bone erosion	Pain, stiffness, swelling, fatigue, weight loss	NSAIDs, Methotrexate, Leflunomide, Hydroxychloroquine, TNF biologics, JAK inhibitors

Current pharmacological remedies provide symptom alleviation from arthritis however are associated with giant facet outcomes that may limit their long-time period use. The Rheumatology/Arthritis Foundation provides steering on contemporary remedy alternatives for arthritis [12,13]. For Osteoarthritis, recommended treatments include oral and topical nonsteroidal anti-inflammatory tablets (NSAIDs), oral pain relievers, serotonin and norepinephrine reuptake inhibitors, and intra-articular corticosteroids [12]. In the case of Rheumatoid arthritis, the remedy targets are aimed toward reducing ache and irritation, with unique pointers depending at the degree and hobby degree of the disease. Treatment for early and mounted Rheumatoid arthritis may additionally contain ailment-editing antirheumatic pills (DMARDs) monotherapy, such as methotrexate for cases of low disease pastime, at the same time as more severe disorder interest may also necessitate an aggregate of DMARDs, biologic dealers, or tofacitinib [13]. The motion mechanisms of modern capsules utilized in treating Osteoarthritis and Rheumatoid arthritis were considerably mentioned in preceding opinions [14].

NSAIDs are connected to dangers of gastrointestinal issues, cardiovascular problems, and kidney harm, proscribing their suitability for ongoing control of arthritis [15,16]. Acetaminophen may purpose liver harm, tramadol can have an effect on the gastrointestinal gadget and principal frightened machine, and the efficacy of intra-articular corticosteroids in treating osteoarthritis remains questionable [17-19]. Non-biologic DMARDs, although powerful, bring capability facet outcomes which includes gastrointestinal disillusioned, liver toxicity, kidney harm, and blood issues [20]. Biologics, used for treating slight to extreme rheumatoid arthritis, pose dangers together with increased susceptibility to infections, cancer, and coronary heart failure [21]. Janus kinase inhibitors, every other remedy for rheumatoid arthritis, additionally present risks related to infections and blood disorders [22]. Thus, it is vital for healthcare companies and sufferers to cautiously remember the advantages and dangers of pharmacological treatments for both osteoarthritis and rheumatoid arthritis.

Amid growing concerns about the safety and cost of conventional arthritis treatments, there is increasing interest in exploring natural remedies, especially herbal therapies, as complementary or alternative treatment options. This review aims to detail the current pharmacological approaches for managing osteoarthritis and rheumatoid arthritis and to provide updated insights into the effectiveness of herbal remedies. It focuses on the mechanisms, safety profiles, and effectiveness of these herbal treatments, particularly their influence on reducing pain and inflammation in both types of arthritis [23].

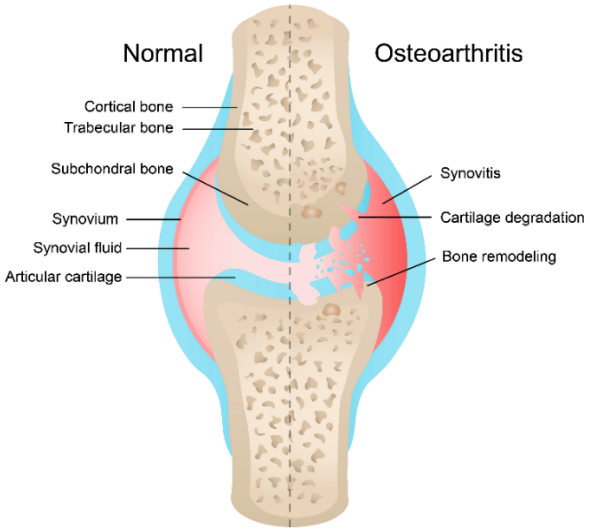

Figure 1: *Healthy vs Osteoarthritis joints. Osteoarthritis is characterized by a loss of cartilage, subchondral bone and inflammation of the synovium [24].*

2. Herbal Drug in the Treatment of Arthritis

The traditional method of managing arthritis has predominantly depended on pharmaceutical drugs, which are often seen as the conventional choice. Yet, due to variations in how individuals respond to these drugs and the possibility of side effects and adverse reactions, finding the most effective drug combination for arthritis treatment can be complex. Arthritis medications fall into two primary categories:

1) Those that relieve pain, inflammation, and muscle stiffness,
2) Those that alter the disease's progression or induce remission.

Herbal medicine offers an alternative approach, with a longstanding history in treating various ailments that dates back to ancient times [25, 26]. Herbal drugs benefit from centuries of therapeutic knowledge accumulated by generations of physicians across various ancient medical systems [27]. With the significant side effects linked to conventional allopathic medications, modern researchers are increasingly focusing on plant-based medicinal agents [28-30]. Herbal plants, widely distributed globally, provide a rich source of therapeutic agents and are used by approximately 80% of the world population for primary health care, according to the World Health Organization (WHO). Herbal treatments have been pivotal in disease management since the beginning of civilization. In India, traditional health systems such as Ayurveda, Unani, Sidha,

Homeopathy, and Naturopathy utilize over 2500 plant species as herbal medicines [31-32]. These plants have been employed both as traditional folk remedies and in modern pharmaceutical formulations for over 3000 years. This rich heritage offers potential for discovering new, effective, and cost-efficient drugs. This review gathers information on potent Ayurvedic plants proven effective in managing Rheumatoid Arthritis (RA) without notable side effects [33].

Looking ahead, the treatment of Rheumatoid arthritis aims to enhance effectiveness, with medicinal herbs standing out as a historical resource for managing various ailments, particularly inflammatory conditions like rheumatoid arthritis. Many nations utilize traditional medicine practices to treat inflammatory diseases. Several factors contribute to the risk of developing Rheumatoid arthritis, including genetics, hormones, environment, nutrition, socio-economic conditions, age, sex, ethnicity, smoking, and infections, with a strong association with pain [34]. This document emphasizes herbal formulations currently available in the Indian market, showcasing their potential in treating Rheumatoid Arthritis through the use of individual herbs, herbal drug combinations, or polyherbal formulations.

Table 2. Summary of herbal medications for osteoarthritis and rheumatoid arthritis treatment [1].

Disease	Herbal Drug	Dose/day	Treatment duration in Days	Mechanism of Action	Clinical Implication
Osteoarthritis	Boswellia spp.	100 or 349.3 mg or 10 drops (oil)	42–120	Inhibits inflammatory mediators, reduces apoptosis, slows cartilage degradation, promotes collagen synthesis	Strong anti-inflammatory and antioxidative activities, mimics anti-arthritis activities with fewer adverse effects
	Curcuma spp.	180 or 500 mg	28–56		
	Withania somnifera	125 or 250 mg	8 or 28		
Rheumatoid Arthritis	Eremostachys laciniata	0.5% topical ointment	14	Inhibits PGE2, leukotriene B4, NO, ROS, induces apoptosis in lymphocytes and synovial fibroblasts, inhibits histamine and bradykinin production	
	Matricaria chamomilla L.	6 g tea	42		
	Tripterygium wilfordii Hook F	30–570 mg	112–16 8		

3. Herbal formulation for the treatment of Arthritis

The standard method for treating arthritis typically involves pharmaceutical drugs, which are commonly accepted as the conventional mode of treatment. However, due to individual variations in drug response and the likelihood of side effects and adverse reactions, finding the most effective arthritis drug combination can be challenging. Arthritis drug therapy is generally divided into two types:

1) those that relieve pain, inflammation, and muscle stiffness, and
2) those that are intended to alter the disease's progression or induce remission.

3.1 *Herbal Gel Formulation for the Treatment of Arthritis*

A new herbal gel components designed for arthritis remedy become created using the mature fresh leaves of Vitex negundo and Cardiospermum halicacabum, which were accrued from Palakkad, Kerala, and authenticated by way of GVS Murthy, Director of the Botanical Survey of India. The ingredients for the formulation, such as Freund's complete adjuvant, diclofenac sodium, triethanolamine, propylene glycol, and disodium edetate, have been sourced. The coaching technique concerned cleansing the leaves to dispose of any dirt and residue, observed via color drying and methanol extraction. The extracts had been then concentrated and preserved for subsequent use. To put together the gel base, Carbopol 934 became dissolved in demineralized water, and disodium edetate, triethanolamine, and propylene glycol have been delivered to form a clear gel base with a neutral pH ~7.5.

Twelve distinct topical gel formulations (F1 to F12) were produced the usage of the methanol extracts of Cardiospermum halicacabum (CHME) and Vitex negundo (VNME). The first six formulations (F1 to F6) used carbopol 934 as the gel base, while the subsequent six (F7 to F12) used carbopol 940. Among these, the F4 formulation, which used Carbopol 934, demonstrated superior satisfactory characteristics and become selected for in addition assessment of its anti-arthritic effectiveness. This study introduces a progressive natural gel system that holds promise for future therapeutic applications within the remedy of arthritis [47].

3.2 *Herbal Cream for the Treatment of Arthritis:*

The development of an herbal cream for arthritis treatment is grounded in the widespread cultural acceptance and compatibility with the human body, with herbal medicines being a cornerstone for 75-80% of the global population, particularly in underdeveloped regions. Herbal medicines, derived from plants, have a rich history as the world's oldest method of health treatment, offering remedies for injuries, diseases, and overall health promotion. The herbal cream formulation, incorporating various oils such as Coconut oil, Lemongrass oil, Wintergreen oil, Peppermint, Garlic Oil, and camphor, exhibits high homogeneity, stability, and anti-rheumatic arthritis action. The BHA and Chlorocresol recipe emerges as the optimal choice, showcasing superior extrudability, spreadability, and rheological qualities. Notably, formulations F5, F6, and F7 demonstrate the highest efficacy in anti-rheumatic arthritis activity, highlighting the potential of polyherbal preparations for achieving this effect.

In conclusion, the herbal cream developed presents a promising avenue for arthritis treatment, leveraging the benefits of herbal medicines with the synergistic effects of multiple oils. The preference for polyherbal formulations, specifically formulations F5, F6, and F7, indicates a potential breakthrough in anti-rheumatic arthritis therapies, offering a holistic approach to health care. The use of quality ingredients, including coconut oil, lemongrass oil, and other essential components, reinforces the formulation's potential success in providing effective and culturally accepted arthritis relief in the future [48].

3.3 *Herbo-synthetic Approach for arthritis:*

The herbo-synthetic approach addresses the considerable economic, social, and health impacts of arthritis, with 10% to 15% of people over 60 experiencing varying degrees of the condition. Women are particularly prone to arthritis, and its incidence differs across EU countries. This condition, characterized as a slowly progressing, non-inflammatory disorder, leads to the degradation of articular cartilage, manifesting symptoms such as stiffness, pain, reduced flexibility, swelling, and bone spurs. Contributing factors include obesity, sedentary lifestyle, genetic predisposition, bone density issues, occupational hazards, and physical trauma.

Emerging techniques like hydrogels, micro/nano-sized particles, and topical gels provide benefits such as extended release and controlled degradation, enhancing drug efficacy in the joints. A study using celecoxib-loaded PEA microspheres in male Lewis rats has shown that these microspheres are biocompatible and degrade appropriately, indicating that such systems could offer a self-regulating, safe method for managing knee osteoarthritis pain [49].

These advanced drug delivery systems represent a promising direction for accurate and safe medication administration in arthritis therapy. Herbal medications, known for their efficacy and lower side effect profile, are increasingly being integrated into treatment regimes. The herbo-synthetic strategy, which blends herbal and synthetic medications, presents a novel method to capitalize on the strengths of each while reducing unwanted side effects, thus paving the way for effective and well-tolerated arthritis treatments in the future [50].

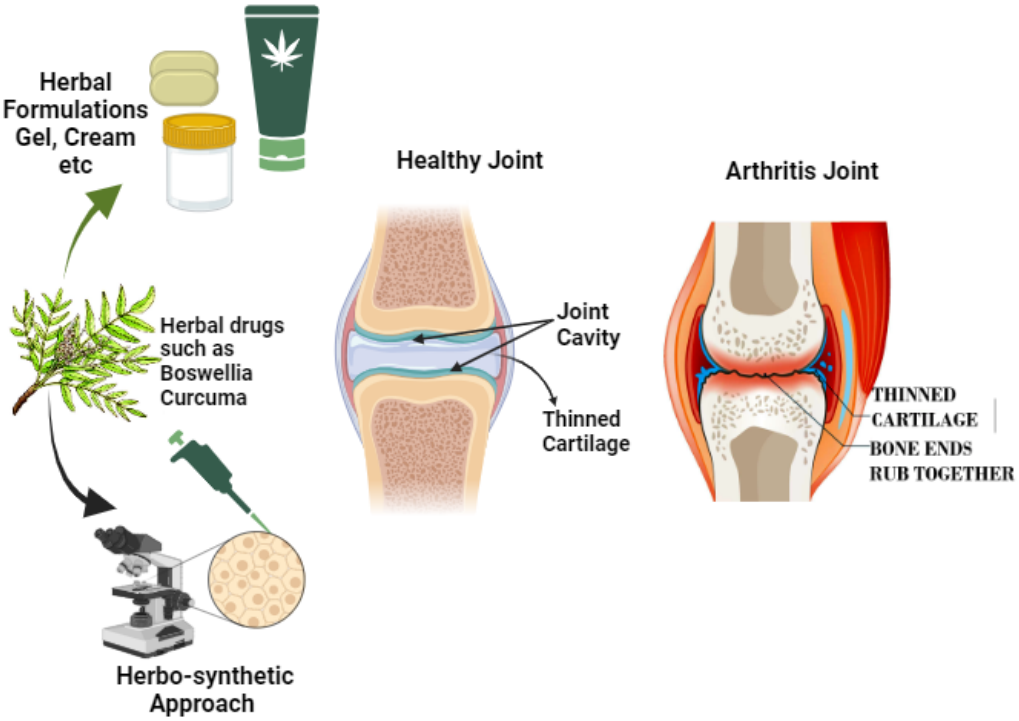

Figure 2: A Hypothesis for the treatment of Arthritis through Herbal constituents

4. Conclusion and Future Prospect

Arthritis, marked by using chronic joint inflammation main to swelling and deformity, stays a chief health project. While traditional drug remedies offer diverse treatments, natural remedy is more and more preferred for its effectiveness and decreased facet consequences. Extensive worldwide studies into indigenous flowers helps their use in treating rheumatic and anti-inflammatory conditions, mainly in polyherbal combos. Emerging revolutionary drug delivery systems promise particular and secure medicinal drug delivery, while the herbo-artificial method pursuits to mix the blessings of herbal and artificial drugs with minimal side results. Clinical trials validate the efficacy of 9 key herbs that substantially alleviate arthritis signs and symptoms via offering pain alleviation and decreasing irritation and oxidative stress thru numerous mechanisms, inclusive of modulation of inflammatory signaling pathways and immune mobile capabilities. Current remedies for osteoarthritis and rheumatoid arthritis vary in long-time period effectiveness and safety, but herbal medicines provide safer, similar, or advanced options. Further studies ought to focus on additional medical trials to confirm the safety and efficacy of herbal drug treatments, look into specific herbal compounds for focused therapy, and expand formulations with most excellent bioavailability and pharmacokinetics.

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