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Herbal Approaches to Arthritis: A Detailed Review on the Medicinal Potential of *Dichanthium annulatum, Pithecellobium dulce Bergenia ciliata, and Ludwigia adscendens*

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Abstract

Rheumatoid arthritis (RA) is a chronic systemic autoimmune disease characterized by persistent synovial inflammation, progressive joint destruction, and significant disability. Although substantial advances have been achieved with conventional disease-modifying antirheumatic drugs, biologics, and targeted synthetic therapies, their long-term use is often limited by adverse effects, high costs, and variable patient responses. Medicinal plants constitute a rich source of bioactive compounds, including flavonoids, alkaloids, terpenoids, and polyphenols, which exhibit potent anti-inflammatory, antioxidant, and immunomodulatory activities. Emerging evidence suggests that plant-derived compounds can modulate key molecular pathways involved in RA pathogenesis, such as cytokine signaling, oxidative stress, and immune cell activation.

This review summarizes the current understanding of RA pathophysiology, highlights emerging therapeutic targets, and critically examines the role of plant-based interventions in RA management, with particular emphasis on selected medicinal plants including *Dichanthium annulatum*, *Pithecellobium dulce* and *Bergenia ciliata*. The integration of traditional medicinal knowledge with modern pharmacological research may support the development of safer, multi-targeted, and cost-effective therapeutic approaches for rheumatoid arthritis.

Keywords: Rheumatoid arthritis, Medicinal plants, *Dichanthium annulatum*, *Bergenia ciliata*, *Pithecellobium dulce*

Introduction

Over the years, global population growth, aging, and an accelerated rate of epidemiologic transition have resulted in lower communicable disease mortality and an increased burden of non-communicable diseases (Piret & Boivin 2021). Emerging infectious diseases (EIDs) pose a significant economic and public health burden (Sohail et al. 2021). Their emergence is thought to have been primarily influenced by socioeconomic, environmental, and ecological factors. Developing, non-developed, and vulnerable countries are experiencing severe humanitarian disasters, and the declining economies of some developed countries have resulted in collapsed healthcare facilities. As a result, an increasing number of people are opting for a more traditional approach to meet some of their primary healthcare needs (Xego et al., 2021).

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In recent years, the traditional knowledge associated with medicinal plants is gaining importance worldwide. This can be attributed to the emergence of new infectious diseases (Mothibe & Sibanda 2019). Recently coronavirus disease manifested itself in Wuhan, China, as unexplained pneumonia. The disease quickly became a pandemic and was called coronavirus disease 2019 (COVID-19) (Lim, Teh & Tan 2021). The International Committee on Virus Taxonomy has named the causative virus SARS-CoV-2. Pharmaceutical companies and researchers have been competing to develop a cure. Phytotherapy and phytomedicines have been recognised as effective immunity boosters with the potential to eliminate viral infection (Lim et al. 2021).

Phytomedicine, also known as alternative medicine, comprises plant metabolites with therapeutic properties. Various plant parts, including roots, stems, leaves, and flowers, are used in these mixtures. The past decade has seen a significant rise in the interest and utilization of medicinal plants, highlighting their positive health effects due to bioactive compounds specific to certain species. Despite advancements in pharmacology, plant-based therapies remain widely used, especially in developing countries, where the World Health Organization indicates that 80% of the population relies on traditional, plant-based medicines for primary healthcare.

1.1. Rheumatoid Arthritis: Introduction

Rheumatoid arthritis (RA) is a systemic autoimmune disease characterized by inflammatory arthritis and extra-articular involvement. It is a chronic inflammatory disorder caused in many cases by the interaction between genes and environmental factors, including tobacco that primarily involves synovial joints (Klareskog et al., 2020). It typically starts in small peripheral joints, is usually symmetric, and progresses to involve proximal joints if left untreated (Aletaha & Smolen et al., 2018: Bullock et al., 2019). Joint inflammation over time leads to the destruction of the joint with loss of cartilage and bone erosions. RA with symptom duration of fewer than six months is defined as early RA, and when the symptoms have been present for more than six months, it is defined as established RA. RA, if untreated, is a progressive disease with morbidity and increased mortality (Pincus et al., 1999).

Rheumatoid arthritis (RA) is an idiopathic disease characterized by inflammation in synovial tissues of joints, cartilage, and bones (Sparks et al., 2016). RA is thought to be driven by genetic and epigenetic factors, but environmental factors such as cigarette smoke and dust exposure also play crucial roles (Scherer et al., 2020: Alam et al., 2017). Uncontrolled RA can lead to joint degradation, severe disability, reduced quality of life, comorbidities, and premature death, posing a significant societal burden (Alam et al., 2017: Cross et al., 2014). Approximately 70% of RA patients in India suffer from anxiety and depression (Almutairi et al., 2021). A cross-sectional, hospital-based study conducted in a tertiary care private multi-specialty hospital in Tamil Nadu revealed that the average annual medical expenditure for treating RA was 44,700 rupees ($543), with a median of 39,210 rupees ($476) (Bagepally et al., 2023). The global prevalence of RA varies, with an estimated 0.5 to 1% of adults affected (Almutairi et al., 2021). The prevalence is generally higher in industrialized countries, possibly due to environmental risk factors, genetic predispositions, and underreporting in other regions (Finckh et al., 2022). Recent reviews indicate that the prevalence of RA in India ranges from 0.28 to 0.7%, based on only four studies (Handa et al., 2016). There is a lack of nationwide epidemiological research on RA in India.

The Global Burden of Disease (GBD) database, established by the Global Burden of Disease Study, is a comprehensive repository maintained by the Institute for Health Metrics and Evaluation (IHME). It systematically quantifies and assesses the impact of major diseases, injuries, and health risk factors globally, regionally, and nationally (Murray et al., 2024). This study leverages GBD 2021 data to analyze the incidence and prevalence of RA in India and estimates the disease burden and trends across different age groups, providing a basis for developing effective RA prevention and control strategies.

Epidemiology

Worldwide, prevalence of RA is relatively stable, ranging from 0.5 to 1.0%; however, it is more prevalent among certain communities, such as indigenous North American tribes such as Indian Pimas (5.3%) and Indian Chippewas (6.8%) (Almutairi et al., 2021). As per the findings of the Global Burden of Disease research, there are approximately 18.5 million RA cases worldwide, and it is estimated that new cases detected per year will increase by 40% from 1.07 million in 2019 to around 1.5 million by 2040 (Shi et al., 2023). The prevalence of RA in India as reported by various studies ranged from 0.28 to 0.7%. (Handa et al., 2016).

Pathophysiology of Arthritis

Although the pathophysiological mechanisms for RA are not fully elucidated, several hypotheses have been postulated. It has been reported that immunological processes can occur many years before symptoms of joint inflammation are noticed, the so-called pre-RA phase (Firestein & McInnes et al., 2017). The interactions between epigenetic modifications on the genomic structure and environmental factors can lead to modified self-antigens as in the case of immunoglobulin G (IgG), type 2 collagen and vimentin. These proteins with arginine residues can be converted to citrulline by peptidyl arginine deiminases in a post-translational modification called citrullination (Curran et al., 2020: Scherer et al., 2020). Moreover, joint disorders like synovial hyperplasia or synovial infections can trigger cytokine release that may cause joint inflammation and also modified self-antigens (Damerau & Gaber et al., 2020). Due to the susceptibility genes HLA-DR1 and HLA-DR4, the immune system is no longer able to recognize citrullinated proteins (vimentin, type II collagen, histones, fibrin, fibronectin, Epstein-Barr nuclear antigen 1, α-enolase) as self-structures (Van & Holoshitz et al., 2017). Antigens are taken up by antigen-presenting cells (APC), which are dendritic cells that are activated to initiate an immune response. The whole complex migrates to the lymph node, where the activation of CD4 helper T cells takes place. Furthermore, the germinal center of the lymph node contains B cells that get activated by reciprocal and sequential signals with T cells, an immunological process called costimulation.

An example of costimulation is the interaction between CD28 and CD80/86 (Frauwirth & Thompson et al., 2002: Isaacs et al., 2008). At this level, B cells undergo somatic hypermutation or class-switch recombination and start to proliferate and differentiate intro plasma cells that produce autoantibodies depending on the receptors of the precursor cells (Stavnezer et al., 2008). Autoantibodies are proteins produced by an immune system that no longer discriminates self from non-self-structures, so self-tissues and organs are accidentally targeted. RF and ACPA are the most studied autoantibodies involved in RA. RF is an IgM antibody with a testing specificity of 85% in RA patients, which targets the Fc portion of IgG, also called the constant region (Ingegnoli et al., 2013). It also forms an immune complex with IgG and complement protein, a complex able to migrate in the synovial fluid. However, ACPA is more specific for RA and targets citrullinated proteins and after their binding interactions, immune complexes are formed with an accumulation in the synovial fluid (Yu et al., 2019).

Bioactive compounds in plants

Bioactive compounds in plants form the cornerstone of their therapeutic potential, offering a vast and diverse array of chemical constituents that contribute to their medicinal properties. These compounds are synthesized by plants as secondary metabolites, playing crucial roles in defense mechanisms, environmental adaptation, and interactions with other organisms. The pharmacologically active components found in various plant species have been the subject of intense scientific investigation, leading to a deeper understanding of their potential applications in medicine. One prominent group of bioactive compounds is alkaloids, nitrogen-containing organic compounds with pronounced physiological effects. Examples include morphine from the opium poppy (*Papaver somniferum*), quinine from the cinchona tree (*Cinchona officinalis*), and caffeine from coffee beans (Coffea spp.). Alkaloids often exhibit analgesic, anti-inflammatory, or psychoactive properties, making them valuable in pharmaceutical development. Flavonoids, another significant

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class of bioactive compounds, are widely distributed in fruits, vegetables, and medicinal herbs (Gaur et al., 2007). These polyphenolic compounds contribute to the vibrant colors of many plants and demonstrate antioxidant, anti-inflammatory, and antiviral activities. Quercetin in onions, epigallocatechin gallate (EGCG) in green tea, and resveratrol ingrapes are well-known flavonoids with health-promoting properties. Terpenoids, characterized by their diverse structures derived from isoprene units, represent a vast and varied group of bioactive compounds. Essential oils, found in plants such as lavender, mint, and eucalyptus, are composed of terpenoids and possess antimicrobial and anti-inflammatory properties. Taxol, derived from the Pacific yew tree (Taxus brevifolia), is a terpenoid with potent anticancer effects. Polyphenols, encompassing flavonoids and other compounds, are abundant in fruits, vegetables, tea, and red wine (Lang et al., 2001). These bioactive compounds contribute to the health benefits associated with a diet rich in plant-derived foods. Resveratrol, found in red grapes, has been linked to cardiovascular health, while curcumin in turmeric exhibits anti-inflammatory and antioxidant properties. Understanding the bioactive compounds in plants is essential for unlocking their therapeutic potential. As research advances, the identification and isolation of specific compounds continue to drive the development of herbal medicines and contribute to the integration of plant-based therapies into mainstream healthcare. The intricate chemistry of these compounds reflects the complex relationship between plants and human health, offering a rich source for innovative pharmaceutical exploration (Gaur et al., 2007).

Plant Description

Dichanthium annulatum

Dichanthium annulatum, or Kleberg bluestem, is a resilient perennial grass native to Africa and spread globally in tropical and subtropical areas. Characterized by tufted growth and bluish-green leaves, it thrives in varying environmental conditions, demonstrating drought tolerance and the ability to stabilize soil, making it valuable for land reclamation. However, it can become invasive, outcompeting native species and reducing biodiversity. Management efforts in problematic regions include targeted grazing and mechanical control to mitigate its impact while leveraging its benefits for pasture improvement. The species exemplifies plant adaptability and the need for responsible ecological management (Kumbhare et al., 2012).

Figure 1: *Dichanthium annulatum*

Studying the chemical constituents and pharmacological properties of *Dichanthium annulatum* is essential for its therapeutic applications and ecological insight. Phytochemical analysis helps identify bioactive compounds that may lead to drug discovery (Heuze et al., 2015). Research into its pharmacological activities reveals potential therapeutic effects including anti-inflammatory, antioxidant, antimicrobial, antidiabetic, and anticancer properties. This research supports traditional medicinal practices and enhances our understanding of ecological interactions, highlighting the need for interdisciplinary approaches to optimize plant biodiversity for health and conservation (Fatima et al., 2018).

Pithecellobium dulce

Figure 2: *Pithecellobium dulce*

Pithecellobium dulce (Roxb.) Benth *(Syn. Mimosa dulcis Roxb.*; *Inga dulcis Wild*.; *Inga lanceolata Blanco*.) belongs to family Leguminosae, is an evergreen tree widely distributed in the greater part of India and is also found in Southeast Asia. Plant locally is known by various names at different regions. *P. dulce* (Family: Leguminosae, sub family Mimosoideae) is one of 100-200 species in this genus (Katekhaye & Kale, 2012). Pithecellobium dulce is the only species that has become widespread outside its origin. It is now common and naturalized in India and tropical Africa, especially along coasts. It is notably weedy in the Caribbean islands (including Cuba, Jamaica, Puerto Rico, and St. Croix), and in Florida and Hawaii, USA, but less so where population and animal pressure keep it contained. *Pithecellobium dulce*, originating from South America, is a widely distributed host plant for certain caterpillars and moths. Typically reaching heights of 10-15 meters, it features a broad crown with bipinnate leaves and small white flowers (Aleman et al., 2024). The tree's gray bark becomes rough and eventually peels. Its distinct reddish-brown pods contain shiny black seeds. Traditionally, the plant is used for various medicinal purposes including antiseptic properties, weight loss aid, and treatment of ailments such as jaundice and malaria. Its nutritional profile includes essential vitamins and minerals, contributing to health benefits such as improved circulation and blood sugar regulation (Sneha et al., 2020).

Bergenia ciliata

The Bergenia is a genus of 10 species of flowering plants in the family Saxifragaceae native to Central Asia, from Afghanistan to China and Himalayas. They are evergreen perennial plants with spirally arranged of rosette of leaves 6-35 cm long and 4-15 cm broad and pink flower produced in cyme. The leaves of Bergenia create wonderful foliage throughout the year. They can be described as leathery or somewhat rubbery. Leaf shape and texture of Bergenia has earned the plants with some interesting nicknames. In addition to elephant ear, Bergenia may be called heartleaf, pigsqueak, picnic plates, or leather cabbages. Leaf size may vary in length from 5.08-30.48 cm and in width from 2.54-15.24 cm. Plant spread is about 45.72-60.96 cm, so Bergenia should be planted about two feet apart from full ground cover. Bergenia are becoming more popular plants among the environmentally conscious because they are drought resistance. The leaves do tend to attract slugs and snails, though spreading coca beans around the plant can help naturally keep these pests away

Figure 3: ***Bergenia ciliate***

Toxicological studies indicate severe toxicity with symptoms including breathing problems and gastrointestinal issues. The rhizome exhibits several medicinal properties, including anti-inflammatory effects comparable to Diclofenac sodium, anti-tussive activity effective against cough, and potent antiviral effects against herpes simplex and influenza viruses. Furthermore, it shows gastroprotective effects in gastric ulcer models, potential anti-cancer properties with cytotoxicity in cell lines, and notable antioxidant activity in both methanolic and aqueous extracts. These findings underscore *Bergenia ciliata*'s significance in traditional medicine and its potential as a source for therapeutic agents.

Ludwigia adscendens,

Ludwingia adscendens the water primrose, is a species of flowering plant in the evening primrose family. Its native distribution is unclear. It is now a common weed of rice paddies in Asia and occurs also in Australia and Africa, but may have originated in South America.

This plant is a perennial floating herb with white spongy buoys, and can float on water surface as well as creep over the surface of wetlands. The plant has simple leaves with elliptic blades, which are 0.4–7 cm long and 0.7–3 cm wide. Its petioles are 0.5–1.0 cm short. Its cream flowers emerge

singly at axils, and each have 5 sepals, 5 petals, and 10 stamens.

Ludwigia adscendens,

Table 1: Pharmacological activity of *Dichanthium annulatum, Bergenia ciliata* and *Bergenia ciliata*.

Sr. No.	Common Disease / Pharmacological Activity	*Dichanthium annulatum* (Marvel grass)	*Bergenia ciliata*	*Bergenia ciliata*	References
1	Antioxidant activity	Strong DPPH, ABTS and SOR radical scavenging activity; ethanol extract IC_{50} = 32.803 ± 9.66 µg/ml	DPPH assay IC50 values indicated a range of antioxidant activity: 150.23 µg/ml (MB), 16.83 µg/ml (AB), 250.32 µg/ml (ML), and 18.30 µg/ml (AL). The extracts demonstrated significant free radical scavenging and iron chelation, with reducing power correlating positively to extract concentration	Free radical (DPPH● and ● OH) scavenging potential of the extracts revealed that both extracts to be active radical scavengers. Reducing (Fe+3-Fe+2) power and lipid peroxidation inhibition efficiency (TBARS assay) of both extracts were also evaluated and both extracts showed promising activity in preventing lipid peroxidation and might prevent oxidative damages to biomolecules.	(Katekhaye & Kale et al., 2012 Chauhan et al., 2013, Rajkumaret al., 2010)
2	Anti-inflammatory activity	ROS scavenging reduces oxidative stress–mediated inflammation	Compounds were determined using HPLC at a scanning wavelength of λmax 280 nm. The altitudes of the collection location were shown to have a positive correlation with the amounts of the targeted chemicals A–D. In contrast to compound C and D concentrations (r = 0.1297,	Polyphenols (epicatechin, catechin) exhibit anti-inflammatory effects	(Sukantha et al., 2014; Srivastava et al., 2015

			0.3245), only compound A and B contents (r = 0.6892, 0.6398) showed a strong association.		
3	Antibacterial activity	Ethyl acetate extract effective against *E. coli* and *C. albicans*	With Minimum Inhibitory Concentration (MIC) and Minimum Bactericidal Concentration (MBC) values ranging from 1 mg to 5 mg for different bacterial strains, notable antibacterial effects were seen that were equivalent to those of chloramphenic ol.	The methanolic extract of B. ciliata rhizome showed a wide spectrum of concentration dependent antibacterial activity of methanolic extract of *B. ciliata* rhizomes at a concentration of 200-1000 µg/disc	(Pradeepa et al., 2014; Sukantha et al., 2014; Sinha et al., 2001)
4	Antidiabetic)	Diabetes was brought on by an intraperitoneal injection of STZ (65 mg/kg). Over a 15-day period, body weight and blood glucose levels were monitored; at the end of the study, lipid profiles and pancreatic histology were assessed.	The methanolic crude extract of P. dulce seed was tested in Streptozotocin (STZ)-induced diabetic rat (albino Wistar male model) and the extract has the ability to protect the functional β-cells that produce and maintain the insulin level in the blood	In the rat gut, α-glucosidase and α-amylase were considerably inhibited by the two active compounds (-)-3-O-galloylepicatechin and (-)-3-O-galloylcatechin that were recovered from the 50% aqueous methanol extract of the rhizome section. Standard IC50 values for [(-)-3-Ogalloylepicatechin] were 560, 334, and 739 µM for sucrose, maltase, and αamylase, and 297, 150, and 401 µM for (-)-3-O-galloylcatechin.	(Gupta et al., 2025; Fu et al., 2013 Bhandari et al., 2008)
5	Anti hyperlipidimc disorders	-	The methanolic crude extract of P. dulce seed on STZ-induced diabetic rat model. The histopathological analysis showed the increased levels of HDLC and the very low-density lipoproteins cholesterol (VLDLC), low-density lipoproteins cholesterol (LDLC), serum cholesterol, and triglycerides level were significantly decreased in	-	(Nagmoti et al., 2015)

			the P. dulce treated rats		
6	Anti-pyretic activity	The Freund's Complete Adjuvant (FCA)-induced arthritis paradigm was used to assess the anti-arthritic impact in Wistar rats. Paw edema was considerably decreased by oral administration of the extract (200 mg/kg and 400 mg/kg), which also improved biochemical (ALP, AST, ALT, CRP)	-	- The antipyretic effects of *Bergenia ciliata* Sternb. rhizome methanol extract on both normal body temperature and yeast-induced pyrexia in rats have been assessed. At oral dosages of 100, 200, and 300 mgkg-1, it showed notable action in both models.	(Khandare et al., 2025: Sinha et al., 2000:)

Herbal Medicines in Rheumatoid Arthritis

RA conventional treatments have several issues with safety and effectiveness. A number of patients seek out complementary and alternative medicine (CAM) solutions as a means of managing this incapacitating illness due to the adverse effects of synthetic medications. Studies have shown that individuals with chronic pain and those who are not pleased with their present care are very inclined to opt for CAM. It is estimated that 60-90% of individuals with arthritis use CAM. There is a need for research on the safety and effectiveness of herbal medicines as individuals with RA are becoming more interested in them. RA is treated using a multidisciplinary strategy aimed at reducing inflammation, easing discomfort and restoring joint function. Herbal medicines that interact with inflammatory mediators have become increasingly popular in the treatment of rheumatoid arthritis (Asif et al., 2011).

Herbal remedies are often perceived as more 'natural' compared to synthetic medications. Some individuals prefer herbal treatments as they feel more comfortable with substances derived directly from plants (Arulselvan et al., 2016). In some cases, herbal remedies may be associated with fewer side-effects compared to certain conventional medications. Cultural and traditional beliefs may influence the preference for herbal remedies. In some cultures, traditional herbal medicine has a long history of use and is deeply rooted in local practices (Tsoupras et al., 2018). They are sometimes seen as part of a holistic approach to health, addressing not only the symptoms but also focusing on overall well-being and lifestyle changes. They may be more readily available and accessible to some individuals, particularly in regions where conventional medications may be less accessible or more expensive. Natural product consumption may be

advantageous for RA patients in the context of antioxidants. Since there is currently minimal research available in this area, there is conflicting evidence regarding the role of antioxidants in RA. However, the value of antioxidants in reducing inflammation is well-established, which explains why natural products' antioxidant properties are frequently assessed and typically come first in vitro evaluations before their anti-inflammatory properties (Yahfoufi et al., 2018).

Table 2: Plant in Rheumatoid Arthritis

Sr. No.	Biological Source (Family)	Part Used	Active Ingredient(s)	Therapeutic Uses	Extract	Reference
1	*Annona montana* (Annonaceae)	Leaves, fruit, seeds, bark, roots	Cyclomontanins A–D, annomuricatin C, (+)-corytuberine	Anti-rheumatic, anthelmintic, anticonvulsant, antidepressant, antimicrobial, antineoplastic, antiparasitic, antispasmodic, antiviral, astringent, cardiodepressant, cytotoxic, febrifuge, hypotensive, insecticide, sedative, stomachic, vasodilator, vermifuge	Methanol	(Chuang et al., 2008)
2	*Abrus precatorius* (Fabaceae)	Fresh leaves	Triterpenoids (Abrusosides A–D)	Colds, cough, convulsion, fever, rheumatism, conjunctivitis, ulcers	Methanol	(Georgewill et al., 2009)
3	*Aristolochia bracteolata* (Aristolochiaceae)	Whole plant	Ceryl alcohol, β-sitosterol, aristolochic acid, alkaloids, fatty acids, aristolactam, magnoflorine	Anthelmintic, fever, purgative, painful joints	Petroleum ether, chloroform, methanol	(Chitme & Patel et al., 2009)
4	*Alpinia conchigera Griff.* (Zingiberaceae)	Rhizomes	Galangoflavonoid, acetoxychavicol acetate, β-sitosterol diglucoside	Analgesic, anti-inflammatory	Ethanol	(Sulaiman et al., 2010– Lee et al., 2006)
5	*Alchornea cordifolia* (Euphorbiaceae)	Leaves	Tannins, phenolic acids, flavonoids, alkaloids	Anti-inflammatory, wound healing, ulcers, toothache, conjunctivitis	Aqueous decoction, methanol	(Manga et al., 2004)
6	*Asparagus racemosus* (Liliaceae)	Roots, leaves, flowers, fruits	Steroidal glycosides (Shatavarins I–IV), diosgenin, flavonoids	Antioxidant, anti-ulcer, gout, dyspnoea	Methanol	(Alok et al., 2013)
7	*Anacardium occidentale* (Anacardiaceae)	Leaves	Myricetin, quercetin, kaempferol, apigenin	Anti-inflammatory, diabetes, skin diseases, ulcers	Ethanol & fractions	(Patil et al., 2003)
8	*Azadirachta indica*	Leaves	Alkaloids, flavonoids,	Anti-inflammatory, antipyretic, antimalarial,	Hydro-alcoholic,	(Jagadeesh et al., 2014)

	(Meliaceae)		triterpenoids, phenolics	antidiabetic	ethyl acetate, n-butanol	
9	*Allium cepa* (Liliaceae)	Bulbs	Organosulfur compounds, flavonoids, sterols, saponins	Antimicrobial, anti-inflammatory	Petroleum ether, methanol, aqueous	(Mosaddek et al., 2008)
10	*Antrodia cinnamomea* (Fomitopsidaceae)	Fruiting bodies	Antrocamphin A, triterpenoids, polyacetylenes	Anti-inflammatory, antioxidant, anticancer	Methanol	(Wen et al., 2011)
11	*Butea frondosa* (Fabaceae)	Roots, leaves	Flavonoids, glucosides, lectins	Anti-inflammatory	Aqueous	(Kumar et al., 2011)
12	*Barringtonia racemosa* (Lecythidaceae)	Fruits, leaves	Diterpenoids, triterpenoids, lycopene, bartogenic acid	Anti-inflammatory, anti-tumor, antimicrobial	Hexane, ethanol, methanol	[47]
13	*Boswellia serrata Roxb*. (Burseraceae)	Oleogum resin	Boswellic acids (AKBA, KBA)	Anti-inflammatory, arthritis, asthma, psoriasis	Petroleum ether	(Gowri et al., 2007)
14	*Borassus flabellifer L*. (Arecaceae)	Male flowers	Alkaloids, terpenoids, steroidal saponins	Anti-inflammatory, diuretic, immunosuppressant	Ethanol	(Paschapur et al., 2009)

New Perspectives and Future Directions in the Treatment of RA

The management of RA has changed significantly over the last decades, resulting in improved quality of life and outcomes for RA patients. This has been made feasible by the successful

discovery of several pathways involved in the pathogenesis of RA. However, both the mechanisms underlying the inflammatory processes and the pharmacological effects of therapeutic molecules are still incompletely elucidated, leading to some unmet needs in the management of RA. These include a deeper understanding of how different therapies have such comparable efficacies; elucidating why certain patients become less responsive over time; detecting pre-RA and establishing an early and aggressive treatment; and improving the efficacy and safety profiles of novel compounds, especially JAKis (Smolen et al., 2016). Several ways to improve RA treatment are now being tested in different experimental models. Numerous new therapeutic targets are being researched and potential therapeutic agents are in various stages of testing in order to obtain a complete remission of RA.

Huang et al. (2021), updated and considered complex information about small molecular metabolite targets (prostaglandins, thromboxane A2, leukotriene B4 receptor, platelet-activating factor, cannabinoid receptors, inducible nitric oxide, etc.) and epigenetic targets (DNA methylation, RNA methylation, histone modification, etc.) and other protein targets (p38 mitogen-activated protein kinase, complex G protein-coupled receptor kinase 2, granulocyte-macrophage colony-stimulating factor), along with potential therapeutic agents (Huang et al., 2021).

Mesenchymal stem cells (MSCs) are also a promising therapeutic approach due to their ability to differentiate into new tissues like bone and cartilage and they have been reported to have immunosuppressive properties in vitro by suppressing T cell activation. Moreover, treatment with MSCs in both animal model studies and clinical trials in RA patients have shown a decrease in the proinflammatory response and an improvement of RA symptoms by reducing the blood levels of IL-1, IL-6, IL-8 and TNF-α (Lin et al., 2020).

Toll-like receptor 4 has a confirmed role in RA pathogenesis, promoting joint inflammation. Thus, therapeutic compounds targeting this receptor or its ligands, such as heat-shock protein crystalline or tenascin C can be optimized (Lin et al., 2020). Therapeutic options for RA are increasingly diverse, and numerous ongoing studies can contribute to a significant improvement for RA patients by discovering new molecular targets, new therapeutic agents, and new methods to counteract side effects. A personalized approach based on genetic studies doubled by evidence-based medicine can transform the future of medicine and succeed in curing the incurable (Köhler et al., 2019).

Conclusion

Rheumatoid arthritis remains a complex autoimmune disorder with significant unmet therapeutic needs despite advances in biologic and targeted synthetic agents. Limitations related to long-term safety, cost, and variable treatment responses necessitate the exploration of complementary strategies. Plant-derived bioactive compounds have gained increasing attention due to their anti-inflammatory, antioxidant, and immunomodulatory properties, with growing evidence supporting their ability to modulate key molecular pathways involved in RA pathogenesis. Medicinal plants such as *Dichanthium annulatum*, *Pithecellobium dulce* and *Bergenia ciliata* represent promising sources of potential anti-arthritic agents. Integrating traditional medicinal knowledge with modern pharmacological and molecular research may facilitate the development of safer, cost-effective, and multi-targeted therapeutic options for rheumatoid arthritis. Continued systematic preclinical and clinical investigations are essential to validate their efficacy and translational potential.

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