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Beyond the Canopy: Antiarthritic Potential of Phytochemicals from Plant Roots, Rhizomes, Fruits, Barks, and Leaves – An *In-Vivo* Review

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Abstract. Medicinal plants have been utilized around the world to address a variety of disorders, including arthritis, and they come in many different formulations. This study aims to review the in vivo research that explores the antiarthritic potential of the natural compounds found in these various plant parts. We detailed the categories of phytochemicals, botanical families, key compounds, active ingredients, effective dosages, types of extracts, duration of experiments, and methods of arthritis induction. In this review, we came across 35 different plants that demonstrate antiarthritic activity in their roots, rhizomes, fruits, barks, and leaf extracts. We also outlined the mechanisms of action for the most common types of compounds. Our research indicates that flavonoids, glycosides, steroids, phenols, alkaloids, tannins, phytosterols, and saponins are the most abundant natural compounds found in the roots, rhizomes, fruits, barks, and leaves of these plants that show antiarthritic properties. Phytochemicals from plant parts like roots, rhizomes, fruits, barks, and leaves show potential in reducing inflammation, oxidative stress, and joint damage, while improving immune response and relieving arthritis symptoms. These plant-based compounds offer promising leads for future arthritis treatments.

1 Introduction

Rheumatoid arthritis (RA) is a chronic autoimmune disorder marked by persistent joint inflammation and progressive tissue damage [1]. Although incurable, early diagnosis and timely treatment are essential to control disease activity and prevent irreversible joint destruction [1]. Globally, RA affects 0.5–1% of the population, with higher prevalence in developed nations due to improved diagnostics and aging demographics. Incidence ranges

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from 5 to 50 cases per 100,000 person-years, influenced by ethnicity and geography [2]. Late-Onset Rheumatoid Arthritis (LORA) is rising in aging societies [3]. Women are affected twice as often as men, with onset typically between 40 and 60 years, though cases in older adults are increasing [4]. The burden is greater in North America and Europe compared to Asia and Africa [5].RA etiology is multifactorial, involving genetics, obesity, smoking, and environmental exposures [6]. Pathologically, synovial inflammation and hyperplasia occur, with autoantibodies such as rheumatoid factor (RF) and anti-citrullinated protein antibodies (ACPA). Over time, cartilage erosion, bone deformities, and systemic complications affecting lungs, heart, bones, and mental health develop [7]. Smoking, infections, and autoantibody presence further contribute [8]. Aberrant immune activity drives pannus formation, invading bone and cartilage [9]. Inflammatory cascades worsen damage: IgM immune complexes activate complement, releasing TNF-α and IL-1, while lysosomal enzymes degrade cartilage and prostaglandins intensify pain. Cytokines including IL-17, IL-18, and RANKL promote synovial proliferation and chronic inflammation [10].Complications include depression, affecting nearly 40% of corticosteroid-treated patients [11], infections from immunosuppressants [12], cardiovascular disease [13], and malignancies such as lymphoma, lung cancer, and skin cancer [14, 15].Therapies include NSAIDs, steroids, and DMARDs, while biologics such as anti-TNF-α, anti-CD20, and abatacept provide efficacy but cause side effects. COX-2 upregulation drives prostaglandin-mediated pain; NSAIDs inhibit COX activity, with COX-2 inhibition offering targeted benefits [16–18]. Due to side effects, herbal alternatives are gaining attention. Plant-based remedies are widely recognized [19, 20]; nearly half of modern drugs derive from natural sources [21], and WHO notes reliance on herbal medicine in developing regions [22]. Medicinal plants are valued for safety and affordability [23], with bioactive compounds such as flavonoids and terpenoids reducing inflammation [24, 25]. The Ayurvedic principle of Polyherbalism, described in *Sarangdhar Samhita* (1300 AD), combines herbs for synergistic benefits [26]. Modern studies confirm polyherbal formulations enhance efficacy, reduce toxicity, and broaden therapeutic use [27, 28].

2 Methods

To gather and analyze data for this review, we tapped into a variety of databases and search engines, such as Web of Knowledge, Springer, Elsevier, PubMed, Science Direct, Taylor & Francis, and Google Scholar. The keywords we focused on included “medicinal plant roots,” “anti-arthritic natural products,” “arthritis rats,” “*in vivo* studies,” and “herbal medicine.” We made sure to exclude any in vitro studies or investigations that didn’t involve roots, rhizomes, fruits, or leaves. Our search was limited to studies published in English, covering a time frame from 1980 to 2024.

3. Results and discussion

In recent decades, different parts of medicinal plants have been used to treat arthritis, and many traditional plant-based therapies are now supported by in vitro, in vivo, and clinical studies. Roots, rhizomes, fruits, barks, and leaves contain diverse phytochemicals such as flavonoids, glycosides, steroids, phenols, alkaloids, tannins, phytosterols, and saponins, some of which are produced mainly in these tissues. These bioactive compounds show anti-inflammatory, antioxidant, and immunomodulatory effects, contributing to their usefulness against arthritis. From our literature review, we discovered that 35 different plant species across 29 families have antiarthritic compounds present in their roots, rhizomes, fruits, barks, and leaves (Table 1). The plant families that popped up most often in the

studies we reviewed were *Orchidaceae, Malvaceae, Euphorbiaceae, Cyperaceae, Solanaceae*, and *Zingiberaceae*, in that order. Although not every study we looked at lists the specific chemical constituents or bioactive compounds, the findings indicated that flavonoids, glycosides, steroids, phenols, alkaloids, tannins, phytosterols, and saponins were the most prevalent bioactive components found in plant roots, rhizomes, fruits, barks, and leaves. The studies we reviewed utilized a variety of solvents for extracting these natural constituents. The most common were Methanolic extract: 22.5%, Ethanolic extract: 22.5%, Hydroalcoholic extract: 15%, Hydroethanolic extract: 2.5%, Alcoholic extract: 5%, Aqueous extract: 20%, N-hexane extract: 2.5%, Ole-gum resin extract: 2.5%, Hydroalcoholic extract & aqueous extract: 2.5%, Aquo-alcoholic extract: 2.5%, Ethyl acetate extract: 2.5% and Acetone extract: 5%.

The duration of the experiments reported across the studies ranged from 6 hours to 2160 hours (90 days). To simplify interpretation, we grouped these durations into two types: short-term studies (<25 days) and long-term studies (>25 days). Based on this classification, 77.1% of the experiments were completed within a single day (short-term), whereas 22.9% extended beyond one day (long-term).

Table 1 The list of plants with antiarthritic activity in their roots, rhizomes, fruits, barks and leaves extracts.

Scientific name	**Common name**	**Family**	**Major chemical constituents**	**Bioactive compound**	**Extract type**	**Dose (mg/kg)**	**Effective dose (mg/kg)**	**Time (Hrs or days)**	**Induction of arthritis**	**Experimental animals**
Vanda roxburghii	Rasna	Orchidaceae	Alkaloids, steroids, tannins, glycosides, flavonoids	Alkyl perulate and β-sitosterol-D-glucoside	Methanolic extract	50, 100	100	6 hrs	Carragenan induced	Swiss albino mice
Sida cordifolia	Bala	Malvaceae	Alkaloids, flavonoids, glycosides, steroids, carbohydrate	Ephedrine, stearic and β – sitosterol	Ethanolic extract	100, 600, 1200, 1800, 2000	250, 500	12 days	Adjuvant induced	Swiss albino mice
Ricinus communis	Aeranda	Euphorbiaceae	Alkaloids, flavonoids, tannins, steroids, glycosides	Ricinine, Erandone, lupeol	Hydroalcoholic extract	250, 500	500	17 days	Complete Freund's adjuvant induced	Wistar rats
Acorus calamus	Vacha	Araceae	Alkaloids, flavonoids, steroids, terpenoids, Volatile Oil	α- and β-asarone	Ethanolic extract	100, 200	200	28 days	Freund's complete adjuvant induced	Wistar rats
Zingiber officinale	Sunthi	Zingiberaceae	Flavonoids, Volatile Oil, phenolic compounds	Zingiberene, Gingerol	Hydroalcoholic ginger extract	50, 100, 200	200	25 days	Collagen induced	Sprague Dawley rats
Vitex negundo	Nirgundi	Lamiaceae	Alkaloids, flavonoids, steroids, terpenoids, volatile oil	nishindine, flavones, luteolin-7-glucoside, β – sitosterol	hydroethanolic extract	200	200	13 days	Freund's complete adjuvant induced	Wistar albino rats
Adhatoda vasica	Vasa	Acanthaceae	Alkaloids, flavonoids, glycosides,	Pyrroloquinazoline	Methanolic extract	50, 100, 200	50, 200	17 days	Collagen induced	Swiss albino mice

			Steroids, volatile oil						
Cyperus rotundus	Musta	Cyperaceae	Alkaloids, flavonoids, Terpenoids, glycosides, volatile oil	Triterpenoid	Alcoholic extract	300, 500	500	10 days	Formaldehyde induced	Wistar albino rats
Tinospora cordifolia	Gudu chi	Menispermaceae	Alkaloids, glycosides, flavonoids, steroids, phenolic compounds	berberine, cordiofolioside A,	Methanolic extract	150	150	13 days	Adjuvant induced	Lewis rats
Pedalium murex	Gokhru	Pedaliaceae	Alkaloids, flavonoids, tannins, glycosides, steroids, Terpenoids	Quercetin, 20,40,50-trihytlroxy-5,7-dimethoxy flavone, diosgenin	Methanolic extract	70	70	90 days	Carragenan induced	Wistar albino rats
Withania somnifera	Ashwagandha	Solanaceae	Alkaloids, flavonoids, steroids, Steroidal lactones	Withaferin-A, withanolide	Aqueous extract	500, 1000	500	12 days	Complete Freund's adjuvant induced	Wistar albino rats
Piper longum	Pippali	Piperaceae	Alkaloids, flavonoids, steroids, volatile oil, phenolic compounds	Piperine and piperlongumine	Aqueous extract	200, 400	200, 400	14 days	Complete Freund's adjuvant induced	Wistar albino rats
Emblica officinalis	Amla	Phyllanthaceae	Alkaloids, flavonoids, tannins, carbohydrates, phenolic compounds	Gallic acid, Ellagic acid, quercetin, kaempferol	Hydroalcoholic extract	250, 500, 750	500	21 days	Freund's complete adjuvant induced	Wistar albino rats
Boerhavia diffusa	Punarnava	Nyctaginaceae	Alkaloids, glycosides flavonoids, terpenoids carbohydrates, proteins, amino acids, phenolic compounds	Flavonoids, alkaloids, phenolic compounds, terpenoids	Methanolic extract	200, 400	200	21 days	Freund's complete adjuvant induced	Wistar albino rats
Curcuma longa	Turmeric	Zingiberaceae	volatile oil, resins, starch grains	curcuminoids	N-hexane extract	200	200	28 days	Complete Freund's	Wistar albino rats

Acyranthus aspera	Devil's horse whip	Amaranthaceae	Alkaloids, Carbohydrates, glycosides, phenolic compound, flavonoids, tannin, proteins	Alkaloids, glycosides, flavonoids, phenolic compounds	Aqueous extract	125, 250, 500	250, 500	28 days	Formaldehyde induced adjuvant induced	Swiss Albino mice, Wister rats

3.1. Alkaloids

Alkaloids are nitrogen-containing natural compounds derived mainly from amino acids and are found in plants, fungi, and bacteria [29, 30]. They are defined by a nitrogen atom not part of an amide group and originate from amino acids such as histidine, lysine, ornithine, tryptophan, and tyrosine [31, 32]. These compounds often serve as plant defense molecules. Alkaloids occur widely across plant families like Solanaceae, Fabaceae, Papaveraceae, Berberidaceae, and Cannabaceae, and are classified by their ring structure or botanical source. Well-known examples include nicotine, atropine, berberine, morphine, and caffeine, used for conditions ranging from cardiovascular and inflammatory disorders to mental health issues [33, 34]. Besides central nervous system and anti-inflammatory effects, some alkaloids also show antidiabetic potential [35]. Berberine, notable for its therapeutic activity, reduces rheumatoid arthritis severity in Wistar rats by lowering IL-6 and IL-17, increasing IL-10 and TGF-β, and decreasing synovial hyperplasia and inflammatory cell infiltration [36].

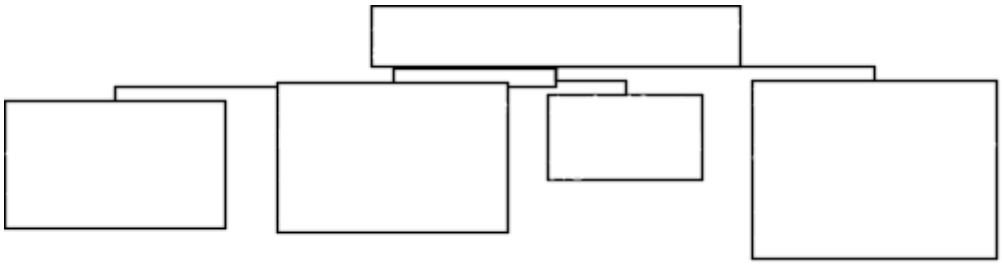

Fig. 1. Alkaloids and saponins: key bioactive effects in RA.FLS – fibroblast-like synoviocytes; NFkB – nuclear factor κB; IL – interleukin; IFN – interferon; TNF – tumor necrosis factor; ROS – reactive oxygen species; NO – nitric oxide.

3.2. Phenolic compounds

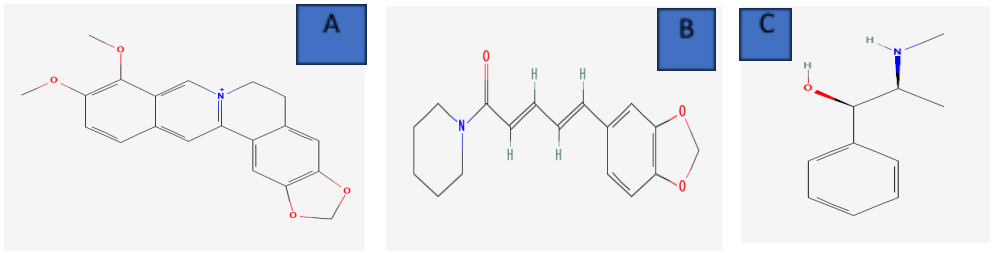

Fig. 2. Chemical structure of selected bioactive compounds in Phenolic compound-A-Berberine,B-Piperin,C-Ephedrin

Phenolic compounds—including flavonoids, resveratrol, emodin, rosmarinic acid, and mangiferin—manage RHA by modulating pro-inflammatory pathways. Flavonoids, abundant in plants and fruits, exhibit potent antioxidant activity [38–41]. Since ROS drive RHA, antioxidants scavenge free radicals and suppress nitric oxide, IL-6, IL-1β, and chemokines [42,43]. Flavonoids also inhibit NF-κB signaling. Notably, dried plum supplementation in transgenic mice reduced TNF-α, slowed bone erosion& delayed RHA onset,highlighting therapeutic potential [44].

3.3. Flavonoids

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Flavonoids are plant-derived secondary metabolites, with over 6,000 identified, regulating physiological and metabolic processes [45, 46]. Found in tea, wine, beer, grains, legumes, berries, herbs, fruits, and vegetables [47, 48], they share a 2-phenylbenzopyrone backbone synthesized via the phenylpropanoid pathway [45, 49]. Classified into six groups, they exhibit antioxidant [50–53] and anti-inflammatory effects by suppressing cytokines, nitric oxide, eicosanoids, and NF-κB/AP-1 signaling [54, 55].

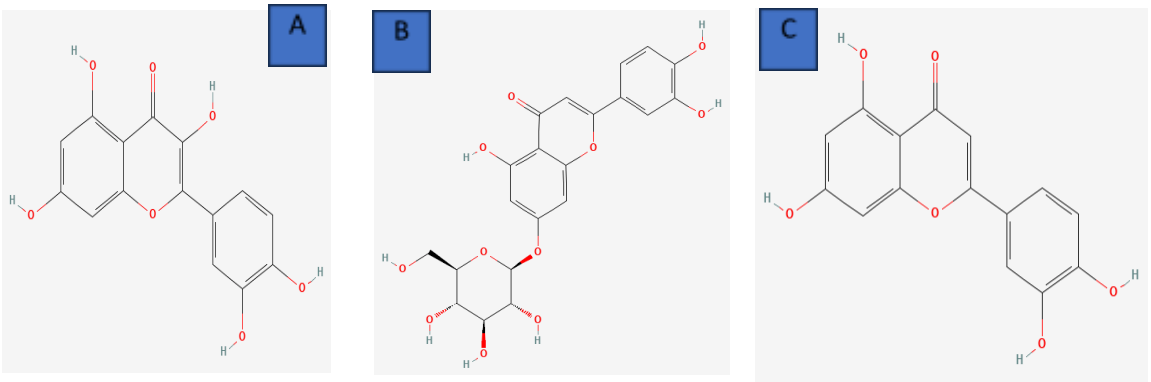


Fig. 3 Chemical structure of selected bioactive compounds in Flavonoid-A-Quercetin,B-Luteolin 7-O-glucoside, C-Luteolin

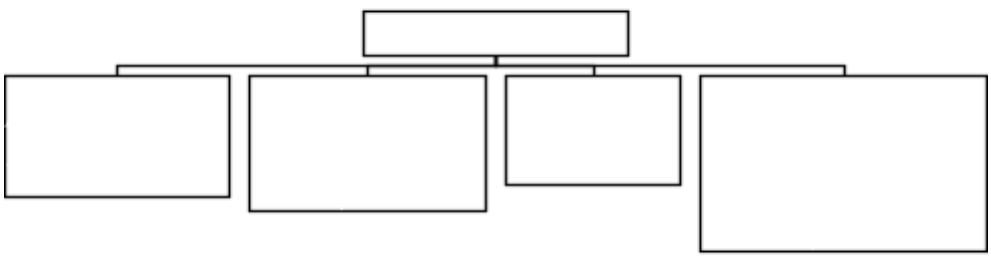


Fig. 4 Biological activities of flavonoids in RA.

3.4.Glycosides :

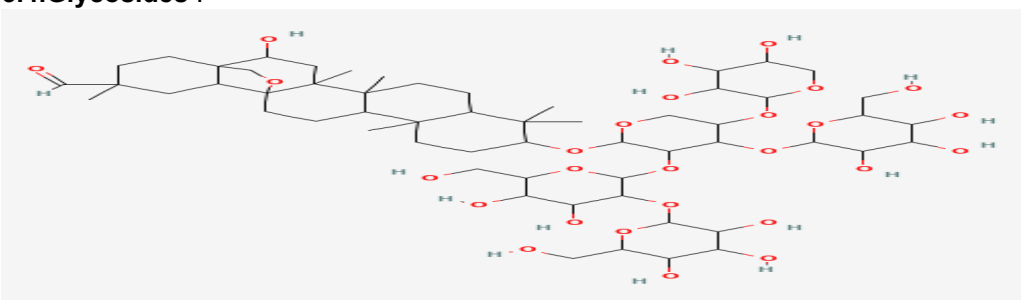


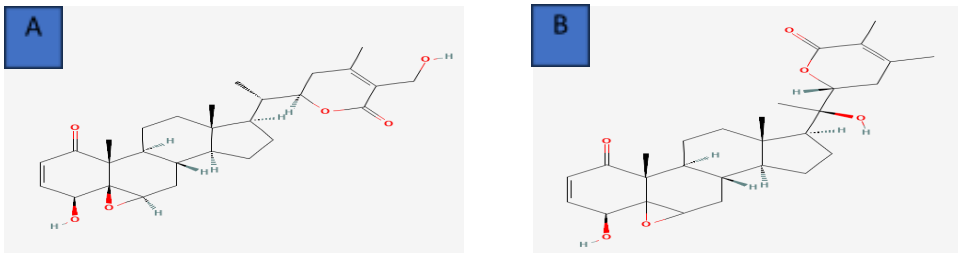
Fig. 5 Chemical structure of selected bioactive compounds in Glycosides--Saponin

Glycosides are fascinating compounds that feature a glycosidic bond, which forms when a sugar molecule connects with another functional group, resulting in O-, N-, or C-glycosidic bonds. There's been a lot of research showing the bioactivity of many glycosides, and

they've been used traditionally for various purposes. Interestingly, some studies have also highlighted the potential effects of glycosides in combating osteoarthritis [56, 57, 58].

3.5. Phytosteroids

Phytosteroids are plant-produced secondary metabolites formed through the acetate–mevalonate pathway, where S-squalene-2,3-epoxide cyclizes into cycloartenol and



is later

Fig. 6 Chemical structure of selected bioactive compounds in Phytosteroids-A-Withaferin A, B-Withanolide

converted into active compounds such as stigmasterol and β-sitosterol [59]. These molecules often bind with sugars to form glycosides like steroidal saponins, glycoalkaloids, and cardiac glycosides. Steroids are important in modern drug development due to their wide pharmacological actions, including immunomodulatory, hepatoprotective, anticancer, antimicrobial, antifungal, anti-inflammatory, and cardiotonic effects, functioning similarly to mammalian steroid and plant growth hormones [60]. Clinically, they are used to treat inflammatory conditions such as rheumatoid arthritis, multiple sclerosis, cardiovascular disorders, inflammatory bowel diseases, Crohn's disease, high cholesterol, and type I diabetes mellitus [61]. Phytosterols like ergosterol, β-sitosterol, stigmasterol, campesterol, and ergosterol acetate show strong anti-inflammatory effects by inhibiting nitric oxide release and reducing TNF-α, COX-2, iNOS, and ERK activity in LPS-stimulated macrophages, with β-sitosterol exhibiting the most potent activity [62].

3.6. Tannins

Polyphenolic tannins protect plants from herbivores but may also inhibit neighbouring plant growth. They are divided into hydrolyzable tannins—formed when a polyhydric alcohol is

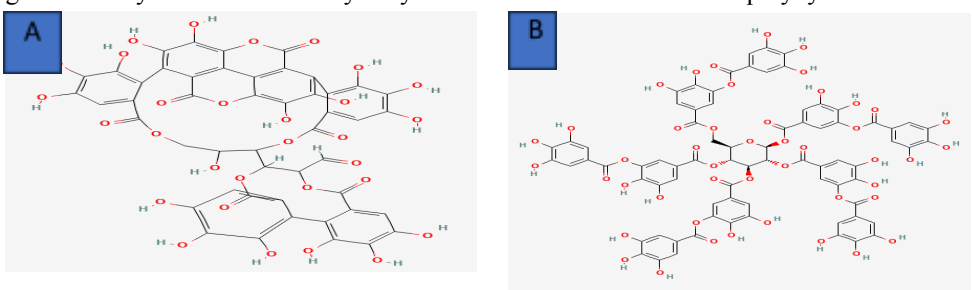


Fig. 7 Chemical structure of A-Punicalagin ,B-Gallotannin tannins

esterified with phenolic acids like gallic acid (gallotannins) or hexahydroxydiphenic acid (ellagitannins)—and non-hydrolyzable tannins, which are polymers of flavan-3-ols and flavan-3,4-diols [63]. Terminalia chebula (TC) is especially rich in hydrolyzable tannins,

making up 30–45% of its content, concentrated in the fruit pericarp. These include compounds such as gallic acid, ellagic acid, chebulic acid, chebulinic acid, punicalagin, chebulagic acid, chebulanin, corilagin, and multiple galloyl-glucose derivatives, along with terchebulin and phyllanemblinin analogues [64–66]. In arthritis studies, tannin-rich fractions (100–400 mg/kg p.o.) found dose-dependent reductions in paw volume, arthritic score, spleen index, and cytokines such as TNF-α, IL-1β, and IL-6, comparable to methotrexate .

3.7. Terpenoids

Terpenes (isoprenoids) are diverse plant secondary metabolites composed of hydrocarbons. They serve key functions such as acting as hormones (abscisic acid, gibberellins), electron carriers (ubiquinone), photosynthetic pigments (carotenoids), and membrane components (phytosterols) [68]. Terpenoids originate from one or more isoprene units (C5H8) and occur widely in plants. They are classified by the number of isoprene units into hemi-, mono-, sesqui-, di-, sester-, tri-, tetra-, and polyterpenoids. Many of them exhibit notable antibacterial, antifungal, and anti-inflammatory properties [69, 70].Myrcene, a monoterpene from *Eryngium duriaei* subsp. *Juresianum* and *Lavandula luisieri*, shows strong anti-inflammatory, pro-anabolic, and anti-catabolic effects. It reduces IL-1β–induced nitric oxide formation and inhibits NF-κB, p38, and JNK activation. It also upregulates anti-catabolic genes (TIMP-1, TIMP-3) and downregulates MMP-1 and MMP-13, helping suppress osteoarthritis-related cartilage degradation [71].Given their significant anti-inflammatory activity, terpenoids across various classes show promising potential in alleviating rheumatoid arthritis symptoms [72–74].

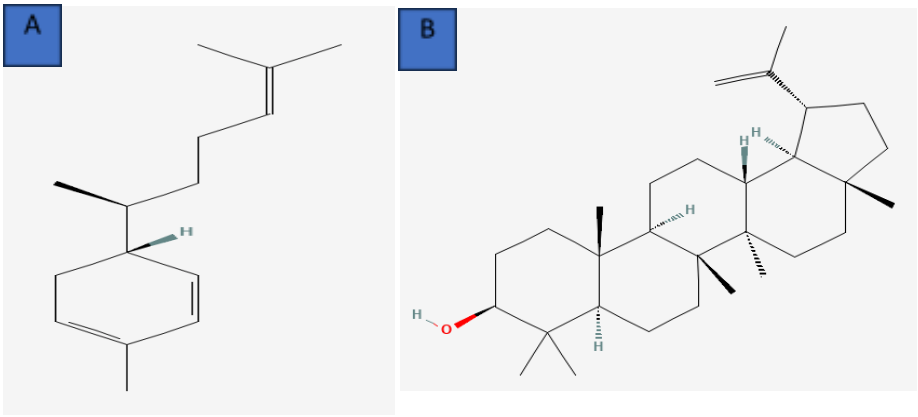


Fig. 8 Chemical structure of selected bioactive compounds in Terpenoids-A-Zingiberene,B-Lupeol

3.8. Volatile oils

Volatile oils are derived from specific parts of aromatic plants—such as buds, flowers, leaves, stems, seeds, berries, roots, wood, and bark—where they are stored in specialized cells or cavities [75]. These oils are widely used in perfumery, therapeutics, and the food industry due to their safety and broad biological activities. Preclinical studies demonstrate that volatile oils exhibit notable antitumor, anti-inflammatory, antioxidant, and antibacterial effects across various animal models and bioassays [76–79].Their strong antioxidant activity, mainly through free radical scavenging, contributes to potential benefits in managing cancers, neurodegenerative and cardiovascular diseases, and immune-related disorders [80]. Among the tested volatile oils, fennel (FEN) and cumin (CUMIN) showed

the strongest anti-inflammatory effects. Fennel exhibited the highest inhibition of fMLF/CB-induced superoxide anion production (IC50: 3.81 µg/ml), followed by cumin (IC50: 16.67 µg/ml) [81].

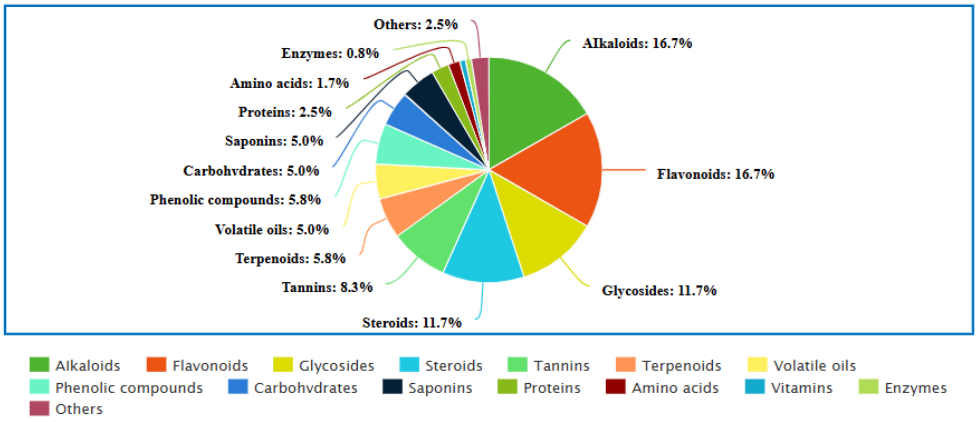


Fig. 9 The class of compounds with antiarthritic bioactivity in plant roots, rhizomes, fruits, barks and leaves

4. Conclusion

This review explores the in vivo antiarthritic potential of plant extracts derived from roots, rhizomes, fruits, barks, and leaves, tested primarily in adjuvant-induced arthritis (AIA) and collagen-induced arthritis (CIA) models in mice and rats. Evidence suggests that phytochemicals present in these plant parts—such as flavonoids, glycosides, steroids, phenols, alkaloids, tannins, phytosterols, and saponins—play a significant role in alleviating arthritic symptoms. Their mechanisms include reducing inflammation, lowering oxidative stress, easing joint swelling and pain, and modulating immune responses. Despite promising findings, there remains a notable gap in in vivo studies focusing on purified secondary metabolites, leaving these plant sources as an underexplored reservoir of potential therapeutic agents.The review identifies plant families such as Orchidaceae, Malvaceae, Euphorbiaceae, Cyperaceae, Solanaceae, and Zingiberaceae as particularly rich in bioactive compounds with antiarthritic properties. Interestingly, most existing research emphasizes aerial parts, while roots, rhizomes, fruits, barks, and leaves remain overlooked despite their pharmacological promise. This article is original, prepared solely for academic and informational purposes, without financial support or sponsorship. All contributors analyzed therapeutic potentials, integrated traditional knowledge with modern pharmacology, and approved the final manuscript. The findings underscore the untapped potential of diverse plant parts in developing novel antiarthritic therapies.

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