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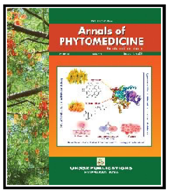

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Drynaria quercifolia (L.) J. Sm.: Phytochemicals, ethnomedicinal use, and therapeutic prospects of a medicinal epiphytic fern

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Abstract

Drynaria quercifolia (L.) J. Sm., a Polypodiaceae epiphytic fern, has received considerable ethnopharmacological attention owing to its frequent use in traditional medicine and complex profile of bioactive compounds. The review here attempts to summarize the existing scientific literature on the phytochemical profile and therapeutic potential of this fern, traditionally used in South and Southeast Asia for bone formation, cognitive stimulation, and therapeutic intervention of inflammatory disorders. Systematic identification of bioactive molecules like flavonoids (naringin, kaempferol), phenolic acids, tannins, glycosides, and terpenoids (β-sitosterol) is carried out in this review, along with the respective pharmacological actions, being critically assessed. The pharmacological properties, including neuroprotective, antioxidant, antimicrobial, osteogenic, hepatoprotective, and anti-inflammatory activities, have also been comprehensively reviewed with supporting evidence from preclinical studies. Apart from the mapping of potential therapeutic indications, the review identifies key gaps in existing knowledge, mainly towards the realization of molecular mechanisms and the establishment of clinical efficacy. The study promotes innovative methodological interventions like focused bioassays for the validation of traditional claims and expansion of therapeutic uses. This review integrates ethnobotanical knowledge with conventional scientific validation, highlighting *D. quercifolia* as a promising candidate for the development of natural product-based therapeutics within the framework of integrative medicine.

1. Introduction

Ferns are one of the oldest vascular plant groups and have existed for approximately 360 million years (Wolf *et al*., 1998). Presently, there are almost 12,000 species, and they are the second most diverse vascular plant group. This indicates how well they adapt to their environment (Nitta *et al*., 2022). The majority of ferns are epiphytes (approximately 75%), *i.e.,* they grow upon other plants and obtain their minerals from outside the soil, utilizing water and nutrients from the environment rather than touching the ground. Their position tall in the forest gives them benefits such as more access to light and less competition, as well as changing the environment of the plants they are growing on and the surrounding landscape.

Ferns or vascular cryptogams or free-living tracheophytes hold a special place in evolution between seedless plants and seed plants. They possess a system known as leptosporangiate, consisting of about 2,800 species, of which 10% are epiphytic. Of these, *Drynaria quercifolia* (L.) J. Sm., or oak-leaf fern, is significant because it has various uses in traditional medicine and holds promise for useful chemicals. The plant is in the Polypodiaceae family and possesses several specialized characteristics that enable it to survive on other plants, including possessing two forms of leaves, nesting leaves to trap nutrients, leafy structures to produce food from sunlight, and a dense, creeping root system (Aparna and Radhika, 2022; Mani *et al*., 2023). It naturally occurs in the Himalayan region, Northeast India, Southeast Asia, and northern Australia, and it thrives in wet, shaded areas where its specialized mechanisms enable it to survive.

D. quercifolia, a medicinally important epiphytic fern, has shown promise in the management of metabolic disorders. Animal studies have suggested that supplementation with plant extracts may exert antidiabetic effects, as evidenced by reductions in fasting blood glucose and glycated haemoglobin levels in diabetic models, highlighting its potential role in glycaemic regulation (Deepikakrishnaveni *et al*., 2024). Traditional medicine systems such as Ayurveda, Siddha, and other indigenous systems have been using the roots of *D. quercifolia* to treat bone fractures, inflammation, alopecia, respiratory disorders, and reproductive health ailments (Anuja *et al*., 2014) (Table 1). These applications form a significant component of local traditional healing practices, though there is a lack of extensive scientific evidence to support them. Phytochemical investigations have identified a wide

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array of bioactive constituents in the plant, including flavonoids such as naringin, kaempferol, rutin, and various C-glycosylated flavones as well as triterpenoids and sesquiterpenoids (Mani *et al.*, 2023; Modak *et al.*, 2021; Rajendran *et al.*, 2014). Recent pharmacological research has revealed that, in addition to its traditional applications, *D. quercifolia* holds future potential in the fields of neuroprotection, immunomodulation, and oncology, and is therefore a potential candidate for future evidence-based therapeutic applications. The present review aims to holistically synthesize the botanical, ethnomedicinal, phytochemical, and pharmacological information on *D. quercifolia*. It emphasizes new therapeutic avenues, points out existing research gaps, and suggests strategic areas of research to facilitate the scientific and medicinal development of this precious epiphytic fern.

Table 1: Summary of medicinal application of *D. quercifolia*

Medicinal application	Pharmacological activity	Study type/model	References
Wound healing	Accelerated tissue regeneration, anti-inflammatory	*In vitro* and *in vivo* studies	Padhy *et al.*, 2014
Neuroprotection (memory enhancement)	Antioxidant, anti-cholinesterase, neuroprotective	*In vitro* and *in vivo* studies	Ahn *et al.*, 2024
Bone regeneration (osteogenic)	Promotes osteoblast proliferation, calcium deposition	*In vitro* (osteoblast cell culture)	Poon *et al.*, 2011; Lei *et al.*, 2024
Anti-inflammatory	Inhibition of NO and pro-inflammatory cytokines	*In vitro* and *in vivo* studies	Modak *et al.*, 2021
Antioxidant	Scavenging of free radicals (DPPH, ABTS assays)	*In vitro*	Chaity *et al.*, 2016
Hepatoprotective	Restoration of liver enzymes, hepatocyte repair	*In vivo* (CCl_4-induced hepatotoxicity in rats)	Anuja *et al.*, 2018
Antimicrobial	Broad-spectrum activity	*In vitro* (agar well diffusion)	Kandhasamy *et al.*, 2008
Antidiabetic	Inhibits α-glucosidase, enhances insulin sensitivity	*In vivo* and *in vitro* studies	Prasanna *et al.*, 2019
Hair tonic/ traditional hair growth agent	Promotes follicle activity, improves hair texture	Ethnomedicinal reports	Prasanna and Anuradha, 2016

2. Botanical overview of *D. quercifolia*

2.1 Habit and habitat adaptation

D. quercifolia is a tropical epiphyte plant species that grows in a diverse range of areas, such as India, Malaysia, Indonesia, Southeast Asia, and northern Australia. The plant grows in shaded, humid conditions such as forest canopies, rocky crevices, and walls (Mani *et al.*, 2023). It is a soilless substrate grower, obtaining moisture and nutrients from atmospheric sources and the organic debris deposited around it (Aparna and Radhika, 2022). One of the physical adaptations of *D. quercifolia* is its dimorphic frond habit: nest fronds, which are sterile and used to trap moisture and detritus, and fertile foliage fronds that bear reproductive spores (Figure 1).

The plant has a creeping and fleshy rhizome, measuring up to 18 cm in length and 8 cm in width. It is reddish-brown scaled across its surface, which protects the plant from environmental stress and desiccation. This makes the plant store water efficiently in the canopy (Lubos and Amoroso, 2013). The plant propagates using spores, which are wind-borne and require specific conditions in the environment to grow and develop (Mazumder *et al.*, 2011). *D. quercifolia* also hosts a wide range of fungi at various times of the year, particularly during summer, contributing to the diversity of the canopies (Karamchand and Sridhar, 2009).

2.2 Microscopic and phytochemical insights into the rhizome

Microscopic observation of the rhizome reveals a wavy, thin outer cover consisting of tightly packed cells. In between is a thick inner cover and rectangular-shaped cells. Vascular bundles in the plant transport system are diverse, smaller on the periphery and larger, oval, or rounded towards the centre. The metaxylem, composed of thick walls up to 30 µm, the protoxylem, and the surrounding phloem constitute the vascular bundles. There are thin-walled cells containing stored nutrients and supportive bundles for ground tissue. The powder consists of spiral and reticulated xylem tracheids, hair-like structures, and scales. It is brownish, rough, and has a mild smell.

On analysis, the rhizome powder shows flavonoids, sterols, terpenoids, saponins, tannins, proteins, and carbohydrates. Alkaloids, glycosides, and fixed oils are not found. The physicochemical figures (9.93% total ash, 4.49% acid-insoluble ash, 6.96% water soluble ash, and 16.34% aqueous extractive yield) show that it is of good quality for its use (Korwar *et al.*, 2010). Structurally, the rhizome supports the plant, stores nutrients, and creates active substances. This makes it therapeutically and traditionally useful in the treatment of diseases like inflammation, metabolic disorders, infection, and degeneration (Janarthanan *et al.*, 2016).

3. Ethnopharmacological background

D. quercifolia or oak leaf fern, has been used for long periods in Asian traditional medicine to treat fractures, wounds, and inflammation. The current pharmacological research supports the ethnomedicinal properties of its rhizome, used in India, China, and Southeast Asia. Bioactive molecules, particularly flavonoids and terpenoids, display osteogenic, anti-inflammatory, antimicrobial, hepatoprotective, antioxidant, and wound-healing properties. The combination of ethnopharmacological information and contemporary studies supports the drug discovery potential and the value of the species for evidence-based medicine.

Figure 1: Morphological features of *D. quercifolia.*

3.1 Ayurvedic medicine

D. quercifolia, or Ashvakatri in Ayurvedic medicine, is valued for its Vata and Kapha dosha-controlling properties. It is usually utilized in decoctions, medicated oils, or powders, often in polyherbal combinations like Asthishrinkala and Lakshadi Guggulu (Nithin *et al*., 2020). In Asthi Bhagna (bone fracture), the rhizome promotes bone growth and healing (Raj *et al*., 2022). In Amavata (rheumatoid arthritis), it is combined with anti-inflammatory drugs and has exhibited a strong anti-inflammatory effect (Raj *et al*., 2022). In Kasa (chronic cough), *D. quercifolia* helps remove mucus and reduce respiratory inflammation, calming mucous membranes (Anuja *et al*., 2014).

3.2 Siddha medicine

In Tamil Siddha medicine, *Drynaria quercifolia* (Attukkal) is categorized based on taste (Suvai), nature (Thanmai), and bio-transformation (Pirivu), pointing to its therapeutic versatility. It is astringent (Thuvarppu) and bitter (Kaippu) in taste, drying and detoxifying in nature. Its hot nature (Veppam) is utilized to treat cold or dampness in the body. Its pungent bio-transformation (karppu pirivu) is a metabolic and digestive stimulant. *D. quercifolia* is utilized in the management of several diseases, including azhalkeelvayu (osteoarthritis), where it alleviates joint pain and rigidity (Wilson *et al*., 2007). In veppunoi (febrile diseases), its heat-releasing quality induces sweating and toxin expulsion (Meena and Ramaswamy, 2015). In peenisam (sinusitis), its astringency reduces mucus and inflammation (Wilson *et al*., 2007), and in vellai noi (leucorrhea), its properties correct excessive discharge (Meena and Ramaswamy, 2015). Synthesis of traditional knowledge of *D. quercifolia* with modern pharmacological confirmation is needed for scientific validation and therapeutic application (Kaliyaperumal *et al*., 2012).

3.3 Traditional chinese medicine (TCM)

D. quercifolia, or 'Li ye hu jue' in chinese medicine, is recognized for its significant medicinal value, especially in strengthening bones and muscles. The plant is used extensively to strengthen bones and tendons, relieve low back pain, treat sprain of ligaments, and treat wind dampness and musculoskeletal diseases (Shi *et al*., 2020; Wang *et al*., 2024). The rhizome is steamed alone or with medicines such as *Eucommia ulmoides* and *Cibotium barometz* to strengthen joints and relieve osteoporosis and arthritis (Lei *et al*., 2023). A decoction of 120 g a day may relieve alzheimer's and improve brain health. *D. quercifolia* has been used as a hair tonic for decades, either alone or combined with *Asparagus racemosus*, to feed hair, tighten the scalp, and prevent hair loss (Aparna and Radhika, 2022). It is used for other purposes, such as relieving toothache and gum bleeding, and repeated use strengthens the teeth. Traditionally, the rhizome relieves tinnitus and prepares tonics for the liver and kidney, which are essential in TCM (Chen *et al*., 2019). Additionally, applying a rhizome paste to the forehead is a popular remedy for headaches.

4. Indigenous and tribal medicinal applications

4.1 Western ghats tribal communities

The Toda, Kurumba, and Irula tribes of the Nilgiris Biosphere Reserve have been using *D. quercifolia* as a medicine for decades, showing their affection for nature. The fern is applied to cure chronic skin diseases, fungal infections, gum disease, male infertility, and nerve pain. The Kurumba tribe refers to its use in children's skin disease, typically associated with hygiene (Deepak and Gopal, 2014). There is little data on *D. quercifolia* for dental care, but it can cure mouth ulcers and oral issues when combined with other plants. It also enhances male fertility, though there are fewer studies on this. Its analgesic property cures headaches and nerve pain, as with other local treatments (Pradheeps and Poyyamoli, 2013). The tribes apply it in various forms, including fresh juice, Bhasma (ash process) for active molecules, and effective fermented extracts (Rangasamy *et al*., 2023). Though a traditional treatment, there is concern about losing this knowledge and plant populations as a result of modernization and habitat loss (Pradheeps and Poyyamoli, 2013).

4.2 Southeast Asian indigenous practices

D. quercifolia is employed generously in Southeast Asia, particularly Thailand, Malaysia, and Indonesia, for traditional medicine by indigenous populations. It assists in postpartum recovery and maternal health, utilizing herbal remedies such as extracts and pastes for the recovery of body and mind (Elter *et al*., 2016; Jaroenn-garmsamer *et al*., 2019). Rhizome is considered for the treatment of hepatobiliary diseases, owing to flavonoid and saponin content, yielding hepatoprotective activity. *D. quercifolia* is also helpful in diabetes management and its complications by normalizing blood glucose. It is found to have antimicrobial and anti-inflammatory activity, hence helpful in the treatment of various skin diseases and alopecia, frequently applied externally as a paste (Mani *et al*., 2023).

4.3 Northeast indian tribes

The Meghalaya Khasi, Garo, and Jaintia use *D. quercifolia* rhizome for various medicinal purposes, indicating their traditional knowledge. Ground rhizome is used on wounds to heal and guard against infection (Kumar *et al*., 2023). It also reduces swelling in arthritic joints (Das *et al*., 2022; Kalita, 2022) and acts as an antidote to snake and insect bites (Devi and Sinha, 2022). Decoction consumed internally aids in relieving congestion in the chest and keeping the respiratory system in good health (Kalita, 2022), and treats reproductive disorders, indicating its therapeutic versatility.

5. Phytochemical profile

D. quercifolia has vast therapeutic potential owing to the abundance of phytochemicals. Gas Chromatography-Mass Spectrometry (GC-MS) has detected significant bioactive compounds that augment its medicinally valuable properties. The plant contains various phytochemicals such as flavonoids, saponins, steroids, triterpenoids, phenolics, alkaloids, and tannins (Table 2). GC-MS analysis detected 38 compounds where dodecanoic acid possesses drug-like potential (Ragavan and Srinivasan, 2024), and ethanolic rhizome extracts contained 11 bioactives, where the most dominant was 2-myristynol-glycinamide (Nithin *et al*., 2020).

Table 2: Major compounds and health benefits of *D. quercifolia*

Phytochemical class	Compound name	Concentration / activity	Trigger biological activities	Mechanisms of action	References
Flavonoids	Naringin	IC_{50}: 76.5 µg/ml (DPPH)	Neuroprotective, antioxidant, anti-inflammatory	Neutralizes harmful free radicals, reduces inflammation by blocking the NF-κB pathway, and lowers levels of inflammatory cytokines (TNF-α, IL-1β). Helps regulate amyloid-beta, involved in brain disorders	Hussain *et al*., 2022; Santos-Buelga and Feliciano, 2017
	Kaempferol	Not specified	Antioxidant, anti-inflammatory, anticancer, antimicrobial	Boosts antioxidant enzyme activity (like SOD), blocks enzymes involved in inflammation, adjusts key signaling pathways linked to inflammation and induces apoptosis, cell cycle arrest	Hussain *et al*., 2024; Kaur *et al*., 2024; Kumar *et al.*, 2020; Periferakis *et al.*, 2022; Rajendran *et al.*, 2014; Roghan *et al*., 2024
	Rutin	Not specified	Vasoprotective, antioxidant, antidiabetic, hepatoprotective	Strengthens blood vessels, inhibits the α-glucosidase, slows down sugar absorption, and binds harmful metal ions	AEh and Chiriapkin, 2023; Iriti *et al*., 2023; Madkour *et al*., 2024; Pandey *et al*., 2022; Talukder *et al*., 2024
	Quercetin	ORAC: 14.3 µmol TE/g	Antioxidant, anti-inflammatory, antiallergic, antiproliferative	Prevents fat oxidation damage, modulating the Th1/Th2 immune balance & reducing antigen-specific IgE production, and blocks cell survival pathways	Kumar and Ponpandian, 2022; Jafarinia *et al*., 2020; Mlcek *et al*., 2016; Nweze *et al*., 2022; Park *et al*., 2019
	C-glycosylated flavones	Not specified	CNS-active, antihyperglycemic, Photoprotective	Exhibits anxiolytic and CNS modulatory effects, stable in the body for longer action, prevents breakdown of complex sugars	Courts and Williamson, 2015; Tremmel *et al*., 2021; Vanegas *et al*., 2018; Xiao *et al*., 2016
Triterpenoids	Friedelin	0.42-0.78 mg/g	Anti-inflammatory, hepatoprotective	Not specified	Ghosh, 2020
	β-Amyrin	0.35-0.63 mg/g	Antinociceptive, gastroprotective	Not specified	Ghosh, 2020
	Oleanolic acid	0.28-0.49 mg/g	Hepatoprotective, anti-inflammatory	Not specified	Kamran *et al*., 2022
	Ursolic acid	0.31-0.54 mg/g	Antimicrobial, anticancer	Not specified	Câmara *et al*., 2024

Diterpenoids	Labdane-type	Not specified	Antimicrobial, cytotoxic, anti-inflammatory, anticancer	Blocks inflammation-related signaling, promotes cancer cell death, and counters drug resistance	Bandyopadhyay and Gonzalez, 2020; Banu, 2024; Hortelano, 2009
	Clerodane-type	Not specified	Anticancer, anti-inflammatory	Inhibits pro-inflammatory mediators such as COX-2, TNF-α, IL-6	Martínez-Casares *et al.*, 2023; Modak *et al.*, 2021
Sesquiterpenoids	Drynaria lactones	Not specified	Cytotoxic (anticancer potential)	Targeting apoptosis pathway	Jagatheeswari and Prasanna, 2023
	Caryophyllene derivatives	Not specified	Anti-inflammatory, analgesic	Reduces inflammation throughout the body	Anuja *et al.*, 2014; Raj *et al.*, 2022
Phenolic acids (hydroxycinnamic)	Chlorogenic acid	3.5-5.4 mg/g; TEAC: 1.3-1.9 mmol/g	Antioxidant	Neutralizes harmful free radicals	Bialecka-Florjanczyk *et al.*, 2018
	Ferulic acid	2.1-3.8 mg/g	Antioxidant	Protects cells from oxidative stress	Bialecka-Florjanczyk *et al.*, 2018
	Caffeic acid	1.8-3.2 mg/g	Antioxidant	Prevents damage to cell membranes	Bialecka-Florjanczyk *et al.*, 2018
	p-Coumaric acid	1.2-2.5 mg/g	Antioxidant	Reduces oxidative damage	Bialecka-Florjanczyk *et al.*, 2018
Phenolic acids (hydroxybenzoic)	Gallic acid	2.7-4.6 mg/g; MIC: 125–250 μg/ml	Antioxidant, antimicrobial	Cleans up reactive oxygen species; Kills microbes by damaging their cell walls	Sehrawat *et al.*, 2022
	Protocatechuic acid	1.4-2.3 mg/g	Antioxidant	Maintains a balance of oxidants and antioxidants	Sehrawat *et al.*, 2022
	Syringic acid	0.8-1.7 mg/g	Antioxidant	Enhances the body's natural antioxidants	Sehrawat *et al.*, 2022
Tannins	Condensed and Hhdrolyzable tannins	Not quantified	Astringent, wound healing, antidiabetic	Binds to proteins to prevent their activity, an antioxidant, and is an antibacterial	De Bruyne *et al.*, 1999; Bors *et al.*, 2001; Smeriglio *et al.*, 2017
Glycosides	Cardiac glycosides	Not specified	Cardiotonic, antiarrhythmic	Alters ion balance to support heart function, strengthens heart muscle contractions	Akera and Brody, 1989; Bacinschi *et al.*, 2024
Sterols	β-sitosterol, Campesterol, Stigmasterol	Not specified	Cardioprotective, hypocholesterolemic	Regulates fat metabolism and immune responses	Makarevich *et al.*, 1999
Alkaloids	Pyrrolidine, Indole, Isoquinoline types	Not specified	Neuroprotective, CNS modulating	Affects brain signals	Radenkova-Saeva and Atanasov, 2014

6. Emerging role of *D. quercifolia* in neuropharmacology

6.1 Naringin and CNS disorders

D. quercifolia, represents a significant natural source of naringin, containing substantially higher concentrations (15-22 mg/g dry weight) than many other plant sources, including medicinal ferns. This elevated naringin content contributes substantially to the fern's neuroprotective properties and traditional applications in cognitive disorders. Recent studies indicate that extracts of *D. quercifolia* demonstrate neuroprotective properties comparable to those of isolated naringin. These effects include the reduction of β-amyloid plaque accumulation, mitigation of oxidative damage in neuronal tissues, and the regulation of key neurotransmitter systems, highlighting its potential therapeutic role in neurodegenerative conditions (Choi *et al*., 2023; Poudineh *et al*., 2022).

The synergistic action of naringin with other bioactive compounds present in *D. quercifolia*, particularly C-glycosylated flavones and specific triterpenoids, may enhance its neuroprotective efficacy beyond that of naringin alone (Singh and Kumar Singh, 2024). Traditional knowledge across various Asian medical systems has long utilized this fern for memory enhancement and neurological conditions, providing ethnopharmacological validation for modern research findings (Yazdani *et al*., 2024). The ability of *D. quercifolia* extracts to modulate neurotransmitter balance, similar to isolated naringin, further supports its potential applications in mood disorders and neurodegenerative conditions (Mishra *et al*., 2024).

6.2 Proposed mechanisms of neuroprotection

D. quercifolia demonstrates multifaceted neuroprotective mechanisms that collectively contribute to its potential therapeutic applications in neurodegenerative disorders. The fern exerts moderate cholinesterase inhibition, with naringin and related flavonoids showing significant acetylcholinesterase inhibitory properties that help maintain cholinergic signalling critical for cognitive function (Cichon *et al*., 2024; Liu *et al*., 2020). Its potent antioxidant defence mechanisms include enhancement of endogenous antioxidant enzymes and preservation of glutathione levels, with studies demonstrating significant reduction in malondialdehyde (MDA) levels, indicating effective protection against oxidative stress (Ferdous *et al*., 2024).

A key mechanism involves the upregulation of brain-derived neurotrophic factor (BDNF), which promotes neurogenesis and synaptic plasticity essential for maintaining cognitive function and preventing neurodegeneration (Shoaib *et al*., 2023). The anti-inflammatory properties of *D. quercifolia* are particularly noteworthy, as it reduces microglial activation and decreases pro-inflammatory cytokine production, addressing the neuroinflammatory component of neurodegenerative pathology (Das *et al*., 2020). Additionally, the fern's ability to stabilize mitochondrial membrane potential, prevent cytochrome c release, and enhance ATP production in challenged neurons supports mitochondrial preservation, a crucial factor in preventing neuronal damage and maintaining cellular energy homeostasis (Shoaib *et al*., 2023).

7. Unexplored immunomodulatory and anticancer potential

7.1 Immune modulation prospects

D. quercifolia possesses remarkable immunomodulatory properties through its rich flavonoid content, particularly naringin, which exerts multifaceted effects on the immune system. Studies have demonstrated its potent ability to reduce pro-inflammatory Tumor Necrosis Factor alpha (TNF-α) production in macrophages by 58% through NF-κB pathway suppression, a critical mechanism for controlling inflammatory cascades (Leyva-López *et al*., 2016; Pavlova *et al*., 2016). Concurrently, naringin interferes with STAT3 phosphorylation to downregulate Interleukin-6 (IL-6) secretion from activated immune cells, targeting another key pathway in chronic inflammatory conditions (Leyva-López *et al*., 2016).

The immunomodulatory versatility of *D. quercifolia* extends to upregulating anti-inflammatory Interleukin-10 (IL-10) production, with peak effects observed at 75 µM concentration, operating through the PPAR-γ pathway to establish a balanced immune response (Martínez *et al*., 2019). Beyond cytokine modulation, the polysaccharide fraction of *D. quercifolia* significantly enhances innate immunity by increasing macrophage phagocytic activity by 75% and stimulating nitric oxide production, while simultaneously supporting adaptive immunity through T-cell proliferation and B-cell activation (Cruz *et al*., 2022). Additionally, the fern augments natural killer (NK) cell cytotoxicity against cancer cells by 42%, suggesting potential applications in cancer immunotherapy (Middleton Jr and Kandaswami, 1993).

7.2 Anticancer potential

D. quercifolia demonstrates significant anti-cancer potential through various mechanisms, including cytotoxicity against cancer cells and inhibition of angiogenesis and metastasis. Its bioactive compounds, such as naringin, kaempferol, and rutin, play crucial roles in its anti-cancer effects. The plant's cytotoxicity is evident with IC_{50} values ranging from 62.3 µg/ml (MCF-7 breast) to 104.2 µg/ml (A549 lung), showcasing its effectiveness compared to conventional drugs like cisplatin and doxorubicin (Hidayah *et al*., 2023).

D. quercifolia activates the p53 pathway, promoting cell senescence and apoptosis, and modulates the Bcl-2 family to regulate pro-apoptotic proteins (Hidayah, 2023). It also triggers apoptosis via caspase activation and ROS generation, leading to mitochondrial dysfunction (Biswas *et al*., 2022). Additionally, it causes G2/M phase arrest, inhibiting cancer cell proliferation. The plant's antiangiogenic effects include reducing Vascular Endothelial Growth Factor (VEGF) expression and preventing cancer cell migration, thus hindering metastasis. Naringin, kaempferol, and rutin contribute to these effects by inducing apoptosis, arresting the cell cycle, generating ROS, and reducing angiogenesis in various cancer types (Hidayah *et al*., 2023).

7.3 *Insilico* studies

Insilico analysis of naringenin and its O-alkyl derivatives, such as isosakuranetin and 5-O-methylnaringenin, reveals their promising potential as therapeutic agents targeting estrogen receptor-α (ERα), particularly in breast cancer treatment. Molecular docking studies show strong binding interactions between these compounds and ERα (PDB ID: 6VJD), with binding energies ranging from -5.49 to -11.05 kcal/mol, suggesting effective inhibition of ERα signalling pathways that drive breast cancer progression (Joseph and Gupta, 2024) (Muralidharan *et al*., 2022). In addition, the pharmacokinetic properties of these compounds, assessed through Swiss ADME, indicate favourable characteristics such as high absorption rates, water solubility, and the capacity to cross the blood-brain barrier, enhancing their therapeutic scope beyond breast cancer (Joseph and Gupta, 2024).

Moreover, compliance with Lipinski's rule of five further supports their suitability for development as drug candidates. Beyond their effects on ERα, Naringenin and its derivatives exhibit additional mechanisms of action, including the modulation of cholesterol metabolism and the inhibition of key proteins involved in cancer pathways, such as Akt1 and EGFR, reinforcing their potential as multi-target anticancer agents (Muralidharan *et al*., 2022; Pallottini *et al*., 2022). However, attention is necessary due to the complexity of ERα interactions with various ligands, including endocrine disruptors, which could lead to unintended biological effects, emphasizing the need for careful evaluation in therapeutic applications (Sellami *et al*., 2021).

8. Conclusion

As noted by Sibi *et al*. (2024), the Drug Controller General of India is moving toward providing naturally derived medicines with regulatory status equivalent to that of synthetic, compound based pharmaceuticals is an important step in validating and integrating traditional remedies into mainstream healthcare. *D. quercifolia* demonstrates significant pharmacological promise due to its diverse phytochemical composition and broad spectrum biological activities. Although traditional uses are well documented, gaps remain in clinical validation, pharmacokinetics, and standardized therapeutic development. Bridging traditional knowledge with modern scientific approaches will be essential to reposition *D. quercifolia* as a novel source for evidence based therapeutics, particularly in neurodegenerative diseases, cancer, and immune disorders.

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Conflict of interest

The authors declare no conflict of interest relevant to this article.

References

AEh, B. and Chiriapkin, A. (2023). Review of the biological activity of rutin: Antidiabetic, antioxidant, anti-inflammatory and antitumor. Bulletin of Science and Practice, **9**(8):48-57. https://doi.org/10.33619/2414-2948/93/05

Ahn, J. S.; Lee, C. H.; Liu, X.Q.; Hwang, K. W.; Oh, M. H.; Park, S.Y. and Whang, W. K. (2024). Neuroprotective effects of phenolic constituents from drynariae rhizoma. Pharmaceuticals, **17**(8):1061. https://doi.org/10.3390/ph17081061

Akera, T. and Brody, T. M. (1989). Pharmacology of cardiac glycosides. In Physiology and Pathophysiology of the Heart (pp:453-469). Springer. https://doi.org/10.1007/978-1-4613-0873-7-21

Anuja, G.; Latha, P.; Shine, V.; Suja, S. and Rajasekharan, S. (2014). Evaluation of *Drynaria quercifolia*, a medicinal pteridophyte for anti-nociceptive, antiallergic, antilipidperoxidative properties and detection of heavy Metal. Content. Am. J. Exp. Biol., 1(2):85-102.

Anuja, G.; Shine, V.; Latha, P. and Suja, S. (2018). Protective effect of ethyl acetate fraction of *Drynaria quercifolia* against CCl4 induced rat liver fibrosis *via* Nrf2/ARE and NFκB signalling pathway. Journal of Ethnopharmacology, 216:79-88. https://doi.org/10.1016/j.jep.2017.11.015

Aparna, G. and Radhika, C. (2022). *Drynaria quercifolia* Linn. J. smith: A review on ethnomedicinal uses and phytochemical constituents. Kerala Journal of Ayurveda, 1(2). https://doi.org/10.55718/kja.120

Bacinschi, N.; Nica, L.; Rakovskaia, T.; Guu, I. and Caraca', A. (2024). Glicozidele cardiace-trecut, prezent, viitor. Farmacist, 216(1):112-122.

Bandyopadhyay, D. and Gonzalez, F. (2020). Anticancer agents from natural sources. In: Promising drug molecules of natural origin (pp. 83-162). Apple Academic Press. https://doi.org/10.1201/9781003010395-7

Bialecka-Florjañczyk, E.; Fabiszewska, A. and Zieniuk, B. (2018). Phenolic acids derivatives-biotechnological methods of synthesis and bioactivity. Current Pharmaceutical Biotechnology, 19(14):1098-1113. https://doi.org/10.2174/1389201020666181217142051

Biswas, P.; Dey, D.; Biswas, P. K.; Rahaman, T. I.; Saha, S.; Parvez, A.; Khan, D. A.; Lily, N. J.; Saha, K. and Sohel, M. (2022). A comprehensive analysis and anti-cancer activities of quercetin in ROS-mediated cancer and cancer stem cells. International Journal of Molecular Sciences, 23(19):11746. https://doi.org/10.3390/ijms231911746

Bors, W.; Foo, L. Y.; Hertkorn, N.; Michel, C. and Stettmaier, K. (2001). Chemical studies of proanthocyanidins and hydrolyzable tannins. Antioxidants and Redox Signaling, 3(6):995-1008. https://doi.org/10.1089/15230860131720353

Câmara, J. S.; Perestrelo, R.; Ferreira, R.; Berenguer, C. V.; Pereira, J. A. and Castilho, P. C. (2024). Plant-derived terpenoids: A plethora of bioactive compounds with several health functions and industrial applications: A comprehensive overview. Molecules, 29(16):3861. https://doi.org/10.3390/molecules29163861

Chaity, F. R.; Khatun, M. and Rahman, M. S. (2016). *In vitro* membrane stabilizing, thrombolytic and antioxidant potentials of *Drynaria quercifolia* L., a remedial plant of the Garo tribal people of Bangladesh. BMC complementary and alternative medicine, 16:1-9.

Chen, Y.; Yu, R.; Jiang, L.; Zhang, Q.; Li, B.; Liu, H. and Xu, G. (2019). A comprehensive and rapid quality evaluation method of traditional Chinese medicine decoction by integrating UPLC-QTOF-MS and UFLC-QQQ-MS and its application. Molecules, 24(2):374. https://doi.org/10.3390/molecules24020374

Choi, G.Y.; Kim, H.B.; Hwang, E.S.; Park, H.S.; Cho, J.M.; Ham, Y.K.; Kim, J.H.; Mun, M.K.; Maeng, S. and Park, J.H. (2023). Naringin enhances long-term potentiation and recovers learning and memory deficits of amyloid-beta induced Alzheimer's disease-like behavioral rat model. Neurotoxicology, 95:35-45. https://doi.org/10.1016/j.neuro.2022.12.007

Cichon, N.; Grabowska, W.; Gorniak, L.; Stela, M.; Harmata, P.; Ceremuga, M. and Bijak, M. (2024). Mechanistic and therapeutic insights into flavonoid-based inhibition of acetylcholinesterase: Implications for Neurodegenerative Diseases. Nutrients, 17(1):78. https://doi.org/10.3390/nu17010078

Courts, F. L. and Williamson, G. (2015). The occurrence, fate and biological activities of C-glycosyl flavonoids in the human diet. Critical Reviews in Food Science and Nutrition, 55(10):1352-1367. https://doi.org/10.1080/10408398.2012.694497

Cruz, R. C.; Sheashea, M.; Farag, M. A.; Sangwan, N. S. and Modolo, L. V. (2022). Insights into the Modulation of Immune Response, Chemistry, and Mechanisms of Action of Immunomodulatory Phytomolecules. In Plants and Phytomolecules for Immunomodulation: Recent Trends and Advances (pp. 33-51). Springer. https://doi.org/10.1007/978-981-16-8117-2_2

Das, G.; Thou, K.; Mondal, P. and Meeran, S. M. (2022). Ethnomedicinal plants used for wound healing and dermatological problem in the North-Eastern Hill Region of India. Asian Journal of Ethnobiology, 5(2). https://doi.org/10.13057/asianjethnobiol/y050204

Das, S.; Nahar, L.; Nath, R.; Nath, D.; Sarker, S. D. and Talukdar, A. D. (2020). Neuroprotective natural products. In: Annual Reports in Medicinal Chemistry, 55:179-206. https://doi.org/10.1016/bs.armc.20 20.02.009

De Bruyne, T.; Pieters, L.; Dommisse, R.; Kolodziej, H.; Wray, V.; Vanden Berghe, D. and Vlietinck, A. (1999). NMR characterization and biological evaluation of proanthocyanidins: A systematic approach. Plant Polyphenols 2: Chemistry, Biology, Pharmacology, Ecology, 193-209. https://doi.org/10.1007/978-1-4615-4139-4_10

Deepak, P. and Gopal, G. (2014). Ethnomedicinal practices of Kurumba tribes, Niligiri district, Tamil Nadu, India, in treating skin diseases. Global Journal of Research on Medicinal Plants and Indigenous Medicine, 3(1):8.

Devi, S. and Sinha, R. (2022). Northeast India: A treasury of medicinal plants. Emergent Life Sciences Research, 8:5-21. https://doi.org/10.31783/elsr.2022.810521

Elter, P. T.; Kennedy, H. P.; Chesla, C. A. and Yimyam, S. (2016). Spiritual healing practices among rural postpartum Thai women. Journal of Transcultural Nursing, 27(3):249-255. https://doi.org/10.1177/104365961455351

Ferdous, R.; Islam, M. B.; Al-Amin, M. Y.; Dey, A. K.; Mondal, M. O. A.; Islam, M. N.; Alam, A. K.; Rahman, A. A. and Sadik, M. G. (2024). Anticholinesterase and antioxidant activity of *Drynaria quercifolia* and its ameliorative effect in scopolamine-induced memory impairment in mice. Journal of Ethnopharmacology, 319:117095.https://doi.org/10.1016/j.jep.2023.117095

Ghosh, S. (2020). Triterpenoids: structural diversity, biosynthetic pathway, and bioactivity. Studies in Natural Products Chemistry, 67:411-461. https://doi.org/10.1016/B978-0-12-819483-6.00012-6

Hidayah, H.; Widyaningsih, A.; Pangestu, A. D. and Dewi, S. R. (2023). Literatur riview: Flavonoid activity as an anticancer compound. MAHESA: Malahayati Health Student Journal, 3(5):1255-1263.

Hortelano, S. (2009). Molecular basis of the anti-inflammatory effects of terpenoids. Inflammation and Allergy-Drug Targets (Formerly Current Drug Targets-Inflammation and Allergy)(Discontinued), 8(1):28-39.https://doi.org/10.2174/187152809787582534

Hussain, M. S.; Altamimi, A. S. A.; Afzal, M.; Almalki, W. H.; Kazmi, I.; Alzarea, S. I.; Gupta, G.; Shahwan, M.; Kukreti, N. and Wong, L. S. (2024). Kaempferol: Paving the path for advanced treatments in ageing-related diseases. Experimental Gerontology, 188:112389.https://doi.org/10.1016/j.exger.2024.112389

Hussain, S.; Mirza, W.; Murtaza, M.; Nazir, A.; Hanif, I. and Ahmad, M. (2022). Sources and chemistry of flavonoids: An overview of their biological and therapeutic potential. Scientific Inquiry and Review, **6**(2):32-58. https://doi.org/10.32350/sir.62.03

Iriti, M.; Varoni, E. M. and Vitalini, S. (2023). Bioactive compounds in health and disease-focus on rutin. Bioactive Compounds in Health and Disease-Online ISSN: 2574-0334; Print ISSN: 2769-2426, **6**(10):235-242. https://doi.org/10.31989/bchd.v6i10.1145

Jafarinia, M.; Sadat Hosseini, M.; Kasiri, N.; Fazel, N.; Fathi, F.; Ganjalikhani Hakemi, M. and Eskandari, N. (2020). Quercetin with the potential effect on allergic diseases. Allergy, Asthma and Clinical Immunology, **16**:1-11. https://doi.org/10.1186/s13223-020-00434-0

Jagatheeswari, R. and Prasanna, G. (2023). Evaluation of analgesic property of *Drynaria quercifolia* rhizome extract. Uttar Pradesh Journal of Zoology, **44**(21):171-177. https://doi.org/10.56557/upjoz/2023/v44i213684

Janarthanan, L.; Balakrishnan, B.; Jayakar, B.; Senthilkumar, K. and Anadharaj, G. (2016). Pharmacognostical standardization and phytochemical profile of rhizomes of *Drynaria quercifolia* (Linn) J. Smith. Eur. J. Biomed. Pharm. Sci., **3**:278-287.

Jaroenngarmsamer, P.; Ounprasertsuk, J.; Krutchangthong, P. and Dumklieng, W. (2019). Herbal, postpartum care in Thai traditional medicine. International Academic Multidisciplinary Research Conference In London 2019.

Joseph, P. and Gupta, J. (2024). *In silico* analysis of naringenin and its O-alkyl derivatives for its potential binding with estrogen receptor-á. Research Journal of Biotechnology. https://doi.org/10.25303/1909rjbt063071

Kalita, T. (2022). Traditionally used herbal remedies by the indigenous tribes of Meghalaya: A review. Current Research Journal of Pharmaceutical and Allied Sciences, **5**(1):1-14. https://doi.org/10.54059/2022.5(1)crjpas_210

Kaliyaperumal, K.; Kaliyaperumal, J.; Jerome, X.; Jayaraman, V. and Luke, M. (2012). Tamil traditional medicinal system-siddha: An indigenous health practice in the international perspectives. CellMed, **2**(2):12-12.

Kamran, S.; Sinniah, A.; Abdulghani, M. A. and Alshawsh, M. A. (2022). Therapeutic potential of certain terpenoids as anticancer agents: A scoping review. Cancers, **14**(5):1100. https://doi.org/10.3390/cancers14051100

Kandhasamy, M.; Arunachalam, K. and Thatheyus, A. (2008). *Drynaria quercifolia* (L.) J. Sm: A potential resource for antibacterial activity. African Journal of Microbiology Research, **2**:202-205.

Karamchand, K. S. and Sridhar, K. R. (2009). Association of water-borne conidial fungi with epiphytic tree fern [*Drynaria quercifolia*]. Acta Mycologica, **44**(1):19-27.

Kaur, S.; Mendonca, P. and Soliman, K. F. (2024). The anticancer effects and therapeutic potential of kaempferol in triple-negative breast cancer. Nutrients, **16**(15):2392. https://doi.org/10.3390/nu1615 2392

Korwar, P. G.; Beknal, A. K.; Patil, B. S.; Halkai, M.; Kulkarni, U.; Hariprasanna, R. and Soodam, S. R. (2010). A study on phytochemical investigation of *Drynaria quercifolia* Linn rhizome. Int. J. Pharm. Sci. Res. (IJPSR), **1**(12):148-158.

Kumar, K. A.; Ramu, R.; Chandan, S. and Puttaiah, S. H. (2020). Kaempferol: A dietary flavonoid isolated from blepharis integrifolia. Pharmacognosy Research, **12**(3). https://doi.org/10.4103/pr.pr_1 14_19

Kumar, S.; Kushari, S.; Sarma, H. and Laloo, D. (2023). Exploring the traditional system of medicine with special emphasis on the indigenous practice of herbal remedy by the Tribals of North-East India. Practice and Re-emergence of Herbal Medicine, **1**:1.

Kumar, S. R. and Ponpandian, N. (2022). Quercetin bioflavonoids derived from phytomedicinal compounds for targeted drug delivery and their antioxidant properties. In: Nanophytomedicine (pp: 221-234). CRC Press.

Lei, S. S.; Huang, X. W.; Li, L. Z.; Wang, X. P.; Zhang, Y.; Li, B. and Shou, D. (2024). Explorating the mechanism of Epimedii folium-Rhizoma drynariae herbal pair promoted bone defects healing through network pharmacology and experimental studies. Journal of Ethnopharmacology, **319**:117329. https://doi.org/10.1016/j.jep.2023.117329

Leyva-López, N.; Gutierrez-Grijalva, E. P.; Ambriz-Perez, D. L. and Heredia, J. B. (2016). Flavonoids as cytokine modulators: A possible therapy for inflammation related diseases. International Journal of Molecular Sciences, **17**(6):921. https://doi.org/10.3390/ijms17060921

Liu, M.-Y.; Zeng, F.; Shen, Y.; Wang, Y.-Y.; Zhang, N. and Geng, F. (2020). Bioguided isolation and structure identification of acetylcholinesterase enzyme inhibitors from drynariae rhizome. Journal of Analytical Methods in Chemistry, **2020**(1):2971841. https://doi.org/10.1155/2020/2971841

Lubos, L. C. and Amoroso, V. B. (2013). The identity and morphology of the three species of Drynaria (Polypodiaceae) in Bukidnon, Philippines. Asian Journal 0f Biodiversity, **2**(1). http://dx.doi.org/10.7828/ajob.v2i1.91

Madkour, D. A.; Ahmed, M.; Elkirdasy, A. F.; Orabi, S. H. and Mousa, A. A. (2024). Rutin: Chemical properties, pharmacokinetic properties and biological activities. Matrouh Journal of Veterinary Medicine, **4**(1):26-34. https://doi.org/10.21608/mjvm.2024.341806

Makarevich, I.; Kovalev, S.; Slyusarskaya, T. and Zhernoklev, K. (1999). Cardiac glycosides of *Erysimum leptophyllum*. Chemistry of Natural Compounds, **35**(4):473-474. https://doi.org/10.1007/BF02282524

Mani, K.; Aiyalu, R.; Thiruvengadarajan, V.; Arivukkarasu, R. and Suriyapriya, K. (2023). A comprehensive review of *Drynaria quercifolia* (L.) J. Sm. Pharmacognosy Reviews, **17**(34). https://doi.org/10.5530/phrev.2023.17.12

Martínez-Casares, R. M.; Hernández-Vázquez, L.; Mandujano, A.; Sánchez-Pérez, L.; Pérez-Gutiérrez, S. and Pérez-Ramos, J. (2023). Anti-inflammatory and cytotoxic activities of clerodane-type diterpenes. Molecules, **28**(12):4744. https://doi.org/10.3390/molecules28124744

Martínez, G.; Mijares, M. R. and De Sanctis, J. B. (2019). Effects of flavonoids and its derivatives on immune cell responses. Recent Patents on Inflammation and Allergy Drug Discovery, **13**(2):84-104. https://doi.org/10.2174/1872213X13666190426164124

Mazumder, P.; Mazumder, B.; Dutta Choudhury, M. and Sharma, G. (2011). *In vitro* Propagation of *Drynaria quercifolia* (L.) J. Sm., a Medicinal Fern. Assam University Journal of Science and Technology, **7**(1):79-83.

Meena, R. and Ramaswamy, R. (2015). Therapeutic potency of a Siddha formulation Kandhaga Rasayanam: A review. International Journal of Research in Ayurveda and Pharmacy (IJRAP), **6**(1):58-64 http://www.ijrap.net/admin/php/uploads/1300_pdf.pdf

Middleton Jr, E. and Kandaswami, C. (1993). Plant flavonoid modulation of immune and inflammatory cell functions. In: Nutrition and Immunology (pp: 239-266). Springer. https://doi.org/10.1007/978-1-4615-2900-2_12

Mishra, V. H.; Khade, A. and Noman, O. (2024). Drug effects on the nervous system: Mechanisms and future directions in neuro-pharmacological therapy. Advances in Human Biology, **10**:4103. https://doi.org/10.4103/aihb.aihb_166_24

Mlcek, J.; Jurikova, T.; Skrovankova, S. and Sochor, J. (2016). Quercetin and its antiallergic immune response. Molecules, 21(5):623. https://doi.org/10.3390/molecules21050623

Modak, D.; Paul, S.; Sarkar, S.; Thakur, S. and Bhattacharjee, S. (2021). Validating potent anti-inflammatory and antirheumatoid properties of *Drynaria quercifolia* rhizome methanolic extract through *in vitro*, *in vivo*, *in silico* and GC-MS-based profiling. BMC Complementary medicine and therapies, 21:1-20. https://doi.org/10.1186/s12906-021-03265-7

Muralidharan, S.; Velanganni, A. A. J. and Shanmugam, K. (2022). Inhibition of breast cancer proteins by the flavonoid naringenin and its derivative: A molecular docking study. Journal of Natural Remedies, pp:51-64. https://doi.org/10.18311/jnr/2022/28194

Nithin, M.; Veeramani, G. and Sivakrishnan, S. (2020). Phytochemical screening and GC-MS analysis of rhizome of *Drynaria quercifolia*. Research Journal of Pharmacy and Technology, 13(5):2266-2268. https://doi.org/10.5958/0974-360X.2020.00408.4

Nitta, J. H.; Schuettpelz, E.; Ramírez-Barahona, S. and Iwasaki, W. (2022). An open and continuously updated fern tree of life. Frontiers in Plant Science, 13:909768. https://doi.org/10.3389/fpls.2022.909768

Nweze, C. C.; Tsea, W. and Ekpe, I. P. (2022). Anti-inflammatory properties of quercetin: A review. Journal of Drug Delivery and Therapeutics, 12(4). https://doi.org/10.22270/jddt.v12i4.5453

Padhy, R.; Dash, S. K.; Patra, S. and Patro, S. K. (2014). Studies on healing activity Vis-à-vis microflora of acute induced wounds against solvent extracts of rhizome of *Drynaria quercifolia* Linn. Journal of Pharmacy and Biological Sciences, 9(5):38-49.

Pallottini, V.; Segatto, M.; Acconcia, F.; Fiocchetti, M. and Marino, M. (2022). Mechanism underlying naringenin hypocholesterolemic effects: involvement of estrogen receptor α subtype. International Journal of Molecular Sciences, 23(24):15809. https://doi.org/10.3390/ijms232415809

Pandey, A.; Kumar, R.; Mishra, A.; Pandey, A. and Pandey, A. K. (2022). Recent updates on the pharmacological potential of plant-based rutin. Current Nutraceuticals, 3(2):24-33.

Park, S.; Lim, W.; Bazer, F. W.; Whang, K.-Y. and Song, G. (2019). Quercetin inhibits proliferation of endometriosis regulating cyclin D1 and its target micro RNAs *in vitro* and *in vivo*. The Journal of Nutritional Biochemistry, 63:87-100. https://doi.org/10.1016/j.jnutbio.2018.09.024

Pavlova, S.; Albegova, D.; Vorob'eva, Y. S.; Laptev, O. and Kozlov, I. (2016). Flavonoids as potential immunosuppressants affecting intracellular signaling pathways (a review). Pharmaceutical Chemistry Journal, 49:645-652. https://doi.org/10.1007/s11094-016-1345-x

Periferakis, A.; Periferakis, K.; Badarau, I. A.; Petran, E. M.; Popa, D. C.; Caruntu, A.; Costache, R. S.; Scheau, C.; Caruntu, C. and Costache, D. O. (2022). Kaempferol: Antimicrobial properties, sources, clinical, and traditional applications. International Journal of Molecular Sciences, 23(23):15054. https://doi.org/10.3390/ijms232315054

Poon, C.; Abas, W.; Kim, K. and Pingguan-Murphy, B. (2011). Effect of herbal extracts on rat bone marrow stromal cells (BMSCs) derived osteoblast–preliminary result. 5th Kuala Lumpur International Conference on Biomedical Engineering 2011: (BIOMED 2011) 20-23 June 2011, Kuala Lumpur, Malaysia. https://doi.org/10.1007/978-3-642-21729-6_200

Poudineh, M.; Ghotbi, T.; Azizi, F.; Karami, N.; Zolfaghari, Z.; Gheisari, F.; Hormozi, M. and Poudineh, S. (2022). Neuropharmaceutical properties of naringin against Alzheimer's and Parkinson's diseases: Naringin protection against AD and PD. Galen Medical Journal, 11:e2337. https://doi.org/10.31661/gmj.v11i.2337

Pradheeps, M. and Poyyamoli, G. (2013). Ethnobotany and utilization of plant resources in Irula villages (Sigur plateau, Nilgiri Biosphere Reserve, India). Journal of Medicinal Plants Research, 7(6):267-276. https://doi.org/10.5897/JMPR011.1394

Prasanna, G. and Anuradha, R. (2016). A comprehensive review on Phytopharmacological activities of *Drynaria quercifolia* L. Int J Pharmacogn Phytochem Res., 8(8):1304-1313.

Prasanna, G.; Devi, R. and Ishwarya, G. (2019). *In vitro* evaluation of antidiabetic and cytotoxicity potentials of the rhizome extract of *Drynaria quercifolia* (L.) J. Smith. Asian J. Pharm. Clin. Res., 12. https://doi.org/10.22159/ajpcr.2019.v12i11.35078

Radenkova-Saeva, J. and Atanasov, P. (2014). Cardiac glycoside plants self-poisoning. Acta Medica Bulgarica, 41(1):99-104. https://doi.org/10.2478/amb-2014-0013

Ragavan, M. L. and Srinivasan, H. (2024). Therapeutic potential of dietary phytochemicals from *Drynaria quercifolia* to modulate gut microbiome: An *in silico* approach. Journal of Biomolecular Structure and Dynamics, 42(21):11508-11520. https://doi.org/10.1080/07391102.2023.2262602

Raj, G. P.; Shincymol, V.; Ansary, P. and Oommen, S. M. (2022). In vivo anti-inflammatory activity of rhizome of *Drynaria quercifolia* (L.) J. Sm. International Journal of Ayurvedic Medicine, 12(4):912-917.

Rajendran, P.; Rengarajan, T.; Nandakumar, N.; Palaniswami, R.; Nishigaki, Y. and Nishigaki, I. (2014). Kaempferol, a potential cytostatic and cure for inflammatory disorders. European Journal of Medicinal Chemistry, 86:103-112. https://doi.org/10.1016/j.ejmech. 2014.08.011

Rangasamy, D.; Jeyarajan, D. and Gunasekaran, L. (2023). A Study of folklore antifungal medicinal herbs among the Tribal groups of Western Ghats, Coimbatore, Tamil Nadu. International Journal of Pharmaceutical Investigation, 13(4). https;//doi.org/10.5530/ijpi.13.4. 102

Roghan, H. B.; Sekar, I.; Bharathi, B. K. M.; Susikaran, S.; Tilak, M. and Sivakumar, B. (2024). Bioactive compounds in mulberry (*Morus* spp.) and their products in curing human health problems: A comparative analysis. Ann. Phytomed., 13(2):291–297. https://doi.org/10.54085/ap.2024. 13.2.28

Santos-Buelga, C. and Feliciano, A. S. (2017). Flavonoids: From structure to health issues. In MDPI, 22:477. https://doi.org/10.3390/molecules22030477

Sehrawat, R.; Rathee, P.; Akkol, E. K.; Khatkar, S.; Lather, A.; Redhu, N. and Khatkar, A. (2022). Phenolic acids versatile natural moiety with numerous biological applications. Current Topics in Medicinal Chemistry, 22(18):1472-1484. https://doi.org/10.2174/1568026622666220623114450

Sellami, A.; Montes, M. and Lagarde, N. (2021). Predicting potential endocrine disrupting chemicals binding to estrogen receptor α (ERα) using a pipeline combining structure based and ligand-based in silico methods. International Journal of Molecular Sciences, 22(6):2846. https://doi.org/10.3390/ijms22062846

Shi, Y.; Shu, H.; Wang, X.; Zhao, H.; Lu, C.; Lu, A. and He, X. (2020). Potential advantages of bioactive compounds extracted from traditional Chinese medicine to inhibit bone destructions in rheumatoid arthritis. Frontiers in pharmacology, 11:561962. https://doi.org/10.3389/fphar.2020.561962

Shoaib, S.; Ansari, M. A.; Fatease, A. A.; Safhi, A. Y.; Hani, U.; Jahan, R.; Alomary, M. N.; Ansari, M. N.; Ahmed, N. and Wahab, S. (2023). Plant derived bioactive compounds in the management of neurodegenerative disorders: challenges, future directions and molecular mechanisms involved in neuroprotection. Pharmaceutics, **15**(3):749. https://doi.org/10.3390/pharmaceutics15030749

Singh, A. and Kumar Singh, N. (2024). Pre-clinical evidence-based neuroprotective potential of naringin against Alzheimer's disease-like pathology: A comprehensive review. Current Pharmaceutical Biotechnology, **25**(9):1112-1123. https://doi.org/10.2174/1389201024666230801095526

Smeriglio, A.; Barreca, D.; Bellocco, E. and Trombetta, D. (2017). Proanthocyanidins and hydrolysable tannins: Occurrence, dietary intake and pharmacological effects. British Journal of Pharmacology, **174**(11):1244-1262. https://doi.org/10.1111/bph.13630

Talukder, P.; Tandon, R. and Pal, U. (2024). Exploring medical biotechnology-*in vivo, in vitro, in silico*: Biotechnology from Labs to Clinics and Basic to Advanced. CRC Press.

Tremmel, M.; Kiermaier, J. and Heilmann, J. (2021). *In vitro* metabolism of six C-glycosidic flavonoids from *Passiflora incarnata* L. International Journal of Molecular Sciences, **22**(12):6566. https://doi.org/10.3390/ijms22126566

Vanegas, K. G.; Larsen, A. B.; Eichenberger, M.; Fischer, D.; Mortensen, U. H. and Naesby, M. (2018). Indirect and direct routes to C-glycosylated flavones in Saccharomyces cerevisiae. Microbial Cell Factories, **17**:1-10. https://doi.org/10.1186/s12934-018-0952-5

Wang, X.; Tang, P.; Yang, K.; Guo, S.; Tang, Y.; Zhang, H. and Wang, Q. (2024). Regulation of bone homeostasis by traditional Chinese medicine active scaffolds and enhancement for the osteoporosis bone regeneration. Journal of Ethnopharmacology, 118141. https://doi.org/10.1016/j.jep.2024.118141

Wilson, E.; Rajamanickam, G.; Vyas, N.; Agarwal, A. and Dubey, G. (2007). Herbs used in siddha medicine for arthritis a review. Indian Journal of Traditional Knowledge, **6**(4):678-686

Wolf, P. G.; Pryer, K. M.; Smith, A. R. and Hasebe, M. (1998). Phylogenetic studies of extant pteridophytes. In Molecular systematics of plants II: DNA sequencing (pp. 541-556). Springer. https://doi.org/10.1007/978-1-4615-5419-6_19

Xiao, J.; Capanoglu, E.; Jassbi, A. R. and Miron, A. (2016). Advance on the flavonoid C-glycosides and health benefits. Critical Reviews in Food Science and Nutrition, **56**:S29-S45. https://doi.org/10.1080/10408398.2015.1067595

Yazdani, F.; Jahanshahi, M.; Elyasi, L. and Sarkala, H. B. (2024). Naringin reduced the density and total number of aβ plaques and restored memory function and volume of hippocampal ca1 area in alzheimer's disease model rats: A stereological study. Iranian Journal of Psychiatry and Behavioral Sciences, **18**(1). https://doi.org/10.5812/ijpbs-138212

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