

REVIEW

Open Access



Exploring the phytochemistry, extraction techniques, and therapeutic potentials of *Dryopteris* species: a scoping review (2010–2025)

Abinash Sharma¹, Anish Pradhan^{1*}, Kiran Sharma², Phunchok Norbu Sherpa¹, Angila Theengh³, Chamta Gurung³, Binu Chettri⁴ and Bhupendra Shrestha⁵

Abstract

Dryopteris, often referred to as wood or shield ferns, constitutes a globally ubiquitous genus within the *Dryopteridaceae* family, thriving in a wide array of habitats that encompass temperate woodlands to tropical montane ecosystems. This investigation examines the phytochemical constituents, extraction methodologies, and biological activities of *Dryopteris* species documented from 2010 to 2025. Adhering to PRISMA protocols, 77 comprehensive publications were chosen from an initial aggregation of 675 entries sourced from PubMed, Scopus, Web of Science, and Google Scholar. During our review, we identified a total of 34 distinct *Dryopteris* species, with *Dryopteris fragrans*, *Dryopteris crassirhizoma*, and *Dryopteris erythrosora* emerging as the most extensively researched. The predominant focus of the studies was directed towards leaves, rhizomes, and roots, thereby exposing a substantial knowledge deficit regarding stems and shoots. Total phenolic content (TPC) was frequently extracted utilizing methanol; however, the ideal solvent was found to differ based on the species and specific plant part. While the subterranean components of *Dryopteris crassirhizoma* demonstrated higher total flavonoid content (TFC), *Dryopteris dilatata* was noted for its elevated TPC. Contemporary investigations have substantiated the antibacterial, antioxidant, and anticancer properties of *Dryopteris*, which is also utilized in ethnobotanical practices for the treatment of wounds, infections, and gastrointestinal disorders. This review underscores the imperative for additional research on lesser-studied plant parts and species at risk of extinction to comprehensively apprehend and safeguard the ecological and medicinal potential of *Dryopteris*.

Keywords *Dryopteris*, Antioxidant, Anti-inflammation, Anti-bacterial, Anti-viral, Anti- cancer, Extraction, Isolation, Total phenolic content, Total flavanoid content, PRISMA

*Correspondence:

Anish Pradhan

pradhananishpaqa01@gmail.com

¹Government Pharmacy College Sajong, Department of Pharmaceutical Chemistry, Sikkim, India

²Government Pharmacy College Sajong, Department of Pharmaceutics, Sikkim, India

³Government Pharmacy College Sajong, Department of Pharmacology, Sikkim, India

⁴Harsha College of Pharmacy, Department of Pharmaceutical Chemistry, Bengaluru, India

⁵Himalayan Pharmacy Institute, Majhitar, Department of Pharmaceutical Analysis, Sikkim, India

Introduction

Taxonomy and morphology of *Dryopteris*

The genus *Dryopteris*, commonly known as wood ferns or shield ferns, is a globally distributed group within the family Dryopteridaceae and comprises numerous species exhibiting distinct morphological characteristics and ecological adaptations. These ferns inhabit a wide range of environments, from temperate forests to tropical montane ecosystems, demonstrating considerable tolerance to variable environmental condition [1]. The genus is typified by intricately divided, pinnately compound fronds that contribute to its morphological identity and aesthetic appeal. Accurate species identification and clarification of evolutionary relationships within the broader fern phylogeny rely heavily on a detailed understanding of *Dryopteris* taxonomy and morphology [2]. However, due to extensive morphological similarities among several taxa, species-level identification often poses challenges, requiring the integration of molecular tools alongside comprehensive morphological assessments for precise taxonomic resolution.

Ecological importance and conservation

The exploration of *Dryopteris* species is significant owing to their ecological functions, potential medicinal applications, and horticultural value. *Dryopteris* ferns play vital ecological roles by providing habitat for various invertebrates, aiding soil stabilization, and preventing erosion, thereby supporting forest ecosystem integrity. Furthermore, floristic survey data have contributed to understanding the distribution and diversity of *Dryopteris* species [1]. Palynological studies analyzing spore morphology have also been instrumental in differentiating species and elucidating phylogenetic relationships within the genus [3]. Several *Dryopteris* species are listed as threatened in Red Data Books, highlighting the urgency of their conservation. The preservation of these sensitive taxa is essential for maintaining biodiversity and ecosystem balance. Effective conservation strategies necessitate both in vitro and ex situ approaches to protect these species from further decline [4].

Ethnobotany and pharmacological properties

The genus *Dryopteris* encompasses approximately 400 species of tree ferns known for their wide geographic distribution and ecological versatility. These species thrive in diverse microhabitats such as shaded forest understories, rocky terrains, and wetland margins an adaptability attributed to specialized morphological traits such as robust rhizomes, dissected fronds, and peltate indusia [5]. Traditional medicinal practices have long recognized the therapeutic potential of *Dryopteris* species. Various species are reported to possess antimicrobial, antioxidant, and anticancer activities [6]. For instance, the

fronds of *Dryopteris ramosa* are used in folk medicine for their antibiotic, astringent, and febrifuge effects, and they are also employed as a natural pesticide [7]. In Unani medicine, *Dryopteris filix-mas* is valued for its efficacy in treating rheumatoid arthritis and healing wounds. Additionally, it is utilized in traditional Chinese medicine as a tonic and vulnerary in the management of wounds, epistaxis, and menorrhagia [8].

Phytochemistry and research significance

The diverse phytochemical constituents identified across *Dryopteris* species underscore their importance in pharmacological research. Recent chemical investigations have revealed an extensive array of bioactive compounds, reinforcing the need for comprehensive studies to understand their therapeutic potential fully [6]. This scoping review aims to provide an in-depth overview of the potential applications of *Dryopteris* species in addressing major health challenges. It also highlights gaps in current research and emphasizes the necessity of further investigation into the pharmacological attributes of these ferns. Additionally, the review evaluates extraction techniques used to isolate bioactive molecules from *Dryopteris* species, which is essential for their effective integration into modern medicinal research. Understanding the phytochemical diversity present in these ferns may support the development of novel therapeutic agents with applications across a spectrum of diseases.

Methodology

The investigation was executed utilizing a meticulously structured methodological framework, which encompassed the delineation of the research inquiry, the identification of pertinent studies, the selection of qualifying studies, the organization of the data, as well as the synthesis and reporting of the findings [9, 10]. In pursuit of ensuring transparency and reproducibility, the search strategy was meticulously formulated in alignment with PRISMA guidelines. The primary aim of this scoping review is to delineate the extant literature pertaining to the phytochemical constituents, biological activities, and traditional applications of plant species within the *Dryopteris* genus across the temporal span from 2010 to 2025.

The principal research inquiry posits: “What is the contemporary state of understanding concerning the chemical constituents, extraction methodologies, and biological activities of *Dryopteris* species?” Studies were included if they reported on the chemical composition, biological activity, or traditional use of any *Dryopteris* species; were published between 2010 and 2025; appeared in peer-reviewed journals or academic books; and were available in English. Studies were excluded if they focused solely on taxonomy or ecology, were review

articles or meta-analyses, were not in English, or fell outside the specified timeframe since the literature range was restricted to 2010–2025 to ensure inclusion of studies employing modern extraction techniques, contemporary phytochemical characterization tools, updated taxonomic classifications, and internationally accepted pharmacological testing protocols. This timeframe enhances methodological consistency, data reliability, and therapeutic relevance in accordance with PRISMA guidelines.

In accordance with PRISMA guidelines, studies were included if they specifically investigated *Dryopteris* species. Eligible publications were required to report on phytochemical composition, isolation or identification of secondary metabolites, extraction methodologies, or pharmacological/therapeutic activities. Both experimental and computational studies such as molecular docking, in vitro assays, in vivo bioactivity studies, and analytical chemistry investigations were considered. Only peer-reviewed articles, conference papers, and high-quality theses published in English were included. No restrictions were placed on the geographical region, date of publication, or study design to ensure comprehensive coverage of global research outputs on *Dryopteris* species.

Studies were excluded if they did not focus on *Dryopteris* or if they addressed unrelated fern genera. Publications that lacked sufficient methodological detail, did not present primary data (e.g., opinion pieces, editorials, commentary articles), or failed to report identifiable phytochemicals or extract-based pharmacological evaluations were removed. Duplicate records across databases (pubmed, scopus, web of science, and google scholar) were screened and eliminated. Articles not available in full text, non-English manuscripts, and studies focusing solely on ecology, botany (without phytochemistry or pharmacology), or horticultural aspects were also excluded. This systematic filtration ensured that only scientifically rigorous and directly relevant studies were incorporated into the final review dataset.

Results and discussions

The genus *Dryopteris* has been the focal point of extensive investigations over the last several decades. Various species within the *Dryopteris* genus were rigorously analyzed in this review, considering their current profiles of chemical constituents, extraction methodologies, and their biological activities. 675 relevant articles based on the selected keywords were successfully retrieved. Following the rigorous processes of duplication removal and abstract assessment, 256 publications were thoroughly screened. During this phase, certain publications were systematically excluded, resulting in 98 original publications and 158 records being discarded from the review.

While 98 articles were evaluated for eligibility, leading to the exclusion of 21 articles for specified reasons, ultimately culminating in the inclusion of 77 comprehensive full-text articles in the review, with the details of the PRISMA flowchart illustrated in Fig. 1.

Dryopteris: species diversity and research trends

During this review, a total of 34 distinct species within the *Dryopteris* genus have been meticulously identified, encompassing *Dryopteris crassirhizoma* Nakai, *Dryopteris fragrans* (L.) Schott, *Dryopteris cochleate*, *Dryopteris redactopinnata*, *Dryopteris sparsa*, *Dryopteris barbigera* (T. Moore ex Hook.) Kuntze, *Dryopteris blanfordii* (Hope) C, *Dryopteris chrysocoma*, *Dryopteris ramose*, *Dryopteris cristata*, *Dryopteris juxtapostia*, *D. bissetiana*, *D. filix-mas* (L.) Schott, *D. affinis*, *D. hirtipes* (Bl.) Kuntze, *Dryopteris wallichiana*, *Dryopteris erythrosora*, *Dryopteris lacera*, *cycadina*, *Gymnocarpium Dryopteris*, *Dryopteris dilatate*, *Dryopteris stewartia*, *Dryopteris manniana*, *Dryopteris aemula*, *Dryopteris borrieri*, *Dryopteris cambrensis*, *Dryopteris carthusiana*, *Dryopteris caucasica*, *Dryopteris expansa*, *Dryopteris oreades*, *Dryopteris remota*, *Dryopteris schimperiana*, *Dryopteris serrato-dentata*, and *Dryopteris xanthomelas*.

Most research has mainly focused on *Dryopteris fragrans* (L.) Schott and *Dryopteris crassirhizoma* Nakai, with each species being the subject of 15 studies, establishing them as the most prevalent species. Following closely are *Dryopteris filix-mas* and *Dryopteris ramose*, each with 6 studies. Additionally, *Dryopteris erythrosora* has been examined in 5 studies, while *Dryopteris affinis* ssp. *affinis*, *Dryopteris cochleate*, and *Dryopteris dilatate* each garnered 4 studies. Furthermore, *Dryopteris cambrensis* and *Dryopteris borrieri* were the focus of 3 studies each, whereas *Dryopteris blanfordii*, *Dryopteris oreades*, *Dryopteris aemula*, and *Dryopteris remota* each received 2 studies, with all other species represented by a solitary study, as illustrated in Fig. 2.

The year of publication serves as a critical indicator of the recency of research, which is paramount for evaluating its relevance to contemporary scientific discourse and developments. Recent publications are typically deemed more significant in fast-paced fields of study. An elevated number of publications regarding a specific plant species within a given year signifies that the species commands considerable attention from researchers. This heightened interest may stem from its prospective applications, distinct characteristics, or its contribution to tackling pressing scientific or environmental issues. Consequently, based on these assertions, we have gathered data on the volume of publications from 2010 to 2025 concerning the *Dryopteris* genus, as illustrated in Fig. 3. Most studies were conducted in 2022 (15 studies), followed by 2023 (10 studies). In 2019, there were 8 studies; 2018 and 2020

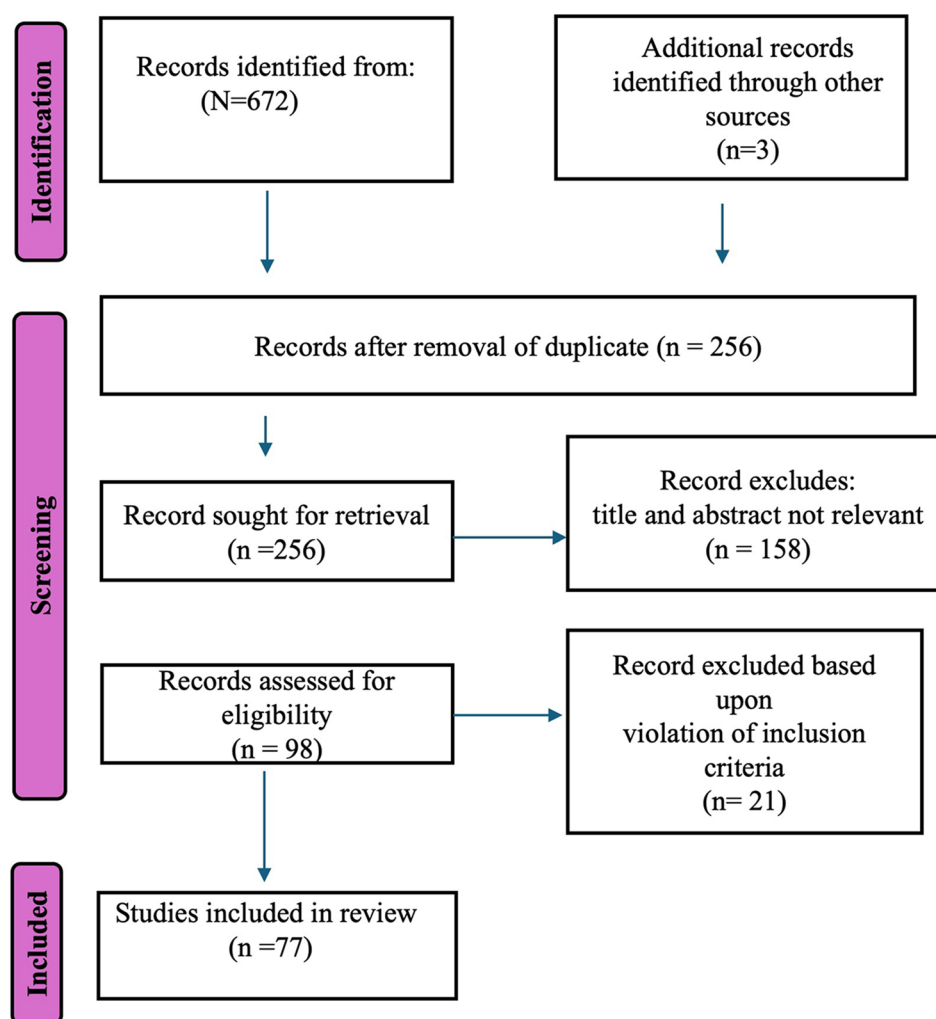


Fig. 1 PRISMA flowchart on literature selection based on inclusion/exclusion criteria

each had 7 studies. 6 studies in 2021, 5 studies was noted in 2024. Years with 4 studies include 2012, 2014, 2017, while 2013, 2015, and 2016 had 2 studies each.

Upon examination and selection of studies, data concerning the specific plant parts scrutinized in each investigation were systematically extracted. This process entailed the precise documentation of the exact plant sections analyzed and the quantification of studies concentrated on each component. The analysis unveiled a substantial distribution of research across various plant elements. Research on the *Dryopteris* genus has primarily concentrated on leaves, rhizomes, and roots. Studies of aerial parts and fronds were conducted later. There have been relatively few investigations concerning stems and shoots, as shown in Fig. 4, indicating a gap in the existing research.

This finding provides a strong basis for future researchers to address these gaps and gain a better understanding of the plant. This information can also be used in future

research to plan studies that improve knowledge of the functional roles and significance of the often-overlooked plant parts in the *Dryopteris* genus. Focusing on these less-explored areas may uncover new bioactive substances, ecological roles, and possible medicinal uses, advancing our understanding of *Dryopteris* species as summarized in the Table 1 below presenting the year, solvents used, and plant parts utilized in these studies.

Compounds isolated from *Dryopteris* genus (2010–2025)

From 2010 to 2025, extensive phytochemical investigations of the genus *Dryopteris* have revealed a remarkable diversity of isolated compounds across multiple species. These studies have identified a wide range of chemical classes, including flavonoids and flavonoid glycosides, phloroglucinol derivatives, coumarins, anthraquinones, and terpenylated acylphloroglucinols. The molecular weights and structural complexity of these compounds vary significantly, reflecting the rich chemical diversity

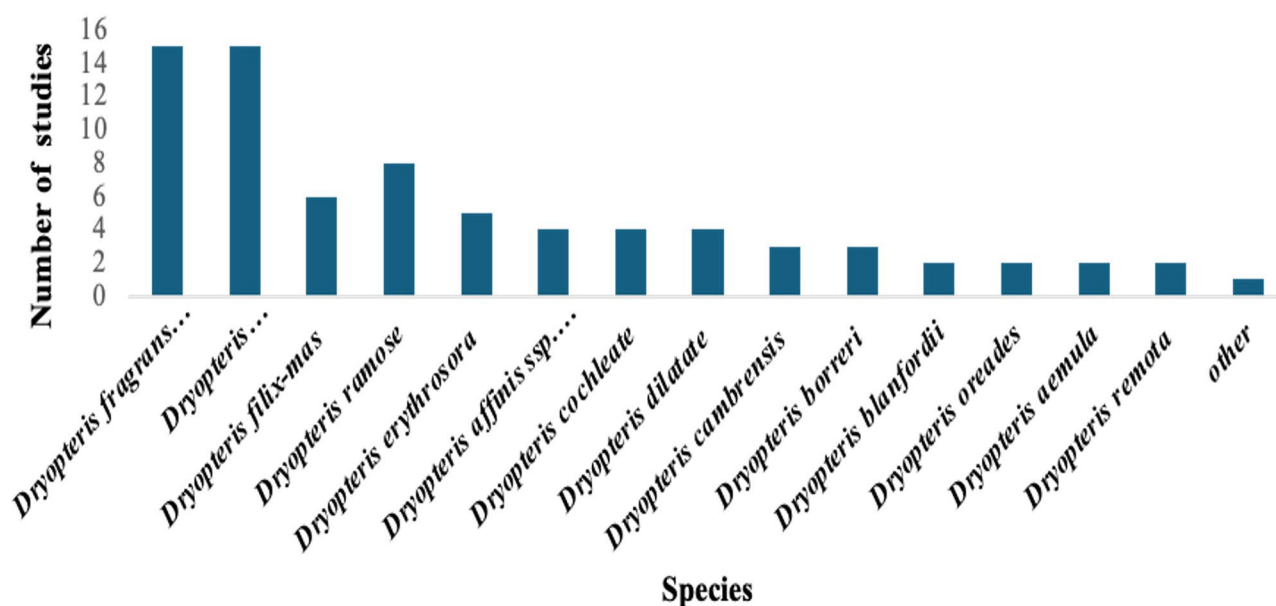


Fig. 2 Studies distribution by plant species within *Dryopteris*

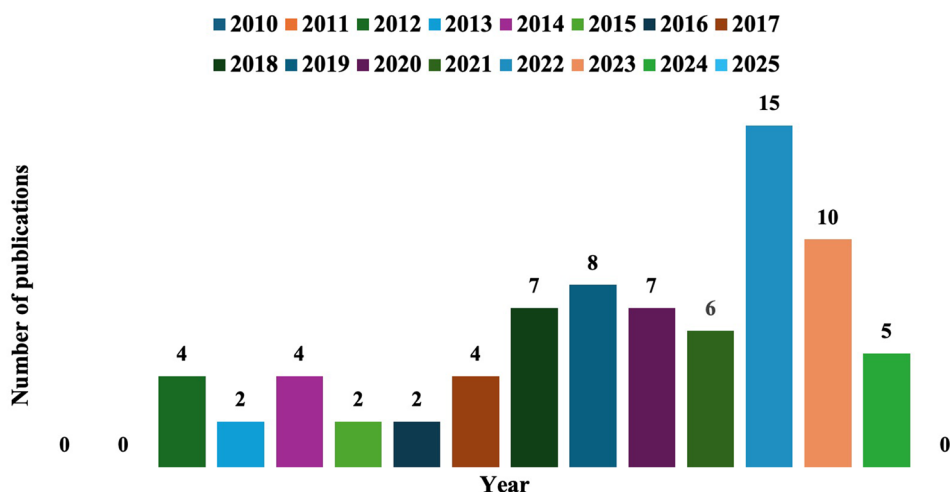


Fig. 3 Frequency of publications within *Dryopteris* (2010–2015)

within the genus (Table 2) and some of the structures of important isolated molecules are highlighted in Fig. 5. This growing body of research underscores the pharmacological potential of *Dryopteris* species and highlights their importance as promising sources of bioactive natural products for future therapeutic development.

Extraction solvents and techniques for phenolic and flavonoid

Methanol is unequivocally recognized as the superior solvent for the extraction of total phenolic content (TPC) from plant materials, due to its exceptional ability to solubilize a wide array of phenolic compounds. Ethanol is also frequently employed for the extraction of phenolic

compounds, particularly when the focus is on flavonoid extraction [87]. It is well established that alcoholic solvents are highly effective in extracting phenolic and flavonoid content from plant source. Our findings from this review unequivocally indicates that the analysis of methanolic extracts from eleven species of *Dryopteris* has yielded the following total phenolic content (TPC) values, articulated in mgGAEq/g 1DW: *Dryopteris aemula* (233.2 ± 17.2), *Dryopteris affinis* (97.9 ± 9.9), *Dryopteris borrieri* (323.2 ± 32.1), *Dryopteris cambrensis* (343.3 ± 40.3), *Dryopteris carthusiana* (272.4 ± 33.3), *Dryopteris caucasica* (232.1 ± 36.2), *Dryopteris dilatate*, (434.3 ± 66.6), *Dryopteris expansa* (265.5 ± 30.9),

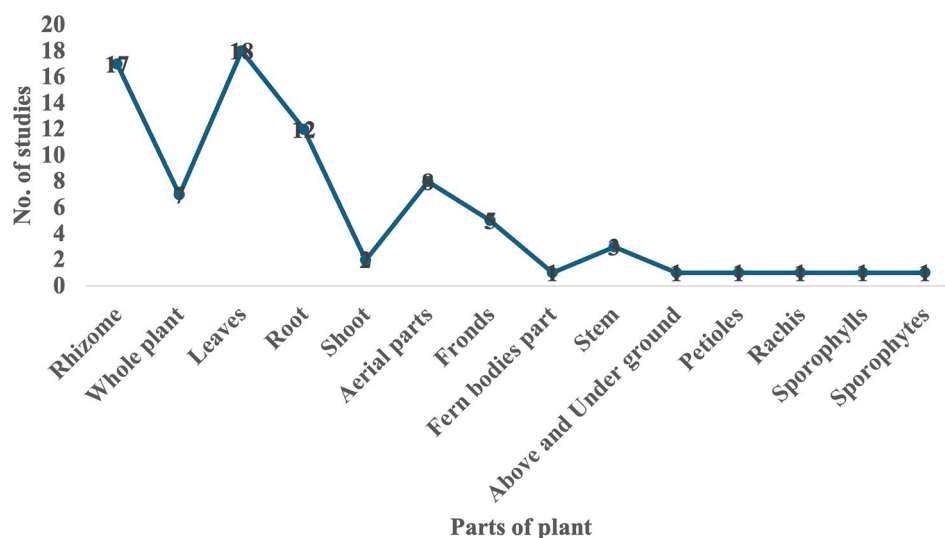


Fig. 4 Frequency of plant parts used in *Dryopteris* phytochemical studies

Dryopteris filix-mas (280.2 ± 43.8), *Dryopteris oreades* (221.2 ± 16.5), and *Dryopteris remota* (319.1 ± 47.1).

Furthermore, in a rigorous comparative analysis of a 70% ethanolic extract derived from both the underground and above-ground portions of *Dryopteris crassirhizoma*, it was determined that the underground section possesses a markedly elevated total flavonoid content of 208.09 ± 5.89 mg RE/g, significantly surpassing that of the above-ground portion, which recorded 129.5 ± 3.82 mg RE/g. The total phenolic content (TPC) of *Dryopteris juxtapostia* has been rigorously assessed utilizing various solvents. The root extracts exhibited a TPC of 222 mg GAE/g when subjected to dichloromethane extraction and 163 mg GAE/g when extracted with methanol. Conversely, the shoot extracts demonstrated inferior TPC values, recording 109 mg GAE/g for dichloromethane and 91.4 mg GAE/g for methanol. The selection of solvents for extraction was paramount in determining the yield of phenolic compounds, whereby dichloromethane proved to be superior for root extracts [56], while both water and petroleum ether extracts presented the lowest concentrations of TPC and TFC, underscoring the critical influence of solvent choice on the extraction efficacy of these compounds. The results decisively indicate that acetone stands as the most potent solvent for isolating phenolic and flavonoid compounds from *Dryopteris cochleata* rhizome [19]. Comprehensive analyses of TPC and TFC are articulated in Table 3.

The predominant solvent system employed was the combination of ethanol alone or an ethanol: water ratio ($n=27$), succeeded by methanol alone or a methanol: water ratio ($n=28$), followed by water ($n=24$), ethyl acetate ($n=10$), hexane and chloroform ($n=7$), petroleum ether ($n=6$), acetone ($n=5$), butanol ($n=4$), dichloromethane (DCM) ($n=3$), diethyl ether ($n=2$), supercritical

CO_2 , butane, benzene, alongside a mixture of ethanol, water, and hydrochloric acid in a 2:1:1 ratio ($n=1$), while 11 studies did not specify the utilization of any solvent ($n=11$), as illustrated in Table 1.

Most of the studies have been conducted using maceration for extracting bioactive compound from *Dryopteris* genus. Because of its simplicity and low operating costs, this procedure has been used over the years. Nevertheless, this approach has many drawbacks, including a lengthy extraction period and poor extraction effectiveness and have significant gap for not utilizing Soxhlet extraction for *Dryopteris* species. Since, extraction is achieved in shorter extraction time and less solvent consumption when compared to maceration or percolation processes. However, this methodology use of high temperatures accelerates the thermal deterioration of compounds [29].

Pharmacological and its therapeutic value

Ferns of the *Dryopteris* species are used extensively in traditional medicine worldwide because of their numerous medicinal applications. These plants have notable pharmacological qualities, including antioxidant, anti-inflammatory, anti-cancer, and anti-microbial effects. Their therapeutic efficacy is increased by the way bioactive substances such as flavonoids, alkaloids, and tannins affect oxidative stress, inflammation, and other biological processes. A natural remedy for rheumatoid arthritis, inflammation, and oxidative-related illnesses could thus be developed using *Dryopteris* species. This section examines the pharmacological effects of *Dryopteris* species, including their antiviral, antibacterial, cytotoxic, antioxidant, anti-inflammatory qualities and other notable activities.

Table 1 Summary of study details on *Dryopteris* genus: year, solvents used, extraction technique and plant parts utilized

Study year	Solvents used	Extraction technique	Plant parts used	Reference
2012	Diethyl ether	Solvent extraction + chromatographic separation	Rhizomes	[11]
	50% ethanol	Ultrasound-assisted solvent extraction	Leaves, Stems, Rachis, and Roots	[12]
	Petroleum ether, chloroform, ethyl acetate, acetone, methanol, and water	Soxhlet extraction	Leaves	[13]
	Methanol	Cold maceration	Root	[14]
2013	95% ethanol	Maceration	Root	[15]
	70% ethanol	Hot maceration	Rhizome	[16]
2014	95% ethanol	Solvent extraction + chromatographic purification	Whole plant	[17]
	95% ethanol	Solvent extraction + isolation	Leaves	[18]
	Petroleum ether, ethyl acetate, acetone, methanol, and water	Soxhlet extraction	Rhizomes	[19]
	Diethyl ether	HS-SPME (Headspace Solid-Phase Microextraction) (volatile extraction)	Aerial parts	[20]
2015	Methanol	Cold maceration	Fern body's part	[21]
	Methanol	Cold maceration	Rhizomes and leaves	[22]
2016	Water	Solvent extraction + chromatographic isolation	Whole Plant	[23]
	Methanol and water	Maceration	Leaves	[24]
2017	Ethanol, water, and petroleum ether	Soxhlet extraction	Rhizomes	[25]
	80% methanol	Solvent extraction + chromatographic isolation	Aerial parts	[26]
	95% ethanol	Solvent extraction + chromatographic isolation	Whole plant	[27]
	90% ethanol	Solvent extraction + bioassay-guided isolation	Rhizome	[28]
2018	95% ethanol, petroleum ether, dichloromethane, ethyl acetate, and n-butanol	Solvent extraction + fractionation	Aerial parts	[29]
	NA	DNA extraction (not phytochemical)	Whole plant	[30]
	Chloroform	Cuticular wax extraction (surface solvent wash)	Fronds	[31]
	60% ethanol	Solvent extraction	Leaves	[32]
	Methanol, ethanol, and water	Maceration	NA	[33]
	95% ethanol	Maceration	NA	[34]
	Water	Solvent extraction + compound isolation	Aerial parts	[35]
	80% aqueous ethanol, n-hexane, ethyl acetate, butanol, and water	Ethanol extraction + fractionation	Leaves	[36]
2019	Petroleum ether, acetone, anhydrous ethanol, and distilled water	Hot-water extraction	Rhizomes	[37]
	Methanol	Maceration	Rhizomes	[38]
	NA	Used previously isolated compound	NA	[39]
	Water, dichloromethane (DCM), ethyl acetate (EtOAc), and butanol (BuOH)	Solvent extraction + compound isolation	Rhizome	[40]
	70% ethanol	Maceration	Rhizome	[41]
	NA	Used dried & powdered root and rhizome	Root and rhizomes	[42]
	NA	No extraction (botanical/herbarium data)	NA	[43]
	Ethyl acetate, methanol, 50% MeOH in water, and distilled water	Solvent extraction + isolation	Rhizomes	[44]
2020	NA	DNA/RNA extraction (not phytochemical)	Roots, sporophylls, and sporophylls with glandular trichomes	[45]
	Ethanol, water, and hydrochloric acid (2:1:1)	Protein extraction	Fronds	[46]
	Ethanol and ethyl acetate	Solvent extraction + fractionation	Leaves	[47]
	Water	Crude extract (technique not specified)	NA	[48]
	n-hexane, chloroform (CHCl ₃), and methanol (MeOH)	Maceration	Root	[49]
	NA	No phytochemical extraction (molecular modification study)	Stem, leaf, and roots	[50]
	Methanol	Solvent extraction + fractionation	Leaves	[51]
	Methanol	Solvent extraction + chromatographic isolation	Rhizomes	[52]

Table 1 (continued)

Study year	Solvents used	Extraction technique	Plant parts used	Reference
2022	Ethyl acetate, methanol, and water	Cold maceration	Fronds	[7]
	Methanol	Solvent extraction combined with ultrasound-assisted extraction	Fronds	[53]
	Methanol	Solvent extraction + chromatographic purification	Aerial parts	[54]
	Methanol	Solvent extraction + chromatographic purification	Aerial parts	[55]
	Dichloromethane and methanol	Maceration	Root and shoot	[56]
	NA	Used already isolated compound	Rhizomes	[57]
	Methanol, n-hexane, chloroform, ethyl acetate, and n-butanol	Solvent extraction for UHPLC-MS metabolomics	Whole plant	[58]
	70% ethanol	Solvent extraction for LC-QTOF profiling	Leaves	[59]
	Methanol	Heat-assisted extraction	Leaves	[60]
	70% ethanol	HS-SPME (Headspace Solid-Phase Microextraction) + solvent extraction	Above and Under-ground parts	[61]
	Methanol	Solvent extraction + compound isolation	Rhizome	[62]
	80% ethanol	Maceration with ethanol	Leaves	[63]
	Distilled water and 99.9% ethanol	Maceration using orbital shaker	NA	[64]
	90% methanol aqueous solution	Solvent extraction + affinity-ultrafiltration	Rhizomes	[65]
	50% ethanol	Solvent extraction + isolation of isoflavaspodic acid	Aerial parts	[66]
	Water	Hot maceratipton	Leaves	[67]
	N-hexane	Soxhlet extraction	Root, shoot, and leaves	[68]
	Water	Cold maceration	Rhizomes	[69]
	NA	Protein extraction	Sporophytes (frond with sporangia)	[70]
2023	Water	Hot-water extraction	Roots, stem, and leaves	[71]
	n-hexane, dichloromethane (DCM), ethyl acetate (EtOAc), and methanol (MeOH)	Organic solvent extraction	Rhizomes	[72]
	70:30 ethanol/water	Solvent extraction	NA	[73]
	NA	Molecular extraction (DNA/protein)	Leaves, petioles, and roots	[74]
2024	Ethanol, butane, hexane, and benzene	Cold maceration	Leaves	[75]
	NA	Solvent extraction + compound isolation	Aerial parts	[76]
	Pet. ether, n-hexane, chloroform, and ethanol	Solvent extraction	Leaves	[77]
	Methanol, ethanol, acetone, and distilled water	Sequential Soxhlet Extraction	NA	[78]
	Methanol	Double maceration (cold maceration)	Root, leaves	[79]
	Methanol	Cold maceration (overnight)	Leaves	[80]
	30% ethanol	Cold maceration (hydroalcoholic extraction)	Rhizomes	[81]
	NA	No extraction—isolated compounds used directly	Whole plant	[82]
	Water	Hot-water infusion for nanoparticle synthesis	NA	[83]
	NA	DNA extraction	Whole plant	[84]
	Ethanol, methanol, ethyl acetate, water, chloroform, acetone, and n-hexane	Solvent extraction	Aerial parts	[85]
2025	Supercritical CO ₂ , ethanol, and methanol	Supercritical CO ₂ extraction (SFE)	Aerial part	[86]

Note: NA = not available

Comparative antioxidant activity

Antioxidants extracted from medicinal ferns, especially those belonging to the *Dryopteris* genus, have attracted considerable attention for their efficacy in addressing disorders linked to oxidative stress. These ferns, historically utilized in traditional medicine for detoxification, possess a wealth of bioactive compounds, including

flavonoids and phenolic acids. Importantly, *Dryopteris crassirhizoma* contains chlorogenic acid, a compound exhibiting potent antioxidant, antibacterial, antiviral, and anti-inflammatory capabilities. Its subterranean components demonstrate prominent antioxidant activity and an elevated flavonoid concentration in comparison to its aerial parts [61]. Numerous *Dryopteris* species

Table 2 List of compounds isolated from *Dryopteris* genus (2010–2025)

Sl.no.	Species	Compound	Plant part used	Extraction solvent	Pharmacological property	Reference
1	<i>D. fragrans</i>	Dryofragone	Aerial part	95% ethanol	Cytotoxic (anticancer)	[29]
2		Dryofracoumarin B				
3		3-O-β-D-Glucopyranosylalbicanol-11-O-β-D-glucopyranoside	Whole plant	95% ethanol	Antifungal	[17]
4		Dihydroconiferylalcohol				
5		(E)-3-(4-Hydroxyphenyl) acrylic acid				
6		Esculetin				
7		5,7-Dihydroxy-2-hydroxymethylchromone				
8		Eriodictyol				
9		Isoorientin				
10	<i>D. shimpiriana</i>	Heptacosanol	Roots	Methanol	Antioxidant	[49]
11		Isorhamnetin			Antibacterial	
12	<i>D. erythrosora</i>	1–1,3-dihydroxy-5-methoxyphenyl-4-O-β-D-glucopyranoside	Aerial part	80% methanol	NA	[26]
13		4-O-β-D-glucopyranosyl-(1"→3")-glucopyranosyl-2-hydroxy-6-methoxy-5-methylphenyl-1-butanone				
14	<i>D. crassirhizoma</i>	Flavaspidic acid AB	Rhizome	Ethyl acetate	Moderate xanthine oxidase inhibition	[44]
15		Flavaspidic acid PB			Weak xanthine oxidase inhibition + antioxidant activity	
16		Flixic acid ABB	Rhizomes	Diethyl ether	Neuraminidase (NA)-inhibitory activity	[11]
17		Flavaspidic acid AP	Rhizome	Ethyl acetate	Xanthine oxidase (XO) inhibitory activity	[44]
18		Aspidinol P	Rhizome	Water extract	Inhibits collagen-stimulated platelet aggregation (antiplatelet).	[40]
19		Aspidinol B			Inhibits platelet aggregation (antiplatelet)	
20		Propionyl-3-methylphloroglucinol			Antiplatelet activity (inhibits aggregation)	
21		Butyryl-3-methylphloroglucinol			Potent antiplatelet	
22		Butyrylphloroglucinol			Antiplatelet activity	
23		Flavaspidic acid BB	Rhizome	Ethyl acetate	Weak or negligible XO inhibition	[44]
24	<i>D. lacera</i>	Diethyl 2-hydroxy-5-oxo-1-cyclohexene-1,4-dicarboxylate	Leaves	70% ethanol	Antioxidant, Predicted Anti-Inflammatory, Mild Antimicrobial, Possible Cytotoxic Potential	[59]

Table 2 (continued)

Sl.no.	Species	Compound	Plant part used	Extraction solvent	Pharmacological property	Reference
25		4',5,7-Trihydroxy-3-methoxyflavone-7-O- α -L-arabinofuranosyl (1 $\rightarrow$ 6)- β -D-glucopyranoside			Antioxidant, Anti-inflammatory, Anticancer, Antimicrobial	
26		6-Hydroxykaempferol-3-O-glucoside			Antimicrobial, Antioxidant, Antitumor, Anti-inflammatory, Antidiabetic	
27		Kaempferol 3-Lathyruside			Antimicrobial, Antioxidant, Antitumor, Anti-inflammatory, Antidiabetic	
28		Kaempferol 3-O- α -L-arabinopyranosyl-7-O- α -L-rhamnopyranoside			Antimicrobial, Antioxidant, Antitumor, Anti-inflammatory, Antidiabetic	
29		Puerarin-4'-O-glucoside			Antimicrobial, Antioxidant, Antitumor, Anti-inflammatory, Antidiabetic	
30		3'-Hydroxypuerarin			Antimicrobial, Antioxidant, Antitumor, Anti-inflammatory, Antidiabetic	
31		1,3,6-Trihydroxy-2-hydroxymethyl-9,10-anthraquinone-3-O-(6'-O-acetyl)- β -D-glucopyranoside			Anticancer activity	
32		Juglanin			Antibacterial	
33		Kaempferol-7-rhamnoside			Antibacterial, Antioxidant, Antitumor	
34	<i>D. bissetiane</i>	Neochlorogenic acid			Antibacterial, Antioxidant, Anti-Inflammatory, Antitumor	
35		6-Hydroxyluteolin 7-O-laminaribioside			Antibacterial activity	
36		(1S)-1,4-Anhydro-1-[8-(β -D-galactopyranosyloxy)-5,7-dihydroxy-2-(4-hydroxyphenyl)-4-oxo-4H-chromen-6-yl]-D-arabinitol			Antioxidant, Anticancer, Antimicrobial, Anti-inflammatory, Possible anti-diabetic	

Table 2 (continued)

Sl.no.	Species	Compound	Plant part used	Extraction solvent	Pharmacological property	Reference
37		Quercetin 3-O-gentiobioside			Antioxidant, Anticancer, Antimicrobial, Anti-inflammatory, Cardioprotective, Neuroprotective	
38		Eucommioside II			Anti-inflammatory, Antimicrobial, Antioxidant	
39		Peltatoside			Antimicrobial	
40		Quercetin 3-O-neohesperidoside			Antioxidant, Anticancer, Antibacterial	
41		Kaempferitrin			Antimicrobial	
42		Hyperoside			Antimicrobial	
43		Astragalin			Antibacterial, Antioxidant	
44		1,3,6-Trihydroxy-2-hydroxymethyl-9,10-anthraquinone-3-O-(6'-O-acetyl)-beta-D-glucopyranoside			Anticancer, Antioxidant, Antimicrobial, Anti-inflammatory, Antiviral, Hepatoprotective	
45	<i>D. wallichiana</i>	Wallichin A (terpenylated acylphloroglucinols)	Diethyl ether	Rhizomes	Moderate nematocidal	[11]
		Wallichin B (terpenylated acylphloroglucinols)			Nematocidal	
46		Wallichin C (terpenylated acylphloroglucinols)				
		Wallichin D (terpenylated acylphloroglucinols)				
47		Filixic acids ABA			Moderate nematocidal	
48		Albaspidins AA				
49		Albaspidins AB				
50	<i>D. ramosa</i>	Iriflophenone-3-C-β-D-glucopyranoside	Methanol	Aerial parts	Antibacterial	[54]
51		Magniferin	Methanol	Aerial part	Antioxidant	[55]
52		Isomagniferin				

Note: NA = not available

have showcased extraordinary antioxidant properties. *D. juxtapostia* crude extracts (DCM and methanol) has exhibited good efficacy across various assays, achieving an IC₅₀ of 42.0 µg/mL in the DPPH assay, a reducing potential of 46.2 mmol/g of Fe²⁺ equivalents per gram of extract in the FRAP assay, and a 71% inhibition rate in the H₂O₂ assay [56]. *D. ramosa* achieved the highest DPPH free radical scavenging rate at 91.95% at 2000 µg/mL (2 mg in 1 ml DMSO) [7], while *D. crassirhizoma* Nakai demonstrated the antioxidant activity, as evidenced by its ability to scavenge DPPH radicals (IC₅₀ of 2.04 mg/mL), hydroxyl radicals (IC₅₀ of 1.70 mg/mL), and superoxide

anions (IC₅₀ of 4.20 mg/mL) in a dose-dependent manner [37]. Furthermore, *D. erythrosora* also exhibited significant DPPH activity, particularly in the stem extracts [32]. Methanolic and ethanolic extracts of *D. dilatata* and *D. blanfordii* showed strong radical scavenging activity. Isorhamnetin from *Dryopteris schimperiana* also exhibited notable antioxidant effects, as did extracts from *D. cochleata*. *D. sparsa* crude methanolic extract of root part comparatively had weaker antioxidant activity, with a higher IC₅₀ value (22.24 µg/mL). *D. ramosa* exhibited notable antimicrobial activity, with MIC values ranging from 31.1 to 125 µg/mL against several pathogenic

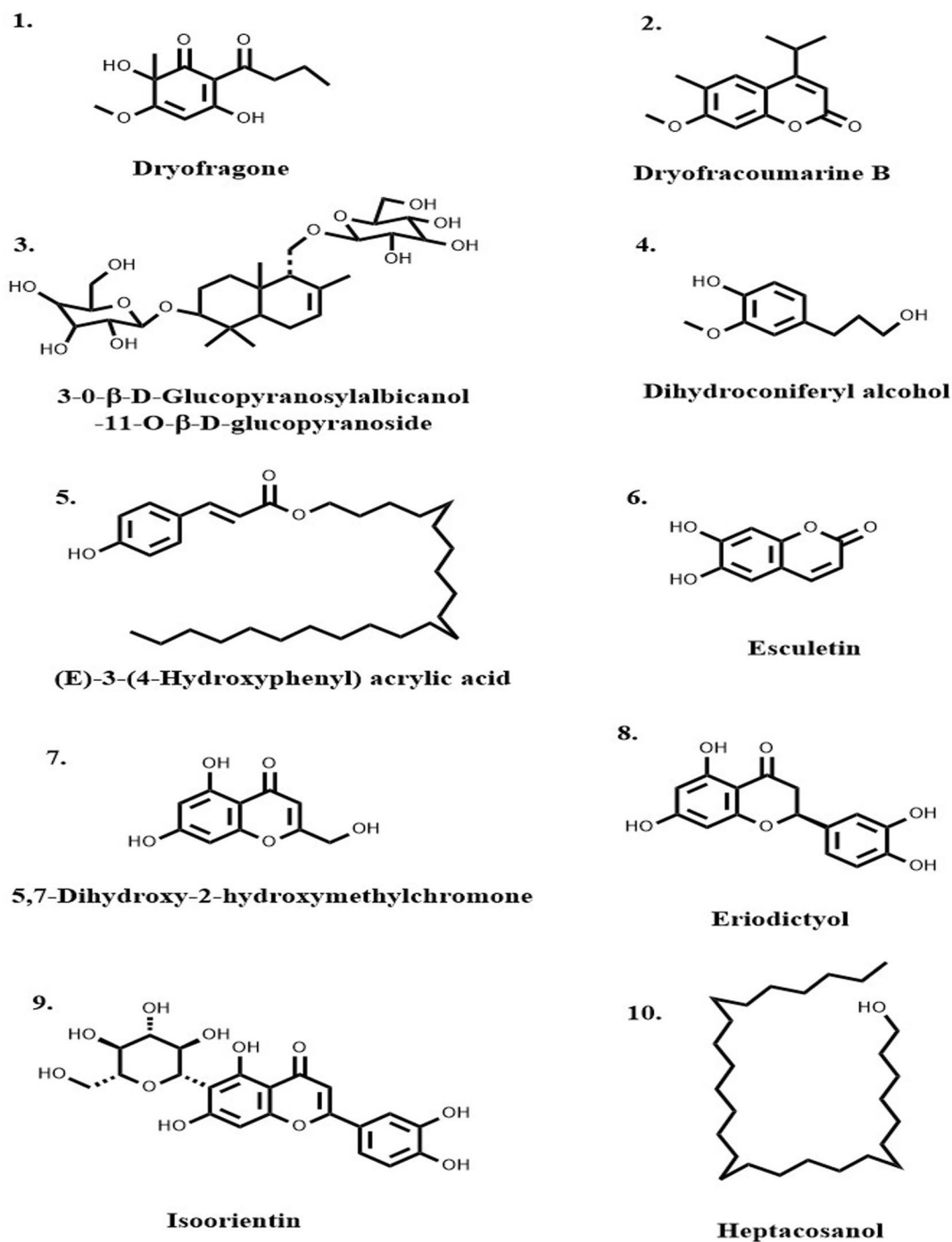
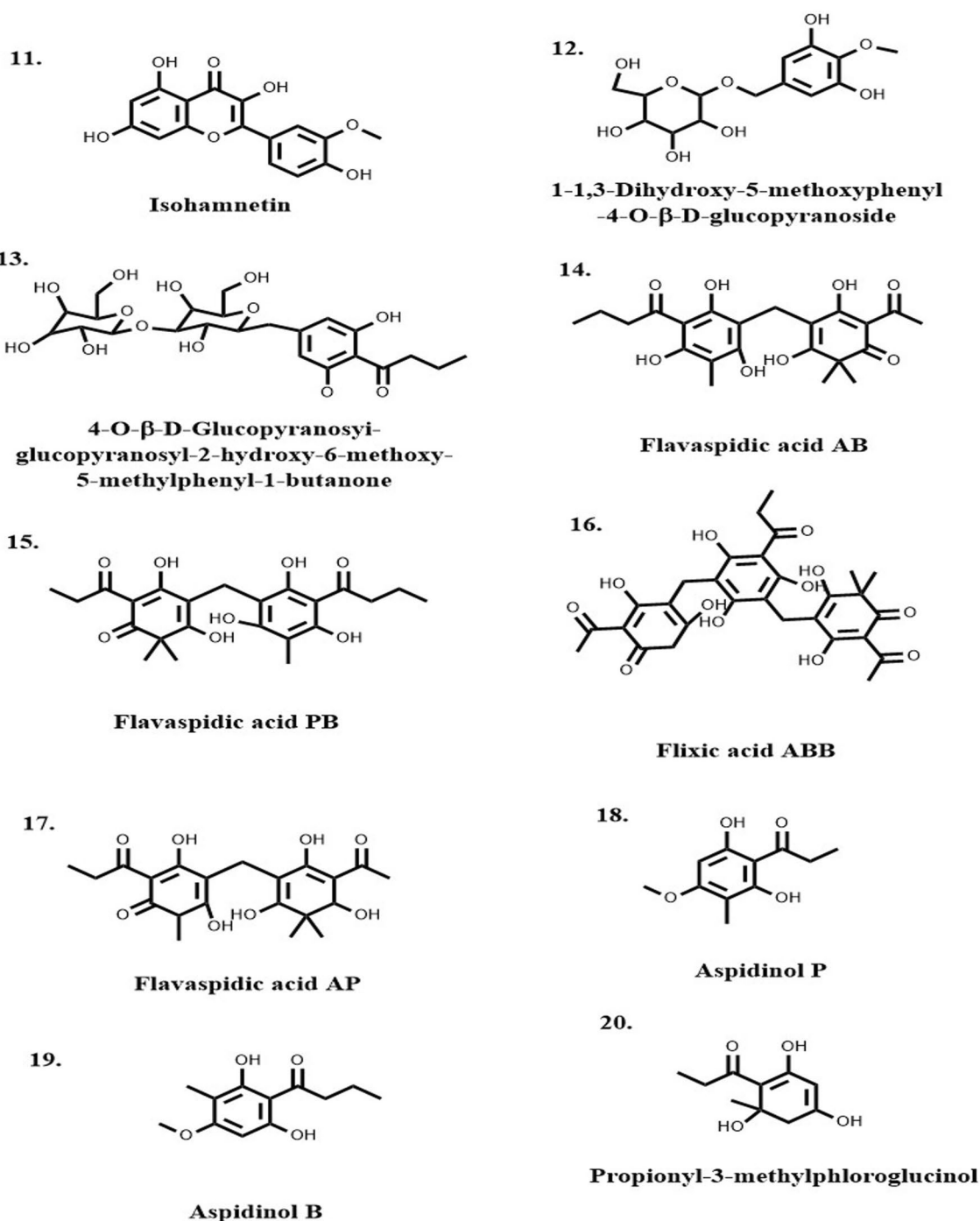


Fig. 5 Structure of some important phytochemical isolated from various *Dryopteris* species

bacteria, while its methanolic extract showed strong DPPH antioxidant potential, where isolated isomangiferin and mangiferin displayed IC_{50} values (Isomangiferin = $55.98 \pm 0.39 \mu\text{g/mL}$, Mangiferin = $60.34 \pm 0.18 \mu\text{g/mL}$) comparable to standard ascorbic acid [54, 55]. Details are summarized in Table 4.

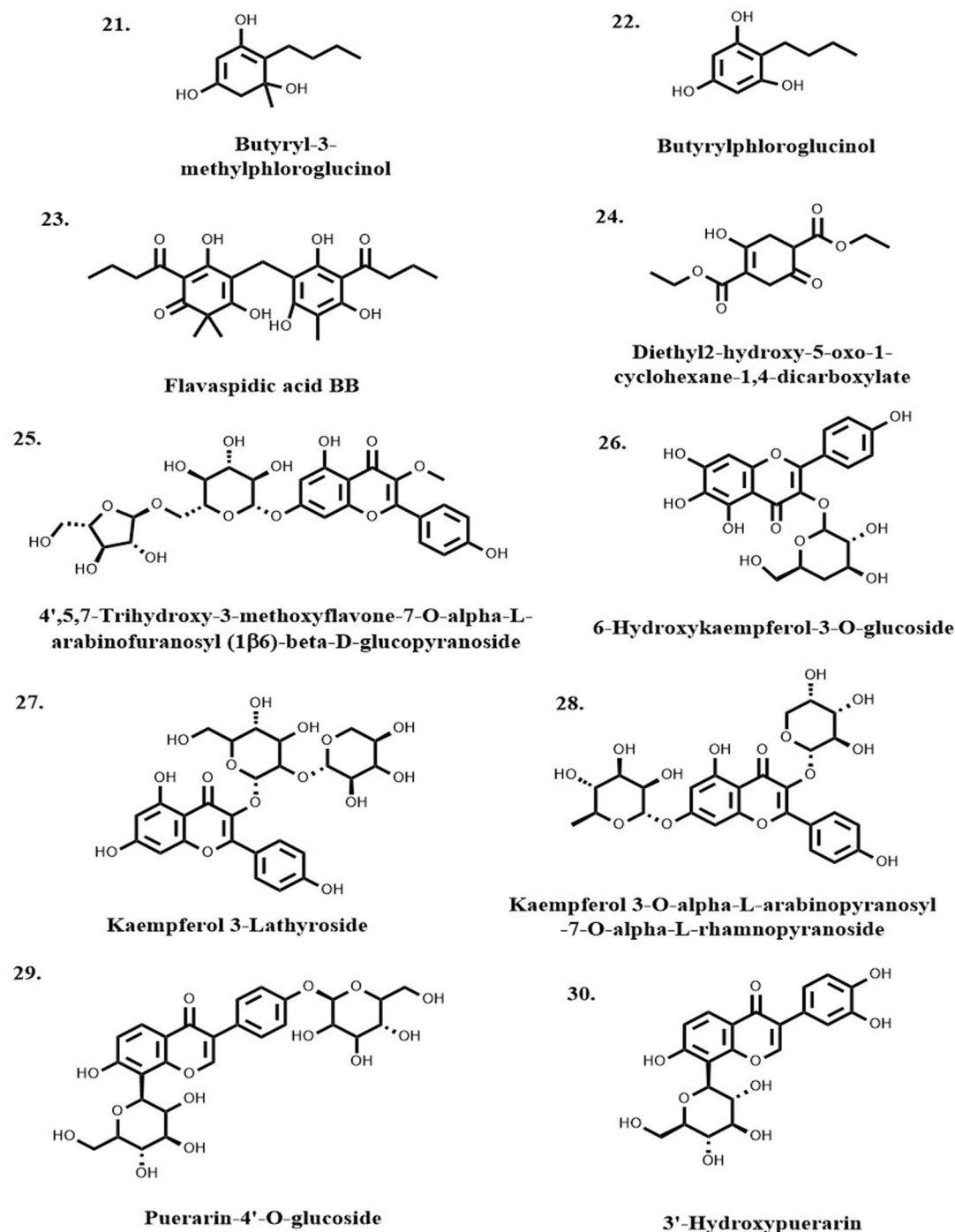
Anti-inflammatory activities

Natural compounds, notably flavonoids and phenolic compounds, have undergone rigorous investigation for their anti-inflammatory capabilities. Flavonoids, prevalent in vascular plants, manifest anti-inflammatory actions in both in vitro and in vivo research. The advantageous effects of these compounds are predominantly due to their interactions with critical enzymes,

**Fig. 5** (continued)

cytokine-associated signaling pathways, and regulatory transcription factors, including NF- κ B [88]. These natural compounds effectively inhibit enzymes that play a role in inflammation, such as cyclooxygenase-2 (COX-2), inducible nitric oxide synthase (iNOS), and 5-lipoxygenase (5-LOX), consequently diminishing the synthesis of inflammatory mediators such as nitric oxide and leukotrienes [89].

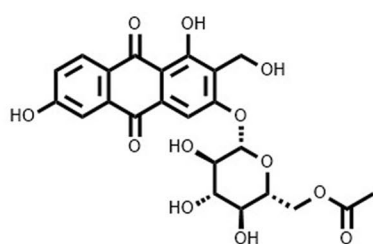
Among the *Dryopteris* species, the dichloromethane extract of *D. juxtapostia* root has demonstrated substantial anti-inflammatory efficacy, achieving 56.7% inhibition in the urease inhibition assay, 61.7% inhibition in the carrageenan-induced paw edema model, and 67.3% inhibition in the formaldehyde-induced paw edema model at an oral dose of 200 mg/kg [56]. Extracts and fractions, specifically ethyl acetate and butanol, from

**Fig. 5** (continued)

D. filix-mas exhibited strong anti-inflammatory activity, where its ethyl acetate and butanol fractions reduced egg-albumin paw edema in a dose-dependent manner, showing maximal inhibition during the 3rd–4th hour at 200–400 mg/kg. The ethyl acetate fraction produced 78.99% xylene-induced ear-edema inhibition, while formaldehyde-induced arthritis decreased by 19.12–31.63% across both fractions [36]. The 95% ethanol extract of *D.*

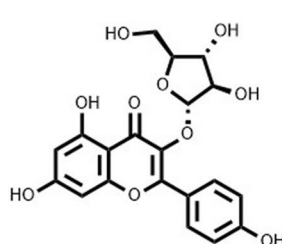
crassirhizoma effectively suppressed the production of inflammatory mediators such as NO and PGE2, down-regulated inflammatory genes including iNOS, COX-2, and TNF- α , and inhibited the ERK/AP-1 and TBK1/IRF3 signaling pathways, thereby reinforcing its anti-inflammatory and anti-infective properties [15]. Furthermore, methanolic extract of *D. ramosa* demonstrated anti-inflammatory action, reducing carrageenan-induced paw

31.



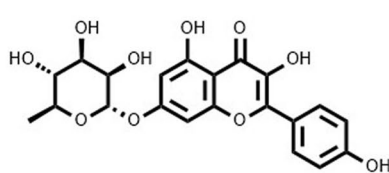
1,3,6-Trihydroxy-2-hydroxymethyl-9,10-anthraquinone-3-O-(6'-O-acetyl)-beta-D-glucopyranoside

32.



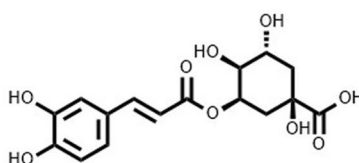
Juglanin

33.



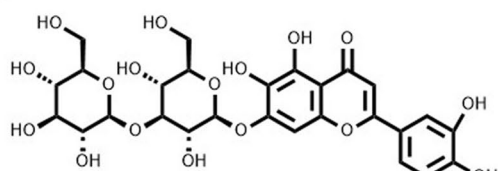
Kaempferol-7-rhamnoside

34.



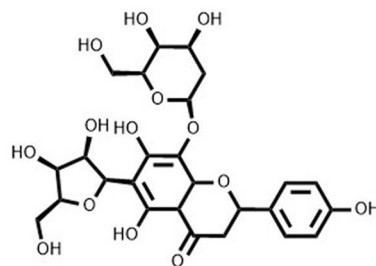
Neochlorogenic acid

35.



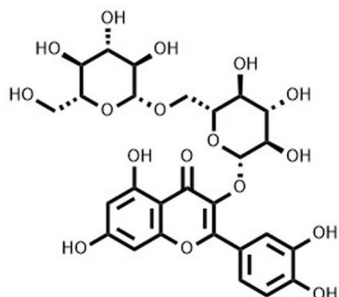
6-hydroxyluteolin 7-O-laminaribioside

36.



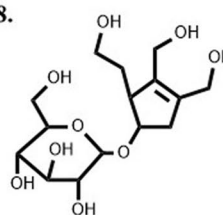
(1S)-1,4-Anhydro-1-[8-(beta-D-galactopyranosyloxy)-5,7-dihydroxyl-2-(4-hydroxyl)-4-oxo-4H-chromen-6-yl]-D-arabinitol

37.



Quercetin 3-O-gentiobioside

38.



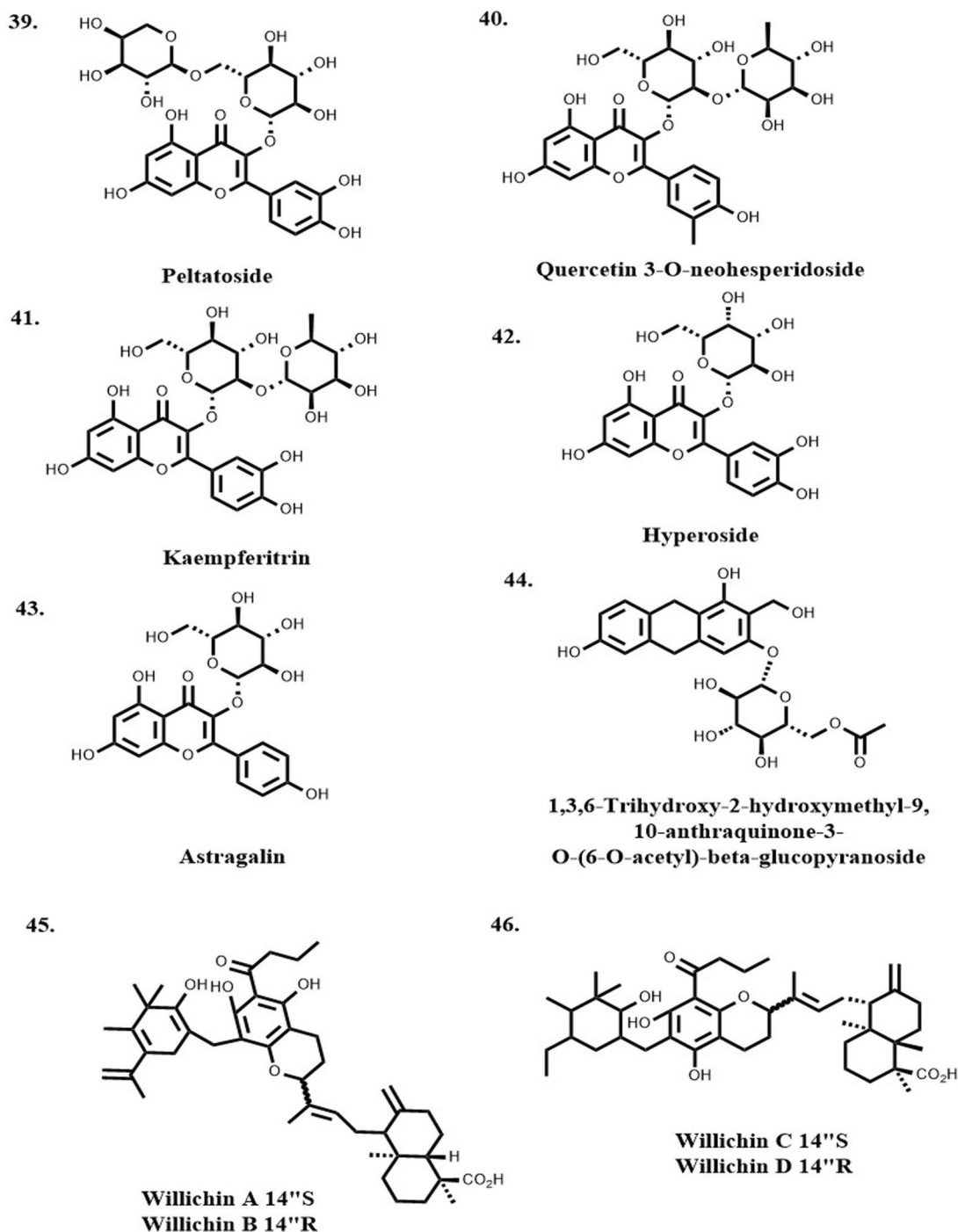
Eucommioside II

Fig. 5 (continued)

edema to 59.554 ± 0.54 and 50.826 ± 0.24 mm at 0.1 g/kg and 0.2 g/kg, respectively [73]. *Dryopteris ramosa* showed strong α -glucosidase inhibition (91.36%) at 1 mg/mL from its ethyl acetate fraction [73], while *D. fragrans* glycosides suppressed NO production with IC_{50} values of 45.8, 65.8, and 49.8 μ M [23], and *D. sparsa* exhibited notable DPPH antioxidant activity ($IC_{50} = 22.24$ μ g/mL) [79]. Table 5 outlines the study details.

Cytotoxic and anticancer activity

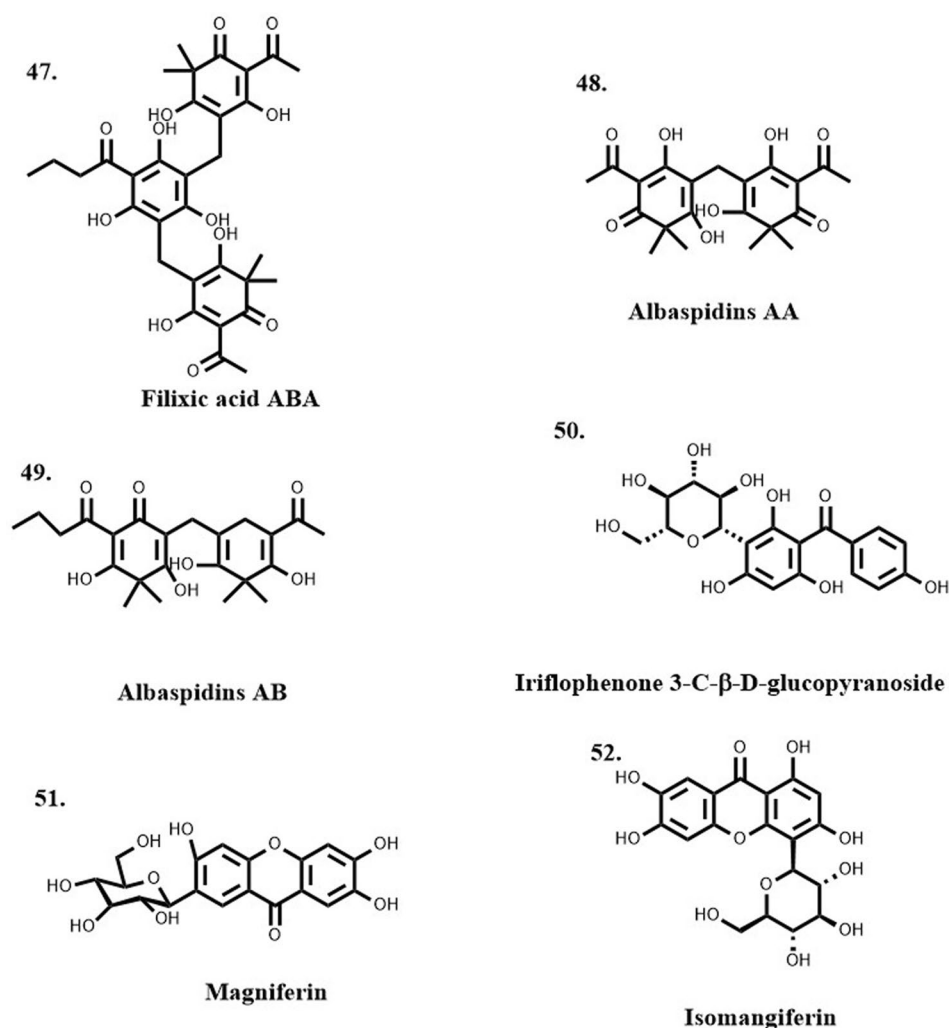
Numerous species within the genus *Dryopteris*, exhibited cytotoxic properties against various cancer cell lines, although the extent of investigation into each species is inconsistent. *D. ramosa* stands out as one of the most thoroughly examined species, with three distinct studies underscoring its anticancer efficacy [58, 85]. One of these critical studies identified a chloroform fraction of

**Fig. 5** (continued)

the fronds part exhibiting remarkable anti-proliferative activity against HepG2 liver cancer cells ($IC_{50} = 53.49 \mu\text{g/mL}$) [58]. Furthermore, *D. ramosa* has demonstrated significant cytotoxic effects against AGS (gastric) and A549 (lung) cancer cell lines, with IC_{50} values consistently reported below $200 \mu\text{g/mL}$ [85].

D. fragrans has garnered extensive scholarly attention in four pivotal studies exploring its cytotoxic capabilities

[18, 27, 29, 35]. These investigations have isolated several bioactive compounds, including a sesquiterpene that has proven effective against A549, MCF-7, HepG2, HeLa, and PC-3 cell lines [27], alongside isoscopoletin, which exhibits activity against lung, breast, and liver cancers [18]. One comprehensive study evaluated *D. fragrans* extracts across nine distinct cell lines, revealing a spectrum of cytotoxic responses [18]. Additionally, one

**Fig. 5** (continued)

study elucidated the cytotoxic effects of *D. marginalis* and *D. juxta-postia*. The dichloromethane extract from *Dryopteris juxta-postia* demonstrated cytotoxicity against prostate (PC3) and cervical (HeLa) cancer cells, with IC_{50} values of 45.2 $\mu\text{g/mL}$ and 17.1 $\mu\text{g/mL}$, respectively [56].

In a similar vein, the ethanolic extract of *Dryopteris marginalis* significantly diminished the viability of MCF-7 breast cancer cells, showing comparability to paclitaxel [73]. Three critical studies on *Dryopteris crassirhizoma* revealed minimal cytotoxicity on MDCK cells, inhibition of oral squamous carcinoma cell migration, and confirmed non-mutagenic, non-clastogenic characteristics [28, 34, 41]. *Dryopteris affinis* showed cytotoxicity in a brine shrimp assay, with rhizomes and leaves displaying different potency levels. Table 6 highlights the varied research focus among species.

Antiviral activities of *Dryopteris* species against coronaviruses

An ethanolic extract derived from *D. crassirhizoma* has unequivocally exhibited potent antiviral properties against a range of coronaviruses, notably including human coronavirus OC43 (HCoV-OC43), SARS-CoV-2, and its variants. This extract targets multiple phases of the viral lifecycle by effectively inhibiting viral entry and suppressing the function of critical viral proteases, Mpro and PLpro [81].

In addition, naturally occurring phloroglucinols isolated from *D. crassirhizoma*, namely dryocin ABA and filixic acid ABA, have been recognized as potent inhibitors of the major protease (MPR) of SARS-CoV-2, with IC_{50} of 46.48 and 39.63, respectively. These compounds also demonstrated antiviral activity against SARS-CoV and MERS-CoV, highlighting their potential as powerful antiviral agents [30]. A summary of the details is highlighted in Table 7.

Table 3 Total phenolic content (TPC) and total flavonoid content (TFC) in *Dryopteris* species: data from previous studies

Plant part used	Species	Extraction solvent	Extraction technique	Total phenolic content	Total flavonoid content	Reference
Fronds	<i>D. aemula</i>	Methanol	Solvent extraction combined with ultrasound-assisted extraction	233.2 mg GAE/g	NA	[53]
	<i>D. affinis</i>			97.9 mg GAE/g		
	<i>D. borrieri</i>			323.2 mg GAE/g		
	<i>D. cambrensis</i>			343.3 mg GAE/g		
	<i>D. carthusiana</i>			272.4 mg GAE/g		
	<i>D. caucasica</i>			232.1 mg GAE/g		
	<i>D. dilatata</i>			434.3 mg GAE/g		
	<i>D. expansa</i>			265.5 mg GAE/g		
	<i>D. filix-mas</i>			280.2 mg GAE/g		
	<i>D. oreades</i>			221.2 mg GAE/g		
	<i>D. remota</i>			319.1 mg GAE/g		
Roots	<i>D. juxtapostia</i>	Dichloromethane, Methanol	Maceration	222 mg GAE/g (DCM); 163 mg GAE/g (MeOH)	NA	[56]
Shoots				109 mg GAE/g (DCM); 91.4 mg GAE/g (MeOH)		
Underground and above-ground parts	<i>D. crassirhizoma</i>	70% ethanol	HS-SPME (Headspace Solid-Phase Microextraction) + solvent extraction	NA	Underground: 208.09 ± 5.89 mg RE/g; Above-ground: 129.5 ± 3.82 mg RE/g	[61]
Rhizome	<i>D. cochleata</i>	Petroleum ether, Ethyl Acetate, Acetone, Methanol, and Water	Soxhlet extraction	Acetone: 141.92 µg/mg; EA: 82.52 µg/mg; MeOH: 80.29 µg/mg; Water: 33.70 ± 0.73 µg/mL; Petroleum ether: 20.59 ± 1.40 µg/mL	Acetone: 127.23 µg/mg; EA: 81.81 µg/mg; MeOH: 62.85 µg/mg; Water: not reported; Petroleum ether: not reported	[19]
Leaves	<i>D. cochleata</i>	Acetone, Ethyl acetate, Chloroform, Methanol, Water, Petroleum ether	Soxhlet extraction	Acetone: 90.45 µg/mL; Water: 28.64 µg/mL (lowest)	EA: 145.78 µg/mL; Chloroform: 122.56 µg/mL; MeOH: 77.71 µg/mL	[13]
Rhizome and leaves	<i>D. affinis</i>	Methanol	Cold maceration	112.54 ± 8.09 mg GAE/g	NA	[22]
Leaves, stems, roots, rachis	<i>D. erythrosora</i>	50% ethanol	Ultrasound-assisted solvent extraction	NA	Stems highest (8.26%); Leaves lowest (2.1%)	[12]
Fronds	<i>D. ramosa</i>	Ethyl acetate, Methanol, Water fractions	Cold maceration	NA	EA: 45.28 µg QE/mg; MeOH: 36.94 µg QE/mg; Water: 25.69 µg QE/mg	[7]

Note: NA = not available

Antibacterial activity

Numerous species within the genus *Dryopteris* have been investigated for their antibacterial properties, as delineated in Table 8, with *D. crassirhizoma* distinguished for its exceptional potential against caries. A study assessed the methanol extract of *D. crassirhizoma* in relation to *Streptococcus mutans* using a microdilution methodology, revealing a Minimum Bactericidal Concentration (MBC) of 250 µg/mL and a Minimum Inhibitory Concentration (MIC) of 62.5 µg/mL. At twice the MBC, the extract markedly reduced viable *S. mutans* counts by

99.9% within one hour and also affected bacterial growth rates and virulence at sub-MIC concentrations [14].

Other *Dryopteris* species have also exhibited significant antibacterial effects against diverse pathogens, albeit through varied mechanisms and targets. For example, silver nanoparticles derived from *D. cristata* demonstrated MICs of 125 µg/mL against *Staphylococcus aureus* and 250 µg/mL against *Escherichia coli* [83]. *D. filix-mas* revealed potent activity against *Proteus mirabilis* and *E. coli* with an MIC of 25 mg/mL utilizing the agar disc diffusion method. Likewise, *D. affinis* showcased

Table 4 Antioxidant properties of *Dryopteris* species: assay methods and principal findings

Species	Plant part used	Extract/fraction	Assay	Result	Reference
<i>D. juxtapostia</i>	Roots	Dichloromethane extract	DPPH, FRAP, H ₂ O ₂ assays	DPPH IC ₅₀ = 42.0 µg/mL; FRAP = 46.2 mmol/g; H ₂ O ₂ inhibition = 71%	[56]
<i>D. crassirhizoma</i> Nakai	Rhizomes	Water	DPPH, Hydroxyl, Superoxide assays	DPPH IC ₅₀ = 2.04 mg/mL; Hydroxyl IC ₅₀ = 1.70 mg/mL; Superoxide IC ₅₀ = 4.20 mg/mL	[37]
<i>D. ramosa</i>	Fronds	Methanol extract; methanol, water, ethyl acetate fractions,	DPPH	DPPH inhibition = crude extract: 91.948% Methanol fraction: 88.25% ± 1.1 Water fraction: 87.28% ± 1.5 Ethyl acetate fraction: 69.97% ± 0.83 at 2000 µg/mL	[7]
<i>D. crassirhizoma</i> Nakai	Underground & above-ground parts	70% Ethanol extract	DPPH, ABTS, Fe ³⁺ reducing assay	DPPH: 80% (underground) vs 76% (above-ground) at 1 mL extract; Higher ABTS & Fe ³⁺ reduction for underground part	[61]
<i>D. erythrosora</i>	Stems, roots, rachis, leaves	70% aqueous ethanol extract	DPPH & Superoxide	DPPH: Stems 79–87.6%; Leaves lowest. Superoxide: Stems highest; Roots lowest when tested at 5–45 µL.	[12]
<i>D. sparsa</i>	Roots	Methanol extract	DPPH	IC ₅₀ = 22.24 µg/mL	[79]
<i>D. ramosa</i>	Aerial part	Methanolic extract	Agar-well diffusion + MIC	• Klebsiella pneumoniae: 31.1 ± 7.2 µg/mL • Staphylococcus aureus: 62.5 ± 7.2 µg/mL • Escherichia coli: 62.5 ± 7.2 µg/mL • Salmonella enterica: 62.5 ± 14.4 µg/mL • Bacillus subtilis: 125 ± 7.2 µg/mL	[54]
<i>D. ramosa</i>	Aerial parts	Methanolic extract	DPPH antioxidant assay	IC ₅₀ : Isomangiferin = 55.98 ± 0.39 µg/mL, Mangiferin = 60.34 ± 0.18 µg/mL	[55]

Table 5 *Dryopteris* species: assay types, experimental models, and main anti-inflammatory findings

Species	Plant part used	Extract/fraction	Assay/model	Result	Reference
<i>D. juxtapostia</i>	Roots	Dichloromethane extract	Urease inhibition assay	56.7% inhibition at an oral dose of 200 mg/kg	[56]
			Carrageenan-induced paw edema	61.7% inhibition at an oral dose of 200 mg/kg	
			Formaldehyde-induced paw edema	67.3% inhibition at an oral dose of 200 mg/kg	
<i>D. filix-mas</i>	Leaves	Ethyl acetate & butanol fractions	Egg-albumin-induced paw edema	Dose-dependent inhibition; the most significant effects were at the 3rd and 4th hour (200/400 mg/kg)	[36]
		Ethyl acetate fraction	Xylene-induced ear edema	78.99% inhibition at 100 µg/ear	
		Ethyl acetate fraction	Formaldehyde-induced arthritis	AUC inhibition: 19.12% (200 mg/kg), 26.08% (400 mg/kg)	
		Butanol fraction	Formaldehyde-induced arthritis	AUC inhibition: 27.51% (200 mg/kg), 31.63% (400 mg/kg)	
<i>D. crassirhizoma</i>	Whole plant	95% ethanol extract (Dc-EE)	NO & PGE ₂ inhibition in LPS-macrophages	NO ↓; PGE ₂ ↓; iNOS & COX-2 downregulated	[15]
<i>D. ramosa</i>	Root & shoot	Ethyl acetate fraction	α-Glucosidase inhibition	91.36% inhibition	[8]
<i>D. fragrans</i>	Aerial	Isolated three pure glycosides from 95% ethanolic crude extract	NO inhibition (cells)	IC ₅₀ = 45.8, 65.8, 49.8 µM	[23]
<i>D. sparsa</i>	Roots	Methanol extract	DPPH assay	IC ₅₀ = 22.24 µg/mL	[79]
<i>D. ramosa</i>	Whole plant	Methanolic	Carrageenan-induced paw edema	59.554 ± 0.54 (0.1 g/kg); 50.826 ± 0.24 (0.2 g/kg)	[73]

Table 6 Cytotoxicity of *Dryopteris* species extracts and compounds on cancer cell lines

Species	Plant part used	Extract/fraction	Assay	Result	Reference
<i>D. juxtapostia</i>	Roots	Dichloromethane extract	MTT assay on HeLa & PC3	IC ₅₀ : HeLa = 17.1 µg/mL; PC3 = 45.2 µg/mL	[56]
<i>D. fragrans</i>	Aerial parts	Methanol extract	MTT assay on A549, MCF7, HepG2	Compound 1: A549 = 6.56 µM, MCF7 = 10.14 µM; Compound 3: HepG2 = 4.76 µM; others vary from inactive to moderate	[18]
<i>D. fragrans</i>	Aerial parts	Petroleum ether fractions (SG1–SG7) & isolated compounds	MTT & CCK-8 on 9 cell lines	Multiple IC ₅₀ values: e.g., Compound 1: A549 = 45.86 µM, HeLa = 25.37 µM; Compound 8: HepG2 = 18.02 µM, HeLa = 17.76 µM, etc.	[29]
<i>D. ramosa</i>	Fronds	Chloroform, n-hexane, crude extract, ethyl acetate	MTT assay on HepG2 & PC3	HepG2 IC ₅₀ : Chloroform = 53.49 µg/mL; n-hexane = 55.36 µg/mL; crude = 85.67 µg/mL; ethyl acetate = 125.00 µg/mL. PC3 IC ₅₀ : n-hexane = 214.53 µg/mL; chloroform = 281.47 µg/mL	[58]
<i>D. affinis</i>	Rhizome & Leaves	Methanol extract	Brine shrimp lethality assay	LC ₅₀ : Rhizome = 323.9 µg/mL; Leaves = 85.5 µg/mL	[22]
<i>D. fragrans</i> (L.) Schott	Whole plant	Ethyl acetate fraction	CCK-8 assay on A549, MCF7, HepG2, HeLa, PC-3	IC ₅₀ : A549 = 2.84 µM; MCF7 = 1.58 µM; HepG2 = 3.53 µM; HeLa = 1.65 µM; PC-3 = 4.62 µM	[27]
<i>D. crassirhizoma</i>	Rhizome	90% ethanol extract	CCK-8 assay on MDCK cells	TC ₅₀ > 400 µM (low cytotoxicity)	[28]
<i>D. crassirhizoma</i>	Rhizome	Ethanol extract	MTT assay (HSC-3 OSCC)	10 µg/mL inhibited cell migration & invasion; no cytotoxicity observed at this dose	[41]
<i>D. crassirhizoma</i>	Rhizome	70% ethanolic extract	Ames test, CHO-K1 chromosomal aberration, mouse micronucleus test	No mutagenicity or genotoxicity detected	[16]
<i>D. fragrans</i> (L.) Schott	Aerial parts	Petroleum ether fraction	MTT assay on A549, MCF7, HepG2, SGC7901	Fragranoside B IC ₅₀ : MCF7 = 2.65 µM. Caffeic acid IC ₅₀ : 8.96–19.44 µM	[35]
<i>D. marginalis</i>	Leaves	Ethanolic extract	MTT assay on MCF-7	<i>Dryopteris marginalis</i> leaf ethanolic extract reduced MCF-7 viability dose-dependently via MTT assay, with 30% inhibition at 60 µg/ml (48 h), less than paclitaxel's 50%	[77]
<i>D. ramosa</i>	Aerial parts	Ethanol, Methanol, Ethyl acetate, Water, Chloroform, Acetone, and n-hexane	MTT assay on AGS, A549, HCT116	IC ₅₀ : AGS: 172.07 ± 0.65 A549: 127.30 ± 0.53 HCT116: 224.04 ± 0.40	[85]
<i>Dryopteris ramosa</i>	Aerial part	Aqueous fraction	Brine Shrimp Lethality Test	LD ₅₀ = 10.037 ± 2.8 µg/mL (non-cytotoxic)	[54]

Table 7 Anti-viral activity in *Dryopteris* species

Species	Assay/method	Active extract/compound	Key Results	Reference
<i>D. crassirhizoma</i>	SARS-CoV-2 Mpro and PLpro inhibition assay	30% ethanolic extract (RDC)	The extract inhibited SARS-CoV-2 Mpro and PLpro in a concentration-dependent manner (1–50 µg/mL) and significantly reduced viral RNA, proteins, and entry in cell-based assays at non-cytotoxic concentrations of 5–25 µg/mL.	[81]
<i>D. crassirhizoma</i>	SARS-CoV-2 Mpro inhibition assay & immunofluorescence antiviral assay	Dryocrassin ABBA and Filixic acid ABA	IC ₅₀ values: Dryocrassin ABBA = 46.48 ± 1.1 µM; Filixic acid ABA = 39.63 ± 1.09 µM	[57]

antibacterial activity against *S. aureus* and *E. coli* with an MIC of 2 µg/mL through broth microdilution [51].

While *D. crassirhizoma* is the most extensively studied due to its anti-caries applications, other species such as *D. cristata*, *Dryopteris filix-mas*, and *D. affinis* also possess noteworthy antibacterial potential. Collectively, the genus *Dryopteris* represents a rich reservoir of bioactive compounds with the capacity to combat bacterial infections [72].

Other notable biological activity

The genus *Dryopteris* exhibits a diverse array of biological activities extending beyond its established anti-inflammatory, antibacterial, antifungal, anticancer, and antiviral properties. Various species within the genus possess distinct ecological and medicinal functions. For example, root and shoot extracts of *D. juxtapostia* have demonstrated hepatoprotective activity [56], while the polysaccharide fraction (DCP-3) from *D. crassirhizoma*

Table 8 Antibacterial assays and Main findings for selected species

Species	Plant part used	Extract/compound	Assay/method	Assay result	Reference
<i>D. ramosa</i>	Whole plant	Purified compounds from methanol extract: Iriflophenone-3-C- β -D-glucopyranoside, Mangiferin, Isomangiferin	Agar well diffusion	Iriflophenone-3-C- β -D-glucopyranoside: <i>E. coli</i> 34 mm; <i>Salmonella</i> 31 mm; <i>K. pneumoniae</i> 30 mm; <i>S. aureus</i> 28 mm. Mangiferin: <i>K. pneumoniae</i> 32 mm; <i>Salmonella</i> 28 mm; weaker against <i>E. coli</i> & <i>P. aeruginosa</i> . Isomangiferin: <i>S. aureus</i> 32 mm; <i>K. pneumoniae</i> 28 mm; least active against <i>P. aeruginosa</i> when tested at 1000 μ g/mL.	[82]
<i>D. cristata</i>	Leaves	DC-AgNPs (silver nanoparticles)	Broth microdilution	MIC: <i>S. aureus</i> 125 μ g/mL; <i>E. coli</i> 250 μ g/mL	[83]
<i>D. filix-mas</i>	Leaves	Methanol extract; DF-6, DF-8 fractions	Agar disc diffusion	MIC: 25 mg/mL; DF-6: 28 mm (<i>P. aeruginosa</i>), 24 mm (<i>E. coli</i>); DF-8: 19 mm (<i>E. coli</i>)	[51]
<i>D. cochleata</i>	Rhizome	Aqueous, ethanol, petroleum ether extracts	Agar well diffusion	Ethanol extract: <i>E. coli</i> 21.33 mm, <i>S. aureus</i> 25.00 mm; Aqueous: 18.33 mm, 21.67 mm; Petroleum ether: 14.33 mm, 16.67 mm at 100 mg/mL	[25]
<i>D. ramosa</i>	Whole plant	Crude methanol extract	Agar well diffusion	Zone of inhibition (mm) 13 mm (<i>P. aeruginosa</i>); MIC = 16 μ g/mL	[7]
<i>D. affinis</i>	Rhizome & leaves	Methanol extract	Broth microdilution	MIC = 2 μ g/mL (<i>E. coli</i> , <i>S. aureus</i>)	[21]
<i>D. erythrosora</i>	Leaves	Ethanol extract	Broth microdilution	MIC (<i>S. aureus</i>) = 0.125 mg/mL	[60]
<i>D. crassirhizoma</i>	Rhizomes	n-hexane extract	Broth microdilution	MIC: 6.25–50 μ g/mL (various bacteria)	[72]
<i>D. schimperiana</i>	Roots	Hexane extract, methanol extract, compounds	Agar well diffusion	Zone of inhibition (mm) Hexane: 9–13 mm; Methanol: 9–10 mm; Isorhamnetin: 17 mm at 5 mg/mL (<i>S. aureus</i>)	[49]
<i>D. cochleata</i>	Rhizomes	Acetone extract	Agar well diffusion	Zone of inhibition (mm) <i>Bacillus subtilis</i> : 15.33 $\pm$ 0.58 mm <i>Enterococcus faecalis</i> : 24.33 $\pm$ 1.53 mm <i>Klebsiella pneumoniae</i> : 17.33 $\pm$ 1.53 mm <i>Staphylococcus aureus</i> : 15.67 $\pm$ 0.58 mm <i>Staphylococcus epidermidis</i> : 16.33 $\pm$ 1.53 mm <i>Shigella flexneri</i> : 11.67 $\pm$ 0.58 mm <i>Proteus vulgaris</i> : 15.67 $\pm$ 0.58 mm <i>Candida albicans</i> : 20.67 $\pm$ 0.58 mm <i>Aspergillus niger</i> : 10.33 $\pm$ 0.58 mm <i>Cryptococcus neoformans</i> : 20.00 $\pm$ 0.00 mm at 50 μ l	[19]
<i>D. fragrans</i>	Aerial Part	Flavaspidic acid BB	Microdilution	MIC (<i>S. haemolyticus</i>): 5–480 μ g/mL	[76]
<i>D. crassirhizoma</i>	Roots	Methanol extract	Microdilution	MIC = 62.5 μ g/mL; MBC = 250 μ g/mL (<i>S. mutans</i>)	[14]

has been shown to exert immunomodulatory effects by stimulating nitric oxide production in macrophages [37].

D. ramosa has exhibited enzyme inhibitory activity; its methanol fraction inhibited acetylcholinesterase by 58.26% at a concentration of 0.5 mg/mL [7]. Additionally, in weight-loss corrosion tests in 1 M H₂SO₄, *D. cochleata* methanol extract inhibition efficiencies increased from ~80% at 400 ppm to ~95% at 2400 ppm, while water extract increased from ~55% to ~72% across the same concentration range [24]. Phloroglucinol derivatives isolated from *Dryopteris crassirhizoma* exhibited potent PTP1B inhibition, with dryocrassin ABBA being the most active compound (IC₅₀ = 3.62 μ M), suggesting potential applications in the treatment of diabetes and obesity [52]. These inhibitory effects were evaluated using electrochemical methods and weight loss assays [43].

Furthermore, the ethyl acetate fraction of *D. ramosa* demonstrated a 91.36% inhibition of alpha-glucosidase

at a concentration of 1 mg/mL, indicating notable anti-diabetic potential at a concentration of 0.5 mg/mL [7]. The identification of four novel terpenylated acylphloroglucinols in *D. wallichiana* further highlights the genus's chemical diversity and therapeutic promise [11].

Other study, evaluated the anthelmintic activity of methanol extracts from eight European ferns, including species from the genus *Dryopteris*, against the nematode *Haemonchus contortus*. The extracts were tested on both drug-susceptible and drug-resistant strains of the parasite using egg hatch and adult viability assays. Results showed that only *D. aemula* extract inhibited egg hatching by 25% at 0.2 mg/mL [80].

In a novel investigation, volatile organic compounds (VOCs) from the aerial parts of six *Dryopteris* species collected in France were profiled for the first time, resulting in the identification of fifty-three biosynthesized VOCs derived from the shikimic, lipidic, and terpenic

Table 9 Toxicological findings reported for *Dryopteris* species

Species	Extract/compound	Model	Toxicological parameter	Key findings	Reference
<i>D. crassirhizoma</i>	70% ethanol extract	Mouse	Genotoxicity	No mutagenic or clastogenic effects	[16]
<i>D. crassirhizoma</i>	90% ethanolic rhizome extract	MDCK cells	TC ₅₀	TC ₅₀ > 400 µM (low cytotoxicity)	[28]
<i>D. juxtapostia</i>	DCM root extract	Rat	Acute toxicity	Dose-dependent biochemical alterations	[56]
<i>D. stewartii</i>	Plant extract	Diabetic mice	Systemic toxicity	Mild toxicity at high dose	[64]
<i>D. filix-mas</i>	Phloroglucinols	Human (historical)	Neurotoxicity	GI distress, neurotoxicity, blindness	[11]

pathways using gas chromatography–mass spectrometry [20].

Toxicological profile

Phloroglucinol derivatives, including dryocrassin, filixic acids, and terpenylated acylphloroglucinols, are reported from several *Dryopteris* species and have been associated with toxic effects in experimental and historical contexts. Adverse outcomes such as neurotoxicity, gastrointestinal disturbances, and visual impairment have primarily been documented in cases of improper use, overdose, or historical medicinal application, particularly in relation to *D. filix-mas*, which was traditionally employed as an anthelmintic.

Recent experimental studies provide species- and dose-specific toxicological evidence rather than uniform toxicity across the genus. Acute oral toxicity and genotoxic effects have been reported for *D. crassirhizoma* in murine models [16]. *D. juxtapostia* demonstrated dose-dependent biochemical alterations indicative of early organ-level stress [56], while *Dryopteris stewartii* showed mild toxicity only at higher administered doses in diabetic mouse models [64]. These findings indicate that toxicological outcomes vary substantially with species, dose, exposure duration, and experimental model.

Given that relatively higher phloroglucinol content has been reported for *D. filix-mas*, *Dryopteris fragrans*, and *D. crassirhizoma* [11, 44], careful dose standardisation and comprehensive safety evaluation are warranted before considering pharmacological applications. Importantly, the absence of severe toxicity at lower or therapeutic dose ranges in some studies should not be interpreted as evidence of safety, underscoring the need for systematic toxicological assessment Table 9.

Pharmacological and human health applications

Extensive experimental work has highlighted the species *Dryopteris* as a source of bioactive secondary metabolites with potential health relevance. Several species have broad spectrum antiviral activity, in particular *D. crassirhizum*, for which phloroglucinols inhibit the proteases Mpro and PLpro of SARS-CoV-2 [57, 81]. The antiviral activity against H5N1 has been confirmed [45]. Strong antibacterial and antifungal properties are documented

in several species, including *D. cristata* nanoparticle formulations [83].

Anti-inflammatory compounds isolated from *D. crassirhizum* and *D. fragrana* modulate the signalling pathways ERK1 and TBK1 [15] or have potent anti-inflammatory and anti-cytokine-suppressive properties [23]. Several phloroglucinols, flavonoids and phenolic glycosides have anti-tumour activity by cytotoxic effects in a variety of tumour cell lines [18, 29, 85]. Further evidence supports the antidiabetic [52, 64], immunosuppressive, antioxidant, anthelmintic and gastroprotective activity of the product [37].

All things considered, these results lend credence to the possible development of *Dryopteris*-based treatments, especially those that target cancer, inflammation-related conditions, viral infections, and metabolic diseases.

Conclusion

The genus *Dryopteris*, a widely distributed group within the Dryopteridaceae family, holds notable ecological and medicinal significance. This scoping review, covering literature from 2010 to 2025, examined the chemical constituents, extraction methods, and biological activities reported for 34 *Dryopteris* species. Ecologically, these ferns contribute to soil stabilization and ground cover, while ethnobotanically they are valued in traditional Asian and Unani medicine for treating wounds, infections, and gastrointestinal disorders.

Most research has focused on *D. fragrans*, *D. crassirhizoma*, *D. erythrosora*, and *D. filix-mas*, primarily using leaves, rhizomes, and roots, whereas stems and shoots remain largely unexplored. Maceration remains the most common extraction technique, with solvent choice critically influencing phenolic and flavonoid yields. Methanol is frequently used for extracting total phenolic content (TPC), with *D. dilatata* showing a particularly high TPC of 434.3 mg GAE/g. Total flavonoid content (TFC) varies across species, exemplified by *D. crassirhizoma* roots exhibiting 208.09 ± 5.89 mg RE/g. Solvents such as dichloromethane and acetone also display variable efficiency depending on species and plant part.

Although significant progress has been made in understanding the phytochemical and biological activity of the species *Dryopteris*, several critical gaps remain.

Systematic toxicological testing is urgently needed since only a few species have been tested in acute and sub chronic conditions, despite the historical reports of serious adverse reactions associated with phloroglucinol-rich plants. Therefore, standardisation and quantification of acylphloroglucinol derivatives is necessary in order to ensure that they are safe for therapeutic use.

Future research should also focus on elucidating the molecular mechanisms underlying antiviral, anti-cancer and anti-inflammatory activity, establishing in vivo pharmacokinetic profiles of key metabolites such as ABBA and filixic acid, and improving bioavailability by new delivery systems. Comparative metabolomics across species and habitats, together with research on endophytic fungi related to *Dryopteris*, offer promising avenues for the discovery of new bioactive compounds. Continued exploration is needed on unexplored parts of plants, adopt advanced extraction techniques and prioritise the protection of endangered species through in vitro and ex-situ strategies. Addressing these shortcomings will improve understanding of the ecological role and therapeutic potential of *Dryopteris*, while promoting its sustainable use and protection of biodiversity.

Abbreviations

ABTS	2,2'-Azino-bis(3-ethylbenzothiazoline-6-sulfonic acid)
AUC	Area Under the Curve
BuOH	Butanol
CCK-8	Cell Counting Kit-8 assay
CHO-K1	Chinese Hamster Ovary cell line
COX-2	Cyclooxygenase-2
DCM	Dichloromethane
DMSO	Dimethyl sulfoxide
DPPH	2,2-Diphenyl-1-picrylhydrazyl
DW	Dry Weight
EA/EtOAc	Ethyl acetate
ERK	Extracellular signal-regulated kinase
FRAP	Ferric Reducing Antioxidant Power
GAE	Gallic Acid Equivalents
HS-SPME	Headspace Solid-Phase Microextraction
H ₂ O ₂	Hydrogen peroxide
IC ₅₀	Half maximal inhibitory concentration
iNOS	Inducible Nitric Oxide Synthase
LC-QTOF	Liquid Chromatography–Quadrupole Time-of-Flight
LPS	Lipopolysaccharide
MeOH	Methanol
MIC	Minimum Inhibitory Concentration
MERS-CoV	Middle East Respiratory Syndrome Coronavirus
Mpro	Main protease
MTT	3-(4,5-Dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide assay
NA	Not Available
NF-κB	Nuclear Factor kappa-light-chain-enhancer of activated B cells
NO	Nitric Oxide
OSCC	Oral Squamous Cell Carcinoma
PC3	Prostate cancer cell line
PGE ₂	Prostaglandin E ₂
PLpro	Papain-like protease
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
QE	Quercetin Equivalents
RAW 264.7	Murine macrophage cell line
RE	Rutin Equivalents
RNA	Ribonucleic Acid

SARS-CoV	Severe Acute Respiratory Syndrome Coronavirus
SARS-CoV-2	Severe Acute Respiratory Syndrome Coronavirus 2
SFE	Supercritical Fluid Extraction
TFC	Total Flavonoid Content
TNF-α	Tumor Necrosis Factor-alpha
TPC	Total Phenolic Content
UHPLC-MS	Ultra-High-Performance Liquid Chromatography–Mass Spectrometry
XO	Xanthine Oxidase

Acknowledgements

NA.

Author contributions

Bhupendra Shrestha had given the major ideas and plan on selection of topic and he has also given expert feedback on designing the whole process. Abinash Sharma and Anish Pradhan are the main author who had designed the review and framed the TOC and also done academic writing part. Kiran Sharma and Phunchok Norbu Sherpa had reviewed the selection of paper in PRISMA. Angila Theengh had worked on selection and collection of isolated molecule in the review. Binu Chettri and Tshamata Gurung had worked on framing table and figures.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sector.

Data availability

No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

Received: 13 September 2025 / Accepted: 3 February 2026

Published online: 06 March 2026

References

- Farias R, Silva I, Pereira AF, Santiago A, Barros I. Inventory of ferns and Lycophytes of the RPPN Pedra D'Antas, Pernambuco state, northeastern Brazil. *Biota Neotropica*/Biota Neotropica. 2017;17(4). <https://doi.org/10.1590/1676-0611-bn-2017-0364>.
- Morajka S, Sajeev S, Hegde S. Spore morphology of selected pteridophytes found in the western ghats of India. *Biosci Biotechnol Res Asia*. 2021;18(1):99–106. <https://doi.org/10.13005/bbra/2899>.
- Balkrishna A, Joshi B, Srivastava A, Shankar R, Tiwari S, Prajapati UB, et al. Some economic aspects of ferns and fern-allies of Seijosa Forest area of Pakke-Kessang District, Arunachal Pradesh. *Int J Adv Res Botany*. 2019;5:22–30. <https://doi.org/10.20431/2455-4316.0503003>.
- Shukla S, Khare P. In vitro conservation of some threatened and economically important ferns belonging to the Indian subcontinent. *J Botany*. 2014. 2014;949028. <https://doi.org/10.1155/2014/949028>.
- Zuo ZY, Zhao T, Du XY, Xiong Y, Lu JM, Li DZ. A revision of *Dryopteris* sect. *Diclisodon* (Dryopteridaceae) based on morphological and molecular evidence with description of a new species. *Plant Diversity*. 2021;44(2):181–90. <https://doi.org/10.1016/j.pld.2021.09.005>.
- Goswami HK, Sen K, Mukhopadhyay R. Pteridophytes: evolutionary boon as medicinal plants. *Plant Genetic Resour*. 2016;14(Spec Iss 4):328–55. <https://doi.org/10.1017/S1479262116000290>.
- Alam F, Khan SHA, Asad MHHB. Phytochemical, antimicrobial, antioxidant, and enzyme inhibitory potential of medicinal plant *Dryopteris ramosa* (Hope)

- C. Chr. BMC Complementary Med Therapies. 2021;21:197. <https://doi.org/10.1186/s12906-021-03370-7>.
8. Bafor EE, Omokaro WO, Uwumangongie OH, Elvis-Offiah UB, Omoruyi O, Viegmann CV, et al. *Dryopteris filix-mas* (Dryopteridaceae) leaves inhibit mouse uterine activity. J Med Plants Econ Devel. 2017;1(1):a25. <https://doi.org/10.4102/jomped.v1i1.25>.
 9. Mak S, Thomas A. Steps for conducting a scoping review. J Graduate Med Educ. 2022;14(5):565–67. <https://doi.org/10.4300/JGME-D-22-00621.1>.
 10. McLeod S. Doing a scoping review: a practical, step-by-step guide. 2024. <http://doi.org/10.13140/RG.2.2.23703.79528>.
 11. Socolsky C, Domínguez L, Asakawa Y, Bardón A. Unusual terpenylated acylphloroglucinols from *Dryopteris wallichiana*. Phytochemistry. 2012;80:115–22. <https://doi.org/10.1016/j.phytochem.2012.04.017>.
 12. Zhang M, Cao J, Dai X, Chen X, Wang Q. Flavonoid contents and free radical scavenging activity of extracts from leaves, stems, rachis and roots of *Dryopteris erythrosora*. Iran J Pharm Res. 2012;11:991–97.
 13. Kathirvel A, Sujatha V. Phytochemical studies, antioxidant activities, and identification of active compounds using GC-MS of *Dryopteris cochleata* leaves. Arabian J Chem. 2012;2:21:1–9. <https://doi.org/10.1016/j.arabjc.2012.03.018>.
 14. Ban S, Kim J, Pandit S, Jeon J. Influences of *Dryopteris crassirhizoma* extract on the viability, Growth and virulence properties of *Streptococcus mutans*. Molecules. 2012;17(8):9231–44. <https://doi.org/10.3390/molecules17089231>.
 15. Yang Y, Lee GJ, Yoon DH, Yu T, Oh J, Jeong D, et al. ERK1- and TBK1-targeted anti-inflammatory activity of an ethanol extract of *Dryopteris crassirhizoma*. J Ethnopharmacol. 2012;145(2):499–508. <https://doi.org/10.1016/j.jep.2012.11.019>.
 16. Hwang Y, Ha H, Yeul J, MA. Acute oral toxicity and genotoxicity of *Dryopteris crassirhizoma*. J Ethnopharmacol. 2013;149(1):133–39. <https://doi.org/10.1016/j.jep.2013.06.011>.
 17. Huang Y, Zeng W, Li G, Liu G, Zhao D, Wang J, et al. Characterization of a New Sesquiterpene and antifungal activities of chemical constituents from *Dryopteris fragrans* (L.) Schott. Molecules. 2014;19(1):507–13. <https://doi.org/10.3390/molecules19010507>.
 18. Zhao D, Zhao Q, Liu L, Chen Z, Zeng W, Lei H, et al. Compounds from *Dryopteris fragrans* (L.) Schott with cytotoxic activity. Molecules. 2014;19(3):3345–55. <https://doi.org/10.3390/molecules19033345>.
 19. Kathirvel A, Rai AK, Maurya G, Sujatha V. *Dryopteris cochleata* rhizome: a nutritional source of essential elements, phytochemicals, antioxidants, and antimicrobials. Int J Pharm Pharm Sci. 2014;6:179–88.
 20. Froissard D, Rapior S, Bessi re J, Fruchier A, Buatois B, Fons F. Volatile Organic compounds of six French *Dryopteris* species: natural odorous and bioactive Resources. Nat Prod Commun. 2014;9(1). <https://doi.org/10.1177/1934578x1400900138>.
 21. Bahadori MB, Mahmoodi F, Bahadori S, Valizadeh H. Antibacterial evaluation and preliminary phytochemical screening of selected ferns from Iran. Res J Pharmacogn. 2015;2:53–59.
 22. Valizadeh H, Sonboli A, Kordi FM, Dehghan H, Bahadori MB. Cytotoxicity, antioxidant activity and phenolic content of eight fern species, from north of Iran. Pharm Sci. 2015;21(1):18–24. <https://doi.org/10.15171/ps.2015.12>.
 23. Peng B, Bai R, Li P, Han X, Wang H, Zhu C, et al. Two new glycosides from *Dryopteris fragrans* with anti-inflammatory activities. J Asian Nat Products Res. 2015;18(1):59–64. <https://doi.org/10.1080/10286020.2015.1121853>.
 24. Nathiya RS, Raj V. Evaluation of *Dryopteris cochleata* leaf extracts as green inhibitor for corrosion of aluminium in 1M H₂SO₄. Egypt J Petroleum. 2016;26:1–10. <https://doi.org/10.1016/j.ejpe.2016.05.002>.
 25. Rajesh N, Subramani A, Devi RK. Antibacterial activity of *drynariaquercifolia* (L.) J. Smith and *Dryopteris cochleata* (Buch. Ham. ex. D. Don). Ann Phytomed Int J. 2017;VI(1):148–54. <https://doi.org/10.21276/ap.2017.6.1.23>.
 26. Yoo G, Park S, Yang H, Nguyen XN, Kim N, Park JH, et al. Two new phenolic glycosides from the aerial part of *Dryopteris erythrosora*. Pharmacogn Mag. 2017;13(52):673. https://doi.org/10.4103/pm.pm_326_16.
 27. Zhong Z, Zhao D, Liu Z, Jiang S, Zhang Y. A New human cancer cell proliferation inhibition Sesquiterpene, dryofraterpene A, from medicinal plant *Dryopteris fragrans* (L.) Schott. Molecules. 2017;22(1):180. <https://doi.org/10.3390/molecules22010180>.
 28. Wang J, Yan Y, Fu S, Peng B, Bao L, Zhang Y, et al. Anti-influenza virus (H5N1) activity screening on the phloroglucinols from Rhizomes of *Dryopteris crassirhizoma*. Molecules. 2017;22(3):431. <https://doi.org/10.3390/molecules22030431>.
 29. Zhang T, Wang L, Duan D, Zhang Y, Huang S, Chang Y. Cytotoxicity-guided isolation of Two New phenolic derivatives from *Dryopteris fragrans* (L.) Schott. Molecules. 2018;23(7):1652. <https://doi.org/10.3390/molecules23071652>.
 30. Gao R, Wang W, Huang Q, Fan R, Wang X, Feng P, et al. Complete chloroplast genome sequence of *Dryopteris fragrans* (L.) Schott and the repeat structures against the thermal environment. Sci Rep. 2018;8(1):16635. <https://doi.org/10.1038/s41598-018-35061-8>.
 31. Guo Y, Li JJ, Busta L, Jetter R. Coverage and composition of cuticular waxes on the fronds of the temperate ferns *Pteridium aquilinum*, *cryptogramma crispa*, *polypodium glycyrrhiza*, *polystichum munitum* and *Gymnocarpium Dryopteris*. Ann Botany. 2018;122(4):555–68. <https://doi.org/10.1093/aob/mcy078>.
 32. Zhang X, Wang X, Wang M, Cao J, Xiao J, Wang Q. Effects of different pretreatments on flavonoids and antioxidant activity of *Dryopteris erythrosora* leave. PLoS One. 2019;14(1):e0200174. <https://doi.org/10.1371/journal.pone.0200174>.
 33. Sher J. Analgesic, anti-inflammatory, antioxidant activity and phytochemical screening of *Dryopteris blanfordii*. 2018 plant.
 34. Liu X, Liu J, Jiang T, Zhang L, Huang Y, Wan J, et al. Analysis of chemical composition and in vitro antidermatophyte activity of ethanol extracts of *Dryopteris fragrans* (L.) Schott. J Ethnopharmacol. 2018;226:36–43. <https://doi.org/10.1016/j.jep.2018.07.030>.
 35. Liu ZD, Zhao DD, Jiang S, Xue B, Zhang YL, Yan XF. Anticancer phenolics from *Dryopteris fragrans* (L.) Schott. Molecules. 2018;23(3):680. <https://doi.org/10.3390/molecules23030680>.
 36. Erhirhie EO, Emeghebo CN, Ilodigwe EE, Ajaghaku DL, Umeokoli BO, Eze PM, et al. *Dryopteris filix-mas* (L.) Schott ethanolic leaf extract and fractions exhibited profound anti-inflammatory activity. Avicenna J Phytomed. 2019;9(4):396–409.
 37. Zhao Y, Hu W, Zhang H, Ding C, Huang Y, Liao J, et al. Antioxidant and immunomodulatory activities of polysaccharides from the rhizome of *Dryopteris crassirhizoma* Nakai. Int J Biol Macromolecules. 2019;130:238–44. <https://doi.org/10.1016/j.jbiomac.2019.02.119>.
 38. Sulamsi ES, Sari RS, Wuriana ZF, Sari MS, Suhadi N, Mawaddah K, et al. Do altitude influence the characterization of *Dryopteris hirtipes* (Bl.) Kuntze biomedical profile? A study of fascinating fern from Baluran National Park and Raden Soerjo Grand Forest Park. IOP Conf Ser Earth Environ Sci. 2019;276(1):012024. <https://doi.org/10.1088/1755-1315/276/1/012024>.
 39. Amin S, Ullah B, Ali M, Rauf A, Khan H, Uriarte E, et al. Potent in vitro α-glucosidase inhibition of secondary metabolites derived from *Dryopteris cycadina*. Molecules. 2019;24(3):427. <https://doi.org/10.3390/molecules24030427>.
 40. Yim N, Lee J, Lee B, Li W, Yeul J, MA. Antiplatelet activity of acylphloroglucinol derivatives isolated from *Dryopteris crassirhizoma*. Molecules. 2019;24(12):2212. <https://doi.org/10.3390/molecules24122212>.
 41. Lee J, Nho YH, Yun SK, Hwang YS. Anti-invasive and anti-tumor effects of *Dryopteris crassirhizoma* extract by disturbing actin polymerization. Integr Cancer Therapies. 2019;18:1534735419851197. <https://doi.org/10.1177/1534735419851197>.
 42. Tiwari S. Insecticidal action of *Dryopteris filix-mas* (Linn.) Schott against larval biochemistry of rice moth *corcyra cephalonica* staint. (Lepidoptera: pyralidae). Int J Zoological Investigations. 2019;5:81–98. <https://doi.org/10.33745/ijzi.2019.v05i01.008>.
 43. Sohail M, Ihsan M, Begum L, Ullah S. List of some selected pteridophytes from maidan valley of dir lower Khyber Pakhtunkhwa Pakistan. Int J Horticulture Food Sci. 2019;1:15.
 44. Yuk HJ, Kim J, Sung Y, Kim D. Phloroglucinol derivatives from *Dryopteris crassirhizoma* as potent Xanthine oxidase inhibitors. Molecules. 2020;26(1):122. <https://doi.org/10.3390/molecules26010122>.
 45. Chen L, Zhang D, Song C, Wang H, Tang X, Chang Y. Transcriptomic analysis and specific expression of transcription factor genes in the Root and sporophyll of *Dryopteris fragrans* (L.) Schott. Int J Mol Sci. 2020;21(19):7296. <https://doi.org/10.3390/ijms21197296>.
 46. Chen X, Liu W, Huang X, Fu H, Wang Q, Wang Y, et al. Arg-type dihydroflavonol 4-reductase genes from the fern *Dryopteris erythrosora* play important roles in the biosynthesis of anthocyanins. PLoS One. 2020;15(5):e0232090. <https://doi.org/10.1371/journal.pone.0232090>.
 47. Earnest E, Ilodigwe E, Ajaghaku D, Umeokoli B, Eze P, Okoye F. Antioxidant activities of the leaf extract and fractions of *Dryopteris filix-mas* (L.) Schott could be attributed to the abundance of polyphenol compounds. Biol, Med, Nat Prod Chem. 2020;9(1):1–6. <https://doi.org/10.14421/biomedich.2020.91.1-6>.
 48. Maqsood M, Te K, Wong F-C, Chai T-T, Low G, Gan SC, et al. Antiviral activity of traditional Chinese medicinal plants *Dryopteris crassirhizoma* and *Morus alba* against dengue virus. J Integr Agriculture. 2020;19:1085–96. [https://doi.org/10.1016/S2095-3119\(19\)62820-0](https://doi.org/10.1016/S2095-3119(19)62820-0).

49. Abdi B, Getaneh E, Gelaw T, Dekebo A, Tesso H, Abdo T, et al. Chemical constituents of the roots extract of *Dryopteris schimperiana* and evaluation for antibacterial and radical scavenging activities. *Ethiopian J Sci Sustain Devel*. 2020;7:1–7. <https://doi.org/10.20372/ejssdstav7.11.2020.153>.
50. Li SS, Chang Y, Li B, Shao SL, Zhen-Zhu Z. Functional analysis of 4-coumarate: CoA ligase from *Dryopteris fragrans* in transgenic tobacco enhances lignin and flavonoids. *Genet Mol Biol*. 2020;43(2):e20180355. <https://doi.org/10.1590/1678-4685-GMB-2018-0355>.
51. Femi-Adepoju A, Oluyori A, Fatoba P, Adepoju A. Phytochemical and antimicrobial analysis of *Dryopteris filix-mas* (L.) Schott. *Rasayan J Chem*. 2021;14(1):616–21. <https://doi.org/10.31788/rjc.2021.1415983>.
52. Phong NV, Oanh VT, Yang SY, Choi JS, Min BS, Kim JA. PTP1B inhibition studies of biological active phloroglucinols from the rhizomes of *Dryopteris crassirhizoma*: kinetic properties and molecular docking simulation. *Int J Biol Macromolecules*. 2021;188:719–28. <https://doi.org/10.1016/j.jbiomac.2021.08.091>.
53. Dvorakova M, Pumpova K, Antonínová Ž, Rezek J, Haisel D, Ekrť L, et al. Nutritional and antioxidant potential of fiddleheads from European ferns. *Foods*. 2021;10(2):460. <https://doi.org/10.3390/foods10020460>.
54. Ishaque M, Bibi Y, Ayoubi S, Masood S, Nisa S, Qayyum A. Iriflophenone-3-C- β -D-glucopyranoside from *Dryopteris ramosa* (Hope) C. Chr. With promising future as Natural antibiotic for gastrointestinal tract infections. *Antibiotics*. 2021;10(9):1128. <https://doi.org/10.3390/antibiotics10091128>.
55. Ishaque M, Bibi Y, Qayyum A, et al. Isolation and structural confirmation of xanthone isomers from *Dryopteris ramosa* (Hope) C. Chr. And their in vitro antioxidant mechanism. *Arab J Sci Eng*. 2021;46:5327–37. <https://doi.org/10.1007/s13369-020-05097-y>.
56. Rani A, Uzair M, Ali S, Qamar M, Ahmad N, Abbas MW, et al. *Dryopteris juxtaopostia* Root and shoot: determination of Phytochemicals; antioxidant, anti-inflammatory, and Hepatoprotective Effects; and toxicity assessment. *Antioxidants*. 2022;11(9):1670. <https://doi.org/10.3390/antiox11091670>.
57. Jin Y, Jeon S, Lee J, Kim S, Jang MS, Park CM, et al. Anticoronaviral activity of the Natural phloroglucinols, *Dryocrassin ABBA* and *Filixic acid ABA* from the Rhizome of *Dryopteris crassirhizoma* by targeting the Main protease of SARS-CoV-2. *Pharmaceutics*. 2022;14(2):376. <https://doi.org/10.3390/pharmaceutics14020376>.
58. Zia-Ur-Rehman N, Rasheed HM, Bashir K, Gurgul A, Wahid F, Che C, et al. UHPLC-MS/MS-GNPS based phytochemical investigation of *Dryopteris ramosa* (Hope) C. Chr. And evaluation of cytotoxicity against liver and prostate cancer cell lines. *Heliyon*. 2022;8(11):e11286. <https://doi.org/10.1016/j.heliyon.2022.e11286>.
59. Kim Y, Lim DJ, Song J, Kim J, Lee B, Son YK. Identification and Comparison of bioactive components of Two *Dryopteris* sp. Extract using LC-QTOF-MS. *Plants*. 2022;11(23):3233. <https://doi.org/10.3390/plants11233233>.
60. Yun S, Bai J. Synergistic antimicrobial effects of *Dryopteris erythrosora* extract and mild heat treatment against *Staphylococcus aureus*. *LWT*. 2022;173:114260. <https://doi.org/10.1016/j.lwt.2022.114260>.
61. Wang Y, Liu B, Wang X, Fan Y. Comparison of constituents and antioxidant activity of above-ground and Underground parts of *Dryopteris crassirhizoma Nakai* based on HS-SPME-GC-MS and UPLC/Q-TOF-MS. *Molecules*. 2022;27(15):4991. <https://doi.org/10.3390/molecules27154991>.
62. Phong NV, Zhao Y, Min BS, Yang SY, Kim JA. Inhibitory activity of bioactive phloroglucinols from the Rhizomes of *Dryopteris crassirhizoma* on *Escherichia coli* β -glucuronidase: kinetic analysis and molecular docking studies. *Metabolites*. 2022;12(10):938. <https://doi.org/10.3390/metabo12100938>.
63. Ikpa CB, Ikezu UJ, Maduwuba MC. In silico docking analysis of anti-malaria and anti-typhoid potentials of phytochemical constituents of ethanol extract of *Dryopteris dilatata*. 2022 May 1. <https://tjnpr.org/index.php/home/article/view/60>.
64. Hanif U, Raza C, Liaquat I, Rani M, Afifi SM, Esatbeyoglu T, et al. Evaluation of safety of Stewart's wood fern (*Dryopteris stewartii*) and its anti-hyperglycemic potential in alloxan-induced diabetic mice. *Int J Mol Sci*. 2022;23(20):12432. <https://doi.org/10.3390/ijms232012432>.
65. Wang Z, Wang N, Han D, Yan H. Characterization of tyrosinase inhibitors in *Dryopteris crassirhizoma* rhizome using a combination of high-speed counter current chromatography, affinity-based ultrafiltration, and liquid chromatography tandem mass spectrometry. *Front Nutr*. 2022;9:862773. <https://doi.org/10.3389/fnut.2022.862773>.
66. Zhang Z, Liu X, Shen Z, Chen Y, Chen C, SiTu Y, et al. Isoflavaspicid acid PB extracted from *Dryopteris fragrans* (L.) Schott Inhibits trichophyton rubrum Growth via membrane permeability alternation and ergosterol biosynthesis disruption. *Biomed Res Int*. 2022;2022(1):6230193. <https://doi.org/10.1155/2022/6230193>.
67. Ejidike IP, Ijimdiya RU, Emmanuel-Akerere HA, Emmanuel GC, Ejidike OM, Bamigboye MO, et al. Biosynthesis, characterization, and antimicrobial assessment of metal nanoparticles from *Dryopteris manniana* (Hook.) C. Chr Leaf Extract. *Bull Pharm Sci Assiut Univ*. 2023;46(1):225–38.
68. Hussain M, Aziz A, Javaid M, Ashraf M, Wasaya A, Majeed M, et al. Evaluating the phytotoxic effects of some plant species of semi-arid regions. *Plant Cell Biotechnol Mol Biol*. 2022;23:1–18. <https://doi.org/10.56557/pcbmb/2022/v23i1-27376>.
69. Atanasov A, Karadjova V, Andonova A, Tsekova D, Lozanov V, Parashkevova B, et al. Synthesis, isolation and biological activity studies of galanthamine derivatives including peptide moiety and tannins from medicinal plants. *Int J Pharm Pharm Sci*. 2022;57:32–38.
70. OjosOjosnegros S, Alvarez JM, Grossmann J, Gagliardini V, Quintanilla LG, Grossniklaus U, et al. The shared proteome of the apomictic fern *Dryopteris affinis* ssp. *affinis* and its sexual relative *Dryopteris oreades*. *Int J Mol Sci*. 2022;23(22):14027. <https://doi.org/10.3390/ijms232214027>.
71. Saimaiti M, Gençcelep H. Thermal and molecular characteristics of novel water-soluble polysaccharide from the *Pteridium aquilinum* and *Dryopteris filix-mas*. *Food Chem Adv*. 2023;3:100401. <https://doi.org/10.1016/j.focha.2023.100401>.
72. Hai P, Gao Y, Yang L, Chen N, Jia H, Wang M, et al. Two New compounds from the endophytic fungi of *Dryopteris crassirhizoma* and their Antimicrobial activities. *Molecules*. 2023;28(24):8043. <https://doi.org/10.3390/molecules28248043>.
73. Iqbal I, Saqib F, Latif MF, Shahzad H, Dima L, Sajer B, et al. Pharmacological basis for Antispasmodic, bronchodilator, and antidiarrheal potential of *Dryopteris ramosa* (Hope) C. via Vitro, Vivo, In Silico Stud ACS Omega. 2023;8(30):26982–7001. <https://doi.org/10.1021/acsomega.3c01907>.
74. Zhang D, Tang X, Chen L, Qiu X, Song C, Wang H, et al. Functional characterization and transcriptional activity analysis of *Dryopteris fragrans* farnesyl diphosphate synthase genes. *Front Plant Sci*. 2023;14:1105240. <https://doi.org/10.3389/fpls.2023.1105240>.
75. Akpotu AE, Ghasi SI, Ajibo DN, Ike AO, Akhator AJ, Enya JI, et al. Free radical scavenging activity and phytochemical investigation of ethanol leaf extract of *Dryopteris dilatata*. *J Complementary Alternative Med Res*. 2023;22(2):37–48. <https://doi.org/10.9734/jocamr/2023v22i2a455>.
76. Liu J, Liu R, Deng R, Zheng S, Shen Z. Evaluation of flavaspicid acid BB from *Dryopteris fragrans* (L.) Schott against resistant *Staphylococcus haemolyticus* in planktonic and biofilm forms. 2023. <https://doi.org/10.21203/rs.3.rs-2931297/v1>.
77. Gupta A, Sharma R, Kumar N, Bansal M. Phytochemical screening, gas chromatography-mass spectrometry, and in vitro antioxidant potential of *Dryopteris marginalis*. *J Adv Sci Res*. 2023;14(10):13–21. <https://doi.org/10.55218/JASR.2023.141004>.
78. Shah A, Rashid S, Mir S. Qualitative phytochemical analysis of some medicinally important fern species collected from conoor and Udthagamandalam, Tamil Nadu, India. *J Pharmacogn Phytochem*. 2023;14:1–5.
79. Lamichhane G, Sharma G, Sapkota B, Adhikari M, Ghimire S, Poudel P, et al. Screening of antioxidant, antibacterial, anti-adipogenic, and anti-inflammatory activities of five selected medicinal plants of Nepal. 2023.
80. Pavičić A, Zajičková M, Šadibolová M, Svobodová G, Matoušková P, Szotáková B, et al. Anthelmintic activity of European fern extracts against *Haemonchus contortus*. *Vet Res*. 2023;54(1). <https://doi.org/10.1186/s13567-023-01192-8>.
81. Habib M, Jin Y, Kim Y, Min JS, Ha JJ, Lee S, et al. Anticoronavirus activity of rhizome of *Dryopteris crassirhizoma* via multistage targeting of virus entry and viral proteases, Mpro and PLpro. *J Ethnopharmacol*. 2024;333:118490. <https://doi.org/10.1016/j.jep.2024.118490>.
82. Khanum A, Bibi Y, Khan I, Mustafa G, Attia KA, Mohammed AA, et al. Molecular docking of bioactive compounds extracted and purified from selected medicinal plant species against covid-19 proteins and in vitro evaluation. *Sci Rep*. 2024;14(1):3736. <https://doi.org/10.1038/s41598-024-54470-6>.
83. Bello ET, Awe S, Bale MI, Awosika A, Oladejo JM, Olaitan FJ, et al. Antibacterial activity of phyto-synthesized silver nanoparticles from *Dryopteris cristata* against *Staphylococcus aureus* ATCC 28923 and *Escherichia coli* ATCC 28922. *Cureus*. 2024;16(10):e70856. <https://doi.org/10.7759/cureus.70856>.
84. Zhao H, Su J, Zhong Z, Xiong T, Dai W, Zhang D, et al. Functional identification and regulatory active site screening of the DFDXS gene of *Dryopteris fragrans*. *Plants*. 2024;13(18):2647. <https://doi.org/10.3390/plants13182647>.
85. Said K, Rauf M, Khan SA, Hussain A, Alhegaili AS, Hussain S, et al. Metabolomics and anticancer potential of the aerial parts of *Dryopteris ramosa* against

- cancerous cell lines assisted with advanced computational approaches. *Curr Pharm Des.* 2024. <https://doi.org/10.2174/0113816128349549241025150229>.
86. Razgonova MP, Okhlopova ZM, Nawaz MA, Egorova PS, Golokhvast KS. Supercritical extraction and identification of bioactive compounds in *Dryopteris fragrans* (L.) Schott. *Pharmaceuticals.* 2025;18(3):299. <https://doi.org/10.3390/ph18030299>.
87. Salih AM, Al-Qurainy F, Nadeem M, Tarroum M, Khan S, Shaikhaldein HO, et al. Optimization method for phenolic compounds extraction from medicinal plant (*Juniperus procera*) and phytochemicals screening. *Molecules.* 2021;26(24):7454. <https://doi.org/10.3390/molecules26247454>.
88. García-Lafuente A, Guillamón E, Villares A, Rostagno MA, Martínez JA. Flavonoids as anti-inflammatory agents: implications in cancer and cardiovascular disease. *Inflammation Res.* 2009;58(9):537–52. <https://doi.org/10.1007/s00011-009-0037-3>.
89. Kumar S, Pandey AK. Flavonoids as potential anti-inflammatory molecules: a review. *Int J Mol Sci.* 2022;23(9):4807. <https://doi.org/10.3390/ijms2309480>.

Publisher's Note

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.