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REVIEW

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Medicinal pteridophytes: ethnopharmacological, phytochemical, and clinical attributes

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Abstract

Background: Almost from the very beginning of human existence, man has been interacting with plants. Throughout human history, plants have provided humans with basic needs such as sustenance, firewood, livestock feed, and wood. The world has approximately 3 million vascular plants. The treatment of primary health problems is provided primarily by traditional medicines by around 80% of the world's population. Compared to other vascular plants, pteridophytes remain underexplored in ethnobotanical aspects, despite being regarded as a valuable component of healthcare for centuries. As an alternative medicine, pteridophytes are being investigated for their pharmacological activity. Almost 2000 years ago, humans were exploring and using plant species from this lineage because of its beneficial properties since pteridophytes were the first vascular plants.

Main body of the abstract: All popular search engines such as PubMed, Google Scholar, ScienceDirect, and Scopus were searched to retrieve the relevant literature using various search strings relevant to the topic. Pteridophytes belonging to thirty different families have been documented as medicinal plants. For instance, *Selaginella* sp. has been demonstrated to have numerous therapeutic properties, including antioxidative, inflammation-reducing, anticarcinogenic, diabetes-fighting, virucidal, antibacterial, and anti-senile dementia effects. In addition, clinical trials and studies performed on pteridophytes and derived compounds are also discussed in details.

Short conclusion: This review offers a compilation of therapeutically valuable pteridophytes utilized by local ethnic groups, as well as the public.

Keywords: Pteridophytes, Ethnobotany, Pharmacology, Phytochemistry

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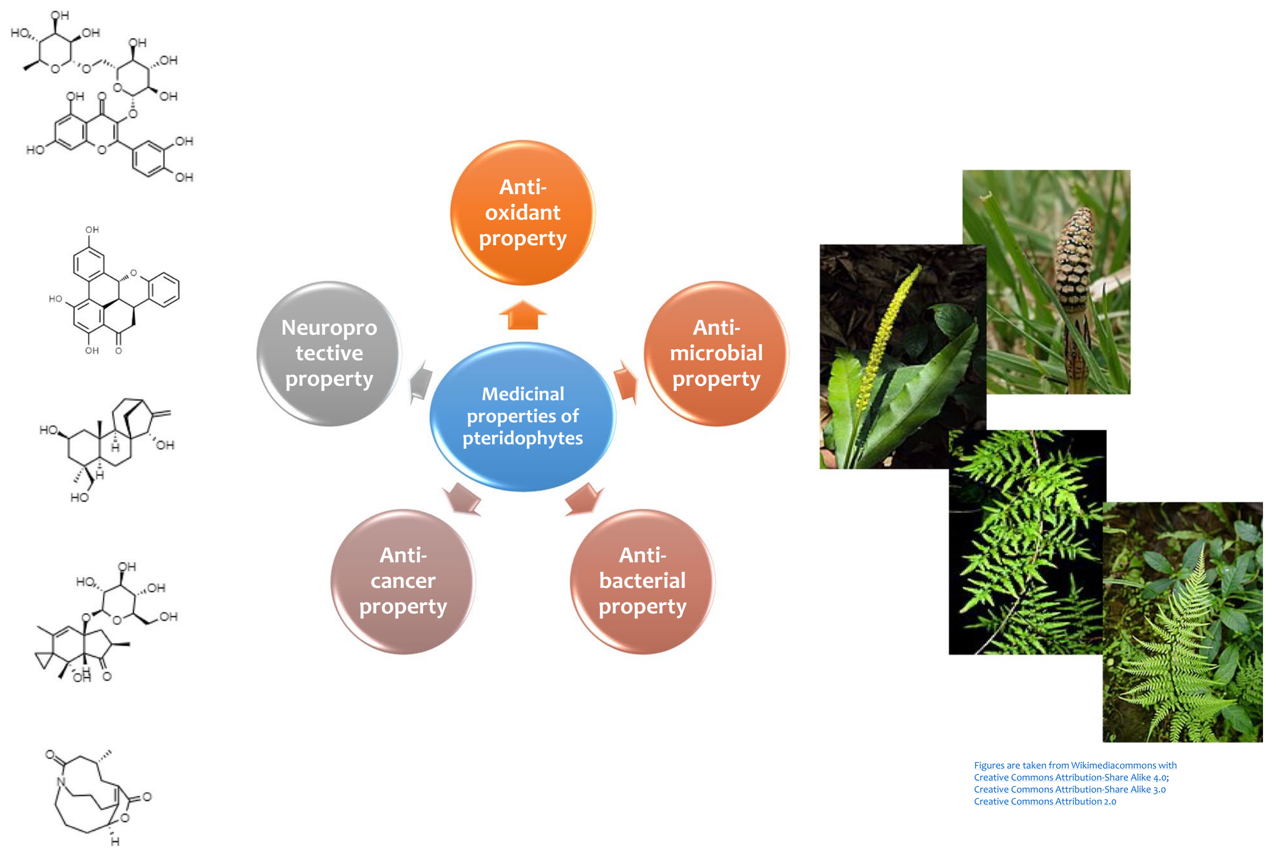
Graphical Abstract



1 Background

People from all continents have utilized medicinal plants as a remedy for several ailments since ancient times [47, 48, 114]. While synthetic organic chemistry has experienced significant growth in the twentieth century, plants are responsible for producing nearly one-quarter of all pharmaceuticals approved by the drug administration boards [120]. Phytochemicals that have antioxidant, antibacterial, or inflammation-fighting abilities have become increasingly sought after for their prospective applications in combating a variety of chronic diseases and infections [6, 70, 134]. Alternative sources of antimicrobial agents, such as plants, might offer potent bioactivity against microbes with pathogenicity, while having fewer adverse effects [11, 13]. There are a number of secondary metabolites in plants, including phenols, which are biologically active [8, 16]. Antimicrobial and antioxidant properties are known to be associated with plant secondary metabolites, with some of them receiving general safety approval [135]. Due to the increasing demand for phyto-compounds, there is a great demand for plants with biomedical properties [3, 33].

Many plants contain phytochemicals that are used as components of the diets of humans and animals. Fruits, nuts, and greens, for example, contain phytochemicals [123]. As plants proceed through their normal metabolic processes, they form phytochemicals. The term "secondary metabolites" refers to the many kinds of chemicals which can be found in plants, namely alkaloids, coumarins, flavonoids, glycosides, gums, phenols, polysaccharides, tannins, terpenes, and terpenoids [80, 126]. Plants also contain other chemical compounds in addition to these. They can be used as adjuvants to reduce unwanted side effects of the active ingredients or as means of assisting with their absorption. Plants are capable of synthesizing an almost infinite number of aromatic compounds, of which 12,000 have been found [104]. The researchers estimate that this is only a small fraction of the total. The active compounds of plants are present in different parts, which can influence the functioning of organs in both humans and animals. Phytochemicals can protect plants from predation by microbes, pests, and grazers, while also exhibiting therapeutic properties for a variety of ailments.

There are over 12,000 species in Ferns and their allies, distributed over 250 different genera in the Pteridophyta [31]. According to Sushruta and Charka, some ferns are prescribed in the Samhita texts of the Ayurvedic systems of medicine. In Unani medicine as well, pteridophytes are used [164]. Native doctors in China recommend ferns in the traditional Chinese medical system [82]. Recent studies have investigated ferns and their allies from an ethnobotanical and advanced pharmacological point of view [34, 35, 50, 51, 140, 169]. Inhibition of the cyclo oxygenase pathway can be associated with anti-inflammatory properties of fern secondary metabolites, flavonoids [95]. Moreover, they possess antioxidative, cancer-preventive, and antibacterial activities [2, 67, 97, 99, 189]. There are a variety of bioactive flavonoids in spider brake fern (*Pteris multifida*), that have thermoregulation, anti-fever, cleansing, antibiotic, inflammation-relieving, and mutagen-suppressive properties [93]. Various bioactive compounds are present in the plant of *P. multifida*, namely, 16-hydroxy-kaurane-2-β-D-glucoside [98], apigenin 4-*O*-α-L-rhamnoside [100, 137], apigenin-7-*O*-β-D-glucoside [73, 100], hyperin, isoquercitrin, kaempferol, luteolin, luteolin-7-*O*-glucoside [117], palmitic acid, quercetin and rutin [73, 100, 175]. Furthermore, *P. multifida* contains bioactive compounds that are cytotoxic to cells, pterosin sesquiterpenes [152]. Terpenoids with bioactive properties, particularly monocyclic sesquiterpene α-caryophyllene, and extracts of Pteris tripartita were found containing these compounds. In addition to acting as anti-carcinogenic, inflammation-reducing, cytotoxic, phytoregulatory, and antibacterial substances, sesquiterpenes are also an important group of secondary metabolites [9]. Humans have known for more than 2000 years that the pteridophytes are medicinal plants. In modern chemotherapy, however, there are very few applications compared to the angiosperms. *Drynaria quercifolia* has been reported to help with flatulence, heartburn, constipation, inflammatory conditions, typhoid, flu, osteoarthritis, migraines, and nausea. Hemoptysis is treated with a rhizome decoction either fresh or dried. Astringents and antiparasitic drugs are also used as a result of its properties. Digestive problems can also be treated using its leaves.

2 Ethnomedicinal properties of pteridophytes

All types of diseases are treated with traditional medicine in urban, rural, and areas rich in aboriginal people [49, 58]. Pteridophytes were first studied by Caius in India for their medicinal properties [20]. The knowledge of ethnobotanical and medicinal uses of pteridophytes was exposed by [38, 124, 124, 170]. The spores and rhizomes of Sporophytes have been proven to have medicinal properties. Many diseases can be cured with the plant extract of pteridophytes. Several pteridophytes are reported to cure human disorders by Theophrastus and Dioscorides in their works from 327 to 287 BC. Also mentioned by Shushurta and Charak are specific ferns such as *Marsilea minuta* and *Adiantum capillus-veneris.* There is evidence that *Selaginella bryopteris and Lycopodium clavatum* are frequently prescribed for neurological disorders and to address the effects of heat stroke in the homeopathic system of medicine. Splinted bones can be treated with *L. clavatum*. Herb Ayurvedic formulations contain *Helenthostachys zeylanica* (Kamraj) as a sexual stimulant and a tonic. Known to boost immunity, marsiline is isolated from *Marsilea minuta* and is also known to treat a variety of conditions, including sleeplessness, flatulence, cough and indigestion. A number of gastrointestinal bacterial strains have been shown to be resistant to the antimicrobial properties of *Pteris vittata*. In addition, pteridophytes would prove themselves to be a vital biological resource for the benefit of humanity due to their enormous importance and vast medicinal scope. Plants, such as ferns, are used as fodder and food in tropical countries. In addition to serving as a supplementary food source, dried fern biomass is used as a strong insulation against extreme temperatures and as an effective absorber of urinal excreta in cattle sheds. Listed below are some important plants and their ethnobotanical significance.

2.1 *Acrostichum aureum* L. (Pteridaceae)

A paste made from leaves is used to treat headaches. Tender leaves can be eaten raw or cooked as a vegetable. Besom and fish attractors can be made from the fronds. Paste of rhizomes is frequently used for healing wounds and boils [149].

2.2 *Actiniopteris dichotoma* Kuhn. (Actiniopteridaceae)

A number of conditions are treated with rhizomes, including chronic cough, gallstones, gastrointestinal problems, infection, Hansen's disease, skin conditions, high blood sugar, and hyperthermia. For sore throats, the leaves are chewed, and to remove dandruff, the rhizomes are boiled and then applied [158].

3 *A. radiata* (J. Koenig ex Sw.) Link (Actiniopteridaceae)

Rhizomes and leaves are employed as disinfectants, to treat asthma, and for disorders related to the female reproductive system. Tuberculosis is treated with dried fronds [149, 156]. Watery stool and high temperatures are treated using the juice from the stem twice daily [79]. For treatment of leukorrhoea and fertility enhancement, fresh leaves paste or powdered leaves are taken twice a day with honey [20]. Five to six leaves are taken twice a day with sugar as a philter and tonic to stimulate fertility in women [127].

3.1 *Adiantum capillus-veneris* L. (Adiantaceae)

Aphrodisiac properties are associated with rhizomes and leaves [12]. India's indigenous community uses the juice of fresh plants to treat cough and blood sugar levels. The juice is also administered to children as a nutritional supplement. High temperatures and acute respiratory infections may be treated by leaf extraction. Chicken pox can be controlled by placing rhizomes and leaves next to the bed [156]. In combination with honey, the leaves are used to make ophthalmic to speed up the healing process, applying *Aloe vera* gel along with paste made from leaves, stems, and rhizomes is prevalent among several communities. To promote hair growth, the leaves, stems, and roots of the plant are mashed together [79]. Astringent and diuretic properties have also been attributed to it [149]. Leaf chewing is used to treat mouth ulcers. Leaf, stem, and rhizome pastes are also used as urine promoters, stimulants, mucoprotective agent, mucoactive agent, and anti-pyretic agent [166].

3.2 *A. caudatum* L.

Foliage extracts are used to treat wounds, to get relief in cough and fever [144]. Antihelmintic properties are associated with rhizomes [149]. In addition to its uses as an Mucoactive agent, it is used in the treatment of dermatological conditions, blood sugar disorders, coughing, and high temperatures [158, 161]. Blisterd, wounds, and abrasions can be treated with leaf paste.

3.3 *A. incisum* forsk

Leaf dust is consumed with butter, thus relieving the feeling of burning in the body [144]. Additionally, it is used for cough relief, lowering blood sugar levels, and for treating dermatological disorders [156, 166].

3.4 *A. lunulatum* Burm.

Acute abdominal cramps, Hansen's disease, and flu are treated by this plant. For a centipede bite, fronds and rhizomes are mixed together into a paste. Blood-related diseases, such as epilepsy and rabies, can also be treated with it. Rhizomes are recommended for strange symptoms and fever caused by elephantiasis. Loose motion, soreness, and discomfort are treated with crushed leaves and juice [161].

3.5 *A. philippense* L.

Chronic nasal congestion, cough, bronchitis, swelling of the throat, and swollen glands of the face can be treated with the plant. The fresh frond extract is used for treating dysentery, blood diseases, ulcers, and burning sensations. For immediate relief from gastric problems, fresh frond paste about 1 gm can be given twice daily on an unfilled stomach for two weeks.

Curing glandular swelling with rhizome is an effective remedy. A powdered rhizome of about one gram combined with water can be used as a contraceptive by tribal women once every 3 to 5 days during menstruation.

Menstrual irregularities are treated with fresh leaf extracts [158–160]. In addition to treating respiratory diseases, it also helps in treating pyrexia, Hansen's disease and thinning hair [155, 166]. This substance is found in Hansraj, the Indian cough medicine. As a remedy for pyrexia and Filariasis, rhizome is considered useful [83]. Also, rhizome is used as an antidote when treating Snakebite envenoming and dog bites [158].

3.6 *Cheilanthes bicolor* (Roxb.) Griff. ex Fras.-Jenk. (Sinopteridaceae)

In Indian medicine, leaves and rhizomes are used as a stimulant and also as a remedy for preventing fear among children. Young girls use the stems as nasal and ear ornaments [156].

3.7 *C. farinosa* (Forsk.) Kaulf

The leaves of the plant are brewed into a decoction, which is taken orally for seven days to treat menstrual irregularities. Additionally, the decoction is used to treat colds and pyrexia. To cure wounds and Atopic dermatitis, rhizome paste is applied. Stomach pain is treated with extracts of rhizome [158].

3.8 *C. tenuifolia* (Burm.f.) Sw.

To liberate pus from abscesses, leaves paste is applied as a cataplasm or used in pyrexia. Indian tribal people drink a bouillon of roots and rhizomes to improve their immunity [53].

3.9 *Diplazium esculentum* (Retz.) Sw. (Athyriaceae)

The leaves and stems of this plant are either fried or consumed raw. Rhizome and root extracts are used as general stimulants by indigenous people [53]. Roots have medicinal properties. The infusion of the plant is used as a hair cleanser and nourisher. Pests and insects are kept at bay by storing rhizome in granaries. As a green vegetable, young fronds are suitable for a salad or for cooking [156, 161]. Sarcoptic mange is treated with a tincture of leaves.

Various respiratory ailments, cough, and icterus can be treated with the juice. Broth made from of young fronds is effective in treating toothaches and dental caries. As a protection against labor pains, pregnant women eat fronds and leaves [122].

3.10 *Helminthostachys zeylanica* (L.) Hook. (Helminthostachyaceae)

Sciatic neuritis is treated using this plant because it is sedative, pain-relieving, and inflammation-reducing. Fronds have been used as sexual stimulant, euphoriant, tranquilizer [156]. Rhizomes are used to treat pertussis and in sexual dysfunction.

3.11 *Hypodematium crenatum* (Forssk.) Kuhn (Woodsiaceae)

A powder made from dried fronds blended within cow milk can be taken by women after five days of period for about a week to improve conception [122].

3.12 *Nephrolepis cordifolia* (L.) Presl, (Nephrolepidaceae)

To prevent bleeding from wounds, frost's paste is applied. Phytochemicals in pinna have bactericidal and fungicidal properties and are used in cough, cuts, and icterus treatment [88]. Approximately 10–15 ml of rhizome extract is administered once during menstruation to sterilize a woman permanently. It is used as a birth control method [50, 51, 159, 160]. The rhizome of this plant has bactericidal activity and is used in, Joint pain, seasonal allergies, nasal congestion, and appetite loss. [157]. Tuber extracts are used for digestive problems. Fresh tubers used to treat ulcers, and in indigestion it is simmered in brine water and consumed to soothe stomach upset [156, 166].

3.13 *Tectaria cicutaria* (L.) Copal (Tectariaceae)

Antibacterial properties are present in the plant. Chest cold, stings from honeybees, and breathing problems are treated with it [157]. Children with irregular bowel movements and dysentery can benefit from a decoction made from the fresh root. [54]. The roots can be used as a stimulant, blood cleanser, and infectious diarrhea. In cases of menstrual problems, rhizomes containing *Zingiber purpureum* and *Croton roxburgii* are prescribed [158]. A stomach-ache is treated with the fresh boiled stem [105].

3.14 *Tectaria coadunata* C. Chr.

A condition that causes inflammatory conditions of the colon's inner lining can be treated with an extract from the plant. Children suffering from stomach problems are given root extracts [166]. For those suffering from chest cold, leaves are extracted or leaves combined with honey are administered. Woodcutters use leaves paste to alleviate pain caused by centipede and honey bee stings [150].

3.15 *Tectaria wightii* (Clarke) Ching.

Disinfectant are made from the roots of this plant [54].

3.16 *Thelypteris arida* D.Don (Thelypteridaceae)

On lesions and abrasions, leaves and rhizome paste are applied [166].

3.17 *Vittaria elongata* Sw. (Vittariaceae)

Its leaves are used to treat joint pain in Andaman and Nicobar Islands. [88].

3.18 *Woodwardia unigemmata* (Makino) Nakai (Blechnaceae)

Diseases like dysentery, abdominal pain may be treated with it [62]

4 Medicinal properties of pteridophytes

4.1 Antioxidant property

There is a growing body of evidence that phenolic compounds in plants have many potential health benefits. Phenolic compounds are by far the most widespread secondary metabolites in plants. When plants are stressed, they produce phenolic compounds. A recent study showed the signaling enzyme phenylalanine ammonia lyase (PAL) is involved in the synthesis of flavonoids, especially anthocyanins and flavones [138] and the presence of phenolics protects DNA from UV-B damage and thereby prevents DNA dimerization and degradation [43]. Thus, plants growing in high mountains must cope with issues such as low temperatures, low partial pressure of oxygen, high UV levels, and arid conditions which result in the accumulation of flavonoids [145]. A high total phenolic content (TPC) can partly be explained by the presence of this conditions in places where the ferns are found. Like, *C. latebrosa, C. barometz, D. quercifolia, B. orientale* and *D. linearis*. Their habitats include areas with direct sunlight, as well as mountainous terrain up to an altitude of 1500–1700 m.

Several fern species have been reported to have antioxidant activity, including *A. penangiana, Braomea* insignis, *Cheilanthes anceps* Swartz, *Davallia divaricata,*

Table 1 Pteridophytes and their antioxidant potential

Family	Species	Method	References
Thelypteridaceae	*Abacopteris penangiana*	TEAC assay	Zhao et al. [194]
Sinopteridaceae	*Cheilanthes anceps*	DPPH assay	Chowdhary et al. [37]
Selaginellaceae	*Selaginella* sp.	In vitro lipid peroxidation	Gayathri et al. [63]
Selaginellaceae	*Selaginella labordei*	In vitro xanthine oxidase inhibition	Tan et al. [163]
Pteridaceae	*Pteris ensiformis*	TEAC assays	Wei et al. [180]
Pteridaceae	*Pteris multifida*	Superoxide scavenging activity	Wang et al. .[177]
Pteridaceae	*Pteris tripartita*	Metal chelating activity	Baskaran and Jeyachandran [10]
Pteridaceae	*Pteris vittata*	DPPH assays	Lai and Lim, [90]
Polypodiaceae	*Polypodium leucotomus*	FRAP assays	Gombau et al. [65]
Marsileaceae	*Marsilea quadrifolia*	DPPH assay	Ripa et al. [142]
Gleicheniaceae	*Dicranopteris linearis*	DPPH assay	[112]
Equisetaceae	*Equesitum* sp.	Total antioxidant capacity	Milovanovic et al. [113]
Dryopteridaceae	*Polystichum semifertile*	ABTS•+assay	Chen et al. [34, 35]
Dryopteridaceae	*Nothoperanema hendersonii*	ABTS•+assay	Chen et al. [34, 35]
Blechnaceae	*Blechnum orientale*	DPPH assay	Lai et al. [89]
Athyriaceae	*Diplazium polypodioides*	DPPH assay	Kshirsagar and Upadhyay [87]

Davallia mariesii, Davallia solida, Dicranopteris linearis, Drynaria fortunei, Drynaria quercifolia, E. arvense, Equesitum sylvaticum, Humata griffithiana, Marsilea quadrifolia, Nothoperanema hendersonii, P. multifida, P. tripartita, Polyopodium leucotomus, Polystichum semifertile, Pseudodrynaria coronans, Pteris ensiformis Burm., *Selaginella* sp. [10, 30, 35–37, 61, 63, 65, 112, 113, 142, 153, 177, 180, 191, 194]. Table 1 represents a list of pteridophytes and their antioxidant potential.

4.2 Anti-microbial property

Antibiotics are available for treating a wide range of conditions currently, namely chloramphenicol, tetracycline, erythromycin, penicillin G, ampicillin, cephalosporin, ciprofloxacin, kanamycin, gentamicin, neomycin, amoxycillin, nystatin, amphotericin-B, and ketaconazole. Despite the availability of several antibiotics to treat bacterial and fungal infections, these medications may not always be effective at combating pathogens. A number of ferns were used in ancient Indian medicine to treat a variety of ailments. Some ferns were recommended for medicinal use by Susruta and Charaka.

In high concentrations of extract and their solvents, pteridophyte extracts and their solvents effectively inhibited microbial growth. *Lygodium altum* extracts in both ethanol and acetone displayed good activity against *B. cerus*. *Salvinia molesta* showed considerable inhibitory activity against *B. cerus* only in its methanolic extract. *Salvinia cuculata* and *Helminthostachys zeylanica*, two plants whose solvent extracts have no antibacterial activity, don't produce such results. Its antimicrobial properties cover both gram-positive and gram-negative bacteria, with *Dryopteris filixmas* showing the strongest antimicrobial effects. Antimicrobial substances are produced by three species of ferns. Folk medicine commonly uses the ferns to treat dermal infections, tonsillitis, abscesses, blisters, ulcers, and skin wounds [7].

4.3 Antibacterial property

An alcoholic and an aqueous extract of the leaves of *A. lunulatum* and *A. pectinatum*, as well as aqueous leaf extracts from *D. cochleata* and *M. minuta* and alcoholic extractions of *C. dentatus* and *H. crenatum* did not show any inhibitory effects on *A. tumefaciens*. With the exception of water-soluble and alcoholic extracts of *A. pectinatum*, aqueous extract of *A. incisum* and *H. crenatum* and alcoholic extract of *C. dentatus*, each of which was effective for combating E.coli. Furthermore, both water-soluble and alcoholic extracts of the leaves of *M. minuta* inhibited the disease-causing strain of *E. coli* better than tetracycline. Additionally, water-soluble and alcoholic extracts of *A. incisum* and *D. cochleata*, as well as aqueous extracts from *A. capillus-veneris* and *M. minuta* and alcoholic extract of leaves of *C. albomarginata, C. dentatus* and *H. crenatum* failed to inhibit *Salmonella arizonae*. But few other extracts showed effectiveness in combating bacteria. In addition, with the exception of the alcoholic and aqueous extracts of *A.pectinatum* and the aqueous extract of leaves of *C. albomarginata*, each of these extracts has demonstrated inhibition of *S. typhi*. Also found to be active were water soluble and alcoholic extracts of the leaves of *A. pectinatum*, aqueous extract of leaves of *A. incisum* and *D. cochleata* and alcoholic extract of leaves of *C. dentatus* and *D. cochleata*, neither of these compounds inhibited the growth of *S. aureus*. [128]

4.4 Anti-carcinogenic properties

Plants, marine organisms, and microorganisms are some of the most common natural sources of anticancer agents [41, 119]. Most cytostatic drugs are derived from plants—paclitaxel, vinblastine and vincristine, topotecan and irinotecan, the camptothecin derivatives, and etoposide.

There are reports that *Microsorum grossum* can cure liver cancer [44, 130]. *A. evecta* [44] and *Pteris polyphylla* [93] also possess anticancer properties. In Chinese traditional medicine, Gushuibu is regarded as having anticancer and anti-inflammatory properties. Various ferns' rhizomes are used to make it, including *D. fortunei* (Kze.) J. Sm., *P. coronans* (Wall. Ex Mett.) Ching, *D. divaricata* BL., *D. mariesii* Moore ex-Bak, *D. solida* (Forst.) Sw., and *H. griffithiana* (Hk.) C. Chr. [19, 32, 39, 42]. Medicinal uses of *M. quadrifolia* include treating various cancers, diabetic conditions, and diseases related to inflammation and diuresis [165]. *Phlebodium decumanum*, also known as the bear paw fern, has been used for centuries as an anticancer and ulcer remedy [136]. Foliage and rootstocks of *H. arifolia* (Burm.) Moore and complete specimens of *Adiantum capillus-veneris* L. are used by the tribal communities of Tamil Nadu for hypoglycaemia and cancer prevention [146].

4.5 Lycopodiales and Isoetales

Lycopodiales, which contain more than 1,200 known existing species, and the associated orders Sellaginelales and Isoetales [21], are characterized by a distinctive set of secondary metabolic compounds. Lycopodiaceae has been reported to contain more than 200 quinolizidine, pyridine, and alpha-pyridone alkaloids, including lycopodine, lycodine, and fawcettimine [55, 102]. In terms of their anticholinergic and inflammation-reducing properties, some of the alkaloids show potential [102, 174]. There are also anticancer flavones in the Lycopodiaceae and Isoetaceae, including apigenin, chrysoeriol, luteolin and tricin, as well as their O-glycosylated or C-glycosylated forms [22, 66, 107]. Furthermore, lycopodine was found to reduce viability with a concentration of 50 μg/mL that can trigger cell death in HeLa cells [106]. In looking into the mechanisms of action, Bishayee et al. [14] revealed that *L. clavatum* spore-derived lycopodine inhibited cell growth and caused apoptosis in prostate cancer cells. In turn, this occurs because of downregulation of 5-lipoxygenase, the 5-oxo-ETE receptor (OXE receptor1) and the EGF receptor, which results in depolarization of the membrane potential of the mitochondria, but without affecting p53 activity.

4.6 Phenolic compounds

A majority of the anticancer activity of ferns is reported to be attributed to phenolic compounds, particularly flavonoids and their *O*-glycosides. In vivo as well as in vitro, flavonoids are powerful antioxidants with anticancer properties. Flavonoids from different plants, including ferns, show both of these properties [24]. Ferns have been studied extensively for their patterning, and they are probably present in all of them. The amentoflavone found in Psilotaceae and its monomer apigenin is primarily contained in this family of plants [22, 172]. It has only been discovered that biflavonoids occur in Osmundaceae and Cyatheaceae so far [66]. Flavonols are the main constituents of Ophioglossaceae [66, 179]. Flavonoids have been found to be abundant in *Helminthostachys zeylanica* (L.) Hook [75]. Marratiales contain flavones in large amounts [173],flavonols are less common. In almost all of the leptosporangiate fern families, different flavonoid types can be detected, including flavonols. Several flavonoids derived from ferns along with their O-glycosides can be found in most plant kingdoms. Flavonoids such as quercetin and kaempferol; the flavanone naringenin; the flavones apigenin, isoorientin, tricetin, vicenin-2, and vitexin; and the 3-deoxyanthocyanins apigenidin and luteolinidin, etc. Among the mechanisms by which they work are a reduction in DNA polymerase activity, suppression of NF-κB, decreased Bcl-2 expression, as well as suppression of MMP-1, p38 MAPK, and c-Jun N-terminal kinase (JNK activation. There is consequently an increase in apoptosis, a decline in cell growth, and migration and invasion of cells [74, 96, 109, 118, 151, 181, 184, 185]. Table 2 presents the diverse phytochemical compositions of pteridophytes.

4.7 Selaginella

There are approximately 700 extant species of *Selaginella* (spikemoss) found in the tropics [131]. Species found in primary tropical rainforests have the widest diversity of spikemoss, as well as xerophytes that can withstand drought and plants indigenous to tundra biomes in the arctic and alpine regions of the world. Many morphological [76] and molecular phylogenetic classifications have been published [85]. In some cases, it has also been shown that extracts of some plants of various taxa, mostly originating in Asia, including South, Southeast, and East Asia, but also from Australia and the Pacific, can inhibit the growth of cancer cells. *S.doederleinii* Hieron's crude extract inhibited cancer cell viability [86] in addition to reversing multidrug resistance [59]. Patients with

Table 2 Diverse phytochemical compositions of Pteridophytes

Family	Species	Biologically active chemicals	References
Equisetaceae	*i. Equisetum arvense*	Equisetolic acid, kaempferol, peteosinsn, quercetin-glucoside	Dos Santos Jr. et al. [56], Singh et al. [154]
Gleicheniaceae	*i. D. prelata* *ii. Dicranopteris dichotoma,* *iii. G. blotiana,* *iv. G. hirta,* *v. Gleichenia quadriparitta,*	Ecdysteroids	Cao et al. [23]
Helminthostachyaceae	*i. Helminthostachys zeylanica*	Prenylated flavonoids, thermalic acids, ugonins	Cao et al. [23]
Huperziaceae	*i. Huperzia serrata* *ii. Lycopodium serratum* *iii. Phlegariurus spp.*	Huperzine, lycobeline alkaloids, lycoclavanol, lycopodine, serratine, serratine-diols	Jiang et al.[77] Ma et al. [103] Yang et al. [186] Ying et al.[188]
Lygodiaceae	*i. L. japonicum* *ii. Lygodium venustum*	Acacetin, phenyl propanoids, glucosides, rutinoside	Cao et al. [23] Morais-Braga et al. [116]
Ophioglossaceae	*i. Botrychium ternatum* *ii. Ophioglossum. petiolotum,* *iii. O. thermale,* *iv.O. pedunculosum,*	Glucopyranosides, kaempferol, ophioglonin, quercetin glycosides	Cao et al. [23]
Polypodiaceae	*i. Polypodium hastata* *ii. P. triloba* *iii. P. leucotomos*	Caffeic acid, coumaric acid, gallic acid, glucopyranoside	Cao et al. [23]
Pteridaceae	*i. P. aquilinum* *ii. P. esculentum* *iii. P. Multifida,* *iv. P. Semipinnata* *v. Pityrogramma calomelanos* *vi. Pteridium spp.* *vii. Pteris semipinnata*	Apigenin, caffeic acid, kaurene, kauroic acid, luteolin, multifedoside ptaquiloside, pterosine, rutin	Bai et al. [5] Reinaldo et al. [141] Wang et al. [178]
Selaginellaceae	*i . Selaginella longistrobilina* *ii. S. bryopteris,* *iii. S. delicatula,* *iv. S. involvens,* *v. S. tamariscina,* *vi. S. wangpeishanii* *vii. S. amassae,*	Biflavonoids-amentoflavone, hinokiflavone, involvenflavone; phenolics, selaginellins, terpenoids	Chandran and Muralidhara [27, 28] Chandran et al. [26, 29] Girish and Muralidhara [64] Ha et al. [68] Lee et al. [92]

cancer who were administered it produced intrinsic tumour necrosis factor [183]. Cao et al. [25] evaluated the cytotoxic potential of flavonoid extracts of several ferns and their allies against adenocarcinoma cells. There is a Southeast-Asian variant that has proven to be particularly effective, the *Selaginella frondosa* Warb. The mitotic activity of glandular stomach epithelium was reduced in rats exposed to a carcinogen followed by feeding *S.tamariscina* (Beauv.) Spring [94].

4.8 Neuroprotective properties

First, antioxidants and anti-inflammatory effects are evaluated in order to determine the neuromodulatory potency of phytochemicals. Among the most widespread fern families, Pteridaceae plants grow in a range of habitats, including tropical to temperate, on flat to hilly terrain, in arid and irrigated conditions, and along the coast and in interior areas. The pharmacological applications of members of the Pteridaceae have been cited in tribal medicine. Researchers have isolated a variety of bioactive compounds from the family Pteridaceae, including alkaloids, flavonoids, and derivatives of their glucosides including kaurene, kauroic acid, apigenin, caffeic acid, rutin, luteolin, ptaquiloside, and pterosine [5, 178]. The cognitive symptoms of Alzheimer's disease can be alleviated with acetylcholinesterase inhibitors. Phytoextracts of *Huperzia* can be used to treat schizophrenia [77], strains, swells, and contusions [77]. A notable fern bioactive is huperzine A, from *Huperzia* spp. that has been found to inhibit Acetylcholinesterase (AChE) activity [103]. As an acetylcholinesterase inhibitor (AChEI), hyperzine A can be used to treat mild-moderate cognitive decline, and its safety, tolerability, and efficacy have also been evaluated in clinical trials [139]. Patients using this alkaloid reported improvements in learning, and it has been reported that rats using it demonstrated neuroprotective properties by protecting cortical neurons against oxidative stress and amyloid beta-induced apoptosis, which is an inherent feature of Alzheimer's disease.

Accordingly, huperzine A has emerged as a major lead for finding a new anti-Alzheimer's drug [162, 182]. There are currently drugs available in China and Europe for Alzheimer's disease and related diseases based on hyperzine A. Research shows that hyperzine A is a good AChEI that has a higher in-mouth bioavailability than some AChEIs, crosses the blood–brain barrier easily, and also has a longer in vivo half-life. In the same manner as huperzine, its analogues like 12-deoxyhuperzine O also inhibit NMDA receptors with an impressively low IC50 value (0.92 μM) [186]. *Huperzia* bioactive has neuroameliorating properties that extend beyond its AChEI activity. Huperzine A and specific triterpenoids in alcohol extractions of *H. serrata* have been demonstrated to possess growth inhibitory effects against human leukemia cells (HL-60) through

Table 3 Pharmacologically significant pteridophyte species and their few representative bioactive chemical compounds

Class	Bioactive compounds	IUPAC name	Family
Alkaloids	Huperzine A ($C_{15}H_{18}N_2O$)	(1R,9R,13E)-1-Amino-13-ethylidene-11-methyl-6-azatricyclo[7.3.1.0^{2,7}]trideca-2(7),3,10-trien-5-one	Lycopodiaceae
	Huperzine B ($C_{16}H_{20}N_2O$)	(1R,9R,10R)-16-Methyl-6,14-diazatetracyclo[7.5.3.0^{1,10}.0^{2,7}]heptadeca-2(7),3,16-trien-5-one	
	Huperzine R ($C_{15}H_{21}NO_3$)	(1S,6R)-6-Methyl-2-oxa-9-azatricyclo[7.4.3.0^{4,13}]hexadec-4(13)-ene-3,8-dione	
	Cernuine ($C_{16}H_{26}N_2O$)	(3aS,5S,6aR,7aS,12aS)-5-Methyltetradecahydro-11H-pyrido[1′,2′:3,4]pyrimido[2,1,6-de]quinolizin-11-one	
	Lycocernuine ($C_{14}H_{14}O_2$)	3-[2-(4-Hydroxyphenyl)ethyl]phenol	
	Lycopodine ($C_{16}H_{25}NO$)	(15R)-15-Methyllycopodan-5-one	
Flavonoids	Apigenin ($C_{15}H_{10}O_5$)	5,7-Dihydroxy-2-(4-hydroxyphenyl)-4H-chromen-4-one	Marattiaceae
	Luteolin ($C_{15}H_{10}O_6$)	2-(3,4-Dihydroxyphenyl)-5,7-dihydroxy-4H-chromen-4-one	
	Violanthin ($C_{27}H_{30}O_{14}$)	5,7-Dihydroxy-2-(4-hydroxyphenyl)-6-[(2S,3R,4R,5S,6R)-3,4,5-trihydroxy-6-(hydroxymethyl)tetrahydro-2H-pyran-2-yl]-8-[(2S,3R,4R,5R,6S)-3,4,5-trihydroxy-6-methyltetrahydro-2H-pyran-2-yl]-4H-chromen-4-on e	
	Isoviolanthin ($C_{27}H_{30}O_{14}$)	5,7-Dihydroxy-2-(4-hydroxyphenyl)-8-[(2S,3R,4R,5S,6R)-3,4,5-trihydroxy-6-(hydroxymethyl)tetrahydro-2H-pyran-2-yl]-6-[(2S,3R,4R,5R,6S)-3,4,5-trihydroxy-6-methyltetrahydro-2H-pyran-2-yl]-4H-chromen-4-on e	
	Muxiangrine III ($C_{23}H_{24}O_6$)	2-[3,4-dihydroxy-5-(3-methylbut-2-enyl)phenyl]-5-hydroxy-7-methoxy-6,8-dimethylchromen-4-one	
Phenolics	Rutin ($C_{27}H_{30}O_{16}$)	2-(3,4-Dihydroxyphenyl)-5,7-dihydroxy-4-oxo-4H-chromen-3-yl 6-O-(6-deoxy-α-L-mannopyranosyl)-β-D-glucopyranoside	Pteridaceae, Adiantaceae, Aspleniaceae, Davalliaceae
	Cinnamic acids ($C_9H_8O_2$)	(E)-3-Phenylprop-2-enoic acid	
	caffeic acid ($C_9H_8O_4$)	(2E)-3-(3,4-Dihydroxyphenyl)acrylic acid	
	Quinic acid ($C_7H_{12}O$)	(1S,3R,4S,5R)-1,3,4,5-Tetrahydroxycyclohexanecarboxylic acid	
	Catechin ($C_{15}H_{14}O_6$)	(2R,3S)-2-(3,4-Dihydroxyphenyl)-3,5,7-chromanetriol	
	Coumarin ($C_9H_6O_2$)	2H-Chromen-2-one	
	Anthraquinone ($C_{14}H_8O_2$)	9,10-Anthracenedione	
	Dihydrochalcone ($C_{15}H_{14}O$)	1,3-Diphenyl-1-propanone	
Diterpenoid	Pterokaurane M1($C_{20}H_{32}O_3$)	(2β,5β,8α,9β,10α,13α,15α)-Kaur-16-ene-2,15,19-triol	Pteridaceae
Sesquiterpenoids	2,5,7-Trimethyl-indan-1-one ($C_{12}H_{14}O$)	2,5,7-Trimethyl-1-indanone	Pteridaceae
	Pterosin Z ($C_{15}H_{20}O_2$)	6-(2-Hydroxyethyl)-2,2,5,7-tetramethyl-1-indanone	
	Ptaquiloside ($C_{20}H_{30}O_8$)	(2′R,3a′R,4′S,7a′R)-4′-Hydroxy-2′,4′,6′-trimethyl-3′-oxo-2′,3′,3a′,4′-tetrahydrospiro[cyclopropane-1,5′-inden]-7a′(1′H)-yl β-D-glucopyranoside	
Triterpenoids	β-sitosterol ($C_{29}H_{50}O$)	(3β)-Stigmast-5-en-3-ol	Polypodiaceae
	Scaphopetalone ($C_{21}H_{26}O_6$)	4-[(1R,2S,3S)-2,3-Bis(hydroxymethyl)-6,7-dimethoxy-1,2,3,4-tetrahydro-1-naphthalenyl]-2-methoxyphenol	
	Neohop-13(18)-ene ($C_{30}H_{50}$)	(3R,3aR,5aS,5bR,7aS,11aS,11bR)-3-Isopropyl-3a,5a,5b,8,8,11a-hexamethyl-2,3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13-octadecahydro-1H-cyclopenta[a]chrysene	
	Diploptene ($C_{30}H_{50}$)	Hop-22(29)-ene	

Table 4 Medicinal properties of some pteridophytes

Name	Part used	Medicinal properties
Adiantum capillusveneris	Entire plant	Treats constipation, common cold, growth of hair follicles, Irregular menstruation, snake bite
Adiantum caudatum	Entire plant	High blood glucose, dermal disorders, common cold
Adiantum incisum	Entire plant	Urinary tract infection, high blood glucose, dermal disorders
Adiantum philippens	Entire plant	Infectious diarrhea, promotes diuresis, growth of hair follicles, cuts and bruises, induces female infertility
Adiantum venustum	Entire plant	Promotes diuresis, insect bites, cuts and bruises, cluster headache
Marsilea minuta	Entire plant	Dermatitis, sleeplessness, sore muscle, tranquilizer
Onychium japonicum	Entire plant	Dermatitis, pyrexia
Diplazium esculentum	Entire plant, fronds	Pyrexia, Infectious diarrhea, stimulant, promotes bowel movement, fatigue
Pteris cretica	Entire plant, fronds	Cuts and bruises, pyrexia
Selaginella chrysocaulos	Entire plant, Spores	Pyrexia
Asplenium dalhousiae	Fronds	Burns and blisters, dermal disorders, pyrexia
Asplenium tricomanes	Fronds	Treats constipation, Irregular menstruation, hepatic disorders, treats parasitic infections
Onychium contiguum	Fronds	Urinary tract infections
Pteris vittata	Fronds	Burns and blisters
Hypodematium crenatum	Fronds	Female fertility, insect bite
Athyrium pectinatum	Rhizome	Treats parasitic infections
Cheilanthes bicolor	Rhizome	Pyrexia, stimulant
Woodwardia unigemmata	Rhizome, frond	Infectious diarrhea
Dryopteris cochleata	Rhizome, fronds	Dermatitis, blood cleanser, stimulant, cuts and bruises, infections in GI tract, sore muscle

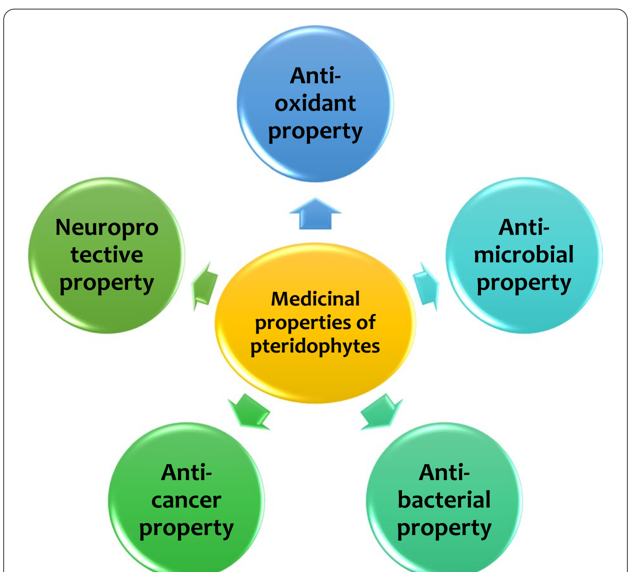


Fig. 1 Pharmacological/medicinal properties of pteridophytes

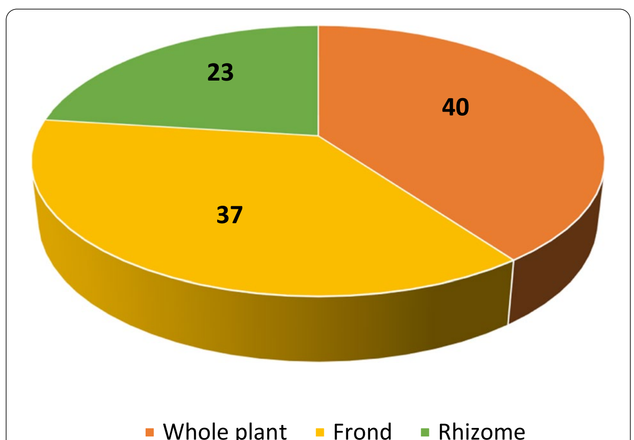


Fig. 2 Illustration of the parts used in medicinal pteridophytes to treat several ailments

induction of proapoptotic mechanisms [71]. Furthermore, huperzine A has been shown to stimulate the production of new hippocampal neurons and alleviate cognitive impairment in rats undergoing acute hypobaric hypoxia [101]. An interesting finding was that in a spinal cord injury model it significantly ameliorated chronic pain phenotypes in rats [190]. Table 3 presents the pharmacologically significant pteridophyte species and their few representative bioactive chemical compounds. Table 4 presents medicinal properties of some pteridophytes. Figure 1 presents some pharmacological/medicinal properties of pteridophytes. Figure 2 illustrates the parts used in medicinal pteridophytes to treat several ailments. Figure 3 represents some phytochemicals of pteridophytes (from ChemDraw).

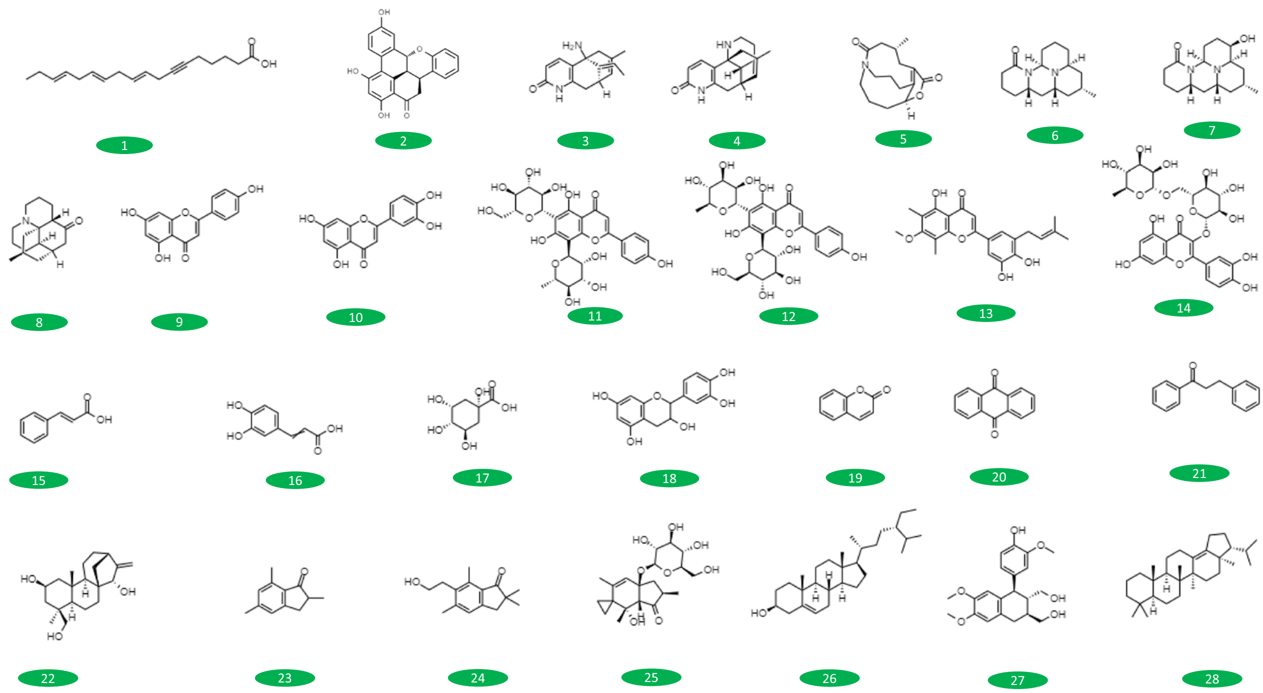


Fig. 3 Some phytochemicals of pteridophytes (from ChemDraw). 1. Dicranin, 2. Ohioensin A, 3. Huperzine A, 4. Huperzine B, 5. Huperzine R, 6. Cernuine, 7. Lycocernuine, 8. Lycopodine, 9. Apigenin, 10. Luteolin, 11. Violanthin, 12. Isoviolanthin, 13. Muxiangrine III, 14. Rutin, 15. Cinnamic acid, 16. Caffeic acid, 17. Quinic acid, 18. Catechin, 19. Coumarin, 20. Anthraquinone, 21. Dihydrochalcone, 22. Pterokaurane M1, 23. 2,5,7-Trimethyl-indan-1-one, 24. Pterosin Z, 25. Ptaquiloside, 26. β-sitosterol, 27. Scaphopetalone, 28. Neohop-13(18)-ene

4.9 Clinical trials

The saponin calagualine was shown to have anti-tumor activity in clinical trials and studies performed in vitro and in vivo in 1967 [18]. Also, humans who have uncontrolled, abnormal growth of tissues or cells benefited from the procedure without causing any complications. When the extract was administered orally to patients at high risk of melanoma, sensitivity to UV radiation was significantly reduced. [1]. The anti-neoplasic activity of antioxidants and immunomodulators is a topic of further study. Rhizome saponins inhibited the insertion of nucleoproteins into cells in an antagonistic manner to that of cytostatics [168]. On hairless mice, researchers observed reductions in UV-induced expression of Cox-2, inflammatory responses, and gene mutation [192]; suppression of excessive epithelial cell growth, elevated p53 activity, and increased antioxidant capacity in the blood [143]; and retardation of skin tumor formation.

Currently, only dermatological benefits of *Phlebodium* spp extract are known. In the treatment of psoriasis, it has been validated in clinical trials since 1974 [125]. When administered to normal volunteers, it reduced lymphocyte proliferation in response to mutation-triggering agents, OKT8 + cells, and immunoglobulin levels. It may explain why the extract benefited patients with psoriasis [78]. A placebo-controlled, randomized study found the extract to be more effective than standard treatment in treating psoriasis [45]. Volunteers also reported protection from UV-induced skin damage [111] and from skin cancer caused by ultraviolet radiation [110].

Apart from this, pteridophyte-derived compounds are also effective against neurodegenerative disorders. Despite their distinct clinical and etiopathogenic differences, neurodegenerative disorders share common traits, including protein deposition abnormalities, dysfunctional cellular transport, impaired mitochondrial function, inflammatory response, excessive Ca^{2+} inside the cell, uncontrolled ROS production, and overstimulation of receptors [52, 84]. In addition, reactive astroglia and microglia play an important role in the pathogenesis of all essential neurodegenerative disorders [4, 57]. It has been suggested that natural substances can be used in conjunction with conventional medicines to help treat neurodegenerative disorders [52]. Since Alzheimer's disease is a neurodegenerative disease with numerous causes and a complex pathophysiology, the development of drugs that offer a combination of multiple targets is becoming increasingly important for treating Alzheimer's disease. Omega-3 fatty acids, for example, have anti-inflammatory properties and inhibit cell toxicity in Alzheimer's

[17]. Plant-derived compounds, including lunasin and tannins, may be useful in treating Alzheimer's disease [46]. The Hup A treatment has been used on more than 1 million people in China. Based on these studies, Hup A improves cognitive functioning and is a feasible medication. 202 Alzheimer's disease patients were enrolled in a double-blind, random, trial involving numerous hospitals in 2002 by Zhang et al. Hup A was administered to 100 patients for 12 weeks at 400 mg per day, and placebos were given to 102 patients. Alzheimer's disease Assessment Scale results showed cognitive improvements in the treatment group, as well as behavior improvements and improvements in daily living skills. [193].

In the same way, treatments for Parkinson's Disorder often involve Levodopa, which, in the brain, is almost exclusively transformed into dopamine with the help of the enzyme dopa decarboxylase, thus producing therapeutic benefits [69, 91]. Neuronal mitochondrial dysfunction has been linked to the progression of Parkinson's Disorder [115, 129]. A major contributing factor to the malfunction is excessive buildup of alpha-synuclein. The mitochondrial dysfunction leads to oxidative stress and neuronal degeneration. [81, 171]. A second peculiar feature of Parkinson's Disorder is the presence of neuroinflammation, which appears to contribute to the progression of the disease. Furthermore, inflammation is also dependent on mitochondrial dysfunction, which activates microglia and produces proinflammatory mediators, namely cytokines, chemokines, complement, and ROS [40]. In addition, most Parkinson's Disorder patients also struggle with non-motor complications, including sleep–wake cycle disorders, cognitive impairments, and mood disorders. All of these symptoms are often worsened by impaired sensory perception and pain. There has been a recent increase in the use of functional foods or nutritional supplements in the management of diseases associated with aging, such as Parkinson's. There is no doubt that diets high in vitamins, dietary minerals, and dietary salts may reduce symptoms of Parkinson's disease and its associated pathologies [40]. Pteridophyte-derived phytochemicals have been shown to improve motor function, reduce oxidative stress, and enhance neurogenesis [15]. Patients with Parkinson's disease were treated with Hup A (0.1 mg) in conjunction with cognitive retraining exercises, as demonstrated by Yao and his colleagues. Yao et al. found that the patients' cognitive function enhanced after six weeks of three daily treatments. [187]. Additionally, Wang et al. administered 0.3 mg Hup A subcutaneously 30 min in advance of general anesthesia to 15 patients. During recovery, acetylcholine levels in the brain were found to be elevated, a factor that helped restore cholinergic nerve conduction [176]. Diabetes patients who took Hup A (0.1 mg) three times daily for eight weeks exhibited improved Mini-mental state examination scores, latency and amplitude. The trial course lengths and sample numbers were small, and positive controls did not exist for most of the trials.

4.10 Negative effect of pteridophytes

Cancer has been linked to only one plant in the vascular system, *Pteridium aquilinum* (L.) Kuhn. Bracken is the most common fern in the world today, and it is also an extremely aggressive weed. The toxic effects of bracken, including its carcinogenic, mutagenic and teratogenic effects on animals and human beings, have been thoroughly examined several times. Bovine enzootic haematuria is caused by feeding on bracken in cattle and sheep. It causes tumours in the bladder which can be either benign or malignant. Additionally, it leads to the formation of rumen papillomas, squamous cell malignancies of the gastrointestinal tract, and cancer of fibroblasts of teeth [108]. A water extract of bracken has been shown to cause carcinoma of the bladder, breast, and intestine in rodents [60, 72, 147, 148]. In addition, the norsesquiterpene glucoside ptaquiloside has been identified as a mutation-inducing, chromosome disrupting and cancer-causing component of bracken [121, 167]. Upon exposure to alkaline conditions, ptaquiloside decomposes into an intermediate dienone known as 'activated ptaquiloside'. This dienone is decomposed in weakly acidic conditions, leading to the production of pterosin B, which can additionally be synthesized directly from ptaquiloside at acidic pH values [148]. By utilizing its cyclopropyl ring, the unstable dienone forms covalently bonded DNA adducts, mostly at adenine's N-3 [132]. Initially alkylating adenine with ptaquiloside or its aglycon ptaquilosin in codon 61 of H-ras accompanied by depurination and faulty DNA synthesis results in the triggering of the H-ras proto-oncogene [133].

4.11 Future prospects

It is estimated that there are 13,000 species belonging to nearly 48 plant families in Pteridophytes; however, few species have been studied and 30 families have been studied. As a result, we strongly encourage pteridophyte researchers to explore the therapeutic potential of the plants and their bioactive components. With the help of biotechnology, researchers could increase the effectiveness of biologically active substances by studying in vitro culture, biochemical processes, mechanism of action, and genetic modification. Multidrug therapies should be developed from early tracheophytes and pteridophytes, as well as studying their biological processes, drug kinetics, and toxicity evaluations. A secondary metabolite analysis could help in identifying the genetic relationships among pteridophytes. Extraction of phytochemicals from *B. orientale, C. thalictroides, D. heterophyllum, D. linearis, H. arifolia, L. ensifolia, N. multiflora, P. calomelanos, P. confusa* and the rhizomes and leaves of *D. quercifolia* were found to contain sugars, steroids, flavonoids, tannins, saponins, carboxylic acid, xanthoprotein, and phenols. Research on the antimicrobial properties of *B. orientale, D. linearis, H. arifolia* and roots *of D. quercifolia* suggests they contain one or more of these phytoconstituents. Numerous phytochemicals discovered have been documented to have medicinal and industrial benefits. There is huge therapeutic potential in plants that contain antimicrobial compounds because they are free of side effects common to synthesized antimicrobials. After extensive investigation, it appears that plants can be used as antimicrobial bioactive agents with broad-spectrum activity. In future work, the objective will be to identify and characterize the underlying mechanisms for bioefficacy and bioactivity.

5 Conclusion

Phytochemical and pharmacological characteristics of pteridophytes by Indian minority groups are poorly understood as are their medicinal uses. Research on pteridophytes has grown over time in recent decades, and more reports have been published on ethnobotany of pteridophytes. The objective of this review is to provide baseline data for scientific research on medicinally important pteridophytes and to categorize them. Pteridophytes haven't been studied extensively in several mountainous regions, particularly the central Western Ghats and the seven sister states. Pteridophyte species are found in large numbers in the North East Indian states, but ethnomedicinal uses are in short supply. The lack of knowledge about pteridophyte species by people residing in these regions may be due to the ecological conditions in these states. Unless these states' underexplored and unexplored territories are explored, researchers must document the ethnomedicinal uses of pteridophytes. It should be given top priority to preserve traditional knowledge records to ensure that resources are conserved and the knowledge of these practices is protected before they disappear from future generations. Pteridophytes are widely used in India, but there are few publications about their therapeutic effects. The scientific literature has not explored much about a neglected group of pteridophytes, so further studies are needed to focus on them. In order to experimentally validate prevailing traditional knowledge as a solution to healthcare problems, the existence of the scientific steps discussed in this review needs to be taken into account. Based on the conclusions of this review, monographs and recommendations about Indian ethnomedicinally important pteridophytes could be formulated based on the data presented here. Pteridophytes are a group of plants with medicinal applications that by studying their phytochemical and pharmacological properties may reveal the presence of active compounds that can be developed into novel therapeutics. Pteridophytes are poorly understood in terms of phytochemistry, pharmacology, and pharmacognosy. To develop new drugs from underexplored plant groups, it is essential to encourage intensive scientific research on unexplored plant species to contribute to the on-going search for alternative and affordable treatments in India. For the purposes of conducting preclinical and clinical trials, a thorough investigation of toxicology is necessary. The study suggests that ethnobotanical investigations are crucial among indigenous communities, as well as the need for detailed studies of available cryptogams, potentially leading to the development of new and novel pharmaceuticals. Therefore, if ethnobotanical research is combined with biochemical analysis or physiological investigations, useful drugs could be discovered.

Abbreviations
AChEI: Acetylcholinesterase inhibitors; PAL: Phenylalanine ammonia lyase; TPC: Total phenolic content.

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Authors' contributions
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Consent for publication
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