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Pteridophytes: evolutionary boon as medicinal plants

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Abstract

Selective use of crude plant extracts has been the oldest ritual in ancient Indian Medicinal System 'Ayurveda', as well as in Traditional Chinese Medicine system for thousands of years. This has been well documented that herbal medicines of Chinese, Indian, Korean and Native American people had included bryophytes, lichens, lycophytes and ferns. Since antiquity, most of the ferns and fern allies have given many health benefits to ancient civilizations who had used them for food, tea and drugs. Modern approaches have combined multidisciplinary technologies and have specific chemical compounds extracted and identified for producing very particulate medicines from plant parts. Plants, which yield appreciable quality and quantity of polysaccharides, steroids, terpenoids, flavonoids, alkaloids and antibiotics are suitable for dragging out drugs for many ailments/diseases, including cancer treatments. Modern explorations on the functional activities of pteridophytes for human health by discovering specific compounds and their usage in medicines have widened the scope of pteridophytes by shaping these plants as a great boon for pharmaceutical companies and related industries. Even 'fern weeds', which invade our freshwater bodies and reduce the freshwater wealth of a lake, e.g. *Azolla, Salvinia, Marsilea, Ceratopteris*, etc. can be utilized to produce life saving drugs because they are reservoirs of very many organic compounds that are useful as medicines. Some of the fern genera have a few unique secondary metabolites, which have not been discovered in higher plants. Polyphenols are useful phytochemicals, which provide health benefits such as antioxidants. From experiments on screening of total polyphenol contents of 37 ferns and fern allies, *Polystichum lepidocaulon* and *Polystichum polyblepharum* were reported to have more than 13% of total polyphenols from dried materials of both fronds and rhizomes. In addition, fronds of *Davallia mariesii* and rhizomes of *Cyrtomium fortune, Dicranopteris pedata, Athyrium niponicum* and *Dryopteris nipponensis* showed more than 10% of total polyphenols from dried materials. High bioactivities of traditional medicinal ferns have been studied internationally to underscore their roles in medicine. These attempts have confirmed various bioactivities, such as antioxidant, antimicrobial, antiviral, anti-inflammatory, antitumor and anti-HIV, etc. The occurrence of antibiotic activity in the extracts of more than 200 species of pteridophytes has been shown to be of prime significance within the period of 1975–2015. The active substances in many cases were found to be antibacterial to penicillin-resistant *Staphylococcus aureus, Mycobacterium phlei, Salmonella typhi, Vibrio cholera*, and *Pseudomonas aeruginosa*. *Dryopteris cochleata* was active against both bacteria and fungi. Five other species of *Dryopteris* showed remarkable antibacterial activity. The ferns of 'Adiantum group' have been found to be particularly active against Gram-positive bacteria. The polypodiaceous ferns constitute a rich group of which *Microsorum alternifolium, Leptochillus decurrens, Polypodium*

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irioides, Pyrrosia mannii and *Phymatodes ebenipes* deserve special mention. Several thelypteroid, davallioid and athyrioid ferns, in addition to antibiotic activity have also been found to show most useful bioactivity for our life – the antioxidant activity. The latter superb biochemical quality of ferns alone makes most ferns of great advantage to human health. Lycophytes particularly *Lycopodium clavatum* and *Equisetum hyemale* and ferns (*Dryopteris* and Adiantums) have had constituted the backbone of Homeopathic medicines and now many more genera have been added to the network of modern medicinal approaches in the drug industry. These pteridophytes are indispensably integral parts of forests world over. A few of the aquatic ferns (*Azolla, Salvinia*) serve as excellent biofertilizers and bioremediation agents. Medicinal plants are under cultivation and cultured world over. Botanically, say a thousand years ago, these were wild and many of them were weeds. As pteridophytes have survived since Paleozoic, they have undergone *series* of disruptive adaptive changes of environment than any other vascular plants. These plants most likely, could withstand the tests of geological time on account of their being guarded with genetic capability of possessing many useful oils, phytochemicals (secondary metabolites) such as flavonoids, steroids, alkaloids, phenols, triterpenoid compounds, varieties of amino acids and fatty acids, which in turn offer inherent tolerance and defense system . Additionally, from evolutionary point of view majority of ferns have constituted carpet flora and have worked as 'cradles' in natural forests so as to nurture small animals particularly reptiles and mammals. Ferns are denominators of prevalent rich biodiversity in almost every part of the earth. Comparison of evolutionary adaptations and natural innovations illuminate the genetic basis for the development of organisms. It is emphasized that there should be good field stations just in the peripheral region of reserved forests with large green houses to function as 'Fernariums/ Mossariums/ and/or Lichenariums' to conserve and maintain rare, endangered and medicinally superlative species found in those areas/forests. Gene networks (DNA stretches) that retain similar wiring diagrams (some or many similar DNA sequences) among related, distantly related or even totally diverse organisms point to the ways in which regulatory regions of the genome have evolved. Indisputably, comparative genomics can help us in deciphering evolvability of gene network and conservation modes during vast geological journey in evolution. We need exhaustive genomics and multidimensional molecular genetic studies on pteridophytes so as to discover unique DNA sequences, which could turn the gates of modern medicine.

Keywords: Huperzine, medicinal pteridophytes, pharmaceutical drugs from ferns, pteridophytes as ecofriendly plants, secondary metabolites from ferns, genomic conservation of lycophytes and ferns, utilization of aquatic fern weeds

Introduction

Entire biological world has survived on the basis of unity, diversity and interdependence among unicellular and multicellular organisms. Millions of species so evolved have inhabited this planet for millions and millions of years. Forests are the products of prolific biological activities. The forest types, their forms and sizes are the cumulative effect of thousands of species corresponding to micro- and macro-organisms interacting with their genetic potentials and environmental factors. Obviously, forests are not merely a jungle of trees housing animals, but are the first rate natural well knitted web comprising herbs, shrubs, climbers and trees for the basic survival of all organisms living in- and out-side of the forest ecosystems (Goswami, 1981). Animals, more so the lower mammals depend on food and shelters under the covers of trees and shrubs. The essential carpet flora enriching the soil is microflora and for mechanical support on ground are the bryophytes and pteridophytes. Lichens, mosses and ferns thrive as terrestrial as well as epiphytic flora thereby offering nutritionally rich and biologically safe forests. Intriguingly, most of these lower groups of plants particularly lichens (Boustie and Grube, 2005), bryophytes (Harris, 2008, 2009) and pteridophytes are equally superior grade of medicinal plants. During the 16th–18th centuries the 'most effective composite group of plants' in the Traditional Chinese Medicine and folk medicine culture was called as 'moss' (Dillenius, 1763: cited from Harris, 2008, 2009). Botanically these 'moss' were a mixture of dried bryophytes (*Sphagnum, Rhodobryum giganteum, Polytrichum*, etc.), lichens (*Cladonia*, and others, so called tree moss the lichens growing on the tree), lycophytes (Club moss: *Selaginella, Lycopodium*), a few dried leaves of small ferns and even angiosperms (often called Spanish moss: *Tillandsia usneoides*).

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There are about 12,000 species of pteridophytes distributed world wide in different ecological niches. Out of these, 10,000 species are ferns and the rest belong to fern-allies. Smith *et al.* (2006) on the basis of morphological and gene sequencing techniques have considered pteridophytes as paraphyletic assemblage of lycophytes and filicophytes. Pteridophytes, though the second largest group of vascular plants, represent only 5–7% of the total vascular plants, but still have important ecological role particularly in the tropical vegetation (Page, 1979). Pteridophytes used as medicinal plants have been recorded since the time of Theophrastus (ca. 372–287 BC) Charak (ca. 100 AD) and Shushruta (ca. 100 AD) (Puri, 1970; Parihar *et al.*, 2004). Charak and Sushruta the two medical giants of ancient India recommended medicinal values of pteridophytes in 'samhitas'. Also, Discorides (ca. 50 AD) referred in his 'de Materia Medica' (Li, 2004) to a number of ferns including the bracken fern (*Pteridium aquilinum* (L) Kuhn) and *Dryopteris filix-mas* (L) Schott) as having medicinal values.

Most popular ancient Indian herbal medicine was a pteridophyte

From ancient point of view the traditional Indian drug 'Sanjeevani' said to be the life-saving/reviving drug mentioned in ancient religious Indian texts is considered to be a group of lycophyte species mainly *Selaginella bryopteris* (Fig. 1(a)). On scientific inquiry *S. bryopteris* has been found to be superior grade of medicinal herb (Antony and Thomas, 2011). This species initially thought to be occurring in Himalayas is now known to be growing in many places. Whereas, there may be many other species, e.g. *Selaginella pulvinata*, and other ferns viz. *Cheilanthes, Actiniopteris*, etc. that are restricted to Himalayas (Fraser Jenkins, 2012), but *S. bryopteris* extracts are found to be far superior in curing wounds. Most of such plants are vegetatively propagated (Renzaglia *et al.*, 2000).

Pteridophytes as herbal medicine across the globe

Having discovered greater potential of medicinal uses of ferns there has been an increasing trend to explore economic feasibility and medicinal uses of pteridophytes in comparison with the angiosperms (Nayar, 1959; Kumar and Kaushik, 1999; Kumar *et al.*, 2001; Remesh *et al.*, 2001; Manickam *et al.*, 2005; Benjamin and Manickam, 2007). In a recent publication from Botanical Survey of India (Singh, 2011), there is an enumeration of 1261 species of pteridophytes occurring in India. Though this figure represents a rich heritage of pteridophytes in India their ethnomedico-botanical uses are not very well known (Dhiman, 1998) despite the fact that these have been used since the advent of ancient Indian Ayurvedic medicinal culture. Similarly, over more than 5000 years the older civilizations in China, Korea, Japan and also Egypt have used herbal medicines, of which nearly 50% is constituted by lower plants, e.g. species of *Lycopodium, Selaginella, Pteridium, Christella* (=*Thelypteris*), *Actiniopteris, Angiopteris, Isoetes, Ophioglossum*, etc. (Goswami, 2009b). Over the past four decades there has been increased interest in drug discovery from this group of plants. A large number of extraction and microbiological testing studies have been conducted in several laboratories in India, Japan and elsewhere to test the antimicrobial activity of ferns indicating the presence of good amount of substances such as phenolic compounds, glycosides, flavonoids and alkaloids (Sen and Nandi, 1951; Banerjee and Sen, 1980; Guha *et al.*, 2004, 2005, 2006; Kumari, 2011; Basak *et al.*, 2012; Abraham *et al.*, 2015). Phytochemical analyses have been done on a large number of pteridophytes to explore presence of phenolic compounds (Bohm and Tryon, 1967; Patric *et al.*, 1995; Singh, 1999; Singh *et al.*, 2008a, b; Shinozaki *et al.*, 2008; Shin and Lee, 2010; Lee and Shin, 2011; Bessa Pereira *et al.*, 2012; Anto *et al.*, 2015). Studies on estimation of primary metabolites, their seasonal quantitative variations and role in ecophysiology have also been undertaken (Rathore and Sharma, 1988, 1991; Sharma *et al.*, 1995; Hopkins *et al.*, 2001; Guha *et al.*, 2006). Lately, genomic studies are gaining wider popularity so as to identify specific DNA sequences responsible for producing hundreds of compounds of medicinal importance (polyphenols, flavonoids, antioxidants, etc.), and prospecting specific fern genera and species with high medicinal potential.

Ethnomedicinal significance

Usage of many fern genera by the tribal people for curing various diseases such as asthma, dyspepsia, bronchitis, phthisis, etc. have long been reported in early literature (Puri and Arora, 1961; Puri, 1970; Pandey *et al.*, 2009). In India, aborigines (tribal folk) inhabiting Andaman and Nicobar Islands are among the most primitive people said to have settled around 35–60,000 years ago (Mazumdar, 1952; Wells, 2002). Ethnomedicinal information obtained from these people has led to huge curiosity to initiate scientific inquiry into the usage of pteridophytes. As a follow-up, Dagar and Dagar (1987) detailed out ethnomedicinal uses of 46 species of pteridophytes. On further investigation, Dagar (1989) had specifically mentioned 10 species that are more particularly used by traditional Vaidyas (local medical practitioners) among Nicobarese. Pandey *et al.* (2009) have surveyed and had published an exhaustive list of medicinal plants, which included many pteridophytes

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Fig. 1. Representative pictures of some important pteridophytes : (a) *Selaginella bryopteris*, commonly called also as 'sanjeevani' can be cultivated in the suitable environment in the garden, (b) *Lycopodium clavatum*, is among the oldest lycophytes being used in the Homeopathic and Unani medicinal practices for centuries, (c) *Osmunda regalis*, in its natural habitat growing in the rock crevices by the side of the flowing water, (d) but this can also be cultivated when grown under suitable environment (e) freshwater free floating fern *Azolla pinnata* with rosette of green to reddish brown, (f) *Salvinia cucullata* often seen in many lakes or ponds.

including epiphytic ferns such as *Microsorum punctatum, Nephrolepis biserrata, Phymatosorus scolopendria* and several terrestrial species.

Most ferns are rich source of phytochemicals and have been found to possess a variety of biological activities (Tables 1 and 2) including antioxidant potential. Exhaustive studies conducted on biological potential of ferns suggest that most ferns have huge potential abilities as antioxidants (Lee and Shin, 2011; Sessa and Der, 2016). Analytical investigations conducted on antioxidant activities of many ferns particularly of the families Dryopteridaceae, Osmundaceae, Woodsiaceae exhibited powerful antioxidant activities. Among these, the antioxidant activities (DPPH radical and ABTS radical cation scavenging) of frond and rhizome extracts of several genera such as *Adiantum, Davallia, Hypolepis, Pteridium, Cytominum, Dryopteris, Polystichum, Dicranopteris, Lycopodium, Osmunda, Ceratopteris, Coniogramme,*

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Table 1. Pteridophytes in medicinal usage

Name of the plant (family)	Medicinal uses	Source reference
Actinopteris dichotoma (Actinopteridaceae)	Rhizome stypic anthelmintic, fronds chewed for sore throat, rhizome decoction anti-dandruff	May (1978)
Actinopteris radiata (Sw.) Link Actinopteridaceae	Anthelmintic, stypic and astringent in haemorrhage; used in bronchitis and gynecological disorders, dry leaves used in tuberculosis	Chopra *et al*. (1956); Parihar and Parihar (2006); Mannan *et al*. (2008); Upreti *et al*. (2009)
Acrostichum aureum L.(Pteridaceae)	Promote healthy pregnancy, as a purgative, wound healing sore throat and for the treatment of Elephantiasis; Heal wounds and boils; rhizome is vulnerary in healing inveterate ulcers, leaves emollient, fertile fronds for syphilitic ulcers	Quisumbing (1951); Mannan *et al*. (2008); Ho *et al*. (2011)
Adiantum aethiopicum L. (Adiantaceae)	Cough and cold and parturition; Decoction of whole plant used as tonic against bruises, gangrenous, wounds, expectorant, diuretic disorders; leaf smoked for head cold, demulcent drink, emetic use of chest	May (1978); Nwosu (2002); Mannan *et al*. (2008) see also Laware and Limaye (2012)
Adiantum capillus-veneris L. (Adiantaceae)	Astringent, expectorant, emmenagogue, catarrhal and menstrual problem; cough, cold and bronchial diseases; infertility and Women's disease, remove hair dandruff, powdered rhizome mixed with camphor and palm carnel oil used against lice; anticancerous, hypoglycaemic, purgative; dry leaves used for bronchitis and fever; fronds are used against cough and cold and also chewed for mouth blisters, used in eye ointment. Also used as anti-diabetic drug	Caius (1935); Asolkar *et al*. (1992); Gaur and Bhatt (1994); Nwosu (2002); Parihar and Parihar (2006); Mannan *et al*. (2008); Upreti *et al*. (2009); Ho *et al*. (2011)
Adiantum caudatum L. (Adiantaceae)	Demulcent, expectorant and tonic; cough fever and skin disease, diabetes; Used for treating jaundice in animals, against scabies, abdominal pain, constipation; Also as antidiabetic medicine	Gaur and Bhatt (1994); Nwosu (2002); Mannan *et al*. (2008); Paul *et al*. (2012)
Adiantum ceneatum L. (Adiantaceae)	Pain killer	Ho *et al*. (2011)
Adiantum flabellulatumL. (Adiantaceae)	Nail cicatrization and snake bite treatment; cough	Mannan *et al*. (2008); Ho *et al*. (2011)
Adiantum incisum Linn. (Adiantaceae)	Diabetes and cough, skin disease, eczema and rashes; infusion of young fronds used as treatment against malaria and bronchial disease; Control of herpes and viral infection; leaf powder mixed with butter and used for controlling the internal burning of the body, cough, diabetes, fever and skin diseases	Sarin (1990); Gaur and Bhatt (1994); Nwosu (2002); Parihar and Parihar (2006); Upreti *et al*. (2009); Laware and Limaye (2012); Rai *et al*. (2016)
Adiantum lunulatum Burm (Syn. Adi antum philippense L.) Adiantaceae	Dysentery, blood purifier; Sterility treatment of women; demulcent, astringent, emenagouge; ulcers, erysipelas, urinary diseases and bleeding from nose; used in cough, asthma, fever, leprosy and hair falling	Hosagoudar and Henry (1993); Parihar and Parihar (2006); Mannan *et al*. (2008); Upreti *et al*. (2009); Ho *et al*. (2011)

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Table 1. (*Cont.*)

Name of the plant (family)	Medicinal uses	Source reference
Adiantum soboliferum L. (Adiantaceae)	Nail cicatrization	Ho *et al.* (2011)
Adiantum pedatum (Adiantaceae)	Fronds used to stop bleeding, fronds are chewed for chests, stomach trouble, used to stop bleeding, soaked and used as infusion for dirty hairs, female disorders, respiratory ailments	May (1978)
Adiantum venustum D.Don (Adiantaceae)	Rhizome and frond extract used in diabetes and liver problem, diuretic, infusion used in circulatory disorders; hydrophobia, tumours; Fronds are used as tonic, expectorant, astringent, emetic, diuretic, etc. decoction of frond used in fever and scorpion bite	Gaur and Bhatt, (1994); Mannan *et al.* (2008); Upreti *et al.* (2009)
Adiantum vogelii (Adiantaceae)	Plants used for faints, treatment of debility, oedema and skin lesions of leprosy	May (1978)
Alsophila costularis (Cyatheaceae)	Hepatitis treatment	Ho *et al.* (2011)
Angiopteris evecta Hoffm. (Angiopteridaceae)	Rhizome and rachis powder mixed with water used in diarrhoea; wound healing	Upreti *et al.* (2009); Ho *et al.* (2011)
Arthromeris wallichiana (*Spr.*) *Ching* (Polypodiaceae)	Dysentery; leaves paste used in sprains, mixed with egg albumen used in fractured bone for resetting	Gaur and Bhatt, (1994); Nwosu (2002)
Asplenium achillerfolium (*Lamb.*) *C.Ch.* (Aspleniaceae)	Decoction of leaves and root drunks as health tea, purge, paste of leaves used as facial beauty mask, powder from roots mixed with palm-kernel oil taken internally to relief stomachache and intestinal worms	Nwosu (2002)
Asplenium adiantum –nigrum L. (Aspleniaceae)	Inflammation, spleen disease, jaundice; extract of fronds drunk with castor oil as purge to remove intestinal worms especially tapeworms (*Taenia* sp.) decoction of leaves taken against urinary disorders, tonic used as antiseptic after ear-piercing, anthelmintic, emetic, laxative, useful in opthalmia	May (1978); Nwosu (2002); Mannan *et al.* (2008)
Asplenium bulbiferum L. (Aspleniaceae)	Paste prepared from leaves applied externally for haemorrhoids, decoction of fronds taken for liver problems	Nwosu (2002)
Asplenium ceterach (Aspleniaceae)	Cure enlarged spleen, pectoral, aperient	May (1978)
Asplenium cuneatum	Emetic	May (1978)
Asplenium falcatum Lam. (Aspleniaceae)	Enlarged spleen, calculus, jaundice, malaria; incontinence of urine,	May (1978); Mannan *et al.* (2008)
Asplenium furcatum (Aspleniaceae)	Rhizome anthelmintic	May (1978)
Asplenium indicum (Aspleniaceae)	Gonorrhoea	Ho *et al.* (2011)
Asplenium laciniatum (Aspleniaceae)	Leucorrhoea	Ho *et al.* (2011)
Asplenium monanthes (Aspleniaceae)	Leaves smoked for head cold, diaphoretic	May (1978)
Asplenium nidusL. (Aspleniaceae)	Antipyretic, treatment of elephantiasis, emollient in cough and chest diseases, leaves are smoked to cure cold; depurative, sedative; spleen enlargement, jaundice, malaria	May (1978); Benjamin and Manickam (2007); Mannan *et al.* (2008); Upreti *et al.* (2009); Ho *et al.* (2011)
Asplenium trichomanes L. (Aspleniaceae)	Abscess of uterus; laxative medicine, leaf is smoked for colds in head and chest, used as an expectorant	Mannan *et al.* (2008); Upreti *et al.* (2009)

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Table 1. (*Cont.*)

Name of the plant (family)	Medicinal uses	Source reference
Asplenium polydon L. (Aspleniaceae)	To promote parturition, as anticancer agent	Benjamin and Manickam (2007)
Asplenium pumilum var. hymenophylloides (Aspleniaceae)	Depurative, sedative, sores and ulcers	Parihar and Parihar (2006)
Asplenium repandum	Decoction of leaves gonorrhoea	May (1978)
Asplenium ruta-muraria L. (Aspleniaceae)	Cold, rickets and swelling; roots anthelmintic, astringent, leaves pectoral, diuretic	May (1978); Mannan *et al.* (2008)
Asplenium pseudolaserpittifolium (Aspleniaceae)	Rheumatoid arthritis	Ho *et al.* (2011)
Asplenium singaporianum (Aspleniaceae)	Decoction of leaves used after childbirth	May (1978)
Asplenium trichomanes (Aspleniaceae)	Plant laxative, expectorant, leaves smoked for cold	May (1978)
Athyrium pectinatum (*Wall. ex Mett.*) *T. Moore* (Athyriaceae)	Anthelmintic	Parihar and Parihar (2006)
Blechnum orientale L.(Blechnaceae)	Impotence, used as poultice in boils, rhizome as anthelmintic, used in typhoid; rhizome treats intestinal worms, bladder complaints; diaphoretic, aromatic, aperative	May (1978); Dhiman (1998); Upreti *et al.* (2009)
Blechnum occidentale (Blechnaceae)	Anti-inflammatory, in urinary infections, in pulmonary and liver disease treatments	Ho *et al.* (2011)
Blechnum spicant (Blechnaceae)	Inner part of rhizome diarrhoea medicine, held in mouth and only saliva swallowed; lung trouble, stomach distress, colic	May (1978)
Botrychium lanuginosum Wall. ex Hook et Grev. (Botrychiaceae)	Dysentery, ointment in the cuts and bruises; boiled rhizomes used in treating pneumonia, catarrh, expectorant, paste from roots used as facial mask	Gaur and Bhatt (1994); Nwosu (2002)
Botrychium lunaria (Botrychiaceae)	Fronds are vulnerary	May (1978)
Botrychium ternatum (*Thunb.*) *Sw.* (Botrychiaceae)	Plant used as healing of wounds; roots prescribed in dysentery	Gaur and Bhatt (1994); Mannan *et al.* (2008); Upreti *et al.* (2009)
Botrychium lunaria L. (Botrychiaceae)	Dysentery	Mannan *et al.* (2008)
Botrychium verginatum Sw. (Botrychiaceae)	Cuts and wounds	Mannan *et al.* (2008)
Camptosorus rhizophyllum (Aspleniaceae)	Herb is tonic, astringent, mucilaginous	May (1978)
Ceratopteris thallictroides (Pteridaceae)	Leaves poultice skin complaints, plant toxic and stypic	May (1978)
Cephalomanes javanicum (*Bl*) (Hymenophyllaceae)	Headache	Mannan *et al.* (2008)
Ceterach officinarum Willd.(Aspleniaceae)	Diuretic and astringent, spleen enlargement, incontinence of urine, calculus and jaundice	Mannan *et al.* (2008)
Cheilanthes albomarginata Clarke Sinopteridaceae (syn. *Aleuritopteris albomarginata*)	decoction of whole plant taken internally against peptic ulcer, fronds powder used in infertility of women, infusion taken in dysentery; as a general tonic for chidren and weak people, Recovery of weakness caused due to tuberculosis	Nwosu (2002)

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Table 1. (*Cont.*)

Name of the plant (family)	Medicinal uses	Source reference
Cheilanthes anceps Sinopteridaceae	To cure cough, asthma, tuberculosis and joint pain by tribal folk of Kumaon Himalaya	Chowdhury *et al.* (2010)
Cheilanthes bicolor Roxb. Fraser-Jenkins Sinopteridaceae	Curing cold fever; plant powder mixed with cow's ghee to use as an incense to keep off fear in children; root used in sickness	Asolkar *et al.* (1992); Upreti *et al.* (2009)
Cheilanthes farinosa Kaulf. Sinopteridaceae	Curing discharge of yellow urine; cure eczema and stomachache	Lal *et al.* (1996); Mannan *et al.* (2008)
Cheilanthes farinosa (Forsk.) *Kaulf* Sinopteridaceae	Gaddis tibe of Himachal Pradesh, India has been using this fern to treat liver damage; anti-inflammatory skin disorders	Yonathan *et al.* (2006)
Cheilanthes fragrans (L.F.) Pteridaceae	Cold and sore throat	Mannan *et al.* (2008)
Cheilanthes glauca (Cav.) Mett. Pteridaceae	Polyphenols reduce oxidative stress and could protect diabetes mellitus patients against hyperglycemia mediated lens-damage	Pastene *et al.* (2007)
Cheilnanthes tenuifolia (*Burm. F.*) *Sw.* Sinopteridaceae	Recovery from sickness; general tonic, cure wounds	Kaushik and Dhiman (1995); Mannan *et al.* (2008)
Cibotium barometz L. (Cyatheaceae)	Soft hairs used to stop bleeding, used to arrest capillary bleeding, antrirheumatic, stimulating to liver, kidney, hairy filament of stipe haemostatic, treats tropical wounds, ulcers; Treatment of lumbago, antihaemorrhagic	May (1978); Mannan *et al.* (2008); Ho *et al.* (2011)
Cibotium djambianum (Cyatheaceae)	Used to stop bleeding	May (1978)
Cibotium glaucescens (Cyatheaceae)	Hairs used to stop bleeding	May (1978)
Coniogramme caudate Hemionitidaceae	Relieve headache; Extract of fronds taken internally to relieve urinary disorders, backache and gall stones	Gaur and Bhatt (1994); Nwosu (2002)
Cyathea affinis (Cyatheaceae)	Haemostatic	Ho *et al.* (2011)
Cyathea medullaris (Cyatheaceae)	Haemostatic	Ho *et al.* (2011)
Cyathea phalerata (Cyatheaceeae)	Varicose veins and haemorrhoid treatment, anti-inflammatory	Ho *et al.* (2011)
Cyathea Mexicana (Cyatheaceeae)	Frond scales stop bleeding of external wounds	May (1978)
Cyathea usambarensis (Cyatheaceeae)	Worm remedy from leaf and core	May (1978)
Cyclosorus striatus (Thelypteridaceae)	Plant decoction, liver ailments	May (1978)
Cystopteris fragilis (Dryopteridaceae)	Pectoral, mucilaginous, expectorant, refrigerant tonic	May (1978)
Davalia fijiensis (Davaliaceae)	Healing of fractured bones	Ho *et al.* (2011)
Davallia mariesii (Davaliaceae)	Healing of fractured bones, pain-killer, anti-inflammatory, anti-cancer, anti-ageing, haemostasis	Ho *et al.* (2011)
Davallia solida (Davaliaceae)	Dysmenorrhoeal, gonorrhoea, leucorrhoea, sore throat, asthma, purgative, wound healing, antitiemetic, in sprain, healing of fractured bones	Ho *et al.* (2011)
Dennstaedtia puntilobula (Dennstaedtiaceae)	Nodules at crown of root used for blood haemorrhages of lungs	May (1978)
Dicranopteris linearis (Burm.) Underwood (Gleic heniaceae)	Anthelminthic, cure asthma and removing sterility in women	Asolkar *et al.* (1992); Upreti *et al.* (2009)

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Table 1. (*Cont.*)

Name of the plant (family)	Medicinal uses	Source reference
Diplazium esculentum (*Retz.*) *Sw.* (*Athyriaceae*)	Infusion of fronds used for toothache, fronds used by pregnant women as protection against difficult child birth; Rhizomes are kept in granaries to check them from insects and pests; decoction used for haemoptysis and cough	May (1978); Nwosu (2002); Upreti *et al.* (2009)
Diplazium esculantum (Retz.) Sw. (Athyriaceae)	Young fronds cooked and taken as food to improve general health	Kaushik and Dhiman (1995)
Diplazium polypodioides Blume (Athyriaceae)	Relieve dysentery	Gaur and Bhatt (1994)
Drynaria quercifolia L. (Polypodiaceae)	Wound healing; Lumbago treatment; rhizome astringent, hectic fever, cough pthisis	May (1978); Gaur and Bhatt (1994)
Drynaria fortunei (Polypodiaceae)	Rhizome decoction in rheumatism, haemostatic for gangrene of fingers; lumbago treatment	May (1978); Ho *et al.* (2011)
Drynaria rigidula (Polypodiaceae)	Rhizome decoction, gonorrhoea, dysentery	May (1978)
Drynaria rosii (Polypodiaceae)	Haematochezia, diarrhoea, febrifuge, diuretic	Ho *et al.* (2011)
Dryopteris anthelmentica (Dryopteridaceae)	Leaves for worms	May (1978)
Dryopteris barbigera (Dryopteridaceae)	Intestinal worms	May (1978)
Dryopteris blandfordii (Dryopteridaceae)	Intestinal worms	May (1978)
Dryopteris cochleata (*D. Don*) *C.Chr L. Dryopteridaceae*	Diarrhoea; to cure eczema and anthelmintic	Gaur and Bhatt (1994); Parihar and Parihar (2006)
Dryopteris crassirhizoma (Dryopteridaceae)	Rhizome and stipe cure stomachache, ease bruising	May (1978)
Dryopteris cristata (Dryopteridaceae)	Intestinal worms	May (1978)
Dryopteris dilatata (Dryopteridaceae)	Rhizome applied to cuts,	May (1978)
Dryopteris heterocarpa (Dryopteridaceae)	Fronds treat leucodermia	May (1978)
Dryopteris schimperiana (Dryopteridaceae)	Rhizome treat worms	May (1978)
Drymoglossum piloselloides L. (Dryopteridaceae)	Reduce swelling, sprains and relieving pain	Mannan *et al.* (2008)
Dryopteris filix-mas L.(Dryopteridaceae)	Young circinately coiled fronds used as vermifuge	Nwosu (2002)
Dryopteris odontoloma L. (Dryopteridaceae)	Dysentery	Gaur and Bhatt (1994)
Dryopteris wallichiana L. (Dryopteridaceae)	Dysentery; tonics from roots drunk against rheumatism	Gaur and Bhatt (1994); Nwosu (2002)
Elaphoglossum petiolatum	Root decoction sore throats	May (1978)
Equisetum arvense L.Equisetaceae	Psychomedicine, gonorrhoeal disease; diuretic, reduce acidity	Gaur and Bhatt (1994); Mannan *et al.* (2008)
Equisetum diffusum D.Don Equisetaceae	Diuretic	Gaur and Bhatt (1994)
Equisetum hymenale Equisetaceae	Root juice eye wash	May (1978)
Equisetum ramosissimum Equisetaceae	Improve the fertility of women, diuretic, haemostatic, antirheumatic, antifgungal, antivirul, in bone injury, cooling medicine for gonorrhoea	May (1978); Parihar and Parihar (2006); Benjamin and Manickam (2007); Upreti *et al.* (2009)

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Table 1. (*Cont.*)

Name of the plant (family)	Medicinal uses	Source reference
Equisetum diffusum D. Don Equisetaceae	Decoction of roots used for treatment of psychosis, dried leaves powder mixed with water used as insect repellant	Nwosu (2002)
Equisetum myriochaetum (Equisetaceae)	Anti-diabetic	Cetto *et al*. (2000)
Equisetum xylochaetum Equisetaceae	Treat ulcer, diuretic	May (1978)
Glaphyropteridopsis erubescens (*Wall ex Hook*.) *Ching Thelypteridaceae*	Gonorrhoea especially for leucorrhoea; Decoction of young fronds used against indigestion for adults, rheumatism, scorpion bite	Gaur and Bhatt (1994); Nwosu (2002)
Gleichenia linearis L. Gleicheniaceae	Administered internally to children suffering from convulsion; gonorrhoea treatment, hernia	Nwosu (2002); Ho *et al*. (2011)
Helminthostachys zeylanica (*Linn*.) *Hook. f. Helminthostachyceae*	Promote vitality and vigour, curing impotency, to relieve blisters on the tongue and also improve memory; intoxicant, anodyne and used in sciatica; dysentery, sciatica, malaria	May (1978); Singh and Maheswari (1989, 1992); Singh *et al*. (1989); Mannan *et al*. (2008); Upreti *et al*. (2009)
Hemionitis arifolia (*Burm*) Hemionitidaceae	Used for burns; antidiabetic	Mannan *et al*. (2008); Ho *et al*. (2011)
Hemitelia stokesii (*Cyatheaceae*)	Haemostatic	Ho *et al*. (2011)
Huperzia subulifolia (*Wall. ex Hook. et Grev*.) *Huperziaceae*	Cough and uneasiness in the chest	Gaur and Bhatt (1994)
Huperzia serrata Huperziaceae	Febrifuge, blood disorder treatment, contusion, strains, swelling, myasthemia gravis, schizophrenia	Ma *et al*. (2007)
Hypodematium crenatum (*Forssk*.) *Kuhn & Deck Hypodematiaceae*	Used in insect bite	Parihar and Parihar (2006)
Isoetes coromandeliana (Isoetaceae)	Treatment of spleen and liver diseases	Benjamin and Manickam (2007)
Lecanopteris carnosum (Polypoodiaceae)	Fronds pectoral, diuretic, astringent, rheumatism	May (1978)
Lemmaphylum carnosum (*Sm*)	Urinary calculus and rheumatism and stop the haemorrhages	Mannan *et al*. (2008)
Lemmaphylum microphyllum	Rheumatoid arthritis, sore throat and cough treatment	Ho *et al*. (2011)
Isoetes rajasthanensis Gena & Bhardwaja Isoetaceae	Spleen and liver diseases	Parihar and Parihar (2006)
Lepisorus clathratus (*Clarke*) *Ching Polypodiaceae*	Deteriorate wounds	Gaur and Bhatt (1994)
Lycopodiella cernuum L. Lycopodiaceae	Decoction of plant is used as beri-beri lotion, used in cough and skin eruption; antitussive; Used for coughs and uneasiness in the chest; rheumatism	May (1978); Mannan *et al*. (2008); Upreti *et al*. (2009); Ho *et al*. (2011)
Lycopodium clavatum L. Lycopodiaceae	Spasmodic retention of urine in infants, gastritis, emollient, urinary or kidney disorders, catarrhal cystitis; dyspepsia, hepatic congestion and pustular skin eruptions, rheumatism, cramps and varices; Ulcer, diarrhoea, dysentery; homeopathic medicine	Hahnemann (1835); Gaur and Bhatt (1994); Nwosu (2002); Mannan *et al*. (2008)
Lycopodium japonicum Thunb. (*Lycopodiaceae*)	Diuretic, antispasmodic, used in rheumatism and diseases of lungs and kidney	Upreti *et al*. (2009)
Lycopodium rubrum (Lycopodiaceae)	Leaves treat elephantitis	May (1978)

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Table 1. (*Cont.*)

Name of the plant (family)	Medicinal uses	Source reference
Lycopodium selago L. Lycopodiaceae	Eczema, snake bite; spore vermifuge	May (1978); Nwosu (2002)
Lygodium circinnatum (Lygodiaceae)	Stipe chewed, applied to bite of venomous snake or insect to neutralize	May (1978)
Lygodium conforme (Lygodiaceae)	Hepatitis treatment	Ho *et al*. (2011)
Lygodium flexuosum (*Linn*.) *Sw*. (Lygodiaceae)	Spermatorrhoea, dysmenorrhoea, jaundice and skin diseases; expectorant, rheumatism, sprains, scabies, eczema and cut wounds	Gaur and Bhatt (1994); Dhiman (1998); Mannan *et al*. (2008); Upreti *et al*. (2009)
Lygodium volubile Sw. Lygodiaceae	Rhizome decoctions for heat and veneral diseases	Wong (1976)
Lygodium japonicum (*Thunb*.) *Sw. Lygodiaceae*	Expectorant	Mannan *et al*. (2008)
Lygodium flexuosum (*L*.) *Sw. Lygodiaceae*	Infusion of leaves for treating female infertility, fractured bones, against haemorrhoids	Nwosu (2002)
Lygodium microphyllum	Crushed leaves cure hiccough	May (1978)
Lygodium palmatum (*L*.) *Sw. Lygodiaceae*	Young frond extract in boils, abscess, swelling; used as astringent, emollient and cosmetics	Nwosu (2002)
Lygodium reticulatum Lygodiaceae	Dysmenorrhoea, digestive, contraceptive, healing of fractured bones, haemorrhoids, impotence	Ho *et al*. (2011)
Marattia fraxinea (Marattiaceae)	Remedy for ancyclostomiasis	May (1978); Benjamin and Manickam (2007)
Marattia salicina (Marattiaceae)	Wound healing, antibacterial	Ho *et al*. (2011)
Marattia douglasii (Marattiaceae)	Decoction bronchitis, diarrhoea from rhizome	May (1978)
Marsilea minuta L. Marsileaceae	Epilepsy, used in cough, spastic conditions of leg muscles, sedation and insomnia	Parihar and Parihar (2006); Mannan *et al*. (2008); Upreti *et al*. (2009)
Marsilea quadrifolia L. Marsileaceae	Aphordisiac	Nwosu (2002)
Microsorum commutatum Polypodiaceae	Renal and urological disorders; Healing of fractured bones, as a painkiller, in influenza, diarrhoea, stomachache treatment, muscle relaxant	Ho *et al*. (2011)
Microsorum membranifolium Polypodiaceae	Cleansing bath for newborn, in dysmenorrhoeal, gonorrhoea, leucorrhoea, sore throat, asthma, purgative, wound healing, anti-emetic, sprains, healing of fractured bones	Ho *et al*. (2011)
Microsorum scolopendria (*Polypodiaceae*)	Skin inflammation treatment, wound healing, purgative	Ho *et al*. (2011)
Microsorum membranaceum (*D. Don*) *Ching Polypodiaceae*	Relieve chest pain, cough and cold of infant, diarrhoea and dysentery	Gaur and Bhatt (1994)
Microsorum punctatum Polypodiaceae	Leaves and juice purgative, diuretic and wound healer	May (1978)
Mohria caffrorum (Schizaeceae)	Smoke of burnt leaves is inhaled by children with nightmares, dried frond ointment in burns	May (1978)
Nephrolepis biserrata (*Nephrolepidaceae*)	Haemostatic treatments for wounds	May (1978)

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Table 1. (*Cont.*)

Name of the plant (family)	Medicinal uses	Source reference
Nephrolepis cordifolia (*L.*) *Presl.* (*Nephrolepidaceae*)	Reduce cough; Amnesia; paste of the leaves applied in wound to check bleeding, decoction of tubers is given to cure cough and intestinal disorders, Fresh watery tubers used in stomach ulcer and acidity	May (1978); Nwosu (2002); Mannan *et al*. (2008); Upreti *et al*. (2009)
Nephrolepis exaltata (*Nephrolepidaceae*)	Newborn umbilical cicatrization	Ho *et al*. (2011)
Nephrolepis hirsulata (*Nephrolepidaceae*)	Postpartum care, bellyache	Ho *et al*. (2011)
Nephrolepis hirsutula (*Nephrolepidaceae*)	Newborn umbilical cicatrization	Ho *et al*. (2011)
Notholaena eckloniana Kuntze L. (Pteridaceae)	Relieves cold in head and chest, applied as an ointment in the scalp	Mannan *et al*. (2008)
Odontosoria chinensis	In chronic enteritis	Benjamin and Manickam (2007)
Oleandra colubrine (*Oleandraceae*)	Rhizome remedy for snakebite; stipe emmenagogue	May (1978)
Oleandra neriiformia (Oleandraceae)	Stipe emmensgogue, rhizome snake bite	May (1978)
Oleandra undulata (*Willd.*) *Ching* (Oleandraceae)	Antidote against snake bites	Gaur and Bhatt (1994)
Onychium siliculosum	Juice of crushed leaves prevents falling hair	May (1978)
Ophioglossum capense (Ophioglossaceae)	Warm rhizome decoction in boils	May (1978)
Ophioglossum ovatum (Ophioglossaceae)	Plant juice emollient	May (1978)
Ophioglossum pendulum L. Ophioglossaceae	Spores given to babies at birth to purge meconium; improve the hair	May (1978); Mannan *et al*. (2008)
Ophioglossum reticulatum L. Ophioglossaceae	Paste of the plant used on burns as cooling agents, leaf extraction used in vulnerary	Upreti *et al*. (2009)
Ophioglossum vulgatum L. Ophioglossaceae	Sore eyes as a detergent, antiseptic; Pulmonary, bronchial and heart disease, ulcerated sores and wounds; jaundice and hepatitis treatment	Gaur and Bhatt (1994); Nwosu, (2002); Mannan *et al*. (2008); Ho *et al*. (2011)
Ophioglossum grande L. Ophioglossaceae	Antidote for snakebite	Nwosu (2002)
Ophioglossum nudicaule Linn. Ophioglossaceae	Inflammation and wound, stypic and haemorrages	Parihar and Parihar (2006)
Osmunda regalis L.Osmundaceae	Rickets, rheumatism, intestinal gripping and stypic; Psychosis, moon-madness, malaria and jaundice	Nwosu (2002); Mannan *et al*. (2008)
Osmunda claytoniana L. Osmundaceae	Wound healing	Gaur and Bhatt (1994)
Osmundopteris lanuginose Osmundaceae	Hypertension treatment	Ho *et al*. (2011)
Pellaea atropurpurea Pteridaceae	Entire plant astringent, anthelmintic	May (1978)
Pellaea calemelanos Sw. Pteridaceae	Asthma, cold in the head and chest	Mannan *et al*. (2008)
Pellaea involuta Pteridaceae	Rhizome spider bite and diarrhoea remedy	May (1978)
Phymatosorus scolopendria Burm. (Polypodiaceae)	Chronic diarrhoea; anti-inflammatory, pulmonary and liver disease treatment	Mannan *et al*. (2008); Ho *et al*. (2011)
Phyllitis scolopendrium (Aspleniaceae)	Diuretic, astringent, expectorant, wound healing; anti-inflammatory, pulmonary and liver disease treatment	Ho *et al*. (2011)
Pityrogramma calomelanos (*L.*) *Link* (Pteridaceae)	Kidney troubles; For flu, cough, amenorrhoea, consumption, hypertension, menorrhagia, fever	Wong (1976); Mannan *et al*. (2008)
Pityrogramma triangularis (Pteridaceae)	Fronds chewed for toothache, pain of childbirth	May (1978)
Pleopeltis lanceolata (*Linn.*) (Polypodiaceae)	Relieves cold and sore throat	Mannan *et al*. (2008)

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Table 1. (*Cont.*)

Name of the plant (family)	Medicinal uses	Source reference
Polypodium aureum (Polypodiaceae)	Cough and fever sudorific	May (1978)
Polypodium californicum (Polypodiaceae)	Juice used for sores, rheumatism, root expectorant, diuretic	May (1978)
Polypodium furfuraceum (Polypodiaceae)	Analgesic	May (1978)
Polypodium lanceolatum (Polypodiaceae)	Rhizome febrifuge, coughs, decoction cold and sore throat	May (1978)
Polypodium microrhizoma Clarke ex Baker Polypodiaceae	Joint pain, rheumatism; gastrointestinal disorders, backache, jaundice, wound healing	Gaur and Bhatt (1994); Nwosu (2002)
Polypodium plebejum (Polypodiaceae)	Rhizome coughs, purgative	May (1978)
Polypodium angustifolium Polypodiaceae	Anti-inflammatory	Ho *et al.* (2011)
Polypodium decumanum Polypodiaceae	Skin disorders, psoriasis treatment	Ho *et al.* (2011)
Polypodium leucotomos (Polypodiaceae)	Antiphlogistic, antitumoral, anti-inflammatory for skin disease, psoriasis treatment, general tonic	Ho *et al.* (2011)
	DIFUR capsules have been produced [An extract of the fern *P. leucotomos* (Difur) [=Phlebodium aureum]	
Polypodium subamoenum Clarke Polypodiaceae	Psychomedicine	Gaur and Bhatt (1994)
Polypodium subpetiolatum Polypodiaceae	Anti-inflammatory	Ho *et al.* (2011)
Polypodium scolopendrium (Polypodiaceae)	Headache, sore lotion	May (1978)
Polypodium vulgare (Polypodiaceae)	Respiratory ailments, epilepsy, cough, apetiteless, skin disease	May (1978)
Polypodium vulgare L. Polypodiaceae	Purgative, vulnerary medicine; Jaundice	Gaur and Bhatt (1994); Ho *et al.* (2011)
Polystichum munitum	Spores cure sore	May (1978)
Polystichum nepalense (*Spr.*) *C. Chr.*	Digestive relief, skin allergies	Gaur and Bhatt (1994)
Polystichum pungens	Wound healing	Ho *et al.* (2011)
Pronephrium gymnopteridifrans	Cold	Ho *et al.* (2011)
Psilotum nudum L.(Psilotaceae)	Arrest diarrhoea	Mannan *et al.* (2008)
Pteridium aquilinum (*L.*) *Kuhn. v. Decken* (Pteridaceae)	Treatment of chronic disorders; Herbal health tea; astringent, anthelmintic, useful in diarrhoea	Mannan *et al.* (2008); Nwosu (2002); Ho *et al.* (2011)
Pteris biaurita (Pteridaceae)	Chronic disorders	Ho *et al.* (2011)
Pteris ensiformis Burm. (Pteridaceae)	Glandular swelling of neck; Dysmenorrhoea, rheumatoid arthritis, digestive, purgative	May (1978); Mannan *et al.* (2008); Ho *et al.* (2011)
Pteris quadriaurita Retz. (Pteridaceae)	Antiseptic, wound healing; Astringent, emollient, insect repellant especially for red ants or termites	Gaur and Bhatt (1994); Nwosu (2002)
Pteris multifida Poir (Pteridaceae)	Dysentery; haemostatic, to treat colds	Mannan *et al.* (2008); Ho *et al.* (2011)
Pteris semipinnata (Pteridaceae)	Snake bite treatment	Ho *et al.* (2011)
Pteris wallichiana (Pteridaceae)	Astringent, dysentery and skin infection	Upreti *et al.* (2009)
Psilotum nudum (Psilotaceae)	Toxic and growth reducing effects on *Ostrinia nubilalis*, a polyphagous lepidopteran; laxative, general tonic	Amason *et al.* (1986); Ho *et al.* (2011)
Pyrrosia adnascens (Polypodiaceae)	Rheumatoid arthritis treatment	Ho *et al.* (2011)

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Table 1. (*Cont.*)

Name of the plant (family)	Medicinal uses	Source reference
Pyrrosia lanceolata (Polypodiaceae)	Skin disorders with intense irritation; Colds and sore throat	Benjamin & Manickam (2007)
Pyrrosia lingua (Polypodiaceae)	Cystitis treatment	Ho *et al.* (2011)
Pyrrosia nuda (Polypodiaceae)	Cystitis treatment	Ho *et al.* (2011)
Schizaea dichotoma L.(Schizeaceae)	Cough and throat infection	Mannan *et al.* (2008)
Tmesipteris tannensis (Psilotaceae)	Toxic and growth reducing effects on *Ostrinia nubilalis*, a polyphagous lepidopteran	Amason *et al.* (1986)
Marsilea minuta L. (Marsileaseae)	Curing cough and bronchial troubles, curing eye diseases	
Selaginella bryopteris (L.) Baker (Selaginellaceae)	Curing gonorrhoea and other veneral diseases, also in stomachache; Reduces heat shock	Sah *et al.* (2005)
Selaginella doederleinii, (Selaginellaceae)	Anticancer herb, contribute to reversible bone-marrow suppression	Pan *et al.* (2001)
Selaginella cinerascens L. (Selaginellaceae)	Emollient, gastrointestinal disorders such as heart burns	Nwosu (2002)
Selaginella involvens Sw. (Selaginellaceae)	High fever	Mannan *et al.* (2008)
Selaginella lepidophylla (Selaginellaceae)	Diuretic	May (1978)
Selaginella serpens Spring (Selaginellaceae)	Liver problems, hepatoma, antiseptic	Nwosu (2002)
Selaginella pallescens (*C.Prest*) *Spring* (Selaginellaceae)	Rheumatism, insomnia, haemorrhoids, fistulus	Nwosu (2002)
Selaginella tamariscina (Beauv.) Spring (Selaginellaceae)	Cough, prolapsed of rectum, amenorrhoea and bowel bleeding; Anti-diabetic	May (1978); Zheng *et al.* (2011)
Selaginella tamariscina (Beauv.) Spring (Selaginellaceae)	Inhibit induction of nitric oxide and production of prostaglandins	Yang *et al.* (2006)
Selaginella moellendorffi (Selaginellaceae)	Inhibit growth of cancer cells by inducing apoptosis	Sun *et al.* (1997)
Selaginella uncinata (Selaginellaceae)	Used against respiratory syncytial virus	Ma *et al.* (2003)
Selaginella uncinata (Desv.) Spring (Selaginellaceae)	Jaundice, dysentery, oedema and rheumatism in traditional Chinese medicine	Zheng *et al.* (2016)
Selaginella wallichii Hook. & Grev. (Selaginellaceae)	Protective medicine after child birth	Mannan *et al.* (2008)
Sphenomeris chinensis	Diuretic, chronic enteritis and sprain treatment	Benjamin and Manickam (2007)
Stenochlaena palustris Burm. (Blechnaceae)	Cures fever	Mannan *et al.* (2008)
Tectaria macrodonta (*Fee*) *Chr.*(=*syn. Tectaria coadunata* (*J. Smith*) *C.Chr.* Tectariaceaae)	Running stomach of cattles, placental expulsion of livestock, foot etching and gonorrhoea; asthma, bronchitis, stings of honey bee and centipeds; colitis, stomachache	Nwosu (2002); Parihar and Parihar (2006); Upreti *et al.* (2009)
Thelypteris arida (Thelypteridaceae)	Wound healing	Upreti *et al.* (2009)
Thelypteris kunthii (Thelypteridaceae)	Boiled plant used to clean and close cuts	May (1978)
Woodwardia unigemmata (*Mak.*) *Nakai* (Blechnaceae)	Purgative; Skin disease (ring worm), infertility of women, abdominal pain, constipation and sore throat	Gaur and Bhatt (1994); Nwosu (2002)
Woodwardia virginica (Blechnaceae)	Leaves astringent	May (1978)

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Table 2. Major pharmaceutically active principles known to be produced in Lycophytes and Fern Genera

Sl. no.	Name of the plant (family)	Main compound	Source reference
1.	*Cheilanthes anceps* Blanford (Sinopteridaceae)	Mono and 3,7-di-O-glycosides of Kaempherol and Quercetin	Chowdhary *et al.* (2010)
2.	*Cheilanthes dalhousiae* (Hook.) (Sinopteridaceae)	Quercetin-3-methyl ether 5-O-glucoside, Kaempferol-3-methyl ether -5-O-*β*-(6′-malonyl) glycoside	Mishra and Verma (2010)
3.	*Cheilanthes grisea* Blanford (Sinopteridaceae)	Quercetin-3-OCH_3-5-O-*β*-d-glucoside, Kaempferol-3-OCH_3-5-O-*β*-d-glucoside, Quercetin-3,4′-dimethyl ether-5-O-*β*-D-glucoside	Mishra and Verma (2009)
4.	*Selaginella tamariscina* (Beauv.) Spring (Selaginellaceae)	Total flavonoids	Zheng *et al.* (2011)
5	*Equisetum myriochaetum* (Equisetaceae)	Three kaempferol glucosides and one caffeoyl glucoside	Cetto *et al.* (2000)
6	*Psilotum nudum* (Psilotaceae)	Psilotin [6-(4′-*β*-D-glucopyranosyloxyphenyl)-5,6-dihydro-2-oxo-2H-pyran], phenolic glycoside	Amason *et al.* (1986)
7	*Tmesipteris tannensis*	Psilotin [6-(4′-*β*-D-glucopyranosyloxyphenyl)-5,6-dihydro-2-oxo-2H-pyran], the major phenolic glycoside	Amason *et al.* (1986)
8	*Selaginella delicatula*	Robustaflavone 4′-methyl ether(1), robustaflavone 7,4′-dimethylether(2), 2″ 3″dihydrorobustaflavone 7, 4′ –dimethyl ether(3)	Lin *et al.* (2000)
		2″3″dihydrorobustaflavone 7, 4, 7″ –trimethyl ether(4)	
9	*Selaginella moellendorffi*	Ginkgetin (biflavone)	Sun *et al.* (1997)
10	*Selaginella uncinata* (Desv.) Spring	five flavone di-*C*-glycosides, schaftoside	Zheng *et al.* (2016)
		(**1**), isoschaftoside (**2**), 6,8-di-*C*-*β*-L-arabinopyranoside-apigenin (**3**), 6-*C*-*α*-L-arabinopyranosyl-8-*C*-*β*-L-arabinopyranosylapigenin	
		(**4**), and 6-*C*-*β*-L-arabinopyranosyl-8-*C*-*α*-L-arabinopyranosyl-apigenin (**5**),	
11	*Selaginella uncinata* (Desv.) Spring	5-hydroxy-2,6,8-trimethylchromone 7-O-beta-D-glucopyranoside (uncinoside A) and 5-acetoxyl-2,6,8-trimethylchromone 7-O-beta-D-glucopyranoside (uncinoside B).	Ma *et al.* (2003)
12	*Huperzia serrata*	Huperzine A, Huperzine B	Liu *et al.* (1986)
13	*Salvinia natans*	Methylbenzoate 3,4-dihydroxy methylbenzoate Natansnin Several complex compounds of medicinal importance have been isolated from *Azolla* and *Salvinia*; the common aquatic weeds of most ponds/lakes	Narasimhulu *et al.* (2010)/Srilaxmi *et al.* (2010)/, Ashalata abstracts; (2010) Also visit WorldWideScience.org
14	*Adiantum aethiopicum* L.	It contains compounds such as triterpenes, flavonoids, carotenes and phenylpropanoides.	Laware and Limaye (2012)
		Apart from that, chemical compounds such as rutin, isoqercetin, quinic acid and astragalin have been reported for their anticancer, antiviral, choleretic, antileukaemic activities, respectively. Also the dimeric protein 15.0 and 15.5 kDa protein isolated from Adiantum was found to be very effective	

Polypodium, Pyrrosia, Pteris, Lygodium, Selaginella, Thelypteris, Athyrium, Matteuccia, Onoclea and *Woodsia* have proved to be of great medicinal relevance. List of such ferns is increasing every year (Sen and Nandi, 1951; Puri and Arora, 1961; Patric *et al.*, 1995; Lopez *et al.*, 2001; Lee *et al.*, 2008; Wong *et al.*, 2009; Shin and Lee, 2010; Wolf *et al.*, 2015; Sessa and Der, 2016; Wani *et al.*, 2016; Srivastava and Paul, 2016).

Natural antioxidants are in high demand for application as nutraceuticals, biopharmaceuticals, as well as food additives. This has been established by various population surveys that increased dietary intake of natural phenolic antioxidants, related with decline in cardiovascular problems. In tribal populations of India and elsewhere, edible ferns have been the most preferred staple food as passing through forests were the major part of their routine (Copeland, 1942; Hernandez and Volpata, 2004). It may be underpinned that further systematic studies on realization of antioxidant potential of ferns as natural ingredient may result in the development of health-care products for ageing and chronic disease on account of their high bioactivities.

Evolutionary and ecological importance of ferns

Evolutionary novelty of lycophytes and ferns has been established by modern genomic studies that have enabled to resolve intricate evolutionary relationships among plants and underscored their ecological importance. Comparative genomics have made it clear that lycophytes first diverged from euphyllophytes and these euphyllophytes then diverged into two sister clades monilophytes (comprising of ferns, psilopsids and sphenopsids) and the spermatophytes (seed plants) during the Devonian (about 380 mya). These non flowering plants have had dominated vegetation world until the evolution of angiosperms. Though flowering plants took over larger distribution during late Cretaceous, but the ferns flourished well and continued to be the integral part of each and every part of forests everywhere (Pryer *et al.*, 2001, 2004; Schneider *et al.*, 2004).

As of today, almost in every part of the globe, tropical, subtropical, remote tropical islands and in different habitats or even in deeper rainforests, the ferns play a definitive role to constitute the strong carpet flora and undercover vegetation. Their network of strong roots, which are enormously rich in organic compounds with strong soil binding capacity also serve as the cradle for a large number of smaller mammals, rodents as well as amphibians, invertebrates, even arthropods and insects (Balick *et al.*, 1978; Cooper-Driver, 1978; Gerson, 1979). Ferns are strong ecologically natural obligations of a rich forest (Goswami, 2009b; Mehltreter *et al.*, 2010). Apart from this natural habitat, several ferns are too hardy, which can colonize and adapt to survive and reproduce in disturbed or barren land with the modest possibility of moisture and drain water. Ferns adapt to xeric environments. These can be frequent colonizers following disturbances such as hurricanes, landslides, fire, floods and even volcanoes (Mehltreter *et al.*, 2010). According to Page (1979) there are five major environments in which ferns are found; these are tropical mesic, tropical xeric epiphytic, tropical xeric terrestrial, tropical alpine and temperate. *Acrosticium aureum* grows in salty water; *Pteris vittata* in particular is often seen growing on the soil near the water drainage pipelines, on walls and even on cement – calcareous waste matter. Most ecologists have referred them to be suitable to be disseminated in barren lands. Since ferns also multiply aggressively by vegetative means, an open area can be better utilized for ferns' inhabitation before nasty invasive species occupy the space. Even a tree fern *Dicksonia antarctica* (Arosa *et al.*, 2012) becomes invasive in So Miguel Island. Ferns can survive drought and even can be grown in man-made destructions on account of huge modern constructions and cement concrete-residue land mass though, these genera may be different from the original populations.

Enrichment of the flora in nature

Speciation by natural interspecific hybridization is very common among lycophytes and ferns. A large number of species have evolved by natural hybridizations in ferns (Haufler, 2008; Kato, 2009), which are capable of adapting to changing natural climatic conditions. The offspring of natural hybrids are expected to have genotypes combining the alleles of the parental species, and are expected to be genetically diverse. Often we expect that heterozygosity may support better adaptive strategies though not always so. For example, the genus *Osmunda* (Fig. 1(c)) of the leptosporangiate fern family Osmundaceae has natural hybrids (Kato, 2009; Tsutsumi *et al.*, 2011), so also are the genera *Ophioglossum, Isoetes* (Goswami, 2009a, 2013) and lot many more (see Haufler, 2008). Hybridization often speeds up speciation process and many such individual segregates do adapt to newer situations. A follow-up study for three decades had revealed that the newly evolved hybrid species, which is practically a segregate of natural hybridization between *Isoetes coromandelina* and *I. sampathkumarini* (as is *Isoetes pantii*) grows on the outer margins of the lake water and can even be collected during winter while both putative parents grow submerged in water and end their rainy season-annual life mostly by the end of October, i.e. onset of winter in India (H.K. Goswami, pers. observ.). Many fern species, e.g. *Asplenium platyneuron, Blechnum spicant, Pteris multifida, Lygodium microphyllum, Lygodium japonicum,*

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Dryopteris carthusiana, Sadleria cyatheoides, Osmunda lancea, etc. are generally effective colonizers because of the capability of intra-gametophytic selfing, i.e. by the union of sperm and egg from the same bisexual gametophyte (Tsutsumi *et al.*, 2011). Such species have an advantage in expanding its distribution along various rivers or similar niches. Cultivation of a fern genus *Osmunda regalis* is a testimony to this. As a natural habitat *O. regalis* always grows by the side of flowing water (Fig. 1(c)) but lately at Pachmarhi (Central India) the planted *O. regalis* is growing well in garden plots (Fig. 1(d)) with modest supply of water (H. K. Goswami, pers. observ.). We have planned to attempt to shift and grow representatives of rare and medicinally important flora to a manageable place so that the original pocket in the reserved forest may be at a distance away from undesired anthropogenic disturbances. For example a lycophyte, *Lycopodium* (Fig. 1(b)) used in Homeopathic medicine is equally cultured in open land area in a designed protected garden. These plants have the tendency to produce many kinds of secondary metabolites in severe conditions (Bohm and Tryon, 1967; Chen *et al.*, 2007; Ding *et al.*, 2008; Ganguly *et al.*, 2011; Chai *et al.*, 2012; Andrade *et al.*, 2014; Dubal and Kale, 2014 and others; see also, Table 2), which offer enhanced adaptive capabilities and also such secondary metabolites (Table 2, Fig. 2) that can be exploited for medicinal uses.

Phytochemical significance

Since the appearance of Vascular land plants, pteridophytes had acquired several apomorphies such as vascular tissue, lignin and sclerenchyma (Pryer *et al.*, 2001, 2004) and evolution of biochemical conversion of certain primary metabolites to secondary products in order to realize protection from UV light, parasites, fungi, protozoa and other predators to adapt on land surface and also to defend themselves against biotic or abiotic stress, such as high light intensity, extremely high or low temperature, high salinity, drought and natural enemies. Interestingly, secondary metabolites are promising as the source of new drugs. Three main classes of secondary metabolite, namely terpenoids, alkaloids and phenylpropanoid and allied phenolic compounds that are known to be produced by Lycophytes and ferns have gained attention as the source of new drugs (Caius, 1935; Bray and Thorp, 1954; Dhar *et al.*, 1968; Adams, 1989; Anishmom and Thomas, 2005; Chen *et al.*, 2007; Chowdhary *et al.*, 2010; Ashihara *et al.*, 2012; Ceyhan *et al.*, 2012; Andrade *et al.*, 2014; Augustin and Thomas, 2015; Wani *et al.*, 2016). Ferns in particular have gained international recognition and for about two decades a large number of laboratories are busy with extracting various compounds that have value in preparation of life saving drugs. Fern rhizomes have not only become stable

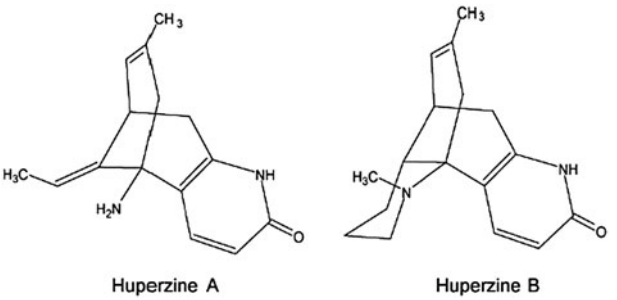


Fig. 2. Structural formulae of medicinally important compounds: Huperzin A and -B (Liu *et al.*, 1998).

refreshment for herbivores, but many rodents are seen feeding on roots and their exudates in the interior forest areas of Bastar (now in Chhatisgarh) and in uphills of Nagaland, India. Chemical components in roots and rhizomes are directly related to adaptive responses of the plant species. For example high sabinene content facilitates adaptation to different climatic and edaphic conditions as observed in an invasive angiosperm species *Hyptis suaveolens* (fam. Lamiaceae) samples (Noudogbessi *et al.*, 2013) studied from different places. Similar studies on *Ophioglossum* (called as Adder's tongue fern) had revealed that higher content of sulphur containing aminoacids (cysteine, ornithine) in roots is directly correlated with excessive vegetative propagation (Fowden, 1965; Goswami and Khandelwal, 1976; Khandelwal and Goswami, 1976; Khandelwal *et al.*, 1980). There are several studies, which indicate that the presence of specific compound supports some or the other biological function in a species. For example, the amino acid proline is generally associated with drought resistance. Proline acts as osmolyte, giving stress relief to plants (Hopkins *et al.*, 2001). There is also an increase of proline content with age in all the three species of *Adiantum* (Guha *et al.*, 2006). Detection of proline in *Ophioglossum* corms of different species, (Goswami and Khandelwal, 1976; Khandelwal and Goswami, 1976) obviously account for regeneration and reappearance of new *Ophioglossum* plants after the summer every year in the next rainy season. Higher amount of proline content in rhizome than that of frond has also been reported by Joseph *et al.* (2003) in Dryopteridaceae. Adaptive distribution of plants appears to be dependent on specific compounds present and active within the basal organs. Carotenoids are found more in amount in drought resistant ferns. Precisely, if at any place any plant species becomes or behaves as an invasive species the species is bound to have some specific organic components, which are helpful in its prolific reproductive rate. There is a need to explore such chemical constituents in detail and work out their utility for medicinal purposes. In this context, we must recall that a few of the ferns have already reached up to the pharmaceutical development and marketing drugs such as, Huperzine A and

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Huperzine B (Fig. 2) from *Huperzia serrata* and Calaguline from *Polypodium leucomotos*. Further, many such attempts on *Selaginella* and *Lycopodium* have also been exploited for producing useful drugs (Liu *et al.*, 1998; Ma *et al.*, 2003; Ho *et al.*, 2011; Zhu *et al.*, 2000).

Phytochemical assays

From sporophytic phase (main plant body)

Phytochemical studies have rightfully gained paramount importance for clinical trials for detecting antimicrobial agents. Earlier these were mainly used in chemotaxonomy of pteridophytes (Banerjee and Sen, 1980; Gottlieb *et al.*, 1991). Of the 13 species examined by Sen and Nandi (1951), 10 species showed antibiotic activity; and the activity was particularly pronounced against the Gram-positive bacteria. Maruzzella (1961) conducted extensive survey of antibiotic activity among the ferns. Thirty-three of the 34 ferns examined by him were found to be fairly active and half of them were active against both Gram-positive and Gram-negative bacteria, including plant pathogens. Mickell (1959) published a review on the antibiotic activity of vascular plants, which included 26 ferns, of which 17 species were reported to be active as antibiotics. Horvath *et al.* (1967) and Creasey (1969) showed antitumoral activity in *Polypodium leucotomos* and *Cibotium schiedei*, respectively. Bhakuni *et al.* (1969) observed anticancerous activity in *Dicranopteris linearis* and *Selaginella plumosa*.

The importance of studying secondary metabolites and their active constituents for antimicrobial properties has gained importance gradually as there is a global need to tap new sources of natural drugs to combat the resistant strains of microorganisms. The frond, rhizome and rachis of ferns are covered by glands densely. These epidermal glands (Manickam *et al.*, 2005) contain substances such as phenolic compounds, glycosides, flavonoids and alkaloids. These substances are largely responsible for the antimicrobial activity and are being soluble in organic solvents easily extracted in ethanol but less soluble in water (Banerjee and Sen, 1980). Depending upon the requirements to obtain medicinally important chemicals, most of the phytochemical studies have been related to antimicrobial assessments from main plant body (sporophytic phase of life cycle; Guha *et al.*, 2003; Parihar *et al.*, 2004; Sarkar *et al.*, 2011), while gametophytes also yield antimicrobial compounds in axenic cultures (Guha *et al.*, 2004, 2005; Ganguly *et al.*, 2011).

From gametophyte

Seedless vascular plants bear two phases in their life cycle: Gametophytic and sporophytic. Gametophytic phase of the life cycle is ephemeral and gametophytic tissue is miniature in size. Francisco and Driver (1984) attempted to measure the pattern of flavonoid distribution in the gametophytic tissue of *Polypodium aureus, Thelypteris patens, T. normalis, Asplenium aethiopicum, Cyrtomium falcatum, Gymnopteris rufa* and *Pteris straminea*. Stable lines of gametophytic tissue of *P. aquilinum* resistant to Streptomycin were isolated by Breznovits and Sheffield (1990). *Adiantum capillus-veneris* was explored for antimicrobial activity of crude extracts and extracted phenols to compare the antibacterial and antifungal activity of sporophytic and gametophytic plants, whereby it was observed that gametophytic plant parts have higher antimicrobial activity. Also seasonal accumulation of phenol content was measured in different parts of sporophytic plant body. It was maximum in winter season and in the immature pinnules of all the plant parts studied separately (Guha *et al.*, 2004, 2005).

Control of pathogens: microbiological assays/ antibiotic activities

An important characteristic of plant extracts and their components is their hydrophobicity, which enable them to partition the lipids of the bacterial cell membrane and mitochondria, disturbing the cell structures and rendering them more permeable. The Gram-negative and/or Gram-positive bacteria were found to be susceptible to extracts from various parts of ferns owing to the presence of broad spectrum of antibiotic compounds present in the selected ferns by many workers (Sen and Nandi, 1951; Bhabbie *et al.*, 1972; Banerjee and Sen, 1980; Lopez *et al.*, 2001; Gracelin *et al.*, 2012; Anto *et al.*, 2015). This is considered an eco-friendly, biocontrol traditional method. The methanol extracts of fronds of five ferns, namely *Adiantum caudatum, Angiopteris evecta, Pteris confusa, Pteris argyraea* and *Lygodium microphyllum* exhibited antibacterial activity against pathogenic bacteria (Kumar and Kaushik, 1999; Anishmon and Thomas, 2005). Phytochemical analysis of all the extracts revealed that antibacterial activity is due to the presence of alkaloids, flavonoids and phenolic compounds. According to the results of Minimum Inhibitory Concentration (MIC) and Relative Percentage Inhibition (RPI) values, *Angiopteris evecta* could be used as potential plant for the management of pathogenic bacterium, *X. c.* pv. *c*, which is known to cause diseases on many vegetables and cash crops, particularly *Centella asiatica*. In a recent review, Srivastava and Paul (2016) have presented excellent treatise on rhizospheric microflora, phyllospheric microflora and endophytic microflora of these ferns and opined enormous biotechnological potential.

Not all parts of the same plant contain the same compounds or even if they do, the amount proportionately

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would be different. Antimicrobial activities of three plant parts such as rhizome, rachis and frond extracts of *Cyclosorus interruptus* (Willd) H, *Gleichenia microphylla* R.Br, and *Microsorum pteropus* (Bl.) Copel, revealed that frond and rhizome extracts of all these three species had higher antimicrobial activity than rachis (Pal, 2013). Also lot many experiments have been conducted on isolation and characterization of human pathogenic bacteria and the effect of various fractions of *Ceratopteris thalictroides, Christella dentata, Lygodium flexuosum, P. vittata* and *Salvinia molesta* on human pathogenic bacteria under *in vitro* conditions. The antibacterial activity of *C. thalictroides, C. dentata, L. flexuosum, P. vittata, S. molesta* are reported against some human pathogenic bacteria such as *Escherichia coli, Klebsiella pneumoniae, Bacillus cereus* and *Staphylococus aureus* (Mandal and Mondal, 2011; Anto *et al*., 2015). Current microbial resistance to antibiotics has become a global concern, as all known classes of natural compounds for antimicrobial therapy are becoming resistant (Boller, 1995). We will have to search for such gene reservoirs in fern genomes because fern genomes have survived the rise and fall of huge populations, natural turmoils and geological stresses over millions and millions of years. We are bound to get many unexplored gene complexes within these genomes as ferns and fern allies have survived from Paleozoic times and have adapted with many more various changes of environment than the other primitive vascular plants (Wallace *et al*., 1991).

As explicitly documented in hundreds of published research papers, ferns possess useful phytochemicals, e.g. flavonoids, steroids, alkaloids, phenols, triterpenoid compounds, varieties of amino acids and fatty acids, etc. (Sen and Nandi, 1951; Bray and Thorp, 1954; Bohm and Tryon, 1967; Adams, 1989; Patric *et al*., 1995; Dalli *et al*., 2007; Hirasawa *et al*., 2012; Morias-Braga, 2012a, b; Pielesz, 2012). There has been increasing emphasis on obtaining plant derived polyphenolic compounds in preparing modern medicines as these posses anti tumour/cancer (Creasey, 1969; Shon *et al*., 2004; Radhika *et al*., 2010) and apoptosis inducing properties. Obviously, role of plant derived polyphenols in chemoprevention of cancer is emerging as a challenging area for future medicine. Needless to mention, natural antioxidants and most of their pharmacological properties are considered to be due to their antioxidant potential, which influence physiological functions (Ames *et al*., 1995a, b; Singh *et al*., 2008a, b; Adamu *et al*., 2012; Zheng *et al*., 2016).

Antifungal and antiviral activities

Apart from antibacterial effects of *Adiantum capillus veneris*, the antiviral, antifungal and antimicrobial activities of *Adiantum latifolium* have also been reported. Alcoholic and aqueous extracts of different sporophytic plant parts of three species of *Adiantum* were tested against the growth of human pathogenic bacteria *Salmonella typhi*, the causal organism of typhoid fever, by Parihar *et al*. (2004). Maximum response has been noted by the extracts of rhizome of *A. lunulatum*, which is even higher than the performance of 10% dilution of Tetracyline. Parihar *et al*. (2004) found antifungal activities of *Cheilanthes albomarginata* and *Marsilea minuta* against the phytopathogen *Aspergillus flavus*. Guha *et al*. (2004, 2005) studied the antibacterial and antifungal activities of crude extracts and extracted phenols from gametophyes and sporophytic plant parts of *Adianutm capillus-veneris* and *Adiantum lunulatum*. They found that the gametophytes are more potent or bioactive in combating fungal or bacterial strains than the sporophytes. Ganguly *et al*. (2011) noted that the crude extract of an epiphyte *Arthromeris himalayensis* (a member of Polypodiaceae) is more responsive than the extracted phenols to control Gram (+ve) bacteria than the Gram (−ve) bacteria. Probably, the Gram (+ve) bacteria are more susceptible than Gram (−ve) bacteria due to their structural pattern of cell wall membrane. Sarkar *et al*. (2011) noted antifungal effects of crude extracts and extracted phenols from different sporophytic plant parts of *Ampelopteris prolifera, C. dentata* and *Pronephrium nudatum* against *Aspergillus niger*. *Christella dentata* is found to have the most effective antifungal property among these three thelypteroid ferns. Sterile leaf parts of all these members contained higher amounts of phenolic substances. There are a large number of studies on antifungal, antiviral and antibacterial activities of fern extracts (Lopez *et al*., 2001; Ma *et al*., 2003; Lee *et al*., 2008; Tiwary and Ganguly, 2016).

Pharmaceutical products – recent progress

A brief account about the production of marketable medicinal products obtainable from Pteridophytes is outlined below

Huperzine (Fig. 2): Since Tang dynasty, China extract of plant *H. serrata* was used and prescribed as Quing Ceng ta in Chinese Traditional medicine. The drug was prescribed for a number of ailments such as contusion, strains, swellings, schizophrenia, myasthemia gravis and now organophosphate poisoning (Ma *et al*., 2003, 2007). Later on Hup A was isolated from Quing Ceng ta (*H. serrata*) by Chinese scientist Liu *et al*. (1998), and established this for its anticholinesterase activity to treat Alzheimer's disease. Since 1996, it was marketed as Shuangyiping tablet (Zhu *et al*., 1999, 2000).

Calaguline: Calaguline isolated from leaves of *Polypodium* has medicinal applications arthritis, psoriasis, atopic dermatitis. Calaguline can block NF-$\kappa\beta$ activation so

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it has the potential of blocking proliferation, inflammation, promotion and metastasis. Structural elucidation has revealed that calaguline contains a new glycoside (Kaempferol 3-O-β-xylopyranosyl (1–2)-β-D arabinopyranoside), two known flavonoid glycosides, rutin and kaempferol 3-O-α-arabinopyranoside (Gombau *et al.*, 2006; Ho *et al.*, 2011). Hydrophilic extract of *P. leucomotos* prevented UV-induced cell damage and its morphological changes in human fibroblasts, namely F-actin-based cytoskeletal structure, coalescence of the tubulin cytoskeleton and mislocalization of adhesion molecule such as cadherins and integrins. So it is used as sun-burning and skin pathologies and with uv-mediated damage (Gonzalez and Pathak, 1996).

Many other useful compounds

From Male Fern (*Dryopteris*): Male fern is used to treat nosebleeds, heavy menstrual bleeding, wounds and tumours. It is also used to expel worms, typically tapeworms, from the intestines. Some veterinarians use male fern to treat worms in animals. The chief constituent of male fern is a yellow amorphous substance of an acid nature, termed filmarone, to which the properties of male fern as a vermifuge are attributed. In solution it slowly decomposes into filicic acid and aspidinol, both of which also occur preformed in the drug (Mittal and Bir, 2006). Recently, Wani *et al.* (2016) have added a list of compounds of medicinal importance extracted from many pteridophytes. In addition to medicinal products, certain other important chemical compounds are being manufactured from the plant parts, e.g. water soluble polymer from the fronds of the black tree fern, *Cyathea medullaris* (Matia-Merino *et al.*, 2012).

Conservation strategies to exploit genomic potentials

Since, a large number of pteridophytes, bryophytes and lichens are the natural constituents of forests, therefore it is desirable that necessary efforts are made to conserve enormous wealth of these plants in forests to sustain the ecosystems *per se* (Goswami, 1981, 2009b). We must cultivate some of the most widely accepted fern genera for genomic exploitation for medicinal uses. Earlier suggestion (Goswami, 2009b) of establishing Fernaria at different sites holds a strong biological feasibility. Selected genera and species can be cultured in large shaded greenhouses (not necessarily glass house) so as to assess and conduct experiments in genomic trials for the production and microbial assays of antibiotic substances. As such, genomic research on lycophytes and ferns has lagged behind other groups of plants. While nuclear genome sequences are now available for over 100 species of seed plants, there is only one sequenced genome of a lycophyte available, i.e. heterosporous *Selaginella moellendorffii*, and none from any fern, or from any homosporous pteridophyte. But as we pass on, serious attempts in this direction are emerging and genomic data are pouring in (Wolf *et al.*, 2015; Sessa and Der, 2016). We need genome sequences of lycophytes and ferns so that we could ascertain the genes and relevant DNA sequences to understand their fundamental and highly economic, medically useful traits which are helpful. Little is known about the genes involved in arsenic sequestration and transport, but identification of such genes could aid the development of remediation techniques for treating arsenic-contaminated soils and groundwater.

For example there are many genera, which possess unique qualities (Table 2), and could be explored for :

(i). Bioremediation (Bharti and Banerjee, 2012; Mandal *et al.*, 2012a, b);

(ii). Hyperaccumulation of heavy metals and toxins. Certain potential resources are: *P. vittata* for Arsenic, Copper, Cadmium and Zinc; *Osmundastrum cinnamomeum* and *Athyrium yokoscense* for Lead, *Salvinia* sp. for Nickel.

(iii). *Desiccation tolerance*: No study has yet been undertaken to investigate the regulatory and metabolic networks that allow ferns to be desiccation tolerant (DT), but such studies have enormous DT (reviewed by Sessa and Der, 2016). Plants can lose all metabolically active water from their vegetative tissues and recover from that state. True DT is very rare in vascular plants, especially crops but gametophytes of many fern species have been found to be tolerant potential for crop plant improvement, particularly as global climate patterns change and periods of drought and inconsistent precipitation become more common.

(iv). *Stress tolerance:* Phenols play an important role in the metabolism of plants especially during stress. Vyas *et al.* (1989) noted that percentage of increase of phenols during stress is much higher in drought resistant pteridophytes than shade loving ferns. But under normal conditions, the soft, green, laminated leaves, e.g. *Tectaria, Athyrium* have more amounts of phenols than the coriaceous, e.g. *Cheilanthes* and reduced leaf forms, e.g. *Equisetum*.

Prospects of genomic studies

Sessa and Der (2016) in their exhaustive review on this and related topics have highlighted ebulliently the additional and essential uses of genomic studies and urged for extensive studies to be undertaken on lycophytes and ferns. Interestingly, two very unlikely results have been revealed that ferns are at the lower end of protein content estimates

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for land plants because of lower gene density. In other words, there appears to be no correlation between protein content and the large genome size, which in turn has a positive relationship among land plants. Second inference asserts on a different mechanism of genome downsizing than other lineages of land plants (Leitch and Bennett, 2004; Barker and Wolf, 2010; Leitch and Leitch, 2012; Goswami, 2013). Similarly, gene number estimates for seed plants are much less variable: generally, between 20,000 and 40,000 per diploid genome. A single estimate for a fern, *Ceratopteris richardii*, is near the range: 42,300 genes. Wolf *et al*. (2015) and Sessa and Der (2016) have reviewed on nuclear, chloroplast and mitochondrial genomes of a large number of lycophytes and ferns, which can be further studied for detailed genomic information. Intriguingly, ferns have higher proportions of the genome comprised DNA transposons and LINE retrotransposons than do seed plants. These authors have also reviewed in detail about DNA methylation studies and have indicated differential DNA methylation during development. Obviously, genomic studies on ferns have enormous prospects for understanding almost all kinds of molecular genetic studies. Many a workers have started barcoding the medicinally important species so as to exactly identify the relevant species for genomic potential (Hirano *et al*., 2012; Gu *et al*., 2013).

From evolutionary and comparative genomics point of view, the pteridophytes offer exceptionally superior evolutionary tales in the plant kingdom. Both homosporous and heterosporous plants are found in this evolutionary lineage. Giant heterosporous lycopods of Carboniferous must have been polyploids that had dominated the homosporous pteridophytes during Carboniferous (300 mya) until they had to face biological extinction (Goswami, 2013) on account of drastic climatic turmoil during the Mesozoic. After that as estimated by palaeobotanists, giant occupancy on marshy land gradually culminated to greatest reduction series of evolution finally to herbaceous lycopods such as the genus *Isoetes* (quillworts). Also, the homosporous ferns emerged as dominating vegetation (polyploidization might have been helpful) at the same time when angiosperms arose as contemporary flora (Schneider *et al*., 2004). The reduction series imposed on heterosporous plants probably might have also involved natural hybridizations/allopolyploidy (Goswami, 2013), and other mechanisms resulting in downsizing of genomes. Or, there may be a few conjoint molecular mechanisms, e.g. differential/variable DNA methylation events (Goswami *et al*., 2000; Sessa and Der, 2016), which have resulted in genomic reshuffles among evolving heterosporous lycophytes and a few fern groups. The two species of this homosporous aquatic fern genus *Ceratopteris, C. thalictroides* and *C. richardii* (family Parkeriaceae) have not only been extensively studied for all morphological and developmental stages of a typical fern life cycle but also have been found to be highly suitable; hence universally recommended fern species for molecular and genomic studies with particular reference to stable inheritance of trans-genes. The protocols of transformation of gametophyte (prothallus) cells with demonstration of trans-genes in sporophytes and in subsequent generations have established *Ceratopteris* to be a classic genetic model for studying gene functions in ferns (Plackett *et al*., 2015). Nakazato *et al*. (2006, 2008) produced a high-resolution genetic linkage map for *C. richardii* based on 488 doubled haploid lines that were genotyped for 368 RFLP, 358 AFLP and 3 isozyme markers. This mapping experiment recovered 41 linkage groups and revealed that the majority of loci (over 76%) were duplicated, with most duplicates in different linkage groups. Efforts to promote developmental and genomic research on model systems in the horsetail fern clade (for example, *Ceratopteris*) will probably lead to an improved understanding of fundamental aspects of vascular plant development and evolution. They have reported on the basis of exhaustive DNA studies on representatives from all the main lineages of land plants that there are three monophyletic groups of extant vascular plants: (1) lycophytes, (2) seed plants and (3) a clade including equisetophytes (horsetails), psilotophytes (whisk ferns) and all eusporangiate and leptosporangiate ferns. Their studies after maximum-likelihood analysis show that horsetails and ferns together are the closest relatives to seed plants.

Comparative genomics

Most of the 470 million year history of plants on land belongs to bryophytes, pteridophytes and gymnosperms, which eventually yielded to the ecological dominance by angiosperms 90 Myr ago (Pryer *et al*., 2001, 2004; Schneider *et al*., 2004). This is extremely exciting that lycophytes and ferns, grouped together for basic morphological understanding depart from each other in phylogenetic shares of genes. In addition to common evolutionary studies genomic studies with a theme of comparative genomics have enormous information not yet discovered or acknowledged. For example, certain gene sequences inherently found in a few bryophytes and pteridophytes exactly resemble some of the DNA sequences on Y chromosome of man. This when first observed (Nagl, 1991; Goswami and Chandorkar, 1994) was not believed but now we have several investigations confirming (Okada *et al*., 2001) the presence of though, a few only (?) same DNA sequences in plants, which are exactly similar in the human genome. Such findings thereby strongly justify earlier hypothesis (Bajpai and Goswami, 2002; Goswami, 2009a, 2012) that DNA sequences ever since originated and

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evolved, had had ceaselessly multiplied and must have been distributed randomly in the evolving cells during the Pre-Cambrian almost before the evolutionary bipartition of cells into plant and animal cells. We can always find many common DNA sequences among many unrelated organisms, be these even plants. Pteridophytes in particular offer a great potential for probing inherent DNA sequences on the basis of comparative genomics because geologically too old genome had witnessed enormous complications of evolutionary genetics and environmental stresses over millions and millions of years.

We now know that comparison of evolutionary adaptations and natural innovations illuminates the genetic basis for the development of organisms. Gene network (DNA stretches) that retains similar wiring diagrams (some or many similar DNA sequences) among related, distantly related or even totally diverse organisms points the ways in which regulatory regions of the genome may have evolved. Comparative genomics can help us in deciphering evolvability of gene network and conservation modes during vast geological journey in evolution. It is now possible to combine genomics, epigenomics, developmental genetics of model organisms and the comparative method. Whole genome sequencing (WGS) has the potential to identify all kinds of genetic variations. Therefore, WGS is strongly needed for all organisms (Pang *et al*., 2014) to detect mutations and genomic changes during the evolution and development in animals and plants (evo-devo; Editorial, *Nature Genetics*, 2016 – doi:10.1038/ng.3566/http://www.nature.com/natecolevol/)

Save freshwater ecosystems and harvest wealth from aquatic fern-weeds

The freshwater ecosystem is the most precious flowing wealth on our planet. We need to understand very seriously about freshwater conservation and a few fern genera can really offer manifold help.

(I) Medicinal plants particularly ferns can be planted around catchment area of a lake

Some medicinal angiosperms, e.g. *Bacopa, Centella* spp. that grow along lakes are hyper accumulators of lead, cadmium, and mercury. Among the pteridophytes, *Ceratopteris, Marsilea, Pteris* spp., etc. are appropriate alternatives as heavy metal accumulators that can be very well cultivated around the catchment area or in the marginal fringes of the water body (Goswami, 2012).

(II) (Aquatic fern weeds can be positively exploited

All aquatic ferns particularly *Azolla* and *Salvinia* (Fig. 1 (e) and (f)) are rich in organic compounds and are also hyper accumulators of heavy metals (further details at WorldWideScience.org).

(a) Aquatic ferns: *Azolla* and *Salvinia*

Phytochemical studies on *Azolla pinnata* R. Br., *M. minuta* L. and *S. molesta* Mitch by Mithraja *et al*. (2011); Li and Pryer (2014) have indicated the presence of phenolics, tannins, carbohydrates, steroids, saponins, carboxylic acid, flavonoids and a few more bioactive compounds in variable quantities in extracts from leaves. Since phenolics have antioxidative, anticarcinogenic, antimicrobial, antiallergic, antiinflammatory properties the authors have rightly recommended to take best pharmaceutical uses of these aquatic ferns by proper approaches (Pandey and Bhargava, 1980; Pandey, 1994; Shon *et al*., 2004; Schor-Fumbarov, 2005; Shinozaki *et al*., 2008; Lee and Shin 2011; Mithraja *et al*., 2011; Mukhopadhyaya, 2012; Abraham *et al*., 2015). Two of these aquatic ferns viz. *Azolla,* and *Salvinia* are used as biofertilizers and are also strong bioaccumulators of heavy compounds under stress.

Ferns of the genus *Salvinia* comprise 10 species; majority of which grow in freshwater bodies of tropical and subtropical regions in many countries and is widespread as aquatic weed in several parts of India. *Salvinia* varieties have small hairs on their leaves, making them water resistant. Air cavities in the leaves help the tiny plant to stay afloat (Fig. 1(f)). Since this plant is a potential removal of heavy metals such as lead (Pb), cadmium (Cd), nickel (Ni), copper (Cu), chromium (Cr) and mercury (Hg) from waste water, this has been used as a decontaminating agent. Its greater use has been recently discovered that the weed menace, which covers a large surface area of freshwater can be converted to beneficial uses.

The phytochemical investigation on *S. natans* shows that it consists of 96% of amino compounds. Recently, isolation of an unusual novel anti-oxidant viz. dibenzoyl glycoside has been found to have anti-oxidative properties (Patric *et al*., 1995; Lopez *et al*., 2001; Lee *et al*., 2008; Wong *et al*., 2009; Shin and Lee, 2010; Wolf *et al*., 2015; Sessa and Der, 2016; Srivastava and Paul, 2016). Li *et al*. (2012, 2014) had investigated the presence and distribution of 22 antibiotics, including eight quinolones, nine sulfonamides and five macrolides, in the water, sediments, and biota samples from Baiyangdian Lake, China mainly covered with *Salvinia*. A total of 132 samples were collected in 2008 and 2010, and laboratory analyses revealed that antibiotics were widely distributed in the lake. Sulfonamides were the dominant antibiotics in the water (0.86–1563 ng/l), while quinolones were prominent in sediments (65.5–1166 µg/kg) and aquatic plants (8.37–6532 µg/kg). Quinolones (17.8–167 µg/kg) and macrolides [from below detection limit (BDL) to 182 µg/kg] were often found in aquatic animals and birds. *Salvinia natans*

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exhibited the highest bioaccumulation capability for quinolones among three species of aquatic plants. Geographical differences of antibiotic concentrations were greatly due to anthropogenic activities. Sewage discharged from Baoding City was likely the main source of antibiotics in the lake. Risk assessment of antibiotics on aquatic organisms suggested that algae and aquatic plants might be at risk in surface water, while animals were likely not at risk. Antibiotics from *Salvinia* are indeed very useful in treatment of industrial waste disposal and sewage irrigation would need further investigations as it would open a very prospective usage of this aquatic fern weed.

Ferns as indoor–outdoor air purifiers

Formaldehyde is the most common indoor volatile organic compound (VOC) with substantially high concentrations. Formaldehyde has several side effects to human beings such as nausea, sore throat, watery eyes, eye burning sensations, headaches, fatigue and so on. Therefore, the formaldehyde-absorbing ability is one of the most effective functions of ornamental plants. Also according to KRDA (Korea Rural Development Administration; Lee and Shin, 2011), several ferns and fern allies show high efficiency of formaldehyde removal indoors. They tested the formaldehyde removal effects of 84 species of plants. *Osmunda japonica* was observed to be the best formaldehyde removal in chamber. In addition, *Selaginella tamariscina, Davallia mariesii, Polypodium formosanum* and *Pteris multifida* have been ranked as highly efficient formaldehyde-removing plants. Other ferns, such as *Pteris dispar, Cyrtomium caryotideum* var. *koreanum* and *Sceptrium ternatum*, showed better formaldehyde removal than areca palm tree (the best air purifying plant ranked by NASA). So, ferns could purify the air just by keeping them indoors or outdoors (Morajkar *et al.*, 2015). Also we expect that many ferns in addition to the above-mentioned genera may have efficient formaldehyde removal activities. They also could remove many other VOCs. Obviously, more studies about the air purifying ability of ferns are becoming necessary. Since ferns grow well in shady places, they can be adapted to indoor, even restrooms in use. Even otherwise lycophytes (Ma *et al.*, 2003, 2007; Lee *et al.*, 2008) as well as ferns are being used as high quality ornamental plants, edible and folklore plants (May, 1978; Nwosu, 2002; Mannan *et al.*, 2008) in different parts of the world. Obviously, these lower vascular plants owe great pharmaceutical relevance.

Concluding remarks

We intend to infer and draw specific attention of all organic and biochemists, evolutionary and molecular geneticists and pharmaceutical personnel to concentrate on pteridophytes to utilize enormous genetic potentials of these plants for not only producing useful drugs but also to conserve forest ecosystems and maintain balance among ecosystems. As so well known by now, these seedless vascular plants or pteridophytes (Lycophytes and Ferns) are still being used by tribal people/isolated populations in different regions of the world for different ailments or disorders. Many well established compounds of medicinal uses are being extracted from these plants (Tables 1 and 2). The healing properties of these plants are known since antiquity as exemplified by many small herbs 'Sanjeevani' or *S. bryopteris*, anticancerous uses of *Blechnum orientale*. Lately, *H. serrata* plant is being used to ameliorate neuronal disorders such as Alzheimer. Also, variation over seasons, gametophytic and sporophytic plant parts are observed with respect to biological activity and potential. More efforts are needed in this direction to search for the onset of genes in haploid and diploid phases of the same plant. Pharmaceutical development of the Huperzin A and -B has enhanced greater chances for future development of drugs. It is underpinned that being the component of basal chain in evolutionary network, and also in their metabolic organization, the genome of pteridophytes could offer unique opportunity in elucidating gene–metabolite relationship and thus necessitating their conservation efforts. Ferns are eco-friendly by virtue of being masters of versatile adaptive ranges. These plants occur at high altitude, high latitude, Arctic-alpine situations to the heart of tropical rainforests and from sub-desert scrub of continental interiors to rocks of sea-coast and, mangrove swamps. In forests these plants enrich biodiversity; are integral part of carpet flora, grow on rock-crevices as well as epiphytes. Lower fauna of the forest is offered homely survival. Therefore we need them for our survival too.

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