Journal of Biomedical and Pharmaceutical Research
Available Online at www.jbpr.in
CODEN: - JBPRAU (Source: - American Chemical Society)
NLM (National Library of Medicine): ID: (101671502)
Index Copernicus Value 2022: 83.058
Volume 12, Issue 5, September-October: 2023, 36-46

ISSN (Online): 2279-0594
ISSN (Print): 2589-8752

Review Article

Anticancer Potential of Ferns from Uttarakhand Region

Akhil Gupta[1*], Rakesh Sharma[1], Neeraj Kumar[2], Mayank Bansal[1], Rupesh Dudhe[3], Shiv Kumar Gupta[4]

[1] Jaipur College of Pharmacy Tonk Road, Sitapur, Jaipur, Rajasthan

[2] Galgotias College of Pharmacy Greater Noida

[3]Aadarsh Institute of Pharmacy, Azamshah layout, GreatNag Road Nagpur, Maharastra

[4] Devsthali Vidyapeeth College of Pharmacy, Lalpur, Rurapur, U.S. Nagar, Uttrakhand

Article Info: Received: 13-08-2023 / Revised: 18-09-2023 / Accepted: 11-10-2023
Corresponding author: Akhil Gupta
DOI :https://doi.org/10.32553/jbpr.v12i5.1026
Conflict of interest statement: No conflict of interest

Abstract:
The current study deals with the anticancer potential of ferns in Uttarakhand region. The ferns are widely used by the local people of the Uttarakhand Himalaya. The present study documents anticancer and antioxidant activity of some fern plants, which are prevalent in study area along with botanical name, family, chemical constituents and their activity for medicinal use. Among all the pteridophytes examined taxa from the Pteridaceae, Polypodiaceae, and Adiantaceae exhibited significant medicinal activity. Based on our review, many pteridophytes have properties that could be used in alternative medicine for treatment of cancer.
Keywords: Anti-cancer, Anti-oxidants, Ferns, Uttarakhand.

Introduction

Cancer is a complaint that's characterized by proliferation of the body cells, due to failures in cellular modulation and inhibition of cell cycle progression, and thereby inspiring nasty excrescence cells conformation with the possibility of getting metastatic [1]. Cancer is presently the prominent root of death encyclopedically [2]; and the number of deaths from cancer is on the rise daily. The number of recorded deaths of persons as a result of cancer rise by 17 between 2005 and 2015, and thus, there's the critical need for further ferocious exploration into the development of new anticancer medicines in addition to the living bones. Plant excerpts are extensively used in Uttarakhand as important sources of chemotherapeutic agents in malignancy of the use of synthetic medicine by vast maturity of the crowd. Medicinal shops have been in nonstop use over the times for the operation of cancer [3].

Uttarakhand state covering an area of km^2 is rich in diversity of medicinal shops. Since, medicinal shops represent an important health element to the state, it's essential to furnish the important shops being used as anti-cancerous. Still there are only many shops which are so far being delved. Hence an attempt has been made to review important medicinal shops used for forestallment and treatment of cancer in the state. Pteridophytes have been used in the traditional systems of drug similar as Ayurveda and Unani for the treatment of colorful forms of ails. Still, studies toward the scientific evaluation of the cytotoxic exertion of this species against mortal cancer cells weren't available Caius JF. Pteridophytes comprise a group of seedless but spore producing shops, formed by two lineages, lycophytesfronds with no splint gap in the stem stele (Lycophylls) and Monilophytes or ferns-fronds with splint gap in the stem stele (Euphylls) [4,5].

They constitute an important element of earth's foliage for millions of times [4]. Presently there are about 300 rubrics of pteridophytes containing roughly 9600 ferns and about 1400 lycophytes worldwide with loftiest diversity in the tropics [6]. The current revised treatment of fern and fern abettors from India revealed 1150 species [7]. Pteridophytes are one of the oldest land factory groups on earth and constitute a vast group of vascular cryptograms. The position of the Pteridophytes as intermediate between the lower cryptograms and advanced vascular shops has made the group fascinating. Pteridophytes have a long geological history on our earth. They were known as far back as 380 million times agone. In India, ferns are mainly distributed in the Himalayan and littoral regions [8]. documented 356 species of ferns from Western Himalaya. Pteridophytes prefer shady, wettish territories with moderate temperature but also do throughout a veritably different range of territories from high altitude. Like other groups of shops, Pteridophytes are also show medicinal mileage and numerous of them are being used medicinally from ancient time. The ethnical communities, ethnic groups and myth throughout the world are exercising factory corridor like rhizome, stem, fronds, pinnae and spores in colorful ways for the treatment of colorful pabulum since ancient time. The figures of donation about the taxonomy, ecology and distribution of Pteridophytes have been published from time to time but enough attention haven't been paid towards their medicinal useful aspects [9]. In the present attempt have been made to explore ethno medicinally important Pteridophytes and duly proved their useful aspect.

The pteridophytes (Ferns and fern abettors) represented by over 1200 taxa belonging to 204 rubrics (ca10,) species of the world, grow in varied climatic zones of different phytogeographical regions of India. Subhash Chandra in his ferns of India has enumerated 1100 species belonging to 144 rubrics under 34 families from the Indian regions, Published an account of pteridophytes from Upper Gangetic plains, which include corridor of Uttarakhand, plains of Uttar Pradesh, Bihar and part of West Bengal in his illustrated fern foliage of Western Himalaya included 360 species of ferns. Pande and Pande (2002) reported ca 350 species of ferns and fern abettors from Kumaun Himalaya. Dixit and Kumar (2002) listed 487 species and 32 infra specific taxa belonging to 108 rubrics under 50 families. Eighteen species are aboriginal to Uttarakhand, of these, 10 species and 2 kinds confined these distributions only to Uttarakhand state and remaining six taxa also show their circumstance in other corridor of India beside Uttarakhand. About 57 species are fairly of rare circumstance being aboriginal, rare and risked due to other anthropogenic factors.

Antioxidant exertion According to Kshirsagar and Upadhyay (2009), methanol excerpts of Diplazium polypodioides and ethyl acetate or water excerpts of Blechnum orientale show strong antioxidant capacity [11]. Presence of phenolics in excerpts of Dicksonia sellowiana may contribute directly to its antioxidant parcels [12, 13]. Ethanolic and ethyl acetate excerpts showed good antioxidant action grounded on the DPPH radical scavenging assay in Microgramma vacciniifolia [14]. Methanol splint excerpts of P. multifida showed stronger antioxidant exertion than ethanol excerpts [15]. In a DPPH assay of S. confidante-ustris, antioxidant exertion was advanced in mature rich (2.29 mg TE/ mg GAE; TE Trolox fellow; GAE gallic acid fellow) and sterile (2.07 mg TE/ mg GAE) fronds than in youthful rich (1.99 mg TE/ mg GAE) and sterile (1.80 mg TE/ mg GAE) fronds. Table 2 summarizes the antioxidant exertion of pteridophytes.

Anticancer Activity

The rubric Pteris is a rich source of bioactive entkaurane diterpenoids. Numerous composites in this class exhibition veritably good anticancer exertion; [16], and it has been reported that the Michael- accepting capability of their, β-unsaturated ketone halves is essential for this cytotoxicity [17]. Pteris semipinn at al. is used as a medicinal factory for the treatment of poisonous snake mouthfuls in Chinese folk drug. In recent times, pharmacological examinations on this species have primarily concentrated on the ent-kaurane diterpenoid ent-11α-hydroxy-15-oxo-kaur-16-en-19-oic-acid, which was shown to parade significant cytotoxicity and anticancer exertion [18]. Ent 11α-Hydroxy-15-oxo-kaur-16-en-19-oic-acid has inhibitory goods in colorful cancer cell lines it induces apoptosis in mortal colon cancer HT-29 cells by adding the cornucopia of p38 and iNOS. Still, this effect can be eased by overexpression of Bcl-2 or Bcl-xL, which upregulates NF-κB exertion and leads to apoptotic offset [19]. Interestingly, ent-11α-hydroxy-15-oxo-kaur-16-en-19-oic-acid displayed stronger cytotoxicity in the gastric cancer cell line MKN-45, which expresses the wild- type p53 protein, than in the affiliated gastric cancer line MKN-28, which expresses a p53 variant with a missense mutation. Farther examinations revealed that ent-11α-hydroxy-15-oxo-kaur-16-en-19-oic-acid induces apoptosis in MNK-45 (in the presence of wild- type p53) by causing the translocation of Bax into mitochondria, leading to a reduction DNA fragmentation [20]. In addition, the release of cytochrome-C and apoptosis converting factor from mitochondria into the cytosol was also observed during the apoptosis of anaplastic thyroid melanoma cells treated with ent-11α-hydroxy-15-oxo-kaur-16-en-19-oic-acid [21]. In vitro trials showed ent-11α-hydroxy-15-oxo-kaur-16-en-19-oic-acid inhibits the proliferation of the mortal lung cancer cell lines A549, NCI-H23 and CRL-2066, arrested the cell cycle in the G2 phase, and convinced apoptosis through a mitochondria-intermediated pathway. In keeping with former results, mechanistic examinations indicated that ent-11α-hydroxy-15-oxo-kaur-16-en-19-oic-acid induces apoptosis by driving the overexpression and translocation of Bax into the mitochondria, leading to the release of cytochrome c into cytosol, activation of caspase-3, and translocation of AIF from mitochondria into the nexus [22]. In addition, ent-11α-hydroxy-15-oxokaur-16-en-19-oic-acid significantly inhibited the development of NNK-convinced mouse lung cancer in vivo by converting apoptosis and plying anti-proliferation goods with minimum side goods [23]. In vivo and in vitro examinations verified that ent-11α-hydroxy-15-oxo-kaur-16-en-19-oic-acid effectively inhibits hepatocellular melanoma (HCC), significantly reducing the number of excrescence foci and the size of excrescences in a diethyl nitrosamine-convinced mouse HCC model with minimum side goods. It also convinced the death of HCC cells by stabilizing IkBα to inhibit NF-κB [24]. In tests against CNE-2Z nasopharyngeal melanoma (NPC) cells, ent-11α-hydroxy-15-oxo-kaur-16-en-19-oic-acid exhibits significant inhibitory goods, causing cell cycle arrest in G2 phase and apoptosis by adding the Bax/ Bcl-2 rate and the position of cytochrome c in the cytosol while reducing situations of NF-κB-p65 and adding those of IκB [25]. Eventually, ent-11α-hydroxy-15-oxo-kaur-16-en-19-oic-acid sensitised A549 cells to cisplatin despite reducing cisplatin- convinced ROS product [26]. In addition to ent-11α-hydroxy-15-oxo-kaur-16-en-19-oic-acid,-dihydroxy and-dihydroxy from P. semipinnata can inhibit lung adenocarcinoma cells by acting as impediments of DNA topoisomerases (TOPO) and tyrosine protein kinase (TPK) [27]. 7, 9-Dihydroxy inhibited TOPO II at an attention of0.01 mg/ L, while-dihydroxy was a relatively potent asset of membrane TPK and also reduced the expression of the oncogene c-myc [28].

Bracken (Pteridiumspp.) illudane glycosidess are labile biologically active terpenoids that suffer corruption under mildly acidic or alkaline conditions, under heating, or in the presence of degradative enzymes [29]. The new bi-homo flavanonol pteridium III, which has an unknown shell, was insulated from P. aquilinum and exhibits in vitro antitumor exertion against NCI-H46 lung cancer cells, A375 carcinoma cells, and U-7MG glioma cells with IC50 values of 22.9, 106.7, and 1540.5 µmol/ L, independently [30]. The pterosins are a large group of naturally being sesquiterpenes with indanone configurations. They are extensively distributed among the Pteridophyte and parade both cytotoxicity and smooth muscle relaxant exertion. Pterosin Z and acetyl-Δ2-dehydropterosin B were plant to be particularly cytotoxic [31]. Pterosin Z was latterly insulated from Microlepia speluncae (L.) Moore, M. trapeziformis (Roxb. partner Griff.) Kuhn and M. substrigosa Tagawa [32]. In addition, bi-muti pterosins A and B, insulated from Pteris multifida, displayed cytotoxicity against the HL60 mortal leukemia cell line [33]. The pterosin sesquiterpenes 2R, 3R-13-hydroxypterosin L 3-O – D-glucopyranoside, 2R, 3S-acetylpterosin C, and 2S, 3S-acetylpterosin C also showed cytotoxicity against HL60 cells with IC50 values of 14.6, 48.3 and 35.7 mM, independently [34]. The newC14 pterosin-sesquiterpenoids multifidosides A and B showed cytotoxicity against the HepG2 excrescence cell line, with IC50 values below 10 µM, and also displayed inhibitory goods on K562 cells with IC50 values of 10.63 and 9.57 µM, independently. The new diterpene 5, 11, 12-trihydroxy-15-oxo-ent-kuar-16-en-19-oic acid and the sesquiterpene 1, 3-dihydroxylnorpterosin C from Pteris dispar showed potent cytotoxicity against KB cells in vitro, with IC50 values of 59.8 and 36.5 spook/ L by the MTT system [35]. Pterosin B, one of the main pterosins plant in the rubric Pteris, exhibits potent cytotoxic exertion against HL60 (mortal leukemia) cells. While searching for the carcinogenic element of bracken, covered the development of cytotoxicity related morphological changes in HeLa cells upon incubation with bracken factors. These studies failed to descry the potent carcinogen ptaquiloside, but did lead to the insulation of several indanone- type sesquiterpenoids pterosins and their glycosides, the pterosides. The in vitro antitumor exertion of P. calomelanos and its insulated dihydrochalcones (DHCs) was estimated in India by Sukumaran and Kuttan using the trypan blue rejection assay with Dalton’s carcinoma ascites excrescence cells (DLA cells) and Ehrlich ascites excrescence cells (EA cells). The excerpt attention leading to 50 cytotoxicity in these cell lines were 16 and 18 µg/ mL, independently. The insulated DHCs displayed lesser cytotoxicity against these cell lines, with IC50 values of 6.1 and11.5 µg/ mL, independently. They also wielded cytotoxic goods in mortal myelogenous leukemia K562 cells and mortal nasopharyngeal KB cells, with IC50 values of1.1 and 8 µg/ mL, independently. A liposome medication of the insulated DHCs was also tested in vivo in womanish Swiss albino mice to estimate its effect on their survival after injection with Ehrlich ascites excrescence cells. The treatment increased the creatures’ lifetime by 52 and 57 when applied at boluses of 5 and 25 mg/ kg, independently. Because excrescences are characterized by rapid-fire cell division, the capacity of DHC to inhibit DNA conflation was delved by covering the objectification of labelled thymidine in excrescence cells, yielding an estimated IC50 of 8 µg/ mL. These results indicate that P. calomelanos has antitumor exertion and is cytotoxic because of its DHC content. In addition to the promising results bandied over, an ethanol excerpt of Adiantum venustum Don. Was shown to increase the mean survival time in melanoma- bearing mice relative to a positive control group treated with the established medicine vincristine [36].

Table 1: Antioxidant and anticancer properties of pteridophytes

Sr. No.	Fern name	Family	Chemical constituents	Medicinal activity	Refrence
1	Carralluma adscendens	Apocynaceae	Pregnane glycosides Flavones glycosides saponins	Antioxidant	J.B.naik Et.al,2010
2	Diplazium esculentum	Athyriaceae	n-hexadecanoic acid antioxidant nematiside pesticide	Anticancer	Z. Zuraini1,et.al.2010
3	Pterris vittata	Pteridaceae	Pyrogallol, Coumaric Ellagic acid, Ferulic acid	Cytotoxic effects, Antioxidant activity	Maneesha Singh,et al.2016
4	Pteris biaurita	Pteridaceae	Steroids Alkaloids Flavonoids Saponins Tannins	Antioxidant	A.k dalli, et.al,2006
5	Salvinia minima	Salviniaceae	Ellagic acids,catechol,catechin,flavonoids	Anti-cancerous Anti-inflammatory	S.S Panda, et.al.2013
6	Polypodium vulgare L.	Polypodiaceae	Polyphenols (particularly flavonoids) terpenoids, steroids, and alkaloids	Anticancer, antiaging	Adrià Farràs,et al**.**
7	Asplenium adiantum-nigrum L.	Adiantaceae	polyphenols(particularly flavonoids), terpenoids, steroids, and alkaloids	Anticancer, antiaging	Adrià Farràs,et al.
8	Asplenium trichomanes L	Adiantaceae	polyphenols(particularly flavonoids), terpenoids, steroids, and alkaloids	Anticancer, antiaging	Adrià Farràs,et al**.**
9	Ceterach officinarum	Aspiaceae	polyphenols(particularly flavonoids), terpenoids, steroids, and alkaloids	Anticancer, antiaging	Adrià Farràs,et al**.**
10	Abacopteris penangiana	Thelypteridaceae	Glycosides flavonoids	Antioxident	Zhongxiang Zhao,et al
11	Adiantum capillus veneris	Pteridophyta	Proteins, lipids, phenols, flavonoids, alkaloids, saponins, and tannins.	Anti-oxidant, anti-bacteria, anti fungall	Satabdi Rautraay, et al
12	*Pteris quadriureta* L	Pteridophyta	Proteins, lipids, phenols, flavonoids, alkaloids, saponins and tannins.	Anti-oxidant	Satabdi Rautray, et al
13	Blechinum Orientale .L	Blechnaceae	Proteins, lipids, phenols, flavonoids, alkaloids, saponins, and tannins.	Antioxidant	Deepa Jayarama Naik, et al
14	Cyathea contaminans	Cyatheaceae	Sugars, flavonoids56 phenolic compound, alkaloids, steroids, acidic molecules,fatty acids.	Antioxidant	Ahmad faizal et al
15	Calahuala	Polypodiaceae	Phenolics, terpenoids, and alkaloids, Flavonoids, hydroxycinnamic acids	Antioxidant, photo-protective and immunomodulatory	Caceres, Armando, et al
16	Cyathea latebrosa	Cyatheaceae	xycinnamic acidsphenolics, terpenoids, and alkaloids, Flavonoids, hydro	Antioxidant;	Tsun-Thai Chai, et.al
17	Dicranopteris curranii	Gleicheniaceae	xycinnamic acidsphenolics, terpenoids, and alkaloids, Flavonoids, hydro	Antioxidant	Tsun-Thai Chai, et.al
18	Gleichenia truncata	Gleicheniaceae	xycinnamic acidsphenolics, terpenoids, and alkaloids, Flavonoids, hydro	Antioxidant	Tsun-Thai Chai, et.al
19	Phymatopteris triloba	Polypodiaceae	Triterpenes, flavonoids and phloroglucinols	Antioxidant	Tsun-Thai Chai, et.al
20	Dryopteris crassirhizoma Nakai	Dryopteridaceae	Alkaloids, glycosides, saponins, phytosterols, tannins	anticancer, antioxidant,	Yuqing Zhao, et al.

				anti-inflammatory and antitumor	
21	*Drynaria quercifolia*	Polypodiaceae	Alkaloids, glycosides, saponins, phytosterols, tannins	anticancer activity	Joash Ban Lee Tan
22	*Drynaria rigidula*	Polypodiaceae	Alkaloids, glycosides, saponins, phytosterols, tannins	anticancer activity	Joash Ban Lee Tan
23	*Drynaria sparsisora*	Polypodiaceae	Saponins, tannins, terpenoids, flavonoids and alkaloids.	anticancer activity	Joash Ban Lee Tan
24	*Blechnum orientale* Linn	*Blechnaceae*	Flavonoids and terpenoids, flavonoids, phenols and saponins,	antioxidant, anticancer activity	How Y Lai, et al
25	Nephrolepis falcata	Nephrolepidaceae	Flavonoids and terpenoids, flavonoids, phenols and saponins,	Antioxidant, Anti-inflammatory	Ismiarni Komala,et al
26	Pyrrosia lanceolata.	Polypodiaceae	xanthophyll pigments and essential fatty acids	Antioxidant, Anti-inflammatory	Ismiarni Komala,et al
27	Matteuccia struthiopteris	Onocleaceae	flavonoid glycosides, mainly kaempferol, quercetin, luteolin and apigenin derivatives	antioxidant activity	John M. DeLong
28	*Dryopteris crassirhizoma*	Dryopteridaceae	Triterpenes, phenolic acids and flavonoids	Antichemotactic, antioxidant, antibacterial	Juliana MM Andrade
29	*Asplenium serra*.	Aspleniaceae	Triterpenes, phenolic acids and flavonoids	Antichemotactic, antioxidant	Juliana MM Andrade
30	*Cyathea phalerata*	Cyatheaceae	Triterpenes, phenolic acids and flavonoids	Antichemotactic, antioxidant	Juliana MM Andrade
31	*Lastreopsis amplissima*	Dryopteridaceae	Hydroxybenzoic acids, four hydroxycinnamic acids, and three flavonoids	Antichemotactic, antioxidant	Juliana MM Andrade
32	Pichi Serm.	Polypodiaceae	Flavonoids, phenolics, alkaloids, steroids, triterpenes and polysaccharides	Anti-proliferative, Anti-oxidant, Iron-chelating	Tsun-Thai Chai,et al
33	*Polypodium interjectum* Shivas	Polypodiaceae	Flavonoids, phenolics, alkaloids, steroids, triterpenes and polysaccharides	antioxidant, anti-tumor, and anti-inflammatory activities	Hassan Valizadeh, et al
34	*Polystichum woronowii* Fomin	Dryopteridaceae	Flavonoids, phenolics, alkaloids, steroids, triterpenes and polysaccharides	antioxidant, anti-tumor, and anti-inflammatory activities	Hassan Valizadeh,et al
35	*Polystichum aculeatum* (L.) Schott	Dryopteridaceae	Flavonoids, phenolics, alkaloids, steroids, triterpenes and polysaccharides	antioxidant, anti-tumor, and anti-inflammatory activities	Hassan Valizadeh,et al ,
36	*Dryopteris affinis*	Dryopteridaceae	Flavonoids, phenolics, alkaloids, steroids, triterpenes and polysaccharides	antioxidant, anti-tumor, and anti-inflammatory activities	Hassan Valizadeh,et al
37	*Athyrium filix-femina*	Woodsiaceae	Flavonoids, phenolics, alkaloids, steroids, triterpenes and polysaccharides	antioxidant, anti-tumor, and anti-inflammatory activities	Hassan Valizadeh,et al
38	*Asplenium scolopendrium L.*	Aspleniaceae	Flavonoids, phenolics, alkaloids, steroids, triterpenes and polysaccharides	antioxidant, anti-tumor, and anti-inflammatory activities	Hassan Valizadeh,et al

39	*Asplenium adiantum-nigrum* L.	Aspleniaceae	Flavonoids, phenolics, alkaloids, steroids, triterpenes and polysaccharides	antioxidant, anti-tumor, and anti-inflammatory activities	Hassan Valizadeh,et al
	Pteris cretica L.	Pteridaceae	Sugars, flavonoidsphenolic compound alkaloids, steroids, acidic molecules,fatty acids.	antioxidant, anti-tumor, and anti-inflammatory activities	Hassan Valizadeh,et al

Conclusion:

In uttarakhand, several plants were used for maintaining the health and treatment of several diseases including cancer. These plants possess various compounds having anti-cancerous activity. Beside anti-cancerous activity these plants also possesses various other biological activities. The medicinal plants presented in this article have versatile remedial properties against tumor which still require a detailed research.

References

1. GBD (2015) Mortality and causes of death collaborators: global, regional, and national life expectancy, all-cause mortality, and cause-specific mortality for 249 causes of death, 1980-2015: A systematic analysis for the global burden of disease study 2015. Lancet 388(10053):1459–1544.
2. Caius JF. The medicinal and poisonous ferns of India. J Bombay Nat His Soc 1935; 38:341-61.
3. Jacobsen WBG, Jacobsen NHG. 1989. Comparison of the pteridophyte floras of Southern and Eastern Africa, with special reference to high elevation species. Bulletin du Jardin Botanique de Belgique 59: 261-317.
4. Shu JC, Liu JQ, Zhong YQ, et al., 2012. Two new pteros in sesquiterpenes from Pteris multifida Poir. Phyto chem. Lett, 5(2): 276-279.
5. Li S, Zhao M, Li Y, et al., 2014. Preparative isolation of six antitumour biflavonoids from Selaginell adoederleinii Hieron by high-speed counter current chromatography. Phytochem Anal, 25(2):127-133.
6. Baskaran X, Jeyachandran R, 2010. Evaluation of antioxidant and phytochemical analysis of Pteristripartita Sw. acritically endangered fern from South India. J Fairy Lake Bot Gard, 9(3):28-34.
7. Hu HB, Cao H, Jian YF, et al., 2008. Chemical constituents and antimicrobial activities of extracts from Pterismul tifida. Chem Nat Comp, 44(1):106-108.
8. Chao LR, Seguin E, Tillequin F, et al., 1987. New alkaloid glycosides from Selaginel ladoederleinii. J Nat Prod, 50(3):422-426.
9. Murakami T, Machashi NT, 1985. Chemical and chemo taxonomical studies on filices. J Pharm Soc Japan, 105(7):640-648.
10. LuH, XuJ, Zhang LX, et al.,1999. Bioactive constituents from Pteris multifida. Plant Med, 65(6):586-587.
11. Liu Q, Qin M, 2002. Studies on chemical constituents of rhizomes of Pteris multifidi Poir. Chin Trad Herb Drugs, 33(2):114.
12. Qin B, Zhu D, Jiang S, et al., 2006. Chemical constituents of Pteris multifida and their inhibitory effects on growth ofrat prostatic epithelial cells in vitro. Chin J Nat Med, 4(6):428-431.
13. Wang HB, Wong MH, Lan CY, et al., 2010. Effect of arsenic on flavonoid contents in Pteris species. Biochem Syst Ecol, 38(4):529-537.
14. Shu JC, Liu JQ, Zhong YQ, et al., 2012. Two new pteros in sesquiterpenes from Pteris multifida Poir. Phytochem Lett,5(2):276-279.
15. Zhao Z, Jin J, Ruan J, et al., 2007. Antioxidant flavonoid glycosides from aerial parts of the fern Abacopteris penangiana. J Nat Prod, 70 (10):1683-1686.
16. Michael SF, Gillian CD, 1984. Antimicrobial activity of phenolic acids in Pteridiuma quilinium. Am Fern J, 74(3):87-96.

17. Ma SC, But PP, Ooi VE, et al., 2001. Antiviral amento flavones from Selaginell asinensis. Biol Pharm Bull, 24 (3): 311-312.
18. Radulovic N, Stojanovic G, Palic R, 2006. Composition and antimicrobial activity of Equisetumarvense L. essential oil. Phytother Res, 20(1):85-88.
19. Milovanovic V, Radulovic N, Todorovic Z, et al., 2007. Antioxidant, antimicrobial and genotoxicity screening of hydroalcoholic extracts of five Serbian Equisetum species. Plant Foods Hum Nutr, 62(3):113-119.
20. Mimica DN, Natasa S, Jelena C, et al., 2008. Phenolic compounds in field horse tail (Equisetumarvense L.) as natural antioxidants. Molecules, 13(7):1455-1464.
21. Gombau L, Garcia F, Lahoz A, et al., 2006. Polypodium leucotomos extract: anti oxidant activity and disposition. Toxicol in Vitro, 20(4): 464-471.
22. Taylor L, 2003. Herbal Secrets of the Rainforest, 2nd Ed., Sage Press.
23. Lee SM, Na MK, An RB, etal., 2003. Antioxidant activity of two phloroglucinol derivatives from Dryopteris crassi rhizoma. Biol Pharm Bull, 26(9):1354-1356.
24. Hort MA, Dalbo S, Brighente IMC, et al., 2008. Antioxidantand hepatoprotective effects of Cyathea phalerata Mart.(Cyatheaceae). Basic Clin Pharmacol Toxicol, 103(1):17-24.
25. Salatino A, Salatino MLF, Yara D, etal., 2000. Distribution and evolution of secondary metabolites in Eriocaulaceae, Lythraceae and Velloziaceae from“camposrupestres”.Genet Molecul Biol, 23(4):931-940.
26. Singh M, Govindarajan R, Rawat AKS, et al., 2008b. Anti-microbial flavonoid rutin from Pteris vittata L. against pathogenic gastrointestinal micro flora. Am Fern J, 98(2):98-103.
27. Garcia F, Pivel JP, Guerrero A, et al., 2006. Phenolic components and antioxidant activity of Fern block, an aqueous extract of the aerial parts of the fern Polypodium leucotomos. Methods Find Exp Clin Pharmacol, 28(3):157-160.
28. Twentyman PR, Fox NE, Rees JK, 1989. Chemosensitivity testing of fresh leukaemia cell susing the MTT colorimetric assay. Br J Haematol, 71(1):19-24.
29. He J, Wu XD, Liu F, et al., 2014. Lycopodine-type alkaloids from Lycopodium japonicum. Nat Prod Bio prospect, 4(4): 213-219.
30. Hirasawa Y, Morita H, Shiro M, et al., 2003. A novel tetracyclic alkaloid from Lycopodium sieboldii, inhibit in g-acetyl cholinesterase. Org Lett, 5(21):3991-3993.
31. Shen YC, Chen CH, 1994. Alkaloids from Lycopodium casuarinoides. J Nat Prod, 57(6): 824-826.
32. Bi YF, Zheng XK, Feng WS, et al., 2004. Isolation and struc-tural identification of chemical constituents from Selaginella tamariscina (Beauv.) Spring. Acta Pharmaceut Sin, 39 (1):41-45(in Chinese).
33. Raja DP, Manickam VS, de Britto AJ, et al., 1995. Chemical and chemo taxonomical studies on Dicrano pteris species. Chem Pharm Bull, 43(10):1800-1803.
34. Staerk D, Larsen J, Larsen LA, et al., 2004. Selagoline, a new alkaloid from Huper ziaselago. Nat Prod Res, 18 (3):197-203.
35. Yang S, Liu M, Liang N, et al., 2013. Discovery and antitumor activities of constituents from Cyrtomium fortunei (J.) Smith rhizomes. Chem Central J, 7(24):1-10.
36. Duh PD, Tu YY, Yen GC, 1999. Antioxidative activity of water extracts of Hamg jyur (Chrysanthemum morifolium). Lebnesmittel–Wissens chaft Technol, 32(5):269-277.
37. Peres MTLP, Simionatto E, Hess SC, et al., 2009. Chemical and biological studies of Microgramma vaccinii folia (Langsd. & Fisch.) Copel (Polypodiaceae). Quim Nova,32(4):897-901.
38. Hoang L, Tran H, 2014. In vitro antioxidant and anti-cancer properties of active compounds from methanolic extract of Pteris multifida Poir. Leaves. Eur J Med Plants, 4(3):292-302.

39. Chen K, Plumb GW, Bennett RN, et al., 2005. Antioxidant activities of extracts from five anti-viral medicinal plants. J Ethno pharmacol, 96 (1-2):201-205.
40. Gayathri V, Asha V, Subromaniam A, 2005. Preliminary studies on the immunomodulatory and antioxidant properties of Selaginella species. Ind J Pharmacol, 37(6):381-385.
41. Garcia F, Pivel JP, Guerrero A, et al., 2006. Phenolic components and antioxidant activity of Fernblock, an aqueousextract of the aerial parts of the fern Polypodium leucotomos. Methods Find Exp Clin Pharmacol, 28(3):157-160.
42. Gombau L, Garcia F, Lahoz A, et al., 2006. Polypodium leucotomos extract: antioxidant activity and disposition. Toxicol in Vitro, 20(4):464-471.
43. Milovanovic V, Radulovic N, Todorovic Z, et al., 2007. Antioxidant, antimicrobial and genotoxicity screening of hydroalcoholic extracts of five Serbian Equisetum species. Plant Foods Hum Nutr, 62(3):113-119.
44. Zhao Z, Jin J, Ruan J, et al., 2007. Antioxidant flavonoid glycosides from aerial parts of the fern Abacopteri spenangiana. J Nat Prod, 70(10):1683-1686.
45. Ripa FA, Nahar L, Haque M, et al., 2009. Antibacterial, cytotoxic and antioxidant activity of crude extract of Marsilea quadric folia. EuropJ SciRes,33(1):123-129.
46. Shyur LF, Tsung JH, Chen JH, et al., 2005. Antioxidant properties of extracts from medicinal plants popular lyusedin Taiwan. Int J Appl Sci Eng, 3(3):195-202.
47. Baskaran X, Jeyachandran R, 2010. Evaluation of antioxidant and phytochemical analysis of Pteristri partita Sw. a critically endangered fern from South India. J Fairy Lake Bot Gard, 9(3):28-34.
48. Milan CM, Avijit D, Abdur R, et al., 2013. Evaluation of antioxidant, cytotoxic and antimicrobial properties of Drynaria quercifolia. Int Res J Pharm,4(7):46-48.
49. Tan WJ, Xu JC, Li L, et al., 2009. Bioactive compounds of inhibiting xanthine oxidase from Selaginella labordei.Nat Prod Res, 23(4):393-398.
50. Lai HY, Lim YY, Kim KH, 2010. Blechnum orientale Linn.—a fern with potential as antioxidant, anti-cancerand antibacterial agent. BMC Complement Alternat Med,10(15):1-8.
51. Bora H, Miguel OG, Andrade CA, et al., 2005. Determination of the level of polyphenols and their antioxidant potential in different fraction of leaf extracts from Dicksonia sellowiana (Presl.) Hook, Dicksoniaciae.Vis Academic, 6(2):38-47.
52. Peres MTLP, Simionatto E, Hess SC, et al., 2009. Chemical and biological studies of Microgramma vacciniifolia (Langsd. & Fisch.) Copel (Polypodiaceae). Quim Nova, 32(4):897-901.
53. Gombau L, Garcia F, Lahoz A, et al., 2006. Polypodiumleu-cotomos extract: antioxidant activity and disposition.Toxicol in Vitro, 20(4):464-471.
54. Shin SL, Lee CH, 2010. Antioxidant effects of the methanol extracts obtained from aerial part and rhizomes of ferns native to Korea. Korean J Plant Res, 23(1):38-46.
55. Gupta SK, Ghosal M, Biswas R, et al., 2014. Evaluation of in-vitro antioxidant activity of methanolic extracts of some ferns from Mawsynram of Meghalaya, India. Int J Curr Sci, 12:E87-E97.
56. Soare LC, Ferdes M, Stefanov S, et al., 2012a. Antioxidant activity, polyphenols content and antimicrobial activity of several native pteridophytes of Romania. Not Bot Hort Agrobo, 40(1):53-57.
57. Kathirvel A, Rai AK, Maurya GS, et al., 2014. Dryopteriscochleata rhizome: a nutritional source of essential ele-ments, phytochemicals, antioxidants and antimicrobials.IntJ Pharm Sci,6(2):179-188.
58. Liu Y. Q., Tian J., Qian K., Zhao X. B., Susan L. M., Yang L., et al. . (2015). Recent progress on c-4 modified Podophyllotoxin analogs as potent antitumor agents. Med. Res. Rev. 35, 1–62. 10.1002/med.21319.
59. Cai Y, Luo Q, Sun M, et al., 2004. Antioxidant activity and phenolic

compounds of 112 traditional Chinese medicinal plants associated with anti-cancer. Life Sci, 74(17):2157-2184.
60. Guha S, Ghosal S, Chattopadhyay U, 1996. Antitumor, immunomodulatory and anti-HIV effects mangiferin, a naturally occurring glucosylxanthone. Chemotherapy, 42(6): 443-451.
61. Hadi SM, Asad SF, Singh S, et al., 2000. Putative mechanism for anti-cancer and apoptosis-inducing properties of plant derived polyphenolic compounds. IUBMB Life, 50(3): 167-171.
62. Hoang L, Tran H, 2014. In vitro antioxidant and anti-cancer properties of active compounds from methanolic extract of Pteris multifida Poir. Leaves. Eur J Med Plants, 4(3): 292-302.
63. Kapadia GJ, Tokuda H, Konoshinma T, 1996. Anti-tumor promoting activity of Dryopteris Phlorophenone derivatives. Cancer Lett, 105(2):161-165.
64. Kaur P, Kaur V, Kumar M, et al., 2014. Suppression of SOS response in Escherichia coli PQ37, antioxidant potential and antiproliferative action of methanolic extract of Pteris vittata L. on human MCF-7 breast cancer cells. Food Chem Toxicol, 74:326-333.
65. Konoshima T, Takasaki M, Tokuda H, et al., 1996. Antitumor-promoting activities of triterpenoids from ferns. Biol Pharm Bull, 19(7):962-965.
66. Kumar S, Chashoo G, Saxena AK, et al., 2013b. Parthenium hysterophorus: a probable source of anti-cancer, antioxidant and anti-HIV agents. Biol Med Res Int, 2013: 810734.
67. Lai HY, Lim YY, Kim KH, 2010. Blechnum orientale Linn.—a fern with potential as antioxidant, anti-cancer and antibacterial agent. BMC Complement Alternat Med, 10(15):1-8.
68. Lee IS, Nishikawa A, Furukawa F, et al., 1999. Effects of Selaginella tamariscina on in vitro tumor cell growth, p53 expression, G1 arrest and in vivo gastric cell proliferation. Cancer Lett, 144(1):93-99.
69. Li JH, He CW, Liang NC, et al., 1999. Effects of antitumor compounds isolated from Pteris semipinnata L. on DNA topoisomerases and cell cycle of HL-60 cells. Acta Pharmacol Sin, 20(6):541-545.
70. Delong JM, Mark Hodges D, Prange RP, et al., 2011. The unique fatty acid and antioxidant composition of Ostrich fern (Matteuccia struthiopteris) fiddle heads. Can J Plant Sci, 91(5):919-930.
71. Gayathri V, Asha V, Subromaniam A, 2005. Preliminary studies on the immune modulatory and antioxidant properties of Selaginella species. Ind J Pharmacol, 37(6): 381-385.
72. Firdaus M, Prihanto AA, Nurdiani R, 2013. Antioxidant and cytotoxic activity of Acanthus ilicifolius flower. Asian Pac J Trop Biomed, 3(1):17-21.
73. Fotsis T, Pepper MS, Aktas E, 1997. Flavonoids, dietary derived inhibitors of cell proliferation and in vitro angiogenesis. Cancer Res, 57:2916-2921.
74. Hoang L, Tran H, 2014. In vitro antioxidant and anti-cancer properties of active compounds from methanolic extract of Pteris multifida Poir. Leaves. Eur J Med Plants, 4(3): 292-302.
75. Hadi SM, Asad SF, Singh S, et al., 2000. Putative mechanism for anti-cancer and apoptosis-inducing properties of plant derived polyphenolic compounds. IUBMB Life, 50(3): 167-171.
76. Kumar S, Chashoo G, Saxena AK, et al., 2013b. Parthenium hysterophorus: a probable source of anti-cancer, antioxidant and anti-HIV agents. Biol Med Res Int, 2013: 810734.
77. Kaur P, Kaur V, Kumar M, et al., 2014. Suppression of SOS response in Escherichia coli PQ37, antioxidant potential and antiproliferative action of methanolic extract of Pteris vittata L. on human MCF-7 breast cancer cells. Food Chem Toxicol, 74:326-333.
78. Lai HY, Lim YY, Kim KH, 2010. Blechnum orientale Linn.—a fern with potential as antioxidant, anti-cancer and antibacterial

agent. BMC Complement Alternat Med, 10(15):1-8.
79. Petard P, Raau T, 1972. The Use of Polynesia Medicinal Plants in Tahitian Medicine. Technical Paper No. 167. South Pacific Commission. Noumea, New Caledonia.
80. Uma R, Pravin B, 2013. In-vitro cytotoxic activity of Marsileaquadri folia Linn. of MCF-7 cells of human breast cancer. Int Res J Med Sci,1(1):10-13.
81. Santhosh KS, Samydurai P, Nagarajan N, 2014. Indigenous knowledge on some medicinal pteridophytic plant species among the Malasartribe'sin Valparai Hills, Western Ghats of Tamil Nadu. Am J Ethnomed, 1(3):164-173.
82. Konoshima T, Takasaki M, Tokuda H, et al., 1996. Anti-tumor promoting activities of triterpenoids from ferns. Biol Pharm Bull, 19(7):962-965.
83. Zakaria ZA, Mohamed AM, Jamil NSM, et al., 2011. In vitro cytotoxic and antioxidant properties of the aqueous, chloroform and methanol extracts of Dicranopteris line-aris leaves. Afr J Biotechnol, 10(2): 273-282.
84. Sarker MAQ, Mondol PC, Alam MJ, et al., 2011. Comparative study on antitumor activity of three pteridophytes ethanol extracts. Int J Agric Tech, 7(6):1661-1671.