INTERNATIONAL JOURNAL OF
Clinical and Pharmaceutical Innovations
An International Peer Reviewed Open Access Journal

Research Article

ISSN (Online): 3142-8665

2026, Volume 1, Issue 3, Page No: 80-86.

IN-SILICO VIRTUAL SCREENING AND COMPARATIVE SOLVENT EXTRACTION STUDIES OF ADIANTUM RADDIANUM C. PRESL FOR ENHANCING PHARMACOLOGICAL ACTIVITY

Vandana K.[1*], Aliya Khan[2], Fathima Fida[3], Fida Sherin T. S.[4], Hasniya T.[5], Mishba Sherin N. K.[6], Anoob Kumar K. I.[7], Lal Prasanth M. L.[8]

[1*]Associate Professor, Department of Pharmaceutical Chemistry, Dr. Moopen's College of Pharmacy, Wayanad, Kerala.
[2,3,4,5,6]Final Year B. Pharm Student, Dr. Moopen's College of Pharmacy, Wayanad, Kerala.
[7]Professor, Department of Pharmaceutical Chemistry, Dr. Moopen's College of Pharmacy, Wayanad, Kerala.
[8]Principal, Professor, Department of Pharmaceutical Chemistry, Dr. Moopen's College of Pharmacy, Wayanad, Kerala.

Article Info: **Received:** 23 April 2026, **Revised:** 13 May 2026, **Accepted:** 02 June 2026

***Corresponding Author: Vandana K.**

Associate Professor, Department of Pharmaceutical Chemistry, Dr. Moopen's College of Pharmacy, Wayanad, Kerala.

Citation:
Vandana K.[1*], Aliya Khan[2], Fathima Fida[3], Fida Sherin T. S.[4], Hasniya T.[5], Mishba Sherin N. K.[6], Anoob Kumar K. I.[7], Lal Prasanth M. L.[8]. (2026). In-silico Virtual Screening And Comparative Solvent Extraction Studies Of Adiantum Raddianum C. Presl For Enhancing Pharmacological Activity. International Journal of Clinical and Pharmaceutical Innovations, 1(3), 80-86.
DOI: https://doi.org/10.5281/zenodo.20581473

ABSTRACT
The present study was investigated for its phytochemical composition, potential bioactivity through in silico drug design, and in vitro pharmacological evaluation of *Adiantum raddianum*, a medicinal pteridophyte known for its therapeutic potential. The study aimed to evaluate its phytochemical profile and antioxidant potential through experimental and anti-inflammatory activity through computational approaches. Fresh plant material of *Adiantum raddianum* was collected, authenticated, dried, and subjected to Soxhlet extraction using a n-hexane, chloroform and ethanol solvent system. The extract was standardized through preliminary phytochemical screening, which revealed the presence of important secondary metabolites such as flavonoids, tannins, saponins, phenolic compounds, and carbohydrates, all of which are known to contribute to antioxidant activity. The antioxidant activity was evaluated using the DPPH (2,2-diphenyl-1-picrylhydrazyl) free radical scavenging assay, with ascorbic acid used as the standard reference. The ethanolic plant extract exhibited significant radical scavenging activity, showing a comparable effect to that of ascorbic acid, indicating strong antioxidant potential. In additional, molecular docking studies were carried out using an appropriate target protein associated to inflammation indicating significant binding affinities. The docking analysis aimed to identify compounds with superior binding affinity. A compound showing a higher docking score than the standard was selected, isolated, and further evaluated for its anti-inflammatory activity. The results suggest that the ethanolic plant extract of *Adiantum raddianum* possesses potent antioxidant properties. This highlights its potential as a natural source of antioxidant agents and supports further research for its application in the development of novel therapeutic compounds.

KEYWORDS: Adiantum Raddianum, Antioxidant, Anti-inflammatory, Molecular docking, Soxhlet extraction.

INTRODUCTION

Pharmacotherapy has historically benefited greatly from natural compounds and their structural equivalents, particularly for infectious disorders and cancer.[7,9] However, the pharmaceutical industry pursuit of natural products declined starting in the 1990s due to technical difficulties with screening, isolation, characterization, and optimization. These issues are being addressed and new opportunities are being created in recent years by a number of scientific and technological advancements, such as better analytical tools, genome mining and engineering techniques, and improvements in microbial culturing.[4,5] As a result, there is a renewed interest in using natural compounds as pharmacological leads, especially to combat antimicrobial resistance.[1,10, 25]

The earliest known medical treatment is herbal medicine. Throughout history, all cultures have utilized herbs. It contributed to the advancement of contemporary civilization. Overtime, each tribe expanded its knowledge base to include the therapeutic properties of local herbs. The most widely used medications come from herbs. Eighty percent of people worldwide utilize herbal medicine as their primary form of treatment, according to estimates from the World Health Organization (WHO).[2,6]

In several countries, fern species are used in traditional medicine to treat a range of ailments. The primary effects of these pharmacological effects include purgative, antibacterial, treatment of gastric and renal infections, diuretic, painkiller (for headaches, stomachaches, and gastrointestinal aches), and anti-inflammatory properties.[6,12] Despite their widespread use, ferns have not been completely investigated by phytochemical studies, which are often unrelated to the observed pharmacological features. Most ferns are responsible for its toxicity and carcinogenic consequences. Moreover, ferns with suitable biological activity are rare, and determining their active constituents requires a combination of efficient separation methods and suitable bioassays.[24,26]

Ferns contain phenolic (flavonoids) and saccharides, which are secondary metabolites with ant oxidative properties. This explains how ferns were used in the past and identifies the derivatives of ferns that have toxic effects on both humans and animals, with the potential to cause acute or chronic damage through direct or indirect effects. Such a metabolite can be hazardous to humans and animals.[14,16] Secondary metabolites, including as cyanogenic glycosides, tannins, Phyto ecdysones, and certain volatile terpenoids, are mostly used by ferns to protect themselves from animal attacks. Certain ferns, or their secondary metabolites, are safe biological substitutes for pesticides. To properly evaluate the prospective uses in therapy, biotechnology, and medicine, more study is needed in this field, particularly with regard to identification, measurement, and biological impacts.[2, 3]

Antimicrobial Activity

Sharma et al. (2013) evaluated the antimicrobial potential of Adiantum raddianum and observed considerable antibacterial activity of its ethanol extracts against pseudomonas aeruginosa and staphylococcus aureus.[20,23] This activity comparable to the antibiotic netilmicin. The methanol extracts were also observed to inhibit s. aureus. Species of the genus Adiantum have been considered to be good sources of antimicrobial agents and the methanol extracts of some species of Adiantum were found to exhibit higher antimicrobial activity than commercial antibiotics, such a gentamicin and ketoconazole.[6,15]

Anthelmintic activity

Methanolic leaf extract of *Adiantum raddianum* shows anthelmintic activity against *Caenorhabditis elegans* when evaluated using a microdilution method. At a tested concentration of 500 µg/mL, the extract resulted in a worm mortality rate of 14.941%, reflecting a moderate level of activity. This effect is considered preliminary and is likely linked to the presence of phytochemical constituents such as flavonoids, polyphenols, and terpenoids. While these findings indicate that *A. raddianum* could serve as a potential natural source of anthelmintic agents, additional research is necessary to validate its effectiveness, optimize dosage, and identify the active compounds responsible for the observed activity. Overall, all extracts of *A. raddianum* like methanolic, n hexane and distilled water exhibited strong antinematodal activity against *C. elegans*, with effectiveness increasing alongside concentration.[6,13]

Antioxidant Activity

A. raddianum also exhibits strong antioxidant activity. The phenolic compounds of A. raddianum possess primary (the compounds react with peroxide radicals and convert them into stable substances) and secondary (oxygen scavengers suppress the formation of free radicals) antioxidant activity (Lai and Lim 2011).[22,27] Other species of the genus Adiantum, such as Adiantum caudatum (Ahmed et al. 2015) and Adiantum philippense L., have been reported to be good sources of antioxidants (Ali et al. 2013). Promising results have been demonstrated for the antioxidant activity of Adiantum capillus-veneris.[8,11]

Adiantum raddianum, commonly known as maidenhair fern, has been used traditionally to manage respiratory problems, inflammation, and fever. Despite its long-standing use, modern scientific studies exploring its pharmacological potential are limited. Understanding the bioactive compounds responsible for its therapeutic effects is essential to validate traditional knowledge and potentially develop safe, effective natural remedies.[18,21]

The method of extraction significantly affects which compounds are obtained from the plant. Different solvents extract different classes of phytochemicals, and a comparative study helps identify the solvent system. At

the same time, virtual screening offers a rapid, cost-effective approaches.[28,28]

By integrating comparative solvent extraction with *in silico* virtual screening, this study aims to identify potent bioactive compounds, optimize extraction methods, and enhance the pharmacological activity of *Adiantum raddianum*, bridging traditional knowledge with modern scientific research.[23]

MATERIALS AND METHODS

Analytical and synthetic grade chemicals and reagents including n-hexane, ethanol, methanol, chloroform, DPPH, Mayer's reagent, Dragendorff's reagent, Wagner's reagent, Fehling's reagent, Molisch's reagent, ferric chloride, acetic anhydride, sulphuric acid, hydrochloric acid, ammonia, pyridine, sodium nitroprusside, and benzene were procured from NICE Chemicals. Instruments used included an electronic balance, heating mantle, hot plate, microwave oven, Soxhlet apparatus, UV–Visible spectrophotometer, and mixer grinder.

The whole plant of *Adiantum raddianum* was collected from Vythiri, Wayanad, Kerala, India, during November 2024. Plant authentication was carried out by Dr. Raji, Associate Professor, Department of Botany, St. Mary's Arts and Science College, Sulthan Bathery, Wayanad.

Preparation of Plant Extract

The collected plant material was washed with distilled water, shade dried for two weeks, and powdered using a blender. Soxhlet extraction was performed using ethanol, n-hexane, and chloroform as solvents. Ten grams of powdered material was extracted with 100 mL of solvent for 6 h, and the extraction was repeated twice to ensure maximum yield. The extracts were concentrated by solvent evaporation.[8, 19]

Data Collection and Experimental Methods

Macroscopic evaluation of the plant material was conducted based on colour, odour, taste, texture, and morphological characteristics. Preliminary phytochemical screening of the extracts was carried out using standard qualitative tests for carbohydrates, glycosides, alkaloids, triterpenoids, phenols, and flavonoids.[6,17]

Antioxidant activity was evaluated using the DPPH radical scavenging assay. Briefly, 0.1 mL of extract was mixed with 3 mL of 0.004% methanolic DPPH solution and incubated for 30 min. Absorbance was measured at 517 nm using a UV–Visible spectrophotometer, and percentage inhibition was calculated.[9, 12]

Molecular docking studies were performed using AutoDock software to predict ligand–receptor interactions, binding affinity, and energetically favourable conformations through grid-based docking and genetic algorithm approaches.[11,30]

RESULTS AND DISCUSSION

Extraction Yield and Phytochemical Analysis

Different solvent extracts of *Adiantum raddianum* were obtained through Soxhlet extraction with yields ranging from 8.2–8.9% (Table 1). Preliminary phytochemical screening revealed the presence of alkaloids, flavonoids, glycosides, terpenoids, carbohydrates, and phenolic compounds. Ethanolic extract showed comparatively higher occurrence of phenols, flavonoids, and glycosides, indicating better extraction efficiency for polar phytoconstituents.

Table no 1: Percentage yield of the different plant extracts of *Adiantum raddianum*.

Extracts of *Adiantum Raddianum*	**Colour of dried Extract**	**Physical nature of dried extract**	**% Yield w/w**
n-Hexane extract of *Adiantum raddianum*	Dark green	Powder	8.9
Chloroform extract of *Adiantum raddianum*	Dark green	Powder	8.4
Ethanol extract of *Adiantum raddianum*	Light green	Powder	8.2

PHYTOCHEMICAL SCREENING

The preliminary phytochemical screening, n-Hexane, Chloroform and ethanolic extract of Adiantum raddianum, showed significant positive results in the tests for alkaloids, glycosides. Flavonoids, terpenoids etc.

Table no. 2: Phytochemical screening of the different plant extracts of Adiantum Raddianum.

S NO	CHEMICAL TEST	n-HEXANE	CHLOROFORM	ETHANOL
1	**Alkaloids**			
A	Mayer's test	+	+	+
B	Wagner's test	+	+	+
2	**Carbohydrate**			
A	Molisch's test	_	+	+
B	Fehling's test	_	_	+
3	**Terpenoids**			
A	Salkowski's test	_	+	+
4	**Phenols**			
A	Ferric chloride	_	_	+
5	**Glycosides**			
A	Legal's test	_	_	+
B	Borntrager's test	+	_	+
6	**Flavanoids**			
A	Aqueous NaOH test	+	+	+
B	Alkaline reagent test	+	+	+

In the preliminary phytochemical evaluation of the plant extracts, it was able to identify the presence of alkaloids, carbohydrates, glycosides, phenolic compounds, flavonoids, and terpenoids. The significant presence of Flavanoids in the n-hexane, chloroform and ethanol extract and it was reported that the alkaloids interfere with the cell division process, thus possess the antioxidant property. In the present study, the n-hexane, chloroform and ethanol extract of Adiantum raddianum showed a strong positive result in the test for flavonoids thus possess antioxidant activity.

DPPH SCAVENGING ASSAY

The DPPH (2, 2-diphenyl-1-picrylhydrazyl) assay is a widely used method for evaluating the antioxidant activity of compounds or extracts. The principle of the DPPH assay is based on the ability of antioxidants to scavenge the stable radical DPPH. When an antioxidant is added to the DPPH solution, it reacts with the DPPH radical, resulting in the formation of a stable molecule, which leads to a color change from purple to yellow. This color change is measured spectrophotometrically at 517 nm, and the antioxidant activity is calculated by measuring the decrease in absorbance, which is directly proportional to the amount of antioxidant present.[12]

The DPPH radical scavenging activities of the total extract of the plant and of ascorbic acid. The extract of Adiantum raddianum has comparatively same radical scavenging activity with the standard.

Table no. 3: Antioxidant activity of different solvent extracts of Adiantum raddianum.

Sl.NO	Solvent used	Concentration	
		50 mg/ml	100 mg/ml
1	Ascorbic acid	96.28	97.87
2	Ethanol	90	92
3	Chloroform	68	88.49
4	n-hexane	37.53	66.37

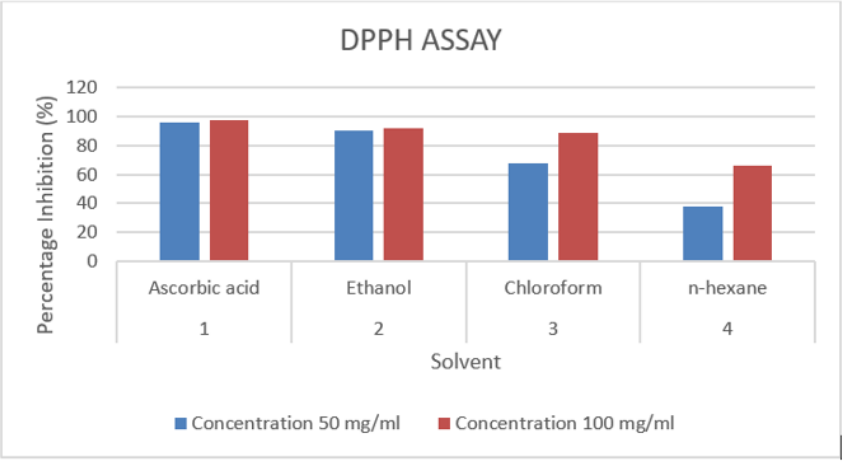

Figure 1: Bar graph showing antioxidant activity of different solvent extracts of Adiantum raddianum.

MOLECULAR DOCKING

In this investigation, molecular docking studies were carried using AutodockVina, and the resulting outcomes were compared with those of the standard Celecoxib. The ligands bind at the active site of the target receptor 4M11 and the binding affinity were expressed as docking scores as given in table. Among them Ketohakonanol had the best score of -7.8 kcal mol-1, which is comparable to standard drug celecoxib (-7.5).

Table 4: Molecular docking score of Ketohakonanol.

Compounds	PDB ID	Binding Affinity (Kcal/mol)
Ketohakonanol	4M11	-7.8
CELECOXIB	4M11	-7.5

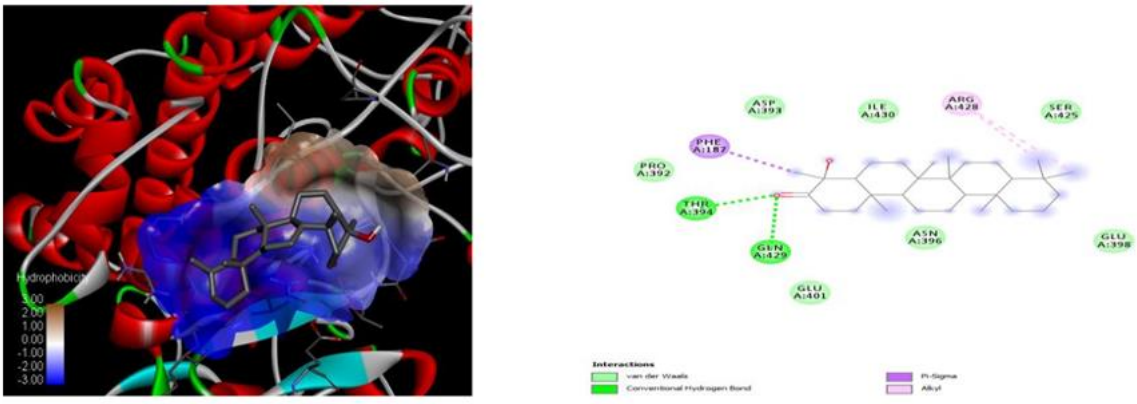

Figure 2: Ketohakonanol at active site Figure 3 2D Interaction with COX-2. (PDB ID: 4M11)

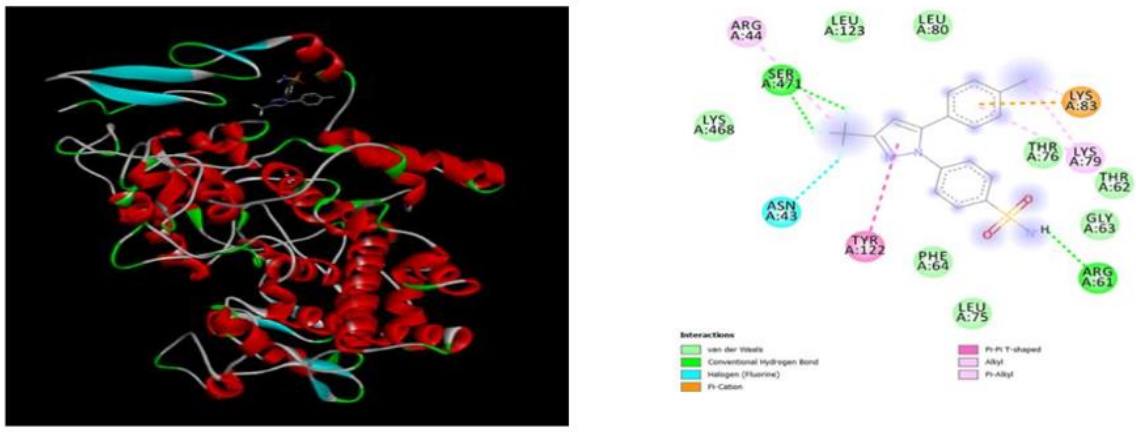

Figure 4: Celecoxib at active site Figure 5 2D Interaction of Celecoxib with COX2.

SUMMARY AND CONCLUSION

The present study was mainly focused to identify the bioactive constituent from Adiantum raddianum. The plant Adiantum raddianum is a maidenhair fern widely distributed in tropical and subtropical regions and is known for its medicinal properties. The plant was authenticated for the present study. The dried plant of Adiantum raddianum were subjected to Soxhlet extraction using ethanol, chloroform, and n-hexane in a comparative study to evaluate the effect of solvent polarity on extract yield and phytochemical content. The n Hexane, Chloroform and Ethanol plant extracts showed percentage yields of 8.9%w/w, 8.4%w/w and 8.2%w/w respectively, indicating efficient extraction of phytoconstituents.

The phytochemical studies of the plant extract of Adiantum raddianum revealed the presence of alkaloids, flavonoids, terpenoids, and phenolic compounds. The antioxidant activity was evaluated using the DPPH stable free radical scavenging assay. The DPPH radical scavenging activity of the plant extract was compared with standard ascorbic acid. The ethanolic plant extract exhibited significant radical scavenging activity with percentage inhibition 90% (50 µg/ml) and 92% (100 µg/ml), showing a comparable effect to that of ascorbic acid, indicating strong antioxidant potential. The Chloroform plant extract exhibited shows radical scavenging activity with percentage inhibition 68% (50 µg/ml) and 88.49% (100 µg/ml) and in case of n Hexane plant extract exhibited comparatively least percentage inhibition with 53% (50 µg/ml) and 66.37% (100 µg/ml) with that of standard.

In this study, molecular docking analysis was performed. The docking process aimed to identify novel compounds with better binding affinity. Molecular docking studies of Ketohakonanol an isolated compound from Adiantum raddianum, showed good binding affinity (- 7.8 Kcal/mol), indicating good binding affinity when compared with the standard drug Celecoxib. Based on docking results, the compound showing a higher docking score thus can be selected for further study and synthesis. Encouraged by the insilico results, the compound was subjected to biological evaluation, confirming that Adiantum raddianum possesses potent anti-inflammatory properties. Overall, this comparative solvent and in silico study highlights the plant's therapeutic potential and supports its use as a source for novel anti-inflammatory agents.

REFERENCE

1. Silva GB, Ionashiro M, Carrara TB, Crivellari AC, Tiné MA, Prado J, Carpita NC, Buckeridge MS. Cell wall polysaccharides from fern leaves: evidence for a mannan-rich Type III cell wall in Adiantum raddianum. Phytochemistry, 2011 Dec. 1; 72(18): 2352 60.
2. Santos MG, Kelecom A, Paiva SR, Moraes MG, Rocha L, Garrett R. Phytochemical studies in pteridophytes growing in Brazil: A review. Am J Plant Sci Biotechnol, 2010; 4(1): 113-25.
3. Irshad MJ, Sajid M, Khalil MI, Zahoor S. Antinematodal Potential of Leaf Extracts of Adiantum Raddianum and Artemisia Absinthium with the Model Organism Caenorhabditis elegans. International Journal of Research Studies, 2023; 1(1).
4. Singh M, Singh N, Khare PB, Rawat AK. Antimicrobial activity of some important Adiantum species used traditionally in indigenous systems of medicine. Journal of ethnopharmacology, 2008 Jan 17; 115(2): 327-9.
5. Kimta N, Puri S, Kumari A, Verma R, Sharma R, Khan KA, Chen KT, Kumar D. Applications of Pteridophytes in Nanotechnology: a class that has not yet explored to the extent of its potential. Green Chemistry Letters and Reviews, 2025 Dec 31; 18(1): 2460641.
6. Santos MG, Kelecom A, Paiva SR, Moraes MG, Rocha L, Garrett R. Phytochemical studies in pteridophytes growing in Brazil: A review. Am J Plant Sci Biotechnol, 2010; 4(1): 113-25.
7. Halder K, Chakraborty S. An account of antioxidant potential in pteridophytes: a biochemical perspective. International Journal of Bioinformatics

and Biological Science, 2018; 6(1): 15-24.
8. Ali MS, Amin MR, Kamal CM, Hossain MA. In vitro antioxidant, cytotoxic, thrombolytic activities and phytochemical evaluation of methanol extract of the A. philippense L. leaves. Asian Pacific Journal of Tropical Biomedicine, 2013 Jun 1; 3(6): 464-9.
9. Qadir SA, Awlqadr FH, Qadir MH, Qadir AM, Faraj AM, Salih SA, Saeed MN, Arab K, Hosseini SM. Adiantum capillus-veneris: A Comprehensive Review of Its Medicinal Properties, Bioactive Compounds, and Advanced Extraction Techniques. Food Science & Nutrition, 2025 Oct; 13(10): e71118.
10. Ibraheim ZZ, Ahmed AS, Gouda YG. Phytochemical and biological studies of Adiantum capillus-veneris L. Saudi Pharmaceutical Journal, 2011 Apr 1; 19(2): 65-74.
11. Hirai RY, Schuettpelz E, Huiet L, Pryer KM, Smith AR, Prado J. Phylogeny and relationships of the neotropical Adiantum raddianum group (Pteridaceae). Taxon, 2016 Dec; 65(6): 1225-35.
12. Reinaldo RC, Feitosa IS, Santiago AC, Albuquerque UP. Adiantum raddianum C. Presl. In Medicinal and Aromatic Plants of South America: Brazil, 2018 Oct 25; (pp. 89-96).
13. Lestari WS, Adjie B. Studies on fern of Lesser Sunda Islands I: Checklist of the genus Adiantum (Pteridaceae). Jurnal Biodjati, 2020 May; 5(1): 107-14.
14. Zurakowski KA, Gifford EM. Quantitative studies of pinnule development in the ferns Adiantum raddianum and Cheilanthes viridis. American Journal of Botany, 1988 Oct; 75(10): 1559-70.
15. Hirai RY, Prado J. Neotropical species of the Adiantum raddianum group (Pteridaceae). Willdenowia, 2019 Nov; 49(3): 295-317.
16. Huiet L, Li FW, Kao TT, Prado J, Smith AR, Schuettpelz E, Pryeri KM. A worldwide phylogeny of Adiantum (Pteridaceae) reveals remarkable convergent evolution in leaf blade architecture. Taxon, 2018 Jun; 67(3): 488-502.
17. Santos-Silva F, Mastroberti AA, Mariath JE. Development of the epidermal cells of the pinnules of Adiantum raddianum C. Presl (Pteridaceae): environmental adaptive plastidial characteristics. American Fern Journal, 2011 Jul; 101(3): 172-81.
18. Rajurkar NS, Gaikwad K. Evaluation of phytochemicals, antioxidant activity and elemental content of Adiantum capillus veneris leaves. Journal of Chemical and Pharmaceutical Research, 2012 Feb 29; 4(1): 365-74.
19. Van Doorn WG, Zagory D, Reid MS. Role of ethylene and bacteria in vascular blockage of cut fronds from the fern Adiantum raddianum. Scientia horticulturae, 1991 Feb 1; 46(1-2): 161-9.
20. Korpelainen H, de Britto J, Doublet J, Pravin S. Four tropical, closely related fern species belonging to the genus Adiantum L. are genetically distinct as revealed by ISSR fingerprinting. Genetica, 2005 Nov; 125(2): 283-91.
21. Lai H, Lim Y. Evaluation of antioxidant activities of the methanolic extracts of selected ferns in Malaysia. International Journal of Environmental Science and Development, 2011 Dec 1; 2(6): 442.9
22. Yogisuari G, Reza RF, Rachma LN, Raras TY, Pratama AN, Nugraha AS, Triatmoko B. Assessment of the phytochemicals and anthelminthic activities of Adiantum raddianum and Kibatalia arborea extracts. Pharmacy Education, 2023 Oct 10; 23(4): 284-8.
23. Govindarajan M, AlQahtani FS, AlShebly MM, Benelli G. One-pot and eco-friendly synthesis of silver nanocrystals using Adiantum raddianum: Toxicity against mosquito vectors of medical and veterinary importance. Journal of Applied Biomedicine, 2017 May 1; 15(2): 87-95.
24. Van Doorn WG, Zagory D, Reid MS. Role of ethylene and bacteria in vascular blockage of cut fronds from the fern Adiantum raddianum. Scientia horticulturae, 1991 Feb 1; 46(1-2): 161-9.
25. Fierascu I, Fierascu RC, Ungureanu C, Draghiceanu OA, Soare LC. Application of polypodiopsida class in nanotechnology–potential towards development of more effective bioactive solutions. Antioxidants, 2021 May 8; 10(5): 748.
26. Kimta N, Puri S, Kumari A, Verma R, Sharma R, Khan KA, Chen KT, Kumar D. Applications of Pteridophytes in Nanotechnology: a class that has not yet explored to the extent of its potential. Green Chemistry Letters and Reviews, 2025 Dec 31; 18(1): 2460641.
27. Marimuthu Govindarajan MG, AlQahtani FS, AlShebly MM, Benelli G. One-pot and eco-friendly synthesis of silver nanocrystals using Adiantum raddianum: toxicity against mosquito vectors of medical and veterinary importance.
28. Fujino DW, Reid MS, Vandermolen GE. Identification of vascular blockages in rachides of cut maidenhair (Adiantum raddianum) fronds. Scientia Horticulturae, 1983 Dec 1; 21(4): 381-8.
29. Van Doorn WG, Clerkx A, Boekestein A. Bacteria as a cause of vascular occlusion in cut fronds of Adiantum raddianum: a scanning electron microscope study. Scientia horticulturae, 1991 Nov 1; 48(3-4): 299-309.
30. Yumkham SD, Singh PK, Khomdram SD. Observations on indusia in Adiantum L. (Pteridaceae: Vittarioideae) of North-East India. Pleione, 2017; 11: 241-8.

