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Review Article

Plant profile, Phytochemistry and pharmacological activity of Plant Adiantum capillus veneris Linn. (Hansraj)

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Abstract

More than half of the world's population relies on traditional medicine and the main role of traditional medicine including the use of plant extract and their active constituents. Among them Adiantum capillus veneris Linn. A small size wooden herb plant of the family Adiantaceae commonly called Parsioshan, Hansraj, Maidenhair fern, and Ghodkhuri. The plant has leaves, stem, and root that have been reported for possessing antioxidant, anti-microbial, anti-fungal, anti-diabetic, antipyretic, wound healing action and it is contraindicated in pregnancy due to its anti-implantation effect. It is most common in the treatment of hair fall and skin disease. The screening of phytochemical analysis showed the presence of flavonoids, alkaloids, tannins, saponins, cardiac glycosides, terpenoids, steroids, and reducing sugars. The present review focuses on details of geographical distribution, phytochemical parameters, phytoconstituents, and pharmacological properties of Adiantum capillus veneris Linn (Hansraj) so far.

Keywords: Adiantum cappilus veneris L; Hapane; neohopane; antidibetic pharmacology

Introduction

One of the most crucial sources of medicine is plants. Herbal medicine is the oldest form of healthcare known to mankind. Herbs had been used by all cultures throughout history Most of the populations of developing countries utilize plant based traditional medicine for their primary health care needs. Ethnobotanical plants have a strong base in Indian systems of medicine, such as Ayurveda, Unani, and Siddha, and several other local medicines such as the Chinese and Tibetan systems. The practices of traditional medicine are not the same all over the world and vary depending on culture and philosophy .According to World Health Organization, about 80% of the world's population depends on the natural product for their health because of the general belief that herbal drugs are without any side effects besides being cheap and locally available Herbal medicine is a chief constituent in all indigenous peoples' tradition, a common element in Ayurveda, homeopathic, naturopathic, traditional oriental, and Native American Indian medicine. It is also estimated that, of the 119 plant-derived pharmaceutical medicines, about 74% are used in modern medicine in ways that correlated directly with their traditional uses as plant medicines by inhabitant cultures In developing countries like India, the use of traditional medicines holds a great promise as an easily available source as effective medicinal agents to cure a wide range of many diseases and Herbal medicines are now in great demand in the developing world for primary health care .Hansraj (Adiantum capillus-veneris L.) is an herbal plant used in the Unani system of medicine since ancient times [1] (Figure1). Adiantum capillus-veneris L. belonging to the Adiantaceae family is one of the most common and broadly distributed species. Ethnomedicinally, the species has been used as tonic and diuretic; in the treatment of cold, fever, cough, and bronchial disorders, as a stimulant, emollient, purgative, demulcent,

general tonic, and hair tonic, in addition to skin diseases, tumors of the spleen, liver [2]. Pteridophytes are one of the oldest and ancient vascular plant groups on earth. Pteridophytes do not have seeds or flowers either; instead, they reproduce via spores. There are over 250 various genera and 12,000 species of ferns reported all over the world. They play a major role in the earth's plant diversity and form a significant dominant part of many plant communities mainly in the tropical and temperate regions. Pteridophytes have been poorly studied and considered the economically less important group of plants in the plant kingdom The Pteridophytes which contain ferns and fern allies have been well-known to man for more than 2000 years and also have been mentioned in ancient literature [3].It has been observed that Pteridophytes are not infected by microbial pathogens, which might be one of the important factors for the evolutionary success of Pteridophytes and the fact that they survived for more than 350 million years. In India Pteridophytes are geographically distributed in Himalaya, Western Ghats, Jammu Kashmir, and Vindhya, hilly areas of Bihar, Orissa and Madhya Pradesh as well as in the Aravalli, mainly in Mount Abu in Rajasthan.

Figure A: Plants of Adiantum capillus-veneris L.

Figure B: Leaves.

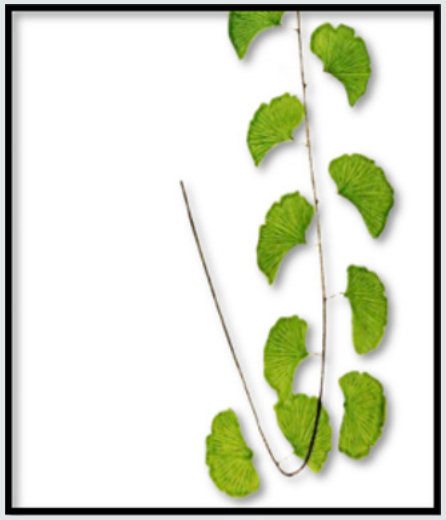


Figure C: Stem.

Figure 1: Parts of Adiantum capillus-veneris L.

Geographical Distribution

A native of tropical America Adiantum capillus-veneris Linn is found all over the world in moist and shady places. It is often found growing on limestone cliffs away from direct sunlight and out of the way of drying southwest winds It is also found in western and southern Europe, Africa, North, and Central America In India, it is distributed in Tamil Nadu up to 1800 meters on the mountains and the western Himalayas and extending up to Manipur. Also grows in Punjab, Bihar, Maharashtra, South India, Kashmir, Nainital, Shimla, Dulhossy, and Mussorie. It is infrequently found in Baluchistan and Afghanistan way to Arabia, Syberia, Southern, and Central Europe, Ireland, and southwest England [4][1].

History

As early as 100 A.C. Dioscorides described Adiantum capillus-veneris by the name of Adiavrovfor having leaves serrated at the top like coriander. The Western Arabs, however, appear to use Adiantum capillus-veneris, as they call the plant Kuzburat-el biror "coriander of the wall", indicating a habitat where A. venestumis not found. Other Arabic names for the genus Adiantum are shaar-el-jinn i.e. "fairies hair", shaar-el-jibali.e. "hair of the mountains"; shaar-el-fual i.e. "hair of omens"; sak-el-aswadi.e. "black stem" and Nasif-el-Aswad i.e. "black veil," Ibn Sina and other medical writers describe the drug under the name of Barsiawashan, which is the Arabic form of its Persian name Parsiawashan. It is considered to be deobstruent and resolvent, useful for clearing the primaviae of bile, and phlegmatic humor; also, expectorant, diuretic, emmenagogue, and alexipharmic properties are ascribed to it. Used as a plaster, it is considered to be discutient and is applied to chronic tu mors' of various kinds. Theophrastus mentions two kinds of Adiantum, "white" and "black," used in making hair oil. Greek synonyms for the plant are polytrichon, calitrichon, trichomenis, and ebinotrichon [4].

Morphology of Plant

Adiantum capillus-veneris is a wooden herb with a height of about 35 centimeters, with a crowning rhizome [5]. It is glabrous and shiny. It has Bi-pinnate fronds having short and terminal pinnae and many laterals on each side. It is also having cuneate segments which are 1.5-2.5 cm broad. Rounded sinuses of crenation have sori born [4]. It is described in the following manner- Frond 3-4 pinnate, pinnules firm, membranous- chartaceous, glabrous, rarely subrhomboid – acuminate, striated, the superior margin rounded, finely dentate- serrate, fertile lobes with 2 notches or rarely 3 notches each notch sub membranous, stripes, glossy and glabrous. 12. It is plants that possess leaves like coriander but are smaller. Its branches are thin and reddish black. It grows in shady and damp areas near the pounds and walls. [1]. Adiantum capillus-veneris Linn (Table. 1) shows Scientific classification, vernacular names, and local names of the Adiantum capillus-veneris Linn [4][1].

Table 1: Scientific classification, vernacular names, and local names of the Adiantum capillus-veneris *Linn*.

Scientific Classification	Local names	Verniculars name
Kingdom: Plantae	Hindi:Hansraj, Kalujhap	Arabic: Kuzburat-el bir, Shaar-ul-jibal, Shaarul-arz
Division: Pteridophyta	Marathi:Mubaraka	English: Maidenhair fern, Lady's hair
Class: Pteridopsida	Gujarati: Hanspadi	Persian:Paresiyan- washan,
Order: Pteridales	Kannada: Hansraj	
Family: Adiantaceae	Sanskrit: Hanspadi	
Sub Family: Adiantaceae	Tamil: Seruppadai	India: Adiantum capillusveneris L
Synonym: Adiantum capillus	Unani :Barsioshan, Kazbaratul Ber	
Genus: Adiantum		
Species: Capillus- veneris Botanical name:capillus-veneris Linn		

Traditional Uses

Numerous Adiantum species were mentioned in traditional literature of Ayurveda and Materia Medica for the treatment of various disease conditions. Adiantum species were used for chest complaints, cough, and cold, as an expectorant, to increase lactation, to aid kidney function, antiparasitic, and dandruff. The fresh or dried leafy fronds were used as, antitussive, antidandruff, demulcent, astringent, emetic, depurative, emollient, febrifuge, weak expectorant, galactagogue, laxative, stimulant, refrigerant, pectoral, and tonic. Moreover, the plant species have been reported for various pharmacological activities and are listed in Tab le no 02 [6]. Thefern is used as a pectoral demulcent, expectorant, emmenagogue, diuretic, and tonic. It is also used as detoxicant in alcoholism and to expel worms from the body. The dried whole plant is used as an antipyretic and diuretic, and also in the treatment of bronchitis in folklore medicine in China. Adiantum capillus-veneris is used asa diuretic, febrifuge, as a hair tonic, in chest diseases, in catarrhal infection, to treat hard tumors in the spleen, antimicrobial and anticancer [5] (Table 2).

Table 2: Biological investigation of plants from Adiantum species

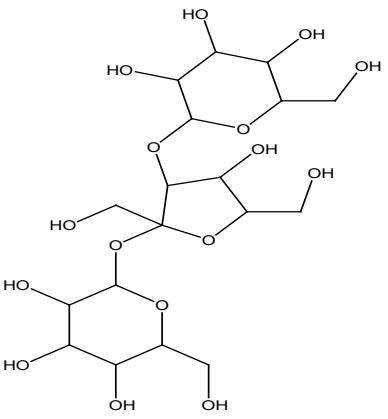
Adiantum species	parts used	Reported activity	References
Adiantum capillus venerisL	Leaves	Antioxidant	Rajurkarand Gaikwad., 2012
Adiantum capillus venerisL	Leaves	Antimicrobial, Antifungal	Hussein et al. [12]
	Stem, root		Saqib Ishaq et al.,
Adiantum capillus veneris L	Leaves	Anti-inflammatory	Haider et al. [17]
Adiantum capillus veneris L	Leaves	Antinociceptive,	Haider et al. [17]
AdiantumIncisumForsk.	Leaves	Hepatotoxicity	Frank et al. [18]
Adiantum capillus veneris L	Leaves	Hypoglycemic Antihyperglycemic	Ibraheim et al. [7]
Adiantum capillus veneris L	Leaves	Diuretic	Aziz and Dizaye.,
Adiantum capillus veneris L	Leaves	Hypocholesterolemic	Al-Hallaq et al. [20]
Adiantum capillus veneris L	Leaves	Hair growth-promoting	Noubarani et al. [21]
Adiantum capillus veneris L	Leaves	Antiobesity	Kasabri et al. [22]
Adiantum capillus veneris L	Leaves	Antiurolithiasic	Ahmed et al. [23]
Adiantum capillus veneris L	Leaves	Goiterogenic, antithyroid	Vijayalakshmi.,

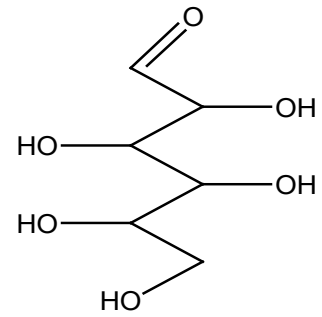
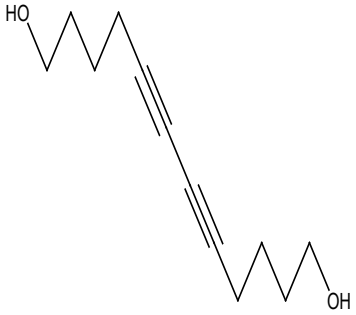
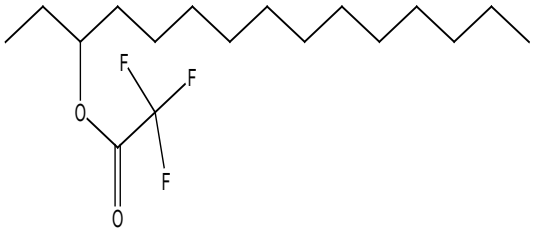
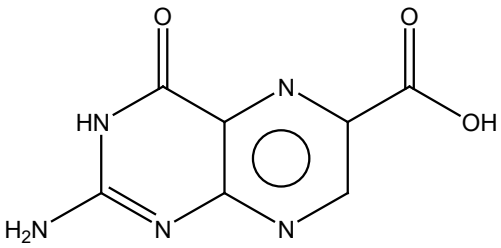
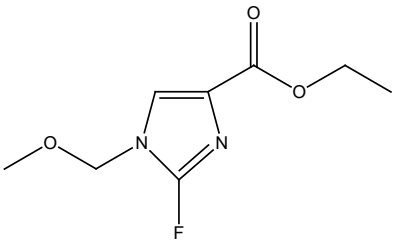
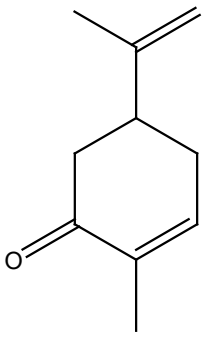
Adiantum capillus veneris L	Leaves	Antidiarrheal, Antispasmodic	Mehmood et al. [10]
Adiantum capillus veneris L	Leaves	Antiasthmatic,	Anbu et al. [25]
Adiantum capillus veneris L	Leaves	Reproductive toxicity	Yousaf et al. [26]
Adiantum capillus veneris L	Leaves	Anticancer	Rautray et al. [27]
Adiantum lunulatumBurm	Whole plant	Antifertility	Sharma et al. [28]
Adiantum incisumforsk	Leaves	Antimicrobial	Parihar et al. [29]
Adiantum incisum	Leaves	Antimicrobial	Parihar et al. [29]
Adiantum lunulatum	Leaves	Antimicrobial	Parihar et al. [29]
Adiantum cuneatum	Leaves	Antimicrobial	M.M. De Souza et al.,
Adiantum peruvianum	Leaves	Antimicrobial	M.Singh et al.,
Adiantum venustum	Leaves	Antimicrobial	M.Singh et al.,
Adiantum caudatum	Leaves	Antimicrobial	M.Singh et al.,
Adiantum venustum	Leaves	Anticancer	Viral et al.,
Adiantum capillus veneris L	Aerial part	cytotoxic	Roy et al.,
Adiantum capillus veneris L	fronds and rhizomes Antidiabetic	Anti Yeast	Sallam et al.,
Adiantum capillus veneris L	Leaves	Antipyretic	Ullah et al. [9]

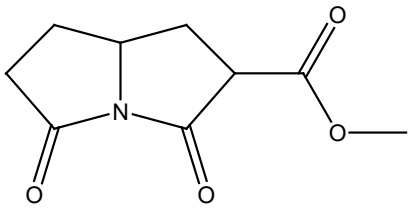
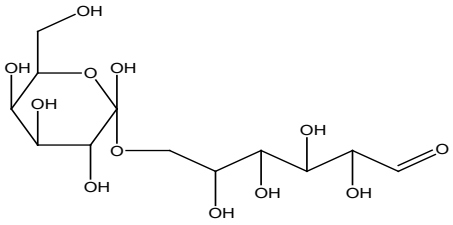
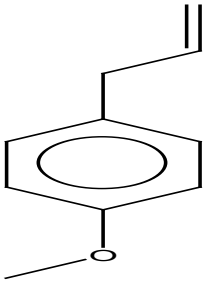
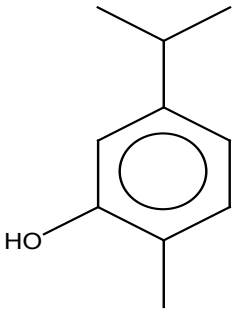
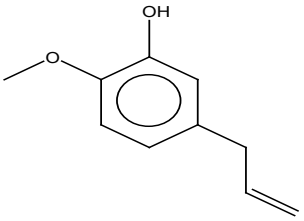
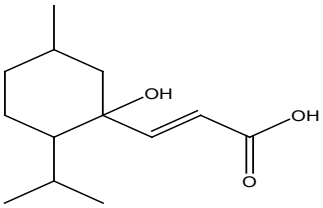
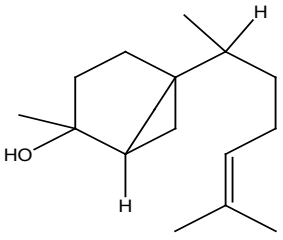
Phytochemical Contents

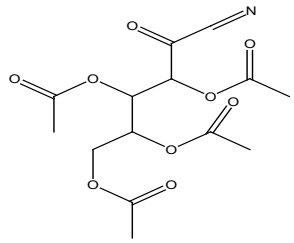
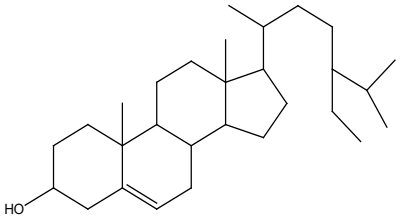
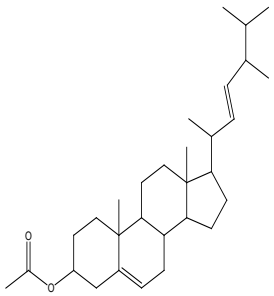
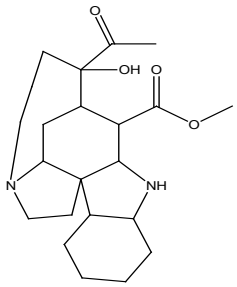
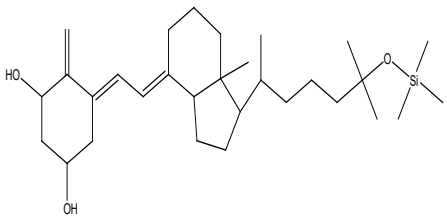
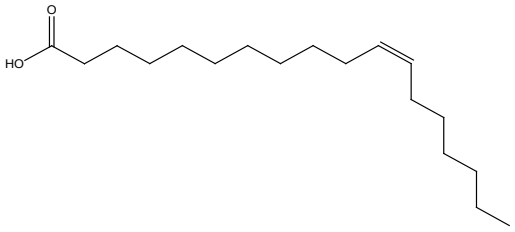
The chemical composite obtainable in plants is called phytochemicals. Phytochemicals constitute one of the most plentiful and broadly distributed groups of substances in the plant kingdom. Performance of phytochemical screening of all extract of leaves, stems, roots of Adiantum capillus veneris L. shows the occurrence of alkaloids, flavonoids, tannins, terpenoids, steroids, glycosides, and reducing sugars which is resemble with other global studies carried out. an additional instrumental study with FTIR shows the presence of compounds like carboxylic acid, aldehyde, amides, ether, ketones, etc [5]. Around 85 Triterpenoids have been estimated from genus Adiantum andphytochemical investigations have revealed that the Triterpenoids, belonging to the hopane, norhopane, neohopane, adiane, fernane, and filicane series, form the main phytochemical groupto which the compounds isolated from Adiantum species [7][8]. Chemical analysis of Adiantum species also has Quercetin, Flavonoids, kaempferol and their glycosides are the most common flavonols of this genus. Quercetin 3-O-(6”-malonyl)-D- rutin, galactoside, isoquercetin, kaempferol 3-glucuronide, querciturone, kaempferol 3-sulphate, astragal in, nicotiflorin, kaempferol 3,7diglucoside, and kaempferol 3-O-rutinoside sulfate were isolated from Adiantum capillus-veneris L Phenyl propanoids, 1-p-coumarylglucose 6-sulphate, lcaffeylglucose 3-sulphate, l-p-coumarylglucose 2-sulphate,1-caffeylgalactose 6-sulphate and 1-caffeylglucose were isolated from Adiantum capillus veneris L[1]. Four sulphate esters of hydroxycinnamic acid-sugar derivatives were isolated from the fronds of Adiantum capillus-veneris. L. These compounds are 1-p-coumarylglucose 6-sulphate, 1-p-coumarylglucose 2- sulphate, 1-caffeylgalactose 3-sulphate, and 1- caffeylgalactose 6-sulphate. The leaves of Adiantum capillus-veneris was reported to contain different flavonoids like rutin, quercetin, quercetin-3-O-glucoside, querciturone, isoquercitrin, nicotiflorin, naringin, populnin, procyanidin, prodelphinidin, and kaempferol-3-sulfate [9]. Alicyclic acids, shikimic acid and quinic acid, and steroids containing b-Sitosterol were isolated from Adiantum capillus-veneris [8] (Table 3).

Table 3: SStructures of some phytochemicals of *Adiantum capillus veneris L.* (Hussein et al 2016).

Phytochemical Name	Structure
α-D-Glucopyranoside O-α-D-glucopyranosyl (1-fwdarw3)-D-fruc	

d-Mannose	
5,7-Dodecadiyn-1,12-diol	
3-Triflouoracetox pentadecane	
Pterin-6-carboxylic acid	
Imidazole-4-carboxylic acid ,2-fluo-ro-1-methoxymethyl-,ethyl ester	
D-Carvone	

Pyrrolizin-1,7-dione-6-carboxylic acid , methyl (ester)	
D-Glucose ,6-O-α-D-galactopyranosyl	
Estragole	
Phenol,2-methyl-5-(1-methylethyl)	
3-Allyl-6-methoxyphenol	
Ppropiolic acid , 3-(1-hydroxy-2-isopropyl-5-methylcyclohexyl)-	
7-epi-trans-sesquisabinene hydrate	

Tetraacetyl-d-xylonic nitrile	
y-Sitosterol	
Ergosta-5,22-dien-3-ol, acetate , (3ß,22E)-	
Curan-17-oic acid ,2,16-didehydro-20-hydroxy-19-oxo,methyl ester	
9,10-Secocholesta -5,7,10(19)-triene-1,3-diol,25-[(trimethylsilyl)oxy	
Cis-Vaccenic acid	

Pharmacological Properties

Antioxidant activity

Medicinal plants are recognized as sources of natural antioxidants that can protect the biological system from oxidative stress. In this study, the antioxidative potential of different solvent extracts (water, methanol, and ethanol) of plant Adiantum capillus veneris L. were evaluated using different in vitro methods. The antioxidant activity of Adiantum capillus veneris L. Leaves was observed by various methods like DPPH, assays showed that its antioxidant activity was close to that of standard Ascorbic acid. The DPPH free radical scavenging activity of Adiantum capillus veneris L. leaves

extracts were found results obtained for samples were compared with that of standard (Ascorbic acid) and control (Rutin). The antioxidant activity was expressed as an effective concentration at 50% Ethanol extract, with an IC50 value of 0.3986mg/gm, showed particularly high free-radical scavenging activity, close to the activity of standard i.e. ascorbic acid (0.2969 mg/gm) and control i.e. rutin (0.3253 mg/gm). The aqueous extract showed approximately four times lower activity with IC50 of 1.448 mg/gm. The results suggested that the ethanol extract exhibited a goodantioxidant activity i.e. 66.61% with less IC50 value than other extracts [10].

Antimicrobial and Antifungal Activity

The antibacterial activity of Adiantum capillus veneris L. extracts was screened byagar-well diffusion method by using Streptomycin; Rifampin; Kanamycin; Cefotoxime and chloramphenicol are standard antibiotics and Methanol as control. The antibacterial activity of methanolic extracts carried out against five bacteria namely, (Bacillus subtilis, Pseudomonas eurogenosa, Streptococcus faecalis, Salmonella typhi, and Staphylococcus aureus, and antifungal activity of the extract was carried out against fourteen fungi and yeast Aspergillus niger, Aspergillus terreus, Aspergillus flavus, Aspergillus fumigatus, Candida albicans, Saccharomyces cerevisiae, Fusarium sp., Microsporumcanis, Streptococcus faecalis, Mucor sp., Penicillium expansum, Trichoderma viride, Trichoderma horzianum, and Trichophyton mentagrophytesby using Fluconazole and Amphotericin B as standard antifungal agent and methanol as control. antifungal activity of Adiantum capillus-veneris was highly active against Aspergillus terreus (7.09±0.32). The zones of inhibition were compared with different standard antibiotics. The diameters of inhibition zones ranged from 3.07±0.21 to 7.09±0.32 mm for all treatments. The extract showed remarkable inhibition of zone for bacterial and fungal growth and the result obtained was compared with that of standards drugs against the tested organisms [5].

Anti-inflammatory activity

The leaves extract of Adiantum capillus veneris L. Was screened for anti-inflammatory using carrageenan-induced rat paw oedema test on albino Wistar rats of either sex (150–200 g). The animals were divided into six groups of six in each. The standard drug Indomethacin (20 mg/kg PO) was given orally as a positive control. The control group was administered orally with 0.9% of 0.1 mL of saline solution only. The test groups were administered orally with the ethanolic extract and its various fractions at the dosages of 200 and 300 mg/kg body weight, one hour before the administration of carrageenan. All the extracts have shown optimal anti-edema activity at 300 mg/kg dosages. However, they exhibited moderate anti-edema activity at a dosageof 200 mg/kg. Amongst these fractions ethyl acetate fraction produced significant inhibition of paw edema at 300 mg/kg dosage as its p-value is extremely significant ($p < 0.001$) at the end of 3 h with inhibition of 67.27% as compared to the standard drug Indomethacin (63.63%) [11].

Antinociceptive activity

The leaves extract of Adiantum capillus veneris L. was screened for anti-nociceptive activities using the Tail immersion method on albino Wistar rats of either sex (150–200 g). The animals were divided into six groups of six in each. Before the experiment, the animals were screened for the sensitivity test by immersing the tail of the rats gently in hot water maintained at 55 ◦C. The animals flicking their tail from hot water in 5 s were selected for the study to avoid any thermal injury to the tail. The selected rats were then divided into six groups of six rats each. The control group was administered orally with 0.9% of 0.1 mL of saline solution only. The standard drug, i.e. ibuprofen was given orally at a dose of 20 mg/kg body weight. The ethanolic extract and its various fractions were given orally at a dose of 300 mg/kg. All the fractions show optimal anti-edema activity at 300 mg/kg dosage, the same dosage is used for analgesic studies. The results of analgesic studies revealed that the ethylacetate fraction (3.48±0.27 min, $p < 0.01$) showed significant analgesic activity after 120 min. The petroleum ether fraction exhibited moderate analgesic (3.19±0.26 min, $p < 0.05$) effect along with methanolic fraction (3.23±0.35 min, $p < 0.05$) and ethanolic extract(3.22±0.41 min, $p < 0.05$) respectively, after 120 min. The ethyl acetate fraction showed significant protection (47.8%, $p < 0.001$) as compared to ibuprofen (47.6%, $p < 0.001$) [11].

Hypoglycemic effects

The alcoholic extract of fronds of Adiantum capillus veneris L. was screened for hypoglycemic activity on Adult male mice (25–30 g) by using the glucose oxidase method. Sixty-six mice were divided into 11groups (six mice, each). The animals were kept for7 days with a 12 h light/dark cycle. Fasted mice (18 h) were divided into three groups of six animals each. Group I (control group) received vehicle (2%PEG-400), while group II received the total alcoholic extract at dose 400 mg/kg body weight via stomach tube. Group III received glipizide at dose 8 mg/kg body weight as a reference standard drug. Blood samples were withdrawn from the cavernoussinus with a capillary tube and the blood glucose levels were estimated (mg/dl) at 0.0, 30, 60, 90, 120, and 150 minusing a one-touch glucometer. The hypoglycemic study of the total alcoholic extract showed significant activity [2].

Antihyperglycemic activity (OGTT)

The alcoholic extract of fronds (leaves) of Adiantum capillus veneris L. was screened for hypoglycemic activity on healthy rabbits (1.2–1.5 kg) by using the glucose oxidase method. nine rabbits were used divided into3 groups (three rabbits, each). The overnight fasted rabbits were divided into three groups of three animals each. Group I was given glucose solution (2.25 g/kg body weight) orally using a stomach tube, the total alcoholic extract (600 mg/kg) was administered simultaneously (groupII) and 30 min before glucose loading (group III). Blood samples were collected from the

ear vein at zero time and after 30, 60, 120, and 240 min. after the glucose administration. The OGTT using the rabbit model showed a significant hypoglycemic effect started after 30 min for group II and continued for 4 hours; this effect may be due to the non-insulin mechanism. When the alcoholic extract was given 30 min before glucose loading, a significant decrease in blood glucose level was observed after 30 min of glucose loading which may be due to enhancing insulin secretion from b-cells. The hypoglycemic effects of the alcoholic extract may be due to the presence of flavonoids which are known for their hypoglycemic [2].

Diuretic activity

The Diuretic activity of Adiantum capillus veneris Linn was evaluated on healthy albino female Wistar strain rats weighing190–240 gm by using hypertensive rats. Hypertension was induced through oral administration of 40 mg/kg/day of NG-nitro-Largininemethyl ester (L-NAME) for 21 days. By the end of this period, a significant increase in blood pressure was observed. A CODA tail-cuff monitor (Kent Scientific, USA) was used to measure systolic pressure and heart rate at weekly intervals. The experiment was conducted in eight groups of six rats; each group. Group I: Normal rats served as a negative control; they were given a placebo (distilled water).Group II: Normal rats treated with AC(100mg/kg/day).Group III: Hypertensive rats served as a positive control; they were given a placebo (distilled water).Group IV: Hypertensive rats received AC aqueous extract (100mg/kg/day).Group V: Hypertensive rats received chlorthalidone CLTD (5 mg/kg).Group VI: Hypertensive rats received 24mg/kg of a flavonoid compound extracted from AC. Group VII: Hypertensive rats received 4mg/kg of an alkaloid compound extracted from AC. Group VII: Hypertensive rats received 30mg/kg of phenolics extracted from AC. The subjects' glomerular filtration rate, urea and creatinine levels, and serum electrolyte concentration and excretion rates were measured. The results were then compared with the results of the standard antihypertensive drug chlorthalidone. Aqueous extract of AC reduced blood pressure andinduced a significant increase in urine flow and the Na+ excretion rate in both normal and hypertensive rats. Constituents apart from flavonoids, alkaloids, or phenolics could be responsible for this effect. Flavonoids, alkaloids, and phenolics extracted from AC produced a decline in serum urea and creatinine [12].

Hypocholesterolemic Effect

The aqueous extract of the hypocholesterolemic effectof Adiantum capillus veneris Linn was evaluated on healthy on locally inbred male Wistar rats of 212.5 ± 1.9 g average body weight (b.wt) was used in the experiments. Rats were divided into4 groups (n=6). Group 1: The negative control group was given only the control diet ad libitum for 10 weeks. Group 2: The hypercholesterolemic control group was given the control diet ad libitum and a high cholesterol diet (HCD)once daily for 10 weeks. Group 3: The treatment group was given the control diet adlibitum and HCD once daily for 10 weeks, while A. capillaveneris500 mg /Kg b.wt was fed in the last four weeks once daily for the last 4 weeks (week 7-10).Group 4: The positive control group was given the control dietad libitum and HCD once daily for 10 weeks. To this group, atorvastatin (10 mg/kg) was administered once daily for the 4weeks (weeks 7-10). Atorvastatin was administered to rats daily at 5:00- 6:00 pm. The median lethal dose was determined on locally inbred mice (Mus musculus) of both sexes with average body weight (b.wt) of 24.25 ± 1.59 g were used for the determination of LD50 of water extract. Mice of both sexes were divided into 2 groups each of 4 mice (2 males and2 females). Group1 served as a control (untreated, given only distilled water), group 2 was given the aqueous extract. Mice have fasted overnight before treatment and they were observed for lethality throughout 24 hrs and the following 7 days. For the determination of LD50, a single dose of1 ml/mouse was administered orally. The highest dose administered was 8g/Kg b.wt (no infusion could be prepared in higher concentration with the plant material), no fatalities were encountered. Accordingly, 500 mg/Kg (equivalent to6%) of the highest prepared dose was selected; lethality was observed neither after 24hrs nor after one week. Moreover, all animals exhibited normal behavior. At the end of day 7, animals were sacrificed; macroscopically gross anatomy and blood biochemistry were performed. Blood was collected in heparinized capillary tubes from all mice of groups 1 and 2 for the determination of red blood cells (RBC), white blood cells (WBC), and hemoglobin (Hb). RBC and WBC were counted manually using the Neubauer counting chamber, while Hb was determined according to the Sahli method. In brief, HCL, 0.1 N, is placed in the graduated tub eof the Sahli outfit, 20 µl of blood is added to yield acid hematin. HCL was added dropwise until the color of thetube corresponds exactly to the color of the standard. Readings from the graduated tube are multiplied by 17.3, the Sahli standard. It was found that the median lethal dose (LD50) blood parameters were within the normal range compared to the untreated animals. No organ abnormalities were observed. Accordingly, it was decided to continue the chronic study with a dose of 500 mg/Kg. b.wt based on its safety profile. This selected dose corresponds to 35 g of the plant material/ 70 Kgb.wt (average human b.wt).This represents approximately a handful of plant material used inthe traditional medicine for the preparation of herbal remedies Exceeding atorvastatin 10 mg/Kg b.wt effectiveness ($p<0.05$, n=6 rats/group), 10-week administration of A. capillus veneris extract in HCD-fed rats decreased highlysignificantly the total cholesterol (TC), LDL and VLDL serum levels. VLDL serum levels in both intervention groups weresubstantially ($p<0.001$) and comparably decreased. Neither treatment could affect HDL serum levels. Besides, the atherogenic indexparameter of TC/HDL was normalized in A. capillus veneris-treated rats. A. capillus veneris can be considered as a potential candidate for the management of hypercholesterolemia and its atherosclerotic complications [13].

Hair growth-promoting effects

The ethanol extracts of hair growth-promoting effects of Adiantum capillus-veneris L. was evaluated on albino mice (2 – 3 month) using a testosterone-induced alopecia model. Twenty-six adult male albino mice 2–3 months of age were randomly allocated in five groups of six animals per group (except group E with two mice). The various groups were treated as follows: (A) Testosterone solution only; (B) Testosterone + Finasteride solution (2%); (C) Testosterone + vehicle; (D) Testosterone + A. capillus-veneris solution (1%); (E) intact control (without testosterone). Mice in all groups except group E were administered testosterone (1 mg) subcutaneously (SC). Animals of groups B, C and D were also received topical application of finasteride (2%), 0.5 mL vehicle, and A. capillus-veneris solution (1%), respectively, on back skin once a day for 21 days. Hair growth was evaluated by visual observation and histological study of several skin sections via various parameters as follicle density (number of follicles/mm) and anagen/telogen ratio. After 21 days, a patch of diffuse hair loss was seen in animals that received testosterone while animals treated with A. capillus-veneris showed less hair loss as compared to those treated with testosterone only. The follicular density observed in the A. capillus-veneris-treated group was 1.92 ± 0.47, compared to 1.05 ± 0.21 in the testosterone-group and 2.05 ± 0.49 in finasteride-treated animals. Anagen/telogen ratio was significantly affected by A. capillus-veneris, which was 0.92 ± 0.06 as compared with 0.23 ± 0.03 and 1.12 ± 0.06 for testosterone and finasteride-treated groups, respectively. According to visual observation and quantitative data (follicular density and anagen/telogen ratio), A. capillus-veneris was found to possess good activity against testosterone-induced alopecia (Noubarani et al., 2013)

Antiobesity effects

The aerial parts ethanolic extract of Adiantum capillus veneris L. was screened for antiobesity effects. In vitro, enzymatic starch digestion was assayed with acarbose as the reference drug. The extent of polysaccharide breakdown into glucose was evaluated in a concentration range of different parts of plant AE 1, 5, 10, 12.5, 25, 50, and100 mg/mL. The chlorogenic acid tested concentration gradient was 0.0625, 0.125, 0.25, 0.5, 1 and 2 mg/mL. The effects of acarbose at 1000 lg/mL concentration were evaluated as well. Control (tap water only) samples did not contain acarbose, plant extract, or chlorogenic acid.PL inhibition is one of the most widely studied mechanisms to determine the potential efficacy of natural products and ethnomedicinal botanicals as obesity modulating agents. In this study, the pancreatic triacylglycerol anti-lipase activity profiles of the crude AEs of A. capillus-veneris and its bioactive phytoconstituents (chlorogenic acid, ellagic acid, and ferulic acid). These significant anti-lipase effects may be solidly related to the effect of the major compounds identified in the crude extract. Its contents of rutin and quercetin were recognized for their in vitro antilipolytic properties. In effect, the results indicate that the pancreatic triacylglycerol lipase (PL) inhibitory efficacy of A. capillus-veneris may be attributable to its multiple components acting additively or synergistically in an optimal ratio. In vitro glucose movement was assayed. To imitate the viscosity-based diffusion hindrance of gel-forming dietary fibers, and hence, their postprandial glucose-lowering efficacies in vitro, guar gum 50 mg/mL were used asa classical positive control, and 10, 25, and 50 mg/mL of A. capillus-veneris AEs in 0.22 M glucose in triplicates were dialyzed against 0.15 M NaCl overnight at 37 _C with gentle shaking and a parallel plant-free (negative) control was included. Like acarbose, A. capillus-veneris as well as chlorogenic acid, with respective IC50 values (mg/mL) of 0.8 ± 0.0 and 0.2 ± 0.0, were identified as in vitro potent dual inhibitors of a-amylase/a-glucosidase. Unlike guar gum, A. capillus-veneris had no glucose diffusion hindrance capacity. Equivalent to orlistat, A. capillus-veneris and its phytoconstituents inhibited PL in vitro with an ascending order of PL- IC50 values (lg/mL): ferulic acid; 0.48 ± 0.06<ellagic acid; 13.53 ± 1.83<chlorogenic acid; 38.4 ± 2.8<A. capillus-veneris; 1600 ± 100.A. capillus-veneris bioactive Phyto-principle exerted highly significant concentration dependent inhibitions of polymeric starch enzymatic digestion. Adiantum capillus veneris L. exerted significant antiobesity effect [14].

Antiurolithiasic effect

The antiurolithiasic effect of the hydroalcoholic extract of Adiantum capillus veneris Linn was investigated on ethylene glycol and ammonium chloride-induced calcium oxalate urolithiasis, in male Sprague Dawley rats weighing 180–210 g. Plain control rats were treated with distilled water only, throughout the study period, whereas in other groups nephrolithiasis was induced by providing drinking water containing 0.75% ethylene glycol and 1% ammonium chloride for 7 days. The hydroalcoholic extract (127.6 mg/kg and 255.2 mg/kg) was administered orally for 21 days. Cystone (750 mg/kg) was used as a standard control for 21 days. At the end of the experiment, several crystals in urine and levels of calcium, phosphorus, urea, and creatinine in serum were observed. Histopathological study of the kidney was done by light microscopy. It was observed that calcium oxalate stones were formed in urine in good quantity and the size of the stone was also large, which almost dissolved after the administration of the test drug. It indicated that the test drug broke the calcium particle into subtle constituents that were not visible or prevented the aggregation and thereby the formation of stones. Also, there was a remarkable reduction in serum creatinine. Histopathology of the kidney showed almost normal kidney architecture intreated groups. The findings thus demonstrated that Adiantum capillus-veneris produced significant lithotriptic activity [15].

Goiterogenic and antithyroid activity

The Goiterogenic and antithyroid activity of the ethanolic extract of Adiantum capillus veneris Linn was investigated on thyroid dysfunction hypothyroidism. Hypothyroidism was induced

in animals by propylthiouracil administration, as the compound prevents the transformation of iodides to iodine and in consequence, prevents the formation of T3 into T4. In PTU (propylthiouracil) induced hypothyroidism. The thyroid peroxidase activity, serum T4 and T3 levels were increased significantly in animals treated with the ethanol plantextract (500 mg/kg) while a decrease in the level of thyroid-stimulating hormone and reversal of the thiouracil-induced increase in thyroid weight (goiter)suggesting its thyroid hormone enhancing effect and anti-goitrogenic effect. The results of Adiantum capillus-veneris L could be used in the regulation of hypothyroidism. However, there is a need to test lower doses of the extract for evaluating their actual anti-goitrogenic potential [16].

Antidiarrheal and Antispasmodic activity

The antidiarrheal and Antispasmodic activity of leaves extract of Adiantum capillus veneris Linn was examined in vivo and Invitro assay. The myorelaxant effect of the crude extract of A. capillus-veneris L. was assessed on spontaneously contracting isolated rabbit jejunum. For clarification of the possible mechanism of spasmolytic effect, low K+ (25 mM) and high K+ (80 mM) were used to depolarize the isolated tissues which in turn produced sustained contractions,which are considered useful for determining the different inhibitory mechanisms like, K+ channels activation or Ca++channel blockade, respectively. Oral administration of the crude extract of Adiantum capillus veneris exhibited dose-dependent inhibitory effect against castor oil-induced diarrhea in mice by producing40 and 60% protection at respective doses of 300and 500 mg/kg. The positive control of loperamidecaused 100% protection at the dose of 10 mg/kg, whilethe group-administered only saline and castor oil showed no protection against diarrhea. Similarly to the activity pattern of cromakalim, an ATP-dependent K+ channel opener. Interestingly, its inhibitory effect on spontaneous contractions was potentiated in the presence of atropine. Adiantum capillus veneris L. possesses antidiarrheal and antispasmodic properties mediated possibly through ATP-dependent K+ channels activation, thus providing a scientific basis to its folk use in abdominal colic and diarrhea [17].

Antiasthmatic activity

The antiasthmatic activity of leaves ethanolic extract of Adiantum capillus veneris Linn was evaluated. Experimental bronchial asthma was induced in guinea pigs by exposing them to histamine. Overnight fasted guinea pigs of either sex (350-450) were selected and randomly divided into five groups each consisting of six animals. Group I was treated as control, Animals belonging to groups IV, V were administered Adiantum capillus veneris L. ethanolic extract in dose (250,500 mg/kg). All the doses were given orally. Before drug treatment, each guinea pigs were exposed to an atomized fine mist of 2% w/v histamine dihydrochloride aerosol (dissolved in normal saline) using a nebulizer in the histamine chamber. Guinea pigs exposed to histamine aerosol showed progressive signs of difficulty in breathing leading to convulsions, asphyxia, and death. The time until signs of convulsion appeared is called pre-convulsion time (PCT) and was determined from the time of exposure to onset of convulsions. Histamine induced bronchoconstriction is the traditional immunological model of antigen-induced airway obstruction. Histamine when inhaled causes hypoxia and leads to convulsion in the guinea pigs and causes very strong smooth muscle contraction, profound hypotension, and capillary dilation in the cardiovascular system. A prominent effect caused by histamine is severe bronchoconstriction in the guinea pigs that causes asphyxia and death. Histamine was released after degranulation of mast cells by an antigen exposure by antigenic stimulation causing smooth muscle contraction, increased vascular permeability, and mucus formation. In vivo study of ethanolic extract, Adiantum capillus (EEAC) have been also shown a significant increase in pre-convulsion time at the dose of 250 and 500 m/kg of body weight of guinea pigs, when the guinea pigs were exposed to histamine. The results of ethanolic extract Adiantum capillus (EEAC) suggested that it is effective in reducing the symptoms of bronchial asthma and also improves the lung function parameters of asthmatic subjects.

Reproductive toxicity

The reproductive toxicity of leaves aqueous extract of Adiantum capillus veneris Linn was examined on testicular toxicity induced by bisphenol A. Twentyfive adult male albino rats (6–8 weeks) with an average weight of 180.39± 0.69 g were used. Adult male albino rats were divided into five groups of five animals each: A (control), B (vehicle control), C (toxic), D (protective), and E (ameliorative) were served distilled water, olive oil, bisphenol A (BPA) at 100 mg/kg body weight, A. capillus veneris plant extract at 25 mg/kg body weight, and BPA + Adiantum capillus-veneris L, respectively. All of the doses were administered orally for 15 days, and the rats were then sacrificed. Blood samples for the testosterone assay and both testes were collected for histological examination. The body weight, paired testes weight, relative tissue weight index, Johnsen. scoring of tubules and the level of serum testosterone decreased in BPA-treated rats. Similarly, histological examination of the testes in BPA-treated animals revealed a lower number of Leydig cells, an irregular basement membrane, sloughing of germinal layers, vacuolization, a lower number of spermatocytes, and debris in the lumen. However, co-administration of A. capillus-veneris with BPA increased the total antioxidative capacity (330.82 ± 22.46 µmol/mg protein) of the testes and restored the serum testosterone level (1.70 ng/ml); histological features showed restoration in the stages of spermatogenesis. A. capillus-veneris plant extract overcomes the estrogenic effects of BPA on the reproductive system of rats and protects rats' testes against BPA-induced injury/dama gevia an antioxidative mechanism that appears to be conciliated [18].

Neuropharmacological activities

Neuropharmacological activities of the plant ethanolic extract were evaluated by using various methods. The plant revealed

significant anticonvulsant effect through prolonging the onset of action and reduction in the period of seizures in the PTZ-induced convulsion model, besides by decrease in the time of different phases of seizure through MES-induced seizure method.

Wound Healing

The Wound Healing potential fraction of extract of Adiantum capillus veneris Linn was examined on angiogenesis and proliferation of endothelial cells in vitro. In addition to Invitro test for protection against damage to fibroblasts by oxygen free radicals. The Aerial parts of the aqueous partition of the methanolic extract promoted angiogenic effects through both capillary-like tubular formations and proliferation of endothelial cells in vitro. Besides, in the tests for protection against damage to fibroblasts by oxygen free radicals, aqueous and butanol fractions showed significant protective effects in comparison with a control group with no significant toxicity in the MTT (3-(4,5-Dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide) assays on normal human dermal fibroblasts and with weak irritation in the HET-CAM bioassay at the vascular level on the CAM of the chicken. The consequence suggested that Adiantum capillus-veneris local application for prevention of chronic wounds after radiation therapy and healing of external wounds similar to bedsores and burns [19].

Conclusion

Over the last decades, plants have been recognized as crucial source of medicines. Investigation of phytochemicals derived from different plant parts as a potential bioactive agent has become a fascinating strategy. The present study has been conducted in attempts to focus on multiple aspects of Adiantum capillus veneris L. traditionally it was used to treat several diseases. It contains flavonoids, alkaloids, tannins, saponins, cardiac glycosides, terpenoids, steroids, and reducing sugars, which could be responsible for different therapeutic activities. Phytopharmacological properties indicated that Adiantum capillus veneris L. had a vital ability to manage different disease conditions. The present study ascertains the value of Adiantum capillus veneris L. plant which could be of considerable interest in the development of plant-based new drugs. This review also explores the entire information of Adiantum capillus veneris L. which might be helpful to researchers and scientists working on plant-based bioactive agents.

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