THE CHEMICAL CONSTITUENTS AND PHARMACOLOGICAL EFFECTS OF ADIANTUM CAPILLUS-VENERIS - A REVIEW

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ABSTRACT
The previous studies showed that Adiantum capillus-veneris contained many secondary metabolites and exerted antimicrobial, antiinflammatory, analgesic, hypoglycemic, antioxidant, antilithiasic, antiproliferative, antidermatitis, neuroprotective, anticholesterolemic and many other effects. The present review will highlight the chemical constituents and the pharmacological and therapeutic effects of Adiantum capillus-veneris.

Key words: Adiantum capillus-veneris, pharmacology, chemical constituents.

INTRODUCTION
Herbal medicine is the oldest form of healthcare known to mankind. Herbs had been used by all cultures throughout history. It was an integral part of the development of modern civilization. As time went on, each tribe added the medicinal power of herbs in their area to its knowledgebase. Many drugs commonly used today are of herbal origin. The World Health Organization (WHO) estimates that 80 percent of the world populations presently use herbal medicine for some aspect of primary health care.

Adiantum capillus-veneris was one on the most common species with potential importance for medicinal and nutritive purpose. It contained flavonoids, triterpenoids, aoleananes, phenylpropanoids, carbohydrates, carotenoids, alicyclics and many other chemicals. It exerted antimicrobial, anti-inflammatory, analgesic, hypoglycemic, antioxidant, antilithiasic, antiproliferative, antidermatitis, neuroprotective, anticholesterolemic and many other effects.

Synonyms: Adiantum capillus, A. michelii, A. modestum, A. Schaffneri and A. Tenerum [1]

Common names
Arabic : Kuzburat-el bir, Shaar- ul-jin, Shaar-ul-jibal, Shaar-ul-arz ; Ayurvedic: Hansaaraja, hansapadi; English: Maiden hair fern, Maria’s fern, Our Lady’s hair; Gujarati: Hanspadi; Hindi: Hansraj, Mubarak, Pursha; Kannada: Hansraj, Persian: Sarsiapeshane; Tamil: Seruppadai; Kashmir: Dumtuli; Urdu: Persia- ushan; Unani: Barsioshan, Kazbaratul Ber [1-3].

Taxonomical Classification
Kingdom: Plantae; Division: Pteridophyta; Class: Pteridopsida; Order: Pteridales; Family: Adiantaceae; Genus: Adiantum, Species: Adiantum capillus- veneris [2,4].

Description
Adiantum capillus-veneris is often found growing on limestone cliffs away from direct sunlight and out of the way of drying southwest winds. Stems short-creeping; scales golden brown to medium brown, concolored, iridescent, margins entire or occasionally with single broad tooth near base. Leaves lax-arching or pendent, closely spaced, 15-75 cm. Petiole 0.5-1.5 mm diameter, glabrous, occasionally glaucous. Blade lanceolate, pinnate, 10-45 × 4-15 cm, glabrous, gradually reduced distally; proximal pinnae 3(-4) pinnate; rachis straight to flexuous, glabrous, not glauous. Segment stalks 0.5-3.5 mm, dark color extending into segment base. Ultimate segments various, generally cuneate or fan-shaped to irregularly rhombic (plants in American southwest occasionally with segments nearly round), about as long as broad; base broadly to narrowly cuneate; margins shallowly to deeply lobed, incisions 0.5-7 mm, occasionally ± laciniate, sharply denticulate in sterile segments; apex rounded to acute. Indusia transversely oblong or crescent-shaped, 1-3(-7) mm, glabrous. Spores mostly 40-50 µm diameter [5].

Distribution: It was found throughout the world in moist and shady places. In Europe, it was found in Atlantic coast...

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as far as Ireland [6-8].

Traditional uses

Adiantum capillus-veneris was one on the most common species with potential importance for medicinal and nutritive purpose. Adiantum species were used for chest complaints, cough and cold, as expectorant, to increase lactation, to aid kidney function, antiparasitic and dandruff. The fresh or dried leafy fronds were used as antidiarrhoeal, antitussive, astringent, demulcent, depurative, emetic, weak emmenagogue, emollient, weak expectorant, febrifuge, galactogogue, laxative, pectoral, refrigerant, stimulant, sudorific and tonic. The dried fronds of the plants were used to make a tea for the same purposes [2, 6-8].

Part used

The fresh or dried leafy fronds, dried herb with rhizome and roots were used medicinally [6].

Physicochemical constants

Loss on drying at 105°C: 7.36%, solid contents: 74.48%; ash values (total ash: 7.81%, acid insoluble ash: 4.42%, and water soluble ash: 0.42%); and successive extractive values (petroleum ether: 60-80°C: 4.49%, chloroform: 3.03%, acetone: 4.60%, ethanol: 9.27% and distilled water: 14.07%) [2].

Chemical constituents

Chemical analysis of Adiantum capillus-veneris showed that it contained flavonoids, triterpenoids, aloeananes, phenylpropanoids, carbohydrates, carotenoids, and alicyclics. Many triterpenoids: 21-hydroxy diadontane, triterpenoid epoxide (adiantoxide), Fern-9(11)-en-12-one, isoadiantone, isoglaucanone, hdoxyhopane, isoadiantol, hydroxyadiantone, olean-12-en-3-one, olean-18-en-3-one, fern-9(11)-ene, ferne-7a, 9(11)-diene, 7-ferrene, hop-22(29)-ene, filic-3-ene, nafenop-12-ene, pteron-14-en-7a-ol, fern-9(11)-en- 3a-ol, fern-7-en-3a-ol, adian-5(10)-en-3a-ol, adian-5-en-3a-ol, fern-9(11)-en-28-O, fern-9(11)-en-12- beta-ol and 4-α-hydroxyfulvan-3-one were isolated from the leaves of Adiantum capillus-veneris [9-21]. Four sulphate esters of hydroxycinnamic acid-sugar derivatives were isolated from the fronds of Adiantum capillus-veneris. L. These compounds have been shown to be 1-p-coumarylgucose 6-sulphate, 1-p-coumarylgucose 2-sulphate, 1-caffeylgalactose 3-sulphate, and 1-caffeylgalactose 6-sulphate [22]

The leaves of Adiantum capillus-veneris was reported to contain different flavonoids like rutin, quercetin, quercetin-3-O-glucoside, quercitrone, isoquercitin, nicotiflorin, naringin, astragalin, populin, procyanidin, prodelphinidin, and kaempferol-3-sulfate [23-26]. The total phenolics and total flavonoids in the leaves were 224.76 ± 9.75 and 49.62 ± 0.875 in the aqueous extract, 156.34 ± 9.70 and 78.18 ± 1.741 in the methanolic extract and 36.53 ± 3.65 and 50.15 ± 4.79 mg/100g in the ethanolic extract, respectively [27].

Leaves contained 8.3 % moisture, 11.44 % ethanol extractable matter and 24.00 % water extractable matter. The soxhlet extraction of Adiantum capillus-veneris showed the presence of phenolics and terpenoids (2.73 %), fats and waxes (0.20 %), alkaloids (0.53 %), quaternary and noxides (26.33 %) and fiber (67.23 %). Ten trace elements (Mg, Ca, K, Mn, Fe, Co, Na, Ni, Cu, and Zn) were determined in leaves extracts. Ca and K were found to be at major level [23].

PHARMACOLOGICAL ACTIVITIES

Antimicrobial activity

The methanolic extracts of Adiantum capillus-veneris aerial part showed antimicrobial properties in concentrations between 0.5-2 mg/ml of the extract against Bacillus, E. coli, Staphylococcus, Proteus, Pseudomonas, and Candida [28]. The methanolic extract of Adiantum capillus-veneris was also tested for its antimicrobial activity against five Grams positive (including multi-resistant Staphylococcus aureus), six Grams negative bacteria and against eight fungal strains. The extract showed broad antibacterial activity and a very low minimum inhibitory concentration value (0.48 mg/ml) against Escherichia coli [29]. The aqueous and alcoholic leaves extract of Adiantum capillus-veneris were found to be effective against Agrobacterium tumefaciens, Escherichia coli, Salmonella arizonae, Salmonella typhi and Staphylococcus aureus bacterial strains [30]. The water extracts and extracted phenols from gametophytes of Adiantum capillus-veneris showed antifungal activity against Aspergillus niger and Rhizopus stolonifer [31]. Ethanol extract from the rhizome of Adiantum capillus-veneris exerted in vitro antiviral activity against vesicular stomatitis virus [32].

Anti-inflammatory and analgesic effects

Alcoholic extract of Adiantum capillus-veneris and its hexane fraction exerted significant anti-inflammatory activity against formalin induced inflammation. The hexane fraction showed topical anti-inflammatory activity after 6h and continued for 30h in croton oil- induced inflammation. The ethyl acetate fraction of the ethanolic extract of Adiantum capillus-veneris showed significant inhibition of hind paw edema induced by carrageenan. The chronic anti-inflammatory activity of the ethanol extract was also evaluated by carrageen-induced paw edema method. The results, at the two dose levels tested in rats, indicate significant anti-inflammatory activity. The maximum inhibition of inflammation (71.15 %) was recorded with 100 mg/kg of plant extract. The analgesic activity of the ethanol extract of Adiantum capillus-veneris and its fraction carried out by tail flick method and writhing test, the result showed significant analgesic activity with insignificant gastric ulceration as compared to the standard anti-inflammatory analgesic antipyretic drugs [26, 33-34].
The anti-inflammatory and anti-nociceptive activities of the crude ethanolic extract of *Adiantum capillus veneris* and its various fractions was studied using carrageenan induced hind paw edema, tail-flick method and writhing test at a dosage of 300 mg/kg po. Gastric ulceration studies have been further carried out for the ethanolic extract and its various fractions at dose of 900 mg/kg body weight. Amongst the tested fractions, the ethyl acetate fraction exhibited better anti-inflammatory effect (67.27%) at 300 mg/kg po dosage when compared to the standard drug, indomethacin (63.63%) after 3h in the carrageenan induced hind paw edema. The anti-inflammatory activity of the ethanolic extract and its various fractions appear to be related to the inhibition of NO release, and the decreasing TNF-α level. The ethanolic extract and all its fractions especially the ethyl acetate (p<0.01) showed significant analgesic activity with insignificant ulceration as compared to the standard drug, ibuprofen. The histopathological study of the effect of ethanolic extract and its fractions in the stomach, reveals that none of them cause ulcer [33].

The anti-inflammatory effect of ethanolic extracts of *Adiantum capillus veneris* and the involvement of NF-κB signaling in the regulation of inflammation was studied. The plant ethanolic extracts effectively suppressed PGE2, IL-6 and TNFα release with an IC50 less than 50μg/ml. Moreover, luciferase expression could be specifically blocked in HepG2 cells, showing that the plant extracts displayed a cell-specific pattern on NF-κB gene transcription. The assayed biological activity also depended on the order of adding TNF-α and the plant extracts because the plant extracts could only block the NF-κB activation if added earlier but were unable to stop the signal when added after TNF-α. However, the plant extracts did not exert any effect on ubiquitination which regulates several steps in the NF-κB pathway. Additionally, the plant extracts down-regulated phosphorylation of IKKα/β at S176/180, p38 at T180/Y182 and p65 at S536, but not p65 at S276. This was confirmed by their ability to selectively abrogate the induction of IL-8 transcription, whereas the ICAM-1 gene, which is not transcribed selectively by an NF-κB complex containing a form of p65 phosphorylated on Ser536, did not change. Finally, the plant extracts at 200 μg/mg could normalize the LPS-induced elevation of spleen index as well as NF-κB and p38 activations in CD1 mice [35].

**Hypoglycemic activity**

When the total extract of the plant prepared by boiling the dried material with water was given to mice (25 mg/kg) orally, it reduced glucose-induced hyperglycemia. However, the extract of the plant prepared by maceration with 80% ethanol, showed no hypoglycemic activity when given to mice in a dose of (25 mg/kg) orally [36]. The alcoholic extract of *Adiantum capillus-veneris* showed significant hypoglycaemic effect in rabbit model, started after 30 min of administration of the extract and continued for 4 hours [26]. El-Tantawy et al., recorded the anti-diabetic and diuretic effects of the alcohol and aqueous extracts of *Adiantum capillus-veneris* as well as its isolated mucilage [37].

**Antioxidant activity**

Antioxidant potential of leaf extract of *Adiantum capillus-veneris* was studied in vitro against H2O2 induced oxidative damage in peripheral blood lymphocytes. Pretreatment with plant leave extract for 18 hours inhibited lipid peroxidation and enhanced the activities of antioxidant enzymes and glutathione content significantly. The results attributed to its direct potential in scavenging free radicals and modulating the antioxidant defense system. Total flavonoids from *Adiantum capillus-veneris* showed high scavenging activity on hydroxyl radicals [38-39].

Ethanol extract showed good antioxidant activity as compared to ascorbic acid, it exhibits low IC50 value, 0.3986 mg/gm for DPPH assay and 0.695 mg/gm for ABTS assay. The results obtained indicated that *Adiantum capillus-veneris* leaves were endowed with free radical scavenging molecules and it can be used as a potential source of natural antioxidants and nutrients [27].

**Antilithiastic activity**

In vitro antilithiastic activity of hydroalcoholic extract of *Adiantum capillus-veneris* was evaluated by crystallization, aggregation and nucleation assays. The result showed that the extract was significantly inhibited crystallization and aggregation which was further confirmed by in vivo study against ethylene glycol (0.75%) and ammonium chloride (1%) induced urolithiasis in male Sprague Dawley rats. Urine microscopy showed significant reduction in the number of crystals in test groups [40].

The antilithiastic effect of the hydroalcoholic extract of *Adiantum capillus-veneris* was also evaluated in male rats. Urine microscopy showed significant reduction (p<0.001) in the number of crystals. Serum levels of calcium, phosphorous, and blood urea were found to be decreased significantly. Serum creatinine level was found to be similar to plain control. The animals treated with test drug showed much improvement in body weight. Histopathology of kidney showed almost normal kidney architecture in treated groups [41].

**Hair growth-promoting effect**

The hair growth-promoting activity of a preparation of the *Adiantum capillus-veneris* was evaluated on albino mice using a testosterone-induced alopecia model. *Adiantum capillus-veneris* solution was applied topically to the back skin of animals and 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 received testosterone while animals treated with *Adiantum capillus-
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**veneris** showed less hair loss as compared to those treated with testosterone only. The follicular density observed in the Adiantum capillus–veneris -treated group was 1.92 ± 0.47, compared to 1.05 ± 0.21 in testosterone-group and 2.05 ± 0.49 (follicles/mm) in finasteride-treated animals. Anagen/telogen ratio was significantly affected by Adiantum 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 [42].

**Other pharmacological activities of the plant constituents**

The compounds isolated from the plant showed many pharmacological effects. Astragalin exerted antiproliferative activity. It inhibited human mesangial cell proliferation and matrix over-synthesis possibly through decreasing beta-1-integrin gene over-expression. These effects may prevent the progression of chronic renal disease. It also exerted antidermatitis activity. It reduced the severity of pre-existing dermatitis and prevented the development of atopic dermatitis. Shikimic acid act as neuroprotective. It reduced focal cerebral ischemic injury induced by middle cerebral artery thrombosis. Rutin exerted anticholesterolemic. It reduced total cholesterol, LDL, VLDL and triglycerides with no reduction in HDL. It also exerted gastroprotective effects. It protected against reflux oesophagitis by inhibiting gastric acid secretion, oxidative stress, inflammatory cytokine production and intracellular calcium mobilization. Naringin showed antioxidant effects. It increased hepatic superoxide dismutase and catalase activity, decreased hepatic mitochondrial hydrogen peroxide and increased plasma vitamin E concentration. It also exerted anticholesterolemic by lowering plasma cholesterol and triglyceride concentrations as well as HMG-CoA reductase activity. Naringin also had DNA protecting effect, so it protected mouse bone marrow cells against gamma radiation induced DNA damage [43-49].

**Adverse reactions and contraindications**

No health hazards or side effects are known in conjunction with the proper administration of designated therapeutic dosages [49]. However, it was documented that the plant lowered blood sugar levels in animal studies. People with diabetes and people with hypoglycemia should use this plant with caution and monitor their blood sugar levels accordingly. The plant has a long history of use in herbal medicine systems to stimulate the uterus and promote menstruation, therefore, it was contraindicated in pregnancy. The plant has shown to have an anti-implantation effect in animal studies and may prevent conception. Couples seeking fertility treatment or pregnancy should not take the plant. Due to its effect on fertility and menstruation, it may have estrogen-like effects and should probably be avoided by women with estrogen-positive cancers [1].

**Dosage**

The drug is taken internally as a tea prepared from the ground or powdered drug. The standard single dose is 1.5 gm of the drug to 1 cup of liquid [3,50].

**CONCLUSION**

Adiantum capillus-veneris is a plant with wide range of chemical constituents which exerted many pharmacological effects. There is a great promise for development of novel drugs from Adiantum capillus-veneris to treat many human diseases as a result of its effectiveness and safety.
obial activity of some important Adiantum species used traditionally.


50. PDR for Herbal Medicines. Medical Economics Company, Inc. at Montvale, 2000, 491.