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Review Article

Adiantum capillus-veneris. L: Phytochemical Constituents, Traditional Uses and Pharmacological Properties: A Review

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ABSTRACT

Since ancient times, *Adiantum capillus-veneris L* is used as remedies in traditional therapy in Iran. It has always had an important role to play in medicine and public health. *Adiantum capillus-veneris L* of *Adiantaceae* family is one of most common plants that have found diverse medicinal uses in the indigenous systems of medicine. The systematic phytochemical studies on the whole plant material have resulted in the isolation and structure elucidation of many compounds such as triterpenoids, flavonoids, phenylpropanoids, oleananes, alicyclic, and carotenoids. The leaves of plant have pharmacologically been studied for various activities like antibacterial, antiimplantation, antihyperglycemic, hypoglycemic, antiyeast, antiviral activities etc. The present report that reviews the entire investigations done on this plant will possibly help to its effective remedies in traditional therapy, and will be the window for its usage in discovery of new drugs.

Keywords: *Adiantum capillus-veneris. L*; Adiantaceae; Phytochemical constituents; Pharmacological properties

1. INTRODUCTION

From the very beginning of human existence, man has familiarized himself with plants and used them in a variety of ways throughout the ages. In search of food and to scope successfully with human suffering, primitive man began to distinguish those plants suitable for nutritional purpose from others with definitive pharmacological action. This relationship has grown between plants and man, and many plants came to be used as drugs. The growth of knowledge to cure disease continues at an accelerating pace, and number of new plant-derived drugs increases likewise [1]. Herbal drugs or medicinal plants, their extracts and their isolated compound(s) have demonstrated spectrum of biological activities and ethno-pharmacological studies on such herbs/medicinally important plants continue to interest investigators throughout the world [2]. *Adiantum capillus-veneris. L* (Fig.1) is a wooden herb with a height of about 35 centimeters, with crowning rhizome. It grows in south Europe, on the Alps Mountains, on the Atlantic seashore and also in Iran [3]. The synonyms of the plant include *Adiantum capillus, A. michelii, A. modestum, A. schaffneri*, and *A. tenerum*. Its most common names are avenca and maidenhair fern [4]. The plant prefers light (sandy), medium (loamy) and heavy (clay) soils and requires well-drained soil.

The plant prefers neutral and basic (alkaline) soils. It can grow in semi-shade (light woodland). It requires moist soil [5]. Its dried root is indicated as a medicine, and its leaves are used as remedy for some diseases in throughout the world (Table. 1). Despite the plant's ancient history of uses for various diseases, no comprehensive review describing phytochemical constituents, traditional uses and pharmacological properties has been reported on *Adiantum capillus-veneris. L*. The present report that reviews the entire investigations done on this plant will possibly help to its effective remedies in traditional therapy, and will be the window for discovery of new drugs from it.

Fig. 1: Photographs of Adiantum capillus-veneris. L. [4]

2. TRADITIONAL USES

Adiantum capillus-veneris. L. has a long history of medicinal use and was the main ingredient of a popular cough syrup called 'Capillaire', which remained in use until the nineteenth century [6]. The fresh or dried leafy fronds are antidandruff,

Table 1: Traditional uses of Adiantum capillus-veneris. L [4]

Worldwide Ethnomedical Uses	
Amazonia	For blood cleansing, coughs, excessive mucous, menstrual problems, respiratory problems, urinary disorders, urinary insufficiency, and to increase perspiration
Brazil	for asthma, bronchitis, childbirth, cough, digestion, excessive mucous, flu, hair loss, kidney problems, laryngitis, menstrual disorders, respiratory problems, rheumatism, throat (sore) urinary insufficiency, and to stimulate the appetite
Egypt	for asthma, chest colds, cough, edema, flu, hepatitis, snakebite, spider bite, splenetic, urinary insufficiency, and to increase perspiration
England	for asthma, cough, hair loss, jaundice, kidney stones, menstrual disorders, pleurisy, shortness of breath, swellings, urinary insufficiency, yellow jaundice
Europe	for alcoholism, bronchitis, bronchial diseases, cough, dandruff, detoxification, diabetes, excessive mucous, flu, hair loss, menstrual problems and to sooth mucous membrane
India	for boils, bronchial diseases, colds, diabetes, eczema, fever, menstrual problems, skin diseases, wounds
Iraq	for bronchitis, colds, cough, excessive mucous, flu, menstrual disorders, respiratory difficulty, reducing secretions, urinary insufficiency and to increase perspiration
Mexico	for birth control, bladder problems, blood cleansing, constipation, hair loss, kidney stones, liver function, menstrual disorders, respiratory distress
Peru	for asthma, colds, cough, congestion, excessive mucous, flu, gallstones, hair loss, heartburn, hydrophobia, liver problems, menstrual disorders, respiratory problems, sore throat, stomach problems, urinary insufficiency, and to increase perspiration
U.S.	for chills, coughs, excessive mucous, fever, flu, lung problems, menstrual disorders, menstrual pain, respiratory ailments, sclerosis (spleen), sores, urinary insufficiency and to sooth membranes and increase perspiration c

antitussive, astringent, demulcent, depurative, emetic, weakly emmenagogue, emollient, weakly expectorant, febrifuge, galactogogue, laxative, pectoral, refrigerant, stimulant, sudorific and tonic [6-15].

A tea or syrup is used in the treatment of coughs, throat afflictions and bronchitis [15]. It is also used as detoxicant in alcoholism and to expel worms from the body [8, 14]. Externally, it is used as a poultice on snake bites, bee stings etc. [13-16]. In Nepal, a paste made from the fronds is applied to the forehead to relieve headaches and to the chest to relieve chest pains [17]. The plant is best used fresh, though it can also be harvested in the summer and dried for later use [8, 9]. It is effective with female conditions and is used to regulate menstruation, dysmenorrhoea, and facilitate childbirth by speeding up the labor. It seems most effective for young women and those having trouble getting back on cycle after birthing, nursing, or coming off birth control pills [18, 19]. A decoction of the whole plant is also mixed with milk and drunk as an anti-icteric. Externally, it is rubbed to prevent hair loss [20]; this hair-stimulant effect has also been observed in the Venezia Giullia region of Italy [21]. The Mexican Kickapoo Indians use a decoction of the entire plant for its claimed antifertility effect, for which it is mixed with *Dryopteris normalis* (*Polypodiaceae*) and drunk for four consecutive mornings following intercourse [22]. In Iran, a decoction made from leaves is used as an expectorant and diaphoretic in the common cold, chronic or acute catarrh and bronchitis [3].

3. PHYTOCHEMISTRY

Chemical analysis of *Adiantum capillus-veneris* reveals an array of compounds including flavonoids, triterpenoids, oleananes, phenylpropanoids, carbohydrates, carotenoids, and alicyclics. The primal phytochemical investigation on the leaf extract of *Adiantum capillus-veneris. L* exhibited a triterpenoid as 21-Hydroxy Adiantone that its structure was elucidated by spectroscopic analyses [23]. In continuation of this study, a triterpenoid epoxide was isolated that was identified by NMR and mass spectra as adiantoxide [24]. Actually, Adiantoxide is an epoxidation product of filic-3-ene, which is derived from squalene via isohopanyl cation with extensive Wagner-Meerwein rearrangements [25].

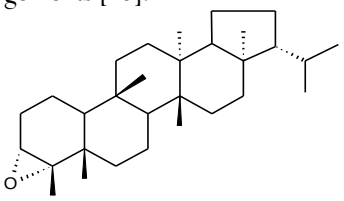


Fig. 2: Chemical structure of Adiantoxide

Many kinds of triterpenoids such as Adiantone, Fern-9(11)-en-12-one, Isoadiantone, Isoglaucanone, Hydoxyhopane, Isoadiantol and Hydroxyadiantone were isolated from leaves of *Adiantum capillus-veneris* [26, 27]. In addition, the isolation of Olean-12-en-3-one and Olean-18-en-3-one was reported [28]. In fact, these oleananes were the first examples of oleanane compounds from *Adiantum* ferns. Several other triterpenoids like Fern-9(11)-ene, Ferna-7, 9(11)-diene, 7-Fernene, Hop-22(29)-ene, Filic-3-ene and Neohop-12-ene were isolated from the leaves of plant, and their structures were determined by spectral and chemical methods [29].

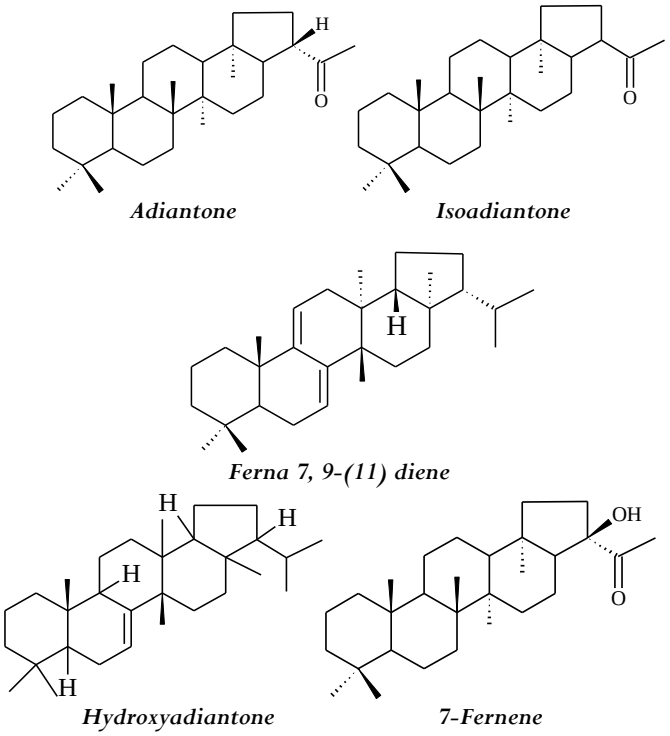


Fig. 3: Chemical structure of some triterpenoids of Adiantum Capillus-Veneries. L

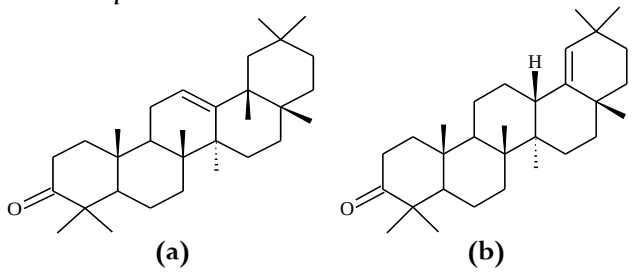


Fig. 4: Chemical structures of a) Olean-12-en-3-one b) Olean-18-en-3-one

During chemotaxonomic investigation on *Adiantum capillus-veneris. L*, a detailed chemical investigation was carried out on the fresh fronds of plant (collected at Yokohama city) that let to isolation of six new migrated hopane triterpenoid alcohols characterized as 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 and Fern-9(11)-en-28-ol. The triterpenoid constituents from the hexane extract of the fresh fronds were purified by various chromatographic techniques to afford the pure triterpenoids. Their structures were elucidated by detailed two dimensional-NMR analyses and/or chemical correlations [30]. Further investigation of plant collected in China has resulted in the isolation of two new triterpenoids; viz. Fern-9(11)-en-12-beta-ol and 4-α-hydroxyfilican-3-one. The constituents of the crude hexane extract of these fronds were purified by various chromatographic techniques to give above mentioned triterpenoids along with many other known triterpenoids from *Adiantum capillus-veneris. L*. The structures of isolated compounds were elucidated by spectroscopic analyses [31].

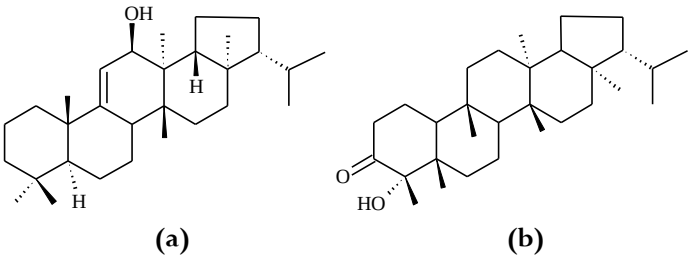


Fig. 5: Chemical structures of a) Fern-9(11)-en-12beta-ol b) 4-α-hydroxyfilican-3-one

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-coumarylglucose 6-sulphate **(a)**, 1-p-coumarylglucose 2-sulphate **(b)**, 1-caffeylgalactose 3-sulphate **(c)**, and 1-caffeylgalactose 6-sulphate **(d)** [32].

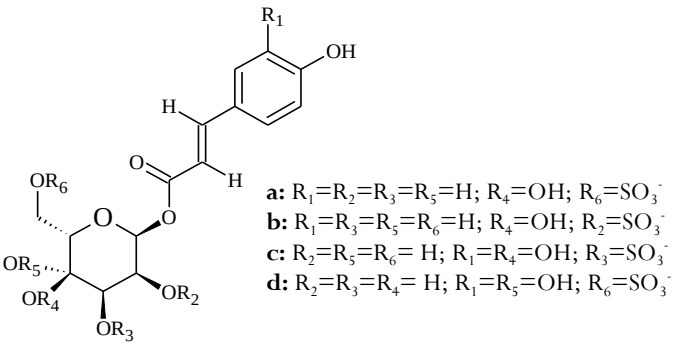
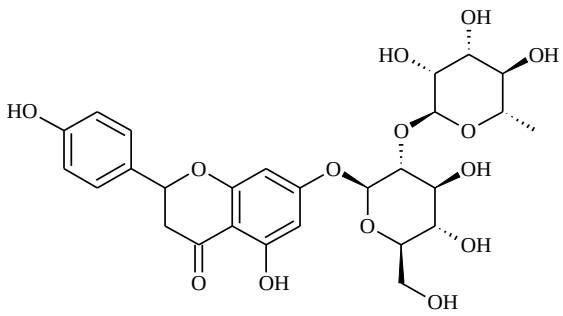
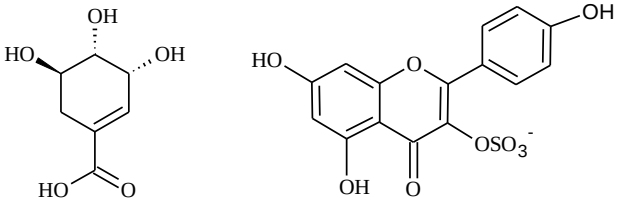


Fig. 6: General structure for sulphate esters of Hydroxycinnamic acid-sugar derivatives from Adiantum capillus-veneris. L

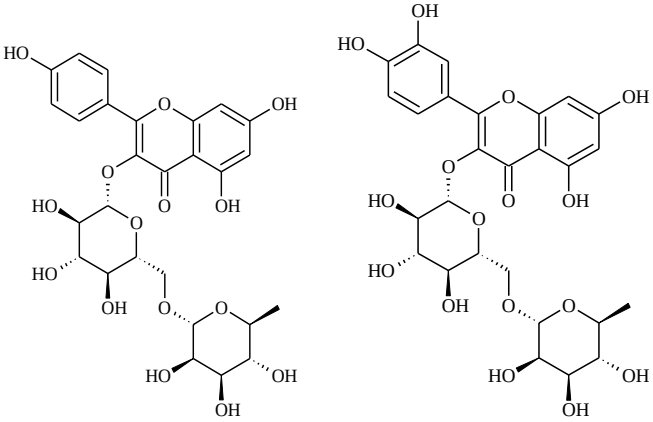


Naringin



Shikimic Acid *Kaempferol-3-sulfate*

Fig. 7: Chemical structure of some flavonoids of Adiantum Capillus-Veneris. L



(a) **(b)**

Fig. 8: Chemical structures of a) Nicotiflorin b) Rutin

The leaves of *Adiantum capillus-veneris. L* was reported to contain different flavonoids like Rutin, Querciturone, Isoquercitrin, Nicotiflorin, Naringin, Astragalin, Populnin, Procyanidin, Prodelphinidin, and Kaempferol-3-sulfate [33-35]. Interestingly, despite its ancient use, there has been a shortage of specific research on *Adiantum capillus*-veneris L to test its extract and chemicals for biological activities. In animal studies, pet ether extract of *Adiantum capillus*-veneris. L dried leaves exhibited potent anti-fertility effect in rats, preventing conception [18, 19].

4. HYPOGLYCEMIC ACTIVITY

Water extract of the entire plant had hypoglycemic activity when given to mice (10 mg/kg) orally [36]. In other research *in vivo* hypoglycemic properties of Adiantum *Capillus-Veneris. L* in mice was successfully confirmed. Total extract of the plant was prepared by boiling the dried material with water. The extract was given to mice (25 mg/kg) orally and found to reduce glucose-induced hyperglycemia. In continuation of study, total extract of the plant was prepared by macerating it with 80% ethanol. The resulting extract was given to mice (25 mg/kg) orally, and showed no activity [37].

5. ANTI-VIRAL ACTIVITY

Ethanol (100%) extract from the rhizome of *Adiantum capillus-veneris. L* evidenced antiviral properties in vitro against Vesicular stomatitis virus [38]. This could be another reason that it is so useful in the fight against respiratory and urinary infections as well as helping to sooth the bowel.

6. ANTI-MICROBIAL ACTIVITY

The methanolic extraction of 20 g *Adiantum capillus-veneris. L* aerial part powder yielded 18% and demonstrated antimicrobial properties. The obtained extract antimicrobial potency was examined by using the set of microorganisms such as *Bacillus, E. coli, Staphylococcus, Proteus, Pseudomonas*, and *Candida*. Concentrations between 0.5-2 Mg/mL of the extract were used and their antimicrobial activity recorded. The remarkable activity exhibited by the 2 mg/ml concentration has been evaluated as a very promising result. All test microbes including the Candida species were affected [39]. In other work, the methanolic extract of *Adiantum capillus-veneris. L* was tested for its antimicrobial activity against five grams positive and six grams negative (including multi-resistant *Staphylococcus Aurous*) bacteria and against eight fungal strains using the standard micro-dilution assay. The extract of this herb had a very low MIC (minimum inhibitory concentration) value (0.48 mug/ml) against *Escherichia coli* [40]. The water extracts and extracted phenols from gametophytes of *Adiantum capillus-veneris. L* was investigated for their antifungal activity against *Aspergillus niger* and *Rhizopus stolonifer*. Both crude extracts and extracted phenols of gametophytes and different parts of sporophytes of plant were found to be bioactive against the fungal strains [41].

7. ANTI-OXIDANT ACTIVITY

Whole part of Iranian *Adiantum capillus-veneris. L* was extracted in methanol by maceration (48 h), and its antioxidant activity was investigated. It was found that the radical scavenging activity in the plant extract is IC_{50}=2.03 mg/ml, showing low antioxidant activity of *Adiantum capillus-veneris. L* (IC_{50} values denote the concentration of sample, which is required to scavenge 50% of DPPH free radicals) [42].

8. OTHER ACTIVITIES

Some of the major compounds isolated from *Adiantum capillus-veneris. L* has been reported to possess many biological activities that are shown in Table 2.

Table 2: Biological activities for compounds of Adiantum capillus-veneris. L

Compound Tested	Activity Tested For	Notes/Organism tested	Ref.
Astragalin	Antiproliferative Activity	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.	43
	Antidermatitis Activity	Reduced the severity of pre-existing dermatitis and prevented the development of atopic dermatitis.	44
Zeaxanthin	Photoreceptor	Protected photoreceptors from light-induced death.	45
Shikimic acid	Neuroprotective	Reduced focal cerebral ischemic injury induced by middle cerebral artery thrombosis.	46
Rutin	Anticholesterolemic	Reduced total cholesterol, LDL, VLDL and triglycerols. No reduction in HDL seen.	47
	Gastroprotective	Protected against reflux oesophagitis by inhibiting gastric acid secretion, oxidative stress, inflammatory cytokine production and intracellular calcium mobilization in PMNs.	48
Naringin	Antioxidant Activity	Increased hepatic superoxide dismutase and catalase activity. Decreased hepatic mitochondrial hydrogen peroxide. Increased plasma vitamin E concentrations.	49
	Anticholesterolemic	Lowered plasma cholesterol and triglyceride concentrations as well as HMG-CoA reductase activity.	50
	DNA Protecting Effect	Protected mouse bone marrow cells against gamma radiation induced DNA damage and reduced cell proliferation.	51

9. CONCLUSION

Adiantum capillus-veneris. L is a common fern and used as a medicinal plant in traditional remedies. Several importance secondary metabolites have been isolated from its leaves, roots, and rhizomes. Many of these secondary metabolites have also been found to possess interesting pharmacological activities and some have served as curves for human and livestock diseases. In addition, the various solvent extracts from leaves have been reported to exhibit biological activities include antibacterial, antiviral, antifertility, anti-implantation, hypoglycemic, antioxidant, etc. The biological activities and chemical constituents reported in present review confirm the therapeutic value of *Adiantum capillus-veneris. L*. Herbalists and healthcare practitioners throughout the world continue to use of *Adiantum capillus-veneris. L* based on its traditional uses for respiratory disorders and hair loss, and to regulate menstruation, though no clinical research has been done to validate these traditional uses. Thus, doing all pharmacological studies on plant many different uses will come in front of us and this will be an important resource for the discovery of new drugs. We should not forget that the advent of new high throughput screening techniques, and new extraction methods like microwave extraction, much better ways of looking for new plant drugs have come available.

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