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REVIEW ARTICLE

Adiantum Capillus-Veneris L.: A Comprehensive Review of Its Phytochemical Composition, Pharmacological Activities, and Therapeutic Potential

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ABSTRACT

Adiantaceae is distributed extensively over the world from cool temperature zones to hot tropical regions. Adiantum capillus-veneris L. was shown to include triterpenoids, flavonoids, aoleananes, polysaccharides, phenylpropanoids, carotenoids, and alicyclics by chemical analysis, which participate in several medical properties. The alcoholic and aqueous leaf extract was proven efficient against several Gram-positive and Gram-negative bacteria strains and also has antifungal properties. An analysis of the antioxidant activity, phytochemicals, and component content reveals that Adiantum capillus-veneris leaves are a rich source of molecules that act as scavengers of free radicals, an ethanolic extract of the leaves of Adiantum capillus-veneris was found to inhibition the oxidative damage caused by hydrogen peroxide by increased antioxidant enzymes levels, such as those of SOD, CAT, Gpx, and glutathione, were increased. The ethanolic extract inhibits the NO release and lowers TNF-α levels. It has anti-inflammatory activity and shows therapeutic results in ulcerative colitis in rats due to the presence of phenolic components, flavonoids such as rutin and isoquercetin, triterpenoids, and mucilage, all of which exhibit antioxidant, anti-inflammatory. The presence of tannins and flavonoids may cause the antidiabetic effect, The plant also has wound-healing properties and enhanced angiogenesis. The important role of an extract made of ethanol from the aerial part of Adiantum capillus-veneris was reported as anticancer activity against cancer cell lines like breast (A549), lung (A549), and colon (HCT-116). The investigation revealed encouraging suppression of cancer cells' growth in vitro for all fractions. The antidiarrheal action crude extract of dried leaves of Adiantum capillus-veneris was demonstrated in a mouse model. Other properties such as hypocholesterolemic effect, the effect of anti-testosterone on hair loss, and urinary tract effect by decreasing colony-forming units and treating urinary tract infections, it is also decrease levels of calcium, phosphorus, and blood urea.

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INTRODUCTION

Pteridophytes are a major contributor to the variety of plants on Earth and are a prominent dominating element of many plant communities, particularly those found in temperate and tropical climates [1]. About 200 species of ferns of the genus Adiantum belong to the family Pteridaceae, while other experts classify them under their own family, Adiantaceae. They are widely spread throughout the world, from hot tropical regions to cold temperate zones [2]. Maidenhair fern is a robust plant up to 35 cm tall with an attractive smell and a spreading rhizome. Plant leaves are typically double-rowed, delicate, and glabrous, measuring up to 50 cm length. The petals of the plant are shiny and black. that is covered with hair at the base. The species' leaf blades range from oval to oblong-ovate. The medicinal portions include fronds, rhizomes, and roots [3]. Among its various secondary metabolites, Adiantum capillus-veneris has shown antibacterial, anti-inflammatory, analgesic, hypoglycemic, antioxidant, antilithiasic, antiproliferative, antidermatitis, neuroprotective, and anticholesterolemic properties [4]. The names shaar-el- Dioscorides, who lived in the early 100s A.C., used the term "Adiavrov" to symbolize Adiantum capillus-veneris because of its leaves' coriander-like serrations on top. Theophrastus described the use of "black" and "white" adiantum in the preparation of hair oils. The plant was not advised to be used while pregnant since it has a lengthy history of inducing menstruation and stimulating the uterus in herbal therapy. The fern in question is commonly referred to by Western Arabs as Kuzburat-el bir or coriander of the wall, denoting jibal, which means hair of the mountains, shaar-el-jinn, which means fairies' hair, sak-el-aswad, which means black stem, shaarel-fual, which means "hair of omens," and Nasif-el-aswad, which means black veil are the names of the genus Adiantum in Arabic. This fern is said to have resolved and DE obstruent properties, making it useful for discharging phlegmatic humors. It is also having emmenagogue, diuretic, expectorant, and alexipharmic qualities. It also used for several types of long-term cancers. It is considered controversial, applied as a plaster, and has been demonstrated in animals to have an anti-implantation impact and prevent pregnancy. Greek terms ebinotrichon, polytrichon trichomenis, and calitrichon are used to refer to this fern[5]. Adiantum Capillus-veneris L. has a long history of medicinal use. In Egypt, it is used to treat asthma, chest colds, coughs, edema, flu, hepatitis, snakebite, spider bite, spleen, urinary insufficiency, and to enhance sweating. In Europe, it is used to treat alcoholism, bronchitis, bronchial disorders, cough, dandruff, detoxification, diabetes, excessive mucus, flu, hair loss, menstruation issues, and to soothe mucous membranes. In India, it is used to treat boils, bronchitis, colds, diabetes, eczema, fever, menstruation issues, skin ailments, and wounds. In Iraq, it is used to treat bronchitis, colds, coughs, excessive mucous, flu, menstrual disorders, respiratory difficulties, reducing secretions, urinary insufficiency, and increasing perspiration, while in Mexico, it is used for birth control, bladder problems, blood cleansing, constipation, hair loss, kidney stones, liver function, menstrual disorders, and respiratory distress [6].

Geographical Distribution

The genus Adiantum is extensively distributed through the worldwide from cold to hot tropical climates [7]. Even though ferns can withstand occasional winter temperatures as low as -2 ˚C, the fronds swiftly wilt at first frost. It occasionally survives winter temperatures as low as -2 ˚C, but it perishes when the temperature drops below -18˚C. It is instigated in different types of soils such as light, sandy, loamy and heavy clay, and requires well-drained soil. It grows best in neutral and basic alkaline soils [6]. Adiantum capillus-veneris is distributed throughout the world. It is indigenous to South America, North America, Africa, Europe, China, Pakistan, Australia, Taiwan, America, Bhutan, Turkey, Afghanistan, Iran, Japan, Nepal and Sri Lanka. In India it is cultivated as an ornamental plant and found in Darjeeling, Himalayas, Dalhousie, Coimbatore plains, Palni-Nilgiri hills, Nainital, Kangra, Tamil Nadu, West side of Tamil Nadu, Kashmir, Gujarat, Patal Kot, Shimla, Kulu, Pachmarhi, Maharashtra, Tamia, and Missouri [8 9] . Also, it is found in Kurdistan, northern Iraq[10].

Scientific classification of Adiantum cappilus- veneris [11 12]

Kingdom: Plantae

SubKingdome : Traciobionta

Division : Pteridophyta

Class : Filicopsida

Order : Polypodials

Family : Pteridaceae

Genus : Adiantum. L.

Species : Adiantum cappilus- veneris

Common Names

There are many vernacular names including Khuzbaratul Ber, Shar-ul-jibal, Shaer-ul-jin, and Shaer-ul-Arz in Arabic; in English, Venus's hair, Maidenhair fern, maria's fern, our lady's hair; in Latin: Marathi Mubaraka, Adiantum capillus-veneris and other names according to countries [4 13 14] .

Botanical Description

The genus name, Adiantum, comes from the Greek term unwetted. since its leaves retain moisture. The Latin terms "capillus" and "veneris," which translate to "hair of Venus," give this plant its chosen common name, "the Venus maidenhair fern." [15] . As shown in Figure 1 Adiantum capillus-veneris L. is a drooping herb from the Pteridaceae family, It attains a height from 14–35 cm, , spreading, or drooping, with a short, brown rhizome. Petiole (stipe): 6–8 cm long, smooth, slender, wiry black or dark brown. Fronds blade up to 25 cm long, bi or tripinnate, with a midrib (rachis) morphology similar to a petiole. The fronds were divided into green leaflets, measuring 1-1.50.7-1.5 cm, which were either rhomboid or deltoid and had lobed or serrated along the margins Veins reach the leaflet boundary in

an open dichotomous vein without veinlets [10] . The spores are thick, smooth, transparent, triangular, tetrahedral, and have obtuse-rounded corners and slightly convex sides. Stomata are dispersed across the whole surface of the extended lamina and are always found on the inferior surface of the pinnae, indicating that they are hypo-stomatic [15]

Figure 1 Adiantum capillus-veneris L. [6]

Chemical Constituents

Chemical components of Adiantum capillus-veneris L. were shown to include triterpenoids, flavonoids, aoleananes, polysaccharides, phenylpropanoids, carotenoids, and alicyclics by chemical analysis. Numerous triterpenoids Triterpenoid epoxide (adiantoxide), 21- hydroxy adiantone, Fern-9(11)-en-12-one, isoadiantone, hydroxyhopane, isoglaucanone, isoadiantol, hydroxyadiantone, olean-12-en-3-one, olean-18-en-3-one, fern-9(11)-ene, ferna-7, 9(11)-diene, 7-fernene, neohop-12-ene, hop-22(29)-ene, filic-3-ene, Adiantum capillus-veneris leaves were used to isolate pteron-14-en-7a-ol, fern9(11)-en-3a-ol, fern-7-en-3a-ol, , fern-9(11)-en-28-O, fern-9(11)-en-12-beta-ol, adian-5(10)-en-3a-ol, adian5-en-3a-ol, fern-9(11)-en-28-O, fern-9(11)-en-12-beta-ol, and 4-α-hydroxyfilican- 3-one [2 6]. According to reports, Adiantum capillus-veneris leaves contain a variety of flavonoids, including populnin, rutin, quercetin-3-O-glucoside, quercetin, querciturone, nicotiflorin, isoquercitrin, astragalin, procyanidin, populnin, kaempferol-3-sulfate, and prodelphinidin[16 17] . The percentages of moisture, ethanol extractable matter (11.44%), and water extractable matter (24.00%) in leaves were as follows. Adiantum capillus-veneris was subjected to a soxhlet extraction, which revealed the terpenoids and phenolics present (2.73%), alkaloids (0.53%), lipids and waxes (0.20%), fiber (67.23%) and quaternary, and noxides (26.33%). Extracts from leaves were tested

for ten trace elements: magnesium, calcium, potassium, manganese, iron, cobalt, sodium, nickel, copper, and zinc. Akabori and Hasagava (1969) [18] pointed out that the levels of Ca and K were important. A saponin glycoside is one of the components in the Adiantum capillus-veneris plant, thus studying the hydrolytic products of the saponin to get a triterpenoid hydroxy hopanoneaglycon and the components of sugar: xylose, galactose, and rhamnose. However, Adiantum capillus-veneris contains protein, steroids [19] and alicyclic acids [20] .

Medical Properties

The extracts of various plants have demonstrated the presence of flavonoids whish work as antibacterial and antifungal agents [21 22 23 24 25] , with an anti-diabetic effect[26] . Other studies have indicated that plant extracts and its essential oil have anticancer activity against several human cancer cell lines [27 28 29 30]. Below we have summarized some of the medical applications of Adiantum capillus-veneris L.

1-Antimicrobial activity

The antibacterial activity of 12 pteridophyte species was studied utilizing a disc diffusion method. Adiantum capillus-veneris Linn's alcoholic and aqueous leaf extract(10%) was discovered to be efficient against strains of, Escherichia coli (MTCC No. 443), Salmonella arizonae (MTCC No.660), Salmonella typhi (MTCC No. 734), Staphylococcus aureus (MTCC No. 96) and Agrobacterium tumefaciens (MTCC No. 431) [31] . The antibacterial properties of the methanolic extract of A. capillus-veneris against helicobacter pylori, E. coli, and S. aureus using a disc diffusion method have been proven[32] . Using the disk diffusion technique, the antibacterial activity on Muller Hinton agar was measured. Different extracts from all the parts used have been revealed to possess antibacterial and antifungal properties as shown in Figure 2[33].

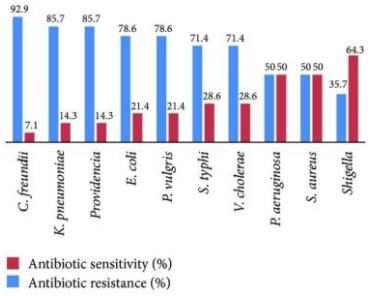

Figure 2 Percentage of antibiotic resistance and sensitivity of multidrug-resistant MDR bacterial strains [33] .

Using the disc diffusion technique, Maidenhair fern's antimicrobial properties against strains of multidrug-resistant (MDR) bacteria was assessed. Maximum zone of inhibition was shown by the species' leaves methanol extract against Salmonella typhi, Proteus vulgaris, Vibrio cholera, Klebsiella pneumoniae, Shigella, and Providencia. The extract from stem methanol had great potency against K. pneumoniae, S. typhi, and E.coli. While the species' stem water extract showed little ZI against E. coli, S. typhi, Shigella, K.

pneumonia, Proteus vulgaris, and Providencia, its leaf water extract was quite effective against all bacterial strains [34] . Well diffusion method for evaluation of antimicrobial activity extracts of Adiantum plant. The ethanolic extract of Adiantum capillus veneris leaves was shown to have antimicrobial properties against a variety of fungi, including Aspergillus species, Bacillus subtilis, Salmonella typhi, Pseudomonas aeruginosa, and Staphylococcus aureus [35]. Researchers found that the essential oil of Adiantum capillus-veneris contains carvacrol,carvone, hexadecanoic acid, hexahydrofarnicyl acetone, and nonanal. Its antibacterial activity was highest against Staphylococcus aureus, Streptococcus pyogenes and diphtheroid during a 100 mg/ml concentration. The flavonoids found in the oil have therapeutic and medicinal uses, as they prevent the growth of disease-causing bacteria [36].Adiantum capillus-veneris hydromethanolic extract exhibited a moderate of antibacterial activity against five different bacterial strains, with Streptococcus pneumoniae demonstrating the highest sensitivity [37]. Hadi and Hussein (2016) [35] used a methanolic extract of Adiantum capillus-veneris to conduct antifungal studies against yeast and fungi (in vitro). The antifungal activity against fungi (Aspergillus niger, Aspergillus terreus, Aspergillus flavus, Aspergillus fumigatus, Candida albicans, Saccharomyces cerevisiae, Fusarium sp, etc.) is due to the plant constituents in this extract. These plant components have antibacterial properties as well. Adiantum capillus-veneris rhizome ethanol extract demonstrated antiviral efficacy against the vesicular stomatitis virus in vitro [38].

2- Antioxidant activity

The 2,2-Diphenyl-1-picrylhydrazyl (DPPH) test was used to confirm the plant essential oil's antioxidant activity. Carvone, carvacrol, and thymol are an instance of phyto-constituents that provide essential oils their antioxidant properties [39]. Using human lymphocytes, in vitro tests were performed to assess Adiantum capillus-veneris's antioxidant potential. The capacity of a 59% alcoholic extract of Adiantum capillus-veneris leaves to shield peripheral blood cells from hydrogen peroxide-induced oxidative damage was investigated at concentrations of 5 μl/10 μl/20 μl. Consequently, the findings validate its antioxidant characteristics. In comparison to cells treated with H2O2, the recovery was slow as the concentration of the leaf extract increased (significant, $P < 0.05$) [40]. The DPPH radical scavenging result of the antioxidant analysis showed that the antioxidant capacity of the methanolic extracts was greater than the petroleum ether extracts [41]. In an in vitro and in vivo antioxidant activity investigation, the antioxidant properties of isolated flavonoids from A. capillus-veneris were shown to be on par with or higher than those of synthetic ethylenediaminetetraacetic acid (EDTA), butylated hydroxytoluene (BHT), and ascorbic acid [42]. Adiantum capullus-veneris has strong levels of carvone, carvacrol, and thymol in the essential oil that is extracted from the plant using the GC-Mass technique. These antioxidant qualities of the plant allow A. capullus-veneris to scavenge radicals. This was done by 5 mL of a 0.004% chloroform solution of DPPH was mixed with 5 mL of each essential oil concentration (Khodaie et al., 2015). An analysis of the phytochemicals, antioxidant activity, and elemental content of Adiantum capillus-veneris leaves reveals that the leaves are a rich source of molecules that scavenge free radicals, including terpenoids, saponins,

tannins, flavonoids, and reducing sugar. Because of this, Adiantum capitalis-veneris has antioxidant properties [43].

3- Anti-inflammatory activity

Adiantum capillus-veneris alcoholic extract and its hexane fraction indicated significant anti-inflammatory efficacy against inflammation produced by formalin. In croton oil-induced inflammation, the hexane fraction and compounds 3, 4 shown topical anti-inflammatory effect after 6 hours and persisted for 30 hours [44]. The ethyl acetate portion of the plant ethanolic extract has shown considerable anti-inflammatory efficacy by inhibiting NO release and lowering TNF-α levels. Triterpenes may have a significant role in the plant's anti-inflammatory properties [45].

Male Westa rats were given oral (by mouth) doses of A. capillus-veneris aqueous extract (ACAE; 150, 300, and 600 mg/kg) and aqueous alcoholic extract (ACHE; 150, 300, and 600 mg/kg). These extracts' anti-inflammatory, ulcer-healing, and antioxidant properties were responsible for the dose-related positive effects on acetic acid-induced colitis.Capillus-veneris Adiantum, The ulcer score, area, and ulcer index were considerably lower in all groups treated with ACAE and ACHE extracts than in the untreated control group (at least $p<0.05$), with the exception of the ACAE (150 mg/kg) group[46]. The study found that Adiantum capillus-veneris extract reduced the toxicity of methyl-2-benzimidazole carbamate-CBZ in rats' hepatic tissues by reducing inflammation, combating oxidative stress, upregulating antioxidant genes, downregulating NF-κB and pro-inflammatory genes, alleviating negative pathological signs, and improving hepatic functioning after CBZ exposure, see Figure 3[47]

4- Anti-diabetic activity

A streptozocin-induced diabetic rat model was used to assess the anti-diabetic properties of Adiantum capillus-veneris aqueous and methanol extracts. The species has excellent anti-diabetic properties with little adverse effects, as demonstrated by the improvement in fasting blood sugar levels. The antidiabetic effect may be caused by the presence of flavonoids and tannins [48]. (100 mg/kg) of the aqueous extract given once daily to rats showed a significant increase in the amylase enzyme and rat body weight, as well as a drop in blood glucose. The plant's ability to repair injured hepato-renal cells is allows it to put on weight. Additionally, substances in the species that resemble insulin and influence pancreatic function for amylase production are the cause of the rise in blood amylase [49]. The species was shown to exhibit antihyperglycemic properties when measured against the reference medication, acarbose [50].

5- Wound healing property

Adiantum capillus-veneris was reported to have wound-healing properties in an in vitro investigation. By using both endothelial cell proliferation and capillary-like tube forms, the plant's water extract significantly enhanced angiogenesis ($P < 0.05$). Additionally, Significant protection against oxygen free radical damage to fibroblasts has been demonstrated by aqueous and butanol fractions [51]. Adiantum capillus-veneris whole plant extract can scav-

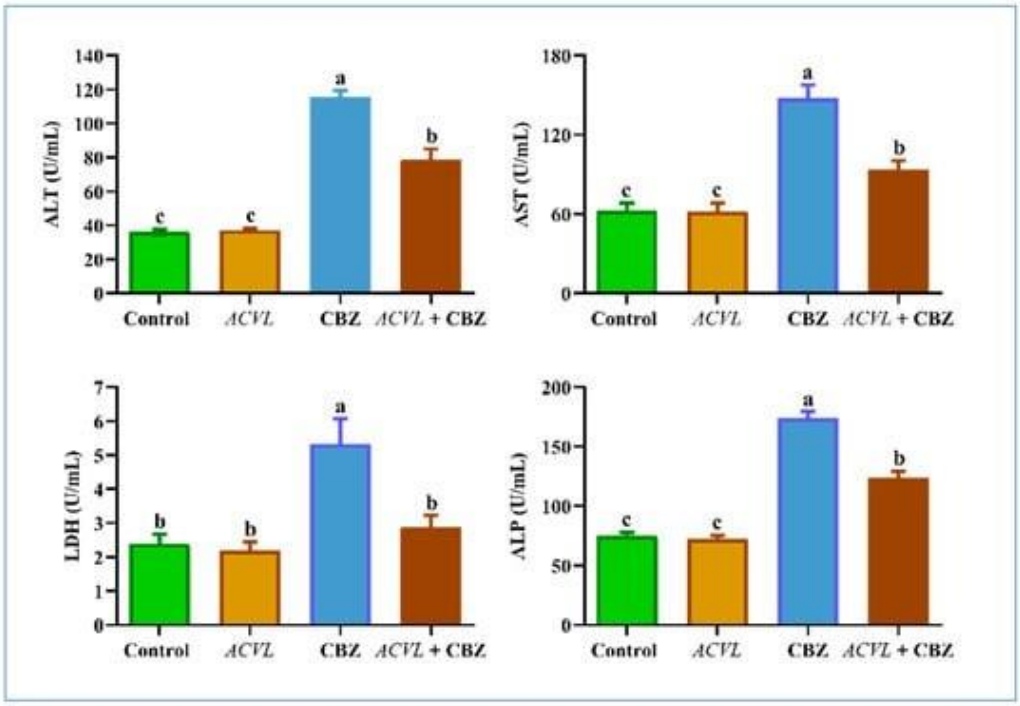

Figure 3 Hepatic antioxidant biomarkers at protein and gene levels in different experimental groups [47]

enge free radical molecules and may be a useful source of natural antioxidants for wound healing remedies [52]. Research discovered that an ointment made of Aloe vera, Myrrha, Henna, and Maidenhair fern healed diabetic rats' wounds [53]. Other study demonstrated the positive benefits of Adiantum capillus-veneris aqueous and hydroalcoholic extracts on ulcer healing at dose-related levels [46].

6- Anticancer activity

Concentrations)0, 10, 25, 50, 100, and 200 μg/mL(of the ethanolic extract's in vitro cytotoxic activity against several human cancer cell lines, including colon (HCT-116), lung (A549), and breast (A549), was investigated in relation to the aerial component of Adiantum capillus-veneris. The MTT test was utilized to evaluate the proliferation/inhibition of, pancreatic (MIA PaCa-2), MCF-7, and tumor cells. Additionally, a mouse model of ascites carcinoma (EAC) was used to assess the hexane fraction's in vivo anticancer efficacy. Examining the extract on several human cancer cell lines revealed encouraging suppression of cancer cell growth in vitro for all fractions of the ethanolic extract[15]. The anticancer properties of ACV extract and gold nanoparticles were examined in MCF7 cell line. ACV twenty-three bioactive components, the results of the investigation demonstrated that the crude extract and nanoparticles exhibited anti-apoptotic and anti-proliferative effects on the MCF7 cell line [54].

Phenolic content of methanol and dichloromethane extracts of Adiantum capillus-sveneris leaves from Duhok, Iraq. Concentrations (25, 50, 100 and 200 μg/ml) were used, the extracts showed antiproliferative activity on A549 cells with increasing concentration[55].

7- Antidiarrheal and antispasmodic activities

Capillus-veneris inhibited castor oil-induced diarrhea in mice in both in vivo and in vitro tests, offering 40 and 60% protection at doses of 300 and 500 mg/kg, respectively. These results demonstrate that A. capillus-veneris possesses antispasmodic and antidiarrheal properties [56].

8- Antiviral activity

Using the vesicular stomatitis virus in monkey cell cultures as the test organism, it was shown that extracts from Adiantum capillus-veneris exhibited antiviral activity [2]

9- Hypocholesterolemic effect

A. capillus-veneris water extract's hypocholesterolemic impact was examined in rats fed a high-cholesterol diet (HCD) paradigm. The findings showed that blood levels of total cholesterol (TC), LDL, and VLDL were significantly reduced, whereas HDL levels were unaffected. Furthermore, animals given A. capillus-veneris treatment showed an approximate normalization of the atherogenic index of TC/HDL [57]

10- Anti testosterone-induced hair loss effect

The impact of A. capillus-veneris ethanolic extract on hair growth was proven in mice using a testosterone-induced alopecia paradigm. The anagen/telogen ratio and follicular density have significantly increased ($p < 0.05$), according to the data [58] .

11- Analgesic and antinociceptive activities

The analgesic effectiveness of the ethanolic extract of Adiantum capillus-veneris and its fractions was assessed in albino Wistar rats using the tail- flick and torsion test at a dosage of 300 mg/kg orally. The ethanolic extract and its components, particularly ethyl acetate ($p < 0.01$), provided substantial analgesic effectiveness with little ulceration compared to the conventional medication, ibuprofen[59]. Similar studies using hot plate and tail immersion tests on rats showed a potent analgesic effect of the ethanolic extract of Adiantum capillus-veneris at doses of 200 mg/kg and 400 mg/kg of animal body weight, and the 400 mg/kg dose was found to be more effective than the extract at a dose of 200 mg/kg of body weight[44] . In the writhing test, 4-α-hydroxyfilican-3-on, which was extracted from the ethanolic extract of the plant, exhibited exceptional anti-noceptive efficacy [60].

12- Urinary tract effect

The urinary tract was used to determine the effectiveness of Adiantum capillus-veneris water extract. In this experiment, the outcome had an inhibitory impact on every examined type of bacteria. Mice with a systemic Candida albicans infected model were used to assess the plant's preventive properties. It also improved the renal pathological features and

reduced the number of Candida albican colony-forming units (CFU) in the spleen. Additionally, it showed twofold effects on the activity of diuresis. Urine production was typically increased by low dosage and severely decreased by high dosage. One possible application for Adiantum capillus-veneris is to treat urinary tract infections (UTIs) [61]. In another study, male rats were used to assess the anticalcium oxalate urolithiasic properties of an ethanolic extract of Adiantum capillus-veneris. The quantity of crystals and the levels of phosphorus, calcium, and blood urea in the serum were discovered to have significantly decreased ($p<0.01$), according to the data [62] .

CONCLUSION:

In conclusion, in this review, we discussed the properties of Adiantum capillusveneris L. that can be beneficial and save agents as a medical plant, in addition to it is chemical components, including triterpenoids, flavonoids, aoleananes, polysaccharides, phenylpropanoids, carotenoids, and alicyclics. most of of Adiantum capillusveneris L. components have medical properties that act as antimicrobial activity, antioxidant activity, anti-inflammatory activity, anti-diabetic activity, wound healing property, anticancer activity, antiviral activity, and others. Thus, it is advised that more research be done to cover its effects in other diseases and its benefits for human health.

Authors' Contributions

All authors contributed equally to the conception and design of the study, sample collection, laboratory analysis, data interpretation, and manuscript preparation. Each author critically revised the work for intellectual content, approved the final version of the manuscript, and agrees to be accountable for all aspects of the work.

Conflict of interest

The authors declare that they have no potential conflicts of interest.

Data availability

The data that support the findings of this study are available on request from the corresponding author.

The Ethical Approval

The research was reviewed and approved by a recognized ethics committee to make sure it follows medical research standards and protects participants' rights. Everyone who took part gave their permission, and their information was kept private and used only for scientific purposes.

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