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REVIEW ARTICLE

An Updated Phytopharmacological Review on Medicinal Plant of Arab Region: *Apium graveolens* Linn

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ABSTRACT

Apium graveolens Linn. (Karafs) is used in traditional medicine for the treatment of the various ailments. There is a need to explore and authenticate the pharmacological profile and medicinal importance of the Karafs. In this paper, the literature and the published work on Apium were collected using online resources "Google scholar", "Web of science", "Scopus" and "PubMed". Each of the pharmacological activity was searched individually using the keywords "Apium/Karafs/*Apium graveolens* + individual pharmacological activity". We documented the most cited and most recent literatures. The current findings illuminate the importance Karafs in the traditional medicine and their impact in treating various diseases. This review strongly supports the fact that the Apium has emerged as a good source of medicine in treating various diseases. There is also a need to isolate the bioactive phytochemicals present in this plant.

Key words: *Apium graveolens*, Arab Medicine, Karafs, Traditional Arab and Islamic Medicine

INTRODUCTION

Since the ancient times, the human being is facing with the disease and discomfort and is struggling to antagonize it with different approaches. Among all the treatments, herbs are continuously used for the treatment of all the ailments.

Nowadays, the herbal drug is not in the list of the mainline therapies; however, due to the unwanted toxicity and side effects, the tilt toward the herbal therapy is again gaining momentum. Herbal medicine is now an accepted medicine as complementary and alternative therapy in combination with the main line therapies. Herbal medicine is now recognized in Europe and America. The sales of herb as dietary products was increased in America by around 7% in 2014. The estimated cost of the current herbal market is more than $6.4 billion. The growth is increasing continuously since the last 11 years in a row.[1,2] In Europe, an estimated 18.8% of the population who has been surveyed is using at least one plant supplements.[3] Because of the popularity of the herbal medicine in global market, it is logical to focus on the herbs which are used for the medicinal purpose. Due to this fact, *Apium graveolens*, a commonly used plant of Arab traditional medicine, has been reviewed.

A. graveolens is a biennial plant locally known as "Karafs", belonging to family Apiaceae. Various parts of *A. graveolens* are used in hepatic and spleen disorders, brain disorders, body pain, and sleep disturbances.

Previously published data show that *A. graveolens* have antifungal, antihypertensive, hypolipidemic, hepatoprotective, diuretic, and anticancer properties.[4-6]

BOTANICAL CLASSIFICATION

Kingdom – Plantae
Subkingdom – Tracheobionta
Superdivision – Spermatophyta
Division – Magnoliopsida
Subclass – Rosidae
Order – Apiales
Family – Apiaceae
Genus – *Apium*
Species – *A graveolens* Linn.

NOMENCLATURE IN DIFFERENT LANGUAGE

Arabic - Karafs; Chinese - Qin cai; English - Celery; Greek - Udasaliyon; Hindi - Ajmud; Persian - Karafs; Roman - Baatrakhiyun; Urdu - Ajmod.[7]

GEOGRAPHICAL INDICATION

Celery was first cultivated as a food plant in Europe, mainly in Italy and France. From here, the plant spreads to Sweden, Algeria, Egypt, and Ethiopia and then to Kingdom of Saudi Arabia (KSA). Central

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Region (Najd) is said to be the main geographical region of this plant in the KSA.[8,9]

PLANT DESCRIPTION

Macroscopy

The root of the *A. graveolens* is shallow and thickened in the middle. The stem is branched, furrowed, succulent, and rigid. The leaves are pinnate and ovate in shape. The size of flower is small and it is white/greenish-white. The inflorescence is a compound dumbbell. Calyx is obsolete; petals are roundish entire; disk is depressed. Fruits are schizocarp with two mericarps, suborbicular to ellipsoid in shape, and slightly bitter in taste.[4,10]

Part used

The dried ripe fruit (sometimes called as seed) is mainly used for the medicinal purposes and commercially available in the market. The celery fruits are separated mericarp, each cremocarp is brown roundish ovoid, laterally compressed, and about 1.0–1.5 mm long, 1.5 mm wide, and 1.5 mm thick. The seeds are orthospermous. The odor and taste of the seed are aromatic.[7]

The transverse section of the plant showed a wavy outline. Each mericarp is composed of five ridges and 6–9 vittae. The epicarp of the fruit is divided into exocarp, mesocarp, and endocarp. Exocarp is made up of parenchymatous cells that are single-layered, thin-walled, and rectangular in shape. The outer part of the exocarp is coated with cuticle. Mesocarp also consists of polygonal- to oval-shaped parenchymatous cells. Endocarp also contains large parenchymatous cells. Testa is made up of single-layered elongated cells. Endosperm contains aleurone grains and calcium oxalate crystals.[11]

THE USE OF *APIUM* IN TRADITIONAL ARAB AND ISLAMIC MEDICINE

The plant is mentioned in the Traditional Arab and Islamic Medicine with the name "Karafs." According to old literature, it was also called as Udasaliyon in the Greece. Arab and Islamic literature mentioned five different types of the Karafs, which are known as Bustani, Maiee, Sakhuri, Nabti, and Jabli. As the name suggests, the Bustani is a locally cultivated plant while Jabli grows on mountains, Sakhuri grows in stony areas, Nabti grows in sheltered area, and the Maiee is the one which grows near water and ponds.[12]

The plant is also mentioned by the famous Arab scholars in their literature. Al-Biruni stated that the Karafs is called as Sumbul by the people from Tirmidh, Khatl, and Bukhara. Avicenna also documented the five types of Karafs.[13,14] According to Al-Rhazes, the plant Maiee variety is bigger in size as compared to Bustani while Jabli and Sakhuri are Roman in origin and pungent in taste.[15]

Imam Ibn-al-Qayyim, who wrote a famous book on the prophetic medicine, describes that wet celery leaves help to cool the stomach & liver and also acts as diuretic and helps in menstrual problem and kidney stones.[16]

Celery also stimulates semen production and relieves offensive breath. Al-Rajhi said that one should avoid eating celery if he/she fears that he/she might suffer a scorpion sting.

PHYTOCHEMICAL CONSTITUENTS

The constituents of the celery include glycosides, steroids, and different types of phenolic including furanocoumarins, flavones, and trace elements (sodium, potassium, calcium and iron).[17,18]

There is variability of the constituents in the different parts of the plants. The main chemical constituents present in each part of the plant are as follows:

Roots

The roots contains falcarinol, falcarindiol, panaxidol, and polyacetylene 8-O-methylfalcarindiol.[19]

Stems

The stem contains pectic polysaccharide (apiuman) containing d-galacturonic acid, 1-rhamnose, 1-arabinose, and d-galactose.[20]

Leaves

Twenty-eight components are obtained from gas chromatography-mass spectrometry study of the volatile oil obtained from the leaf. The important compounds are 1-dodecanol, 9-octadecen-12-ynoic acid, methyl ester, and tetradecence-1-ol acetate.[21]

Fruits/seed

Caffeic acid, chlorogenic acid, apiin, apigenin, rutaretin, ocimene, bergapten, and isopimpinellin are reported to be found in celery seed. The other substances such as seslin, isoimperatorin, osthenol, and gravebioside A and B were also found in the seeds.[22] Literature also showed that seslin, isoimperatorin, osthenol, gravebioside A and B, umbelliferone are present in the seeds of the plants.

The seed oil is composed of palmitic acid, stearic acid, oleic acid, linoleic acid, petroselinic acid, d-limonene, selinene, terpineol, and santolol. The aroma of the oil is due to the presence of sedanonic anhydride and sedanolide in the seed oil.[23,24] The maximum concentration of the oil was found in 5-week-old fruits.[25]

The different group of chemical constituents found in the *A. graveolens* is enlisted in Table 1.

TRADITIONAL USES

Celery has been used in the traditional system of medicine to treat spasm and stomach problems and as diuretic, laxative, and sedative. It is used as heart tonic to lower the blood pressure in African traditional medicine in Trinidad and Tobago.[82] There is also a report to the use of celery in joint problems.[4] The celery seed is well known as libido stimulant in the traditional system of medicine due to its protective role against the sodium valproate in testes and amplification of the sperm profile.[83,84] It also increases the secretion of breast milk.[85]

PHARMACOLOGICAL ACTIVITY

Hepatoprotective activity

The methanolic extract of *A. graveolens* seed was found to have significant activity against paracetamol-induced[5] and carbon tetra chloride-induced[86] liver damage. *A. graveolens* extract dose-dependently attenuated the rise in various hepatotoxicity markers including aspartate transaminase, alanine transaminase, alkaline phosphatase, albumin, and total protein when compared with silymarin. Histopathological studies also showed the reversal of paracetamol-induced structural changes of liver tissues.

In another study, dietary intake of celery along with chicory and barley attenuates the elevated serum liver enzymes, total cholesterol, triglycerides and improves lipid profile in cholesterol-fed diets.[87]

Antioxidant activity

A. graveolens is a big source phenolic compounds, which provides a good source of antioxidants.[88] The antioxidant activity of Karafs leaf was

Table 1: The chemical constituent of the *Apium graveolens* Linn.

Group of chemicals	Chemical constituents	Reported activity	References
Glycosides	Apigenin	Neurogenesis stimulator (used in the Alzheimer disease), antitumor, antioxidant, antiviral	[26-28]
Organic acid	Caffeic acid	Antioxidant, antitumor	[29,30]
Organic acid ester	Chlorogenic acid	Anticancer, antioxidants, anti-inflammatory, analgesic	[31-34]
Furanocoumarins	Bergapten	Anti-psoriatic, anticancer	[35,36]
	Isopimpinellin	Anticancer	[37]
	Isoimperatorin	CYP450 inhibitor	[38]
	8-hydroxyl-5-methoxypsoralen	Antipsoriatic, CYP450 inhibitor	[39]
7-hydroxycoumarins	Osthenol	Antifungal, antibacterial	[40,41]
	Umbelliferone	Anti-inflammatory, analgesic, antioxidant, neuroprotective	[42-45]
Fatty acids	Myristic acid	Bioavailability enhancer	[46,47]
	Octadecanoic acid	Antimicrobial, immunomodulatory	[48,49]
	Palmitic acid	Antioxidant, anti-cholesterol	[47,50-52]
	Oleic acid	Increase fatty acid oxidation (by inducing cAMP/PKA and SIRT1 Ser-434 phosphorylation)	[51,53]
	Linoleic acid	Anti-CHF, anticancer	[54,55]
	Stearic acid	Antitumor, anti-cholesterol	[51,56]
Essential oil	d-limonene	Aromatherapy, anticancer, acaricidal, spasmolytic	[57-60]
	d-selinene	Antimicrobial	[61,62]
	Sedanolide	Antioxidant, anticancer, antimicrobial	[63-65]
	Terpineol	Anticonvulsant, antioxidant, antimicrobial	[66-69]
	Santalol	Antitumor	[70,71]
	Selinene	Antimicrobial, antioxidant	[72]
	Nerolidol	Antileshmanial, antimicrobial	[73,74]
	β-pinene	Antibacterial, antifungal, antioxidant	[75-77]
	d-carvone	Acaricidal, spasmolytic, antifungal	[59,60,69]
	β-myrcene	Antioxidant, antiulcer, anticancer, neuroprotective	[78-81]

CYP450 = Cytchrome P450, CHF = Congestive heart failure, cAMP = Cyclic adenosine monophosphate, PKA = Protein kinase A

investigated (by scavenging of the 1,1-diphenyl 2-picrylhydrazyl [DPPH] radical activity) and found to be a strong natural antioxidant by inhibiting oxidant process.[21] It may be attributed to its antioxidant constituents including L-tryptophan and derivatives of methoxy-phenyl chromenone.[89]

In another experiment, the organic and inorganic extracts of celery were tested and both of the extracts were found to a good scavenger of OH and DPPH radicals. *In vivo* experiments with CCl_4-induced toxicity also showed the significant protective effects.[90]

Larvicidal and mosquito repellent activity

The seed oil of the celery has a strong larvicidal, adulticidal, and repellent activity against the *Aedes aegypti* larva, the vector of dengue hemorrhage fever.[91,92] In another study, the mosquito repellent activity of celery oil (with 5% vanillin) was found better repellent activity than a number of commercially used repellent.[93]

Anticancer activity

Nonpolar extract of root and bulbs of *A. graveolens* was tested against the lymphoblastic leukemia cell lines CEM-C7H2 cell lines. The extract showed the significant cytotoxicity.[19]

Antidiabetic activity

The antidiabetic effect of the aqueous extract of the celery seed was tested on the diabetic rat. It was that intraperitoneal administration of the extract leads to changes in the lipid profile.[94]

Anti-inflammatory activity

The anti-inflammatory activity of celery was studied in croton oil-induced ear test model in mice. Results showed that the potency of the anti-inflammatory was seven times lower than the indomethacin. The mechanism involved in the anti-inflammatory activity may be due to the inhibitory activity of its active constituents apiin against inducible nitric oxide synthase (iNOS) and nitride oxide (NO) production.[95] Apiuman, a pectic polysaccharide found in the celery, has also been found to decrease the interleukin-1β and increased interleukin-10 production and diminish the neutrophils migra, which may also be the cause of its anti-inflammatory activity.[20] The stems of the celery plant also possessed significant anti-inflammatory activity due to the presence of polar constituents in the aqueous extract.[96]

Antimicrobial activity

A. graveolens has been found to exhibit antibacterial activity against *Escherichia coli*. The activity was more in the ethanolic extracts as compared to the aqueous and hexane extract.[97]

Analgesic activity

The ethanolic extract of the seed of celery possessed significant analgesic activity when tested against acetic acid-induced writhing and hot plate method.[98] The analgesic effect of celery is attributed to the involvement of celery in the cytochrome P450, which was found to be decreased in the liver homogenate.[99]

Antiulcer activity

The ethanolic extract of celery seed significantly protects the indomethacin and cytodestructive agents (80% ethanol, 0.2 M NaOH, and 25% NaCl) induced gastric ulcer. The results were assessed by biochemical and histopathological analysis of the control and treated samples. Extract significantly protects the gastric mucosa and suppresses the basal gastric secretion in rats possibly through its antioxidant potential that is evident from the presence of antioxidants compound (flavonoids, tannins) in the extract.[100]

Anti-spasmolytic activity

Ethanolic extract of the *A. graveolens* showed a significant anti-spasmolytic activity. It inhibited the ileum concentration in a

dose-dependent manner. The activity may be attributed due to the presence of a flavonoid, apigenin.[101]

Anti-infertility activity

The celery extracts were found to have a protective effect against the sodium valproate-induced testicular toxicity in rats. The histopathological analysis supported the results. Apigenin found as a major constituent in the extract may be responsible for the activity.[84] Protective study of the *Apium* was also studied against the chemically induced rat testis damage. It was found that celery has positive effect in the recovery of testis and sexual.[102-104]

Antiplatelet activity

A. graveolens has been found to have a potent antiplatelet activity. The effect is due to the presence of apigenin found in the extract. Apigenin inhibits the collagen, adenosine diphosphate (ADP), and arachiadonic acid induced aggregation of platelet. In addition, apigenin also inhibited collagen-ADP-induced aggregation in blood.[105]

Hypocholesterolemic activity

The hydroalcoholic extract of celery (*A. graveolens*) has been investigated for its effect on lipid profile of rats fed a high-fat diet. The result showed that celery significantly decreased the cholesterol, triglycerides, and low-density lipoprotein in the treated group as compared to the control group.[106,107]

The mechanism of hypocholesterolemic activity is attributed to its effect on bile acid secretion as well as the presence of polar compounds with sugar/amino acid moiety in the extract.[108]

Cardiotonic activity

It was found that apigenin isolated from the celery inhibited the contraction of aortic ring caused by cumulative concentration of calcium in high potassium medium. This relaxation of thoracic aorta may be attributed the Ca^{2+} ion suppressing effect of celery through both voltage and receptor operated calcium channels.[109]

In another study, derivative of 3-butylpathalide isolated from the celery showed significance cardiotonic activity. It acts by inhibiting the calcium dependent and independent release of glutamate from synaptosomes. It also decreases the nitric oxide (NO) content and NOS activity in the global cerebral ischemia-reperfusion model in rats. In addition, it also significantly inhibits the expression of the inducible NOS protein.[110]

The celery juice has also been tested on the doxorubicin-induced cardiotoxicity in rats. The content of reduced glutathione, activity of catalase, xanthine oxidase, glutathione peroxidase, and lipid peroxidation intensity in the liver homogenate and blood hemolysate was measured. The results showed the cardioprotective activity as compared to toxic group.[111]

TOXICITY AND SAFETY

The plant is generally safe for the common use. Although it causes the allergy in the central European population. The most important allergen are PR-10 (Api g 1), nonspecific lipid transfer protein – LTP 1 (Api g 2), profilin (Api g 4), and flavoprotein (Api g 5). Api g 2 and Api g 4 are potentially dangerous for allergic individuals because these allergens may induce an anaphylactic reaction.[112]

The plant is also reported to be infected with the fungus *Sclerotinia sclerotiorum* that causes dermatitis in sensitive people. This is common in Caucasians. Some people are allergic to the cress and it may cause anaphylaxis. The consumption should be avoided in case of pregnancy as it has uterine stimulant activity.[17]

CONCLUSION

The ancient literature and the practice among the local population clearly indicate that herbal medicine is being practiced in the Arab region since long back.

In this review, we documented the medicinal importance of the *A. graveolens* (Karafs) that is being used as anthelmintic, antispasmodic, carminative, diuretic, laxative, sedative stimulants in the Arab traditional medicine. The description of the plants and its medicinal importance as per the old Arab literature has been summarized. In addition, the phytochemical investigation the pharmacological activity which has been carried out so far has been summarized.

There is a need to preserve the pharmacological profile and the medicinal importance of the Karafs. There is also need to isolate the bioactive phytochemicals that are present in the plants. Karafs needs effective utilization to make a hallmark to treat the various diseases and to be available for ordinary population.

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Conflicts of interest

There are no conflicts of interest.

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