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Review Paper

Unani description of Tukhme Karafs (Seeds of *Apium graveolens* Linn) and its Scientific reports

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Abstract

Apium graveolens Linn commonly known as salad and Karafs in Unani literature, belongs to the family Apiaceae. Karafs is used in many diseases and is considered as one of the best diuretic and lithotriptic according to Unani literature.

Key words: Celery, karafs, *Apium graveolens*, Unani system of medicine.

Introduction

Tukhme Karafs (Celery) is the seed of *Apium graveolens* Linn commonly known as salad. Karafs is a well known drug used in the Unani system of medicine for a number of diseases and is one of the constituent of many pharmacopoeal preparations. Though the entire plant contains medicinal value however, its seeds and root are more commonly used therapeutically for diverse pathological conditions. It belongs to the family Apiaceae earlier known as Umbellifereae, over 20 species of biennial and perennial plants make up this genus.

Taxonomical classification

Kingdom – Plantae; Sub kingdom – Tracheobionta; Superdivision – Spermatophyta; Division – Magonliopisida; Subclass – Rosidae; Order – Apiales; Family – Apiaceae; Genus – *Apium;* Species – *A graveolens* Linn[1].

Nomenclature: Tukhme Karafs (seeds of *Apium graveolens* Linn) is known by different names worldwide.

Language/Region Nomenclature: Arabic- Bazrul Karafs; Bengali- Chanu, Randhuni; Bombay-Ajmud, Budiajamoda; Chinese- Qin cai; Kannada- Selerina; English- Celery; Greek- Eleioselinon, Udasaliyun; Hindi- Ajmud, Boriajmud; Pakistan- Karafs ajowan; Persian- Karasb, Karafs; Roman- Baatrakhiyun; Sanskrit- Ajmoda Andhapatrika,Brahmakoshi; Tamil- Asham tagam; Telugu- Ashu magada voman, Ajmudah; Urdu- Ajmod[2]

Description of Karafs as described in Unani literature: In Unani system of medicine the names of drugs are adopted from Persian or Arabic nomenclature. In Persian *Apium graveolens* Linn is known as Karafs. Hence the drug Karafs means the same as *Apium graveolens* Linn and the seeds are called as Tukhme Karafs. Hussain writes that Karafs is the Celery of Europeans and the Udasaliyon of Greeks. He mentions five varieties of Karafs namely Bustani, Jabli, Nabti, Sakhuri, Maiee (Tari). Bustani is cultivated variety while Jabli grows in hills, Sakhuri on stony surface, Nabti in shady places and Maiee or Tari near water or ponds. According to Hussain, Sakhuri, Nabti and Maiee varieties of Karafs are called in Greek, as Fiturasaliyun, Akusaliyun and Samarniyun respectively[3]. Al Biruni writes that the people of Tirmidh, Khatl and Bukharistan called Karafs as Sumbul[4]. Avicenna and Baitar have also mentioned five types of Karafs i.e. Jabli, Sakhuri, Bustani, Mashriqi and Qabrisi[5,6]. The Nomenclature of the five different varieties of Karafs as described in the literature related to Unani system of medicine is below (table-1). This classification of Karafs appears to be based on its origin[3-6]. The Arabs probably obtained their knowledge of Tukhme Karafs from the Greeks. Dioscorides describes five kinds of Karafs, the Selnion of Theophrastus was probably Celery. Dioscorides further mentions that wild varieties (Jabli and Sakhuri) have different sub varieties. One of them has bud similar to garlic, second is fragrant having a rose like bud, and third has a milky white bud[7]. Baitar quotes Dioscorides in describing the seeds of Fiturasaliyun (Sakhuri). The seeds are similar to those of Ajowan (*Ptycotis ajowan* DC) but having stronger odour[6].

According to Rhazes the variety that grows near water (Tari or Maiee) is larger than the cultivated one (Bustani), whereas the wild variety (Jabli or Sakhuri) is Roman in origin and is bitter in taste. Azam Khan mentions that the various varieties of Karafs are named after their origin or after the regions where they are found. He has described the Bustani variety in brief. According to him the leaves are somewhat round in shape having many lobes with toothed margins. The plant is about one yard in height, the flowers are yellow, fruits round and small; equal in size to Anise seed, black and dull in colour, acrid in taste, and odorous. Its roots are large, black in colour having fibres[8]. Najmul Ghani describes flowers as white, the flowers and seeds are arranged like an umbrella shape. The taste of seeds is

pungent and slightly mint like[9]. The description of the plant based on the modern scientific studies gives almost similar account as mentioned by earlier authors of phamacology[10].

Temperament[9]: Hot 2^0 and Dry 2^0.

Pharmacological Actions: Deobstruent, Carminative, Appetizer, Lithotriptic, Diaphoretic, Diuretic, Emmenogogue, Astringent, Anthelminthic, Semen Procreator, Cardiac tonic, Aphrodisiac[3-9].

Therapeutic uses: In Unani system of medicine, the whole plant of Karafs (seeds, leaves, stem and root) is used as medicine in various forms like decoction, powder, paste etc for many activities. The seeds are used as stimulant, cardiac tonic, carminative, diuretic and antiseptic. The seeds are also used in conditions of asthma, bronchitis, liver and spleen disorders. The important therapeutic actions of its seeds on different systems of the human body which have been described by various authors are as follows:

Urogenital system: The decoction of seeds is said to be a potent medicine as a lithotriptic. It expels the stones of kidneys and bladder. The seeds are also used in different dosage forms in cases of sexual debility. The seeds are therapeutically used to promote diuresis[4, 8, 9].

Gastro-intestinal tract: The seeds are used in protozoal infestation. They are good appetizer and also used in flatulence. They are effective in hiccough, tenesmus and used as adjvent to purgatives[4, 9].

Respiratory system: In the form of decoction it is effective in asthma, breathing difficulties, bronchitis and pleurisy[8].

Inflammation: In the treatment of inflammatory conditions seeds are used with honey. The powder of seeds mixed with barley powder is applied in the form of paste for the treatment of inflammation of eyes. The decoction and poultice of the seeds are used in backache, sciatica, gout and rheumatoid arthritis[4,7,8,9]. Its decoction is also effective in measles and all types of fevers[8]. Hussain writes that its local application on boils is quiet effective[3]. In combination with some other medicines it is also effective in ascitis and jaundice[7].

Adverse effect: The drug Tukhme Karafs has been mentioned to be used cautiously in patients with hot temperament. It is contraindicated in pregnant and lactating women. It has also been mentioned that Tukhme karafs may have adverse effect in patients suffering from epileptic disorders[9].

Correctives: *Pimpinella anisum* Linn and *Pistacia lentiscus* Linn[9].

Substitute: *Hyoscyamus niger* Linn[9].

Dosage: 3 -5 grams[9]

Compound Formulations

Banadiqul buzoori, Dawaul kurkum kabir, Habbe khabsul hadeed, Jawarish falafili, Jawarish safarjali qabiz, Jawaish zarooni sada, Jawarish zarooni ambari, Jawarish shehreyaran, Jawarish narmushk, Majoon jalali, Majoon foodnaj, Majoon hajrul yahood, Majoon jograj gugal, Majoon kalkalanaj, Majoon nankhwah, Majoon dabeedul ward, Sharbat bozoori haar, Sikanjabeen buzoori motadil, Sufoof namak sheikhur raees, Sufoof moya, Sufoof mohazzil, Sufoof habbur rumman, Zimad sumbulut teeb[11].

Description as given in modern literature: The modern description of Tukhme Karafs can be studied under the following categories:

Geographical distribution: Karafs is an erect, annual or biennial plant, native to Europe and now naturalized and occurring wild in the foot-hills of north-western Himalayas and the outlying hills of Punjab, Himachal Pradesh and Uttar Pradesh[12].

Macroscopic features: John Lindley in Flora Medica describes it as herbaceous plant with the root thickened at the neck (figure 1). Stem furrowed, branched. Leaves are pinnate with wedged-shaped cut segments. Umbels axillary or nearly sessile on the apex of the stalk; no involucres; Flowers greenish white; Calyx obsolete; Petals roundish entire; Disk depressed (figure 2). Fruits round, contracted at the side, double. Half-fruits with 5 filiform equal ridges, of which the laterals form the border (figure 3). Dorsal channels with single vittae lateral with 2-3. When wild, growing in wet meadows and in ditches, it is acrid and poisonous; when cultivated in dry ground, and partially blanched[13]. According to Khorey and Katrak its fruit is ovate or globular, surface hairy, slightly tubercled wrinkled and marked with prominent ridges, colour greenish, yellow or brown, 2 mericarps, 5 ribs and 12 oil tubes, taste aromatic, somewhat pungent, slightly mint like at first then bitter, odour coriander like, faintly terbinthaceous[14].

Table-1
Different varieties of Tukhm karafs, its other names and their origin

Sl no	Name of the Variety	Other names	Source of origin
1	Bustani	Saalibiyun	Cultivated
2	Jabli	Aqt Saliyun, Kohi Maqdun	Self growing on hills
3	Sakhuri	Fitursaliyun	Self growing on stony surface
4	Nabti	Akusaliyun Mashriqi, Karafse Azeem	Grown in shady places, now a place in Syria
5	Tari (Maiee)	Samarniyun,Anusaliyun, Qurratulain.	Growing near rivers or canals

Figure-1
Plant

Figure-2
Flowers

Figure-3
Fruit/ Seeds

According to the FDA standards of identity, Celery seeds are the dried fruit of a biennial herb, *Apium graveolens* Linn; light brown to brown-color, having characteristic celery aroma and a warm, bitter taste. The quality characteristics are measured by the volatile oil, non-volatile ether extract, total and acid insoluble ash[15].

Microscopic features: The sectional view of the fruit shows a wavy outline. Each mericarp has mostly five ridges and six to nine vittae. The epicarp consists of single layer of rectangular, thin walled parenchymatous cells coated with irregular cutile on the outer side. The mesocarp region is mostly composed of several layers of moderately thick walled parenchymatous which are polygonal to oval in shape. The sclereids of mesocarp which are rather irregular shaped, i.e. ovoid to elongate rectangular with a slightly sinuous outline. The walls are slightly thickened at corners. Innermost layer of mesocarp is made up of large brown parenchymatous cells which are elongated rectangular in shape, and is attached to the endocarp. The endocarp consists of a single layer of rectangular to squarish thin walled parenchymatous cells. The testa, which is usually associated with the endocarp, is generally single layered consisting of thin walled elongated rectangular and mostly collapsed cells. Beneath which the endospermic region is composed of several layers of rectangular to polygonal thick walled parenchymatous cells containing aleurone grains which are oval to round and are joined in groups. Most of the endospermic cells contain microspheroidal crystals of calcium oxalate. A small amount of vascular tissue and reticulated parenchyma is present. The elements are small and are usually in groups. The vessels show spiral or reticulate thickenings[16].

Cultivaton

The plant is largely cultivated in Amritsar and adjoining parts of Punjab, Haryana and some parts of western Uttar Pradesh for its seeds. In India, Celery has gained importance only recently, more as a seed crop than as a vegetable. Large scale cultivation is done for procurement of seeds. Celery needs a cool climate and is moisture love plant, requiring plenty of water and regular irrigation. For seed production in the plains sowing is done in September-October, the seedlings are transplanted later in December or in January and the seed crop is ready by the middle of May. For raising the seed crop, the seedlings are normally planted in the field in rows 45 cm apart. No major disease and pests have been reported on Celery so far. Hot water treatment of seeds is successful in reducing the incidence of blights. The seed crop is ready for harvest when the flowers lose their white colour and become reddish. The plant are cut and left in the field for 2-3 days for drying and then threshed with sticks to bring out the seeds. The seeds are winnowed through different sieves for grading. The average yield of Celery seed, when cultivated for seed, is estimated at one tonne/ha[12].

Phytochemical studies: i. The chemical constituents include organic and inorganic compounds such as glycosides, steroids, Phenols, flavonoids, sodium, potassium, calcium and iron16. The seeds also contain apiin, apigenin, caffeic acid and chlorogenic acid. It contains four furocumarins, viz. rutaretin (C14H14O5, m p 1980), apiumetin (C14H12O4, m p 1980), bergapten, and isopimpinellin, other substances isolated are seslin, isoimperatorin, osthenol, apigravin (m p 168 - 700), gravebioside A (luteolin – 7 - apiosylglucoside mp 256 - 570), gravebioside B (chrysoeriol – 7 – apiosylglucoside, m p 234 - 350), myristicic acid, 8 – hydroxyl – 5 –methoxypsoralen (m p 2180), umbelliferone, Δ6,7- octadecanoic acid, and Δ7,8-octadecanoic acid[12]. ii. The seeds yield a fatty oil (17%) having Sp gravity at 25º, 0.9282; n25º, 1.4803; acid val, 8.6; sap val, 193.2; iod val, 90.0; and unsapon matter, 6.4%. The fatty acid composition of the oil is as follows: Palmitic, 11.7; oleic, 30.5;

linoleic, 9.7; petroselinic acid, 41.0; and resin acids, 7.0%. The seeds yield a golden yellow essential oil (2-3%) having the following characteristics: Sp gravity15^0, 0.850 to 0.895; [α] 20^0 , +65o to + 82o; *n*20^0 ,1.478-1.486, acid value upto 5, ester value, 15-40; The main constituents of the oil are *d*-limonene (50%), *d*-selinene (10%-15%), sedanonic anhydride (0.5%) and sedanolide (2.5 to 3%). The last two are responsible for the aroma of the oil. The Celery seed oil on standing gives a sludge which contains wax, mp 99.40 (acid value, 25.6; saponification value, 211.3; and iodine value, 47.3)[12]. Huo-ping-Pan and D. W. Kenndy determined the fatty acid constituents of Celery seed oil by Gas Liquid Chromatography (GLC) and reported two more fatty acids namely stearic and linoleic acid[17]. Rai and Muttana have reported the presence of d-limonene 50%, selinene 7%, terpineol 5.6%, santalol 4.6% and a new acid 3.5% with a Keto alcohol 11.3%[18]. Bhatnagar and Handa studied the yield percentage of volatile oil in different parts of Karafs at different stages of growth. They noted that the oil content of the fruits increased from about 1% in the one week old fruits to 2.9% in five weeks old fruits after which the concentration was reduced slightly[19]. Proximate composition of *Apium graveolens* L seeds and the physico-chemical characteristics of the volatile oils were determined by Jagan Mohan and co-workers. In their study the GC-MS analysis of the volatile oils showed the presence of 44 constituents of which limonene (50.9%), β-selinene (19.53%), 3-n-butylphthalide (6.92%), nerolidol (2.29%), α-selinene (1.63%), β-pinene (1.22%), d-carvone (1.86%), n-amylbenzene (1.63%), β-myrcene (1.3%) and cis-limonene oxide (1.12%) were the major constituents. Deterpenation of the volatile oil gave about 13% terpeneless oil. The yield of celery seed oleoresin was about 24% and the oleoresin was found to keep well when stored in cold (8-10°C) for 60 days even without the addition of antioxidants[20].

Scientific Reports

General pharmacology: The LD50 of 50% ethanolic extract of the fruits has been reported more than 1000 mg/kg i.p. in mice and 1000 mg/kg i.p. in rats[21]. Hanefi *et al* determined the lethal doses of fixed and volatile oils extracted from fruits of *Apium graveolens* Linn, using Swiss albino mice by the method of probit analysis. The lethal doses (ml/kg) LD1, LD10, LD50, LD90, LD99 of *Apium graveolens* Linn. essential oil were 0.706, 1.261, 2.568, 5.228, 9.333 and that of fixed oil were 0.789, 1.274, 2.291, 4.120, 6.647, respectively[22].

Central Nervous System: Its fraction (b.p. 176^{0}C) containing α-Limonene was devoid of CNS activity. Maximum CNS activity was found in fractions (b. p.180^0 C) and (b.p.265^{0}C) containing sedanolide and α-selinene respectively. The ED_{50} values by the method of potentiation of pentobarbital narcosis, and conditioned avoidance response were found to be 0.098 ml/100 gm and 0.093 ml/100 gm respectively. The ED50 value by the method of maximal electro shock seizures and Metrazol seizure-threshold test were found to be 0.073 ml/100 gm and 0.103 ml/100 gm respectively. The maximal activity of the fraction appears to be against Maximal electro shock seizures (ED50 values being 0.073 ml/100 gm)[23]. Alkaloid content from the seeds of Karafs was studied for its CNS activity by Kulshresha. It was found to have tranquillizing effect in various animal models as evidenced by reduction in spontaneous motor activity, potentiating of pentobarbital narcosis and abolition of conditioned avoidance response. The extract was reported to reduce mortality in aggregated mice by amphetamine and protected mice in maximal electro shock seizure pattern test, but was ineffective against metrazole and strychnine convulsions in these animals. The ED50 values (in mg/100 gm) were found to be 336 ± 5.5, 29.8 ± 1.4 and 24.3± 3.6 in potentiation of pentobarbital narcosis, conditioned avoidance response test and the test for spontaneous motor activity respectively. However ED50 value of reducing mortality in mice in amphetamine group toxicity test was found to be higher (68 ± 4.6). The ED50 in mice was found to be 110.2 ± 7.6 mg/100 gm. Thus the safety margin of the extract was shown to be two to three folds in animal experiments. The extract did not induce protection against metrazole and strychnine convulsions but did so against MEST in mice (ED50 – 34.6 mg/ 100gm) indicating that the drug acts at a level higher than the brain stem in the central nervous system. This contention was further substantiated by the presence of potent tranquilizing activity in various animal tests. The higher margin of safety and presence of tranquilizing and anticonvulsant activities in the alkaloidal fraction suggest its therapeutic utility in various psychiatric conditions and in grandmal epilepsy[24]. The central depressant activities of 3, n-butylphthalide and a new compound, sedanenolide, were studied in mice. While neither compound affects ethanol sedation, they exhibit similar activities in both prolonging pentobarbital narcosis by prior administration of the test compounds and in inducing sleep immediately following recovery from a prior treatment with barbiturate. Weak sedative activity is also shown to reside in both compounds without potentiation[25].

Anthelminthic activity: Kokate and Verma have reported that 0.1% emulsion of oil in 1% aqueous polysarbate 20 produced paralytic effect in 31 minutes and lethal effect in 78 minutes and 0.2% emulsion of oil in 1% aqueous polysarbate 20 produced paralytic effect in 13 minutes and lethal effect in 44 minutes in comparision to 0.1% piperazine citrate which produced paralysis in 24 minutes and lethal effect in 70 minutes and 0.2% piperazine citrate which produced paralysis in 16 minutes and lethal effect in 44 minutes[26].

Antibacterial activity: The essential oil of Tukhme Karafs showed marked antibacterial activity against, *Bacillus subtilis* 10 mm, *Bacillus pumilus* 11mm, *Vibro cholera* 11 mm, *Staphylcoccus aureus* 13 mm, *Streptococcus Pyrogens* 15 mm, *Salbus* 13 mm, *Shigella dysentrica* 12mm, *Coryne bacterium diphtheria* 15 mm, *Salmonella typhii* 11 mm, *S faecalis* 12 mm, *Pseudomonos solanacearum* 19 mm. The standard antimicrobials used were benzoic acid 1%, Benzyl pencillin (1000u/ml), Streptomycin sulphate (2 mg base/ml), Chlorobenzoic acid 1%, Hexachlorophene 1%, Hamycin 0.5%,

Chlorobutol 1%, Salicylic acid 1%. The essential oil of Tukhme Karafs also showed bacteriostatic effect against all the above microbes[27]. The essential oil of Tukhme Karafs has further been reported to be effective against *S typhii*, *S albus* and *V cholera*[28]. In some other studies the essential oil of Tukhme Karafs has been found effective against *C. albicans, S. aureus, B. subtilis* and *P. Maltocida* [29] and against *Staphylococcus aureus* and *Sarcina lutea*[30].

Antifungal activity: The anifungal activity of steam distilled oil of Tukhme Karafs was carried out by Jain and Jain. They evaluated the antifungal activity of the oil by comparing the inhibition activity of the oil with respect to eight standard antifungal drugs namely Griseofulvin 1%, Hamycin 0.5%, Zinc undecnoate 1%, cetrimide 1%, benzoic acid 1%, Salicylic acid 1%, hexachlorophene 1% and Chlorobenzoic acid 1%. The steam distilled oil of Tukhme Karafs showed marked activity in comparison to standard drugs against *Trichophyton-terrestre, Histoplasma-capsulatum, A niger, A nidulans, Epidermophylon floccosum, Fusarium-oxysporum*[31]. The antifungal activity of essential oil has also been reported by Kher and Chaurasia against fifteen different species of animal and plant pathogenic fungi[32].

Anti inflammatory activity: i. In a study by R. Momin it was found that the Cyclooxygenase inhibitory and antioxidant bioassay-directed extraction and purification of celery seeds yielded sedanolide (1), senkyunolide-N (2), senkyunolide-J (3), 3-hydroxymethyl-6-methoxy- 2,3-dihydro-1H-indol-2-ol (4), L-tryptophan (6), and 7-[3-(3,4-dihydroxy-4-hydroxymethyl-tetrahydro-furan-2-yloxy)-4,5-dihydroxy-6-hydroxymethyl-tetrahydropyran- 2-yloxy]-5-hydroxy-2-(4-hydroxy-3-methoxy-phenyl)-chromen-4-one. The structures of compounds 1–7 were determined using spectroscopic methods. Compound 4 is reported here for the first time. At 250 µg/ ml, (COX-II) inhibitory activities at pH 7. The acetylated product (5) of compound 4 also inhibited COX-I and COX-II enzymes when tested at 250 µg/ ml. Compounds 6 and 7 exhibited good antioxidant activity at concentrations of 125 and 250 µg /ml. Only compounds 1–4, 6 and 7 displayed prostaglandin H endoperoxide synthase-I (COX-I) and prostaglandin H endoperoxide synthase-II compounds 1–3 exhibited topoisomerase-I and -II enzyme inhibitory activity at concentrations of 100, 200 and 200 µg/ ml, respectively[33]. ii. The antinociceptive and anti-inflammatory effects of the aqueous and hexane extracts obtained from *Apium graveolens* L seeds were evaluated by Mina Ramezani et al on Formalin and Xylene-induced ear edema in mice. The hexane fraction was found to be effective against nociception while both fractions showed remarkable antiinflammatory effect which supported the traditional use of *Apium graveolens* in diseases associated with inflammation[34].

Gastro intestinal activity: i. The methanolic extracts of *Apium graveolens* Linn showed hepatoprotective activity comparable with standard drug silymarin. Other extracts namely petroleum ether and acetone also exhibited a potent activity[35]. ii. In an experimental study by Taher *et al,* the effect of volatile oil of seeds of *Apium graveolens* Linn was studied on some hepatic enzymes including SGOT, SGPT and ALP in rats and also to identify the active components of volatile oils by GC/MS. The authors found D-limonen and myrcen as the major active components in volatile oil of *Apium graveolens* Linn. They concluded that active ingredients of Celery may act as an antioxidant or to decrease the production of free radicals, causing stabilization of hepatocyte membrane and decreasing the release of enzymes into the blood[36]. iii. *Apium graveolens* Linn. Has been reported to alleviate most of the Sodium valproate (VPA) induced effect in experimental animals suggesting its protective role through antioxidant activity. Apigenin content was estimated and was found as a major fraction of *A. graveolens* extract[37].

Conclusion

Tukhme karafs is an annual or biennial plant belonging to the family Apiaceae is used as Deobstruent, Carminative, Appetizer, Lithotriptic, Diaphoretic, Diuretic, Emmenogogue, Astringent, Anthelminthic, Semen Procreator, Cardiac tonic, Aphrodisiac activities. Some of these activities are scientifically evaluated and some are yet to be evaluated.

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