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Pharmacological and phytochemical analysis of *Foeniculum vulgare* Mill: A review

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Abstract

Background: Medicinal plants always played an important role in the health development of mankind. *Foeniculum vulgare* is one of the oldest spice plants which, due to its economic importance and significant pharmaceutical industry applications, are considered as one of the world's most important medicinal plants.

Methods: In order to gather the information the keywords *Foeniculum vulgare*, therapeutic, and pharmacology have been searched until March 31, 2019 from journals accessible in databases such as Science Direct, Scopus, EBSCO, Medline, PubMed, Embase, SID, and Iran Medex.

Results: The results showed that this plant has various pharmacological properties including antioxidant, anti-cancer activity, anti-inflammatory, antifungal, Anti-bacterial and estrogenic effects which are probably due to the presence of aromatic compounds such as anethole, estragole and fenshon.

Conclusion: *Foeniculum vulgare* possesses various pharmacological properties and play an important role in human health; hence, it might be used for different drug productions.

Keywords: Medicinal plants, *foeniculum vulgare*, unani medicine, anethole, antioxidant, anti-inflammatory

1. Introduction

The use of herbs to treat diseases has been common since ancient times. Also the use of plants different parts is common in public health. Using natural remedies and herbal medicines is beneficial cost-effective method for treating diseases. Nowadays medicinal herbs are good alternative to chemical drugs, one of the major reason for this is low side effect compared to chemical drugs. Plants have always played an important role in the health and treatment of human society. Medicinal herbs have fewer side effects than synthetic drugs and due to their antioxidant properties they reduce drugs toxicity^[1, 2]. Also, the natural effective ingredients cause biological balance and prevent drug accumulation in body. So medicinal plants can be used in the treatment of various diseases³. *Foeniculum vulgare* is a biennial medicinal and aromatic plant belonging to the family Apiaceae (Umbelliferaceae). It is a hardy, perennial-umbelliferous herb with yellow flowers and feathery leaves. It grows to a height of up to 2.5 m with hollow stems. The leaves grow up to 40 cm long; they are finely dissected with the ultimate segments filiform (thread like) of about 0.5 mm wide. The flowers are produced in terminal compound umbels. The fruit is a dry seed 4–10 mm long. It is generally considered indigenous to the shores of Mediterranean Sea but has become widely naturalised in many parts of the world especially on dry soils near the sea coast and on the river banks. Some authors distinguish two sub-species of fennel, piperitum and vulgare: sub-species piperitum has bitter seeds, while sub-species vulgare has sweet seeds which are used as flavouring agents in baked goods, meat and fish dishes, ice creams, alcoholic beverages, etc due to their characteristic anise odour⁴. Morphological differences between these two sub-species are not always clearly defined.

2. Nomenclature

Arabic:	Bisbas, razianaj
Bengali:	Mauri, p.anmour.
English:	Bitter fennel, common fennel, sweet fennel, wild fennel
Hindi:	Badi, badishep, Bari saunf, badi, saunf, saunp, saunf, sonp
French:	Fenouil
Germany:	Fenchel, fenfchle, bitterfenfchel, wilder fenfchel, dunkler fenfchel,
Chinese:	Hui xiang, xiao Hui xiang

Laotian: Phaksi
 Latin: *Foeniculum, maratrum*
 Loja, Ecuador: Hinojo
 Majorcan area: Fonoll
 Middle Navarra: Hinojo, cenojo

3. Taxonomy

Kingdom: Plantae,
 Division: Tracheophyta,
 Subdivision: Spermatophytina,
 Class: Magnoliopsida,
 Order: Apiales,
 Family: Apiaceae,
 Genus: *Foeniculum*,
 Species: *vulgare*, and
 Botanical name: *Foeniculum vulgare* Mill.

4. Synonym

There are various synonyms of *Foeniculum vulgare*. Like, *Anethum foeniculum* Clairv, *A. foeniculum* L., *A. rupestre* Salisb, *Feniculum commune* Bubani, *Foeniculum azoricum* Mill, *F. capillaceum* Gilib, *F. dulce* DC, *F. foeniculum* (L.) H. Karst, *F. officinale*.

5. Distribution

In India *Foeniculum vulgare* is cultivated in various regions of Assam, Punjab, Maharashtra and Gujarat. It is also cultivated in Europe, Asia, Temperate regions of Africa and South America [5].

6. Botanical description

Foeniculum vulgare is an ancient seasonal herb. The fennel plant originated in the southern Mediterranean region and through naturalization and cultivation it grows wild throughout the Northern, Eastern, and Western hemispheres, specifically in Asia, North America, and Europe. It is cultivated in fields and also grows wild. The herb was well-known to the ancient Egyptians, Romans, Indians, and Chinese. The Romans grew it for its aromatic seeds and the edible fleshy shoots are still a very common vegetable in southern Italy [6]. Emperor Charlemagne was known to have encouraged its cultivation in Central Europe. It is an indispensable ingredient in modern French and Italian cooking. All parts of the plant are aromatic and can be used in many ways.



Fig 1: Leaf of *F. vulgare*



Fig 2: Flowers of *F. vulgare*



Fig 3: Seeds of *F. vulgare*

F. vulgare is an upright, branching perennial herb with soft, feathery, almost hair-like foliage growing up to 6.6 ft. (2 m) tall. This plant looks similar to dill. It is typically grown in vegetable and herb gardens for its anise-flavored foliage and seeds, both of which are commonly harvested for use in cooking. It is erect and cylindrical, bright green, and smooth as to seem polished, with multiple branched leaves cut into the finest of segments. The leaves grow up to 40 cm long; they are finely dissected, with the ultimate segments filiform (threadlike), about 0.5mm wide. The bright golden flowers, produced in large, flat terminal umbels, with thirteen to twenty rays, bloom in July and August.

Foliage: Stem striate, leaves 3-4 pinnate, segments filiform, up to 1.6 in. (4 cm) long; leaf bases sheathing. It has a green, sleek, and slippery stem with upright stiff branches and much divided leaves in linear segments. Rays are 5–30 numbers with 0.39–2.4 inches (1–6cm) long. Flowers are small, yellow, and found in large flat-topped umbels. Fruits are oblong to ovoid with 0.12–0.2 inches (3–5 mm) long and 1.5–2.0mm broad. The stylopodium persists on the fruit. The fruits are elongated and have strong ribs. The most esteemed fennel seeds vary from three to five lines in length and are elliptical, slightly curved, and somewhat obtuse at the ends.

Microscopic characteristic

The mesocarp of fennel consists of brownish colored parenchyma. It also consists of brown epithelial cells which are transversed in the ridges by vascular bundles having one inner xylem strand and two lateral phloem strands. They also contain lignified fibres. The mesocarp consists of brownish parenchyma which is traversed longitudinally by six large schizogenous vittae. Some of the mesocarp cells of vascular bundles possess lignified reticulate cells. Epidermis is covered with smooth cuticle. Epidermis also contains fewer stomata and no hairs. Endocarp of this plant consists of parallel layer of flattened thin walled cells. Endosperm is composed of thick walled polygonal cellulosic parenchyma, which contains fixed oils and micro rosette crystals of calcium oxalate.

Powdered plant material

The powdered plant material of fennel is grayish-brown to grayish-yellow in color. It contains polyglonal secretory cells which are yellowish-brown in color and these cells are associated with the thin-walled transversely elongated cells, which are 2–9 μm wide. It also contains numerous fibre bundles. Endosperm fragments contain aleuronic grains along with very small micro rosette crystals of calcium oxalate, and fibre bundles from the carpophores.

General identity tests

The identity tests have been done for the macroscopic and microscopic examinations of *Foeniculum vulgare*, thin-layer chromatography is used in the presence of anethole and fenchone, and gas chromatography is used in the presence of anethole, fenchone and estragole.

7. *Foeniculum vulgare* in Unani System of Medicine

Name:	Badiyan
Mizaj (Temperament):	Hot ^{2°} & dry ^{2°}
Botanical name:	<i>Foeniculum vulgare</i>
Part used:	Root, Leaf and Seed.
Constituents:	Essential oil.
Actions: Seed:	stimulant, aromatic, stomachic, carminative, Emmenagogue.
Leaf:	Diuretic.
Root:	Purgative.
Oil of seed:	wormicide.
Uses:	Paste of seed or fruit; as cooling drink of fever, burning sensation in passing urine.
Dosage:	Seeds: 4-9gm.
Odor:	characteristic aromatic in nature.
Taste:	Sweet to bitter.

8. Important unani formulations

Some important unani formulations of *Foeniculum vulgare* are as follows-

Syrup Alkuli (Buzuri)
Syrup Fevnil (khakshi)
Syrup Badiyan
Capsule Agerd (Tabkhir)
Tablet Tonalax (Mulaiyan)
Sufoof Moya
Etrifale Badiyan
Jowarish Zarooni
Sufoof Musakkin

9. Chemical constituents

All parts of fennel such as roots, leaves, fruit and especially the seeds are used [7]. Fennel seed contains 6.3% water, 9.5% protein, 10% fat, 13.4% minerals, 18.5% fibers and 42.3% carbohydrates [8]. Its leaves contain vitamins and minerals such as calcium, potassium, sodium, iron, phosphorus, thiamine, riboflavin, niacin and vitamin C [9]. Fruits consist 10 to 12 % of oil that is stored in the cotyledons of seeds. Oil obtained from the fennel fruit has 4% palmitic acid, 22% oleic acid, 14% linoleic acid and 6% petrocyclic acid. The fruit has value of 4 to 6% essence which its essence and combine ingredients vary according to the location of plant growth [10]. The aromatic property of fennel is because of the essence. There are more than 30 types of terpene compounds in the essential oil of fennel, the most important of them are 50 to 80% trans-anethole, 8% fenshon and limonene 5% [11]. This herb also contains phenolic compounds such as flavonoids, phenolic acids, hydroxycinnamic acids, coumarin and tannin [12]. Phenolic acids include 3-O-Caffeoylquinic acid, 4-O-caffeoylquinic acid, 5-O-caffeoylquinic acid, 1, 3-O-di-caffeoylquinic acid, 1, 4-O-di-caffeoylquinic acid and 1, 5-O-di-caffeoylquinic acid. Its flavonoid contains eriodictyol-7-rutinoside, quercetin-3-rutinoside and rosmarinic acid [13]. Also aqueous extract of fennel fruit include quercetin-3-O-galactoside, kaempferol-3-O-rutinoside, kaempferol-3-O-

glucoside, quercetin-3-O-glucuronide, kampferol-3-O-glucuronide, isoquercetin, and isorhamnetin-3-O-glucoside [14].

10. Traditional uses

Foeniculum vulgare subsp. *Vulgare* var *azoricum*, the vegetable form of fennel, is sometimes confused with anise due to a similarity in flavor to the true anise. *Foeniculum vulgare* has many traditional uses in the treatment of various diseases. All of the aerial portions of fennel are edible, including the flowers. Fennel seeds are baked into breads, biscuits, stuffings and Italian sausages, and added to sweet pickles and sauerkraut. Stems can be grilled with fish, meats and vegetables, and leaves can be added to salads, olives, fish, and snails or used as a garnish. The essential oil from the seeds is added to cosmetics perfumes, pharmaceuticals and soaps. Fennel oil, seeds or extracts are also used to flavor prepared foods including meats, ice cream, candy, baked goods and condiments as well as liqueurs like sambuca, non-alcoholic beverages and toothpaste. In traditional medicine, fennel was used as an aphrodisiac and to encourage menstruation and lactation. It has been used as a Galactagogue improving the milk supply of a breastfeeding mother. This is suggested to be due to the presence of phytoestrogens present in fennel which promote growth of breast tissue [15].

11. Pharmacology

Foeniculum vulgare is used traditionally to treat a large number of disorders and diseases, but yet very few pharmacological activities have been found significant. Studies those found to be significant are following:

Antidiabetic activity: Abou N *et al.*, (2011) carried out antidiabetic activity of *Foeniculum vulgare*. Fennel was traditionally reported to be highly recommended for diabetics. The essential oil which is present in *Foeniculum vulgare* possesses to exhibit an antidiabetic effect in Streptozotocin-Induced diabetic Rats. In this study rats were divided into 3 groups 10 rats in each group. Group I was taken as normal control and group II was taken as diabetic control. Group III in which diabetic rats received *Foeniculum vulgare* Mill essential oil (30 mg/kg bw orally). The dose was selected according to the LD50. The results has been reported the marked improvements of hyperglycemia and pathological changes induced by streptozotocin after fennel ingestion which can prove its effect as antidiabetic in folk Medicine. A protective effect was obtained by using *Foeniculum vulgare* Mill essential oil to diabetic rats [16].

Antioxidant activity: Singh G *et al.*, (2006) carried out antioxidant activity of *Foeniculum vulgare* using acetonic extract prepared by soxhlet extraction. Gas chromatography (GC) and Gas chromatography- Mass spectroscopy (GC-MS) were Use for the chemical analysis of the fennel. These techniques showed the presence of 35 components in volatile oils of *Foeniculum vulgare*. Trans-anethole was the major component. Acetonic extract showed the presence of 9 components. Linoleic acid, oleic acid and palmitic acid were the major components. Different techniques were used for the evaluation of the anti-oxidant activity such as petriplate method; the volatile oil showed complete zone inhibition against *Aspergillus niger*, *Aspergillus flavus*,

Fusarium graminearum and *Fusarium moniliforme*. Another technique was food poison technique in which both extract and volatile oils showed good to moderate zone of inhibition. The antioxidant values were carried out by measuring the peroxide and thiobarbituric acid values for linseed oils. The acetic extract and volatile oils showed great zone of inhibition as compared to the butylated hydroxyanisole (BHA) and butylated hydroxytoluene (BHT) [17].

Gastrointestinal effects: *Foeniculum vulgare* has been proven to have gastrointestinal effects by Niiho Y *et al.*, (1977). Intragastric administration of *Foeniculum vulgare* fruits 24.0 mg/kg bw increased spontaneous gastric motility in unanaesthetized rabbits; at a dose of 25.0 mg/kg bw the fruits reversed the reduction of gastric motility induced by pentobarbital [18].

Hypolipidemic and Anti-Atherogenic Activity: Mokkhasmit M *et al.* (2011) carried out hypolipidemic and anti-atherogenic activity of *Foeniculum vulgare*. The aqueous extract of *Foeniculum vulgare* was used for the hypolipidemic and anti-atherogenic activity in mice. Triton WR-1339 (200 mg/kg body weight) induced hyperlipidemia in mice. In this study mice were divided into three groups, Control, hyperlipidemic and hyperlipidemic treated with fennel aqueous extract, administered by a force-feed. A significant decrease of plasma lipid levels occurred. 24 h after treatment, plasma total, cholesterol, triglycerides, LDL-cholesterol and Apolipoprotein B decreased by 40 %, 23 %, 61% and 61%, respectively and increased in HDL-cholesterol and apolipoprotein A-I by 85 % and 58%, respectively. Also, a histological study on heart alterations showed a marked decrease in lipid deposits [19].

Cardiovascular effects: Cardiovascular activity of *Foeniculum vulgare* was carried out by Mokkhasmit M *et al.*, (1971) and Haranath PSRK, *et al.*, (1987). Intravenous administration of a 50% ethanol extract of the fruits reduced blood pressure in dogs. An aqueous extract of the fruits reduced blood pressure in rats. The animals were also pre-treated with atropine for better results [20]. It is highly effective in reducing blood pressures. The effect was blocked by pretreatment of the animals with morphine [20].

Hepatoprotective activity: Fennel essential oil could inhibit the CCl₄ induced acute hepatotoxicity by decreasing levels of serum aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP) and bilirubin. D-limonene and β -myrcene of the oil might be the potential candidates [21].

Anti-inflammatory activity: of the pharmacological effects of fennel plant, anti-inflammatory activity can be noted. Research has shown that the methanol extract of fennel has anti-inflammatory effects. Oral administration of 200 mg per kg of methanol extract of fennel fruit shows inhibitory effects on acute and subacute inflammatory diseases and type 4 allergic reactions. In addition, it decreased the activities of superoxide dismutase (SOD) and catalase (CAT). It also significantly increased plasma levels of HDL cholesterol. In contrast, it significantly reduced the level of malondialdehyde (MDA) as a measure of lipid peroxidation. These results indicate that the methanol extract of fennel

fruit is effective in reducing inflammation [22]. Kataoka *et al.* studied anti-inflammatory effects of fennel. The results showed that the methanol extract of fennel seeds inhibits inflammation through cyclooxygenase and through lipoxygenase pathways [23].

Antithrombotic activity: *Foeniculum vulgare* has been reported to have antiplatelet properties. Tognolini M *et al.*, (2007) carried out antithrombotic activity of *Foeniculum vulgare*. The main component of the oil, anethole, tested in guinea pig plasma was as potent as fennel oil in inhibiting arachidonic acid. It's also helpful in preventing thrombin-induced clot retraction at concentrations similar to fennel oil. *F. vulgare* essential oil/anethole showed a significant antithrombotic activity in mice which prevents the paralysis which is induced by collagen-epinephrine intravenous injection. *F. vulgare* essential oil and anethole (100 mg/kg oral administration) shows significant results toward ethanol induced gastric lesions in rats. In conclusion, these results indicate that the *F. vulgare* essential oil, and its main component anethole, has been used as antithrombotic agent [24].

12. Side effects & safety

Fennel is likely safe when taken by mouth in the amounts commonly found in food. It is possibly safe when used as appropriate doses for a short period of time. Fennel creams are also possibly safe when applied to the skin. There is not enough evidence to know whether fennel is safe when used as medicine for longer periods of time. Although rare, other side effects might include stomach and intestinal upset. Seizures related to taking fennel essential oil by mouth have also been reported. Some people can have allergic skin reactions to fennel. People who are allergic to plants such as celery, carrot, and mugwort are more likely to also be allergic to fennel. Fennel can also make skin extra sensitive to sunlight and make it easier to get sunburn. Wear sun block if you are light-skinned.

13. Special precaution & warnings

Pregnancy and breast-feeding: Not enough is known about the safety of using fennel during pregnancy. It's best to avoid use. During breast-feeding, fennel is possibly unsafe. It's been reported that two breast-feeding infants experienced damage to their nervous systems after their mothers drank an herbal tea that contained fennel.

Children: Fennel products are possibly safe when used at appropriate doses by young infants for colic for up to one week.

Allergy to celery, carrot or mugwort: Fennel might cause an allergic reaction in people who are sensitive to these plants.

Bleeding disorders: Fennel might slow blood clotting. Taking fennel might increase the risk of bleeding or bruising in people with bleeding disorders.

Hormone-sensitive condition such as breast cancer, uterine cancer, ovarian cancer, endometriosis, or uterine fibroids: Fennel might act like estrogen. If you have any condition that might be made worse by exposure to estrogen, do not use fennel.

14. Interactions

Moderate interaction. Be cautious with this combination.

▪ Birth control pills (Contraceptive drugs) interacts with fennel

Some birth control pills contain estrogen. Fennel might have some of the same effects as estrogen. But fennel isn't as strong as the estrogen in birth control pills. Taking fennel along with birth control pills might decrease the effectiveness of birth control pills. If you take birth control pills along with fennel, use an additional form of birth control such as a condom. Some birth control pills include ethinyl estradiol and levonorgestrel (Triphasil), ethinyl estradiol and norethindrone (Ortho-Novum 1/35, Ortho-Novum 7/7/7), and others.

▪ Ciprofloxacin (Cipro) interacts with fennel

Ciprofloxacin (Cipro) is an antibiotic. Fennel might decrease how much ciprofloxacin (Cipro) the body absorbs. Taking fennel along with ciprofloxacin (Cipro) might decrease the effectiveness of ciprofloxacin (Cipro). To avoid this interaction take fennel at least one hour after ciprofloxacin (Cipro).

▪ Estrogens interacts with fennel

Large amounts of fennel might have some of the same effects as estrogen. But fennel isn't as strong as estrogen pills. Taking fennel along with estrogen pills might decrease the effects of estrogen pills. some estrogen pills include conjugated equine estrogens (Premarin), ethinyl estradiol, estradiol, and others.

▪ Tamoxifen (Nolvadex) interacts with fennel

Some types of cancer are affected by hormones in the body. Estrogen-sensitive cancers are cancers that are affected by estrogen levels in the body. Tamoxifen (Nolvadex) is used to help treat and prevent these types of cancer. Fennel seems to also affect estrogen levels in the body. Taking fennel along with tamoxifen might decrease the effectiveness of tamoxifen (Nolvadex). Do not take fennel if you are taking tamoxifen (Nolvadex).

Conclusion

Available researches have shown that extracts of fennel possess different pharmacological properties such as anti-allergic, analgesic, anti-inflammatory, antioxidant, antibacterial, anti-cancer, anti-stress and cytotoxicity activity. Medicinal properties of the plant are due to its different chemical compounds. Among the various compounds found in fennel plant essence and phenolic compounds are considered as the most important and most active compounds of it. The fennel bioactive molecules can be used for different drug production and play an important role in human health. The most prominent and best studies have been conducted on the antioxidant, antimicrobial and fennel estrogenic effects in various experimental models. Few studies have been performed on the anticancer effect of this plant, while a high percentage of worldwide deaths occur as various cancer effects. Therefore, it is recommended that future researches be investigate on the effect of this plant on cancer cell lines.

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Conflict of interest

None to declare.

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