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Review Article

Utilization of Fennel (*Foenirulum vulgare*) as Herb Medicines

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Abstract

Foeniculum species are characterized by the presence of essential oils, sterols, coumarins and flavonoids. Certain bioactivities have been attributed to some Foeniculum species; viz, antioxidant and antimicrobial activities for F. vulgar Mill. aerial part, anti-inflammatory and analgesic activities for the fruits of the same plant. Oils from F. vulgare showed a higher and broader degree of inhibition than that of C. maritimum. Fennel is a major invasive plant in many lower elevation natural areas in coastal California. Fennel is used to treat many bacterial, fungal, viral, and mycobacterial infectious diseases. Fennel has antibacterial activity due to compounds such as, linoleic acid, undecanal,1, 3-benzenediol, oleic acid and 2,4-undecadienal. Fennel has 5-hydroxy-furanocoumarin which has important role antibacterial activity of this plant. Aqueous extract of fennel shows bactericidal activity against Enterococcus faecalis, Staphylococcus aureus, Escherichia coli, Pseudomonas aeruginosa, Salmonella typhi, Salmonella typhimurium, and Shigella flexneri. The essence of plant showed very strong antibacterial activity against pathogens in food such as Escherichia coli, Listeria, monocytogenes, Salmonella typhimurium, Staphylococcus aureus, as well as having enormous activity against Helicobacter pylori and Campylobacter jejuni.

Fennel extract has antibacterial effect on all bacteria strains so it's' extract can be used to control multiple-antibiotic resistant bacteria. Dillapional the derivative of fennel stalk phenyl propanoid has antimicrobial properties against Aspergillus niger, Bacillus subtilis and Cladosporium cladosporioides. Fennel herb has estrogenic effects and has been traditionally used to treat infertile women. It was shown that the extract of fennel increased serum concentrations of follicle-stimulating hormone and decreased the yolk hormones and testosterone in treatment groups. Hypolipidemic and anti-atherogenic activities, this herb could be used for controlling cardiovascular disorders. Oral administration of the extract reduced systolic blood pressure. The fennel extract acts as a diuretic and natriuretic, too. The extract could be useful for the control of blood glucose in diabetic patients and in addition, their daily use could be effective in reducing chronic complications associated with diabetes. Fennel extract improves hyperglycemia in diabetic patients which part of this related to herb effect on oxidation/restored system. Therefore, this plant can be used in the pharmaceutical industry for the manufacture of anti-diabetic drugs. Also, methanol extract of fennel fruit reduced blood glucose and triglycerides and led to higher levels of liver and muscle glycogen.

Foeniculum vulgare (FVE), known as Fennel, has a long history of herbal uses and widely cultivated, both in the native habitat, India and Egypt, and elsewhere, for its edible strongly flavored leaves and seeds. The FVE fruit has a long history of use as both food and medicine. Traditionally, it is believed that the plant acts as a carminative (assists with flatulence control) and increase breast milk production. It has been reported that this plant can also enhance libido, facilitate birth, alleviate the symptoms of the male climacteric, promote menstrual flow, and soothe indigestion and cough. The antioxidant activity of water and ethanol extracts of fennel seeds was evaluated by various antioxidant methods, including total antioxidant, free radical scavenging, superoxide anion radical scavenging, hydrogen peroxide scavenging, metal chelating activities, and reducing power. Thosevarious antioxidant activities were compared to standard antioxidants such as (BHA), (BHT), and alpha-tocopherol. The water and ethanol extracts of fennel seeds showed strong antioxidant activity.

Keywords: foeniculum vulgare; hydrogen peroxide; superoxide anion radical

Introduction

Throughout China it is cultivated and adventive; 200-2600 m. (native to the Mediterranean region; cultivated and adventive worldwide) (Hui xiang, 2005). Foeniculum species are characterized by the presence of essential oils (Ozbek *et al*., 2003), sterols, coumarins (Kwon *et al*., 2002) and flavonoids (Parejo et al., 2004). Certain bioactivities have been attributed to some Foeniculum species; viz, antioxidant and antimicrobial activities for F. vulgar Mill. aerial parts (Ruberto *et al*., 2000), anti-inflammatory and analgesic activities for the fruits of the same plant (Eun and Jae, 2004). It can be an annual, biennial or perennial plant and is native to the Mediterranean areas (Piccaglia and Marotti, 2001). According to Shah and Khan (2006) the vernacular name is sonf, family is Apiaceae, part used is leaves and seeds and it is used as antidiabetics. The stem leaves, and fruit are commonly used as the dietary herb "xiao hui xiang" in traditional Chinese medicine to aid digestion. The leaves are used for flavoring and the fruits are used as a spIt is carminative and commonly used to flavor liquors, bread, fish, salad, soups, cheese and in manufacturing of pickles, perfumes, soaps, cosmetics and cough drops (Garcia-Jamenz *et al*., 2000; Patra *et al*., 2002), while Indians and Egyptians knew it as culinary species (Hui xiang, 2005). Antioxidant and antimicrobial activity of fennel has also been reported (Ruberto *et al*., 2000). The method of distillation significantly affected the essential oil yield and quantitative composition, although the antifungal activity of the oils against some fungi was only slightly altered (Mimica-Dukid *et al*., 2003). The analyses show that fennel oils exhibited different degrees of fungistatic activity depending on the doses (Ozcan et al., 2006). The method of distillation significantly effected the essential oil yield and quantitative composition, although the antifungal activity of the oils against some fungi was only slightly altered (Mimica *et al*., 2003). The significant antibacterial activity of essential oils to the bacterial pathogens of mushrooms appears promising (Lo Cantore *et al*., 2004). The isolates 1-6 were not active against the Escherichia coli (Kwon *et al*., 2002).

In addition, their inhibitory action in linoleic acid system was studied by monitoring peroxide accumulation in emulsion during incubation through ferric thiocyanate method. The results were well correlated with the above results (Singh *et al*., 2006). Oils from the two samples of F. vulgare showed a higher and broader degree of inhibition than that of C. maritimum (Roberto *et al*., 2000). Bell et al. (2008) reported that fennel is a major invasive plant in many lower elevation natural areas in coastal California.

These results on the genetic stability and uniformity of organogenic and embryogenic regenerated fennel plants was supported also by a comparison of the cpDNA microsatellite region with other natural fennel plants where variations were found in some of them except Francia Pernod (Bennici *et al*., 2004).

Zahid et al. (2009) reported that F. vulgare is an important, well-known aromatic and medicinal herb.

Khalil et al. (2007) reported that eight medicinal plants (F. vulgare) were cultivated in the Experimental Farm Station of the National Research Centre at Shalakan Kalubia Governorate, Egypt, during the two consecutive seasons 2003/2004. Mohamed and Abdu (2004) reported that seeds of the aromatic plant F. vulgarewere sown in sandy soil with 0 or 2.5 kg/m2 of organic fertilizer (OF); chicken manure, cattle manure or plant compost. Plants were irrigated three, four, five or six times at 21-day intervals commencing 21 days after sowing and continuing until harvest. The symptoms little leaf disease was temporarily suppressed when treated with tetracycline hydrochloride. This is the first report of a phytoplasma disease on fennel from India (Samad *et al*., 2002). Among these herbs can point to fennel (Foeniculum vulgare Mill) which is of great importance and is used in the pharmaceutical, food, cosmetic and healthcare industries (Abe and Ohtani, 2013). Fennel is one of the oldest spice plants which widely grows in arid and semi-arid and due to its economic importance and pharmaceutical industry usage, it is one of the world's most dimension medicinal herb (Jamshidi *et al*., 2012). This plant has anti-inflammatory, antispasmodic, antiseptic, carminative, diuretic and analgesic effect and is effective in gastrointestinal disorder treatment. Also, with its anti-ulcer and anti-oxidant properties it is used to treat neurological disorders (Birdane *et al*., 2007 and Delaram *et al*., 2011).

On radiating branches linear lines can be diagnosed. Fennel has small seed with a length of about 8 mm and a width of 3 mm with an aromatic odor and sweet taste. Fennel seeds are narrow, long, cylindrical appearance and dimensions vary depending on plant growth. The crack groove light green surface (Ahmadi *et al*., 2007). All parts of fennel such as roots, leaves, fruit and especially the seeds are used (Meireles, 2005). Fennel seed contains 6.3% water, 9.5% protein, 10% fat, 13.4% minerals, 18.5% fibers and 42.3% carbohydrates (Rather *et al*., 2012). Its leaves contain vitamins and minerals such as calcium, potassium, sodium, iron, phosphorus, thiamine, riboflavin, niacin and vitamin C (Miguel *et al*., 2010). 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% (Salehi Surmaghi, 2006). This herb also contains phenolic compounds such as flavonoids, phenolic acids, hydroxycinnamic acids, coumarin and tannin (Rahimi and Ardekani, 2006). 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-caffeoylquinicacid. Its flavonoid contains eriodictyol-7-rutinoside, quercetin-3-rutinoside and rosmarinic acid (Faudale *et al*., 2008). 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 (Parejo *et al*., 2004). In the Middle Ages people believed that chewing the seeds is important to eliminate abdomen noise (Siyahi *et al*., 2009). In the fifth century it was believed that fennel had sedative effect and in 9th to 14th centuries numerous therapeutic properties were attributed to it (Taherian *et al*., 2007). The Romans believed that fennel seed could help supercharge the vision. The English believed that the plant could offer relief from bloating stomach and facilitate digestion. The fennel therapeutic use has been serious since the 18th century, and many studies have been taken (Ranjbarian et al., 2004). Nowadays, the different parts of the plant are used in treatment of many diseases, particularly pain in the digestive system. Also, it is very useful in the treatment of diabetes, bronchitis, chronic cough and kidney stones (Badgujar *et al*., 2014). The herbs is helpful for chronic fever and removing the obstruction in the internal organs, especially the liver, gut, respiratory and urinary tract and also it is used to improve eye diseases such as cataract as well as diseases of the stomach, chronic diarrhea and relieve children colic (Razi, 2000 and Ibn Sina, 2005).

The pharmacological activities of fennel include following items (Tonkaboni, 2007). Fennel is used to treat many bacterial, fungal, viral, and mycobacterial infectious diseases (Duško *et al*., 2006). Fennel has antibacterial activity due to compounds such as, linoleic acid, undecanal, 1, 3-benzenediol, oleic acid and 2,4-undecadienal. Fennel has 5-hydroxy-furanocoumarin which has important role antibacterial activity of this plant (Esquivel-Ferriño et al., 2012). Aqueous extract of fennel shows bactericidal activity against Enterococcus faecalis, Staphylococcus aureus, Escherichia coli, Pseudomonas aeruginosa, Salmonella typhi, Salmonella typhimurium, and Shigella flexneri (Parejo et al., 2004). MIC for aqueous and alcoholic extracts of fennel seed which was in the range of 20-80 mg/ml and 5-15 mg/ml and statistical analysis showed better effect of the plant extract compared to standard antibiotics (Kaur and Arora, 2009). The essence of plant showed very strong antibacterial activity against pathogens in food such as Escherichia coli, Listeria, monocytogenes, Salmonella typhimurium, Staphylococcus aureus, as well as having enormous activity against

Helicobacter pylori and Campylobacter jejuni (Mahady *et al*., 2005 and Cwikla *et al*., 2010).

Jazani et al. studied the antibacterial activity of fennel extract on Acinetobacter baumannii strains which cause nosocomial infection. The results showed that fennel extract has antibacterial effect on all bacteria strains so its' extract can be used to control multiple-antibiotic resistant bacteria (Jazani *et al*., 2009).

Another study showed that dillapional the derivative of fennel stalk phenyl propanoid has antimicrobial properties against Aspergillus niger, Bacillus subtilis and Cladosporium cladosporioides. Also, derivates of coumarin named scopoletin had antimicrobial properties against above micro-organisms but was less important than dillapional (Kwon *et al*., 2000).

Antifungal activity of fennel essence on Sclerotinia sclerotiorum was investigated. The antifungal effect of this plant against Sclerotinia sclerotiorum observed based on survival of the microorganisms (Soylu *et al*., 2009).

A study demonstrated that nitric oxide production in peritoneal macrophages which were treated with fennel extract at a concentration of 10 mg/ml significantly increased. Also, the production of reactive oxygen species compared to the control group increased. Lethality study also showed that treated macrophages with concentrations of 10 and 20 mg ml had anti-candidate effects more than control group. Among chemical compositions of the plant extract anethole had the strongest antifungal activity (Naeini *et al*., 2011). Phenolic compounds in this herb such as caffeoylquinic acid, rosmarinic acid, eriodictyol-7-orutinoside, quercetin-3-O-galactoside, kaempferol-3-O-glucoside showed antioxidant activity. Fennel volatile oil has strong antioxidant activity, too. Plant ethanolic and aqueous extracts in comparison to its essence has less antioxidant activity (Scalbert *et al*., 2005; Chatterjee *et al*., 2012 and Díaz-Maroto *et al*., 2005). The results obtained in this study showed that fennel seed was a potential source of natural antioxidants (Oktay *et al*., 2003). Also, antioxidant activity of the ethanol and aqueous extracts of fennel showed that 100 mg of ethanol and watery extracts respectively had the 99.1% and 77.5% of antioxidant activity which was greater than the alpha-tocopherol (36.1%) antioxidant properties with the same dose (Shahat *et al*., 2011).

These results indicate that the methanol extract of fennel fruit is effective in reducing inflammation (Choi and Hwang, 2004). Kataoka et al. (2002) studied anti-inflammatory effects of fennel. The results showed that the methanol extract of fennel seeds inhibits inflammation through cyclooxygenase and through lipoxygenase pathways (Kataoka et al., 2002).

It was demonstrated that stress levels in treated group with fennel essence compared to control group significantly decreased. Thus, it can be concluded that this plant can hold promising effects in the treatment of anxiety and stress (Mesfin *et al*., 2014).

Koppula et al. investigated the properties of fennel extract in stress reduction and memory enhancement in rats. This study showed that this herb with several functions such as anti-stress proceeding, increase in memory and antioxidant effects may reduce stress and stress-related disorders (Koppula and Kumar, 2013). It has been shown that fennel plant has significant protective effect on gastrointestinal disorders. It was shown that the use of fennel oil emulsions eliminated colic in 65% of treated infants which was considerably better than the control group (Alexandrovich *et al*., 2003). In a study Al-Mofleh et al. investigated the effect of fennel plant on gastric ulcer. The findings showed that the plant had a protective effect on gastric ulcer. In addition, the herb reduced mucosal lining of the stomach. These functions were attributed to its antioxidant capacity (Al-Mofleh *et al*., 2013). The fennel essence showed fewer side effects in the treatment of primary dysmenorrhea. Administration of different doses of fennel extract significantly decreased contractions intensity induced by oxytocin and prostaglandins (Ostad *et al*., 2001). Fennel herb has estrogenic effects and has been traditionally used to treat infertile women. It was shown that the extract of fennel increased serum concentrations of follicle-stimulating hormone and decreased the yolk hormones and testosterone in treatment groups (Mirabolghasemi et al., 2014). As a result because of hypolipidemic and anti-atherogenic activities, this herb could be used for controlling cardiovascular disorders (Oulmouden *et al*., 2014 and Oulmouden *et al*., 2011). In other study, oral administration of the extract reduced systolic blood pressure. The fennel extract acts as a diuretic and natriuretic, too (Bardai *et al*., 2001). The findings exhibited that the extract could be useful for the control of blood glucose in diabetic patients and in addition, their daily use could be effective in reducing chronic complications associated with diabetes (Sushruta *et al*., 2007). To evaluate the effect of fennel on blood sugar reduction, a study was conducted on streptozotocin-diabetic rats. The results showed that fennel extract improves hyperglycemia in diabetic rats which part of this related to herb effect on oxidation/restored system. Therefore, this plant can be used in the pharmaceutical industry for the manufacture of anti-diabetic drugs (El-Soud *et al*., 2011). Also methanol extract of fennel fruit reduced blood glucose and triglycerides and led to higher levels of liver and muscle glycogen (Dongare *et al*., 2010).

The results showed that anethole inhibited cellular responses induced by these cytokines which might explain its role in suppressing cancer. It also specified that the fennel with its antiangiogenic mechanisms inhibits prostate tumor xenograft (Garga *et al*., 2009).

Bogucka-Kocka et al.evaluated apoptotic activity of ethanol extracts of fennel against leukemia.The findings showed that the extract had considerable apoptotic effects on cancer cells (Bogucka-Kocka *et al*., 2008). The results demonstrated that the methanol extract of fennel had significant anticancer activity against breast cancer cells (MCF-7) and liver cancer (Hepg) through modulating lipid peroxidation and increasing antioxidant defense system and inhibitory effect on free radicals (Mohamad *et al*., 2011).

Data from this study showed that this extract reduced the levels of AST (aspartate aminotransferase), ALT (alanine amino transferase), ALP (alkaline phosphatase) and serum bilirubin (Ozbek *et al*., 2004). Also, the effect of fennel on lipid peroxidation in rats with hepatic fibrosis was investigated. After fennel consumption ALT, AST level and MDA content significantly decreased and the TP, ALB and SOD, CAT, GSH-PX activities increased. According to results it might be concluded that fennel probably through effect on regulation of lipid peroxidation might inhibit hepatic fibrosis (Qiang et al., 2011). Wang et al.studied fennel effect on cytokines in rats with hepatic fibrosis. The results demonstrated that degradation of lipids and inflammation was reduced in the fennel treated group. Based on the data obtained from this study can be deduced that fennel might reduce inflammationin the liver and also considerably protect hepatocytes against liver damage (Liu *et al*., 2009). According to these findings it can be derived that fennel might inhibit hepatic fibrosis (Wang *et al*., 2012). Also, the effect of fennel on TNF-α cytokine in liver fibrosis model was examined. In the treated group inflammation was reduced and the amount of TNF-α secretion was reduced by PBMCS (Liu *et al*., 2008).

In Joshi et al. study the effect of fennel extract as a neurotropic factor and anti-acetylcholinesterase in mice were investigated. The findings of this study showed that fennel extract significantly inhibited acetylcholinesterase. According to this study it can be deduced that fennel might be used in treatment of cognitive disorders such as dementia and Alzheimer (Joshi and Parle, 2006).

It is reported that the use of fennel extract for control and treatment of primary dysmenorrhea causes concern about the teratogenicity potential of it, due to its estrogen-like activity. Investigating the herb extract effect showed teratogenic property that may have toxic effects on the cells of the embryo but no evidence of teratogenicity to concentration of 9.3 mg/ml

(Ostad *et al*., 2004). Traditionally, medicinal plants are deliberately cultivated in areas with some level of drought stress condi-tions to elevate their secondary metabolite content (Emami Bistgani *et al*., 2017). Fennel (Foeniculum vulgareMill.) is an importantmedicinal plant grown in many semi-arid regions andcoastal areas with sandy soils (Díaz-López *et al*., 2012). Fennel oil is a richnatural source of anethol and is primarily used as a flavoring agent in culinary preparations, confectionary, cordials, and liqueurs, and is employed in scentingsoaps. Fennel stimulates appetite and aids digestionand is also used to treat kidney stones, menopausalsymptoms, nausea, and obesity (Zahid *et al*., 2009).

Foeniculum vulgare (FVE), known as Fennel, a plant belonging to the family apiaceae, has a long history of herbal uses and widely cultivated, both in the native habitat, India and Egypt, and elsewhere,for its edible strongly flavored leaves and seeds (Roby *et al*., 2013). The FVE fruit has a long history of use as both food and medicine. Traditionally, it is believed that the plant acts as a carminative (assists with flatulence control) and increase breast milk production (Senatore *et al*., 2013). It has been reported that this plant can also enhance libido, facilitate birth, alleviate the symptoms ofthe male climacteric, promote menstrual flow, and soothe indigestion and cough (Namavar *et al*., 2003). The antioxidant activity of water and ethanol extracts of fennel seeds was evaluated by various antioxidant methods, including total antioxidant, free radical scavenging, superoxide anion radical scavenging, hydrogen peroxide scavenging, metal chelating activities, and reducing power (Soleimani *et al*., 2013). Thosevarious antioxidant activities were compared to standard antioxidants such as (BHA), (BHT), and alpha-tocopherol. The water and ethanol extracts offennel seeds showed strong antioxidant activity (Soleimani *et al*., 2013). F. vulgare known as fennel, belonging to the familyApiaceae, is being used for its anti-inflammatory, anti-spasmodic, analgesic, and laxative effects in folk medicine (Delaram *et al*., 2011). Fennel oil contains different ingredients such as anol or dimethylated anethole which may have some estrogenic activity (Mohebbi-Kian *et al*., 2014).

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