ISSN: 2320 - 4230

Journal of Drug Discovery and Therapeutics
Available Online at www.jddt.in
CODEN: - JDDTBP (Source: - American Chemical Society)
Volume 7, Issue 12, December: 2019, 01-13

Review Article

CHEMICAL AND PHARMACOLOGICAL PROPERTIES OF FOENICULUM VULGARE MILL: A REVIEW

Navneet Kumar Verma*, Asheesh Kumar Singh, Prem Chand Mall, Vikas Yadav, Rupali Jaiswal
Faculty of Pharmacy, Buddha Institute of Pharmacy, GIDA, Gorakhpur, UP, India-273209

Article Info: Received 10 December 2019; Accepted 25 December. 2019
Address for Correspondence: *Navneet Kumar Verma*
Disclosure statement: *The authors have no conflicts of interest.*

Abstract:
Foeniculum vulgare is a perennial, aromatic plant belonging to Apiaceae (Umbelliferae) family. The fruits, commonly referred to as seeds, are ridged, aromatic and oblong or ellipsoid shaped. Originally indigenous to the Mediterranean region, it has now been naturalized and cultivated throughout the world and is universally known as fennel and by more than 100 other names. It was well-known to the ancient Egyptians, Greeks, Romans and Chinese. Hippocrates and Dioscorides described it as a diuretic and Emmenagogue and to strengthen eyesight. The fruits are reputed as carminative, stomachic, diuretic, Emmenagogue and Galactagogue and to promote menstruation and facilitate birth. Fennel fruits contain carbohydrates, alkaloids, Phytosterols, phenols, tannins and flvonoids. They are also a rich source of dietary, protein, calcium, iron, magnesium and manganese. Pharmacologically, the fruits possess antioxidant, anti-inflmmatory, Gastro protective, estrogenic, Hepatoprotective and antithrombotic activities. This article reviews the use of fennel in medical practices in various parts of the world and reflects upon the scientific studies conducted and how they reconcile with its traditional uses.
Keywords: Fennel; *Foeniculum Vulgare*; Fenchone; aromatic plant.

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 [1, 2]. Nowadays medicinal herbs are good alternative to chemical drugs, one of the major reason for this is low side effect compared to chemical drugs [3, 4]. Plants have always played an important role in the health and treatment of human society [5]. Medicinal herbs have fewer side effects than synthetic drugs and due to their antioxidant properties they reduce drugs toxicity [6, 7]. Also, the natural effective ingredients cause biological balance and prevent drug accumulation in body [8]. So medicinal plants can be used in the treatment of various diseases [9] From 422000 flowering plants around the world, more than 5000 ones are used for medicinal purposes. 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 [10]. 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 [11]. 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 [12, 13]. According to importance of fennel as a medicinal herb, the aim of the present study was to evaluate the phytochemical characteristics, and therapeutic properties of this medicinal plant.

DESCRIPTION

Foeniculum vulgare is a biennial plant with a thick rootstock, erect, much-branched, and smooth, often 1 meter or more in height. Leaves are 2-, 3-, or 4-pinnate and about 20 centimeters long; the segments are filiform and 2 to 4 centimeters long. Umbels are 5 to 10 centimeters in diameter; the rays number: 8 to 15, about 2 to 3 centimeters long, but longer in fruit, each with 20 to 30 pedicelled yellow flowers. Fruit is ridged, very aromatic, oblong or ellipsoid, about 5 millimeters long. Seeds are somewhat dorsally compressed [14, 15]. Traditional uses: Fennel was considered as

one of the oldest medicinal plants and culinary herbs. It was used over 4000 years ago. Fennel was used by the ancient Egyptians as a food and medicine, and it was considered a snake bite remedy in ancient China. It was used since ancient times to treat menstrual disorders, dyspepsia, flatulence and cough, and to reduce the griping effect of laxatives [16]. Foeniculum vulgare was widely used in traditional Arabian medicine as diuretic, appetizer, and digestive [17]. The fruit, seeds and young leaves were used for flavoring sweets, dishes and dainties. The young leaves, raw or cooked, were used as flavoring. The seeds have an anise-like flavor and used as flavoring. The infused fruits were used as carminative. Roots were employed as purgative. Crushed fruits were inhaled to counter faintness. Infusion of fruit was used for flatulence. Shoots of young plant were used as carminative and in respiratory disorders. Juice of fruit was used to improve eyesight. Decoction was gargled as a breath freshener or applied as eyewash. Decoction of seeds was used to regulate menses and as diuretic and emmenagogue. Poultice was used to relieve breast swelling in nursing mothers. Infusion of seeds was used for stomatitis, abdominal cramps, colic, flatulence. Fennel water (aqua foeniculi) was used for colic and flatulence in children. Hot infusion of fruit and of roots was used for amenorrhea. Infusion of roots was given for toothaches and postpartum pains. Infusion of seeds was used for flatulence in babies. Infusion of root was also used for urinary disorders. Oil was used for flatulence and intestinal worms. Paste of seeds or fruit were used in cooling drinks for fevers. Seeds also used as stimulant and to enhance libido, to increase breast milk production, for the treatment of venereal diseases, easing childbirth and soothing cough [14].

PARTS USED

Whole plant, roots, seeds and oil of seed [14]. Physicochemical parameters of the essential oil of fennel fruit: Moisture %: 3.35- 4.75; Solubility: alcohol, chloroform, carbon tetrachloride, hexane; acid value (mg/KOH/g): 1.5-2.45; Saponification value (mg/KOH/g): 121.50-145.75; Ester value: 116.00-141.30; Peroxide value (m Eq/kg): 5.65-6.45; Iodine value (g/g): 94.25-98.5; Refractive index at 25oC: 1.5465±0.30-1.5575±0.25; Congealing point (16.4oC): 16.4±0.5- 16.7±0.5; Optical rotation (-2.25 ± 0.70 to + 10.25 ± 0.43) - (-2.10 ± 0.36 to + 10.35 ± 0.45) and Specific gravity at 25oC: 0.978±0.035 -0.985±0.032 [18] .

Fig.1: Foeniculum Vulgare plant (copied from google.com)

Fig.2: Foeniculum Vulgare fruit (copied from google.com)

CHEMICAL CONSTITUENTS

The preliminary phytochemical study revealed the presence of saponins, flavonoids, cardiac glycosides, sterols, triterpenes, coumarins and volatile oils [17,19]. It also contained protein, fat, minerals, fibre and carbohydrates. The minerals and vitamins identified in Foeniculum vulgare were included calcium, potassium, sodium, iron,

phosphorus, thiamine, riboflavin and niacin [20] . Triterpenes, flavanoid glycosides, smaller terpenes (monoterpenoids, sesquiterpenoids and diterpenoids) and reducing sugars were isolated from the seeds of Foeniculum vulgare [21]. Total phenolic content in organic fennel oil was 262.59 ± 15.5 mg Gallic Acid Equivalents/l [22]. The phenolics identified in the fruit of this plant were neochlorogenic acid (1.40%), chlorogenic acid (2.98%), gallic acid (0.169%), chlorogenic acid (6.873%), caffeic acid (2.960%), p-coumaric acid (4.325%), ferulic acid-7-o-glucoside (5.223%), quercetin-7-oglucoside (3.219%), ferulic acid (3.555%), 1,5 dicaffeoylquinic acid (4.095%), hesperidin (0.203%), cinnamic acid (0.131%), rosmarinic acid (14.998%), quercetin (17.097%), and apigenin (12.558%) [23]. However, Parejo et al., isolated 3- caffeoylquinic acid, 4- caffeoylquinic acid, 1.5-Odicaffeoylquinicacid, rosmarinic acid, eriodictyol-7-Orutinoside, quercetin-3-O-galactoside, kaempferol-3-Orutinoside, kaempferol-3-O-glucoside, hydroxylcinnamic acid derivatives, flavonoid glycosides and flavonoid aglycones from the aqueous extract of fennel fruits [24]. The furocoumarins imperatorin, psoralen, bergapten, xanthotoxin and isopimpinellin were isolated from the methylene chloride extract. The flavonoids isorhamnetin 3-O-α-rhamnoside, quercetin and kaempferol were isolated from the ethyl acetate extract, whereas quercetin 3-O-rutinoside, kaempferol 3-O-rutinoside and quercetin 3-O- β-glucoside were isolated from the methanol extract [25]. Nutritional analysis showed that the plant contained moisture:90.21 g, Energy: 31 kcal, Protein: 1.24 g (Essential amino acids: Leucine: 0.63 g, Isoleucine: 0.73 g, Phenylalanine: 0.45 g, Tryptophane: 0.53 g and Non-essential amino acid (Glycine: 0.55 g, Proline: 0.53 g), Total lipid (fat): 0.2 g (Fatty acids, total saturated: 0.09 g, Fatty acids, total monounsaturated: 0.068 g, Fatty acids, total polyunsaturated: 0.169 g), Carbohydrate: 7.3 g, Total dietary fiber: 3.1 g, Sugars: 3.93 g, Minerals (Calcium: 49 mg, Iron: 0.73 mg, Magnesium: 17 mg, Phosphorus: 50 mg, Potassium: 414 mg, Sodium: 52 mg, Zinc: 0.2 mg), Vitamins (Vitamin: 12 mg, Thiamin: 0.01 mg, Riboflavin: 0.032 mg, Niacin: 0.64 mg, Vitamin: 0.047 mg, Folate: 27 µg, Vitamin A: 48 µg Vitamin E: 0.58 mg, Vitamin K: 62.8 µg) [25]. Essential oils were isolated from fennel aerial parts collected in Cape Verde and from a commercial fennel EO of Portugal were analyzed by NMR, GC and GC-MS. Trans Anethole (32 and 30%, respectively), limonene (28 and 18%, respectively) and fenchone (10% in both cases) were the main compounds identified in the essential oils isolated from fennel from Cape Verde and Portugal, respectively [26]. Foeniculum vulgare essential oil from Turkey contained 74.8% (E)-anethole, 11.1% limonene, 4.7% methyl chavicol, 2.5% fenchone and 1.3% α-pinene [27] . Sing et al., investigated the chemical components of volatile oil of Foeniculum vulgare (from Gorakhpur), they found that the oil contained (%): acetic acid-ethyl ester: trace, 3-Methylbutanal: 0.1, 2-Methylbutanal: trace, Alpha-Thujene: trace, Alpha-Pinene: 0.2, Camphene: trace, Sabinene: trace, Beta-Pinene: 0.2, Myrcene: 0.1, Delta-3-Carene: 0.1, Alpha-Terpinene: trace, p-Cymene: 3.1, Limonene: 3.1, 1,8-Cineole: 0.1, trans-betaOcimene: 0.1, Gamma-Terpinene: 2.1, Fenchone: 8.6, Linalool: 1.2, Camphor: 0.3, BetaTerpineol: trace, Terpinen-4-ol: 0.2, Alpha-Terpineol: 0.2, Methyl chavicol: 4.7, Fenchyl acetate: 0.2, Cuminal: 0.4, cis-Anethole: 0.4, p-Anisaldehyde: 0.5, trans-Anethole: 70.1, Thymol: 0.1, Alpha-Copaene: 0.1, Beta-Caryophyllene: 0.2, Alpha-Humulene: tracea and Delta-Cadinene: trace [28]. However, Upadhyay , isolated 36 components from the essential oil of Foeniculum vulgare from Gorakhpur, Uttar Pradesh, India. The main constituents of essential oil were identified as 9-octadecenoic acid (18.56%), 8Z)-14-methyl-8-hexadecenal (7.75%), pentad ecanecarboxylic acid (4.25%), o-benzenedicarboxylic acid (14.47%), 1,3,3-trimethyl-2-vinyl-1- cyclohexene (10.77%), 2-methyl-3-oxoestran- 17-yl acetate (5.46%), 1H-benzocycloheptene (10.71). However, the major and minor constituents isolated from Fennel

(Foeniculum vulgare) essential oil were included (0.71%) Tetradecane, Hexadecane; (2.05%) Ethanone, 1-(4-methyl-3-cyclohexen-1-YL)-1-(4-methyl-3-cyclohexen-1-YL) ethanone, 2-propanone; (3.67%) H-Benzocycloheptene, 2,4a,5,6,7,8,9, 9a-octahydro-3,5,5-trimethyl-9-methylene-, Longifolene; (0.15%) Phenylmethyl ester; (2.25%) cis-(-)-2,4a,5,6,9a-Hexahydro-3,5,5,9-tetramethyl (1H)) Benzocycloheptene; (10.71%) 1H-Benzocycloheptene; (0.26%) m-Methyl acetophenone; (0.21%) alpha.-Caryophyllene; (0.14%) 2-Cyclopenten-1-one, 2-hydroxy-3-methyl-Corylon; (0.54%) p-Guaiacol; (0.48%) 2-(4a,8-Dimethyl-2,3,4,4a,5,6-hexahydro-naphthalen-2-yl)-prop2-en-1-ol; (0.66%) Vetivenene Neoisolongifolene, Aromadendrene; (0.90%) Anthracene, 1,2,3,4,5,6,7,8-octahydro-1-methyl-; (1.74%) 1-Methyl-6-(3-methylbuta-1,3-dienyl)-7-oxabicyclo [4.1.0] heptane; (1.12%) 1-hydroxy-2-methoxy-2-methoxy-4-methylbenzene; (0.26%) 1- (2,3-Dihydroindol-1-yl)-4-phenyl-butan-1,4-dione; (0.26%) 5,5 Dimethyl-3-vinyl cyclohex-2-en1-one; (0.54%) 2-Methoxy-4-ethylphenol, 1,2-Dimethoxy-4-methylbenzene; (0.37%) Bis(4-methyl phenyl) methane disulfonate; (0.32%) (-)-5-xatricyclo [8.2.0.0(4,6)] Dodecane, Cedran9-one; (1.22%) 2,2-dimethyl-3-phenylpropanoate; (0.29%) -Methyl-6-(3-methylbuta-1,3- dienyl)-7-oxabicyclo [4.1.0] heptane; (0.45%) 2,7-dimethyloct-7-en-5-yn-4-yl ester; (2.04%) 2-Methyl-6-(4-methyl-1,3-cyclohexadien-1-yl)-2-hepten-4-one; (3.16%) 3-Methyl-2-butenoic acid; 5.46 2-Methyl-3-oxoestran-17-yl acetate; (0.70%) 3,3,6-Trimethyl-1-indanone; (10.77%) 1,3,3-Trimethyl-2-vinyl-1-cyclohexene; (14.47%) o-Benzene dicarboxylic acid; (0.49%) 1- Isopropyl-1,2,3,4-tetrahydroisoquinoline; (0.20%) 3,4-Dimethyl-1,5-cyclooctadiene; (1.84%) 2-hydroxy-1-(hydroxymethyl)ethyl ester; (4.25%) Pentadecanecarboxylic acid; (7.75%) 8Z)- 14-Methyl-8-hexadecenal; (18.56%) 9-octadecenoic acid and (1.00%) 2-cis,cis-9,12-Octadecadienyloxyethanol. Analyses (GC and GC/MS) of Foeniculum vulgare roots and schizocarp (from the city of Niš, Serbia) essential oils and diethyl ether extracts resulted in identification of 89 different components. The most abundant classes of constituents were the phenylpropanoids (69.5-85.5%) and monoterpenoids (11.7-26.9%). The dominant volatile metabolites of schizocarps were fenchone (13.3-18.8%) and (E)-anethole (66.1-69.0%). Contrary to that, terpinolene (6.2-6.5%) and dillapiole (71.4-77.5%) were the major volatiles of fennel roots [29] . The chemical analysis of the aerial parts and fruits of Foeniculum vulgare Mill. subsp. piperitum collected from North Western Mediterranean coastal strip near El-Salloum, Egypt showed the presence of the following fatty acids(%): capric acid 2.83 and3.23, undecanoic acid 18.21 and 20.09, lauric acid 2.13 and 2.45,myristic acid 10.51 and 11.20, pentadecanoic acid 1.79 and 2.10, pentadecenoic acid 7.33 and 7.68, pentadecadienoic acid 9.29 and 10.91, palmitic acid 31.51 and 33.47, stearic acid 0.69 and 0.77, oleic acid 1.55 and 0.40, linolieic acid 0.43 and 0, linolenic acid 0.65 and 0.38, arachidic acid 0.76 and 1.31, behenic acid 0 and 0.41, erucic acid 0.87 and 1.33 and tetracosenoic acid 1.89 and 0 respectively. Hydrocarbons and sterols identified in the aerial parts and fruits of Foeniculum vulgare (100) were included: n-Decane 3.75 and 4.29, n-Dodecane 2.16 and 2.84, n-Tridecane 0.88 and 0.34, n-Pentadecane 0.47 and 1.09, nHexadecane 0.49 and 0.65, n-Heptadecane 1.64 and 1.44, n-Octadecane 1.71 and 2.19, nNonadecane 0 and 1.11, n-Eicosane 5.89 and 10.43 n-Monocosane 2.72 and 1.88, nDocosane 0.96 and 1.39, n-Tricosane 0 and 2.37, n-Tetracosane 0.45 and 0.89, nPentacosane 2.25 and 4.59, n-Hexacosane 2.86 and 5.51, n-Heptacosane 0.41 and 0.27, nOctacosane 0.37 and 0.44, n-Nonacosane 0.79 and 1.76, n-Triacontane 0.53 and 1.35, n Monotriacontane 0.48 and 0.89, n-Dotriacontane 2.09 and 2.28, n-Tetratriacontane 4.52 and 3.34, n-Hexatriacontane 10.27 and 0, n-Octatriacontane 7.91 and 2.83, n-Tetracontane 1.71 and 0.84, Cholesterol 5.52 and 5.95, β–Sitosterol 5.52 and

5.95, Campesterol 3.33 and 4.04 and Stigmasterol 14.86 and19.04 respectively [25] . Cultivated and wild growing samples of Foeniculum vulgare from R. Macedonia were studied for their volatiles and fatty acid composition. The main essential oil components were: trans-anethole >80%, estragole < 6%, limonene < 6%, anisaldehyde < 1% and 0.5 % fenchone. The dominant fatty acid was (petroselinic and oleic acid) 75.0-82.8%, followed by linoleic acid 10.8-16.2%, palmitic 4.3-6.9%, stearic 1.2-1.7% and myristic acid 0-2.9% [30].

PHARMACOLOGICAL PROPERTIES

Anti-bacterial activity

Fennel is used to treat many bacterial, fungal, viral, and mycobacterial infectious diseases [31]. 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 [32]. Aqueous extract of fennel shows bactericidal activity against Enterococcus faecalis, Staphylococcus aureus, Escherichia coli, Pseudomonas aeruginosa, Salmonella typhi, Salmonella typhimurium, and Shigella flexneri [33]. During a study it was found that this plant extract has a significant antibacterial effect against a lot of bacteria except Klebsiella pneumoniae and one strain of Pseudomonas aeruginosa. Also this report determined 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 [34]. 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 [35,36]. 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 [37].

Anti-fungal activity

Fennel extract has antifungal activity against various fungal species such as Candida albicans, species of Aspergillus, and dermatophytes [21]. Also a study on the herb antifungal effect showed significant antifungal activity against fungi in food waste such as Aspergillus niger and Fusarium oxysporum. The MIC of fennel extract for these molds respectively was 750 and 250 micrograms per ml. 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 [38]. 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 [39]. 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 [40].

Antioxidant activity

Fennel is known as an excellent source of natural antioxidants. This plant can inhibit free radicals due to the high content of polyphenols and flavonoids. Phenolic compounds in this herb such as caffeoylquinic acid, rosmarinic acid, eriodictyol-7-orutinoside, quercetin3-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 [33,41-43]. In a research aqueous and methanolic extracts of fennel seed for Total Antioxidant Capacity (TAC) and determination of total phenolic compounds were studied. TAC was measured using the DPPH, H2O2, and FRAP and phenolic compounds using the Folin-ciocalteu reagent. This study showed that fennel extracts could inhibit free radicals and act as primary antioxidant [41]. In another study, the antioxidant activity of aqueous and ethanol extracts of fennel seeds was evaluated by using a variety of antioxidant methods such as total antioxidant, free radical scavenging, superoxide anion radical scavenging, hydrogen peroxide scavenging, metal chelating activity. These antioxidant activities were compared to standard antioxidant such as butylated hydroxyanisole (BHA), and butylated hydroxytoluene (BHT), and a-tocopherol. The results obtained in this study showed that fennel seed was a potential source of natural antioxidants [44]. 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 [45].

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 sub-acute 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 [46]. 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 [47, 48]. Also Choi et al. evaluated fennel methanol extract anti-inflammatory effects. The results showed that the fennel methanol extract had anti-inflammatory activity dependent on the central and peripheral mechanisms [46].

Anti-anxiety activity

Anxiolytic activity of the crude extract of fennel has been reported. Fennel due to phytoestrogens extensively has therapeutic use in the treatment of estrogen deficiency abnormalities. Estrogens are hormones that are involved in the phenomenon of anxiety which appear to act via the GABA A receptors. The results of a study showed that the plant with increase in time spent in the open arm established significant anxiolytic effect. Picrotoxin (GABA receptor antagonist) and Tamoxifen prevented anxiolytic effect. Therefore, fennel probably is an herbal remedy that has anxiolytic effects mediated by GABA-ergic system and estrogen receptors. Mesfin et al. studied the anxiolytic activity of fennel on adult mice. 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 [49]. 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 [50].

Gastro-protective activity

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 [51,52]. 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 [53].

Estrogenic activity

Fennel has been used for thousands of years as an estrogenic agent. Due to this property, fennel increases milk secretion, reduces menstrual pain, facilitates birth and increases sexual desire. Anatole is the main part of fennel plant that operates estrogenic properties. Researches have shown that active pharmaceutical agents such as dianthole and photoanatole are polymers of anthole [48]. 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 [54]. Moderate doses increased mammary gland weight and higher doses increased the weight of oviduct, endometrium, myometrium and cervix [55]. Myrseyed et al. investigated the effect of fennel seed ethanol extract on gonadotropin changes in adult male rats. Testosterone, FSH, LH levels in treatment groups were significantly reduced in comparison to the control group. Significant reduction in the amount of sperm resulting in epididymis weight loss and hormone levels indicates the fennel seed decreases in male reproductive activity [56]. 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 [57]. In another study Devi et al. investigated fennel fruit acetone extract effect on mammary gland and oviduct. The results of this study confirmed the effects of natural estrogen for this plant seed extract [58]. **Cardiovascular and lipid activity**

The study of the anti- cholesterol and anti-atherogenic effect of fennel methanol extract showed that treatment with the extract significantly reduced plasma lipid levels. Also the plant had important anti-atherogenic effects. It reduced triglycerides in fatty liver and facilitated blood flow in the coronary arteries by preventing the buildup of fatty deposit in arteries through reduction of plasma and liver fats. As a result because of hypolipidemic and anti-atherogenic activities, this herb could be used for controlling cardiovascular disorders [59,60]. Also intravenous injection of the extract significantly reduced blood pressure, without affecting the heart rate and respiration. It seems that fennel extract effect on blood pressure was not mediated by adrenergic, muscarinic, ganglion, serotonergic receptors [61]. In other study, oral administration of the extract reduced systolic blood pressure. The fennel extract acts as a diuretic and natriuretic, too [62].

Anti-diabetic activity

A study investigated the effect of aqueous extract Apiaceae family plant such as fennel in lowering blood sugar and anti-diabetic activities. 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 [63]. 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 [64]. Also methanol extract of fennel fruit reduced blood glucose and triglycerides and led to higher levels of liver and muscle glycogen [65].

Anti-cancer activity

It was shown that TNF-α -dependent responses are involved in inflammation and cancer. It was found that anethole in fennel seed has inhibitory effect

on activating TNF-α by transcription factor NF-KB. 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 [66]. 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 [67]. In other study, fennel methanol extract effects on antitumor and cytotoxic activities in mice with cancer were investigated. Data of this study showed that the methanol extract of fennel considerably increased MDA levels and significantly reduced CAT activity and glutathione content in the liver and tumor tissue of mice with cancer. In contrast, the total protein content in the ascites fluid decreased. 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 [68].

Hepato-protective activity

The studies demonstrated that the fennel plant has protective effect on liver. Qiang et al. studied the effect of fennel extract in carbon tetrachloride - induced liver injury rats. 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 [69]. 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 [70]. 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 inflammation in the liver and also considerably protect hepatocytes against liver damage [71]. In other study, the effect of fennel on hepatic fibrosis and the amount of potassium supplements examined. Patient group with fibrosis, liver tissue inflammation and excessive fat degradation after fennel treatment significantly improved. After treatment with fennel of ascites level and HAase content decreased and potassium levels went up. According to these findings it can be derived that fennel might inhibit hepatic fibrosis [72]. 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 [73]. Based on these findings, we can conclude that fennel might reduce TNF-α secretion by single –core cells, inhibit inflammation and improve liver fibrosis.

Memory-protective activity

It is believed that some plants including fennel herbs are used to enhance memory and intelligence. Therefore, the effect of fennel extract on memory in amnesiac rats was examined. The results showed that this extract had memory enhancement property. In Joshi et al. study the effect of fennel extract as a neurotropic factor and anti-acetyl cholinesterase in mice were investigated. The findings of this study showed that fennel extract significantly inhibited acetyl cholinesterase. According to this study it can be deduced that fennel might be used in treatment of cognitive disorders such as dementia and Alzheimer [74].

CONCLUSION

Nevertheless, its use since ancient times is a testament for its usefulness in certain conditions. It is now established that a number of diseases have cellular damage due to oxidative stress as a component of their pathology. Fennel contains significant amounts of antioxidant substances, such

as phenolic compounds and flavonoids that display a broad spectrum of physiological activities and protect against various disease processes. 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 phenolics 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.

REFERENCES

1. Tang SY, Halliwell B. Medicinal plants and antioxidants: what do we learn from cell culture and Caenorhabditis elegans studies? Biochem Biophys Res Commun 2010; 394(1): 1-5.

2. Ghasemi Pirbalouti A. Iranian medicinal and aromatic plants. Shahrekord: Islamic Azad University; 2009.

3. Kooti W, Ghasemiboroon M, Asadi-Samani M, Ahangarpoor A, Zamani M, Amirzargar A, et al. The effect of hydroalcoholic extract of celery leaves on the delivery rate (fertilization and stillbirths), the number, weight and sex ratio of rat off spring. Adv Environ Biol 2014; 8(10): 824-30.

4. Beyrami-Miavagi A, Farokhi F, Asadi-Samani M. A study of the effect of prostodin and hydroalcoholic extract of Malva neglecta on kidney histopathology and renal factors in female rats. Adv Environ Biol 2014; 8(9): 942-7.

5. Kooti W, Mansouri E, Ghasemiboroon M, Harizi M, Ashtary-Larky D, Afrisham R. The Effects of hydroalcoholic extract of apium graveolens leaf on the number of sexual cells and testicular structure in rat. Jundishapur J Nat Pharm Prod 2014; 9(4): e17532.

6. Asadi-Samani M, Rafieian-Kopaei M, Azimi N. Gundelia: a systematic review of medicinal and molecular perspective. Pak J Biol Sci 2013; 16: 1238- 47.

7. Kooti W, Ghasemiboroon M, Asadi-Samani M, Ahangarpoor A, Abadi A, Noori M, et al. The effects of hydro-alcoholic extract of celery on lipid profile of rats fed a high fat diet. Adv Environ Biol 2014; 8(9): 325-30.

8. Asadi-Samani M, Kafash-Farkhad N, Azimi N, Fasihi A, Alinia-Ahandani E, Rafieian-Kopaei M. Medicinal plants with hepatoprotective activity in Iranian folk medicine. Asian Pac J Trop Biomed 2015; 5(2): 146- 57.

9. Kooti W, Mansori E, Ghasemiboroon M, Harizi M, Amirzarga A. Protective effects of celery (Apium Graveolens) on testis and cauda epididymal spermatozoa in rat. Iran J Reprod Med 2014; 12(5): 365-6.

10. Abe R, Ohtani K. An ethnobotanical study of medicinal plants and traditional therapies on Batan Island, the Philippines. J Ethnopharmacol 2013; 145(2): 554-65.

11. Jamshidi E, Ghalavand A, Sefidkon F, Goltaph E. Effects of different nutrition systems (organic and chemical) on quantitative and qualitative characteristics of Fennel (Foeniculum valgare Mill.) under water deficit stress. Iran J Med Aromat Plants 2012; 28(2): 309-23.

12. Birdane FM, Cemek M, Birdane YO, Gulcin I, Buyukokuroglu ME. Beneficial effects of Foeniculum vulgare on ethanol-induced acute gastric mucosal injury in rats. World J Gastroenterol 2007; 13(4): 607.

13. Delaram M, Kheiri S, Hodjati MR. Comparing the effects of echinop hora-platyloba, fennel and placebo on pre-menstrual syndrome. J Reprod Infertil 2011; 12(3): 221-6.

14. Philippine Medicinal Plants, Haras, Anis, Foeniculum vulgare Mill. http://www. stuartxchange.org/Anis.html The chemical

constituents and pharmacological effects of Foeniculum vulgare - A review 103.

15. Badgujar SB, Patel VV and Bandivdekar AH. Foeniculum vulgare Mill: A review of its botany, phytochemistry, pharmacology, contemporary application, and toxicology. Biomed Res Int 2014; 2014: 842674. doi: 10.1155/2014/842674.

16. Fennel- Foeniculum vulgare - Aromatic Studies, https://aromaticstudies. com /fennel – foeniculum-vulgare.

17. Tanira, MOM et al. Pharmacological and toxicological investigations on Foeniculum vulgare dried fruit extract in experimental animals. Phytother Res 1996; 10: 33-36.

18. Saini N, Singh GK and Nagori BP. Physicochemical characterization and spasmolytic activity of essential oil of fennel (Foeniculum vulgare) from Rajasthan. International Journal of Pharmacotherapy 2014; 4(2): 97-103.

19. WHO monographs on selected medicinal plants 2001; 3: 136-138.

20. Elizabeth AA, Josephine G, Muthiah NS and Muniappan M. Evaluation of analgesic and anti-inflammatory effect of Foeniculum vulgare. Research Journal of Pharmaceutical, Biological and Chemical Sciences 2014; 5(2): 658-668.

21. Araujo RO, Souza IA, Sena KXFR, Brondani DJ and Solidonio EG. Biological evaluation of Foeniculum vulgare (Mill.) (Umbelliferae/ Apiaceae). Rev Bras Pl Med Campinas 2013; 15(2): 257-263.

22. Marín I, Sayas-Barberá E, Viuda-Martos M, Navarro C and Sendra E. Chemical composition, antioxidant and antimicrobial activity of essential oils from organic fennel, parsley, and lavender from Spain. Foods 2016; 5: 18.

23. Roby MHH, Sarhan MA, Selim KA, and Khalel KI. Antioxidant and antimicrobial activities of essential oil and extracts of fennel (Foeniculum vulgare L.) and chamomile (Matricaria chamomilla L.). Industrial Crops and Products 2013; 44:437-445.

24. Parejo I, Viladomat F, Bastida J, Schmeda-Hirschman G, Burillo J and Codina C. Bioguided isolation and identification of the nonvolatile antioxidant compounds from fennel (F. vulgare Mill.) waste. J Agric Food Chem 2004; 52: 1890-1897.

25. Nassar MI, El–sayed AA, Makled YA, El–Khrisy EA and Osman AF. Secondary metabolites and pharmacology of Foeniculum vulgare Mill. Subsp. Piperitum. Rev latinoam. quím 2010; 38(2): 103-111.

26. Rocha DK, Matosc O, Novoa MT, Figueiredo AC, Delgado M and Moiteiro C. Larvicidal activity against Aedes aegypti of Foeniculum vulgare essential oils from Portugal and Cape Verde. Nat Prod Commun 2015;10 (4):677-682.

27. Özbek H. The anti-inflammatory activity of the Foeniculum vulgare L. essential oil and investigation of its Medium lethal dose in rats and mice. International Journal of Pharmacology 2005; 1(4): 329-331.

28. Singh G, Maurya S, de Lampasona MP and Catalan C. Chemical constituents, antifungal and antioxidative potential of Foeniculum vulgare volatile oil and its acetone extract. Food Control 2006;17: 745–752. The chemical constituents and pharmacological effects of Foeniculum vulgare - A review 104

29. Upadhyay RK. GC-MS analysis and in vitro antimicrobial susceptibility of Foeniculum vulgare seed essential oil. American Journal of Plant Sciences 2015; 6: 1058-1068.

30. Najdoska-Bogdanov M, Bogdanov JB and Stefova M. Simultaneous determination of essential oil components and fatty acids in fennel using gas chromatography with a polar capillary column. Nat Prod Commun 2015; 10(9): 1619-1626.

31. Duško BL, Comiæ L, Sukdolak S. Antibacterial activity of some plants from family Apiaceae in

relation to selected phytopathogenic bacteria. Kragujevac J Sci 2006; 28: 65-72.

32. Esquivel-Ferriño PC, Favela-Hernández JMJ, GarzaGonzález E, Waksman N, Ríos MY, Camacho-Corona MdR. Antimycobacterial activity of constituents from Foeniculum vulgare var. dulce grown in Mexico. Molecules 2012; 17(7): 8471-82.

33. Parejo I, Jauregui O, Sánchez-Rabaneda F, Viladomat F, Bastida J, Codina C. Separation and characterization of phenolic compounds in fennel (Foeniculum vulgare) using liquid chromatography-negative electrospray ionization tandem mass spectrometry. J Agric Food Chem 2004; 52(12): 3679-87.

34. Kaur GJ, Arora DS. Antibacterial and phytochemical screening of Anethum graveolens, Foeniculum vulgare and Trachyspermum ammi. BMC Complement Altern Med 2009; 9(1): 30.

35. Mahady GB, Pendland SL, Stoia A, Hamill FA, Fabricant D, Dietz BM, et al. In vitro susceptibility of Helicobacter pylori to botanical extracts used traditionally for the treatment of gastrointestinal disorders. Phytother Res 2005; 19(11): 988-91.

36. Cwikla C, Schmidt K, Matthias A, Bone K, Lehmann R, Tiralongo E. Investigations into the antibacterial activities of phytotherapeutics against Helicobacter pylori and Campylobacter jejuni. Phytother Res 2010; 24(5): 649-56.

37. Jazani N, Zartoshti M, Babazadeh H, Ali-Daiee N, Zarrin S, Hosseini S. Antibacterial effects of Iranian fennel essential oil on isolates of Acinetobacter baumannii. Pak J Biol Sci 2009; 12(9): 738.

38. Kwon YS, Choi WG, Kim WJ, Kyung cKim W, Kim MJ, Kang WH, et al. Antimicrobial constituents of Foeniculum vulgare. Arch Pharm Res 2002; 25(2): 154-7.

39. Soylu S, Yigitbas H, Soylu E, Kurt Ş. Antifungal effects of essential oils from oregano and fennel on Sclerotinia sclerotiorum. J Appl Microbiol 2007; 103(4): 1021-30.

40. Naeini A, Naseri M, Kamalinejad M, Khoshzaban F, Rajabian T, Nami H, et al. Study on anti-candida effects of essential oil and extracts of Iranian medicinal plants, in vitro. J Med Plant 2011; 2 (38): 163-72.

41. Scalbert A, Manach C, Morand C, Rémésy C, Jiménez L. Dietary polyphenols and the prevention of diseases. Crit Rev Food Sci Nutr 2005; 45(4): 287-306.

42. Chatterjee S, Goswami N, Bhatnagar P. Estimation of phenolic components and in vitro antioxidant activity of fennel (Foeniculum vulgare) and ajwain (Trachyspermum ammi) seeds. Adv Biores 2012; 3(2): 109-18.

43. Díaz-Maroto MC, Díaz-Maroto Hidalgo IJ, Sánchez-Palomo E, Perez-Coello MS. Volatile components
and key odorants of fennel (Foeniculum vulgare Mill.) and thyme (Thymus vulgaris L.) oil extracts obtained by simultaneous distillation-extraction and supercritical fluid extraction. J Agric Food Chem 2005; 53(13): 5385-9.

44. Oktay M, Gülçin İ, Küfrevioğlu Öİ. Determination of in vitro antioxidant activity of fennel (Foeniculum vulgare) seed extracts. LWT-Food Sci Technol 2003; 36(2): 263-71.

45. Shahat AA, Ibrahim AY, Hendawy SF, Omer EA, Hammouda FM, Abdel-Rahman FH, et al. Chemical composition, antimicrobial and antioxidant activities of essential oils from organically cultivated fennel cultivars. Molecules 2011; 16(2): 1366-77.

46. Choi EM, Hwang JK. Antiinflammatory, analgesic and antioxidant activities of the fruit of Foeniculum vulgare. Fitoterapia 2004; 75(6): 557-65.

47. Kataoka H, Horiyama S, Yamaki M, Oku H, Ishiguro K, Katagi T, et al. Anti-inflammatory and anti-allergic activities of hydroxylamine and related compounds. Biol Pharm Bull 2002; 25(11): 1436-41.

48. Albert-Puleo M. Fennel and anise as estrogenic agents. J Ethnopharmacol 1980; 2(4): 337-44.

49. Mesfin M, Asres K, Shibeshi W. Evaluation of anxiolytic activity of the essential oil of the aerial
part of Foeniculum vulgare Miller in mice. BMC Complement Altern Med 2014; 14(1): 310.

50. Koppula S, Kumar H. Foeniculum vulgare Mill (Umbelliferae) attenuates stress and improves memory in wister rats . Trop J Pharm Res 2013; 12(4): 553-8.

51. Chakŭrski I, Matev M, Koĭchev A, Angelova I, Stefanov G. Treatment of chronic colitis with an herbal combination of Taraxacum officinale, Hipericum perforatum, Melissa officinaliss, Calendula officinalis and Foeniculum vulgare. Vutr Boles 1980; 20(6): 51- 4.

52. Alexandrovich I, Rakovitskaya O, Kolmo E, Sidorova T, Shushunov S. The effect of fennel (Foeniculum vulgare) seed oil emulsion in infantile colic: a randomized, placebo-controlled study. Altern Ther Health Med 2003; 9(4): 58-61.

53. Al-Mofleh I, Al-Sobaihani M, Alqasoumi S, Al-Said M, Al-Dosari M, Al-Yahya M, et al. Fennel" Foeniculum vulgare" treatment protects the gastric mucosa of rats against chemically-induced histological lesions. Int J Pharm 2013; 9(3): 182.

54. Ostad S, Soodi M, Shariffzadeh M, Khorshidi N, Marzban H. The effect of fennel essential oil on uterine contraction as a model for dysmenorrhea, pharmacology and toxicology study. J Ethnopharmacol 2001; 76(3): 299-304.

55. Malini T, Vanithakumari G, Devil Nmsak, Fiango V. Effect of Foeniculum vulgare Mill. seed extract on the genital organs of male and female rats. Indian J Physiol Pharmacol 1985; 29(1): 21-26

56. Myrseyed F, Shiravi A, Nasr-Abadi M. The effect of intraperitoneal injection of alcoholic extract Foeniculum vulgare seed on gonadotropic and testosterone hormones in male wistar rats. J Anim Sci 2088; 1(1): 49-56.

57. Mirabolghasemi G, Alizadeh F. The Effect of hydroalcoholic extract of Fennel (Foeniculum vulgare) seed on serum levels of sexual hormones in female Wistar rats with Polycystic Ovarian Syndrome (PCOS). Arak Med Univ J 2014; 17(5): 70-8.

58. Devi K, Vanithakumari G, Anusya S, Mekala N, Malini T, Elango V. Effect of Foeniculum vulgare seed extract on mammary glands and oviducts of ovariectomised rats. Anc Sci Life 1985; 5(2): 129.

59. Oulmouden F, Ghalim N, El Morhit M, Benomar H, Daoudi EM, Amrani S. Hypolipidemic and AntiAtherogenic effect of methanol extract of Fennel (Foeniculum Vulgare) in hypercholesterolemic mice. Int J Sci Knowl 2014; 3(1): 42-52.

60. Oulmouden F, Saïle R, Gnaoui N, Benomar H, Lkhider M, Amrani S, et al. Hypolipidemic and anti-atherogenic effect of aqueous extract of fennel (Foeniculum Vulgare) extract in an experimental
model of atherosclerosis induced by triton WR-1339. Eur J Sci Res 2011; 52(1): 91-9.

61. Abdul-Ghani AS, Amin R. The vascular action of aqueous extracts of Foeniculum vulgare leaves. J Ethnopharmacol 1988; 24(2): 213-8.

62. Bardai SE, Lyoussi B, Wibo M, Morel N. Pharmacological evidence of hypotensive activity of Marrubium vulgare and Foeniculum vulgare in spontaneously hypertensive rat. Clin Exp Hypertens 2001; 23(4): 329-43.

63. Sushruta K, Satyanarayana S, Srinivas S, Sekhar JR. Evaluation of the blood-glucose reducing effects of aqueous extracts of the selected umbelliferous fruits used in culinary practices. Trop J Pharm Res 2007; 5(2): 613-7.

64. El-Soud N, El-Laithy N, El-Saeed G, Wahby M, Khalil M, Morsy F, et al. Antidiabetic activities of Foeniculum vulgare Mill. Essential oil in streptozotocin-induced diabetic rats. Maced J Med Sci 2011; 4(2): 139-46.

65. Dongare V, Arvindekar A, Magadum C. Hypoglycemic effect of Foeniculum vulgare Mill. fruit on dexamethasone induced insulin

resistance rats. Res J Pharmacogn Phytochem 2010; 2(2): 163-5.

66. Garga C, Khan S, Ansari S, Suman A, Garg M. Chemical composition, therapeutic potential and perspectives of Foeniculum vulgare. Pharmacogn Rev 2009; 3(6): 346-352

67. Bogucka-Kocka A, Smolarz H, Kocki J. Apoptotic activities of ethanol extracts from some Apiaceae on human leukaemia cell lines. Fitoterapia 2008; 79(7): 487-97.

68. Mohamad RH, El-Bastawesy AM, Abdel-Monem MG, Noor AM, Al-Mehdar HA, Sharawy SM, et al. Antioxidant and anticarcinogenic effects of methanolic extract and volatile oil of fennel seeds (Foeniculum vulgare). J Med Food 2011; 14(9):986-1001.

69. Ozbek H, Ugras S, Bayram I, Uygan I, Erdogan E, Ozturk A, et al. Hepatoprotective effect of Foeniculum vulgare essential oil: A carbon-tetrachloride induced liver fibrosis model in rats. Scand J Lab Anim Sci 2004; 31(1): 9-17.

70. Qiang F, Yiming A, Shui-quan W, Zi-ming G. Effects of foeniculum vulgare Mill on lipid peroxidation in rats with liver hepatic fibrosis. Prog Mod Biomed 2011; 21: 13.

71. Liu YP, Xu Y, Gan ZM. The influence of the Foeniculum vulgare Mill on cytokine in hepatic fibrosis rats. J Xinjiang Med Univ 2009; 6: 8.

72. Wang L, Zhang T, Zhang JL, YU Y, Gan ZM. Experimental study of Chinese herb Foeniculum vulgare Mill on liver hepatic fibrosis and potassium supplement in rats. J Xinjiang Med Univ 2012; 9: 12.

73. Liu YP, Xu Y, Gan ZM. The effect on the TNF-αin CCL4-induced liver fibrosis rat by the Foeniculum vulgare Mill [J]. J Xinjiang Med Univ 2008; 4: 21.

74. Joshi H, Parle M. Cholinergic basis of memory strengthening effect of Foeniculum vulgare Linn. J Med Food 2006; 9(3): 413-7.