e - ISSN - 2348 - 2168
Print ISSN - 2348 - 215X

Acta Biomedica Scientia

Journal homepage: www.mcmed.us/journal/abs

PHARMACOLOGICAL IMPORTANCE OF *FOENICULUM VULGARE* IN HUMAN HEALTH CARE – A REVIEW

R. Vinodhini*

Unit of Biochemistry, Department of Medicine, College of Medicine and Health Sciences, Ambo University, P.O. Box. 19, Ambo Town, West Shoa, Ethiopia.

Article Info

Received 29/02/2016
Revised 16/03/2016
Accepted 19/03/2016

Keywords :-
Foeniculum vulgare,
Hepatoprotective effect,
Antioxidants,
Hyperlipidemia.

ABSTRACT

Foeniculum vulgare (Apiaceae) commonly known as fennel is a well-known aromatic plant as well as the essential plant in traditional medicine for its known medicinal value all over the world. The present review deals about the various chemical, therapeutic and protective effect of fennel. The leaves, stalks and seeds (fruits) of the plants are good source of powerful natural antioxidants because of the presence of vitamins, phenolic compounds and oleoresins. Fennel is used as carminative, digestive, diuretic and in the treatment of respiratory and gastrointestinal disorders. Furthermore, anti-inflammatory, anti-diabetic, antitumor, and many other activities of this plant have been revealed by different researches all over the world in different animal models confirmed the biopotential nature and the importance of this medicinal plant. As most of the scientific documentation deals on the fruit part of the *F. vulgare*, it is necessary to carry out more systematic studies to explore the remaining portions of the fennel. Therefore, *F. vulgare* could be an effective source of phytochemical required for the preparation of novel therapeutic agents used to treat different disorders.

INTRODUCTION

The liver is a vital organ of paramount importance involved in the maintenance of metabolic functions and detoxification of the exogenous and endogenous challenges like xenobiotics, drugs, viral infections and chronic alcoholism [1]. About 20,000 deaths occur every year due to liver diseases. The hepatocellular carcinoma is one of the ten most common tumors in the world with over 250,000 new cases each year [2]. Conventional drugs used in the treatment of liver diseases are sometimes inadequate and can have serious adverse effects. A detailed investigation and documentation of plants used in local health traditions and the pharmacological evaluation of these plants can lead to the development of invaluable plant drugs for many dreaded diseases. Plants constitute a rich source of bioactive secondary metabolites. Moreover, they can degrade to non-toxic products. Plant based drugs have gained importance and popularity in recent years because of their safety, efficacy and cost effectiveness. The plants and their products have been have been used as natural alternatives for treatment and management of various diseases including hepatic disorders.

Nowadays most of the advanced techniques and research input focus on the invention of different approaches related to the treatment of alcoholic liver diseases, but still no significant and safe hepatoprotective agents are available in modern therapeutics. Therefore, it is important to optimize the development of plant based hepatoprotective drugs with scientific validation to optimize the drug as effective in healing the variety of liver disorders. According to WHO more than 80% of people in developing countries depend on traditional medicine for their primary health care needs, and a recent survey shows that more than 60% of patients use vitamins or

Corresponding Author:

R. Vinodhini
Email: sivaniswetha@yahoo.com

phytomedicine at some point in their therapy [3]. A large number of plants and formulations have been reported for their hepatoprotective effect. Nearly 160 phytoconstituents from 101 plants have been claimed to possess liver protecting activity [4]. Herbs and spices are generally considered safe and proved to be effective against various human ailments. Medicinal plants have very important place as they not only maintain the health and vitality of human beings but also cure several diseases including liver disorders without causing any toxicity. This review focus on such important and well-documented medicinal plant called *Foeniculum vulgare* Mill. This herbal plant well known all over the world for its use in curing different types of disorders.

METHODOLOGY

The pharmacological information of *Foeniculum vulgare* mill have been searched from journals accessible in databases such as ScienceDirect, Scopus, EBSCO, Medline, PubMed, Embase, SID, Google Scholar, Iran Medex and Standard text books by using key words such as fennel and pharmacology of *F. vulgare*.

RESULTS AND DISCUSSION

BOTANICAL INFORMATION

Fennel is an ancient seasonal herb. The fennel plant originated in the southern Mediterranean Region. Family: Apiaceae, *genus*: *Foeniculum*, *species*: *vulgare*, and *botanical name*: *Foeniculum vulgare* Mill. It is universally known as Fennel and is known by many names worldwide (Table 1). *F. vulgare* is an upright, branching perennial herb with soft, feathery, almost hair-like foliage growing upto 2 m tall. The bright golden flowers, produced in large, flat terminal umbels (Figure 1).

CHEMICAL PROPERTIES OF *F.VULGARE*

It is a small group of annual, biennial or perennial herb belonging to the Umbelliferae (Apiaceae) family with a characteristic aniseed flavour [5]. The leaves, stalks and seeds (fruits) of the plant are edible. It is widely cultivated throughout the temperate and tropical regions of the world for its aromatic fruits, which are used as culinary spices. Fennel is used as a spice and also as an important ingredient in various folklore medicines throughout the world. Moreover, this plant has been investigated extensively for several medicinal and therapeutic activities and has been reported for possessing carminative, flavoring and mosquito repellent properties. Chemically, Foeniculum species are characterized by the presence of essential oils [6], estragol [7], coumarins [8] and flavonoids [9]. The stem leaves, and fruit are commonly used as the dietary herb to aid digestion. The leaves are used for flavoring fish and meat and the fruits are used as a spice giving them a strong aroma and taste, and as an ingredient in cosmetics. The leaves contain vitamins and minerals including calcium, potassium, sodium, iron, phosphorus, thiamine, riboflavin, niacin and vitamin C [10]. 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% petrocylic acid. The fruit has value of 4 to 6% essence which its essence and combine ingredients vary according to the location of plant growth [11]. The essential nutritional values of *F. vulgare* is presented in the Table 2.

THERAPEUTIC EFFECT OF *F. VULGARE*

Fennel is a healthy food which can be used to reduce the potential of lung cancer, asthma and prevent thrombosis and atherosclerosis [12]. Fennel and its herbal drug preparations are used for dyspeptic complaints such as mild, spasmodic gastric-intestinal complaints, bloating and flatulence [13]. The plant acts as a carminative (assists with flatulence control) and increase breast milk production [14].

Fennel is used in herbal remedies for respiratory tract disorders and indigestion and is also used to increase milk flow in nursing mothers [15]. Fennel seeds have been shown to increase milk secretion, promote menstruation, facilitate birth and alleviate the symptoms of dysmenorrhea [16]. The antioxidant activity of *Foeniculum vulgare* seeds [17], leaves [18] and fruits [19] proved that all parts of this plant is act as strong phytotherapeutic agent. The shoots and leaves showed the highest levels of Vitamin E (tocopherols) and vitamin C (ascorbic acid). Fennel interacts synergistically at the membrane-cytosol interface to regenerate membrane-bound oxidized vitamin E [20]

Foeniculum vulgare has been scientifically proved to possess various pharmacological activities, which include anti-diabetic [21], antioxidant [22], hepatoprotective [23], anti-microbial [24], anti-thrombotic [25], anti-spasmodic [26], anti-osteoporotic [27], anti-inflammatory [28], anti-atherosclerotic [29], gastroprotective [30] anxiolytic activity [31], anti-depressant [32] and anti-tumor activity [33].

ANTI-DIABETIC EFFECT

The oral administration of fennel oil slightly decreases hyperglycemia by promoting the sensitivity of insulin and regulate the energy metabolism in cells [34]. A study conducted on the streptozotocin induced diabetes in the kidney and pancreatic tissues of the experimental rat models were found to be reversible and corrected after ingested with fennel oil. The excellent recovery of pancreatic tissue with treatment of fennel oil may enlighten the positive effects of this agent on the production of insulin. The rats pre-treated with fennel oil regenerated the islets of pancreas [21]. Another study carried out to explore the hypoglycemic effect of fennel concludes the therapeutic effect of fennel on diabetes by decreasing the oxidative stress, and preserving the integrity of beta-cells of pancreas [35].

ANTIOXIDANT EFFECT

Foeniculum vulgare has a good radical scavenging activity. This is supported by number of research papers stated the presence of essential oil in fennel has a strong radical scavenging and protective effect against lipid peroxidation [36 – 38]. The possible reason for its scavenging effect is due to the presence of higher content of total phenols and flavonoids. A research on invitro studies to explore the aqueous and ethanolic extract of fennel concluded, the medicinal plant *F. vulgare* is a potent antioxidant [39]. The antioxidant effect of fennel was supported by another research that states a significant enhancement in the activities of antioxidant enzymes in the diets containing fennel [40, 41]. According to Li and Zhou [42], the phenolic compounds containing free hydrogen present in the *F. vulgare* was largely responsible for its antioxidant activity. This statement was supported by another comparative study conducted on the isolation of essential oils on different plant extracts concluded the antioxidant properties fennel could be attributed to the rich content of phenolic compounds [43, 44]. Anethole (t-anethol) is the main compound present in all the volatile oils of fennel are mainly responsible for the significant antioxidant activity. The presence of t-anethol and flavonoids content in fennel lowered and ameliorated the total lipids, cholesterol, triglycerides and LDL – C levels [45] and demonstrated its effect as potent radical scavenger and antioxidant. Pigs supplemented with fennel oil down-regulated the activity of GSHPx, thus indicating that fennel oil attenuated the changes in the pancreatic antioxidant enzymes in response to generation of oxidants [46].

HEPATOPROTECTIVE EFFECT

Fatima et al., [47] reported that fennel seeds extract protects the liver cells against diethyldithiocarbamate induced liver toxicity in rats. A research study carried out to explore the hepatoprotective nature of fennel (*Foeniculum vulgare*) pointed out the presence of D-limonene and β-myrcene compounds in fennel increases the concentration of liver glutathione (GSH) which is required by several enzymes that participate in the formation of disulfide bonds of many proteins [48]. Another research work conducted on the rats intoxicated with paracetamol increased the serum and liver marker enzymes such as SGOT, SGPT, ALP and bilirubin. This condition was reverted and maintained by the treatment of *F. vulgare* at a high dose of 400 mg/kg body weight. The study concluded the extract of *F. vulgare* possess anti- hepatotoxic action [49].

ANTI-MICROBIAL ACTIVITY

Fennel seeds displayed significant antibacterial and antiviral activities [50]. The essential oils obtained from the fruits of fennel showed significant antibacterial activity against E. *coli* and *Bacillus megaterium* [51]. Another research finding concluded that *F. vulgare* had highest antibacterial activity against gram positive bacteria. It represented 75 % inhibition zone of ampicillin. In addition to the antibacterial effect the water extracts of fennel seeds act as effective antifungal agents as compared to reference commercial fungicidal Greseofulvin [52]. The dose at the concentration of 20 µg of Fennel extracts was found to be more effective than Acyclovir [53]. A study carried out on the essential oils of *F. vulgare* showed a prominent antifungal activity against *Candida albicans*. It is suggested by the researchers that fennel could be the candidate for a new antifungal agent for candidiasis and other fungal diseases [54]. Mimica et al., [55] also reported the essential oils of fennel are active against Aspergillus species and the essential oils of the bitter fennel exhibit an inhibitory effect against a wide range of Bacillius species [56]. It is well understood that the isolated essential oils and extracts from spices and herbs have the ability of inhibiting the growth of microbes [57]. Gulfraz et al., [58] reported the essential oil and seed extracts of *F. vulgare* could be a source of pharmaceutical materials required for the preparations of new therapeutic and antimicrobial agents.

ANTI-THROMBOTIC AND GASTROPROTECTIVE EFFECT

The essential oil of *F. vulgare* prevented the thrombin induced clot reaction. Furthermore, the oral administration of essential oil in *F. vulgare* at a concentration of 100 mg/kg provided significant protection towards ethanol induced gastric lesions in rats [25]. A research work carried out on the rats treated with fennel water decreased the tone and amplitude of peristalsis in the stomach. The results of the study inferred the *F. vulgare* has shown a protective effect against ethanol induced gastric mucosal lesions [30]. The study further implies the presence of anethole whose chemical structure is similar like dopamine might be the possible reason for the gastroprotective effect of *F. vulgare*.

ANTI-SPASMODIC EFFECT

The alcoholic extract of fennel oil tested in the isolated smooth muscles (invitro models) has demonstrated a significant antispasmodic activity [59]. A research carried out by Sandhu and Heinrich [60] stated the antispasmodic action appears to be due to an effect on the calcium metabolism in the smooth muscle.

OESTROGENIC EFFECT

A study done on estrogenic activity in cell culture system demonstrated that Fennel extract (5 – 50 µg/ml) can stimulate the proliferation of human bone marrow mesenchymal stem cells (MSCs) reaching peak at 72 h in lower concentration and showing inhibitory effects at high concentration (100µg/ml) [61]. The possible reason for its oestrogenic effect is due to the presence of phytoestrogens, with a structure similar to 17β-estradiol (E2). *F. vulgare*

produces a protective benefit on osteoporosis in post-menopausal women and beneficial effects on women health.

ANTI-INFLAMMATORY EFFECT

The methanolic extract of fruits of *F. vulgare* at a concentration of 200 mg/kg has been reported to show inhibitory effects against inflammatory diseases. *F. vulgare* showed a central analgesic effect by inhibition of the Type IV allergic reactions [62].

HYPOLIPIDEMIC EFFECT

Fennel reduced the gain in body weight due to phytoestrogens like estradiol which turned back the liver total lipids to the normal values [63]. A study done on the mice with the intraperitoneal injection of Triton WR-1339 (Tyloxapol) induces hyperlipedemia in the liver and coronary arteries. The animals treated with methanol extract of *F. vulgare* at a dose of 0.2 g/kg decreases the total cholesterol, triglycerides, LDL and Apo. B and increases the HDL and Apo. AI. The results of the study confirmed the hypolipidemic effect of the fennel [64].

ANTI-DEPRESSANT EFFECT

A study carried out on the administration of methanolic extracts of the whole plant of fennel for four successive days ameliorated the amnesic effect of scopolamine (0.4 mg/kg) and aging induced memory deficits in mice. Further, the extract exhibited antioxidant action by inhibition of lipid peroxidation in both liver and brain homogenates of rats [65]. Another research work conducted on *F. vulgare* at a dose of 500mg/kg showed potent effect to decrease the immobility period as compared to imipramine (30 mg/kg). Thus, the *Foeniculum vulgare* extract may possess an antidepressant like effect [32]. Fennel is also used in the treatment of cognitive disorders such as dementia and Alzheimer's disease [66].

NEPHROPROTECTIVE EFFECT

The albino rabbits intoxicated with gentamycin decreased the urea, creatinine and malondialdehyde concentration and significantly increased and the levels of albumin compared to normal control group. All the intoxicated groups after treated with *F. vulgare* at high doses alone and mixture of *F. vulgare* and *S. nigrum* exhibited nephroprotective effects by significantly lowering the urea, creatinine and the lipid peroxidation. The nephroprotective activity of may be due to the presence of flavonoids and many phenolic compounds, present in *F. vulgare* and *S. nigrum* [67].

ANTI-TUMOR EFFECT

The fennel extract contains 7 phenolic acids all with antitumor activity such as tannic, gallic, caffeic, cinnamic, chlorogenic, ferulic and vanillic acids [68]. The 70% methanolic extract of *F. vulgare* against B16F10 melanoma cell line showed cytoprotection and confirmed the *F. vulgare* has good antitumor activity [33]. A research finding supported the presence of anethole, which is the active component of fennel not only prevents but also treats cancer and other diseases [69]. Al-Harbi et al., [70] carried out a research study to detect the anticarcinogenic potential of anethole on the Ehrlich Ascites Tumor (EATs) in the paws of Swiss albino mice. The results revealed that anethol increases the survival time and reduces tumor weight and volume of the EAT bearing mice. All the above discussed pharmacological activities of the *F. vulgare* is presented systematically in the Table 3.

Table 1. Vernacular names of *Foeniculum vulgare*

Region / language	Local name
Alto, Bolivia	Hinojo
Arabic	Bisbas, razianaj
Aymara, Kechua	Inuju
Balikesir, Turkey	Arapsaci, rezene, malatura, hullebe
Basque	Mieloi
Bengali (Indian language)	Mauri, panmouri
Bosnia	Komoraˇc
Brazil	Endro, erva-doce, funcho
Catalan	Fenoll, fonoll
Central Serbia	Morac
Chinese	Hui xiang, xiao hui xiang
Czech	Fenykl
Dalmatia (Southern Croatia), Poland	Komoraˇc, koromaˇc, kumuraˇc, moraˇc, moroˇc, moraˇca, Koper, wloski
Danish	Almindelig fennikel, fennikel
Denmark	Almindelig
Dutch	Venkel
English	Bitter fennel, common fennel, sweet fennel, wild fennel
France	Fenouille

French	Fenouil
Germany	Fenchel, fenchle, bitterfenchel, wilder fenchel, dunkler fenchel,
Hindi (Indian language)	Badi, badishep, bari saunf, badi saunf, saunp, saunf, sonp, sont
Italy	Finucchio, finucchiello, finochietto, finocchiella,fen`ucciu, fenuc´ettu-sarv`egu
Japanese	Fenneru, uikyou, uikyou, shouikya
Jordan	Shomar
Korea	Sohoehyang
Latin	Foeniculum, maratrum
Nepalese	Madesi sauf
North Iran	Badian
Norway	Fenikkel
Pakistan	Sonef, saunf
Persian	Razianeh
Polish	Fenkuł, koper włoski
Portuguese	Funcho
Slovenian	Sladki komar˘cek
Somali Region, Ethiopia	Kamon
South Europe	Fennel
South Africa	Vinkel, fennel
Spanish	Hinojo, hinojo amargo, fenoll, fiollo, millua
Swedish	F¨ank˚al
Tamil (Indian language)	Perunch siragum, shombu, sohikire
Thai	Phak chi, phak chi duen ha, phak chi lom, thian klaep, yira

Table 2. Essential nutritional values of *F. vulgare*

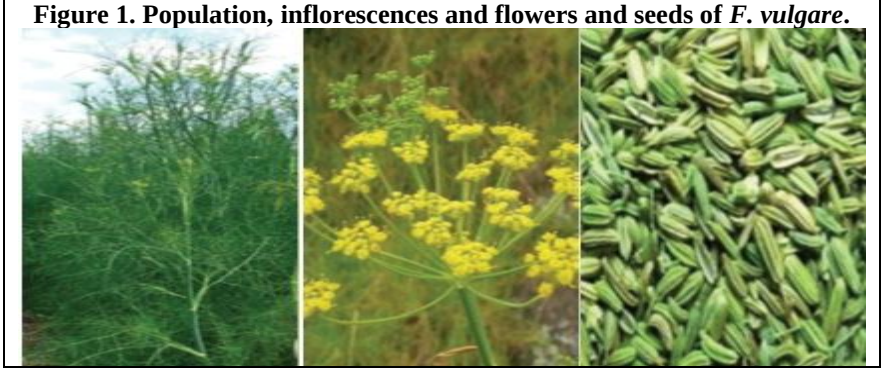
Composition	**Quantity / 100 g**
Phytochemical constituents	
Protein	1.24 g
Total lipid (fat)	0.2 g
Carbohydrate	7.3 g
Total dietary fiber	3.1 g
Sugars	3.93 g
Minerals	
Calcium, Ca	49 mg
Iron, Fe	0.73 mg
Magnesium, Mg	17 mg
Phosphorus, P	50 mg
Potassium, K	414 mg
Sodium, Na	52 mg
Zinc, Zn	0.2 mg
Vitamins	
Vitamin A	48 μg
Vitamin E	0.58 mg
Vitamin K	62.8 μg
Vitamin C	12 mg
Thiamin B-1	0.01 mg
Riboflavin B-2	0.032 mg
Niacin B-3	0.64 mg
Vitamin B-6	0.047 mg
Lipids	
Fatty acids, total saturated	0.09 g
Fatty acids, total polyunsaturated	0.169 g
Fatty acids, total monounsaturated	0.068 g

Curtsey: USDA, New York.

Table 3. Important pharmacological activities of *Foeniculum vulgare*

Activity	Plant part used	Type of extract
Anti-carcinogenic	Seed	Methanolic extract
Anti-depressant	Whole plant	Methanolic extract
Anti-diabetic	Fruit	Fennel oil
Anti-inflammatory	Fruit	Methanolic extract
Anti-microbial	Fruit	Essential oil
Anti-mycobacterial	Aerial parts	Chloroform, hexane, methanol, and aqueous extracts
Antioxidant	Seed	Ethanol and water extract
Anti-spasmodic	Fruit	Fennel oil
Anti-stress	Fruit	Aqueous extracts
Anti-thrombotic	Fruit	Essential oil
Ant-itumor	Fruit	Methanolic extract
Anti-ulcerogenic	Aerial parts	Aqueous extract
Apoptotic	Fruit	Ethanol extract
Cytoprotective	Fruit	Methanolic extract
Cytotoxic	Root (ground part)	Dichloromethane and methanol (1 : 1) extract
Gastroprotective	Fruit	Essential oil
Hepatoprotective	Seed	Essential oil
Hypoglycaemic	Seed	Essential oil
Hypolipidemic	Fruit	Methanolic extract
Nephroprotective	Seed	Methanolic extract
Oestrogenic	Seed	Acetone extract
Therapeutic effect	Whole plant	Aqueous extract
Vascular effects	Leaf	Aqueous extracts

Figure 1. Population, inflorescences and flowers and seeds of *F. vulgare*.



CONCLUSION

The voluminous researches carried out in fennel confirmed its chemical property in healing different types of disorders. *F. vulgare* was considered as a potent medicinal plant because of cluster of chemicals that are diversely distributed in all parts of the plant. It is imperative to stress a point that majority of the available researches are focussing on the fruit portion of the fennel but minimum researches are conducted on the remaining parts of the *F. vulgare* for its antioxidant, antibacterial and hepatoprotective effect. Therefore it is recommended for the future researches to ultimately explore all parts of the *F. vulgare*. This could help the pharmaceutical industries in the development of new alternative medicines in the treatment of different disorders.

CONFLICT OF INTEREST: Nil

REFERENCES

1. Dienstag, JL and Isselbacher KJ. (2001). Toxic and drug induced hepatitis, 15th Edn, Chapter 296, In: Harrison's Principles of internal medicine. The McGraw-Hill Companies, In. 2, 737 – 1742.
2. Kshirsagar AD, Mohite R, Aggrawal AS and Suralkar UR. (2011). Hepatoprotective medicinal plants of ayurveda– a

review. *Asian J Pharmaceut Clin*, Res 4, 1 – 8.
3. Madhuri, S and Govind, P. (2009). Some anticancer medicinal plants of foreign origin. Curr Sci 96(6), 779 – 783.
4. Mohamed STS, Madhusudhana CC, Ramkanth S, Rajan VST, Mahesh Kumar K and Gauthaman K. (2010). Hepatoprotective herbs – A review. *Int J Res Pharm Sci*, 1, 1 – 5.
5. Sharma R. (2000). Medicinal Plants of India: An encyclopedia. Daya publishing house, Delhi. 108 – 109.
6. Özbek H, Ugras S, Bayram I, Uygan I, Erdogan E, Öztürk A and Huyut Z**. (**2004). Hepatoprotective effect of *Foeniculum vulgare* essential oil: A carbon tetrachloride induced liver fibrosis model in rats. Scand. *J Lab Anim Sci*, 1 (31), 9 – 17.
7. Farooq A, Muhammad A, Abdullah I and Muhammad S. (2009). Antioxidant and antimicrobial activities of essential oil and extracts of fennel (*Foeniculum vulgare* Mill.) seeds from Pak. *Flav Fragr, J*, 24,170 – 176.
8. Kwon YS, Choi WG, Kim WJ, Kim WK, Kim MJ, Kang WH and Kim CM. (2002). Antimicrobial constituents of *Foeniculum vulgare*. *Arc Pharmacol Res*, 25, 154 – 157.
9. Parejo I, Valadomat F, Bastida J, Rossa RA, Ferlage N, Burillo J and Codina C. (2002). Comparison between the radical scavenging activities and antioxidant activity of six distilled and non-distilled Mediterranean herbs and aromatic plants. *J Agri Food Chem*, 50, 6882 – 6890.
10. Miguel MG, Cruz C, Faleiro L, Simoes MT, Fiqueiredo AC, Barroso JG and Pedro LG. (2010). *Foeniculum vulgare* essential oils: chemical composition, antioxidant and antimicrobial activities. *Nat Prod Comm*, 5(2), 319 – 328.
11. Ahmadi A, Nasiri NF and Parivar K. (2007). Effect of aqueous extract of the aerial part of the Ruta graveolens on the spermatogenesis of immature Balb / C mice. *Razi J Med Sci*, 14 (56), 13 – 20
12. Vardavas CI, Majchrzak D, Wagner KH, Elmadfa I and Kafatos A. (2006). Lipid concentrations of wild edible greens in Crete. *Food Chem*, 99 (4), 822 – 834.
13. Musharaf K and Shahana M. (2014). *Foeniculum vulgare* Mill. A medicinal herb. Med Plant Res 4(6), 46 – 54.
14. Khazaei M, Montaseri A, Khazaei MR and Khanahmadi M. (2011). Study of *Foeniculum vulgare* effect on Folliculogenesis in female mice. *Int J Fertil Steril*, 5, 122 – 227.
15. Choi M and Hwang JK. (2004). Anti-inflammatory, analgesic and antioxidant activities of the fruit of *Foeniculum vulgare*. *Fitoterapia*, 75, 557 – 565.
16. Rather MA, Dar BA, Sofi SN, Bhat B.A and Qurishi MA. (2012). *Foeniculum vulgare:* A comprehensive review of its traditional use, phytochemistry, pharmacology and safety. *Arab J Chem*, http://dx.doi.org/10.1016/j.arabjc.2012.04.011.
17. Surveswaran S, Cai YZ, Corke H and Sun M. (2007). Systematic evaluation of natural phenolic antioxidants from 133 Indian medicinal plants. *Food Chem*, 102, 938 – 953.
18. Heinrich M. (2005). Co-ordinator of the local food-nutraceuticals consortium, understanding local mediterranean diets: a multidisciplinary pharmacological and ethnobotanical approach. *Pharmacol Res*, 52, 353 – 366.
19. Marino SD, Gala F, Borbone N, Zollo F, Vitalini S, Visioli F and Iorizzi M. (2007). Phenolic glycosides from *Foeniculum vulgare* fruit and evaluation of antioxidative activity. *Phytochemistry*, 68 (13), 1805 – 1812.
20. Li Y and Schellhorn HE. (2007). New developments and novel therapeutic perspectives for vitamin C. *J Nutr*, 137, 2171 – 2184.
21. El-Soud NA, El-Laithy N, El-Saeed G, Wahby MS, Khalil M, Morsy F and Shaffie N. (2011). Antidiabetic Activities of *Foeniculum vulgare* Mill essential oil in Streptozotocin induced diabetic rats. *Mac J Med Sci*, 4(2), 139 – 146.
22. Singh G, Maurya S and Lampasona MN. (2006). Chemical constituents, antifungal and antioxidative potential of *Foeniculum vulgare* volatile oil and its acetone extract. *Food Control*, 745 – 752.
23. Naeem M, Rabeh and Aboraya AO. (2014). Hepatoprotective Effect of Dill (Anethum graveolens L.) and fennel (*Foeniculum vulgare*) oil on hepatotoxic rats. *Pak J Nut*, 13 (6), 303 – 309.
24. Janssen AM, Chin NL, Scheffer JJ and Baerheim SA. (1986). Screening for antimicrobial activity of some essential oils by the agar overlay technique. *Scientific Edition*, 8, 289 – 292.
25. Tognolini M, Ballabeni V, Bertoni S, Bruni R, Impicciatore M and Barocelli E. (2007). Protective effect of *Foeniculum vulgare* essential oil and anethole in an experimental model of thrombosis. *Pharmacol Res*, 56, 254 – 260.
26. Forster HB, Niklas H and Lutz S. (1980). Antispasmodic effects of some medicinal plants. *Planta Medica*, 40, 309 – 319.
27. Fariba J, Alireza G and Hossein N. (2006). Evaluation of prophylactic effect of the fennel essential oil on experimental osteoporosis models in rats. *Int J Pharmaclol*, 2(5), 588 – 592.
28. Chainy GB, Manna SK, Chaturvedi MM and Aggarwal BB. (2000). Anethole blocks both early and late cellular responses transduced by tumor necrosis factor: effect on NF-κB, AP-1, JNK, MAPKK and apoptosis. *Oncogene*, 19, 2943 – 2950.
29. Oulmouden F, Saïle R, Gnaoui NE, Benomar H and Lkhider M. (2011). 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*, 52, 91 – 99.
30. Birdane FM, Cemek M, Birdane YO, Gulcin I and Buyukokuroglu ME. (2007). Beneficial effects of *Foeniculum vulgare* on ethanol-induced acute gastric mucosal injury in rats. *World J Gastroenterol*, 13(4), 607 – 611.
31. Mesfin M, Asres K and Shibeshi W. (2014). Evaluation of anxiolytic activity of the essential oil of the aerial part of

Foeniculum vulgare Miller in mice. *BMC Comp Alter Med*, 14, 310.

32. Singh JN, Sunil K and Rana AC. (2013). Antidepressant activity of methanolic extract of *Foeniculum vulgare* (Fennel) Fruits in Experimental Animal Models. *J App Pharmaceu Sci*, 3 (09), 065 – 070.
33. Pradhan M, Sribhuwaneswari S, Karthikeyan D, Minz S, Sure P, Chandu AN, Mishra U, Kamalakannan K, Saravanankumar A and Sivakumar T. (2008). In-vitro cytoprotection activity of *Foeniculum vulgare* and Helicteres isora in cultured human blood lymphocytes and antitumour activity against B16F10 melanoma cell line. *Res. J Pharm Technol*, 1 (14), 450 – 452.
34. Gonzalez OM, Hernandez GO Hernandez SE and Martinez AE. (2008). Effect of oral L-carnitine administration on insulin sensitivity lipid profile in type 2 diabetes mellitus patients. *Ann Nutr Metab*, 52, 335 – 338.
35. El-Dakhakhny M, Mady N, Lembert N and Ammon HP. (2002). The hypoglycemic effect of fennel oil is mediated by extra pancreatic actions. *Planta Med*, 68, 465 – 466.
36. Faudale M, Viladomat F, Bastida J, Poli F and Codina C. (2008). Antioxidant activity and phenolic composition of wild, edible, and medicinal fennel from different mediterranean countries. *J Agri Food Chem*, 56(6), 1912 – 1920.
37. Ozcan M, Erel O and Herken E. (2009). Antioxidant activity, phenolic content, and peroxide value of essential oil and extracts of some medicinal and aromatic plants used as condiments and herbal teas in Turkey. *J Med Food*, 12(1), 198 – 202.
38. Roby MHH, Sarhan MA, Selim KA and Khalel KI. (2013). Antioxidant and antimicrobial activities of essential oil and extracts of fennel (*Foeniculum vulgare* L.) and chamomile (Matricaria chamomilla L.). *Indus Crops Prod*, 44, 437 – 445,
39. Oktay M, Gulcin I and Kufrevioglu I. (2003). Determination of in vitro antioxidant activity of fennel (*Foeniculum vulgare*) seed extracts. *Food Sci Tech*, 36, 263 – 271.
40. Singh B and Kale RK. (2008). Chemomodulatory action of *Foeniculum vulgare* on skin and forestomach papillomagenesis enzymes associated with xenobiotic metabolism and antioxidant status in murine model system. *Food Chem Toxicol*, 46(12), 3842 – 3850.
41. Nickavar B and Abolhasani FA. (2009). Screening of antioxidant properties of seven umbelliferae fruits from Iran. *Pak J Pharm Sci*, 22(1), 30 – 35.
42. Li X, Li X and Zhou A. (2007). Evaluation of antioxidant activity of the polysaccharides extracted from Lycium barbarum fruits in vitro. *Eur Polymer J*, 43(2), 488 – 497.
43. Barros L, Heleno SA, Carvalho AM and Ferreira IC. (2009). Systematic evaluation of the antioxidant potential of different parts of *Foeniculum vulgare* Mill from Portugal. *Food Chem Toxicol*, 47(10), 2458 – 464.
44. Chang SH, Bassiri A and Jalali H. (2013). Evaluation of antioxidant activity of fennel (*Foeniculum vulgare*) seed extract on oxidative stability of olive oil. *J Chem Health Risks*, 3(2), 53 – 61.
45. Freire RS, Morais SM, Catunda F and Pinheiro D. (2005). Synthesis and antioxidant, anti-inflammatory and gastroprotector activities of anethole and related compounds. *Bioorg Med Chem*, 13, 4353 – 4358.
46. Schöne F, Vetter A, Hartung H, Bergmann H, Biertümpfel A, Richter G, Müller S and Breitschuh G. (2006). Effects of essential oils from fennel (Foeniculi aetheroleum) and caraway (Carvi aetheroleum) in pigs. *J Anim Physiol Anim Nutr*, (Berl) 90 (11-12), 500 – 610.
47. Fatima SK, Abdulaziz AH, Alaa EDH and Shahnaz MQ. (2005). Protective effects of fennel extract (*Foeniculum vulgare* mill.) on diethyldithiocarbamate-induced liver toxicity in rats. Program and abstracts of the Seventh Annual U.A.E. University Al-Ain, Research Conference STD, 95.
48. Eman GEH, Fatma AE and Amira MSAW. (2011). Effect of fennel (*Foeniculum vulgare*) on hyperlipidemic rats. *Egy J Hospital Med*, 43, 212 – 225.
49. Devika V, Mohandass S and Aiswarya PR. (2013). Screening of methanolic extract of *Foeniculum vulgare* for hepatoprotective activity. *Int J Pharm Pharmaceut Sci*, 5(4), 56 – 59.
50. Ruberto G, Baratta MT, Deans SG and Dorman HJ. (2000). Antioxidant and antimicrobial activity of F. vulgare and C. maritimum essential oils. *Planta Med*, 66(8), 689 – 693.
51. Araque M, Rojas LB and Usubillaga A. (2007). Antibacterial activity of essential oil of F. vulgare Miller against multiresistant Gram-negative bacilli from nosocomial infections. *Science*, 15(3), 366 – 370.
52. Zahid NZ, Abbasi NA, Hafiz AI, Hussain A. and Ahmad Z. (2012). Antifungal activity of local fennel (*Foeniculum vulgare* Mill) extracts to growth responses of some soil diseases. *Afr J Microbiol Res*, 6, 46 – 51.
53. Hanan AAT, Mohamed MIH, Wafaa AH and Hassan A. (2013). Chemical composition and biological potentials of aqueous extracts of fennel (*Foeniculum vulgare* L). *J App Sci Res*, 9(3), 1759 – 1767.
54. Park SH and Seong I. (2010). Antifungal effects of the extracts and essential oils from *F. vulgare* and *Illicium verum* against Candida albicans**.** *Kor J Med Mycol*, 15(4), 157 – 164.
55. Mimica D, Bozin B, Sokovic M, Mihajlovic B and Matavulj M. (2003a). Antimicrobial and antioxidant activities of three mentha species essential oils. *Planta Med*, 69, 413 – 419.
56. Ozcan MM, Chalchat JC, Arslan D, Ates A and Unver A. (2006). Comparative essential oil composition and antifungal

effect of bitter fennel (*Foeniculum vulgare* ssp. piperitum) fruit oils obtained during different vegetation. *J Med Food*, 9, 552 – 561.

57. Falzari LM and Menary RC. (2003). Chamomile for oil and dried flowers. RIRDC Publication No. 02/156 RIRDC Project No. UT-28 A, Australia.
58. Gulfraz M, Mehmood S, Minhas N, Jabeen N, Kausar R, Jabeen K and Arshad G. (2008). Composition and antimicrobial properties of essential oil of *Foeniculum vulgare*. *Afr J Biotechnol*, 7 (24), 4364 – 4368.
59. Khan IA and Abourashed EA. (2009). Leung's encyclopedia of common natural ingredients used in food drugs and cosmetics, 3rd Edn, New York, John Wiley and Sons, Inc. 183 – 186.
60. Sandhu DS and Heinrich M. (2005). The use of health foods, spices and other botanicals in the Sikh community in London. *Phytother Res*, 19, 633 – 642.
61. Zahra M, Masoud S, Abbas S, Gholamreza K and Arezoo A. (2013). Effects of *Foeniculum vulgare* ethanol extract on osteogenesis in human mecenchymal stem cells. *Avi J Phytomed*, 3(2), 135 – 142.
62. He W and Huang BA. (2011). Review of chemistry and bioactivities of a medicinal spice: *Foeniculum vulgare*. *J Med Plants Res*, 5(16), 3595 – 3600.
63. Ofir R, Tamir S, Khatib S and Vaya J. (2003). Inhibition of serotonin reuptake by fennel constituents. *J Mol Neurosci*, 20, 135 – 140.
64. Fatiha O, Noreddine G, Mohamed EM, Hakima B, Mustapha D and Souliman A. **(**2014). Hypolipidemic and Anti-atherogenic effect of methanol extract of fennel (*Foeniculum vulgare*) in hypercholesterolemic mice. *Int J Sci Knowl*, 31, 42 – 52.
65. Sushruta K and Hemant K. (2013). *Foeniculum vulgare* Mill (Umbelliferae) attenuates stress and improves memory in wister rats. *Trop J Pharmaceu Res*, 12 (4), 553 – 558.
66. Joshi H. (2006). Cholinergic basis of memory-strengthening effect of F. vulgare Linn. *J Food Med*, 9 (3), 413 – 417.
67. Shaheen U, Manzoor Z, Khaliq T, Kanwal A, Muhammad F, Hassan IJ, Hussain SM and Mazhar H. (2014). Evaluation of nephroprotective effects of *Foeniculum vulgare* Mill, Solanum Nigrum Linn and their mixture against gentamicin-induced nephrotoxicity in albino rabbits. *Int J Pharm Sci Rev Res*, 25(1), 01: 1 – 9.
68. Singh UP, Singh, D.P and Maurya S. (2004). Investigation on the phenolics of some spices having pharmacotherapeutic properties. *J Herb Pharmacother*, 4, 27 – 242.
69. Bharat BA and Shishir S. (2006). Molecular targets of dietary agents for prevention and therapy of cancer. *Biochem Pharmacol*, 71, 1397 – 13142.
70. Al-Harbi MM, Qureshi S, Raza M, Ahmed MM, Giangreco AB and Shah AH. (1995). Influence of anethole treatment on the tumour induced by Ehrlich ascites carcinoma cells in paw of Swiss albino mice. *Eur J Cancer Prev*, 4, 307 – 318.