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# Phytochemistry and Pharmacological Activities of *Foeniculum Vulgare*

**Z.M. Anka[1*] S.N. GIMBA[2] Anshu Nanda[3] Lawan Salisu[2]**

[1]*Department of pharmacy, School of Allied Health science, Sharda University, Greater Noida U.P, India*
[2] *Department of Basic Science, Shehu Sule College of Nursing and Midwifery, Damaturu. Yobe, State. Nigeria*
[3]*Department of Clinical Research, School of Allied Health science, Sharda University, Greater Noida, U.P, India*

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**Abstract:** Foeniculum vulgare Mill (fennel) is a biennial medicinal and aromatic plant. It is a hardy perennial herb with yellow flowers and feathery leaves; it grows to a height of up to 2.5m with hollow stems. The leaves grow up to 40 cm long; they are finely dissected with the ultimate segments filiform (thread like) of about 0.5 mm wide. The flowers are produced in terminal compound umbels. The fruit is a dry seed 4–10 mm long. This research tends to determine what information is available on the traditional uses; botany, phytochemistry, and toxicity of F. vulgare? What pharmacological studies were performed on this plant and how do they validate its traditional uses? What is the future for F. vulgare? Based on the review made it can be concluded that F. vulgare is a medicinal and aromatic plant with a diverse pharmacological spectrum and having considerable importance in particular to food industry. The phenolic molecules present in fennel have been shown to possess potent antioxidant activity in a number of experiments. These bioactive molecules in fennel can be developed as novel pharmacological lead molecules provided their bioavailability, pharmacokinetics, physiological pathways, and importance to human health are known with sufficient detail.

**Keywords: Phytochemistry, Pharmacological, Foeniculum vulgare, Activity, fennel**

## I. INTRODUCTION

*Foeniculum vulgare* also known as fennel is a flowering plant species in the carrot family. (US D. A.N.R.C.S. 2015) F. vulgare Mill is a biennial medicinal and aromatic plant. It is a hardy perennial herb with yellow flowers and feathery leaves; it grows to a height of up to 2.5m with hollow stems. The leaves grow up to 40 cm long; they are finely dissected with the ultimate segments filiform (thread like) of about 0.5 mm wide. The flowers are produced in terminal compound umbels. The fruit is a dry seed 4–10 mm long. It is generally considered indigenous to the shores of Mediterranean Sea but has become widely naturalized in many parts of the world especially on dry soils near the sea coast and on the river banks. Some authors distinguish two sub-species of fennel, piperitum and vulgare: sub-species piperitum has bitter seeds, while sub-species vulgare has sweet seeds which are used as flavoring agents in baked goods, meat & fish dishes, ice creams, alcoholic beverages, etc due to their characteristic anise odour (Diaaz-Maroto et al., 2006). Morphological differences between these two sub-species are not always clearly defined.

It is a highly aromatic and flavorful herb with culinary and medicinal uses. Fennel seeds are anise like in aroma and are used as flavorings in baked goods, meat & fish dishes, ice cream, alcoholic beverages and herb mixtures (Diaaz-Maroto et al., 2005). The bulb, foliage and seeds of the fennel plant are widely used in many of the culinary traditions of the world.

Dried fennel seed is an aromatic, anise-flavored spice, brown or green in colour when fresh, slowly turning a dull grey as the seed ages. For cooking green seeds are the best. The bulb is a crisp, hardy root vegetable and may be saute´ed, stewed, braised, grilled or eaten raw. Fennel features predominantly in Mediterranean cuisine, where bulbs and fronds are used, both raw and cooked, in side dishes, salads, pastas, vegetable dishes. Many cultures in the Indian subcontinent and the Middle East use fennel seeds in their cooking. Fennel is one of the most important spices in Kashmiri Pandit and Gujarati cooking (Grieve, 1931).

It is a traditional and popular herb with a long history of use as a medicine. A series of studies showed that *F. vulgare* effectively controls numerous infectious disorders of bacterial, fungal, viral, mycobacterium, and protozoal origin(Kaur and Arora., 2009), (Manonmani and Abdul Khadir., 2011), (Orhan *et al*., 2012), (Morales *et al*., 2012), (Dua *et al*., 2013). It has antioxidant, antitumor, chemo-preventive, cyto-protective, hepato-protective, hypoglycemic, and oestrogenic activities(Malini *et al*., 1985), (Ozbek *et al*., 2003), (Oktay *et al*., 2003), (Pradhan *et al*., 2008), (El-Soud *et al*., 2011).

Some of the publications stated that *F. vulgare* has a special kind of memory-enhancing effect and can reduce stress (Koppular and Kumar., 2013). Animal experiments and limited clinical trials suggest that chronic use of *F. vulgare* is not harmful. Fennel maybe consumed daily, in raw form as salads and snacks, stewed, boiled, grilled, or baked in several dishes and even used in the preparation of herbal teas or spirits. A diet with desired quantity of fennel could bring potential health benefits due to its valuable nutritional composition with respect to presence of essential fatty acids (Barros *et al*., 2010). In recent years, increased interests in improvement of agricultural yield of fennel due to its medicinal properties and essential oil content has encouraged cultivation of the plant on large scale. Research on *F. vulgare* with current technology has been conducted all over the world.

## II. METHODOLOGY

All available literature on *F. vulgare* were compiled from electronic databases such as Academic Journals (including high impact, non-impact, and non-indexed journals), Ethno-botany, Google Scholar, Scopus link, PubMed, Science Direct, Web of Science, and library search.

A review of the literature from 2001 to 2005 shows only 20% reports published on *F. vulgare* which increased to about 38% from 2006 to 2010. Briefly, in these 10 years a total of 89 claims appeared in the literature on various aspects of *F. vulgare*. It is important to note that about 39% of reports (61 articles) were collected from recent three years, that is, 2013 to 2016. Some of the earlier published reviews of this plant included medicinal properties and phytochemistry (Garg *et al*., 2009), (He and Huang., 2011), (Rather *et al*., 2012), (Jamwal *et al*., 2013), (Grover *et al*), (Rahimi and Ardekani., 2013), but few of them appear in all these reviews. However, there is a need for an inclusive review that bridges the gaps between traditional uses of fennel and it's *in vitro* studies. The present review attempts to collate the available information on the botany, nation wise common vernacular names, cultivation (propagation), nutritive value, and traditional/ contemporary as well as allied applications, phytochemistry, pharmacology, and toxicity of *F. vulgare*. We hope that this review may provide scientific basis that explains the ethno-phytopharmacological role of *F. vulgare* in order to facilitate and guide future researches.

In particular, we aimed to answer the following questions.

1. What information is available on the traditional uses, botany, phytochemistry, and toxicity of *F. vulgare*?
2. What pharmacological studies were performed on this plant and how do they validate its traditional uses?
3. What is the future for *F. vulgare*?

On account of its carminative properties, fennel is chiefly used medicinally with purgatives to allay their side effects and for this purpose forms one of the ingredients of the well known compound liquorices powder. Fennel water has properties similar to those of anise and dill water: mixed with sodium bicarbonate and syrup, these waters constitute the domestic 'gripe water', used to correct flatulence of infants. Fennel tea, also employed as a carminative, is made by pouring boiling water on a teaspoonful of bruised fennel seeds. In the Indian Subcontinent, fennel seeds are eaten raw, sometimes with some sweetener to improve eyesight. Extracts of fennel seeds have been shown in animal studies to have a potential use in the treatment of glaucoma, as a diuretic and a potential drug for the treatment of hypertension. It has been used as a galactagogue improving the milk supply of a breast feeding mother. This is suggested to be due to the presence of phytoestrogens present in fennel which promote growth of breast tissue (Agarwal et al., 2008).

**Images of three stages of F. Vulgare and its seeds**

**a. flower**

**b. Root**

**c. seed**

**d. stem**

**Phytochemistry**

F. vulgare has been reported to contain 6.3% of moisture, 9.5% protein, 10% fat, 13.4% minerals, 18.5% fibre and 42.3% carbohydrates. The minerals and vitamins present in F. vulgare are calcium, potassium, sodium, iron, phosphorus, thiamine, riboflavin, niacin and vitamin C.

**Essential oil**

F. vulgare is well known for its essential oil. The characteristic anise odour of F. vulgare which is due to its essential oil makes it an excellent flavouring agent in baked goods, meat & fish dishes, ice-cream and alcoholic beverages. The major components of F. vulgare seed essential oil have been reported to be trans-anethole, fenchone, estragol (methyl chavicol), and a-phellandrene. The relative concentration of these compounds varies considerably depending on the phonological state and origin of the fennel (Diaaz-Maroto et al., 2006). The essential oil composition of F. vulgare exhibits considerable chemodiversity depending upon the method of extraction and geographical origin. The accumulation of these volatile compounds inside the plant is variable, appearing practically in any of its parts viz. roots, stem, shoots, flowers and fruits (Diaaz-Maroto et al., 2006; Gross et al., 2009). In one study it was reported that the essential oil content and composition varies during the different maturation stages of F. vulgare. The essential oil content was reported to decline with fruit maturity. The content of trans-anethole, the main component, varied between 81.63% and 87.85% (Telci et al., 2009). Another study reported that the phenyl-propenes estragol and trans-anethole which are the major constituents of the oleoresin of the aerial parts of F. vulgare varied during plant development, these two compounds being maximal in flowers and developing mericarps. The pharmacological effects of the F. vulgare fruits are generally attributed to their essential oil. Numerous studies have shown that the essential oil and its individual constituents exhibit novel pharmacological activities. (+) Fenchone and Panisaldehyde were identified as the major acaricidal agents against Dermatophagoides farinae and Dermatoghagoides pteronyssinus. Hence these compounds can be used as potential house dust mite control agents or as lead compounds. In another study, anethole has been reported to be active oestrogenic agent. However, in some studies it has been shown that polymers of anethole i.e. dianethole and photoanethole are the actual oestrogenic agents. Anethole has been also reported to be a safe antithrombotic agent due to its antiplatelet activity, clot destabilising effect and vaso-relaxant action (Tognolini et al., 2007). However, estragole, a main component of F. vulgare has become a cause of concern, as the structurally similar methyleugenol has been recently found to be a potential carcinogen. This has led to the European Union (EU) to allow a new legal limit for estragole of 10 mg/kg in non-alcoholic beverages (Zeller and Rychlik, 2006). The other classes of phytochemicals present in F. vulgare are phenols and phenolic glycosides.

F. vulgare has been reported to contain phenolic acids like 3-O-Caffeoylquinic acid, 4-O-caffeoylquinic acid, 5-O-caffeoylquinic acid, 1,3-O-di-caffeoylquinic acid, 1,4-O-di-caffeoylquinic acid, 1,5-O-di-caffeoylquinic acid. The flavonoids like eriodictyol-7-rutinoside, quercetin-3-rutinoside and rosmarinic acid have also been isolated from F. vulgare (Faudale et al., 2008; Park, 1996). Quercetin-3-O-galactoside, kaempferol-3-O-rutinoside and kaempferol-3-O-glucoside have also been reported to occur in the aqueous extract of F. vulgare. Quercitin-3-O-glucuronide, kampferol-3-O-glucuronide, isoquercitin and isorhamnetin-3-O-glucoside have also been isolated from F. vulgare (Parejo et al., 2004a). The phenolic compounds present in F. vulgare are considered to be associated with the prevention of diseases thought to be induced by oxidative stress such as cardiovascular diseases, cancer and inflammation. These phenolic compounds have received tremendous attention among nutritionists, food scientists and consumers due to their roles in human health. Diglucoside stilbene trimers and benzoisofuranone derivatives have also been isolated from F. vulgare fruit together with cis-miyabenol C, trans-miyabenol C, trans-resveratrol-3-O-b-D-glucopyranoside, sinapyl glycoside, syringin-4-O-b-glucoside, oleanolic acid, 7a-hydroxycampesterol, (3b,5a,8a,22E) 5,8-epidioxy-

ergosta-6,22-dien-3-ol, and 2,3-dihydropropylheptadec-5-onoate (Marino et al., 2007). An acylated kaemferol glycoside from flowers of F. vulgare has also been isolated (Soliman et al., 2002)

**Pharmacology**

**Antibacterial activity**

The essential oil extracted from the fruits of F. vulgare exhibited antibacterial effect against food borne pathogens such as Escherichia coli, Bacillus megaterium and Staphylococcus aureus

(Mohsenzadeh, 2007), E. coli 0157:H7, Listeria monocytogenes and S. aureus (Dadalioglu and Evrendilek, 2004; Cantore et al., 2004). Aqueous and organic extracts of F. vulgare have been reported to show antibacterial activity against some bacterial strains (Kaur and Arora, 2008). The seed essential oil of F. vulgare has also been reported to possess antibacterial activity against some human pathogenic bacteria. Ethanol and water extracts of F. vulgare have shown activity against Campylobacter jejuni and Helicobacter pylori (Mahady et al., 2005). In another study, the F. vulgare essential oil has been shown to exhibit potential for the control of multidrug resistant Acinetobacter baumannii infections. Some chemical constituents from F. vulgare have been identified as active antimicrobial principles such as a phenyl propanoid derivative – Dillapional was found to be the active antimicrobial principle of the F. vulgare stem. Another molecule – Scopoletin which is a coumarin derivative has been isolated from F. vulgare and reported to possess marginal antimicrobial effect (Kwon et al., 2002).

**Antifungal activity**

The fennel essential oil has been reported to exhibit antifungal effect. The fennel essential oil and its seed extracts have been reported to exhibit antimycobacterial and anticandidal activity (Abed, 2007). Various bark extracts of F. vulgare have also been reported to possess antifungal activity against Candida albicans (Pai et al., 2010). The essential oil of F. vulgare hasalso been reported to reduce the mycelial growth and germination of Sclerotinia sclerotiorum and as such could be used as bio fungicide alternative to synthetic fungicides against phytopathogenic fungi (Soylu et al., 2007). The essential oil of F. vulgare has been reported to show complete zone of inhibition against Aspergillum niger, Aspergillum flavus, Fusarium graminearum and Fusarium moniliforme at 6 ll dose (Singh et al., 2006).

**Antioxidant activity**

The antioxidant activity of wild, edible and medicinal fennels from different Mediterranean countries has been determined. Wild fennel has been found to exhibit a radical scavenging activity higher than that of both medicinal and edible fennels (Faudale et al., 2008). The methanolic extract of F. vulgare fruit has also been reported to exhibit antioxidant activity by decreasing the malondialdehyde level in F. vulgare fruit methanol extract group compared to the control group. The essential oil and acetone extracts of F. vulgare have been reported to exhibit strong antioxidant activity in comparison with butylated hydroxyanisole (BHA) and butylated hydroxytoluene (BHT) (Ruberto et al., 2000). The inhibitory action of oil and the acetone extracts in linoleic acid system was studied by monitoring peroxide accumulation in emulsion during incubation through ferric thiocyanate method. F. vulgare fruit extract and the purified compounds namely cis-miyabenol C 11a-O-b-D-glucopyranosyl-(1fi6)-b-D-glucopyranoside, cismiyabenol C, trans-miyabenol C, sinapyl glucoside and syringing 4-O-b-glucoside have been reported to exhibit antioxidant activity. The n-BuOH extract of the F. vulgare fruit showed a moderate activity in the lipid peroxidation assay but strong activity at the higher tested concentration. Pure compounds isolated from F. vulgare showed higher antioxidant activity than the crude extracts (Marino et al., 2007). The isolated phenolic compounds from the residue of flowering aerial parts of the bitter fennel resulting from its distillation for essential oils have been reported to possess strong antiradical scavenging activity which may contribute to the interpretation of the pharmacological effect of F. vulgare. The isolated compounds were characterized as 3-caffeoylquinic acid, 4-caffeoylquinic acid, 1,5-O-dicaffeoylquinic acid, ros marinic acid, eriodictyol-7-rutinoside, quercetin-3-O-galactoside, kaempferol-3-O-rutinoside and kaempferol-3-O-glucoside. (Parejo et al., 2004b). In another study water and ethanol extracts of F. vulgare seeds have been reported to display antioxidant activity. 100 lg of water and ethanol extracts exhibited 99.1% and 77.5% inhibition of peroxidation in linoleic acid system respectively and greater than the same dose of a-tocopherol (36.1%). Both extracts were reported to have effective reducing power, free radical scavenging, superoxide anion radical scavenging, hydrogen peroxide scavenging and metal chelating activities. Essential oils of the fruits of three

Organically grown cultivars of Egyptian fennel (F. vulgare var. azoricum, F. vulgare var. dulce and F. vulgare var. vulgare) were reported to possess antioxidant activity. Essential oils from the azoricum and dulce cultivars were more effective antioxidants than those from the vulgare cultivar (Shahat et al., 2011)

**Antithrombotic activity**

The essential oil of F. vulgare and its main component, anethole has been shown to have a safe antithrombotic activity that originates due to their broad-spectrum antiplatelet activity, clot destabilizing effect and vasorelaxant action. Anethole, the main component of fennel oil tested in guinea pig plasma was as potent as the fennel oil in inhibiting arachidonic acid, collagen-ADP and U46619 induced aggregation. Anethole also prevented thrombin induced clot reaction at concentrations similar to fennel oil. The fennel oil and anethole were tested in rat aorta with or without endothelium and displayed comparable NO-independent vasorelaxant activity at antiplatelet concentrations which have been proved to be free from cytotoxic effects in vitro. Furthermore, both F. vulgare essential oil and anethole (100 mg/kg oral administration) provided significant protection towards ethanol induced gastric lesions in rats (Tognolini et al., 2007).

**Anti-inflammatory activity**

Oral administration of methanol extract of *F. vulgare* fruit to rat and mice exhibited inhibitory effects against acute and sub-acute inflammatory diseases. The anti-inflammatory activity of methanol extract was evaluated by using three screening protocols, namely, carrageenan-induced paw edema, arachidonic acid-induced ear edema, and formaldehyde-induced arthritis. These are widely used for testing non-steroidal anti-inflammatory drugs. For acute inflammation, methanol extract (200mg/kg) exhibits significant inhibition of paw edema (69%) induced by carrageenan injection as compared to the control group of animals. Methanol extract of *F. vulgare* also inhibits ear-edema (70%) induced by arachidonic acid in mice. The level of serum transaminase, aspartate aminotransferase (AST), and alanine aminotransferase (ALT) significantly increases in the presence of methanolic extract of *F. vulgare* on inflammation induced by formaldehyde as compared to control group. The assessment of the level of AST and ALT provides a good and simple tool to measure the anti-inflammatory activity of the target compounds (Kataoka *et al*.,
2002). These overall results seem to suggest that *F. vulgare* FME may act on both the cyclooxygenase and lipoxygenase pathways (Choi and Hwang., 2004)

**Oestrogenic activity**

F. vulgare has been used as an oestrogenic agent for centuries. It has been reported to increase milk secretion, promote menstruation, facilitate birth, and alleviate the symptoms of the male climacteric and increase libido. The main constituent of fennel essential oil, anethole has been considered to be the active oestrogenic agent. Some other studies have suggested that the actual pharmacologically active agents are polymers of anethole, such as dianethole and photoanethole (Albert-puleo, 1980).

**Hepatoprotective activity**

The fennel essential oil has been reported to possess hepatoprotective activity. In a study, the hepatotoxicity produced by acute CCl4 administration was found to be inhibited by fennel essential oil with evidence of decreased levels of serum aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP) and bilirubin (Ozbek et al., 2003).

**Antidiabetic activity**

The essential oil of F. vulgare has been reported to show hypoglycaemic activity in Streptozotocin induced diabetic rats. Ingestion of essential oil of F. vulgare to diabetic rats corrected the hyperglycaemia from (162.5 +3.19 mg/dl) to (81.97+ 1.97 mg/dl) and the activity of serum glutathione peroxidise from (59.72+ 2.78 u/g Hb) to (99.60 +6.38 u/g Hb). This makes the possibility of its inclusion in antidiabetic drug industry (El-Soud et al., 2011).

**Other Activities of F. Vulgare**

**In vitro cytoprotection and antitumour activity**

The methanolic extract of F. vulgare has been reported to exhibit in vitro cytoprotective activity against normal human blood lymphocytes by micronucleus assay and anti-tumour activity against B16F10 melanoma cell line by trypan blue exclusion assay for cell viability. Lymphocyte culture treated with 70% methanolic extract of F. vulgare showed very less percentage of micronucleus i.e. 0.006% as compared to standard drug doxorubicin which showed 0.018% micronucleus. On the other hand 70% methanolic extract of F. vulgare showed good anti-tumour activity at the concentration of 200 lg/ml. This suggests that F. vulgare could be considered as a natural resource of antitumour agents as well as cytoprotective to normal cells (Pradhan et al., 2008).

**Acaricidal activity**

F. vulgare fruit oil has been reported to possess acaricidal activity against D. farinae and D. pteronyssinus using direct contact application and compared with that of the commercial repellent benzyl benzoate. The biologically active constituents of the F. vulgare fruit oil have been identified as P-anisaldehyde, (+)-fenchone, (-)-fenchone, thymol and estragol (Lee, 2004).

The methanol extract of F. vulgare fruit has been reported to exhibit mosquito repellent activity against Aedes aegypti females using skin and patch tests. The biologically active constituents of the Foeniculum fruits were characterised as (+)fenchone and (z)-9-octadecanoic acid (Kim et al., 2002).

**Antihirustism activity**

The ethanolic extract of F. vulgare has been reported to display antihirustism activity. In a double blind study patients were treated with creams containing 1%, 2% of fennel extract and placebo. The cream containing 2% fennel is better than the cream containing 1% fennel (Javidnia et al., 2003).

**Effect on uterine contraction**

The effects of fennel essential oil on the uterine contraction in rats have been reported. Administration of different doses of fennel essential oil reduced the intensity of oxytocin and PGE2 induced contractions significantly (25 and 50 lg/ml for oxytocin and10 and 20 lg/ml for PGE2 respectively). Fennelessential oil also reduced the frequency of contractions induced by PGE2 but not with oxytocin. The estimated LD50 obtained in female rats by moving average method was 1326 mg/kg. Furthermore, no obvious damage was observed in the vital organs of the dead animals (Ostad et al., 2001).

**Human liver Cytochrome P450 3A4 inhibitory activity**

Thirteen compounds isolated from the methanolic extract of fennel have been found to possess human liver cytochrome P450 3A4 inhibitory activity. Among these compounds 5-methoxypsoralen (5-MoP) showed the strongest inhibition with an IC50 value of 18.3µM and with a mixed type of inhibition. (Subehan et al.,2007).

**Environmental Application**

*Foeniculum vulgare*, that is, fennel, not only exhibited pharmacological activities but also revealed a few environmental activities. These activities play a key role in the management of nematode, insect, mosquitoes, and some harmful larvae of malaria producing vector. Thus, the extracts of *F. vulgare* and isolated biologically active compounds have been evaluated for their insecticidal, repellent, acaricidal, larvicidal, and nematicidal activity (Oka *et al*., 2000), (Kim *et al*., 2001), (Kim *et al*., 2002), (Lee *et al*., 2004) and (Sedaghat *et al*., 2011). A brief review on the different type of eco friendly environmental activities as reported on this plant is summarized below.

**Insecticidal Activities:**

The fruit derived phytoconstituents of *F. vulgare* exhibited prominent insecticidal activities against *Sitophilus oryzae*, *Callosobruchus chinensis*, and *Lasioderma serricorne*. This activity was examined using direct contact application and fumigation methods. The biologically active constituents, that is, phenylpropenes (E)- anethole and estragole, and the monoterpene (+)-fenchone were characterized from *Foeniculum* fruit. By using a filter paper diffusion test, estragole (0.168mg cm−2) caused 91% mortality to *S. oryzae* within 1 day after treatment whereas (+)-fenchone and (E)-anethole gave over 90% mortality at 2 and 4 day after treatment, respectively. After 2 days of treatment, all test compounds (0.021 mg cm−2 concentration) revealed potent insecticidal activity against *C. chinensis*. Whereas after 1 day of treatment, (E)- anethole (0.105 mg cm−2) gave 100%mortality of *L. serricorne* whereas 90 and 60% mortality at 4 day after treatment was achieved with estragole and (+)-fenchone, respectively. In a fumigation test, the compounds were much more effective against adults of *S. oryzae*, *C. chinensis*, and *L. serricorne* in closed cups than in open ones, indicating that the insecticidal activity of test compounds was largely attributable to fumigant action. As naturally occurring insect-control agents, the *F. vulgare* fruit-derived materials described could be useful for managing field populations of *S. oryzae*, *C. chinensis*, and *L. serricorne* (Kim *et al*., 2001).

**Acaricidal Activity:**

Fennel oil shows significant acaricidal activity against *Dermatophagoides farinae* and *Dermatophagoides pteronyssinus*. (+)-fenchone and p-anisaldehyde are major constituents of fruit oil of *F. vulgare*. *P*-anisaldehyde was the most toxic compound against *D. farinae* and is much more effective compared with benzyl benzoate, thymol, and estragol (Lee *et al*., 2004).

**Repellent Activity:**

The methanolic extract of fruits of *F. vulgare* was spectroscopically characterized for the presence of biologically active constituents called (+)-fenchone and (E)-9-octadecenoic acid. The repellent activity of these constituents was tested against hungry *Aedes aegypti* females with the help of skin and patch tests and compared with that of the commercial repellent agent called N,N-diethylm- toluamide (DEET) and (Z)-9-octadecenoic acid. In a skin test with female mosquitoes (+)-fenchone and (Z)-9-octadecenoic acid (0.4mg/cm2) exhibited moderate repellent activity at 30 min after treatment, whereas DEET provided >1 h of protection against adult mosquitoes at (0.2 mg/cm2). Thus, (+)-Fenchone and (E)-9-octadecenoic acid are potential mosquito repellent agents or lead compounds (Kim *et al*., 2002).

**Larvicidal Activity:**

Plant extracts and oils may act as alternatives to conventional pesticides for malaria vector control. By considering this aspect, (Sedaghat et al., 2011) investigated the larvicidal activity of essential oils of three plants of *Apiaceae* family against malaria vector called *Anopheles stephensi*. The larvicidal activity was evaluated against laboratory-reared larvae by standard method of WHO. The *F. vulgare* oil was the most effective against *A. stephensi* with LC(50) and LC(90) values of 20.10 and 44.51 ppm, respectively (Sedaghat *et al.*,2011). Additionally, the essential oil extracts from leaves, flowers, and roots of *F. vulgare* exhibit noticeable larvicidal activity against fourth-instar larvae of the mosquito *Culex pipiens molestus*. Terpineol and 1,8-cineole content of *F. vulgare* are the most effective phytoconstituent against *Culex pipiensmolestus* bites offering complete protection for 1.6 and 2 h, respectively (A. F. Traboulsi ., *et ai* 2005). Recently, (Zoubiri et al. 2010) reported the larvicidal activity of essential oil of fennel seed against *Culex pipiens* mosquito.Thus, *F. vulgare* can serve as a natural larvicidal agent.

**Nematicidal Activity:**

Oka et al. investigated the *in vitro* nematicidal activity of essential oils extracted from 27 spices and aromatic plants in pot experiments. Twelve of the twenty-seven essential oils immobilized more than 80% of juveniles of the root-knot nematode *Meloidogyne javanica* at a concentration of 1000 ⍰L/liter. At this concentration, most of these oils also inhibited nematode hatching. Essential oils of *Carum carvi*, *Foeniculum vulgare, Mentha rotundifolia*, and *Mentha spicata* showed the highest nematicidal activity among the *in vitro* tested oils. In 3-liter pot experiments, nematicidal activity of the essential oils and their components was confirmed at 200 and 150mg/kg, respectively.The results suggest that the essential oils and theirmain componentsmay serve as nematicides (Y. Oka., *et al* 2000).

**Safety**

The safety of medicinal and spice plants and of their preparations deserves increased scientific attention. One of the main conditions for use of herbal preparations in medicinal conditions is the absence of such risks as mutagenicity, carcinogenicity, and teratogenicity. In general, such products need to have minimal toxicity and side effects. Generally, the vast majority of herbal remedies are recognised as safe, and individual hypersensitivity is usually considered as the most common but controllable risk. However, for those individual compounds exhibiting toxic effects in laboratory animals, the question of possible negative effects in humans remains open. In the case of F. vulgare some compounds have come under scrutiny, most importantly, estragole.

Estragole (Methylchavicol) is one of the main components of the essential oil of F. vulgare. It has been reported that estragole is associated with the development of malignant tumours in rodents. This was the basis for the recommendations of the Scientific Committee on Food (SCF) of the European Union to restrict the use of this substance (Opinion of the Scientific Committee on Estragole, 2001) but the potential of estragole to induce carcinogenesis in human remains unclear. The ability of estragole to cause genotoxicity and, thus, to be carcinogenic was first described by Drinkwater (Drinkwater et al., 1976) and then followed by numerous in vivo and in vitro studies (Swanson et al., 1979), (Miller et al., 1983), (Paini et al., 2010). It was found that estragole possesses tissue-, species-, and sex-specific carcinogenic effects. According to recent evidence, estragole does not have a direct carcinogenic action.

The essential factor for estragole's carcinogenicity is its metabolic activation, leading to the formation of unstable molecules and active radicals that form adducts with nucleic acids and thus damage DNA (Phillips, 1994). Estragole metabolism is dose-dependent and elevated doses of estragole increase its biotransformation, leading to the formation of mutagenic metabolites (Punt et al., 2008). The biotransformation of the same substance can differ in animals and in humans, which raises the question of whether the mutagenic metabolites of estragole are formed in humans.

## III. CONCLUSION

In conclusion it can be ascertained that F. vulgare is a medicinal and aromatic plant with a diverse pharmacological spectrum and having considerable importance in particular to food industry. Its aroma active compounds such as anethole (and its polymers like dianethole and photoanethole) estragole, (+)-Fenchone and P-anisaldehyde have been recognized as the biologically active molecules possessing oestrogenic, acaricidal and antithrombotic activities. The phenolic molecules present in fennel have been shown to possess potent antioxidant activity in a number of experiments. These bioactive molecules in fennel can be developed as novel pharmacological lead molecules provided their bioavailability, pharmacokinetics, physiological pathways, and importance to human health are known with sufficient detail.

## REFERENCES


[1]. Abed, K.F., 2007. Antimicrobial activity of essential oils of some medicinal plants from Saudi Arabia. Saudi J. Biol. Sci. 14, 53–60.

[2]. Agarwal, R., Gupta, S.K., Agarwal, S.S., Srivastava, S., Saxena, R., 2008. Oculohypotensive effects of Foeniculum vulgare in experimental models of glaucoma. Indian J. Physiol. Pharmacol. 52, 77–83.

[3]. G. J. Kaur and D. S. Arora, "Antibacterial and phytochemical screening of Anethum graveolens, Foeniculum vulgare and Trachyspermum ammi," *BMC Complementary and Alternative Medicine*, vol. 9, article 30, 2009.

[4]. R. Manonmani and V. M. Abdul Khadir, "Antibacterial screening on *Foeniculum vulgare* Mill," *International Journal of Pharma and Bio Sciences*, vol. 2, no. 4, pp. 390–394, 2011.

[5]. I. E. Orhan, B. ¨ Ozc¸elik, M. Kartal, and Y. Kan, "Antimicrobial and antiviral effects of essential oils from selected Umbelliferae and Labiatae plants and individual essential oil components," *Turkish Journal of Biology*, vol. 36, no. 3, pp. 239–246, 2012.

[6]. P. Morales, A. M. Carvalho,M. C. S´anchez-Mata, M. C´amara, M. Molina, and I. C. F. R. Ferreira, "Tocopherol composition and antioxidant activity of Spanish wild vegetables," *Genetic Resources and Crop Evolution*, vol. 59, no. 5, pp. 851–863, 2012.

[7]. A. Dua, G. Garg, and R. Mahajan, "Polyphenols, flavonoids and antimicrobial properties of methanolic extract of fennel (*Foeniculum vulgare Miller*)," *European Journal of Experimental Biology*, vol. 3, no. 4, pp. 203–208, 2013.

[8]. T.Malini, G. Vanithakumari, N.Megala, S.Anusya, K. Devi, and V. Elango, "Effect of *Foeniculum vulgare*. Mill seed extract on the genital organs of male and female rats," *Indian Journal of Physiology and Pharmacology*, vol. 29, no. 1, pp. 21–26, 1985.

[9]. H. Ozbek, S. U˘gras¸, H. D¨ulger et al., "Hepatoprotective effect of *Foeniculum vulgare* essential oil," *Fitoterapia*, vol. 74, no. 3, pp. 317–319, 2003.

[10]. M. Oktay, I. G¨ulc¸in, and ¨ O. I. K¨ufrevioglu, "Determination of in vitro antioxidant activity of fennel (*Foeniculum vulgare*) seed extracts," *LWT-Food Science and Technology*, vol. 36, no. 2, pp. 263–271, 2003.

[11]. M. Pradhan, S. Sribhuwaneswari, D. Karthikeyan et al., "In-vitro cytoprotection activity of *Foeniculum vulgare* and *Helicteres isora* in cultured human blood lymphocytes and antitumour activity against B16F10 melanoma cell line," *Research Journal of Pharmacy and Technology*, vol. 1, no. 4, pp. 450–452, 2008.

[12]. N. A. El-Soud, N. El-Laithy, G. El-Saeed et al., "Antidiabetic activities of *Foeniculum vulgare* mill. Essential oil in streptozotocin-induced diabetic rats," *Macedonian Journal of Medical Sciences*, vol. 4, no. 2, pp. 139–146, 2011.

[13]. S. Koppula and H. Kumar, "*Foeniculum vulgare* Mill (Umbelliferae) attenuates stress and improves memory in wister rats," *Tropical Journal of Pharmaceutical Research*, vol. 12, no. 4, pp.553–558, 2013.

[14]. L. Barros, A. M. Carvalho, and I. C. F. R. Ferreira, "The nutritional composition of fennel (*Foeniculum vulgare*): shoots, leaves, stems and inflorescences," *LWT: Food Science and Technology*, vol. 43, no. 5, pp. 814–818, 2010.

[15]. C. Garg, S. A. Khan, S. H. Ansari, A. Suman, and M. Garg, "Chemical composition, therapeutic potential and perspectives of *Foeniculum vulgare*," *Pharmacognosy Reviews*, vol. 3, no. 6, pp. 346–352, 2009.

[16]. W. He and B. Huang, "A review of chemistry and bioactivities of a medicinal spice: *Foeniculum vulgare*," *Journal of Medicinal Plants Research*, vol. 5, no. 16, pp. 3595–3600, 2011.

[17]. M. A. Rather, B. A. Dar, S. N. Sofi, B. A. Bhat, and M. A. Qurishi, "*Foeniculum vulgare*: a comprehensive review of its traditional use, phytochemistry, pharmacology, and safety," *Arabian Journal of Chemistry*, 2012.

[18]. N. S. Jamwal, S. Kumar, and A. C. Rana, "Phytochemical and pharmacological review on Foeniculum Vulgare," vol. 4, pp. 327–341, 2013.

[19]. S. Grover, C. P. Malik, A. Hora, and H. B. Kushwaha, "Botany, cultivation, chemical constituents and genetic diversity in fennel (*Foeniculum vulgare*Mill): a review," *International Journal of Life Sciences*, vol. 2, no. 2, pp. 128–139.
[20]. R. Rahimi and M. R. S. Ardekani, "Medicinal properties of *Foeniculum vulgare* Mill. in traditional Iranian medicine and modern phytotherapy," *Chinese Journal of Integrative Medicine*,vol. 19, no. 1, pp. 73–79, 2013.
[21]. Albert-Puleo, M., 1980. Fennel and anise as estrogen agents. J. Ethnopharmacol. 2, 337-344.
[22]. Cantore, P.L., Iacobelli, N.S., Marco, A.D., Capasso, F., Senatore, F., 2004. Antibacterial activity of Coriandrum sativum L. and Foeniculumvulgare Miller Var. vulgare (Miller). Essential oils. J. Agric. Food Chem. 52, 7862–7866.
[23]. Choi, E.M., Hwang, J.K., 2004. Anti-inflammatory, analgesic and antioxidant activities of the fruit of Foeniculum vulgare. Fitoterapia 75 (2004), 557–565.
[24]. Dadalioglu, I., Evrendilek, G.A., 2004. Chemical compositions and antibacterial effects of essential oils of Turkish oregano (Origanum minutiflorum), bay laurel (Laurus nobilis), Spanish lavender (Lavandula stoechas L.), and fennel (Foeniculum vulgare) on common foodborne pathogens. J. Agric. Food Chem. 52, 8255–8260.
[25]. Diaaz-Maroto, M.C., Hidalgo, I.J.D., Saa nchez-Palomo, E., Pea¨ rez-Coello, M.S., 2005. 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. 53, 5385–5389.
[26]. Diaaz-Maroto, M.C., Pea rez-Coello, M.S., Esteban, J., Sanz, J., 2006. Comparison of the volatile composition of wild fennel samples (Foeniculum vulgare Mill.) from Central Spain. J. Agric. Food Chem. 54, 6814–6818.
[27]. Drinkwater, N.R., Miller, E.C., Miller, J.A., Pitot, H.C., 1976. Hepatocarcinogenicity of estragole (1-allyl-4-methoxybenzene) and 1-hydroxyestragole in the mouse and mutagenicity of 1-acetoxyestragole in bacteria. J. National Cancer Inst. 57, 1323–1331.
[28]. El-Soud, N.A., El-Laithy, N., El-Saeed, G., Wahby, M.S., Khalil, M., Morsy, F., Shaffie, N., 2011. Antidiabetic activities of Foeniculum vulgare Mill. Essential oil in Streptozotocin induced diabetic rats. Macedonian J. Med. Sci. 173, 1857–5773.
[29]. Faudale, M., Viladomat, F., Bastida, J., Poli, F., Codina, C., 2008. Antioxidant activity and phenolic composition of wild, edible, and medicinal fennel from different mediterranean countries. J. Agric. Food Chem. 56, 1912–1920.
[30]. Grieve, M., 1931. A Modern Herbal: the Medicinal, Culinary, Cosmetic and Economic Properties, Cultivation and Folk-lore of Herbs, Grasses, Fungi, Shrubs & Trees with their Modern Scientific Uses. Brace & Company, Harcourt.
[31]. Gross, M., Lewinsohn, E., Tadmor, Y., Bar, E., Dudai, N., Cohen, y., Friedma, J., 2009. The inheritance of volatile phenylpropenes in bitter fennel (Foeniculum vulgare Mill. var. vulgare Apiaceae) chemotypes and their distribution within the plant. Biochem. Syst. Ecol. 37, 308–316.
[32]. Javidnia, K., Dastgheib, L., Samani, S.M., Nasiri, A., 2003. Antihirsutism activity of Fennel (fruits of Foeniculum vulgare) extract: a double-blind placebo controlled study. Phytomedicine 10, 455–458.
[33]. Kaur, G.J., Arora, D.S., 2008. In-vitro antibacterial activity of three plants belonging to the family Umbelliferae. Int. J. Antimicrob. Agents 31, 393–395.
[34]. Kim, D.H., Kim, S.I., Chang, K.S., Ahn, Y.J., 2002. Repellent activity of constituents identified in Foeniculum vulgare fruit against Aedes aegypti (Diptera: Culicidae). J. Agric. Food Chem. 50, 6993–6996.
[35]. Kwon, Y.S., Choi, W.G., Kim, W.J., Kim, W.K., Kim, M.J., Kang, W.H., Kim, C.M., 2002. Antimicrobial constituents of Foeniculum vulgare. Arch. Pharmacal Res. 25, 154-157.
[36]. Lee, S.H., 2004. Acaricidal activity of constituents identified in Foeniculum vulgare fruit oil against Dermatophagoides spp. (Acari: Pyroglyphidae). J. Agric. Food Chem. 52, 2887–2889.
[37]. Mahady, G.B., Pendland, S.L., Stoia, A., Hamill, F.A., Fabricant, D., Dietz, B.M., Chadwick, L.R., 2005. In-vitro susceptibility of Helicobacter pylori to botanical extracts used traditionally for the treatment of gastro-intestinal disorders. Phytother. Res. 19, 988–999.
[38]. Marino, S.D., Gala, F., Borbone, N., Zollo, F., Vitalini, S., Visioli, F., Iorizzi, M., 2007. Phenolic glycosides from Foeniculum vulgare fruit and evaluation of antioxidative activity. Phytochemistry 68, 1805–1812.
[39]. Miller, J.A., Miller, E.C., 1983. The metabolic activation and nucleic acid adducts of naturally-occurring carcinogens: recent results with ethyl carbamate and the spice flavors safrole and estragole. Brazilian J. Cancer 48, 1–15.

[40]. Miller, E.C., Swanson, A.B., Phillips, D.H., Fletcher, T.L., Liem, A., Miller, J.A., 1983. Structure–activity studies of the carcinogenicities in the mouse and rat of some naturally occurring and synthetic alkenyl-benzene derivatives related to safrole and estragole. Cancer Res. 43, 1124–1134.
[41]. Mohsenzadeh, M., 2007. Evaluation of antibacterial activity of selected Iranian essential oils against Staphylococcus aureus and Escherichia coli in nutrient broth medium. Pak. J. Biol. Sci. 10, 3693–3697.
[42]. Opinion of the Scientific Committee on Food on Estragole (1-Allyl-4-methoxybenzene) (2001), SCF/CS/FLAV/FLAVOUR/6 ADD2 FI-NAL, Brussels, Belgium.
[43]. Ostad, S.N., Soodi, M., Shariffzadeh, M., Khorshidi, N., Marzban, H., 2001. The effect of fennel essential oil on uterine contraction as a model for dysmenorrhea, pharmacology and toxicology study. J. Ethnopharmacol 76, 299–304.
[44]. Ozbek, H., Ugras, S., Dulger, H., Bayram, I., Tuncer, I., Ozturk, G., Ozturk, A., 2003. Hepatoprotective effect of Foeniculum vulgare essential oil. Fitoterapia 74, 317–319.
[45]. Pai, M.B., Prashant, G.M., Murlikrishna, K.S., Shivakumar, K.M., Chandu, G.N., 2010. Antifungal efficacy of Punica granatum, Acacia nilotica, Cuminum cyminum and Foeniculum vulgare on Candida albicans: an in vitro study. Indian J. Dental Res. 21 (3), 334–336.
[46]. Paini, A., Punt, A., Viton, F., Scholz, G., Delatour, T., Marin- Kuan, M., Schilter, B., van Bladeren, P.J., Rietjens, I.M., 2010. A physiologically based biodynamic (PBBD) model for estragole DNA binding in rat liver based on in vitro kinetic data and estragole DNA adduct formation in primary hepatocytes. Toxicol. Appl. Pharmacol. 245, 57–66.
[47]. Parejo, I., Viladomat, F., Bastida, J., Schmeda-Hirschmann, G., Burillo, J., Codina, C., 2004a. Bioguided isolation and identification of the nonvolatile antioxidant compounds from Fennel (Foeniculum vulgare Mill.) waste. J. Agric. Food Chem. 52, 1890–1897.
[48]. Parejo, I., Jauregui, O., Saa¨ nchez-Rabaneda, F., Viladomat, F., Bastida, J., Codina, C., 2004b. Separation and characterization of phenolic compounds in fennel (Foeniculum vulgare) using liquid chromatography–negative electrospray ionization tandem mass spectrometry. J. Agric. Food Chem. 52, 3679–3687.
[49]. S. Zoubiri, A. Baaliouamer, N. Seba, and N. Chamouni, "Chemical composition and larvicidal activity of Algerian *Foeniculum vulgare* seed essential oil," *Arabian Journal of Chemistry*, 2010.
[50]. Y. Oka, S. Nacar, E. Putievsky, U. Ravid, Z. Yaniv, and Y. Spiegel, "Nematicidal activity of essential oils and their components against the root-knot nematode," *Phytopathology*, vol. 90, no. 7, pp. 710–715, 2000.
[51]. D. H. Kim and Y. J. Ahn, "Contact and fumigant activities of constituents of *Foeniculum vulgare* fruit against three coleopteran stored-product insects," *Pest Management Science*, vol. 57, no. 3, pp. 301–306, 2001.
[52]. D. Kim, S. Kim, K. Chang, and Y. Ahn, "Repellent activity of constituents identified in *Foeniculum vulgare* fruit against *Aedes aegypti* (diptera: Culicidae)," *Journal of Agricultural and Food Chemistry*, vol. 50, no. 24, pp. 6993–6996, 2002.
[53]. H. Lee, "Acaricidal activity of constituents identified in *Foeniculum vulgare* fruit oil against dermatophagoides spp. (Acari: Pyroglyphidae)," *Journal of Agricultural and Food Chemistry*, vol. 52, no. 10, pp. 2887–2889, 2004.
[54]. M. M. Sedaghat, A. Sanei Dehkordi, M. R. Abai et al., "Larvicidal activity of essential oils of apiaceae plants against malaria vector, *Anopheles stephensi*," *Journal ofArthropod-Borne Diseases*, vol. 5, no. 2, pp. 51–59, 2011.
[55]. A. F. Traboulsi, S. El-Haj, M. Tueni, K. Taoubi, N. A. Nader, and A. Mrad, "Repellency and toxicity of aromatic plant extracts against the mosquito *Culex pipiens* molestus (Diptera:Culicidae)," *Pest Management Science*, vol. 61, no. 6, pp. 597–604, 2005.
[56]. E. Choi and J.Hwang, "Antiinflammatory, analgesic and antioxidant activities of the fruit of *Foeniculum vulgare*," *Fitoterapia*, vol. 75, no. 6, pp. 557–565, 2004.
[57]. H. Kataoka, S. Horiyama, M. Yamaki et al., "Anti-inflammatory and anti-allergic activities of hydroxylamine and related compounds," *Biological&Pharmaceutical Bulletin*, vol. 25,no. 11,pp. 1436–1441, 2002.

Z.M. Anka, etal. "Phytochemistry and Pharmacological Activities of Foeniculum Vulgare." *IOSR Journal of Pharmacy (IOSRPHR),* 10(1), 2020, pp. 01-10.