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Medicinal Potential of Fennel Seed: A Review

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Abstract: Fennel is a popular fragrant and medicinal plant. Flavonoids, glycosides, and other phytoconstituents found in fennel are utilized as remedies for many illnesses. Fennel contains phenolic chemicals that are beneficial to human health. Bioactive substances like trans-anethole, estragole, fenchone and bioactive compounds kaempferol, quercetin, rosmarinic acid have been isolated from this plant and several associate with prospective human body mechanisms. The aim of the review was to discuss pharmacological activities including antibacterial, antidiabetic, anticancer, antioxidant, and other activities. Also, this review focus on the nutritional value, botanical studies, phytochemicals and some major pharmacological actions of fennel to reveal the medicinal potential and future investigation aspects which may be utilized in the creation of many drugs

Keywords: Fennel extract, Identification test, Pharmacological activities, Medicinal plant, Flavonoids, Glycosides, Phytochemical, Anethole, Estragole, Fenchone

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Introduction

Foeniculum vulgare (Fennel) is a perennial herb. Marathon is the Greek word for fennel. It has an upright, glucose-green stem that can reach a height of up to 2.5 metres (8 feet) and is hollow. The leaves are finely divided, with the final segments being filiform (threadlike) and measuring 0.5 mm in length. The leaves can grow

up to 40 centimetres (16 inches) in length. Its leaves are narrower than dill's but generally similar. Flowering occurs in terminal compound umbels that range in size from 5 to 17.5 cm (2 to 7 inches) wide, with each umbel section having 20 to 50 small yellow flowers on short pedicels. Dry schizocarps that are 4-10 mm long, half that width,

or less, and grooved make up the fruit. Since the fruit's seed is affixed to the pericarp, the entire fruit is frequently referred to as a seed by accident. Despite being grown in many regions of the world on dry soils near rivers or coasts, fennel is still thought of as a native plant of the Mediterranean region. The best growing conditions for fennel are in well-drained, calcareous soils with enough of sunshine. India, Egypt, Turkey, Syria, and Iran are significant fennel producers. India is known to have produced roughly 150,000 tonnes of fennel in 2018 (NHB, 2019), despite the fact that real production data for several other nations are not yet available (Rahman *et al.*, 2020)

Fennel, commonly known as Saunf (*Foeniculum vulgare*) belongs to the Apiaceae family. It is a small group of annual, biennial, or perennial herb. It is widely cultivated in the temperate and subtropical regions of the world. France, Germany, Russia, Italy, India, and the US are the major fennel growing countries. In India it is mainly cultivated in Gujarat, Rajasthan and Uttar Pradesh. It is a highly aromatic perennial herb, erect, and it grows up to a height of 2 m. The flowers are produced in terminal compound umbels, 5–15 cm wide, and each umbel section with 20–50 tiny yellow flowers on short pedicels. The fruit is a dry seed 4–9 cm long and grooved. Fennel is known by the use of its fruits and its essential oil used as a spice for adding flavours to meats, breads, biscuits, candies, and liquors or in the manufacturing of perfumes, dentifrices, soaps, and phytotherapies.

Due to its commercial significance and significant pharmaceutical industry applications, fennel (*Foeniculum vulgare* Mill), one of the world's most significant medicinal herbs, is among the oldest known spice plants.

Fennel is also used in culinary preparations, confectionery applications, and food, beverage and cosmetic industries. It also found a wide range of applications in areas such as the pharmaceutical industry and phototherapy due to its potential

medicinal properties. In medieval times, fennel was used in conjunction with St. John's work to keep away witchcraft and other evils. This might have been originated because fennel was believed to be an effective insect repellent.

It contains C10 and C15 compounds which are called terpenes and is considered as a spice due to the presence of terpenic compounds in its volatile oil. Anethole, estragol, fenchone, d-limonene and α -pinene are the major compounds reported to be present in the fennel oil. It is reported that the percentage of these compounds present in the fennel oil may vary considerably due to the phenological state and geographical origin of the fennel, harvesting season, methods of extraction techniques employed, environmental, genetic and agricultural practices.

Volatile oil recovery from plant materials is generally carried out by solvent extraction, hydro-distillation or steam distillation. Enzyme assisted extraction is the recent approach for extracting bio-ingredients from the plant materials. The applications of enzymes in the extraction of essential oils from oilseeds like sunflower, soybean, rapeseed, corn, coconut, olives, avocado, rice bran oil, etc. are well documented in the literature. Enzymes are used for the pre-treatment of the plant materials, prior to the conventional method of extraction, to get better yield and quality of bio ingredients. Recent studies, employing enzymatic pre-treatment for the extraction of flavor components from various plant materials, have shown an enhancement in aroma recovery. Enzymes such as cellulases, hemicellulases, pectinases, and a combination of these have been used for the pre-treatment of plant materials, resulting in a higher yield of volatile oil and resin. There are reports of increase in the extraction yield of essential oils of garlic, celery, cumin, clove and cardamom due to the application of enzyme assisted extraction method (Rodríguez-Solana *et al.*, 2014).

Industrially, it is very important to improve the quality and yield of spice volatiles especially in

the case of fennel which is expensive and in huge demand. It is imperative to develop an alternative method, which may enhance the extraction yield, because steam distillation alone is inadequate to extract the spice volatiles completely. Hence, prior to steam distillation, enzyme pre-treatment of fennel seeds was employed as an alternative method for the enhanced extraction of volatile oil (Biljana *et al.*, 2005).

The effect of enzyme pretreatment on the important flavor compounds of the oil was also investigated. Scanning electron microscopic (SEM) studies were conducted to scientifically explain the effect of enzymes on the integrity of the cell wall of fennel seeds. A comparison between the physico-chemical properties as well as the variations in major components of the volatile oils obtained by the enzyme pretreatment of fennel seeds with those of the control was also taken into account.

Foeniculum vulgare Mill. is native from the Mediterranean area. Its essential oil or oleoresin is valuable for its pharmacological properties like balsamic, cardiotonic, digestive, lactagogue, and for their antimicrobial, and antioxidant properties. In literature there are different proportions of major fennel essential oils compounds of the same variety, *vulgare* showed that estragole, and trans-anethole were the most abundant volatile compounds in the essential oils from Iberian Peninsula (Spain) fennel seeds, where trans-anethole was the major constituent of the extracts. In other research, about Portuguese fennel seeds, Miguel *et al.* (2010) reported that estragole was the most abundant compound in their essential oils. They studied the chemical variation among indigenous populations of *Foeniculum vulgare* var. *vulgare* and concluded that high proportions of estragole respect trans-anethole were associated with high yearly rainfall. Other authors argue that the ratio of estragole, trans-anethole, and fenchone varies depending on the phenological state and origin of the seeds. The exact amount of estragole in different plants, mainly in fennel

seeds, has been of great importance in recent years due to this volatile compound was declared to be a carcinogen substance being recommended a limit of 0.05 mg/kg in food to avoid a high value of human daily intake of this compound.

Foeniculum is a genus of fewer than half a dozen species, and is best known as saunf in Hindi, treated by some botanists as the sole species of the genus. It is a well known aromatic and medicinal herb, which is native to southern Europe and the Mediterranean region, where it has been used for centuries as a condiment and culinary spice as well as for medicinal purposes. As an important economic crop, fennel has been used and traded internationally for centuries due to its therapeutic and culinary utilisation. In Greece, it was a symbol of success. In Rome, the young fennel shoots were used as food. Though details about its introduction are obscure, it has occurred in California for the past 120 years and is presumed to have escaped from cultivation repeatedly (Grover *et al.*, 2013)

Varieties:

F. vulgare has been intensively cultivated in China and can be divided into different subspecies or varieties on the basis of chemicals presents and its utilisation. The two most important subspecies of *F. vulgare* were *Vulgare* and *Piperitum*, where *Piperitum* have with bitter seeds and is characterised by the presence of rotundifolone, while *vulgare* with sweet seeds, varied with estragole, trans-anethole, limonene and fenchone, by which different chemotypes can be divided. *Vulgare* variety is widely used for flavourings in baked goods, meat and fish dishes, ice cream, and alcoholic beverages, due to its characteristic anise odour. Contrarily, according to some others botanists, *F. vulgare* constitutes two varieties. One is sweet fennel (*F. vulgare* var. *dulce*), which is annuals or biennials with small sweet-tasting fruits and the other one is bitter fennel (*F. vulgare* var. *vulgare*), which is a perennial with fruits having a bitter taste. Different populations of *F. vulgare* contain 10- nonacosanone as a specific

chemical marker and transanethole is the major volatile constituent. This review focuses on the bioactive components of the fennel and their pharmacology, and also provides a platform for further study and utilisation of fennel.

Fennel, is utilised for a variety of traditional therapeutic uses. According to reports, *Foeniculum vulgare* has a moisture content of 6.3%, 9.5% protein, 10% fat, 13.4% minerals, 18.5% fibre, and 42.3% carbs. *Foeniculum vulgare* contains calcium, potassium, sodium, iron, phosphorus, thiamine, riboflavin, niacin, and vitamin C amongst other minerals and vitamins. Information on antimicrobial, antiviral, anti-inflammatory, anti-mutagenic, antinociceptive, antipyretic, antithrombotic, antitumor, hepatoprotective, hypoglycemic, hypolipidemic, and memory-enhancing pharmacological properties *in vitro* and *in vivo* indicates their effectiveness.

The fennel fruit also exhibits diuretic and analgesic properties in addition to antioxidant properties. The distinctive aroma and flavour are provided by the essential oils, which are primarily concentrated in the mericarps. According to Siah *et al.* (2009), phytoestrogen is an active biological compound that functions in a manner similar to oestrogen. Additionally, it boosts libido and milk production while alleviating menopausal symptoms in women. In fact, due to the plant's sedative, estrogenic, analgesic, and anti-inflammatory effects, infusions and essential oils made from its fruits and aerial parts are both part of the herbalist's arsenal.

In addition to its antimicrobial activity due to its potential essential oil constituents and several pharmacological benefits through its bioactive constituents, which are very significant for human health, preliminary phytochemical screening confirmed the presence of flavonoids, tannins, saponins, steroids, glycosides, and terpenoids in fennel.

Many previous studies had extensively reported the pleiotropic activities of fennel using different solvents, and all of them recommended

methanol, ethanol, or hydro-alcoholic extracts so, the current study aimed to assess the ability of ethyl extract (dissolved in 60% ethyl alcohol) of fennel seeds to inhibit the growth of a wide range of indicator microorganisms including Gram-positive bacteria, Gram-negative bacteria, yeasts, and filamentous fungi. Antioxidant, anticancer, and antiviral activities would also be included in this review. As a preliminary method for characterizing an object, GC-MS would anticipate its chemical contents.

Volatile compounds of fennel seeds extracted by simultaneous distillation-extraction (SDE)³ and supercritical fluid extraction (SFE) showed similar compositions, with transanethole, estragole, and fenchone as the main components. All available methods in the analytical scale can be applied to the extraction of flavors of plant origin. However, isolation techniques by either steam distillation or solvent extraction have some shortcomings, namely losses of the movable compounds, low extraction efficiency, long extraction time, degradation of compounds and toxic solvent residue. To overcome these problems several approaches have been used to extract volatile flavor compounds of plant origin. Alternative to conventional techniques, supercritical fluid extraction, subcritical water extraction at temperatures between 100 °C and 374 °C and a pressure high enough to maintain the liquid state, and head space solid-phase microextraction (HS-SPME) are also reported. The purpose of the present study is to develop a simple, rapid, sensitive and reproducible procedure for the quantitative determination of flavor compounds in the fennel and fennel-like samples. The method in the present paper for the extraction and determination of flavor compounds in fennel and fennel-like samples is based on the headspace solid phase trapping solvent extraction (HS-SPTE) and gas chromatography-mass spectrometry (GC/MS) ' Additionally principal component analysis (PCA) has been used for characterizing or classifying eight different fennel-like samples according to origin or other features. This

approach could be employed in pattern recognition problems and chemo-typing to distinguish fennel seed, anise seed, star anise and dill seed, because these samples have similar patterns of flavor compositions (Sadrefozalayi and Farah, 2014)

Chemical constituents:

In the study, various phytoconstituents of methanolic extract of *Foeniculum vulgare* were identified using gas-chromatography mass spectrometry (GC-MS) method. GC-MS method was also applied for the analysis of biomarker fenchone in extract and eight different commercial formulations. The mass of prepared extract and formulations A-D and H (commercial herbal mixtures and commercial extract) used for the analysis of fenchone was 10 g. However, the mass of formulations E-G (soft gelatin capsules) was 100 mg. 57 different phytoconstituents were identified in the methanolic extract of *F. vulgare* using GC-MS technique. The main compounds identified were trans-anethole (31.49%), 2-pentanone (25.01%), fenchone (11.68%) and benzaldehyde-4-methoxy (8.01%). Several other compounds were also identified in higher amounts and some compounds were identified in trace amounts. Many compounds have been reported for the first time in the methanolic extract of *F. vulgare*. The amount of fenchone was found to be maximum in plant extract (9.789 mg/g) in comparison with other commercial formulations by the proposed GC-MS technique. In three different commercial formulations (F, G and H), the amount of fenchone was obtained as more than 1.0 mg/g. However, in five different commercial formulations (A, B, C, D and E), the amount of fenchone was recorded as less than 0.1 mg/g. This method could be utilized for the analysis of fenchone contents in the commercial formulations containing fenchone as an active ingredient. The results obtained in this work could be useful in standardization of commercial formulations containing fenchone (Kumaranthara and Thottiam, 2016; Prawez *et al.*, 2019)

The chemical constituents from the fennel include essential oil, fatty acid, phenylpropanoids, monoterpenoids, sesquiterpenes and coumarins. It also contains triterpenoids, tannins, flavonoids, cardiac glycosides, saponins and other types of compounds. In western countries, essential oil of fennel fruits was used for flavouring purpose, cosmetic and pharmaceutical products. The prominent component of oil was trans-anethole (70.1%) and the most intense odour compounds of fennel fruits were trans-anisole, estragole, fenchone and 1-octen-3-ol. Radulovic and Blagojevic (2010) carried out (GC and GC/MS) analysis of *F. vulgare* Mill. (Fennel) root and schizocarp essential oils and diethyl ether extracts and identified 89 different components (Kumaranthara and Thottiam, 2016).

Flavonoids such as eriodictyol-7-Rutinoside, Quercetin-3-Rutinoside, and Rosmarinic Acid have been isolated from the fennel plant. Flavonoids in fennel such as isorhamnetin 3-O-rhamnoside, quercetin, and kaempferol were isolated from ethyl acetate extract, while quercetin 3-O-Rutinoside, kaempferol 3-O-Rutinoside, and quercetin 3-O-glucoside were isolated from methanol extract. Oral administration of 200 mg/kg methanol extract from fennel fruit to mice showed an inhibitory effect on acute and subacute inflammation. The overall result of this study is that fennel plants have an anti-inflammatory effect through the cyclooxygenase and lipoxygenase pathways. Traditionally in South Africa, the use of infusion or fennel leaf decoction can treat arthritis.

The chemical constituents from the fennel include essential oil, fatty acid, phenylpropanoids, monoterpenoids, sesquiterpenes, coumarins. It also contains triterpenoids, tannins, flavonoids, cardiac glycosides, saponins, and other types of compounds (Prawez *et al.*, 2019).

Fatty acids:

The fruits of fennel contain about 20% fatty acids and petroselinic acid is a characteristic fatty acid of fennel oil. The level of petroselinic acid could be

as high as 70 to 80%. The sweet fennel and bitter fennel showed no obvious differences in oil content and fatty acid composition. The chemical analysis of the acetone extract of fennel showed that linoleic acid (54.9%), palmitic acid (5.4%) and oleic acid (5.4%) were major components in acetone extract.

Phenolic compounds:

There has been a growing interest in phenolic components of fruits and vegetables, which may promote human health or lowering the risk of disease. Aqueous extract of fennel fruits contains rich phenolic compounds. Many of them have antioxidant activities, such as 3-caffeoylquinic acid, 4-caffeoylquinic acid, 1,5-O-dicaffeoylquinic acid, rosmarinic acid, eriodictyol-7-O-rutinoside, quercetin-3-O-galactoside, kaempferol-3-O-rutinoside and kaempferol-3-O-glucoside. Besides, these compounds, fennel was reported containing hydroxycinnamic acid derivatives, flavonoid glycosides and flavonoid aglycones.

Flavonoids:

Flavonoids were generally considered as an important category of antioxidants in the human diet. Flavonoids were rich in the plants of Apiaceae family. It was reported that the presence of flavonol glycosides in fennel species was related to their morphological heterogeneity and variation, and some flavonoids such as quercetin arabinoside were identified from *F. vulgare*.

Essential oil:

In western countries, essential oil of fennel fruits (referred as fennel oil) was used for flavouring purpose, cosmetic and pharmaceutical products. The volatile compounds of fennel fruits were well studied by hydrodistillation, extraction with classical solvents, supercritical fluid extraction (SFE), headspace solvent microextraction and solid-phase microextraction (SPME). The relative content of essential oil in fennel fruits was about 3% by weight. The prominent component of oil was trans-anethole (70.1%) and the most intense

odor compounds of fennel fruits were trans-anisole, estragole, fenchone and 1-octen-3-ol. 78 compounds from fennel fruits were identified by GC-FID-MS, representing more than 98% of the oils. They can be divided into monoterpene hydrocarbons, oxygenated monoterpenes and phenylpropanoids. The main compound estragole was ranging from 34 to 89%. The essential oil of bitter fennel fruits was characterized by relatively high concentrations of α -pentene and fenchone, and low concentrations of trans-anethole and estragole, unlike sweet fennel oils.

The main phytochemical components responsible for the therapeutic effects of fennel were phenolic and volatile compounds.

This review is based on contents from different sources like Text books, Review articles, Reference books, Journals, Internet, etc. Following are the studies which describe the details regarding fennel:

- Rahman *et al.* (2020): They worked on their marketed analysis of fennel seeds.
- Prawez *et al.* (2019): They evaluated chemical constituents of fennel seed extract.
- Al-Snafi (2018): Reviewed the chemical constituents and pharmacological effects of *Foeniculum vulgare*.
- Jamwal *et al.* (2013): They evaluated the procedures, and analysis of their phytochemicals and their pharmacological effects.
- Weiping and Baokang (2011): They reviewed the use of natural products obtained from plant source and to evaluate their chemistry and bioactive components.
- Kumaranthara and Thottiam (2016): They evaluated effect of enzyme pre-treatment on extraction yield and quality of fennel (*Foeniculum vulgare*) volatile oil, Biocatalysis and Agricultural Biotechnology.
- Muckensturm *et al.* (1997): They have studied

phytochemical and chemotaxonomic of *Foeniculum vulgare*.

- Reyes-Jurado *et al.* (2015): They have studied essential oils: antimicrobial activities, extraction methods, and their modeling.
- Jamwal *et al.* (2013): Reviewed phytochemical and pharmacological aspects of *Foeniculum vulgare*.
- Sana *et al.* (2023): Reported pharmacological, nutraceutical, functional and therapeutic properties of fennel (*Foeniculum vulgare*).

Plant Profile:

Fennel:

Synonyms: Fennel fruits, fructus *Foeniculum*

Biological Source: Fennel consist of dried ripe of the plant known as *Foeniculum vulgare* miller

Family: Apiaceae



Fig. 1: Fennel seeds

Geographical source: It is indigenous to Mediterranean countries and largely cultivated in Romania, Russia, France, India and Japan.

Chemical composition: Fennel contains volatile oil (1-4%), fixed oil (9-12%) and proteins (20%). The chief constituents of volatile oil are a phenolic ether anethole (50-60%) and ketone fenchone (18-20%). Anethole has an aromatic odour and sweet taste whereas fenchone has a camphoraceous odour and taste.

Uses: Fennel is used for various digestive problems including heartburn, intestinal gas, bloating, loss of appetite, and colic in infants. It is also used for upper respiratory tract infections, coughs, bronchitis, cholera, backache, bedwetting, and visual problems.

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. *Foeniculum vulgare* was widely used in traditional Arabian medicine as diuretic, appetizer, and digestive. 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 an 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.

Other uses of fennel are as follow:

- Irritable bowel
- Increase urine flow
- Breast enlargement
- Promotes menstruation
- Improves digestive system
- Improves milk flow
- Anxiety
- Arthritis
- Water retention
- Appetite suppressant
- Amenhorrea
- Angina
- Asthma
- Heartburn
- Lower blood pressure
- Boost libido
- Respiratory congestion
- Coughs

Chemical structure of chemical constituent:

1. Anethol:

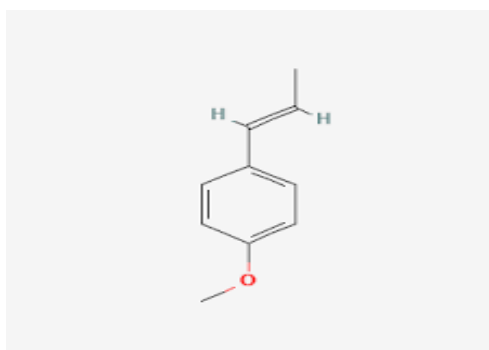


Fig. 2: Anethol structure.

Chemical name: trans-1-methoxy-4-(prop-1-enyl)benzene.

Description of fennel:

Organoleptic characteristic of Fennel:

Colour	Green to yellowish-brown
Odour	Sweet aromatic
Taste	Strongly aromatic
Size	5-10 x 2-4mm
Shape	Straight or slightly curved
Condition	Dried Cremo carp
Surface	Glabrous

Microscopic characteristic of Fennel:

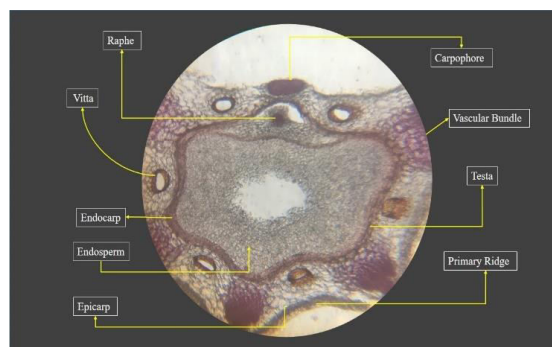


Fig. 3: T.S. fennel

1.	Pericarp:	
	[a] Epicarp	A layer of quadrangular to polygonal cells, with smooth cuticle
	[b] Mesocarp	Reticular, lignified parenchyma surrounding the vascular bundles
	[c] Vascular bundles	Five in number, bicollateral present below ridge (primary ridge)
	[d] Vittae	Schizogenous oil cells, 4 on dorsal side, 2 on commissural surface/ventral surface. About 250 micron in maximum width, the walls are brown.
	[e] Endocarp	Consist of narrow elongated cells having a parquetry arrangement
2.	Seed:	
	[a] Testa	Single layered yellowish brown in colour
	[b] Endosperm	Thick walled, polygonal, cellulosic parenchyma containing oil globules, aleurone, grains and rosette crystal of calcium oxalate
	[c] Raphe	A single ridge of vascular strands appears in the middle of commissural surface
	[d] Carpophore	With very thick walled sclerenchyma in 2 strands

Taxonomic classification:

Kingdom: Plantae, Phylum: Spermatophyta, Subphylum: Angiospermae, Class: Magnoliopsida, Order: Apiales, Family: Apiaceae, Genus: *Foeniculum*, Species: *Foeniculum vulgare*.

Common Names:

- ✓ Arabic: shmar, shumar, bisbas, razianj, haba helwa;
- ✓ Brazil: Endro, erva-doce, funcho;
- ✓ Chinese: hui xiang; Cuba: hinojo común
- ✓ English fennel, common fennel, Florence fennel, Roman fennel, sweet fennel, anise, sweet anise, aniseed, aniseed weed;
- ✓ French: aneth doux, fenouil, fenouil commun, fenuil doux;
- ✓ Germany: Echter Fenchel, Garten- Fenchel, Gemüfefenchel, Gewürzfenchel, wilder Fenchel;
- ✓ Hindi: Badi saunf, Bari saunf, Moti saunf, Saunf, Saumph;
- ✓ Indonesia: adas, adas londo, hades;
- ✓ Iran: Razianeh,
- ✓ Italy: finocchio; Japan: ui-kyo;
- ✓ Laos: phak s'i;
- ✓ Malaysia: adas pedas;
- ✓ Netherlands: venkel Philippines: anis, haras;
- ✓ Portuguese: funcho
- ✓ South Africa: vinkel;
- ✓ Spanish: fonol, hinojo;
- ✓ Sweden: faenkaal, fänkål;
- ✓ Thailand: phakchi-duanha, thian-klap, yira.

Pharmacological activities of fennel:

1. Antibacterial activity:

According to Dadalioglu and Evrendilek (2004); Cantore *et al.* (2004) and Mohsenzadeh (2007), the essential oil extracted from the fruits of *F. vulgare* exhibited antibacterial effect against these

foodborne pathogens -- *E. coli* 0157:H7, *Listeria monocytogenes*, and *S. aureus*. According to Kaur and Arora (2008), both aqueous and organic extracts of *F. vulgare* exhibit antibacterial efficacy against specific bacterial strains. Additionally, it has been claimed that the essential oil from the seeds of *F. vulgare* has antibacterial properties against a few human pathogenic microorganisms. *Campylobacter jejuni* and *Helicobacter pylori* have been demonstrated to be sensitive to ethanol and water extracts of *F. vulgare*. *Acinetobacter baumannii* infections that are resistant to many drugs may be controlled by *F. vulgare* essential oil. A phenyl propanoid derivative known as Dillapional was shown to be the active antibacterial principle of the *F. vulgare* stem. Other chemical components of *F. vulgare* have also been identified as active antimicrobial principles. According to Kwon *et al.* (2002), another chemical called Scopoletin, a coumarin derivative, has been discovered from the *F. vulgare* plant. (Reyes-Jurado *et al.*, 2015)

The disc diffusion method described by Lennette *et al.* (1980) was used for determination of antimicrobial activity of plant extracts and their essential oils, as follows: sterile nutrient agar medium (Merck) was prepared and distributed into Petri plates of 90 mm diameter. The disc diameter used was 6 mm (Whatman No. 1) paper. Different dilutions of the extracts and essential oils were made with methanol. The microbial suspension was streaked over the surface of the nutrient agar using a sterile cotton swab in order to get a uniform microbial growth on both control and test plates. Under aseptic conditions, the discs were placed on the agar plates and then 7.5, 10, 12.5, 15 and 20 g from each of the extracts and essential oil dilutions was put on the discs. A dilution solvent (methanol) was added to the discs on the control plates. The plates were then incubated at optimum temperature (37 °C for bacteria and 25 °C for yeast and fungi) for 24–48 h in order to get reliable microbial growth. Diameters of microbial inhibition zones (mm) were measured and recorded. A microdilution

broth susceptibility assay was used as recommended by Natural Committee for Clinical Laboratory Standard-NCCLS (1999) for the determination of the Minimum inhibitory concentration (MIC). All tests were performed in nutrient broth for bacteria and in potato dextrose broth for yeast and fungi. Concentrations of 7.5, 10, 12.5, 15 and 20 g dry extract or essential oil were added to 1 ml nutrient broth tubes containing 105 CFU/ml of live microorganism's cells. The tubes which contained 10 ml broth were incubated on an incubator shaker as to evenly disperse the extracts and essential oils throughout the broth in the tubes. The highest dilution (lowest concentration), showing no visible growth, was regarded as MIC. Cells from the tubes showing no growth were sub-cultured on nutrient agar plates to determine if the inhibition was reversible or permanent.

2. Antifungal activity:

It has been claimed that the fennel essential oil has an antifungal effect. According to reports, the fennel essential oil and seed extracts contain antimycobacterial and anticandidal properties. According to Pai *et al.* (2010), *F. vulgare* bark extracts have been shown to have antifungal properties against *Candida albicans*. The essential oil of *F. vulgare* has also been shown to inhibit *Sclerotinia sclerotiorum*'s mycelial growth and germination, and as a result, it may be utilised as a natural alternative to synthetic fungicides to combat phytopathogenic fungus. *Aspergillum niger*, *Aspergillum flavus*, *Fusarium graminearum*, and *Fusarium moniliforme* have been shown to be completely inhibited by the essential oil of *F. vulgare*.

3. Antioxidant activity:

It has been established that fennel species from various Mediterranean nations have distinct antioxidant capacities. According to Faudale *et al.* (2008), wild fennel exhibits a higher level of radical scavenging activity than both edible and medicinal varieties. The malondialdehyde level was found to be lower in the *F. vulgare* fruit methanol extract group compared to the control group, suggesting

that the methanolic extract of the fruit has antioxidant action. In comparison to butylated hydroxyanisole (BHA) and butylated hydroxytoluene (BHT), it has been observed that the essential oil and acetone extracts of *F. vulgare* exhibit considerable antioxidant activity Biljana *et al.* (2005). By tracking peroxide accumulation in the emulsion during incubation using the ferric thiocyanate method, it was possible to study the inhibitory activity of oil and acetone extracts in the linoleic acid system. The isolated chemicals cis-miyabenol C, trans-miyabenol C, sinapyl glucoside, and syringing 4-O-glucoside, as well as the fruit extract from *F. vulgare*, have all been shown to have antioxidant activity. A low amount of lipid peroxidation activity was seen in the *F. vulgare* fruit's n-BuOH extract, but a significant amount of activity was seen at the higher concentrations that were examined. According to Marino *et al.* (2007), extracted pure components from *F. vulgare* had better antioxidant activity than crude extracts.

Following its distillation for essential oils, the bitter fennel's flowering aerial parts left behind contained isolated phenolic compounds that were reported to have strong antiradical scavenging activity. This information may help explain the pharmacological effect of *F. vulgare*. According to Parejo *et al.* (2004), the isolated chemicals were identified as 3-caffeoylquinic acid, 4-caffeoylquinic acid, 1,5-O-dicaffeoylquinic acid, rosmarinic acid, eriodictyol-7-rutinoside, quercetin-3-O-galactoside, and kaempferol-3-O-rutinoside. In a different investigation, *F. vulgare* seed extracts in both water and ethanol were found to have antioxidant activity. In comparison to the same amount of -tocopherol (36.1%), 100 g of water and ethanol extracts showed 99.1% and 77.5% inhibition of peroxidation in the linoleic acid system, respectively. Both extracts were said to exhibit potent reducing power, free radical scavenging, superoxide anion radical scavenging, hydrogen peroxide scavenging, and metal chelating activities. Antioxidant activity has been found in the essential oils of the fruits of three Egyptian fennel cultivars that are produced organically: *F. vulgare* var.

azoricum, *F. vulgare* var. *dulce*, and *F. vulgare* var. *vulgare*. Essential oils from the cultivars *azoricum* and *dulce* were more potent antioxidants than those from the *vulgare* cultivar.

4. Antithrombotic activity:

Due to their broad-spectrum antiplatelet activity, clot destabilising effect, and vasorelaxant action, the essential oil of *F. vulgare* and its primary constituent, anethole, have been found to have a safe antithrombotic activity. In guinea pig plasma, anethole, the primary component of fennel oil, was just as effective as fennel oil at inhibiting arachidonic acid, collagen-ADP, and U46619-induced aggregation. At doses comparable to fennel oil, anethole likewise inhibited the thrombin-induced clot response. Both fennel oil and anethole showed equivalent NO-independent vasorelaxant efficacy at antiplatelet doses that were shown to be free of cytotoxic effects *in vitro* when evaluated in rat aortas with or without endothelium. Anethole (100 mg/kg oral dose) and *F. vulgare* essential oil (also combined) significantly protected rats from ethanol-induced stomach ulcers (Reyes-Jurado *et al.*, 2015)

5. Anti-inflammatory properties:

According to Choi and Hwang (2004), oral administration of the methanolic fruit extract of *F. vulgare* (200 mg/kg) has been shown to have inhibitory effects against acute and subacute inflammatory illnesses as well as type IV allergic reactions.

6. Oestrogenic activity:

F. vulgare has been claimed to boost libido, encourage menstruation, ease labour and delivery, enhance milk production, and lessen male climacteric symptoms. The active oestrogenic ingredient in fennel essential oil is thought to be anethole, which makes up the majority of the oil. According to certain other investigations, polymers of anethole such as dianethole and photoanethole are the true pharmacologically active substances.

7. Hepatoprotective activity:

Hepatoprotective characteristics of fennel

essential oil have been established (Ozbek *et al.*, 2003). Aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), and bilirubin levels in the serum were shown to have decreased in a study that examined the effects of fennel essential oil on the hepatotoxicity induced by acute CCl₄ injection (Puji *et al.*, 2020).

8. Antidiabetic activity:

In Streptozotocin-induced diabetic rats, the essential oil of *F. vulgare* has been shown to exhibit hypoglycaemic action. When diabetic rats ingested *F. vulgare* essential oil, their hyperglycemia was reduced from 162.5 ± 3.19 mg/dl to 81.97 ± 1.97 mg/dl and their serum glutathione peroxidase activity was increased. This opens up the prospect of its inclusion in the market for diabetes medications.

9. Antiparasitic effects:

The larvicidal activity of the essential oils and its major constituents were evaluated against third instar larvae of *Aedes aegypti* for 24 h. Pure compounds, such as limonene isomers, were also assayed. The lethal concentrations LC₅₀, C₉₀ and LC₉₉ were determined by probit analysis using mortality rates of bioassays. A 99% mortality of *Ae. aegypti* larvae was estimated at 37.1 and 52.4 µl/l of fennel essential oils from Cape Verde and Portugal, respectively. The repellent activity of (+)-fenchone and (E)-9-octadecenoic acid was tested against *Aedes aegypti* females using skin and patch tests in comparison with the commercial repellent agent (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 30 min after treatment. The larvicidal activity of essential oils was investigated against malaria vector, *Anopheles stephensi*. Among oils of three plants, *Foeniculum vulgare* oil was the most effective against *A. stephensi* with LC₅₀ and LC₉₀ values of 20.10 and 44.51 ppm, respectively. The essential oil of the leaves, flowers, and roots of *Foeniculum vulgare* exerted larvicidal activity

against fourth-instar larvae of the mosquito *Culex pipiens molestus*. Terpeneol and 1,8-cineole content of *Foeniculum vulgare* were the most effective contents against *Culex pipiensmolestus* bites offering complete protection for 1.6 and 2 h, respectively (Weiping and Baokang, 2011)

10. Miscellaneous:

In vitro cytoprotection and antitumour activity:

The methanolic extract of *F. vulgare* has been shown to have anti-tumor activity against the B16F10 melanoma cell line by trypan blue exclusion assay and *in vitro* cytoprotective action against normal human blood cells by micronucleus assay. When lymphocyte cultures were treated with a 70% methanolic extract of *F. vulgare*, the percentage of micronuclei decreased significantly, from 0.018% with doxorubicin to 0.006% with 70% methanolic extract of *F. vulgare*. However, a 70% methanolic extract of *F. vulgare* at a concentration of 200 g/ml demonstrated good anti-tumor action. According to Pradhan *et al.* (2008), *F. vulgare* may be used as a natural source of antitumor drugs in addition to providing cytoprotection for normal cells.

Entomological activity:

Direct contact application of *F. vulgare* fruit oil has been shown to have acaricidal action against *D. farinae* and *D. pteronyssinus* when compared to that of the commercial repellent benzyl benzoate. P-anisaldehyde, (+)-fenchone, fenchone, thymol, and estragol have been identified as the physiologically active components of *F. vulgare* fruit oil.

Using skin and patch testing, it has been discovered that the methanol extract of the fruit of *F. vulgare* exhibits mosquito-repellent properties against female *Aedes aegypti* mosquitoes. (+)-Fenchone and (z)-9-Octadecanoic Acid were identified as the biologically active components of the *Foeniculum* fruits (Weiping and Baokang, 2011).

Antihirustism activity:

F. vulgare's ethanolic extract has been shown to

have antihirustism properties. Patients were administered creams containing 1%, 2%, and placebo fennel extract in a double-blind research. According to Javidnia *et al.* (2003) and Weiping and Baokang (2011) cream with 2% fennel is preferable than cream with 1% fennel.

Effect on uterine contraction:

There have been studies on the effects of fennel essential oil on rat uterine contraction. When fennel essential oil was administered at various quantities (25 and 50 g/ml for oxytocin and 10 and 20 g/ml for PGE2, respectively), oxytocin and PGE2-induced contractions were much less intense. The frequency of contractions brought on by PGE2 but not oxytocin were likewise decreased by fennel essential oil. By using the moving average approach, an estimated LD₅₀ of 1326 mg/kg was achieved in female rats. The dead animals' essential organs also did not appear to have any visible harm

Human liver cytochrome P450 3A4 inhibitory activity:

Human liver cytochrome P450 3A4 inhibitory activity has been discovered in thirteen compounds isolated from the methanolic extract of fennel. The highest inhibition was demonstrated by 5-methoxypsoralen (5-MoP), which had an IC₅₀ value of 18.3 M and a mixed type of inhibition, out of all of these drugs.

Increased scientific research should be focused on the safety of medicinal and spice plants and the products made from them. The lack of dangers including mutagenicity, carcinogenicity, and teratogenicity is one of the primary requirements for using herbal remedies in medical diseases. These goods should, in general, be as safe as possible with few adverse effects (Muckensturm *et al.*, 1997).

Effect on reproductive system:

The anti-fertility effect of *Foeniculim vulgare* seed extract was studied in male rats. Rat groups were orally administered 1 ml of hydro-alkoholic extract of fennel seed in four doses of 35, 70, 140, and 280 mg/kg/bw daily for 60 days. After the last gavage,

the rats were anaesthetised and the caudal part of the right epididymis was used for sperm counting. After fixation of the testes, microscopic sections were prepared and histological changes were evaluated. The number of spermatogonia after doses of 140 and 280 mg/kg and Sertoli cells after a dose of 140 mg/kg decreased significantly as compared with the control group ($P < 0.05$). The number of primary spermatocytes and sperm count decreased significantly in the treated groups (70, 140, and 280 mg/kg) compared to the control group ($P < 0.05$). Furthermore, thickening of the basement membrane, cell apoptosis, and irregular arrangement of the germinal epithelium were observed in the treated groups. The compound anol or anethole, the major active compound of fennel oil, is considered to be an active estrogenic agent due to its structural resemblance to diethylstilbesterol, a synthetic estrogen. The effect of acetone extracts of *Foeniculum vulgare* seeds at different dose levels (50, 150 and 250 $\mu\text{g}/100 \text{ g}$ bw) was investigated on mammary glands and oviducts of castrated rats. The extract was found to increase nucleic acids and protein concentration as well as the organ weights in both tissues. The medium and high doses were very effective. The results confirmed the estrogenic nature of the seed extract. The essential oil of fennel seeds (500, 750, 1000 mg/kg for 30 days) was investigated for its anti-osteoporotic activities in ovariectomized rat osteoporosis model. The findings (assessed on the basis of bone mineral density and uterine weight) showed that the fennel essential oil has a preventive effect on development of osteoporosis in ovariectomized rats. This protective effect on early post-ovariectomy bone loss was dose dependent and at the dose of 1000 mg/kg, it was even more than estradiol of $0.082 \pm 0.008 \text{ g cm}$.

11. Broncho dilatory effects:

The bronchodilatory effects of *Foeniculum vulgare* (aqueous and ethanol extracts and essential oil) were examined by using precontracted isolated tracheal chains of guinea pig. The results indicated bronchodilatory effects of ethanol extract and

essential oil of *Foeniculum vulgare* which was not due to inhibitory properties of the plant on muscarinic and histamine H1 and/or an stimulatory effect on β_2 -adrenergic receptors.

12. Hepatoprotective and nephroprotective effects:

The potential protective effect of fennel essential oils was studied against carbon tetrachloride (CCl_4) induced fibrosis in rats. Administration of CCl_4 (1.5 ml/kg) intrapretoneally (ip) in olive oil (1:7 dilution) for 7 successive weeks resulted in liver damage manifested by significant increase in serum AST, ALT, ALP, decreased total protein and increased triglycerides, total cholesterol, LDL and decreased HDL level. Rats treated orally with essential oil of *Foeniculum vulgare* (Fennel, 200 and 400 kg/bw) for 7 successive weeks showed a significant protection against induced increase in serum liver enzyme (AST, ALT, ALP), restored total protein level and ameliorate the increased triglycerides, total, cholesterol, LDL and decreased the HDL. These protective effects were further confirmed by histopathological examination. The effect of whey protein concentrate (WPC) (0.5g/kg/day) or fennel seed extract (FSE) (200 mg/kg/day) was evaluated on paraoxonase-1 activity (PON1) and oxidative stress in liver of tienilic acid (TA) treated rats. TA administration significantly increased ALT and AST, total- and direct bilirubin levels, serum tumor necrosis factor- α and nitric oxide levels. Furthermore, serum PON1, and hepatic reduced glutathione, glutathione-S-transferase and Na^+/K^+ -ATPase values were diminished with a significant rise in the level of hepatic lipid peroxidation. Triglycerides, total- and LDL-cholesterol levels were significantly elevated, while HDL-cholesterol was unchanged. The administration of either WPC or FSE to TA treated animals significantly protected the liver against the injurious effects of tienilic acid. This appeared from the improvement of hepatic functions, atherogenic markers, Na^+/K^+ -ATPase activity, endogenous antioxidants and hepatic lipid peroxidation level; WPC showed the strongest protection effect. The nephroprotective effects of different oral doses of aqueous extract of *Foeniculum vulgare* seeds 250

mg/kg, *Solanum nigrum* 500 mg/kg fruit and their mixture (250 and 500 mg/kg/oral, respectively) were studied in gentamicin induced nephrotoxicity in albino rabbits. All the treatments were continued for 21 days. Blood samples were taken from all groups at day 21 to determine serum urea, creatinine, albumin, plasma malondialdehyde and catalase. Histopathological parameters of kidneys were also examined at day 21. Gentamicin induced oxidative stress and caused structural changes in the kidneys. The aqueous extract of *Foeniculum vulgare* seeds, *Solanum nigrum* fruit and their mixture significantly prevented renal damage by normalizing increased levels of renal markers. Mixture of both plants at high doses exhibited the more nephroprotective and antioxidant activities (Albert-Puleo, 1980; Ruberto *et al.*, 2000). The renoprotective effect of the aqueous extract of *Foeniculum vulgare* (150 mg/kg bw) was studied in experimental PCOS female rats. The mean values of blood urea nitrogen in PCOS rats treated with low dose of extract of *Foeniculum vulgare* and estradiol valerate and non-treated was significant ($P < 0.05$). Fennel essential oil did not reduce the BUN, Cr, KTDS, KW and body weight. Also, the serum and tissue levels of nitrite were not altered significantly by fennel essential oil (Puji *et al.*, 2020).

13. Antimutagenic and anticancer effects:

The potential antimutagenic and cancer chemoprevention effects of the hot water crude extract of sweet fennel (*Foeniculum vulgare* Mill.) seeds were evaluated in well known genetic model organisms: mice and *Drosophila*, using mutagenicity, molecular and biochemical assays. In mice, mitomycin C (MMC) was administered as a positive control alone before and after treatment with 5 or 0.5 mg/kg bw or in combination with fennel crude extract as acute (24h) and sub acute (5 consecutive days) doses, respectively. Chromosomal aberration assay in mice bone marrow cells revealed slight insignificant effect of fennel extract on aberrant mitosis rate, while it gave remarkable significant reduction of the MMC induced chromosomal aberrations. This effect was found to be dose-dependent. However, random

amplified polymorphism of DNA (RAPD) showed clear variation between different classes of treated and non-treated animals against MMC treatment, which reflected DNA protective effect of fennel extract. The serum uric acid, urea and creatinine (kidneys function) and liver function (GOT and GPT activities) were slightly affected by MMC, which were improved by the ingestion of fennel extract. In *Drosophila*, fennel extract significantly decreased the frequency of colchicine induced aneuploidy and chromosomal aberrations in post and pre-treatments (Albert-Puleo, 1980; Tognolini *et al.*, 2007). The apoptotic activity of crude methanolic *Foeniculum vulgare* leaves ethanolic extract was investigated on cervical cancer cell lines (HeLa). The induction of apoptosis was determined by analyzing DNA fragmentation in cervical cancer cells treated with active fraction of crude methanol extract using agarose gel electrophoresis. Fragmentation of the DNA was observed at different plant sample concentrations. Morphological observations were carried out and apoptosis body was observed at 125 µg/ml of the extract. *Foeniculum vulgare* induced apoptosis on cervical cancer cell line and inhibited cell proliferation through DNA fragmentation. The anticarcinogenic potential of anethole was studied in Ehrlich ascites tumour (EAT) in the paw of Swiss albino mice. The results revealed that anethole increased the survival time, reduce the tumour weight and volume and body weight of the EAT-bearing mice. It caused a significant cytotoxic effect in EAT cells in the paw, reduced the levels of nucleic acids and MDA, and increased NP-SH concentrations. The histopathological changes observed after treatment with anethole were comparable to the standard cytotoxic drug, cyclophosphamide. The results on the frequency of micronuclei and the ratio of polychromatic erythrocytes to normochromatic erythrocytes showed anethole to be mitodepressive and non-clastogenic in the femoral cells of mice.

14. Antiallergic effect:

In order to establish the antiallergic effect of fruits

of *Foeniculum vulgare*, the inhibitory actions of the fruit on 5-lipoxygenase (5-LOX) and β -hexosaminidase release were evaluated. The 70% ethanol extract considerably inhibited 5-LOX-catalyzed leukotriene production from A23187-induced rat basophilic leukemia (RBL)-1 cells. The IC_{50} was 3.2 mg/ml. From this extract, 12 major compounds including sabinene, fenchone, γ -terpinene, apinene, limonene, p-anisylacetone, p-anisylaldehyde, estragole (4-allylanisole), trans-anethole, scopoletin, bergapten and umbelliferone were isolated. It was found that several terpene derivatives including γ -terpinene and fenchone as well as phenylpropanoid, trans-anethole, revealed the considerable inhibitory action of 5-LOX. In particular, the IC_{50} of trans-anethole was 51.6 mM. In contrast, ethanol extract and the isolated compounds did not show considerable inhibitory activity on the degranulation reaction of β -hexosaminidase release from antigen-treated RBL-2H3 cells. Ethanol extract and trans-anethole showed significant inhibition of arachidonic acid-induced ear edema in mice, by oral administration at doses of 100-400 mg/kg (Ozbek *et al.*, 2003).

15. Toxicity and side effects:

The LD_{50} of *Foeniculum vulgare* essential oil was found to be 1.038 ml/kg. However, acute oral toxicity study in female mice revealed that a single high dose (2000 mg/kg) of the essential oil did not show loss of weight, autonomic behavioral changes or other signs of toxicity. There was also no mortality observed during the study period, suggesting that the LD_{50} (median lethal oral dose) of the essential oil is higher than 2000 mg/kg when given orally. The plant extract lethality in mice was tested using three doses (0.5, 1 and 3g/kg, orally). In addition, locomotor activity, bizarre reactions, sensitivity to sound, social interaction, tail posture, aggressive behaviour, ataxia, paralysis, convulsions, tremors, prostration, exophthalmos, pupil size, defaecation, salivation, urination, pattern of respiration, nasal discharge, cyanosis and piloerection was observed over a period of 24 h. The plant extract in doses of 0.5, 1

and 3 g/kg (orally) did not cause any deaths. Only the 3g/kg dose showed signs of reduced locomotor activity and piloerection. Otherwise, all other parameters were negative. No restrictions known for the seed used in infusions and preparations containing an equivalent amount of the essential oil. It was not recommended during pregnancy. No restrictions during lactation (Muckensturm *et al.*, 1997; Ostad *et al.*, 2001).

16. Cytotoxicity:

Due to their complex chemical composition, essential oils have no specific cellular ligands. As lipophilic mixtures, they are able to cross the cell membrane and degrade the layers of polysaccharides, phospholipids and fatty acids, and permeabilize. This cytotoxicity appears to include such membrane damage. In bacteria, the membrane permeabilization is associated with the loss of ions and the reduction of the membrane potential, the collapse of the proton pump and the depletion of the ATP pool. Essential oils may coagulate the cytoplasm and damage lipids and proteins. Damage to the wall and the cell membrane can lead to the leakage of macromolecules and lysis. In addition, essential oils change membrane fluidity, which becomes abnormally permeable, resulting in a leakage of radicals, cytochrome C, the Ca^{2+} ions, and proteins, like in the case of oxidative stress. This permeabilization of the outer and inner membranes causes cell death by apoptosis and necrosis. Ultrastructural alteration of the cell can be observed at a plurality of compartments. The interruption of the viral envelope herpes simplex virus (HSV) by essential oils can also be observed by electron microscopy. The induction of membrane damage was also confirmed by an analysis showing that microtubule *Saccharomyces cerevisiae* genes involved in the biosynthesis of ergosterol, the absorption of sterols, lipid metabolism, the structure and function of cell wall cellular detoxification, and transport are affected by treatment with α -terpinene. Recent work on the yeast *Saccharomyces cerevisiae*, has shown that the

cytotoxicity of some essential oils based on the ability to form colonies differs significantly in relation to their chemical composition. Generally, essential oil cytotoxicity mainly correlates to the presence of phenols, alcohols, and monoterpene aldehydes. The cytotoxic properties of essential oils are of great importance because they assume their use not only against certain human pathogens and animal parasites, but also in the preservation of agricultural and marine products against microbial attack. Indeed, some components of essential oils are effective against a variety of microorganisms as bacteria, viruses, fungi, protozoa, parasites, mites, and others. In addition, α -humulene shows cytotoxicity against breast cancer cells *in vitro*. α -humulene was reported to be responsible for cytotoxicity (CI₅₀ 55 mM). It induced a dose- and time-dependent decrease in cellular glutathione (GSH) content and an increase in reactive oxygen species (ROS) production. Furthermore, some scientist focusing on the effects of carvacrol, one of the main compounds in the EO of oregano, on the DNA synthesis of N-ras transformed mouse myoblast CO25 cells, finding that this monoterpenic phenol was able to inhibit the DNA synthesis in the growth medium and ras-activating medium, which contained dexamethasone. They proposed that it may be valuable in cancer therapy because of its growth inhibition of myoblast cells, even after activation of mutated N-ras-oncogene. The EO of the Anonaceae *Xylopia aethiopica* (Ethiopian pepper), a plant grown in Nigeria, showed, at a concentration of 5 mg/ml, a cytotoxic effect in the carcinoma cell line (Hep-2). Moreover, Yu *et al.* (2007) tested the essential oil of the rhizome of the *Aristolochia mollissima* for its cytotoxicity on four human cancer cell lines (ACHN, Bel-7402, Hep G2, HeLa). The rhizome oil possessed a significantly greater cytotoxic effect on these cell lines than the oil extracted from the aerial plant. Linabool inhibited only moderate cell proliferation; however, in subtoxic concentrations potentiates doxorubicin-induced cytotoxicity and proapoptotic effects in both cell lines, MCF7 WT and MCF7 AdR. This monoterpene improves the

therapeutic index in the management of breast cancer, especially multidrug resistance (MDR) tumors. An *in vitro* cytotoxicity assay indicated that the EO of *Cyperus rotundus* (Cyperaceae) characterized by the predominance of cyperene, α -Cyperone, isolongifolen-5-one, rotundene, and cyperoro-tundene, was very effective against L1210 leukemia cells, which correlates with significantly increased apoptotic DNA fragmentation (Muckensturm *et al.*, 1997).

17. Allelopathic Activity:

According to the International Allelopathy Society (IAS), allelopathy was defined in 1996 as “The science that studies any process involving secondary metabolites produced by plants, algae, bacteria and fungi that influences the growth and development of agricultural and biological systems”. Allelopathic interactions derive from the production of secondary metabolites. The secondary metabolites are synthesized for a wide range defense by plant and microorganisms. The secondary metabolites involved are called allelochemicals. Volatile oils and their constituents are being explored for weed and pest management, and are viewed as an important source of lead molecules in agriculture. Bioactive terpenoids constitute an important part of the defensive mechanisms of a large number of organisms and represent a fairly untapped source of active compounds of potential use both in the agricultural field. In fact, a large number of highly phytotoxic allelochemicals are derived from the terpenoid pathway and the phytotoxicity of essential oils has been investigated. This essential oil has, *in vitro*, an allelopathic ability to control *Trichoderma harzianum*. herbaceous species, including pinene, limonene, p-Cymene, and 1,8-cineole. Moreover, it is well known that monoterpenes in the essential oils have phytotoxic effects that may cause anatomical and physiological changes in plant seedlings leading to accumulation of lipid globules in the cytoplasm, reduction in some organelles such as mitochondria, possibly due to inhibition of DNA synthesis or disruption of membranes

surrounding mitochondria and nuclei. Since the continued use of synthetic herbicides may threaten sustainable agricultural production and result in serious ecological and environmental problems, essential oils with allelopathic properties could be exploited as in alternative strategies leading to the development of biodegradable and non-toxic compounds.

18. Repellent and Insecticidal Activity:

Numerous studies have demonstrated that these compounds, as well as their parent blends, possess biological activity capable of eliciting adverse effects in arthropod pests. The *Foeniculum vulgare* is used as an insect control agent and could be useful in managing field plant populations (Kim *et al.*, 2002). Several factors affecting the commercialization of plant essential oil extracts as repellents include regulatory requirements, intellectual property value, biological activity, product performance, and product quality.

Functional and therapeutic properties of fennel:

For thousands of years, fennel has been used in traditional medicine to treat a number of diseases and has a long history of use by humans. Fennel was thought to have calming characteristics in the fifth century, and from the ninth through the fourteenth centuries, it was credited with a wide range of medicinal benefits. Fennel seed, according to the Romans, might enhance eyesight. The English thought that the herb may help with digestion and provide comfort from a bloated stomach. Since the 18th century, fennel has been used therapeutically, and several research has been conducted. Additionally, it is highly effective in the treatment of kidney stones, bronchitis, diabetes, and persistent cough. Meals with cream use fennel seeds as an ingredient. The plant is used to treat kidney and bladder disorders because of its diuretic properties. It is also used to stop vomiting and ease nausea. The herbs are useful for treating chronic fever as well as obstructions in the hepatic, gastrointestinal, respiratory, and urinary tracts. In addition, they are utilized to treat conditions relating to the eyes, such as cataracts, and the

stomach, such as persistent diarrhea, endocrine, reproductive, and respiratory systems. In addition to that, it is also utilized in the treatment of breastfeeding women as a galactagogue agent (Al-Snafi, 2018).

Conclusion

This review discuss the chemical constituent, pharmacological and therapeutic effects of *Foeniculum vulgare* as promising herbal drug because of its safety and effectiveness. Studies that are presently accessible have shown that fennel extracts have a variety of pharmacological properties, including anti-allergic, analgesic, anti-inflammatory, antioxidant, antibacterial, anti-cancer, anti-stress, and cytotoxicity activities. The plant's numerous chemical components give it its therapeutic properties. Among the many components found in fennel plant essence, phenolic molecules are thought to be the most important and active ones. Fennel contains bioactive chemicals that are essential to preserving human health and are employed in the production of many different medications. Remarkably popular and productive studies have been conducted on the antioxidant, antibacterial, and estrogenic effects of fennel in different animal models.

In traditional medicines the plant has been used as a treatment option against anxiety, arthritis, water retention, appetite suppressant, amenorrhoea, angina etc. Traditional knowledge regarding the use of this plant is many but the scientific research available today to support this knowledge is limited. Here we have tried to compile all the available information from both traditional and published scientific literatures regarding the medicinal uses of *Foeniculum vulgare*. It will be helpful for the future researchers to get the information. This will provide tremendous opportunities for planning and conduct research related to various aspects of this medicinal plant.

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