Antioxidant, Antidiabetic and Antimicrobial Activities of *Foeniculum vulgare*

CHAPTER 27

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SUMMARY

Herbal medicines have healing qualities and beneficial pharmacological effects on human or animal bodies. These are an essential source of new drugs verified widely. About one-tenth of plant species are used in health products and drugs. One of them is fennel (Foeniculum vulgar), also referred to as saunf. A member of the Apiaceae family, the annual plant. Foeniculum vulgar is cultivated for its flavorful leaves, stalks and seeds. Fennel is used for its pleasing aroma, nutritive value and therapeutic effects Fennel contains volatile compounds, bioactive compounds, fatty acids and amino acids. These bioactive compounds make fennel a widely used medicinal plant that has antioxidant, antibacterial, cytotoxic, anti-inflammatory, antiseptic, diuretic, antiparasitic, hypoglycemic, anti-ulcer, memory-enhancing and hepatoprotective qualities. Fennel relieves indigestion, intestinal swelling, bloating, loss of appetite and newborn stomach ache. It is also used to cure bronchiolitis, coughs, cholera, joint pain and vision problems and to demonstrate other bioactivities.

INTRODUCTION

Nature is constantly the best example of significant interdependence occurrences. Natural compounds derived from plants, animals and minerals are the core of treating human ailments. Plants are the framework for all other life forms (Mouneir et al., 2022). They provide all of the food we eat, maintain the oxygen levels of the air and are the primary supplier of vitamins, which are crucial accessory foods. We would starve to death and perish from various deficiency diseases if we did not have plants (Robbins, 1944).

Herbal medicines are those that have healing qualities or have beneficial pharmacological effects on human or animal bodies. Since the beginning of time, plants have been used for various reasons. Using natural substances in Western treatment pharmaceuticals with harmless and active medicine, especially alkaloids, which are easily isolated from other organic compounds, led to a substantial advancement in the treatment of herbal materials (Jantan *et al*., 2015).

Medicinal plants contain compounds that can be used therapeutically or as precursors for producing lucrative medicines. Therapeutic plants have long been a valuable source of both curative and preventive medicinal therapeutic preparations for humans and a source of vital bioactive components for extraction. Nearly 80% of the world's whole population, particularly in third-world nations, is projected to rely on traditional medicine and goods for their healthcare needs regularly. Many people in underdeveloped countries use a combination of conventional therapies. Traditional medicines are frequently less expensive than modern medicines and these are sometimes the only natural therapies available and accessible in rural populations. Rural residents prefer traditional remedies due to their accessibility to traditional healers and the fact that the healers are familiar with their culture, surroundings and patients (Doughari, 2012).

Medicinal plants are an essential source of new drugs, verified widely. About one-tenth of plant species (50,000+) are used in health products and drugs (Venieraki *et al*., 2017). Herbal drugs helped in the establishment of an advanced medical health system that treats human illnesses. Further, by regulating and monitoring the health of active plant-extracted substances (Rasool *et al*., 2020). The value of the date palm is explained in the Holy Quran. "And you consume many drinks and eat a lot of grapes and date palm fruits." The importance of garlic is given in Surah Baqarah. In Surah Baqarah, Verse 61, garlic, cucumber, lentils and onions are all important. Surah Ad-Dahr Chapter no. 76, Verse no. 17 discusses the importance of the ginger significance of many medicinal plant species in Ahaidth (Aslam and Ahmad, 2016).

Current medicinal plant drug research employs a multi-pronged approach incorporating botanical, phytoconstituents, biochemical and molecular approaches. The hunt for novel and

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substantial leads in the treatment of malignancies, HIV/AIDS, malaria and pain, as well as other pharmacologic domains, is ongoing (Gul et al., 2023). Certain plant-derived organic products, such as galantamine, nitisinone and tiotropium, have hit new markets in the United States or are presently in late-stage human medical trials. As part of research with the National Cooperative Drug Discovery Group (NCDDG), various compounds from rainforest plants were discovered that may have antitumor effects. The research has also identified certain compounds that may be useful in chemoprevention, most of which are from consumable plant species or nutraceutical plants. However, the medicinal discovery of plant drugs continues to be a vital source of new pharmacological leads; there are various challenges to face, which include getting materials from plants, choosing the most authentic high-output screening bioassays, and upgrading active ingredients (Ojah, 2020).

Phytoconstituents, which seem non-nutritive substances found in plants and have health-protective characteristics, are a significant source of nutrition in diets high in plant-based foods. Phytochemicals, terpenoids, pigments and additionally natural antioxidants in nuts, whole grains, vegetables and fruits are related to the inhibition or handling of conditions such as heart problems, cancers, hypertension and diabetes, among others. The foods and herbs with the most potent anticancer properties are umbelliferous vegetables, garlic, soybeans, coleslaw, ginger, licorice and cabbage. Citrus fruits are rich in folic acid, potassium, vitamin C and pectin and contain a range of active phytochemicals. Phytochemicals in grains reduce the possibility of cancer and heart disease (Tangapazham *et al*., 2016). Numerous phytochemicals, especially polyphenols such as polyphenolic compounds, flavonoids, tannins and anthocyanins, have been shown to have free radical-scavenging capabilities. As a result, such plants can be studied to learn more about their medical characteristics and their safety and efficacy (Pham-Huy *et al*., 2008).

FENNEL

Fennel enhances mental and physical health (Arzoo & Parle 2017). A member of the Apiaceae (carrot) family, the annual plant *Foeniculum vulgare* (*F. vulgare*), is cultivated for its flavorful leaves, stalks and seeds. People call it fennel. Argentina, which is Syria, India, Egypt, China, Bulgaria, Indonesia and Pakistan are the main fennel-producing countries. It is a resistant herb with fluffy leaves and sturdy yellow blooms. Although it is found all over the world, it is most common on arid soils near rivers and the coast, that's why it is seen on the beaches of the Mediterranean. The plant *F. vulgare* is used for its pleasing aroma, nutritive value and therapeutic effects. It is farmed mostly as an herb or for the fruit it produces. Fruit volatile oil is mainly composed of 15–20% fenchone and 50–60% anethole, which are aroma molecules present in essential oils derived from herbs and seeds. (Malhotra, 2012). Fresh fennel garden herbs and fruits are used to make various therapeutic products that are highly sought after on the international market.

Fennel's nutritive and effective attributes include its antibacterial, antiflatulent, amphetamine and expectorant properties and its adulteration, harmfulness and allergenicity in medicine. Excellent requirements are given for different manufactured items made from fennel, including whole seed, chopped seed, oleoresins and volatile oil. For ages, people have used fennel in both food and medicinal applications. The entire plant has medicinal properties; the more extensive root is consumed as a vegetable; its leaves are added in food; and the seeds are beneficial for the extraction of essential oils (Zafar *et al*., 2023). Structural characterization and bioactive assessments of *F. vulgare* was done by different biochemical techniques. These phytocompounds show remarkable biological activities as shown in Fig. 1 (Karamat et al., 2024).

Fennel Classification

Foeniculum vulgare, member of Apiaceae family and is classified as

- Bitter fennel (*F. vulgare* Mill. var. piperitum Cout).
- Sweet fennel (*F. vulgare* Mill. var. dulce DC Batt. et Trab).
- Florence fennel or fnocchio (*F. vulgare* Mill. var. azoricum Thell).

The three main varieties of Fennel (Seidemann, 2005). Sour *F. vulgare* is cultivated for its seeds and their essential oil, which is used as a vegetable, as opposed to fnocchio fennel, which can be cultivated for its leaves. Sweet fennel is sowed for its wide base of leaves, seeds and valuable oil extracted from the fruits. Although other authors have written about annual, biennial and perennial varieties of fennel, Weiss (2002) classifies varieties as perennial or fragrant herbs. It has 2n = 22 somatic chromosomes and is called a foeniculum.

Biochemical Composition

The chemical composition of *F. vulgare* based on the morphotype, environment, nutrient availability and harvest period. Within each 100 g eatable quantity, seeds have 8.80 g moisture, 15.80 g protein, 36.60 g carbs, 14.90 g lipid and 15.70 g fiber (which includes 1.20 g Calcium, 19 mg iron, 1.70 g potassium, 385 mg Magnesium, 88 mg sodium, 487 mg phosphorous and 28 mg Zinc) (Bernath et al., 1996). Each 100 g contains 135 IU of retinol (vitamin A), 6 mg of niacin, 0.41 mg of thiamine and 0.35 mg of riboflavin, with an energy content of around 1440 kJ. The primary source of the non-volatile compounds are seeds, which contains tannin, mucilage, starchy sugars, aromatic oil and stable oil which contains phytochemicals [Table 1 (Koudela & Petříková, 2008)].

Green Herb and Fennel Bulb

The green "herb" fennel and the bulb is used as garnish just before serving or to flavor dishes as it cooks throughout India and the Central East. Although removing the leaves will stop the bulb from developing, fennel leaves have a comparable flavor. The National Nutrient Database of the United States Department of Agriculture states that per 100 grams of fennel, the following components are present (Badgujar et al., 2014) Carbs 90.21 g, Protein 1.24 g, 7.3 g of zinc 0.2 mg, potassium 414 mg, magnesium 17 mg and calcium 49 mg, B-6 vitamin

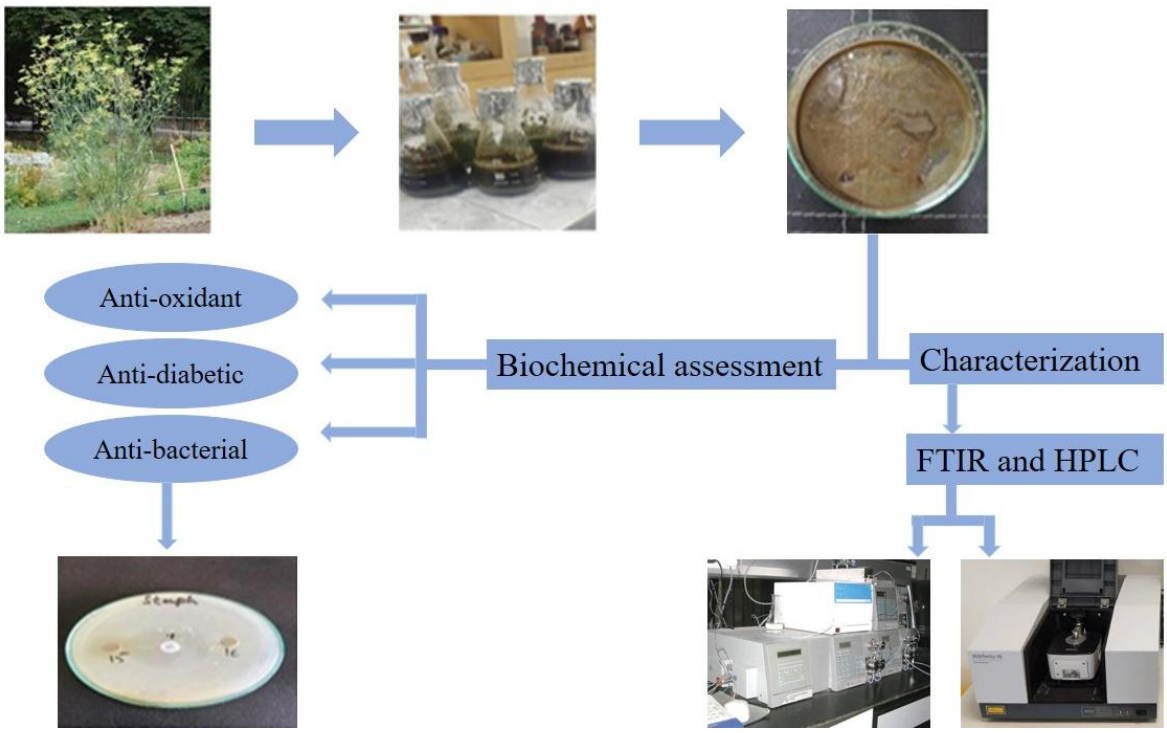

Fig 1. Biochemical assessment and characterization of *Foeniculum vulgare*

0.047 mg, 0.01 mg of thiamin Vitamin A 48 µg, Niacin 0.64 mg and Energy 31 kcal Lipid total: 0.2 g, 3.1 g of dietary fiber, Vitamin C 12 mg, Fe 0.73 mg and Na 52 mg, Riboflavin in milligrams. Because of its high fiber content, fennel bulbs may help diminish cholesterol. The fennel plant and its color variation, Rubrum (golden fennel), have a high antioxidant content.

Its flavorful seeds and leaves, which resemble dill in shape, can also be removed and cooked, marinated or utilized in risotto. The broader leave straws of Florence fennel undergo blanching and are eaten as a vegetable. Typical fennel leaves and seeds are also nice for salads (Chevallier, 2001). Florence fennel can be cooked as a food or mixed with avocado and chicory in Italian and German salads. In addition to being utilized in preparing green teas or juices blended with herbs, green bulbs and the whole plant are decent foundations of calcium, iron, folic acid, vitamins B and C. Under all conditions, the leaves offer their characteristically subtle, anise-like flavour (Zafar et al., 2023).

Fennel Seeds

Fennel seed that has been dehydrated is aromatic and has an anise flavor. The seeds are green or brown when young, but as these get matured, the color becomes a washed-out grey tint. Using green seeds in cooking is the best choice. Anise, a tiny plant with a flavor and exterior similar to fennel, occasionally gets confused with fennel seeds (Javed et al., 2020). Due to its unique, pleasant flavor, fennel seeds are used for chewing after meals. Fennel seeds coated in sugar can also be taken as a snuffle refresher. In some areas of Pakistan and India, cooked fennel seeds are utilized as an organic flavoring or for digestive aid. In rural villages, chewing green fennel seeds is a common practice. It is essential to the Chinese favorite flavor powder and minced Bengali spice. Italian sausages and rye breads from northern Europe are commonly made with fennel seed (Zafar et al., 2023).

Fennel leaves, fresh or dried, are added to many different eggs, seafood and other meals. The whole seed is used as a spice or flavor in several civilizations (India, China and Egypt). A traditional Indian spice, fennel seeds are utilized in many recipes, especially curries. Adding a small amount of whole fennel seeds may completely transform a meal's flavor. They are usually used to improve the flavor of soups, sauces, bread rolls, meat meals and desserts. German breads, English-style soups, spaghetti, pickles, desserts and other dishes of vegetables all contain fennel seed (Farrell, 1998). The seeds of fennel are used as a flavoring agent in liquors and pickles. Fennel seed vinegar is a popular ingredient in salads. It is easily prepared by combining two teaspoons of plant seeds with white wine vinegar (600 mL), letting it settle down in a cold, dark location, and wrapping the container while shaking

Table 1. Phytochemicals of *Foeniculum vulgare*

Phytochemicals	Percentages
Fenchone	15–20%
Lmonene	11%
Anethole	68%
Limonene	22% seeds
Limonene	19.6% (leaf oil)
α-pinene,	0.36%
δ-limonene	0.071%
1,8-cineole	5.08%
Anethone	86.12%
Trans-anethole	60–70%
Protein	15–22%
Fat	13–18%
Leaf oil	51.1%
Seed oil	58.5%

it after every few days. After that, the vinegar must be poured into glass bottles and preserved in a moisture free dark area.

EDIBLE PLANT PARTS AND USES

Consuming the entire plant, including the roots, flowers, seeds, leaves, stems, sprouting seeds, shoots and essential oil is safe. Swelling petioles and their bases are also consumable. Bulb, leaves and seeds of fennel plants are often utilized in salads, pasta meals, vegetable development, sausages and other dishes equally, both raw and cooked, as potential sources of various nutrients (Zafar et al., 2023).

Raw fennel bulbs contain carbs, fibre, protein, ascorbic acid, vitamin B complex and minerals. A fragrant plant called fennel is utilized as a herb for marijuana. It has good essence and various applications in cooking and is used extensively as both a vegetable and a spice. In drinks and confections, essential oil, the entire seed and its powder are used as preservatives, antioxidants and flavoring ingredients. Many cultures commonly use fennel seeds to make pickles, sauces, cakes, soupszz and breads. Fennel is used as an organic flavor to enhance the taste of cooked meats, such as spicy pepperoni and sugary Italian sausages, soft beverages, baked items, soups and ice creams (Farrell, 1998).

The big, fluffy bases of fennel leaves are consumed raw or roasted in England, sometimes as a supplement to cheese. It is a most common staple ingredient in many Italian and German salads, mostly paired with avocado. Before adding it to risotto, it is also marinated, blanched or broiled. Fennel slices, oranges and avocados make a great salad. Chopped fennel is often used with the traditional sandwich toppings of tomato and lettuce. Mint leaves and plain yogurt are served alongside thinly sliced fennel. Fennel makes a delicious side dish for scallops and pairs well with braised fennel and salmon. A tasty side dish is made with sautéed onions and fennel in olive oil (Chevallier, 2001).

There is also the option of cooking and consuming the thick roots. One of the three components of absinthe, a well-known alcoholic beverage in Europe, is Florence fennel. Many European countries cultivate the plant professionally to yield anethol, which is utilised in food products and alcoholic drinks. Fennel pectin includes uronic acid in addition to galactose, arabinose and rhamnose (Giosafatto et al., 2007). Based on phaseolin protein deficiency and occurrence, the extracted pectins are further evaluated as a carb resource to create biopolymer films (Tamang et al., 2021).

Fennel Tea

Fennel tea is made using dried or fresh seeds. The whole seeds are pure herbs that have been treated less than tea bags of herbs, preserving the plant oil and producing a more robust tea (usually prepared by infusion). You may also obtain fennel green tea from fennel bulbs and leaves. Fennel seeds are available online and at herbal shops for use in tincture and infusion recipes. Herb blends made with organic components frequently include calendula flowers, catnip, spearmint, lemongrass, rosemary and sage leaf (Zafar et al., 2023).

Cough Syrups

There are additional syrups with 10% alcohol by volume that are created from honey-infused fennel and naturally occurring herbal components like osha root, marshmallow root, elecampane root, mullein and horehound (Hammerquist, 2024).

Foeniculum vulgare as Natural Medicine

Fennel (*Foeniculum vulgare* mill.) is a widely used medicinal plant that has antioxidant, antibacterial, cytotoxic, anti-inflammatory, antiseptic, diuretic, antiparasitic, hypoglycemic, anti-ulcer, memory-enhancing and hepatoprotective qualities as shown in Fig. 2. Fennel relieves indigestion, intestinal swelling, bloating, loss of appetite and newborn stomach ache. It is also used to cure bronchiolitis, coughs, cholera, joint pain and vision problems and to demonstrate other activities, as summarized in Table 2 (Anka et al., 2020).

Antibacterial activity

The dietary spice fennel is commonly used and in demand. Gas chromatography-mass spectrometry (GC-MS) was used to determine the chemical composition of the essential oil obtained from hydro-distilling fennel seeds and 26 components were identified. The principal constituents (10.42 per cent) were estragole (68.53 per cent) and trans-anethole (68.53 per cent). Essential oils are used to evaluate their antibacterial activity, minimum bactericide concentration (MBC) and minimum inhibitory concentration (MIC) about various food-borne illnesses. Gram-negative and gram-positive bacterial strains showed various susceptibilities to the fennel seed oil, which exhibited antibacterial action against *Bacillus subtilis*, *Staphylococcus albus*, *Shigella dysenteriae* and *E. coli*. MBC and MIC values of 0.25 and 0.125 mg/mL, respectively. *S. dysenteriae* is the microbe most sensitive to essential oils among those under investigation. Furthermore, the kill-time experiment demonstrates that the essential oil significantly impacts the survival rate of *S. dysenteriae*. According to data from assays measuring content losses (proteins, carbs and 260 nm absorbing compounds) and electrolyte leakage, the essential oil's mode of action against *S. dysenteriae* might be described as affecting membrane integrity (Diao et al., 2014).

Bitter fennel essential oils' chemical composition and antimicrobial capabilities were examined against seed-borne and foodborne infections. These essential oils have an antimicrobial effect that helps shield food and seeds from dangerous microorganisms. The pathogens were most

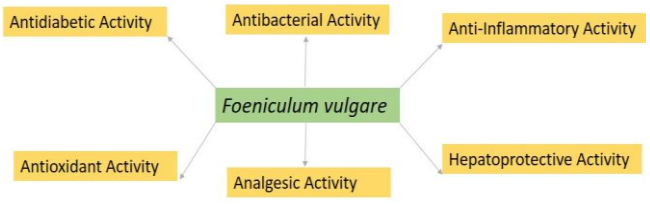

Fig 2. Schematic representation of phytochemical activities of *Foeniculum vulgare*

effectively inhibited by fennel essential oil's antibacterial effectiveness (Fig. 3). Due to their significant restriction of microbial growth, seed disinfectants and food additives utilizing essential oils or their constituents may be helpful against foodborne and seed-borne infections (Soylu et al., 2009).

People have used herbal remedies to treat various illnesses for thousands of years. In light of medication resistance and the unfavourable side effects of chemical antibacterial medicines, researchers are increasingly turning to natural resources. The study's primary objectives were *E. coli* and *S. aureus* to assess the essential oil's chemical composition and

Table 2. Studies on pharmacological activities of *Foeniculum vulgare*

Plant part	Activity	Results	References
Seeds	Determination of the antioxidant activity by using DPPH radical scavenging as well as free radical property	When plant extracts were added, the violet-colored DPPH free radical turned into a non-radical solution that indicated a reduction potential	Oktay et al., 2003
Seeds	Antibacterial activity by using ethanol and methanol extracts by Disc Diffusion Assay	Growth of gram-positive and gram-negative bacteria was not inhibited by lower concentrations of ethanol extract (25 g/disc), even though extracts are more sensitive to gram-negative bacteria.	Lo Cantore et al., 2004
Seeds	Anti-inflammatory activity of seed's essential oil in excision and incision wound model	Through a shorter epithelization duration and a faster rate of wound contraction, the extract (200 mg/kg dose) successfully expedited wound healing.	Özbek, 2005
Fruits	Antidiabetic activity as inhibition of glucose hydrolyzing enzymes by using an *in vitro* assay	The best anti-diabetic activities were found in leaf extract (lower IC50 value = 0.896 mg/mL).	El-Soud et al., 2011
Seeds	Ethyl acetate and ethanol extract are used in Cell lines: Breast cancer with hepatocellular carcinoma (HepG2) (MCF-7)	In comparison to human breast cell lines, ethanol extract demonstrated promising effectiveness against colorectal and neuroblastoma cells.	Akhbari, 2019
Seeds	Antimicrobial activity of zinc oxide nanoparticles synthesized from seed extracts	Particles showed significant effects against foodborne bacteria	Salari et al., 2023
Seeds	Therapeutic qualities were studied	Flavonoids, glycosides and other phytoconstituents were found that can be used as natural medicine	Noreen et al., 2023
Seeds	Determining the chemical components of MeOH extract	Anti-inflammatory activity was observed due to the presence of flavonoids and fatty acids	Cherbal et al., 2023
Seeds	Anti-motion sickness properties and LC-MS analysis	Flavonoids showed anti-motion sickness effects	Zhao et al., 2024
Seeds	Effect of chitosan based nanoparticles in animal model	Polyphenol-rich particles stimulated neurons regeneration in mice	Bajaber et al., 2024
Seeds	Antimicrobial activity of seeds essential oils	With no cytotoxic effects, seed oils are natural antibacterial agents	Khammassi et al., 2024
Seeds	Effect of essential oils from seeds in broiler chickens	Supplement improved the gut micro-biota	İpçak et al., 2024
Stalks	Phytochemical study by GC-MS, FTIR	15 new secondary metabolites not reported previously were identified	Ogbonna et al., 2024

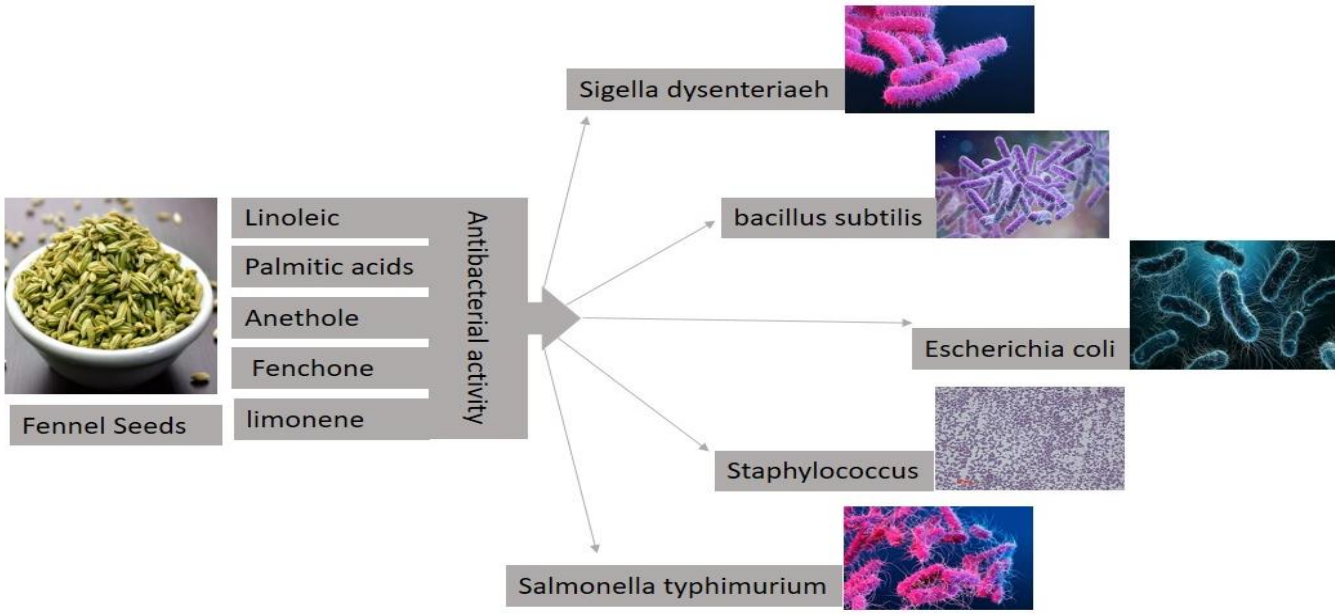

Fig 3. Antibacterial activity of *Foeniculum vulgare*

antibacterial qualities. The chemical composition of the specimen was determined using gas chromatography-mass spectrometry. Agar disc and agar well diffusion techniques were used to assess the antibacterial effects of essential oils. The MIC was determined using the macrobroth tube test. At doses of either 0.003 g/mL or 0.007 g/mL, the essential oil from *F. vulgare* inhibited the growth of both *S. aureus* and *E. coli*, with the Trans-anethole component making up 47.41% of the total. It has been discovered that the plant's antibacterial properties are ineffective against *E. coli* and *S. aureus*. Although various findings support the antibacterial qualities of the essential oil. *F. vulgare* essential oil can be used medicinally or as a preservative (Foroughi et al., 2016).

Antifungal-activity

Fennel essential oil has antifungal effects. Fennel essential oil and seed extracts possess antimycobacterial and anticandidal qualities. There have also been reports of *F. vulgare* bark extracts having antifungal action against *Candida albicans*. Similarly, the essential oil of *F. vulgare* inhibits *Sclerotinia sclerotiorum* germination and mycelial growth and it may be utilized as a bio-fungicide alternate to artificially synthesized fungicides for the control of phytopathogenic fungus (Soylu et al., 2007). The essential oil of *Foeniculum vulgare* exhibits a full zone of inhibition against *Aspergillum niger*, *Aspergillum flavus*, *Fusarium graminearum* and *Fusarium moniliforme* (Singh et al., 2006).

Antioxidant activity

Antioxidant power present in wild, appetizing and therapeutic fennel plants from numerous European countries has been studied. It was discovered that the radical scavenging activity of wild fennel is more significant than both eatable and therapeutic fennel (Vaezi et al., 2010). Additionally, the *F. vulgare* fruit methanolic extract exhibits antioxidant activity compared to the control. Fennel essential oil and acetone extracts showed strong antioxidant activity when compared to butylated hydroxytoluene (BHT) and butylated hydroxyanisole (BHA) (Chatterjee et al., 2000).

The inhibitory effects of oil and acetone extracts in the linoleic acid system were investigated using the ferric thiocyanate method to detect peroxide accumulation in the emulsion during incubation. Fruit extract from *F. vulgare* and its purified constituents. Antioxidant activity was shown by trans-miyabenol C, syringing 4-O-b-glucoside, sinapyl glucoside and cismiyabenol C. In the lipid peroxidation test, the *F. vulgare* fruit n-BuOH extract exhibited considerable activity at the higher tested concentration but only moderate activity otherwise. Compared to crude extracts, pure components derived from *F. vulgare* exhibited better antioxidant activity (Giosafatto et al., 2007).

Strong antiradical scavenging activity was attributed to phenolic compounds isolated from fennel after distillation of essential oils. These compounds may help explain the fennel pharmacological effect. The chemicals that were isolated are as follows: eriodictyol-7-rutinoside, quercetin-3-O-galactoside, kaempferol-3-O-rutinoside, ros marinic acid and 4-caffeoylquinic acid (Oktay et al., 2004). Another investigation has observed the antioxidant activity of *F. vulgare* seed extracts in ethanol and water extracts. In the linoleic acid system, 100g of water and ethanol extracts showed 99.1% and 77.5% prevention of peroxidation, respectively and were higher than the same dose of a-tocopherol (36.1%). Adequate reducing power, free radical scavenging, superoxide anion radical scavenging, hydrogen peroxide scavenging and metal chelating activities were identified for both extracts. The essential oils of three Egyptian fennel cultivars farmed organically *F. vulgare* var. azoricum, *F. vulgare* var. dulce, and *F. vulgare* var. have antioxidant properties in their fruits (Anthon et al., 2011).

Chemo Modulatory Action

Swiss albino mice were used for the estimation of chemomodulatory effects of various doses of a test diet containing *Foeniculum vulgare* seeds against skin papillomagenesis induced by 7,12-dimethylbenz(a)anthracene (DMBA-) and forestomach papillomagenesis induced by benzo(a)pyrene [B(a)P-] at the periinitiational level (Badgujar et al., 2014). Compared to the control group, fennel seeds show a significant decrease in the incidence and multiplicity of cutaneous and fore-stomach tumors. Additionally, phase I enzyme content and activity significantly increased, as demonstrated by biochemical testing, mainly when a 6% test diet of fennel plant and oil extracted from seeds was used for sensitive people; it may cause contact dermatitis (Malhotra, 2012).

At every dosage of the test food that was being investigated, there was a corresponding rise in the phase II enzyme activity. Particularly at the 4% and 6% test meals containing fennel, there was a notable increase in the antioxidant enzyme activity. These results suggested that fennel may have chemopreventive properties against the development of cancer. This is the first study demonstrating the chemopreventive ability of fennel seeds against the development of cancer (Singh & Kale, 2008).

Antidiabetic Activity

Diabetes is a metabolic condition characterized by insulin insufficiency, either absolute or relative. Many treatment techniques are now being developed to reduce postprandial glucose levels and adsorption by inhibiting enzymes such as amylase and glucosidase. These two enzymes are now employed to hydrolyze dietary carbohydrates to maintain glucose levels in diabetic patients (Fig. 4). *In-vitro* antidiabetic activity of three distinct extracts of *Foeniculum vulgare* seeds: ethyl acetate, n-butanol and benzene using alpha-amylase and alpha-glucosidase inhibition assay. Compared to the conventional acarbose values, the acquired data reveals that all three extracts had a higher α-glucosidase inhibitory effect than α-amylase inhibition. According to early phytochemical examination, all of the extracts contained phenols, saponins, terpenoids, tannins and flavonoids. These secondary metabolites can help to keep blood glucose levels stable, making them hypoglycemic agents (Godavari et al., 2018).

To examine the histopathological findings in streptozotocin-induced diabetic rats and the essential fennel oil

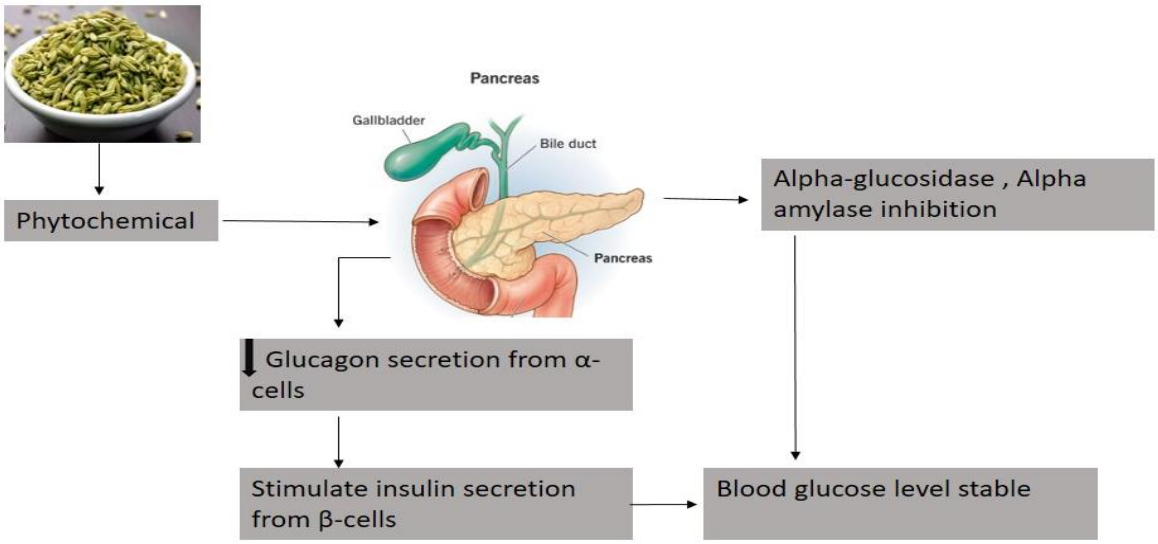

Fig 4. Antidiabetic activity of *Foeniculum vulgare*

for its antioxidant and hypoglycemic effects. Three groups of rats were created: diabetic control, diabetic group and normal control, which were received orally (30 mg/kg bw) *Foeniculum vulgare* essential oil. The essential oil's LD50 was used to determine the dose. The pancreas and kidney of the rats were histologically examined and measurements of whole 28 blood glutathione peroxidase and serum glucose were done. With a p0.05, essential oil ingestion reduced hyperglycemia in diabetic rats, ranging from 81.97-1.97 mg/dL to 162.5-3.19 mg/dL.

Additionally, the pathogenic abnormalities in their kidneys and pancreas were improved. In diabetic rats, the essential oil of fennel reduced pathological abnormalities and hyperglycemia, possibly due to its anti-oxidative activity and restoration of redox balance. As a result, its incorporation into the anti-diabetic medicine market has potential (Abou El-Soud et al., 2011).

Anti-Inflammatory Activity

When Fennel methanol extract was given orally to rats and mice, it showed inhibitory effects against acute and chronic inflammatory disorders. Three screening methods were used to assess the anti-inflammatory effect of methanol extract: formaldehyde-induced arthritis, arachidonic acid-induced ear oedema and carrageenan-induced paw oedema. They are often employed in the testing of nonsteroidal anti-inflammatory medications. Regarding acute inflammation, paw oedema (69%) caused by carrageenan injection is significantly inhibited by methanol extract (200 mg/kg) compared to the animal control group. *F. vulgare* methanol extract prevents mice's 70% ear oedema from arachidonic acid. When *F. vulgare* methanolic extract is applied to formaldehyde-induced inflammation, serum transaminase levels, aspartate aminotransferase (AST) and alanine aminotransferase (ALT) rised noticeably compared to the control group. A practical and straightforward method for determining the target chemicals' anti-inflammatory action is to evaluate the amount of AST and ALP (Kataoka et al., 2002). These findings indicate that *F. vulgare* could affect the pathways for lipoxygenase and cyclooxygenase (Choi & Hwang, 2004).

Hepatoprotective Activity

Rats exposed to acute hepatotoxicity caused by carbon tetrachloride had a strong protective effect against liver damage caused by the essential oil of *F. vulgare* seeds. In comparison to the control group, oral delivery of *F. vulgare* essential oil lowers serum levels of bilirubin, alanine aminotransferase (ALT), aspartate aminotransferase (AST) and alkaline phosphatase (ALP). D-limonene and beta-myrcene, two components of essential oils, might have been crucial in shielding the liver against CCl4 poisoning (Özbek et al., 2003).

SIDE EFFECTS

The fennel herb, seeds, bulb and extractives don't seem to be toxic in any kind. Fennel is not poisonous when taken at proportions commonly found in food (Lal & Meena, 2018). Fennel tea, along with many other formulations, has a broad spectrum of effects and virtually no adverse effects when taken in therapeutic proportions. Excessive usage of oil can cause nausea, vomiting and convulsions. Large doses of fennel should be evaded and it should only be used under the supervision of an herbal health professional, as certain fennel products include estragole. This chemical naturally occurs and causes cancer. Fennel essential oil has the potential to cause cancer when bare to sunlight. Infrequently, allergic reactions involving the skin and respiratory system have been documented. Pregnant females should avoid use of fennel plant, seeds, tincture or essential oil in remedial therapies because it is an oestrogenic herb. Small amounts of fennel used as a spice in meals are safe but large amounts stimulate the uterus. Even in small quantities, fennel essential oil can be dangerous and lead to breathing difficulties, vomiting, skin irritation and seizures. It is not advised to ingest the volatile oil. As a result of fennel's potential teratogenicity due to its oestrogen-like action, fennel oil usage as a primary dysmenorrhea treatment generated concerns (Ostad et al.,

2004). This is why it was necessary to elucidate the safety of fennel oil use. The research revealed that even at doses as small as 0.93 mg/mL, fennel essential oil (FEO) was cytotoxic. Though, as a neutral red cell sustainability trial showed, this decline was related to cell loss rather than a reduction in cell differentiation. Despite the lack of teratogenicity, these data suggest that fennel essential oil may be toxic to fetal cells at the concentrations studied.

Fennel as a Food Allergen

With alterations in diet and the globalization of food, spices are being utilized increasingly often. Prick tests were used to measure children's allergic reactions to cinnamon, fennel, nutmeg, curry, vanilla, coriander, paprika, sesame and cumin. These essential foods were either crushed or diluted in saline (Rancé et al., 1994) conducted experiments with specific spices (fennel, mustard). The spices that caused sensitization were curry, cumin, fennel, mustard and coriander (reported in 46% of cases). Fennel was the cause of a case of recurrent angioedema. The two foods most frequently linked to symptoms are mustard and fennel, which can also cause clinical symptoms. Avoiding some allergies in the diet can be more difficult since they are disguised in combinations.

Toxicity

Researches Acute (24 hours) and long-term (90 days) oral toxicity tests on ethanolic fennel fruit extracts in mice showed no significant acute or long-term mortality as compared to controls. The male mice gained considerable weight throughout treatment, but the female mice given the same extracts either reduced or showed little change in weight. *F. vulgare* essential oil at the tested concentrations may be detrimental to fetal cells, according to *in-vitro* experiments using rat embryo limb mesenchymal cells. However, there was no evidence of teratogenicity (Ostad et al., 2004).

Adverse Effects

According to Türkyılmaz et al. (2008), Long-term use of some drugs, including fennel, which helps babies with gas and regulates intestinal function, might trigger early the larche and should be avoided. When a child grows their breasts before the age of two and shows no other signs of puberty, it is known as isolated early larche. However, it can be connected to long-term treatment and long-term use of herbal therapies; the larche is most frequently associated with hypothyroidism, illnesses of the adrenal glands or ovaries using the use of exogenous hormones.

CONCLUSION

Fennel essential oils' chemical composition have an antimicrobial effect that helps shield food and seeds from dangerous microorganisms. The pathogens were most effectively inhibited by fennel essential oil. Due to their significant restriction of microbial growth, seed disinfectants and food additives utilizing essential oils or their constituents may be helpful against foodborne and seed-borne infections. Radical scavenging activity of wild fennel is more significant than both eatable and therapeutic fennel. Additionally, *F. vulgare* fruit methanolic extract exhibits antioxidant activity compared to the control. Fennel essential oil and acetone extracts showed strong antioxidant activity when compared to butylated hydroxytoluene and butylated hydroxyanisole. Fennel extracts had a higher α-glucosidase inhibitory effect than α-amylase inhibition. Phytochemical examination of all extracts contained phenols, saponins, terpenoids, tannins and flavonoids. These secondary metabolites can help to keep blood glucose levels stable, making them hypoglycemic agents. Further research on the bioactive components of these plants is necessary in order to identify additional advantages for public health and therapeutic uses in the medical industry.

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