



REVIEW ARTICLE

A review on antimicrobial and antibiofilm activity of *Foeniculum vulgare* Miller

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Abstract

Foeniculum vulgare Miller also has been extensively studied for its antimicrobial activity and recently many studies have also revealed its antibiofilm activity. Antibiotic resistance, which is a serious concern, demands the discovery of novel antimicrobial chemicals that can be developed and utilized as antibiotics. Compounds with antibiofilm activity must also be discovered to combat antibiotic resistant biofilm making microorganisms. The present review was conducted with the aim of evaluating current data on the antibacterial and antibiofilm activities of *Foeniculum vulgare* Miller and is the result of a thorough evaluation of the scientific literature on *Foeniculum vulgare* Miller, chemical composition, general medicinal and traditional properties, antimicrobial, antibiofilm activity.

Keywords: *Foeniculum vulgare* Miller, Antimicrobial activity, Antibiofilm.

Introduction

The world is currently experiencing an antibiotic resistance crisis as the microbes are becoming resistant to antibiotics. According to WHO, "Antibiotic resistance leads to higher medical costs, prolonged hospital stays, and increased mortality". Novel antimicrobial compounds are therefore urgently required to treat infectious diseases.

The plant extracts have been evaluated for various therapeutic properties in India. In addition to their medicinal properties, such as anti-inflammatory, nootropic, antianxiety, anti-aging, antitumor, and antiviral effects, plant extracts are also being investigated for antimicrobial activity. Several studies have demonstrated the antimicrobial activity of compounds derived from plants (Archana and Geetha

Bose 2022, Srivastava *et al.* 2021, Ugboko *et al.* 2020).

Foeniculum vulgare Miller commonly known as fennel or saunf is the medicinal plant belonging to the Umbelliferae (Apiaceae) family, known and used by humans since ancient times (Ugboko *et al.* 2020). The seeds of this plant are used as an aromatic to enhance the flavour of Indian cooked meals as well as tea. It's also known as a digestive and is commonly used as a home remedy for stomach problems like indigestion and flatulence. The seeds of *Foeniculum vulgare* Miller are also used in Ayurveda, an Indian traditional medical system.

Furthermore, several studies have revealed that *Foeniculum vulgare* Miller has anti-inflammatory, antitumor, cytoprotective, hepatoprotective, hypoglycemic, oestrogenic, and memory enhancing properties (Badgujar *et al.* 2014) making it a potential treatment choice for a variety of diseases.

Antibiofilm activity is a novel approach for evaluating the antibacterial properties of plant extracts or isolated plant components. A biofilm is an organised bacterial community that is enclosed in a self-produced polymer matrix made of polysaccharide, protein, and DNA. Stressful conditions, such as those with severe temperature and pH, high and low salt concentrations, low nutrition levels, and the presence of antibiotics, cause bacteria to produce biofilm. Biofilms cause antibiotic resistance and interestingly biofilms are resistant to all currently available antibiotics, which results in persistent infections (Roy *et al.* 2018). The difficulty of phagocytosing biofilm makes it harder for even

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body's defense system to combat it. According to Nobile and Johnson, *Candida albicans* biofilms are responsible for approximately 100,000 deaths in United States alone (Nobile and Johnson 2015).

Foeniculum vulgare Miller significance lies in its ability to produce large amounts of essential oil (EO) from various parts of the plant. The extractable EOs, which have a subtle anise flavor, are commonly used in cooking. These EOs are primarily composed of phenylpropanoids like (E)-anethole and estragole, as well as monoterpene hydrocarbons such as α -pinene and α -phellandrene. When the fruit is hydrodistilled, the resulting EO demonstrates strong antibacterial activity against *Escherichia coli*, *Bacillus megaterium*, and *Staphylococcus aureus*, as well as *E. coli* 0157:H7, *Listeria monocytogenes*, and *S. aureus*. The EO extracted from the seeds exhibits antimycobacterial and anticandidal properties. In addition, this plant's EO has shown excellent results as an antioxidant, an antidiabetic agent, and an insecticide. Regenerate response Antibiotic resistance, which is a serious concern, demands the discovery of novel antimicrobial chemicals that can be developed and utilized as antibiotics. Compounds with antibiofilm activity must also be discovered to combat antibiotic resistant biofilm making microbials.

Plants and essential oils have been used since ancient times to treat infectious diseases, even though knowledge of microorganisms did not exist. However, the increasing resistance of pathogens to antibiotics poses a significant threat to public health as it reduces the effectiveness of treatment, potentially leading to increased morbidity and mortality. Gram-negative bacteria such as *Escherichia coli* and *Pseudomonas aeruginosa* have already shown resistance, highlighting the urgent need for alternative antimicrobial agents to combat resistant pathogenic microorganisms. While moulds, actinomycetes, and bacteria are the most important sources of antibiotics, higher plants also contain several secondary metabolites classes with antimicrobial properties. Thus, there are ongoing efforts to evaluate the antimicrobial activity of various natural products, including plant metabolites, to isolate and characterize novel compounds that can inhibit bacteria and fungi or even serve as models for new molecules. Previous studies have shown that fennel essential oils possess antimicrobial activity against several microorganisms (Mota *et al.* 2015).

The herb known as Fennel has various names in different languages. In Sanskrit, it is referred to as madhurikā, mādhuṛī (the sweet), miśreya, miśrt (Egyptian). Its Hindi names include saunf, badi saunf, saunp, while in Bengali, it is called mauri, pānmourī. In Marathi, it is known as badishep, and in Gujarati as hariyal, variyali. Kannada has three different names for it, dodda sopu, dodda jirige, badi sopu, while in Sindhi, it is referred to as saunf. In Telugu, it is called sopu, pedda jilakura, and in Tamil, shombu, sohikire. Fennel is

an ancient seasonal herb. The fennel plant is originated in southern Mediterranean region and through naturalization and cultivation it grows wild throughout the Northern, Eastern and Western hemisphere specifically in Asia, North America and Europe. All parts are aromatic and can be used in many ways. The fennel plant typically reaches a height of 2-3 feet, with a green, glossy and smooth stem, accompanied by upright and firm branches. The leaves are highly divided, appearing as linear segments. Its elongated fruits have distinct and sturdy ribs, and they are colored in a greenish-yellow hue, resembling hay, which explains the origin of the term "fennel" [Madhurikā, saunf or fennel (*Foeniculum vulgare* Miller, Gaertn.) - Namah Journal].

Methodology

The scientific databases, Pubmed, Science Direct, Google Scholar and Web of Science were searched. Textbooks, journals, and websites were also used as sources of information. The keywords "*Foeniculum vulgare* Miller antimicrobial activity" were used in the search engine PUBMED to find out the research papers on antimicrobial activity of fennel seeds. The search yielded a total of 20 results. Total 11 results were research papers on the evaluation of antimicrobial properties of *Foeniculum vulgare* Miller, two were a review articles, and seven results were irrelevant. To find any missing research publications, a separate search was conducted using the keywords "*Foeniculum vulgare* Miller antibacterial activity" and "*Foeniculum vulgare* Miller antifungal activity." It was discovered that the same results were produced when the search term "*Foeniculum vulgare* Miller antimicrobial activity" was used. When keywords "fennel, antimicrobial, antibiofilm, antibacterial, antifungal activity, *Foeniculum vulgare* Miller" were used in Science Direct, 12 results were obtained. Out of those outcomes there were 3 research papers and rest were review articles and book chapters.

Chemical composition and nutritional value of food *Foeniculum vulgare* Miller

The composition of *F. vulgare* Miller has been studied, revealing that it contains 6.3% moisture, 9.5% protein, 10% fat, 13.4% minerals, 18.5% fiber, and 42.3% carbohydrates (De, AK and De M 2022). Calcium, potassium, sodium, iron, phosphorus, thiamine, riboflavin, niacin, and vitamin C are among the minerals and vitamins found in *F. vulgare* Miller. The main constituents of *F. vulgare* Miller essential oil are trans-anethole, fenchone, estragol (methyl chavicol), and α -phellandrene. The proportion of these compounds varies depending on the fennel phenological state and place of origin (Díaz-Maroto *et al.* 2005). Tables 1 and 2 show nutrient content found in dried fennel and different parts of fennel respectively.

The distribution of volatile compounds in *F. vulgare* Miller is not restricted to any specific plant part, with accumulation

being observed in various parts such as the roots, stem, shoots, flowers, and fruits (Díaz-Maroto *et al.* 2005, Gross *et al.* 2009). It has been reported that the essential oil content

Table 1: Nutrients found in dried fennel (USDA, USA)

Composition	Quantity (Per 100 g)	Composition	Quantity (Per 100 g)
Proximates		Riboflavin B-2	0.032 mg
Moisture	90.21 g	Niacin B-3	0.64 mg
Energy	31 kcal	Vitamin B-6	0.047 mg
Protein	1.24 g	Folate	27 µg
Total lipid (fat)	0.2 g	Vitamin A	48 µg
Carbohydrate	7.3 g	Vitamin E	0.58 mg
Total dietary fiber	3.1 g	Vitamin K	62.8 µg
Sugars	3.93 g	Lipids	
Minerals		Fatty acids, total saturated	0.09 g
Calcium, Ca	49 mg	Fatty acids, total monounsaturated	0.068 g
Iron, Fe	0.73 mg	Fatty acids, total polyunsaturated	0.169 g
Magnesium, Mg	17 mg	Essential amino acids	
Phosphorus, P	50 mg	Leucine	0.63 g
Potassium, K	414 mg	Isoleucine	0.73 g
Sodium, Na	52 mg	Phenylalanine	0.45 g
Zinc, Zn	0.2 mg	Tryptophane	0.53 g
Vitamins		Nonessential amino acid	
Vitamin C	12 mg	Glycine	0.55 g
Thiamin B-1	0.01 mg	Proline	0.53 g

decreases as the fruit matures. The percentage of trans-anethole, the primary constituent, ranges from 81.63% to 87.85% (Telci *et al.* 2009). The other classes of phytochemicals present in *F. vulgare* Miller are phenols and phenolic glycosides. Phenolic acids such as 3-O-Caffeoylquinic acid, 4-O-caffeoylquinic acid, 5-O-caffeoylquinic acid, 1,3-O-di-caffeoylquinic acid, 1,4-O-di-caffeoylquinic acid, and 1,5-O-di-caffeoylquinic acid have been reported in *F. vulgare* Miller. Flavonoids like eriodictyol-7-rutinoside, quercetin-3-rutinoside, and rosmarinic acid have also been found in *F. vulgare* Miller (Faudale *et al.* 2008, Park *et al.* 1996). Additionally, quercetin-3-O-galactoside, kaempferol-3-O-rutinoside, and kaempferol-3-O-glucoside have been identified in the aqueous extract of *F. vulgare* Miller, while quercetin-3-O-glucuronide, kaempferol-3-O-glucuronide, isoquercetin, and isorhamnetin-3-O-glucoside have been isolated from *F. vulgare* Miller (Parejo *et al.* 2004). These phenolic compounds are believed to play a role in preventing diseases associated with oxidative stress, including cardiovascular disease, cancer and inflammation.

F. vulgare Miller is one of the highest plant sources of potassium, sodium, phosphorous and calcium. According to the USDA data for the Mission Variety Fennels are richest dietary fiber and vitamins, relative to human needs.

General Medicinal and Traditional Properties of *Foeniculum vulgare* Miller

Foeniculum vulgare Miller, frequently referred to as fennel or saunf, is a medicinal herb belonging to the Umbelliferae (Apiaceae) family that has been known and utilized by humans since ancient times (Rather *et al.* 2016). The general medicinal and traditional properties are shown in Figure 1.

Table 2: Nutrient content of different parts of *Foeniculum vulgare* Miller

Composition	Contents			
	Leaves	Inflorescences	Stems	Shoots
Moisture	76.36 ± 0.33	71.31 ± 4.01	77.46 ± 1.03	73.88 ± 0.83
Asha	3.43 ± 0.04	3.23 ± 0.02	1.62 ± 0.12	2.39 ± 0.02
Fat	0.61 ± 0.16	1.28 ± 0.28	0.45 ± 0.07	0.49 ± 0.05
Protein	1.16 ± 0.03	1.37 ± 0.05	1.08 ± 0.00	1.33 ± 0.04
Carbohydrates	18.44 ± 0.06	22.82 ± 3.06	19.39 ± 0.65	21.91 ± 0.55
Fructose	0.49 ± 0.05	1.10 ± 0.04	1.49 ± 0.04	1.51 ± 0.06
Glucose	0.76 ± 0.12	2.94 ± 0.11	3.43 ± 0.20	4.71 ± 0.15
Sucrose	0.04 ± 0.00	0.03 ± 0.00	Nd	0.35 ± 0.06
Reducing sugars	0.72 ± 0.04	1.20 ± 0.19	1.49 ± 0.29	1.14 ± 0.10
Total SFA ^b	27.99 ± 0.02	37.47 ± 0.25	33.81 ± 0.06	19.95 ± 0.12
Total MUFA	4.96 ± 0.40	5.59 ± 0.13	4.78 ± 0.57	2.72 ± 0.36
Total PUFA ^b	67.05 ± 0.42	56.94 ± 0.12	61.41 ± 0.62	77.33 ± 0.24
Energy	83.90 ± 1.34	108.23 ± 10.37	85.91 ± 3.02	97.37 ± 2.44

Nutrients composition (g/100 g) and energetic value (Kcal/100 g) of the different parts of fennel, nd: not detected. Values are expressed as mean ± SD, n=3 experiments in each group, Source: (Barros *et al.*, 2010)

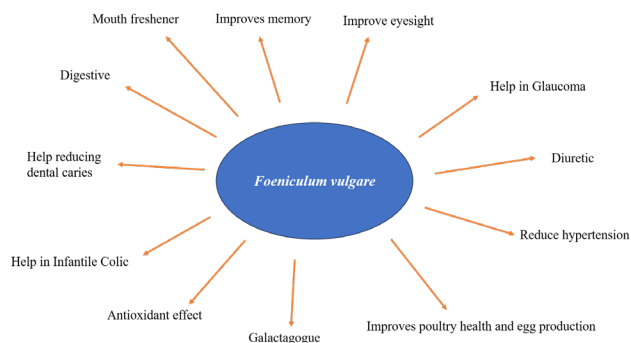


Figure 1: Some general traditional and medicinal uses of *Foeniculum vulgare* Miller

Flavoring agent, digestive and other health benefits

This plant's seeds are used as an aromatic to enhance the flavor of Indian prepared dishes and tea. It is also known as a digestive and is frequently used as a home treatment for stomach issues such as indigestion and flatulence. Ayurveda, an Indian traditional medical practice, also uses the fennel seeds in various Ayurvedic formulations. Fennel tea, a popular carminative, is made by steeping a teaspoon of crushed fennel seeds in hot water. Fennel seeds are ingested raw in the Indian subcontinent, often with sweets, to improve eyesight when it comes to improve eyesight fennel seeds particularly help in glaucoma, acting as diuretic and serve as medication to the hypertension. Fennel has been utilized as a galactagogue to enhance breast milk production in lactating mothers. This is believed to be attributed to the presence of phytoestrogens in fennel, which stimulate the growth of breast tissue (Rather *et al.* 2016).

Mouth freshener

Fennel seeds have been used as an ingredient to remove bad breath since ancient times. Surprisingly, the natural light green dye extracted from leaves is utilized in cosmetics, textile/wooden material colouring, and food colouring. Fennel flowers and leaves are combined to produce yellow and brown dyes (Gordon, 1977). Fennel seeds, both sugar coated and untreated, are utilized in mukhwas (mouth fresheners). Roasted fennel seeds are used as a mouth refresher in various parts of India and Pakistan. Mukhwas is a colourful after-meal mouth freshener or digestive aid. It can be produced from a variety of seeds and nuts, although it is most commonly found with fennel seeds, anise seeds, coconut, and sesame seeds. They are sweet in flavor and highly aromatic due to the presence of sugar and the addition of various essential oils.

Dental caries

Dental caries, the most widespread dental disease affecting humans, is a complex infectious disease caused by various factors, including saliva. Saliva is a crucial body fluid that serves a general protective role for the exposed hard

tissues of the oral cavity, and its decrease contributes to the formation of dental caries. Saliva plays a significant role in protecting against dental caries by maintaining the salivary pH above the critical pH level of 5.5, which prevents the dissolution of dental enamel minerals. Hence, discussing salivary pH is important in the context of dental caries. The use of fennel seeds as a buffering agent for salivary pH following a meal or sugar exposure can be considered effective. This is because the seeds initially increase the pH from its baseline level, but after 30 minutes, there is a significant reduction in pH, although it does not drop below the baseline (Manohar *et al.* 2020).

Infantile colic

Excessive crying in an otherwise healthy baby, known as infantile colic, is a distressing condition, but there is limited evidence to support the numerous treatments available. Despite being a natural and usually benign condition, colic poses a significant problem for infants and can burden parents emotionally, psychologically, and physically. Although dicyclomine hydrochloride is the only pharmacological treatment that has consistently shown efficacy, serious side effects, including death, occur in 5% of infants who receive it. While fennel seed oil has been demonstrated to decrease intestinal spasms and improve motility of the small intestine, there are no clinical studies that confirm its effectiveness (Alexandrovich *et al.* 2003).

Anticancer activity

Kaempferol, a major flavonoid aglycone, is found in several natural products, including fennel seeds, chia seeds, chives, cumin, moringa leaves, endive, garlic, among others. The extensive examination of kaempferol's remarkable properties in fighting cancer underscores its significant potential. The findings of these studies are promising, particularly since kaempferol has been shown to selectively inhibit cancer cells while leaving healthy cells unharmed. However, since the majority of research on kaempferol's anticancer potency has been conducted in vitro, it is challenging to arrive at a definitive conclusion regarding its efficacy (Imran *et al.* 2019).

Studies suggest that administering fennel or its active component trans-Anethole (TA) can safeguard the liver against streptozotocin (STZ)-induced diabetes in rats. These components also have the ability to improve blood glucose levels and regulate the lipid profile in serum. The hypoglycemic properties of fennel extract and TA may partly account for their therapeutic effects. Furthermore, these components may directly protect the liver through other mechanisms, including their antioxidant effects (Samadi-Noshahr *et al.* 2021).

Growth Performance and egg production in Poultry

A study found that feeding laying hens with 50 mg/kg fennel extract resulted in a significant increase in egg production

and shell thickness (Khan *et al.* 2022). A study showed that supplementing quails with phytoestrogens led to improved egg quality variables and overall performance (Akdemir and Sahin 2009). This suggests that fennel contains estrogenic compounds that stimulate egg production.

Antimicrobial and Immune Stimulating Effects in Poultry

The addition of 50 mg/kg of fennel extract to the diet was shown to enhance antibody titers against Newcastle disease (ND) in broilers (Badgajar *et al.* 2014). One study examined the impact of fennel seeds on bird immunity and found that adding fennel seeds to the feed of broilers significantly increased antibody titers against ND (Soltan *et al.* 2008). However, supplementing fennel seed oil with a mannan oligosaccharide combination did not affect bird immunity (Özek *et al.*, 2011). Including fennel extract in the diet of broilers improved Newcastle vaccination efficacy on day 35 and immunoglobulin synthesis on day 42, leading to enhanced immunity against bacterial, viral, and novel infections (Safaei-Cherehh *et al.* 2020).

Antioxidant effects on Poultry

A study was conducted to investigate the impact of fennel seed as a feed additive on the antioxidative quality of chicken meat, in comparison to a control diet with conventional feed additives like antibiotics and probiotics. The results revealed that birds fed with fennel had the lowest levels of oxidative compounds in their meat, while those fed with antibiotics had the highest levels. The study concluded that the oxidative stability of chicken meat could be influenced by both the base diet and feed additives, and that fennel as a feed supplement could potentially enhance the oxidative quality of chicken meat (Khan *et al.* 2022).

Supplementing poultry feed with fennel seeds has numerous advantageous effects on poultry health and growth. However, scientists aim to conduct further research on the precise dosage, bio-availability of active compounds, and innovative delivery methods, which are the focus of future studies.

Antimicrobial and Antibiofilm Activity

Many studies have reported antimicrobial activities of *Foeniculum vulgare* Miller making it a potential candidate for the development of novel antibiotics. An antimicrobial can be a microbicide, which kills bacteria, or a bacteriostatic substance, which prevents their growth. These drugs are classified based on the microorganisms they predominantly target. Antibiotics are generally used to treat bacteria, whilst antifungals are used to treat fungi.

The essential oil (EO) from the leaves of *F. vulgare* Miller subsp. *vulgare* var. *vulgare* has recently been found to have high antibacterial as well as antibiofilm properties (Di Napoli *et al.* 2022). The antibacterial action of EO was tested on *E. coli*, *S. aureus*, *P. aeruginosa* and *S. typhimurium* strains, and

it was discovered to be quite potent, with 100% mortality at 200 µg/mL. At low doses, EO was found to have antibiofilm activity against a non-pathogenic mycobacterium strain. The researchers also performed chemical profiling of the EO and discovered substantial quantities of α pinene (33.75%), a monoterpene hydrocarbon, and estragole (25.06%), a phenylpropanoid. The authors attributed EO's antibacterial effect to these small terpenoids and phenylpropanoids, which have demonstrated efficacy in pure form. In line with this, Marwa *et al* also observed similar results when they tested wild *F. vulgare* Miller grown in South Africa (Khammassi *et al.* 2023). In contrast, (Galgano *et al.* 2022) found no bacteriostatic or bactericidal effect of *F. vulgare* Miller EO on *S. aureus*. However, it showed some activity against *E. coli* strains (Ekhtelat *et al.*, 2019). This group obtained EO from some external source and have not described method of EO extraction, however; Di Napoli *et al* extracted EO from plant leaves by hydrodistillation. The difference in results could be attributed to a number of factors, including the method used for EO extraction or other unknown factors.

In another study, activity of EO obtained from *F. vulgare* Miller from Italy displayed greatest inhibitory activity on ampicillin, ciprofloxacin, and gentamicin resistant *E. coli* strain (D'Aquila *et al.* 2022). Studies on resistant strains are more useful. Galgano *et al.* also used *E. coli* isolates that were resistant to oxacillin, ampicillin, and erythromycin, as well as *S. aureus* isolates that were resistant to oxacillin and ampicillin.

Though EO has received the most attention, aqueous extracts have also shown significant antimicrobial and antibiofilm activity in a few studies. In one study, hydrolates formed as byproducts of distillation of *F. vulgare* Miller for EO were found to have substantial antibacterial action against Gram-positive *S. aureus* and *Ent. faecalis* (Šilha *et al.* 2020). The hydrolates were found to be ineffective against the fungus *Candida albicans* CCM 8186, however it did exhibit antibiofilm efficacy against *A. butzleri*, *A. cryaerophilus*, and *S. aureus* strains. Following a chemical analysis of fennel hydrolate, 13 compounds were identified, with estragole and fenchone being the most abundant. Estragole was discovered to be the primary odorant in fennel (Šilha *et al.* 2020). Therefore, in addition to EO, aqueous hydrolates showed antibacterial and antibiofilm action. This could be due to the presence of common phytochemicals in EO and hydrolates. However, according to the authors hydrolates had a smaller number of phytochemicals as compared to EO.

The antifungal activity of EO from *Foeniculum vulgare* Miller and other plants was investigated against several strains of *Penicillium sp* (Felšöciová *et al.* 2020). In another investigation on ten clinical isolates of *C. albicans*, fennel oil showed substantial antifungal activity when compared with other EOs (Bassyouni *et al.* 2019).

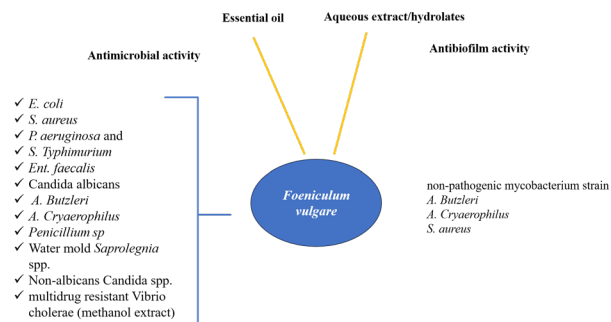


Figure 2: Simple graphical representation of antimicrobial and antibiofilm effects of essential oils and aqueous extract of *Foeniculum vulgare* Miller on various drug resistant and biofilm forming microbial strains

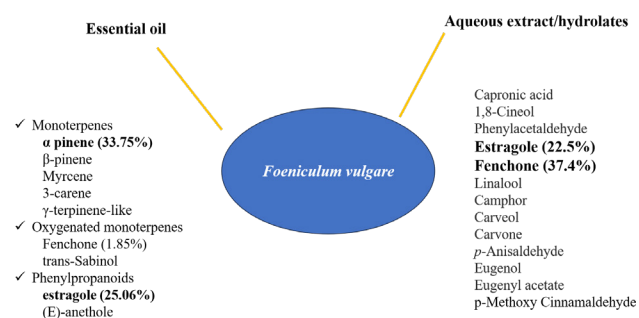


Figure 3: Chemical composition of essential oil and hydrolates of *Foeniculum vulgare* Miller based on studies included in the review. The composition may differ according to different plant species, environments, seasons, extraction methods used

According to Radice *et al* (Radice *et al.* 2022), alpha-phellandrene, a monoterpene found in EO of fennel, has significant, antibacterial activity along with biopesticide and antitumoral effects and hence has potential application. However, another phytocompound (-)-fenchone, a bicyclic monoterpene present in essential oils of plant species, such as *Foeniculum vulgare* Miller showed antifungal but no antibacterial activity (Pessoa *et al.* 2020). Suleiman (Suleiman 2020) studied the chemical composition and antibacterial activity of essential oils produced by hydrodistillation from the fruits of six fennel samples taken from indigenous populations in Portugal's centre and south. The main compounds found were fenchone (16.9 - 34.7%), estragole (2.5 - 66.0%), and trans-anethole (7.9 - 77.7%) out of the 16 compounds identified.

A water mold *Saprolegnia* spp. was not found to be sensitive to fennel EO in one study (Nardoni *et al.* 2019). Researchers (Mandras *et al.* 2021) in 2020 explored several EO on Non-albicans *Candida* Species in attempt to find an effective treatment for yeast infections resistant to existing antifungal medications. (Suleiman 2020) selected several plants based on their antimicrobial profile and prepared the supercritical fluid extract using sophisticated equipment

called supercritical fluid extractor (Suleiman 2020). The crude extract of *F. vulgare* Miller has the greatest antifungal activity against *Candida albicans*, *E. faecalis*, and *Salmonella typhimurium*, and it was found to contain certain unique chemicals such as squalene, eugenol, and isoeugenol.

(Vieira *et al.* 2019) investigated the activity of EO obtained by hydrodistillation of certain plants from apiaceae family on several strains of candida species from oral cavity. All EO were found to be effective on all the strains. The extracts were analysed by GC/MS and *Foeniculum vulgare* Miller showed high presence of Anethole (79.62%) whereas Fenchone (12.19%) and 1R- α - pinene (1.65%) were present in lower concentrations.

In One study conducted by (Chatterjee *et al.* 2016), methanol extract of sweet Fennel seeds was found to inhibit production of cholera toxin in multidrug resistant *Vibrio cholerae* O1 El without affecting viability. They designed this study with the idea that targeting virulence factors would put less pressure on the bacteria to mutate and grow resistant rather than killing them.

Zinc oxide nanoparticles (ZnO NPs) derived from fennel seed extract (FSE) were investigated for antibacterial activity against pathogenic strains of bacteria and yeast in a study conducted by (AlSalhi *et al.* 2020). FSE-derived nanoparticles demonstrated significant antibacterial activity (Kalhapure *et al.*, 2018). In yet another study hydroponically grown fennel plant derived silver nanoparticles inhibited methicillin resistant *Staphylococcus aureus* (MRSA) growth in vitro and in vivo (Fatima *et al.* 2023).

Figure 2 shows the antimicrobial and antibiofilm effects of essential oils and aqueous extract of *Foeniculum vulgare* Miller on various drug resistant and biofilm forming microbial strains based on the studies included in this review. Chemical composition of essential oil and hydrolates of *Foeniculum vulgare* Miller has been depicted in Figure 3.

Conclusion

In most of the studies EO of *Foeniculum vulgare* Miller was used and found to have potent antimicrobial and antibiofilm activity with some exceptions. The water soluble hydrolates were also found to possess antibacterial and antibiofilm activity in one study. More studies on hydrolates are required for explore more. When compared to antimicrobial activity, antibiofilm activity was found to be at low doses. In fact, some studies reported increased biofilm formation by some extracts, indicating that microbes form biofilm to resist antimicrobial compounds as a natural defense. Targeting virulence factors rather than the pathogen itself can be an effective strategy since it puts less pressure on the bacterium to evolve in order to become resistant or to produce biofilms. More such studies are required. Further, more research on antimicrobial and antibiofilm activities of purified compounds extracted from the plant *Foeniculum*

vulgare Miller would strengthen its applicability in drug development.

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