

## Quantitative analysis of antimicrobial activity of *Foeniculum vulgare*: A review

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### Abstract

*Foeniculum vulgare* is a perennial herb that belongs to Apiaceae family. Traditionally, it is used as an antiseptic, carminative, digestive, diuretic, and expectorant agent. This is a systematic review on antimicrobial activity of *Foeniculum vulgare* using the Minimum Inhibitory Concentration (MIC) technique. Essential oil extract had more antimicrobial effect than the alcoholic extract of the same tested microorganisms. *F. vulgare* essential oil, alcoholic, hexane, and diethyl ether extracts had strong inhibitory activity against *Bacillus cereus*, *Escherichia coli*, *Salmonella typhi*, and *Staphylococcus aureus*. Essential oil extract had low MIC values for *Bacillus cereus*, *Bacillus megaterium*, *Bacillus subtilis*, *Escherichia coli*, *Klebsiella sp.*, *Pseudomonas aeruginosa*, *Salmonella typhi*, *Sarcina lutea*, *Shigella boydii*, *Shigella dysenteriae*, *Shigella shiga*, *Shigella sonnie*, *Staphylococcus aureus*, and *Streptococcus-β-haemolyticus*. The alcoholic extract had low MIC values for *Aspergillus flavus*, *Bacillus cereus*, *Candida albicans*, *Escherichia coli*, *Salmonella typhi*, and *Staphylococcus aureus*. Hexane and diethyl ether extracts had low MIC values for *Aspergillus flavus*, *Bacillus cereus*, *Candida albicans*, *Escherichia coli*, *Salmonella typhi*, and *Staphylococcus aureus*. Microbial inhibition can be specific for the species. The antimicrobial activity strength of methanolic extract is similar to that of ethanolic extract. Acetone extract had lower MIC values than those for aqueous extract for the same tested microorganisms. Acetone, diethyl ether, and alcoholic extracts have stronger antifungal effects than essential oil. The essential oil extracted from *F. vulgare* leaves was not as effective as the essential oil extracted from its seeds. *Foeniculum vulgare* extracts have high potential to be an effective antibiotic agent.

**Keywords:** antibacterial activity; antifungal activity; fennel; *Foeniculum vulgare*; medicinal plants.

**Abbreviations:** IZ\_Inhibition Zone; MIC\_Minimum Inhibitory Concentration; ppm\_parts per million; TSST-1\_Toxic Shock Syndrome Toxin 1.

### Introduction

*Foeniculum vulgare*, also known as fennel, is native to southern Europe and the Mediterranean region. Nowadays, it is widely cultivated throughout the temperate and tropical regions of the world (Ferrara 1998). *F. vulgare* can reach a height of up to 2.5 m, with a hollow stem. The leaves are finely dissected with the ultimate segments filiform (thread-like) of about 0.5 mm wide. The flowers are produced in terminal compound umbels. The fruit is a dry seed 4–10 mm long (Díaz-Maroto et al. 2005). The leaves and the fruit of *F. vulgare* are mainly used as ingredients in cosmetics and as flavoring substances for fish and meat to give them a strong aroma and taste (Ruberto et al. 2000). *F. vulgare* essential oil, which is produced by steam distillation of dried fruits, is used for flavoring purposes in Western countries (Husain 1994). *F. vulgare* essential oil has antioxidant, antimicrobial, and hepatoprotective activity (Beaux et al. 1997; Marotti et al. 1993; Muckensturm et al. 1997; Özbek et al. 2003; Singh et al. 2002; Tanira et al. 1996). The essential oil extracted from *F. vulgare* seeds showed antibacterial activity against *Bacillus cereus*, *Bacillus magaterium*, *Bacillus pumilus*, *Bacillus subtilis*, *Escherichia coli*, *Klebsiella pneumonia*, *Micrococcus lutus*, *Pseudomonas aeruginosa*, *Pseudomonas putida*, *Pseudomonas syringae*, *Salmonella typhimurium*, *Shigella dysenteriae*, *Staphylococcus albus*, *Staphylococcus aureus*, and *Streptococcus haemolyticus* (Anwar et al. 2009;

Diao et al. 2014; Gulfranz et al. 2008; Singh et al. 2002). This supports the traditional use of *F. vulgare* extracts as a cure for infectious diseases. In fact, significant inhibitory effect was detected against six Gram positive and nine Gram negative human pathogenic bacteria using *F. vulgare* oil (Kazemi et al. 2012). Moreover, an inhibitory effect using *F. vulgare* oil was detected against food-borne and seed-borne pathogenic bacteria such as *Agrobacterium tumefaciens*, *Clavibacter michiganensis* subsp. *michiganensis*, *Erwinia carotovora* pv. *Carotovora*, *Listeria monocytogenes*, *Salmonella enteritidis*, *Salmonella typhimurium*, and *Xanthomonas axonopodis* pv. *vesicatoria* (Soylu et al. 2009). The seed essential oil had inhibitory activity against *Alternaria*, *Aspergillus fumigatus*, *Aspergillus niger*, *Aureobasidium*, *Fusarium solani*, *Penicillium*, *Phytophthora infestans*, *Rhizopus solani*, *Trichophyton rubrum*, and three *Candida albicans* strains of different origins (Bansod and Rai 2008; Pai et al. 2010; Skrobonja et al. 2013; Soyly et al. 2006). This makes *F. vulgare* essential oil a good candidate as a bio-fungicide and as an alternative to the chemical fungicides against phytopathogenic fungi. In fact, the seed essential oil is able to prevent the mycelia growth responsible for food deterioration (Barkat and Bouguerra 2012). Anethole and fenchone, the main components of *F. vulgare* oil, have antifungal activity against *Cladosporium cladosporioides*, *Penicillium helianthi*, and *Trichophyton mentagrophytes*.

However, *Penicillium funiculosum*, *Penicillium ochrochloron*, and *Trichoderma viride* were not inhibited by the essential oil (Mimica-Dukić et al. 2003; Singh et al. 2006). Moreover, the essential oil can reduce the mycelial growth and germination of *Sclerotinia sclerotiorum* (Soylu et al. 2007). The essential oil extracted from the stem showed a potential for controlling the multidrug-resistant *Acinetobacter baumannii*, a bacterial pathogen associated with hospital-acquired infections (Jazani et al. 2009). The essential oil suppresses the production of *Staphylococcus aureus* exotoxins, enterotoxins (SEs), and toxic shock syndrome toxin 1 (TSST-1). This suppression of *Staphylococcus aureus* toxins was attributed to the high amount of anethole in *F. vulgare* essential oil (Qiu et al. 2012). Therefore, anethole is an important antibiotic and food preservative agent that can be used in the pharmaceutical and food industries (Çetin et al. 2010; Martins et al. 2012).

The essential oils extracted from leaves and fruit (ripe and unripe) of *F. vulgare* showed antimicrobial activity to *Alternaria alternata*, *Bacillus megaterium*, *Escherichia coli*, *Fusarium oxysporum*, *Paenibacillus larvae*, and *Rhizopus solani*, (Araque et al. 2007; El-Adly et al. 2007; Gende et al. 2009; Özcan et al. 2006). Silver nanoparticles were made by the leaf extract of *F. vulgare* engaged with silver nitrate (AgNO<sub>3</sub>). The silver nanoparticles of *F. vulgare* were tested for antibacterial activity in combination with antibiotics against *Escherichia coli* and *Staphylococcus aureus*. The different standard antibiotics (gentamicin, oxacillin, vancomycin, ampicillin, and amoxicillin) showed significant increases in their activity when combined with *F. vulgare* silver nanoparticles. The highest activity against *Escherichia coli* and *Staphylococcus aureus* was with combination of vancomycin (Bonde 2011). The essential oils extracted from the flowers and the roots significantly inhibited both *Aspergillus parasiticus* fungal growth and its production of aflatoxin (B1 and G1). The flower and root essential oil inhibited fungal growth by 65% and inhibited the production of aflatoxin (B1 and G1) by 98% (Alinezhad et al. 2011).

Aqueous, ethanol, and ethyl acetate extracts of *F. vulgare* showed moderate antibacterial activity against *Agrobacterium radiobacter* pv. *tumefaciens*, *Erwinia carotovora*, *Pseudomonas fluorescens*, and *Pseudomonas glycinea* (Duško et al. 2006). Moreover, ethanol seed extract showed inhibitory activity against some pathogenic bacteria species such as *Bacillus cereus*, *Bacillus subtilis*, *Enterobacter aerogenes*, *Enterobacter cloacae*, *Kocuria rhizophila*, and *Staphylococcus aureus*.

Hot water and acetone seed extracts showed inhibitory activity against *Enterococcus faecalis*, *Escherichia coli*, *Pseudomonas aeruginosa*, *Salmonella typhi*, *Salmonella typhimurium* 1, *Shigella flexneri*, and *Staphylococcus aureus* (Arora and Kaur 2007; Kaur and Arora 2009). The aqueous extract moderately inhibited the growth of three soil borne fungi, namely, *Fusarium moniliforme*, *Macrophomina phaseoli*, and *Rhizocotina solani* (Zahid et al. 2012). In fact, the aqueous extract at a concentration of 1.6 mg/ml was inhibitory to *Aspergillus niger*, *Bacillus subtilis*, *Campylobacter jejuni*, *Escherichia coli*, *Pseudomonas aeruginosa*, *Penicillium chrysogenum*, *Staphylococcus aureus*, and *Salmonella typhi*, (Abd El-Malak et al. 2010; Essawi and Srour 2000; Taie et al. 2013). This shows that *F. vulgare* aqueous extract could be used as a natural food preservative agent to enhance food shelf-life.

The methanol extracts of the seeds showed inhibitory activity against enteropathogenic bacteria (*Bacillus pumilus*, *Helicobacter pylori*, *Staphylococcus aureus*), and against *Bacillus cereus*, which is an important food poisoning

pathogen (Alzoreky and Nakahara 2003; Dua et al. 2013; Mahady et al. 2005). Hexane extract of *F. vulgare* var. *dulce* had different inhibitory chemical compounds against multidrug-resistant *Mycobacterium tuberculosis*. In fact, the most inhibitory chemical compound extracted from the hexane extract against *Mycobacterium tuberculosis* was 2,4 undecadienal (Esquivel-Ferriño et al. 2012).

*F. vulgare* is an importance medicinal plant. Many research studies have been conducting to investigate the antimicrobial activity of this plant. The aim of this systematic review is to analyze the antimicrobial data in the literature using MIC values to learn what pathogens are inhibited by which part of *F. vulgare*, using which extraction method, and at what concentrations. This helps investigators to use this data analysis not only for ethanobotanical applications, but also for discovery of new antibiotics.

## Results

### Essential oil extracted from seeds

The antimicrobial activity of the essential oil extracted from seeds measured in MIC can be divided into six categories. The first category has the lowest MIC value of 0.5 ppm and includes *Staphylococcus aureus* and *Streptococcus-B-haemolyticus*. The second category has an MIC value of 1.0 ppm and includes *Bacillus cereus*, *Bacillus megaterium*, *Bacillus subtilis*, *Escherichia coli*, *Pseudomonas aeruginosa*, *Shigella dysenteriae*, and *Shigella shiga*. The third category has an MIC value of 1.5 ppm and includes *klebsiella sp.* and *Sarcina lutea*. The fourth category has an MIC value of 2.0 ppm and includes *Salmonella typhi* and *Shigella boydii*. The fifth category has an MIC value of 5.0 ppm and includes only one microorganism, *Shigella sonnie*. The sixth category includes many microorganisms with high MIC values (Table 1 and Figure 1).

### Alcoholic extracts from the seeds

The classification of tested microorganisms according to MIC value can be divided into four categories, using methanolic and ethanolic extracts of the seeds. The first category has the lowest MIC value of 10 ppm and includes *Aspergillus flavus* using the methanolic extract and *Candida albicans* using either methanolic or ethanolic extracts. The second category of 12.5 ppm MIC value includes *Aspergillus flavus* using ethanolic extract, and *Bacillus cereus* and *Staphylococcus aureus* using methanolic extract for both organisms. The third category of 15 ppm MIC value includes *Bacillus cereus* and *Staphylococcus aureus* using ethanolic extract, *Escherichia coli* and *Salmonella typhi* using either methanolic or ethanolic extracts. The fourth category includes many microorganisms with high MIC values (Table 2 and Figure 2).

### Aqueous and acetone extracts from the seeds

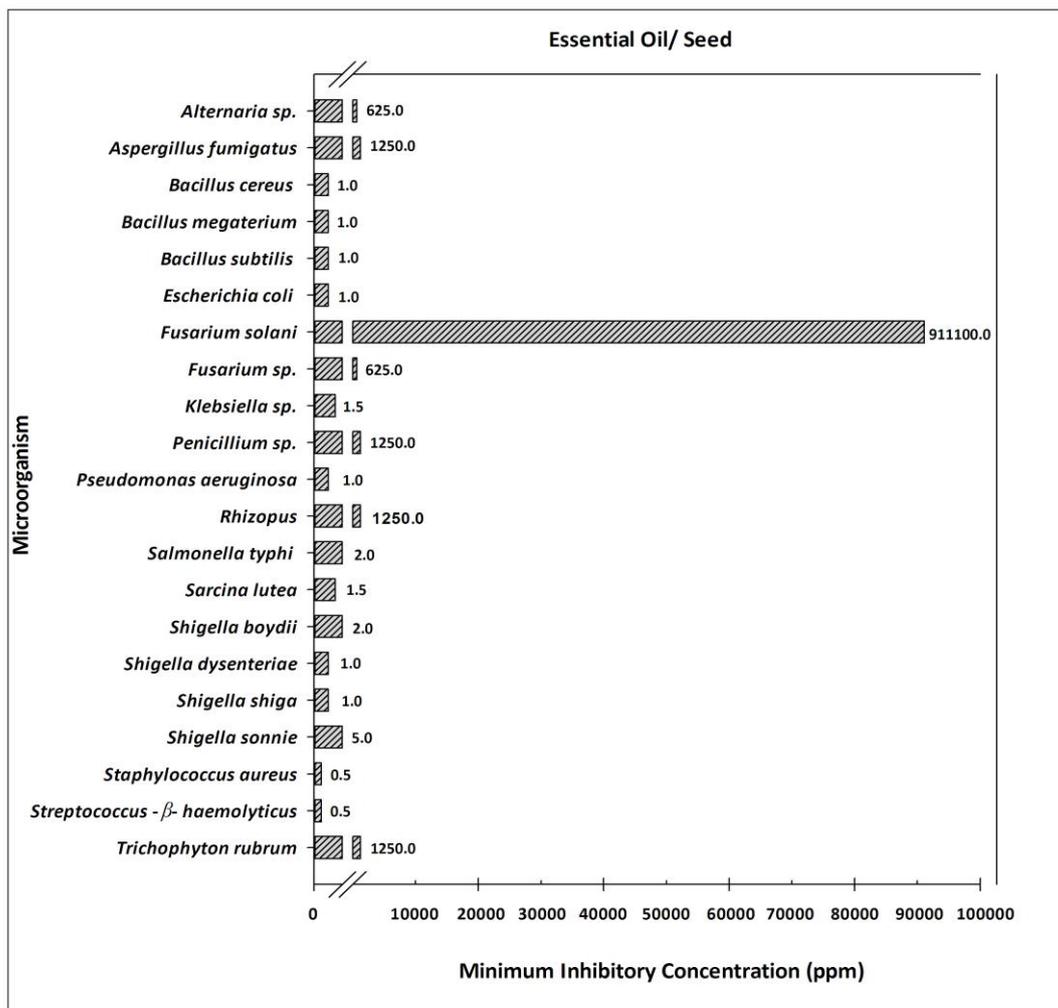
High values of MIC were detected when aqueous or acetone extract of *F. vulgare* seeds was used. Relatively lower MIC values were obtained using acetone extract than aqueous extract (Table 3 and Figure 3).

### Hexane and diethyl ether extracts from the seeds

Hexane and diethyl ether extracts had low MIC values for the tested microorganisms. However, hexane extract showed a

**Table 1.** List of tested microorganisms and the antimicrobial activity of essential oil extracted from *F. vulgare* seeds expressed as MIC values.

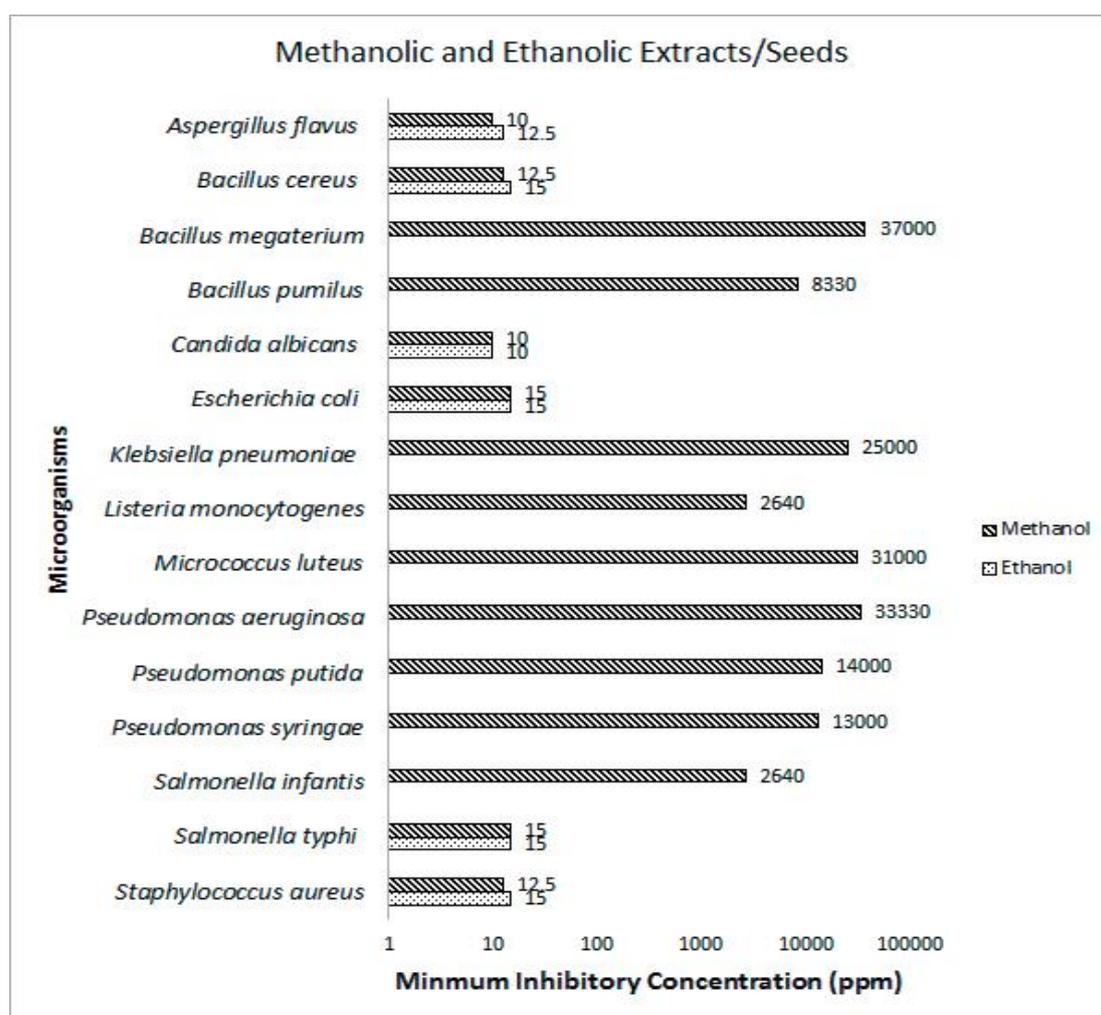
Microorganism	MIC Value	MIC Value (PPM)	Reference
<i>Alternaria sp.</i>	625 µg/ml	625	(Barkat and Bouguerra 2012)
<i>Aspergillus fumigatus</i>	1250 µg/ml	1,250	(Barkat and Bouguerra 2012)
<i>Aspergillus niger</i>	0.5 (% , v/v)	5,000	(Bansod and Rai 2008)
<i>Bacillus cereus</i>	1.0 µg/ml	1	(Kazemi et al. 2012)
<i>Bacillus megaterium</i>	1.0 µg/ml	1	(Kazemi et al. 2012)
<i>Bacillus subtilis</i>	1.0 µg /ml	1	(Kazemi et al. 2012)
<i>Candida albicans</i>	0.4 (% , v/v)	4,000	(Gulfranz et al. 2008)
<i>Escherichia coli</i>	1.0 µg/ml	1	(Kazemi et al. 2012)
<i>Fusarium solani</i>	91.1 mg/ml	91,100	(Anwar et al. 2009)
<i>Fusarium sp.</i>	625 µg/ml	625	(Barkat and Bouguerra 2012)
<i>Klebsiella sp.</i>	1.5 µg/ml	1.5	(Kazemi et al. 2012)
<i>Micrococcus luteus</i>	2.1 (% , v/v)	21,000	(Gulfranz et al. 2008)
<i>Penicillium sp.</i>	1250 µg/ml	1,250	(Barkat and Bouguerra 2012)
<i>Pseudomonas aeruginosa</i>	1.0 µg/ml	1	(Kazemi et al. 2012)
<i>Pseudomonas putida</i>	0.6 (% , v/v)	6,000	(Gulfranz et al. 2008)
<i>Pseudomonas syringae</i>	2.6 (% , v/v)	26,000	(Gulfranz et al. 2008)
<i>Rhizopus</i>	1250 µg/ml	1,250	(Barkat and Bouguerra 2012)
<i>Salmonella typhi</i>	2.0 µg/ml	2	(Kazemi et al. 2012)
<i>Sarcina lutea</i>	1.5 µg/ml	1.5	(Kazemi et al. 2012)
<i>Shigella boydii</i>	2.0 µg/ml	2	(Kazemi et al. 2012)
<i>Shigella dysenteriae</i>	1.0 µg/ml	1	(Kazemi et al. 2012)
<i>Shigella shiga</i>	1.0 µg/ml	1	(Kazemi et al. 2012)
<i>Shigella sonnie</i>	5.0 µg/ml	5	(Kazemi et al. 2012)
<i>Staphylococcus aureus</i>	0.5 µg/ml	0.5	(Kazemi et al. 2012)
<i>Streptococcus-β- haemolyticus</i>	0.5 µg/ml	0.5	(Kazemi et al. 2012)
<i>Trichophyton rubrum</i>	1250 µg/ml	1,250	(Barkat and Bouguerra 2012)



**Fig 1.** Minimum Inhibitory Concentration (MIC) in parts per million (ppm) of essential oil extracted from *F. vulgare* seeds on the tested microorganisms. Most of the experiments in the literature used essential oil of the seeds more than any other plant part. Essential oil extracted from the seeds had low MIC values for many microorganisms.

**Table 2.** List of tested microorganisms and the antimicrobial activity of ethanolic and methanolic extracts of *F. vulgare* seeds expressed as MIC values.

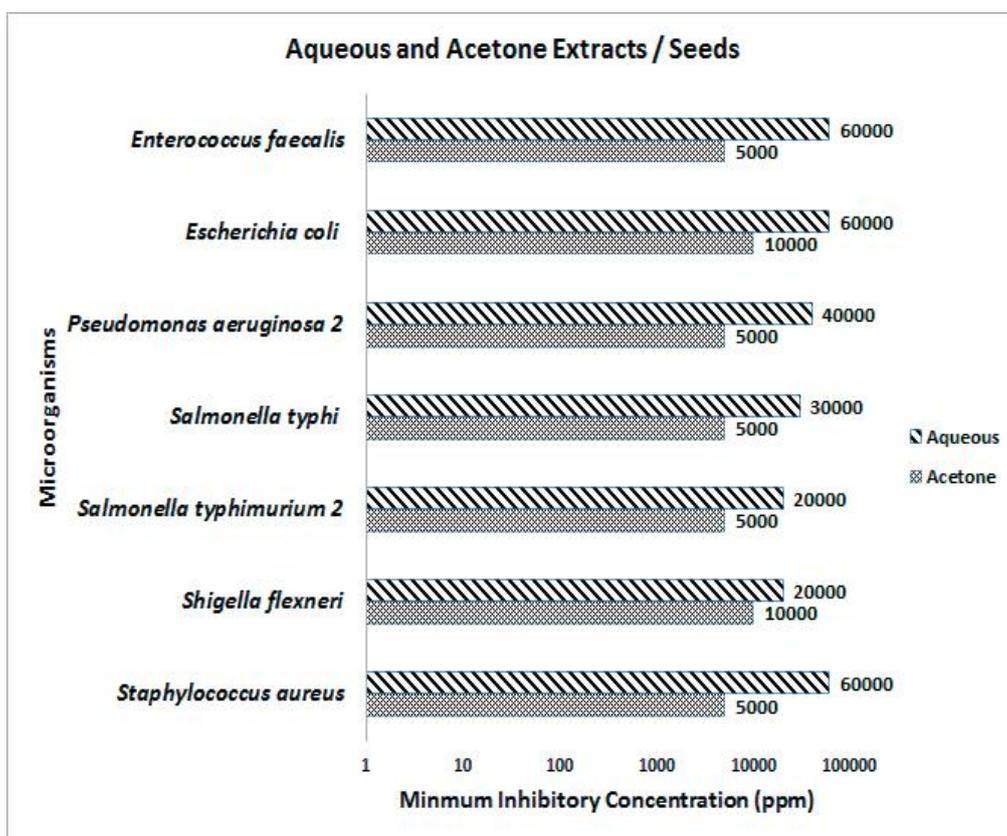
Microorganism	Extraction Method	MIC Value	MIC Value (PPM)	Reference
<i>Aspergillus flavus</i>	Ethanol	12.5 µg/ml	12.5	(Roby et al. 2012)
<i>Aspergillus flavus</i>	Methanol	10 µg/ml	10	(Roby et al. 2012)
<i>Bacillus cereus</i>	Ethanol	15 µg/ml	15	(Roby et al. 2012)
<i>Bacillus cereus</i>	Methanol	12.5 µg/ml	12.5	(Roby et al. 2012)
<i>Bacillus megaterium</i>	Methanol	3.7 (% , v/v)	37,000	(Gulfraz et al. 2008)
<i>Bacillus pumilus</i>	Methanol	8.33 mg/ml	8,330	(Dua et al. 2013)
<i>Candida albicans</i>	Ethanol	10 µg/ml	10	(Roby et al. 2012)
<i>Candida albicans</i>	Methanol	10 µg/ml	10	(Roby et al. 2012)
<i>Escherichia coli</i>	Ethanol	15 µg/ml	15	(Roby et al. 2012)
<i>Escherichia coli</i>	Methanol	15 µg/ml	15	(Roby et al. 2012)
<i>Klebsiella pneumoniae</i>	Methanol	2.5 (% , v/v)	25,000	(Gulfraz et al. 2008)
<i>Listeria monocytogenes</i>	Methanol	>2640 mg/L	2,640	(Alzoreky and Nakahara 2003)
<i>Micrococcus luteus</i>	Methanol	3.1 (% , v/v)	31,000	(Gulfraz et al. 2008)
<i>Pseudomonas aeruginosa</i>	Methanol	>33.33 mg/ml	33,330	(Dua et al. 2013)
<i>Pseudomonas putida</i>	Methanol	1.4 (% , v/v)	14,000	(Gulfraz et al. 2008)
<i>Pseudomonas syringae</i>	Methanol	1.3 (% , v/v)	13,000	(Gulfraz et al. 2008)
<i>Salmonella infantis</i>	Methanol	>2640 mg/L	2,640	(Alzoreky and Nakahara 2003)
<i>Salmonella typhi</i>	Ethanol	15 µg/ml	15	(Roby et al. 2012)
<i>Salmonella typhi</i>	Methanol	15 µg/ml	15	(Roby et al. 2012)
<i>Staphylococcus aureus</i>	Ethanol	15 µg/ml	15	(Roby et al. 2012)
<i>Staphylococcus aureus</i>	Methanol	12.5 µg/ml	12.5	(Roby et al. 2012)



**Fig 2.** Minimum Inhibitory Concentration (MIC) in parts per million (ppm) of methanolic and ethanolic extracts from *F. vulgare* seeds on the tested microorganisms. Methanolic extract is the second most used extract after the essential oil extract. The methanolic and ethanolic extracts have similar MIC values.

**Table 3.** List of tested microorganisms and the antimicrobial activity of acetone and aqueous extracts of *F. vulgare* seeds expressed as MIC values.

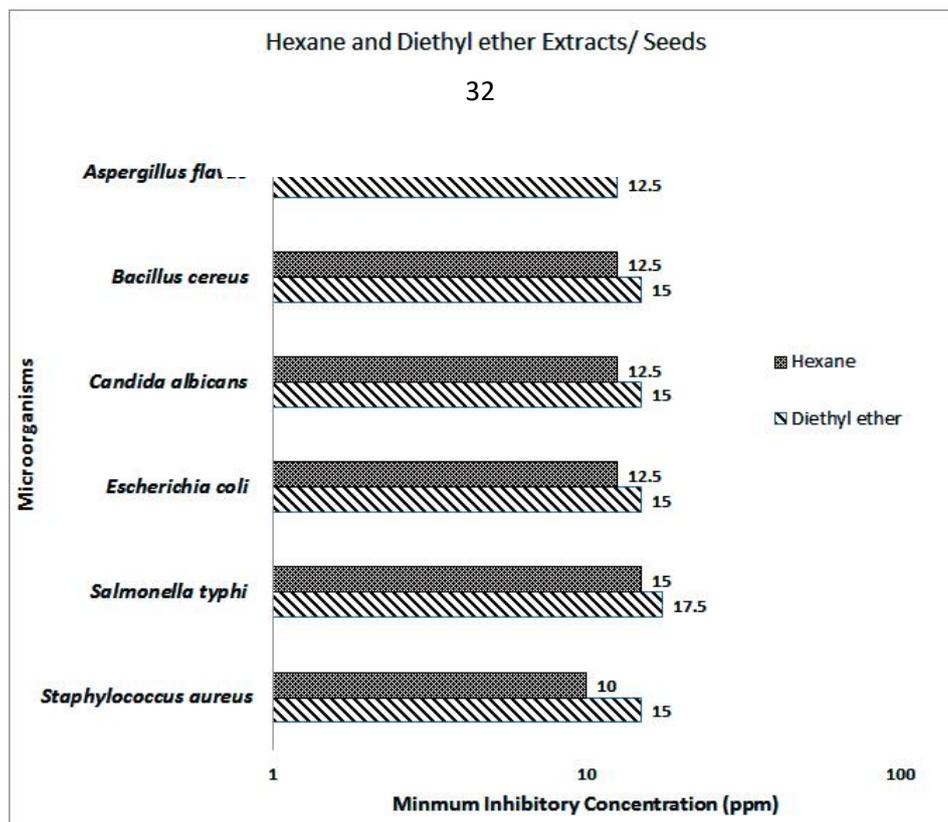
Microorganism	Extraction Method	MIC Value (mg/ml)	MIC Value (ppm)	Reference
<i>Enterococcus faecalis</i>	Acetone	5	5,000	(Kaur and Arora 2009)
<i>Enterococcus faecalis</i>	Aqueous	60	60,000	(Kaur and Arora 2009)
<i>Escherichia coli</i>	Acetone	10	10,000	(Kaur and Arora 2009)
<i>Escherichia coli</i>	Aqueous	60	60,000	(Kaur and Arora 2009)
<i>Pseudomonas aeruginosa 2</i>	Acetone	5	5,000	(Kaur and Arora 2009)
<i>Pseudomonas aeruginosa 2</i>	Aqueous	40	40,000	(Kaur and Arora 2009)
<i>Salmonella typhi</i>	Acetone	5	5,000	(Kaur and Arora 2009)
<i>Salmonella typhi</i>	Aqueous	30	30,000	(Kaur and Arora 2009)
<i>Salmonella typhimurium 2</i>	Acetone	5	5,000	(Kaur and Arora 2009)
<i>Salmonella typhimurium 2</i>	Aqueous	20	20,000	(Kaur and Arora 2009)
<i>Shigella flexneri</i>	Acetone	10	10,000	(Kaur and Arora 2009)
<i>Shigella flexneri</i>	Aqueous	20	20,000	(Kaur and Arora 2009)
<i>Staphylococcus aureus</i>	Acetone	5	5,000	(Kaur and Arora 2009)
<i>Staphylococcus aureus</i>	Aqueous	60	60,000	(Kaur and Arora 2009)



**Fig 3.** Minimum Inhibitory Concentration (MIC) in parts per million (ppm) of aqueous and acetone extracts from *F. vulgare* seeds on the tested microorganisms. The inhibitory effects of aqueous and acetone extracts are not as strong as the essential oil or the alcoholic extracts. The acetone extract has a stronger inhibitory effect than the aqueous extract.

**Table 4.** List of tested microorganisms and the antimicrobial activity of hexane and diethyl ether extracts of *F. vulgare* seeds expressed as MIC values.

Microorganism	Extraction Method	MIC Value ( $\mu\text{g/ml}$ )	MIC Value (ppm)	Reference
<i>Aspergillus flavus</i>	Hexane	10	10	(Roby et al. 2012)
<i>Aspergillus flavus</i>	Diethyl Ether	12.5	12.5	(Roby et al. 2012)
<i>Bacillus cereus</i>	Hexane	12.5	12.5	(Roby et al. 2012)
<i>Bacillus cereus</i>	Diethyl Ether	15	15	(Roby et al. 2012)
<i>Candida albicans</i>	Hexane	12.5	12.5	(Roby et al. 2012)
<i>Candida albicans</i>	Diethyl Ether	15	15	(Roby et al. 2012)
<i>Escherichia coli</i>	Hexane	12.5	12.5	(Roby et al. 2012)
<i>Escherichia coli</i>	Diethyl Ether	15	15	(Roby et al. 2012)
<i>Salmonella typhi</i>	Hexane	15	15	(Roby et al. 2012)
<i>Salmonella typhi</i>	Diethyl Ether	17.5	17.5	(Roby et al. 2012)
<i>Staphylococcus aureus</i>	Hexane	10	10	(Roby et al. 2012)
<i>Staphylococcus aureus</i>	Diethyl Ether	15	15	(Roby et al. 2012)



**Fig 4.** Minimum Inhibitory Concentration (MIC) in parts per million (ppm) of hexane and diethyl ether extracts. Hexane extract has similar antimicrobial activity as diethyl ether extract; however, hexane showed a lower MIC value than that of diethyl ether for all tested microorganisms.

lower MIC value than diethyl ether extract. For most of the tested microorganisms, the MIC value was 2.5 ppm higher using diethyl ether extract than the MIC value using hexane extract for the same tested microorganism. The exception was *Staphylococcus aureus*, which had a difference of 5.0 ppm MIC value between the hexane and diethyl ether extracts (Table 4 and Figure 4).

#### Essential oil extracted from the leaves

Essential oil extracted from *F. vulgare* leaves had much higher MIC values than essential oil extracted from the seeds for the tested microorganisms, except for *Aspergillus niger* (Tables 1 and 5 and Figure 5).

#### Discussion

This is a mathematical approach to compare the data of different experiments of antimicrobial activity of *F. vulgare* using MIC values. MIC is the minimum concentration of the extract that is needed to inhibit the growth of a microorganism. High MIC value does not, necessary, mean that the extract is not inhibitory against the microorganism; however, a low MIC value definitely means the extract is very inhibitory. Essential oil is the most used extract of *F. vulgare* seeds to test for antimicrobial activity. Therefore, the number of microorganisms that showed antimicrobial activity using seeds of *F. vulgare* essential oil is more than the number of microorganisms that showed antimicrobial activity using any other extraction method. Some microorganisms had high MIC value, regardless of the extraction method, such as *Micrococcus luteus*, *Pseudomonas putida*, and

*Pseudomonas syringae*. *Bacillus megaterium* had a low MIC value using the essential oil, but had a high value using the methanolic extract. This could be due to the fact that MIC value of the methanolic extract was calculated from (% v/v) not from (w/v).

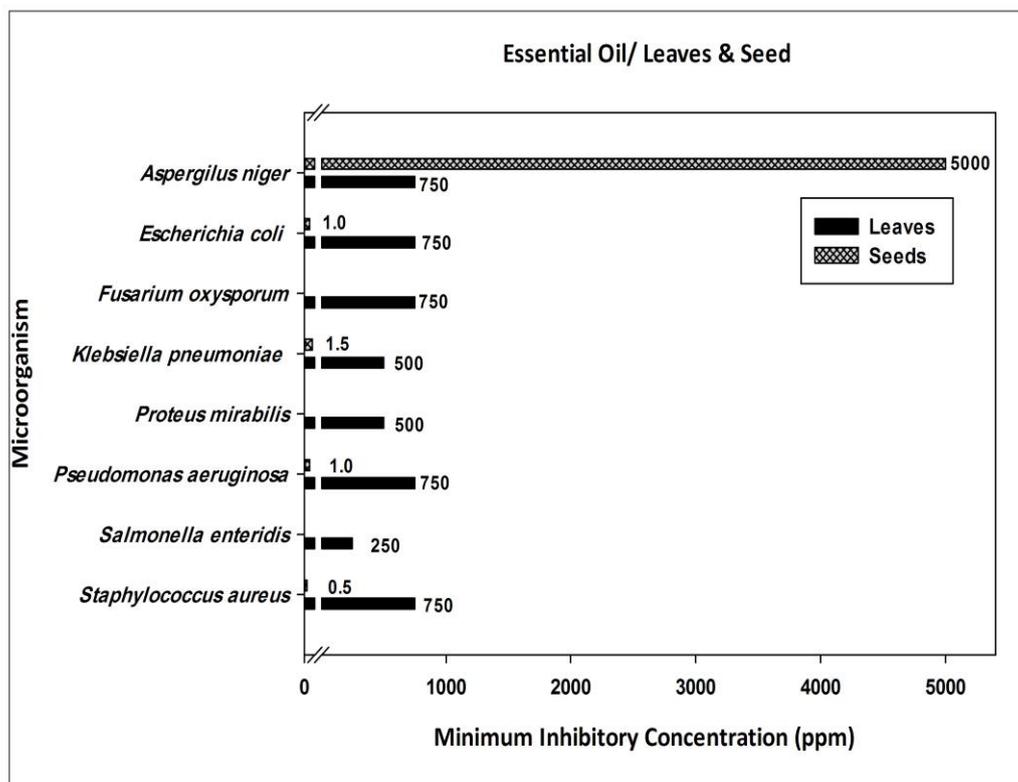
Some extracts showed high inhibitory antimicrobial activity. For instance, *Bacillus cereus*, *Escherichia coli*, *Salmonella typhi*, and *Staphylococcus aureus* have low MIC values when essential oil or alcoholic extract is used as an antimicrobial agent. However, the essential oil extract had more inhibitory effect than that of the alcoholic extracts on the same tested microorganisms. This could be explained by different scenarios. One scenario is that the inhibitory material that exists in the essential oil extract is different than what exists in the alcoholic extracts. The other scenario is that the nature of the inhibitory material is the same in the essential oil and the alcoholic extracts, but the concentration or/and the purity is higher in the essential oil than in the alcoholic extracts.

The inhibition of the microorganism can be specific for the species. For instance, by using essential oil extract, *Pseudomonas putida* and *Pseudomonas syringae* had high MIC values while *Pseudomonas aeruginosa* had a low MIC value. However, this is not always the case. For instance, *Bacillus* had a low MIC value, regardless of the species, using the essential oil extract. Interestingly, using methanolic extract, *Bacillus cereus* had a low MIC value, whereas *Bacillus megaterium* and *Bacillus pumilus* had high MIC values. In this case, the mode of inhibition is dependent on the species.

The antimicrobial activity of methanolic extract is similar to the ethanolic extract. However, methanolic extract had equivalent or lower MIC values than for the ethanol extract

**Table 5.** List of tested microorganisms and the antimicrobial activity of essential oil extract of *F. vulgare* leaves expressed as MIC values.

Microorganism	MIC Value( $\mu\text{g/ml}$ )	MIC Value(ppm)	Reference
<i>Aspergillus niger</i>	750	750	(Martins et al. 2012)
<i>Escherichia coli</i>	750	750	(Martins et al. 2012)
<i>Fusarium oxysporum</i>	750	750	(Martins et al. 2012)
<i>Klebsiella pneumoniae</i>	500	500	(Martins et al. 2012)
<i>Proteus mirabilis</i>	500	500	(Martins et al. 2012)
<i>Pseudomonas aeruginosa</i>	750	750	(Martins et al. 2012)
<i>Salmonella enteridis</i>	250	250	(Martins et al. 2012)
<i>Staphylococcus aureus</i>	750	750	(Martins et al. 2012)



**Fig 5.** Minimum Inhibitory Concentration (MIC) in parts per million (ppm) of essential oil extracted from *F. vulgare* leaves on the tested microorganisms. Essential oil extracted from the leaves had higher MIC values than essential oil extracted from the seed for the same tested microorganisms, except *Aspergillus niger*.

for the same tested microorganisms. This is expected since the chemistry of methanol is close to the chemistry of ethanol. Therefore, the dissolved inhibitory materials of the extract could be similar with the same concentrations. Aqueous and acetone extracts of *F. vulgare* seeds had high MIC values for all tested microorganisms. However, acetone extract had lower MIC values than the MIC values of aqueous extract for the same tested microorganisms. This means that acetone extract of *F. vulgare* seeds is a stronger antimicrobial agent than that of aqueous extract.

Other extraction methods were used for *F. vulgare* seeds. Hexane and diethyl ester had low MIC values for some of the tested microorganisms. However, hexane had lower MIC values for all the tested microorganisms. Hexane, diethyl ether, and alcoholic extracts had lower MIC values than those of the essential oil for the tested fungi *Aspergillus flavus* and *Candida albicans*. This probably indicates that hexane, diethyl ether, and alcoholic extracts contain stronger antifungal agents than those of the essential oil.

Other plant parts, beside the seeds, were used as a source of essential oil. However, most research on *F. vulgare* was focused on the essential oil extracted from the seeds. The

essential oil extracted from *F. vulgare* leaves was not as effective as the essential oil extracted from its seeds. However, the number of the tested microorganisms using the essential oil extracted from the seeds is much more than the number of tested microorganisms using the essential oil extracted from the leaves. Therefore, a fair comparison of the effectiveness of the extracted plant part cannot be made. However, for those tested microorganisms of both plant parts (leaves and seeds), antimicrobial strength, in most cases, is much more in the essential oil extracted from the seeds than that extracted from the leaves. The only exception microorganism is *Aspergillus niger*, which has lower MIC value for leaves than seeds.

### Methodology

Articles related to studying the antimicrobial activity of *F. vulgare* were collected. Information was entered into *Microsoft Excel* and an *Access* database. To make the data analysis quantitative, only those experiments that reported MIC were considered. Since *F. vulgare* has a dry fruit, "fruits" mentioned in the articles was considered as "seeds."

To make a scientific fair comparison between the different experiments in the literature, MIC units reported in the experiments were converted to parts per million (ppm). For those studies that used a value of MIC with bigger sign, the exact maximum MIC value was used in the analysis. Figures were generated using *Microsoft Excel* and *SigmaPlot* programs.

## Conclusion

*F. vulgare* is an important medicinal plant. The plant extract has been proven to work as an antimicrobial agent for many tested microorganisms. The most common extract of *F. vulgare* is the essential oil of the seeds. The seeds have stronger antimicrobial activity than any other plant part. The essential oil extracted from the seeds does not work in the same manner as antimicrobial agent, when compared with the alcoholic extract of the seeds. This could be due to the different chemical compositions of the two extracts. Inhibition selectivity depends not only on the plant extract method, but also on the microorganism species. *F. vulgare* extract has high potential to be an effective antibiotic drug. Further experiments are needed to purify and fractionalize the crude extract to be tested *in vivo* as an antibiotic drug.

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