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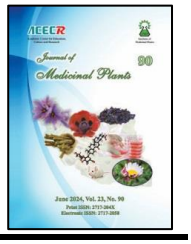

Research Article

Investigation of the antibacterial effect of *Ferula foetida* (Bunge) Regel oleo-gum-resin extracts and essential oil on methicillin-resistant *Staphylococcus aureus* and its simultaneous effect with vancomycin

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ABSTRACT

Background: Nowadays, the decreased susceptibility of *Staphylococcus aureus* (*S. aureus*) to last-resort antibiotics such as vancomycin has caused concern in both human and veterinary medicine. Therefore, the need to find alternative treatments and new antibacterial agents is felt more than ever. **Objective:** The antibacterial effect and simultaneous effect of *Ferula foetida* (Bunge) Regel (*F. foetida*) oleo-gum-resin (OGR) extract and vancomycin on methicillin-resistant *Staphylococcus aureus* (MRSA) were investigated. **Methods:** Aqueous, ethanolic, a mixture of aqueous and ethanolic extracts, and essential oil were prepared from *F. foetida* OGR collected from Beyrut village, Sabzevar, Razavi Khorasan province, Iran. The Checkerboard method was used to determine the minimum inhibitory concentrations (MICs) of vancomycin and plant extracts and essential oil, and their simultaneous effects on MRSA (ATCC 33591). The minimum bactericidal concentrations (MBCs) of these agents were also determined. Ethanolic extract and essential oil of *F. foetida* OGR were analyzed using gas chromatography-mass spectrometry (GC-MS). **Results:** The MICs of vancomycin and aqueous, ethanolic, a mixture of aqueous and ethanolic extracts, and essential oil of *F. foetida* OGR were 0.00195 mg/ml, 8 mg/ml, 0.25 mg/ml, 0.5 mg/ml, and 256 mg/ml, respectively. The MBCs of these agents were 0.0078 mg/ml, 64 mg/ml, 0.5 mg/ml, 2 mg/ml, and more than 512 mg/ml, respectively. The simultaneous use of the extracts and essential oil of this plant with vancomycin on MRSA showed partial synergistic to additive effects. **Conclusion:** The combinations of *F. foetida* OGR extracts or essential oil with vancomycin are expected to reduce the effective dose of vancomycin against MRSA.

Abbreviations: MRSA, Methicillin-resistant *Staphylococcus aureus*; GC-MS, Gas chromatography-mass spectrometry; CAMHB, Cation-adjusted mueller-hinton broth; MIC, Minimum inhibitory concentration; MBC, Minimum bactericidal concentration; FIC, Fractional inhibitory concentration; OD, Optical density; MSSA, Methicillin-sensitive *Staphylococcus aureus*; RT, Retention time; Mw, Molecular weights; FIC_V, Fractional inhibitory concentration of vancomycin; FIC_E, Fractional inhibitory concentration of the *F. foetida* oleo-gum-resin extracts or essential oil; FICI, Fractional inhibitory concentration index

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1. Introduction

Staphylococcus aureus is a commensal bacterium found on the skin and mucous membranes of humans and animals. Its infection begins when the microorganism enters through a break in the skin or mucosa. Thereafter, a wide variety of infections can occur, from superficial skin diseases to deep infections and septicemia [1].

Treatment of infections caused by *S. aureus* relies on antibiotics. So, their resistance to common antibiotics is a therapeutic challenge. *S. aureus*, especially methicillin-resistant *S. aureus* (MRSA), can cause life-threatening invasive infections in humans. These infections can be acquired in the community or a hospital. Moreover, this bacterium is the primary cause of mastitis in dairy cows and results in economic losses in livestock production. Recently, MRSA has been isolated from animals and food of animal origin, raising public concerns about the transmission of MRSA from food of animal origin to humans. Furthermore, direct contact with animals harboring MRSA can lead to the colonization of these strains in contact with humans, and they become a carrier for the transmission of MRSA to others [1, 2].

Vancomycin is an antibiotic of last resort, used only after other antibiotics have failed to treat life-threatening infections caused by Gram-positive bacteria. Currently, vancomycin has become the most common drug of choice for the treatment of MRSA [3]. However, the emergence of vancomycin-resistant MRSA strains has necessitated the development of alternative antimicrobial agents, especially those of plant origin [4].

Plants contain bioactive compounds including alkaloids, flavonoids, tannins, and phenolic compounds. Phytochemicals isolated from medicinal plants exhibit diverse antimicrobial activities. Therefore, they can be used as antimicrobial agents [5].

The genus *Ferula* is a member of the *Apiacae* family and contains approximately 185 species. These plants contain bioactive compounds, such as sulfur-containing compounds, terpenoid coumarins, and sesquiterpenes. Monoterpenes and sesquiterpenes and their oxygenated forms are the major constituents of these plants which have antimicrobial properties [6]. *Ferula foetida* (Bunge) Regel is a plant native to Central Asia (Qezel Qom Desert, Qara Qom Desert, Turkmenistan), eastern Iran, western Afghanistan, and western Pakistan [7]. The gum obtained from this plant has an unpleasant sulfurous odor similar to garlic, so it has been nicknamed the devil's dung. Its gum has been used as an anthelmintic and anti-rheumatism [8, 9]. Most of the previous studies have been conducted on the therapeutic properties of other *Ferula* species [6, 10, 11]. Therefore, in the present study, we investigated the antibacterial and the simultaneous effect of extracts and essential oil of *F. foetida* OGR and vancomycin on MRSA strain. Moreover, the constituents of the extract and essential oil of *F. foetida* oleo-gum-resin (OGR) were also determined using gas chromatography-mass spectrometry (GC-MS) to obtain information about the antibacterial properties of this species of *Ferula* plant.

2. Materials and methods

2.1. Preparation of Plant Extracts and Essential oil

F. foetida OGR was collected from Beyrut village, Sabzevar county, Razavi Khorasan province, Iran. The plant species was confirmed by A.R. Khosravi, a plant taxonomist at Herbarium of Shiraz University (HSHU), Biology Department, School of Sciences, Shiraz

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University, Shiraz, Iran, where a voucher specimen (No. 55122) was deposited.

To prepare *F. foetida* OGR essential oil, 50 g of plant gum was extracted with 1 liter of distilled water using a Clevenger machine for 4 h. Finally, 5504 µL of essential oil was obtained and dehydrated by adding sodium sulfate.

To prepare the ethanolic extract of *F. foetida* OGR, 25 g of the plant gum was shaken with 250 ml of 97 % ethanol for 48 h at 37 °C at 1500 rpm. The obtained solution was filtered through filter paper (Whatman, England). Excess ethanol was removed by a rotary vacuum evaporator (IKA, Germany). After 48 h of storage in an oven at 37 °C, 862 µL of ethanolic extract was obtained.

To prepare the aqueous extract of *F. foetida* OGR, 25 g of plant gum was shaken with 250 ml of distilled water for 48 h at 37°C at 1500 rpm. The obtained solution was filtered with sterile gauze and filter paper (Whatman, England) and freeze-dried (Christ, Germany) for 24 h. Finally, 7.908 g of aqueous extract was obtained.

A mixture of aqueous and ethanolic extracts of *F. foetida* OGR was prepared by mixing equal amounts of aqueous and ethanolic extracts.

2.2. Gas chromatography-mass spectrometry (GC-MS)

The chemical composition of the ethanolic extract and essential oil of *F. foetida* OGR were analyzed using 7890B GC & 5977A series gas chromatography-mass spectrometry (GC-MS) (Agilent Technologies, United States). The essential oil was diluted 1:100 with n-hexane and then injected into the device. Helium gas was used as the carrier gas at a constant flow rate of 1 mL/min. The column temperature reached 60 °C, then increased to 220 °C at a rate of 5 °C/min, and finally to 280 °C at a rate of 3 °C/min. Mass spectra were obtained at 70 eV. The entire GC/MS run took 58 minutes [12].

2.3. Bacteria

MRSA (ATCC 33591, IBRC 10690) was purchased from the National Center for Genetic and Biological Resources of Iran.

2.4. Checkerboard Assay

To evaluate the antibacterial effects of vancomycin and plant extracts or essential oil on MRSA (ATCC 33591, IBRC 10690) both alone and in combinations, the checkerboard assay was performed in 96-well microtiter plates.

To perform the checkerboard assay, 100 µL of 2X cation-adjusted Mueller-Hinton broth (CAMHB) medium (Lab M, UK) was poured into each well of a microtiter plate using a multichannel sampler. Then 100 µL of vancomycin solution (0.0624 mg/ml) was added to wells A (1-11) and serially diluted from wells A to G. Next, 100 µL of vancomycin solution (0.1248 mg/ml) was poured into the A12 well and serially diluted to the G12 well. Then 100 µL of the contents of G (1-12) wells were discarded.

Depending on the experiment, 100 µL aqueous extract of *F. foetida* OGR (512 mg/mL), or ethanolic extract of *F. foetida* OGR (8 mg/mL) or a mixture of aqueous and ethanolic extracts of *F. foetida* OGR (64 mg/mL) or *F. foetida* OGR essential oil (2048 mg/mL) was added to wells 12 (A-H) and serially diluted from wells 12 to wells 2 in each row. Then 100 µL from the contents of 2 (A-H) wells were discarded. After that, 100 µL of a1:100 dilution of bacterial suspension equivalent to 0.5 McFarland standard was added to each microtiter plate well so that the final concentration of MRSA in each well was about 5×10^5 CFU⁄mL.

Based on this method, the minimum inhibitory concentration (MIC) of vancomycin can be determined in column 1 (wells A to G) of the microtiter plate. The MIC of *F. foetida* OGR extracts or essential oil can be determined in row

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H (wells from 12 to 2). The H1 well only contains 2X CAMHB medium and MRSA suspension and did not include vancomycin and plant extracts or essential oil and was considered a bacterial growth control well. The other 77 wells of the microtiter plate had a combination of different concentrations of vancomycin and extracts or essential oil of *F. foetida* OGR and were used to determine the simultaneous effect of vancomycin and extracts or essential oil of plant on MRSA.

Each experiment was repeated at least three times. For each experiment, a background microtiter plate containing all components except the MRSA suspension was prepared. After putting the lid on the microtiter plates, they were incubated for 24 h at 37°C. Next, the optical density (OD) of the contents of each well was read at 600 nm. Subsequently, the ODs of the experiments and the background microtiter plates were compared. The percentage of bacterial growth in each well was calculated using the following equation:

$$\frac{\mathrm{OD(drug\ combination\ well)} - \mathrm{OD(background)}}{\mathrm{OD(drug\ free\ well)} - \mathrm{OD(background)}} \times 100$$

Then, the lowest concentrations of vancomycin, plant extracts, or essential oil that reduce the growth of MRSA by more than 80% were considered as MIC [13].

2.5. Fractional Inhibitory Concentration (FIC) Index

The FIC index is equal to the sum of FIC (extracts or essential oil of *F. foetida*) and FIC (vancomycin). To determine the FIC (*F. foetida* extracts or essential oil), the MIC of the combination of plant extracts or essential oil with vancomycin is divided by the MIC of the plant extracts or essential oil alone. To determine the FIC (vancomycin), the MIC of the combination of plant extracts or essential oil with vancomycin is divided by the MIC of vancomycin alone [14].

FIC index values less than 0.5 indicate a synergistic effect, values between 0.5-0.75 indicate partial synergy, values between 0.76-1 indicate an additive effect, values between 1-4indicate an indifference effect, and values above 4 indicate an antagonism effect [14].

2.6. Minimum Bactericidal Concentration (MBC)

To determine the MBC, which is the lowest concentration of an antimicrobial agent that can kill at least 99.9 % of the initial bacterial inoculum [15], 10 µl of the contents of the clear wells were spread on the Mueller–Hinton agar medium plates. Then the plates were incubated overnight at 37 °C.

3. Results

3.1. GC-MS

GC-MS analysis of essential oil and extract showed the presence of various phytochemicals. The specifications of these compounds are listed in Tables 1 and 2. GC-MS analysis graphs are shown in Figures 1 and 2.

3.2. MIC

The MIC, which is the lowest concentration of an antimicrobial agent that inhibits bacterial growth, was 0.00195 mg/ml, 8 mg/ml, 0.25 mg/ml, 0.5 mg/ml, and 256 mg/ml for vancomycin and aqueous, ethanolic, a mixture of aqueous and ethanolic extracts, and essential oil of *F. foetida* OGR, respectively. Among the studied extracts and essential oils, the ethanolic extract of *F. foetida* OGR showed the highest inhibitory effect and its essential oil showed the lowest inhibitory effect against MRSA.

[DOI: 10.61186/jmp.23.90.82]

3.3. MBC

The MBC of vancomycin and aqueous, ethanolic, a mixture of aqueous and ethanolic extracts, and essential oil of *F. foetida* OGR were 0.0078 mg/mL, 64 mg/mL, 0.5 mg/ml, 2 mg/ml, and more than 512 mg/ml, respectively. Among the studied extracts and essential oil, the ethanolic extract of *F. foetida* OGR showed the highest bactericidal effect and its essential oil showed the lowest bactericidal effect against MRSA.

Table 1. Chemical composition of *F. foetida* OGR ethanolic extract

NO.	RT	Component names	Mw (g/mol)	Chemical classification	Area	Molecular Formula
1	35.914	(2-cyclopropylethenyl)- Benzene	146.23	Aromatic hydrocarbons	22.612	C9H12O
2	25.329	β-Guaiene	204.35	Sesquiterpene	15.263	C15H24
3	19.156	Butanamide, 2-hydroxy-N,3,3-trimethyl-	145.20	Amides	11.38	C7H15NO2
4	32.539	8-Methyl-9-oxapentacyclo[5.4.0.0^{2,11}.0^{3,10}.0^{4,8}]undec-5-ene	160.212	Polycyclic	8.804	C11H12O
5	27.025	Myristic acid	228.37	Long-chain fatty acids	6.526	C14H28O2
6	37.808	Myristic acid β-monoglyceride	302.446	Long-chain fatty acids	5.575	C17H34O4
7	22.63	Lauric acid	200.32	Medium-chain fatty acids	4.706	C12H24O2
8	34.363	Oleic acid	282.5	Omega-9 fatty acid	4.635	C18H34O2
9	12.11	Triethylarsine	162.10	Organoarsenic	3.665	C6H15As
10	11.958	1,3-Dithiolane	106.21	Heterocyclic organic	3.248	C3H6S2
11	30.994	Palmitic acid	256.42	Long-chain fatty acids	2.218	C16H32O2
12	4.905	Styrene	104.15	Aromatic hydrocarbon	2.152	C8H8
13	24.647	(R)-γ-cadinene	204.35	Sesquiterpene	2.054	C15H24
14	11.212	3,5-Dimethylisothiazole	113.18	Heterocyclic organic	1.819	C5H7NS
15	23.225	Guaiol	222.372	Sesquiterpenoid alcohol	1.384	C15H26O
16	23.918	γ-Eudesmol	222.37	Eudesmane sesquiterpenoid	1.338	C15H26O
17	12.576	3,5-Dimethylisothiazole	113.18	Heterocyclic organic	1.116	C5H7NS
18	46.854	Di-n-octyl phthalate	390.6	Benzoic acid esters	0.908	C24H38O4
19	24.857	Bulnesol	222.37	Sesquiterpene alcohol	0.597	C15H26O

RT: Retention time, Mw: Molecular weights, Area %: Concentrations

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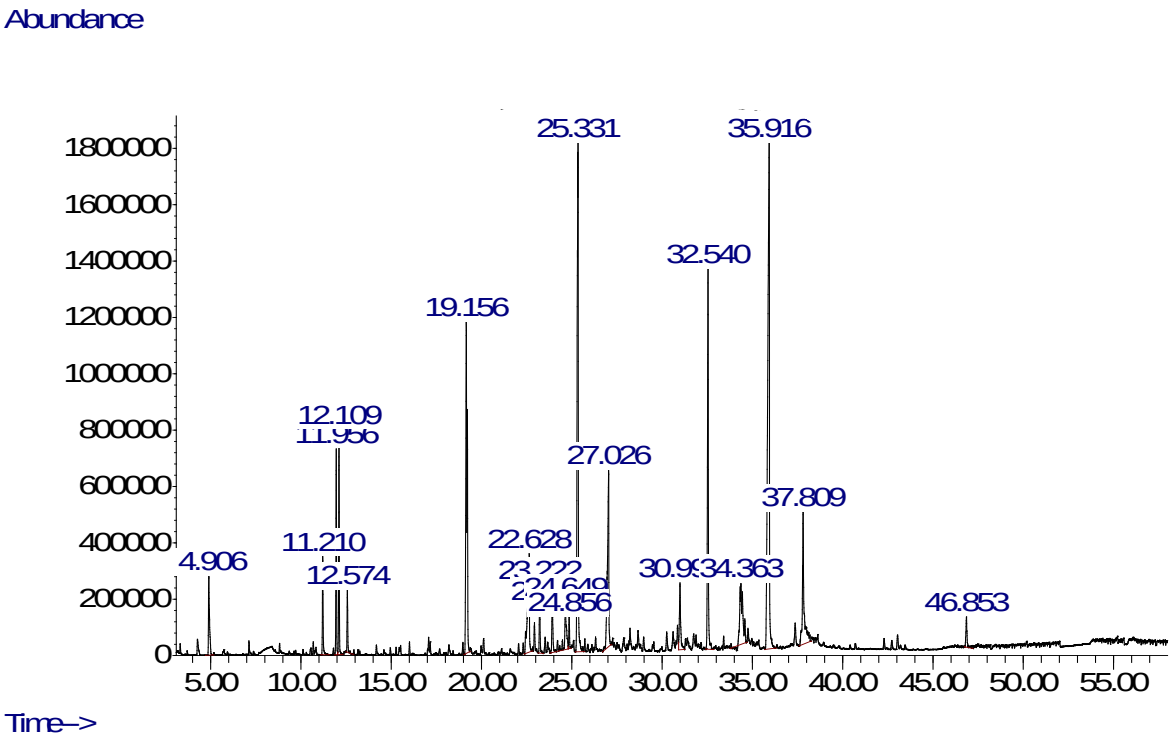

Fig. 1. GC-MS analysis graph of *F. foetida* OGR ethanolic extract

Table 2. Chemical composition of *F. foetida* OGR essential oil

NO.	RT	Component names	Mw (g/mol)	Chemical classification	Area%	Molecular Formula
1	12.209	Triethylarsine	162.10	Organoarsenic	31.347	C6H15As
2	19.407	Dimethyl thioformamide	89.16	Thioamide	27.523	C3H7NS
3	12.389	Triethylarsine	162.10	Organoarsenic	22.721	C6H15As
4	19.477	2-Nitrobenzyl chloride	185.56	Nitrobenzenes	7.329	C7H4ClNO3
5	25.323	4,6-Guaiadiene	202.33	Diene	3.033	C15H22
6	17.116	3,6-Dimethyl-2,4,5,7-tetrathiaoctane	213.998	Alkane	1.59	C12H26
7	20.182	Methane thioamide, N,N-dimethyl-	89.159	Formamides	1.174	C3H7NS
8	17.204	3,6-Dimethyl-2,4,5,7-tetrathiaoctane	213.998	Alkane	1.107	C12H26
9	26.349	Methane thioamide, N,N-dimethyl-	89.159	Formamides	0.84	C3H7NS
10	18.224	Ethanol, 2-(trimethylsilyl)-	118.25	Silyl ethers	0.798	C5H14OSi
11	6.736	β-Pinene	136.237	Hydrocarbon monoterpene	0.507	C10H16
12	4.905	Styrene	104.15	Aromatic hydrocarbon	0.504	C8H8
13	13.2	Butyl disulfide	178.4	Organic sulfur	0.463	C8H18S2
14	23.924	γ-Eudesmol	222.37	Sesquiterpene alcohol	0.393	C15H26O
15	8.403	(E)-β-Ocimene	136.23	Hydrocarbon monoterpene	0.381	C10H16
16	16.026	Camphene	136.23	Hydrocarbon monoterpene	0.287	C10H16

RT: Retention time, Mw: Molecular weights, Area %: Concentrations

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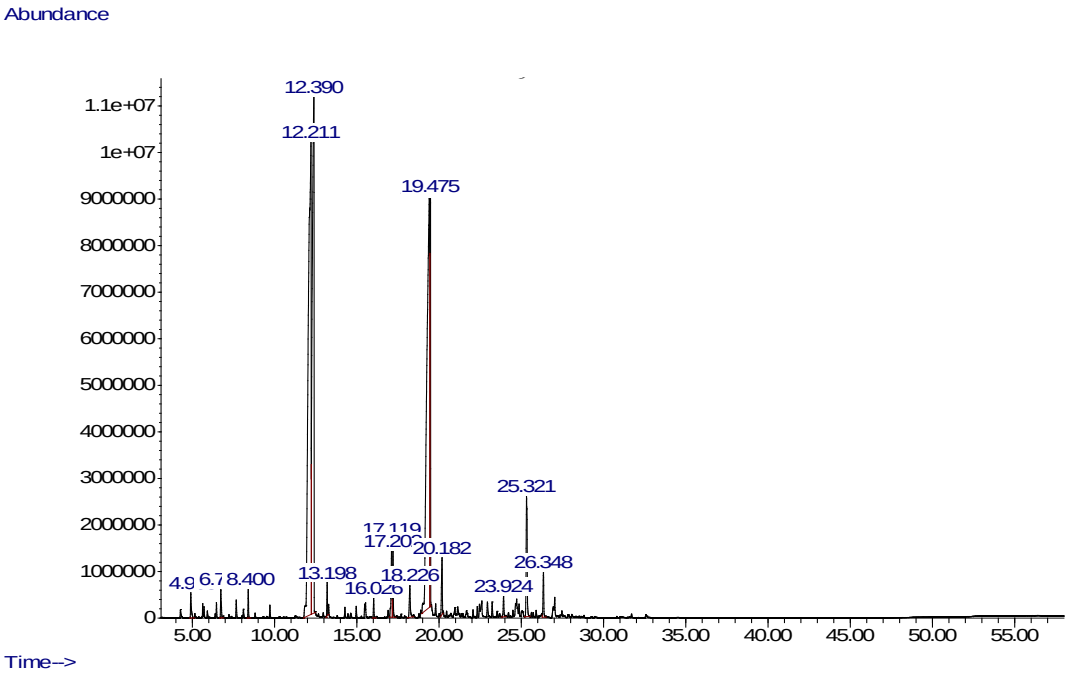

Fig. 2. GC-MS analysis graph of *F. foetida* OGR essential oil

3.4. FIC index

The FIC index and the simultaneous effect of vancomycin and aqueous, ethanolic, a mixture of aqueous and ethanolic extracts, and essential oil of F. foetida OGR on MRSA strain are reported in Table 3.

The combination of ethanolic extract and vancomycin, the combination of a mixture of aqueous and ethanolic extracts with vancomycin, and the combination of essential oil and vancomycin showed a partial synergistic effect on MRSA strain. The combination of *F. foetida* OGR aqueous extract and vancomycin showed an additive effect.

Table 3. FIC index and simultaneous effect of vancomycin and *F. foetida* OGR extracts and essential oil on MRSA strain

Type of extract or essential oil	Concentration of extracts or essential oil (mg/ml)	Concentration of vancomycin (mg/ml)	FIC_V	FIC_E	FICI	Simultaneous effect
Aqueous extract	4	0.00097	0.497	0.5	0.997	**Additive effects**
Ethanolic extract	0.125	0.00048	0.246	0.5	0.746	**Partial synergy**
	0.031	0.00097	0.497	0.124	0.621	**Partial synergy**
Mixture of aqueous and ethanolic extract	0.25	0.00012	0.061	0.5	0.561	**Partial synergy**
Essential oil	8	0.00097	0.497	0.031	0.528	**Partial synergy**

FIC_V: Fractional inhibitory concentration of vancomycin; FIC_E: Fractional inhibitory concentration of *F. foetida* OGR extracts or essential oil; FICI: Fractional inhibitory concentration index

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4. Discussion

In this study, the main compounds of *F. foetida* OGR ethanolic extract were (2-cyclopropyl ethenyl)- benzene (22.612 %) and β-Guaiene (15.263 %). β-Guaiene is a sesquiterpene that has demonstrated various biological activities including antimicrobial, anti-inflammatory and anti-cancer properties [16]. Other sesquiterpene compounds found in the ethanolic extract include (R)-γ -cadinene, Guaiol, γ-Eudesmol and Bulnesol. Sesquiterpenoids can inhibit microorganisms in several ways [17].

Other components identified in the tested ethanolic extract included lauric acid, oleic acid, palmitic acid, myristic acid and myristic acid β-monoglyceride. The antimicrobial properties of these fatty acids have been proven in previous studies [18, 19, 20, 21, 22].

Regarding *F. foetida* OGR essential oil, the main components found in this study were triethylarsine (31.347 %) and dimethyl thioformamide (27.523 %). This essential oil also contains various terpenes including β-Pinene, γ-Eudesmol, (E)-β-Ocimene and camphene. The inhibitory effect of β-Pinene and camphene on various bacteria has been reported [23]. For example, camphene has antibacterial effects against important pathogenic bacteria such as *Enterococcus* spp. and *S. aureus*, including MRSA [24].

It is worth mentioning that in previous studies, there was no report on the content of *F. foetida* OGR essential oil and only the content of *F. assa- foetida* OGR was investigated. Although there are similarities between the components of *F. assa- foetida* OGR essential oil and *F. foetida* OGR essential oil [25, 26, 27, 28, 29]. In the present study, the MIC of vancomycin against MRSA ATCC 33591 was 0.00195 mg/mL. This amount has been reported as 0.002 mg/mL, 0.00391 mg/mL, and 0.001 mg/mL in previous studies [14, 30, 31].

It has been found that the antimicrobial activity of vancomycin can be increased by combining it with other antimicrobial agents. For example, the combination of vancomycin and oxacillin showed a synergistic effect on methicillin-resistant staphylococci [32, 33]. Considering the potential of herbal medicines to treat diseases and the different modes of action of phytochemicals compared to antibiotics, which become ineffective in a short time due to the development of resistance among bacteria, replacing plants with antimicrobial properties or combining them with existing antibiotics can help improve the treatment of the infections [5]. Moreover, in the case of vancomycin, which has toxic effects in high doses, the occurrence of drug resistance and side effects of vancomycin can be prevented by reducing the required dose of vancomycin [34, 4].

Several studies have been conducted on the antimicrobial properties of other species of the *Ferula* plant. For example, the MIC of the ethanolic extract of *F. assa-foetida* against *S. aureus* was 1 mg/mL [35]. The MICs of *F. assa-foetida* against MSSA ATCC 29213 and MRSA ATCC 33591 were 25 and 50 mg/mL, respectively [36]. The MIC of the essential oil of the aerial parts of *Ferula asafetida* against *S. aureus* was 12 mg/mL [37]. The MIC of *Ferula szowitsiana* leaf oil against MRSA was 0.000156 mg/mL [10]. The MICs of *Ferula cupularis* root, leaf, flower, and the stem essential oils against *S. aureus* ATCC 6538 were 2.85, 11.38, 22.75, and 2.85 mg/mL, respectively [11]. In the present study, we investigated the antimicrobial properties of *F. foetida* OGR, and the MICs of aqueous, ethanolic, a mixture of aqueous and ethanolic extracts, and its essential oil were determined to be 8 mg/ml, 0.25 mg/ml, 0.5

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mg/ml, and 256 mg/ml, respectively. Furthermore, with the simultaneous use of the extracts and essential oil of this plant with vancomycin on the MRSA strain, a partial synergistic to an additive effect was determined. Although there were no previous reports on the simultaneous effect of *F. foetida* OGR extracts or essential oil with vancomycin against *S. aureus* strains, several studies investigated the simultaneous effect of other plant extracts and vancomycin on *S. aureus* strains. For instance, the synergistic effect of *Quercus infectoria* gall extract in combination with vancomycin against MRSA, the synergistic effect of *Cryptotanshinone* and vancomycin against clinical strains of MRSA and vancomycin-resistant *S. aureus*, and the synergistic effect of *Canarium odontophyllum* Miq extract together with oxacillin or linezolid against MRSA ATCC 33591was reported [14, 31, 38].

5. Conclusions

The use of vancomycin in combination with *F. foetida* OGR extracts or essential oil is expected to reduce the required effective dose of vancomycin on MRSA strains. As a result, this may reduce the potential side effects and antibiotic resistance caused by higher doses of vancomycin. But more research is needed in this field.

Conflict of Interest

Nothing to declare.

Author Contributions

Z.GF. Investigation, Formal analysis (equal), Writing – original draft; Z.N. Conceptualization (equal), Funding acquisition (equal), Supervision (equal), Project administration (equal), Methodology, Formal analysis (equal), Validation (equal), Writing – review & editing; A.D. Conceptualization (equal), Funding acquisition (equal), Supervision (equal), Project administration (equal), Validation (equal); F.RF. Resources (Plant samples). All authors read and approved the final version of the manuscript.

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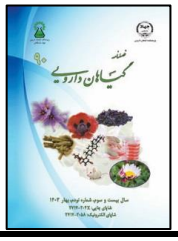

مقاله تحقیقاتی

بررسی اثر ضد باکتریایی عصاره و اسانس صمغ اولئو-رزین گیاه *Ferula foetida* (Bunge) Regel (گندکما) بر روی *Staphylococcus aureus* مقاوم به متی سیلین و اثر همزمان آن با وانکومایسین

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اطلاعات مقاله

گل‌واژگان:
استافیلوکوکوس اورئوس مقاوم به متی‌سیلین
فرولا فوتیدا
وانکومایسین
اثر ضدباکتریایی
چکربورد

چکیده

مقدمه: امروزه کاهش حساسیت *Staphylococcus aureus* نسبت به آنتی بیوتیک‌هایی که به عنوان آخرین راه حل درمانی‌اند مانند وانکومایسین باعث نگرانی هم در حوزه پزشکی و هم در دامپزشکی شده است. بنابراین نیاز به یافتن درمان‌های جایگزین و عوامل ضدباکتریایی جدید بیش از پیش احساس می‌شود. **هدف:** اثر ضدباکتریایی و اثر همزمان عصاره و اسانس صمغ اولئو-رزین (*F. foetida*) *Ferula foetida* (Bunge) Regel و وانکومایسین بر *S. aureus* مقاوم به متی‌سیلین (MRSA) بررسی شد. **روش بررسی:** از صمغ اولئو-رزین گیاه *F. foetida* جمع‌آوری شده از روستای بیروت، سبزوار، استان خراسان رضوی، ایران، عصاره آبی، اتانولی و مخلوطی از عصاره آبی و اتانولی و همچنین اسانس، تهیه شد. جهت تعیین حداقل غلظت‌های مهارکننده رشد (MICs) وانکومایسین و عصاره‌های گیاهی و اسانس و اثرات همزمان آنها بر MRSA (ATCC 33591) از روش چکربورد استفاده شد. حداقل غلظت‌های کشندگی باکتری (MBCs) این عوامل نیز تعیین شد. عصاره اتانولی و اسانس صمغ اولئو-رزین *F. foetida* با روش GC-MS مورد ارزیابی قرار گرفت. **نتایج:** MICs وانکومایسین و عصاره آبی، اتانولی، مخلوطی از عصاره‌های آبی و اتانولی و اسانس صمغ اولئو-رزین *F. foetida* به ترتیب ۰/۰۰۱۹۵ ، ۸ ، ۰/۲۵، ۰/۵ و ۲۵۶ میلی‌گرم در میلی‌لیتر بود. MBCs این عوامل نیز به ترتیب ۰/۰۰۷۸ ، ۶۴ ، ۰/۵، ۲ و بیش از ۵۱۲ میلی‌گرم در میلی‌لیتر بود. استفاده همزمان از عصاره و اسانس این گیاه با وانکومایسین بر روی MRSA اثرات هم‌افزایی نسبی تا جمع‌پذیر نشان دادند. **نتیجه‌گیری:** انتظار می‌رود ترکیبات عصاره یا اسانس *F. foetida* با وانکومایسین، دوز موثر مورد نیاز وانکومایسین بر علیه MRSA را کاهش دهند.

مخففها: MRSA، *Staphylococcus aureus* مقاوم به متی سیلین؛ GC-MS، کروماتوگرافی گازی -طیف سنجی جرمی؛ CAMHB، مولر-هینتون براث تنظیم شده با کاتیون؛ MIC، حداقل غلظت مهارکننده رشد؛ OD، چگالی نوری؛ FIC، غلظت بازدارندگی کسری؛ MBC، حداقل غلظت کشندگی باکتری؛ MSSA، *Staphylococcus aureus* حساس به متی‌سیلین؛ RT، زمان بازداری؛ Mw، جرم مولکولی؛ FIC_v، غلظت بازدارندگی کسری وانکومایسین؛ FIC_E، غلظت بازدارندگی کسری عصاره یا اسانس صمغ *Ferula foetida*؛ FICI، شاخص غلظت بازدارندگی کسری؛ mg، میلی‌گرم؛ mL، میلی‌لیتر؛ µl، میکرولیتر

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