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A Review on Antibacterial Effects of Iranian Herbal Medicine on Methicillin-Resistant *Staphylococcus aureus*

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Abstract

Context: *Staphylococcus aureus* (*S. aureus*) is an opportunistic pathogen that is able to cause different types of life-threatening infections from acute bacteremia to often chronic osteomyelitis, endocarditis, infections of indwelling devices and wound infections. These chronic infections are highly recalcitrant to antibiotic treatment. Owing to the increasing incidence of *S. aureus* infections and resistance with long-term treatment with available antibiotics, *S. aureus* is notorious. Research for new drugs, especially from natural sources is ongoing. Plants were commonly used in the treatment of diseases by a primary human from ancient times. Exhibiting minimum side effects, ease of use, availability, and commonly cost-effective are the advantages of plants. So in the last few decades, research on herbal medicine is getting popularized.
Evidence Acquisition: In this systematic review, we aimed to review antimicrobial potential of essential oil and different extracts (methanolic, ethanolic, ethyl acetate, ether or aqueous extracts) from 31 genera of medical plants, including 83 species against *S. aureus* and its most frequent resistant strain, methicillin-resistant *S. aureus* (MRSA) for introducing them as potent therapeutic agents. To find intended articles, we searched in several databases using a list of suitable keywords.
Results: The essential oil of *T. caucasicus* has the best inhibitory effect on *S. aureus*. However, extract of 8 plant species has also the acceptable inhibitory effect. Surprisingly, essential oil of some plants showed better anti-staphylococcal effect than standard antibiotics. Moreover, twelve plant species have effective inhibitory effect against MRSA.
Conclusions: Some of the evaluated Iranian plants such as *T. parthenium*, *T. vulgaris*, *T. eriocalyx*, *T. persicus*, *A. millefollum*, *P. harmala*, *H. scabrum*, and *S. urmiensis* with acceptable MIC or inhibition zone have the potency of antimicrobial activity, especially against *S. aureus* and MRSA. According to the comparison, essential oil of *Thymus caucasicus* with the MIC value of 0.31 μg/mL for *S. aureus* and 2.5 μg/mL for MRSA has the best inhibitory effect. So the mentioned natural extract, especially essential oil of *T. caucasicus* can be a candidate for drug design with the goal of the treatment of *S. aureus* infections.

Keywords: Herbal Medicine, Antimicrobial Susceptibility, *Staphylococcus aureus*, Chronic Infections

1. Context

Infectious diseases are the second leading cause of death worldwide (1). *Staphylococcus aureus* (*S. aureus*) is one of the important and problematical infectious pathogens (2). It is an opportunistic pathogen and is the primary cause of lower respiratory tract and surgical site infections, and the second leading cause of nosocomial bacteremia, pneumonia, and cardiovascular infections (3). Moreover, *S. aureus* is often found among chronic and recurrent bone infections, and is often the cause of chronic osteomyelitis, endocarditis, infections of indwelling devices and postsurgical wound infections such as chronic biofilm-associated infections in prosthetic devices (4). In recent years, the emergence of antibiotic-resistant forms of pathogenic *S. aureus* is a worldwide problem in clinical medicine (5). Methicillin-resistant *S. aureus* (MRSA) is the most common antibiotic-resistant of all antibiotic-resistant threats. The MRSA was first identified five decades ago (6). Hereafter, MRSA infections have spread in Europe, the Americas, and the Asia-Pacific region (7). Hence the search for newer, safer and more potent antimicrobials with less susceptibility to the resistance is a pressing need (8). Evidence currently shows that improved quality of life is considerably important in the treatment of chronic diseases (9). The negative effects of chronic infection induced by MRSA on the quality of life increase the need to search for newer, safer, and more potent antimicrobial agents with less susceptibility to resistance is a pressing need (8).

Plants were commonly used in the treatment of diseases by a primary human from ancient times. (9). Over the years, the World Health Organization (WHO) advocated traditional medicine as safe remedies for both microbial and non-microbial diseases. According to the WHO in 2008, above 80% of the world's population rely on traditional medicine for their primary healthcare needs (10). On the other hand, almost one-third of all medical products have a plant origin (11). Plants contain a variety of compounds against a variety of pathogens. It means that plants have wide-spreading effects against a different variety of infectious agents, including antibiotic-resistant bacteria. Thus recently, the research is growing on medical plants as safe, cheap, accessible, and more acceptable for peoples than synthetic antibiotics (12).

The diversity of the climate has resulted in a high diversity of plant flora in Iran. So it is possible to identify effective substances in different native plants of the country and to extract these substances in order to produce these materials in large quantities at the industrial level. Evaluation of these capabilities, especially in the case of plants native to Iran is of special importance (13). A considerable number of articles are published annually on the antimicrobial effect of various Iranian plants. Given the growing problem of antibiotic resistance, analyzing and summarizing the results of these articles will be important for their practical use. Moreover, the comparison between pharmaceutical effects of different parts of a medical plant can give a good vision for accomplishing further study with more efficiency.

2. Objectives

The aim of the present systematic review was to deliberate on whether plants, found commonly in Iran, could be used as an alternative for infection therapy. This review would describe some of the Iranian plant species as potent therapeutic agents specifically against *S. aureus* and its frequent resistant strain, MRSA. It also compared the antimicrobial potential of different Iranian herbs to highlight the most functional of them.

3. Data Sources

The present systematic review study was conducted after obtaining prior permission from the Research Ethics Committee (code: IR.AJUMS.REC.1396.150). This review involves searching for available literature about plants and herbal compounds effective against *S. aureus* and MRSA. To find related articles, we searched several databases, including PubMed, Science Direct, Scopus, Springer Link, Wiley Online Library, and Google Scholar databases and Persian databases, including Iran Medex (indexing articles published in Iran biomedical journals), Magiran (Iranian magazines database), and SID (scientific information database) using a list of keywords in MeSH such as medical plant, healing plants, pharmaceutical plants, medical herbs, healing plants, plant extracts, plant drug, Iranian medical plants, antimicrobial susceptibility, *Staphylococcus aureus*, plant antimicrobial extract, microbial sensitivity tests, plant biologically active compounds, methicillin-resistant *Staphylococcus aureus*, as well as a combination of them. We studied all related articles, collected, and classified all relevant data published from January 1, 1974 to January 2017.

4. Study Selection and Data Extraction

All research articles that focused on the antimicrobial assay of essential oil or at least one of the different extracts (methanolic, ethanolic, ethyl acetate, ether or aqueous) from plants, growing in Iran, by Microdilution method and Kirby-Bauer test (zone of inhibition test) against *S. aureus*, published from January 1, 1974 to January 2017 were included in this study. All other relevant research articles that used other antimicrobial assays did not investigate the antimicrobial effect against *S. aureus* or were out of desired time range were excluded from the study. A flow diagram depicts the flow of information through the different phases of this review (Figure 1).

5. Results

This systematic review compared the result of research articles that determined the antimicrobial activity of essential oil and different extracts (methanolic, ethanolic, ethyl acetate, ether or aqueous extracts) from different parts of 31 genera of medical plants, including 83 species, especially against *S. aureus*. All described herbal medicine with the details of using part of the plant, types of extracts, maximum inhibitory concentration (MIC) and inhibition zone against *S. aureus*, location of harvesting, and the references are summarized in Table 1. The map of Iran along with the provinces is shown in Figure 2 so that the harvesting areas of the plants can be traced back to the map.

According to the comparison, essential oil of *T. caucasicus* with the MIC value of 0.31 μg/mL for *S. aureus* and 2.5 μg/mL for MRSA has the best inhibitory effect on *S. aureus* strains (Table 1). However, essential oil of *T. parthenium*, *T. vulgaris*, *T. eriocalyx*, *T. persicus*, *A. millefollum*, ethanolic extract of *P. harmala*, flower extract of *H. scabrum*, and ethyl acetate extract of *S. urmiensis* with MIC value lower than 22 μg/mL have also the acceptable inhibitory effect against

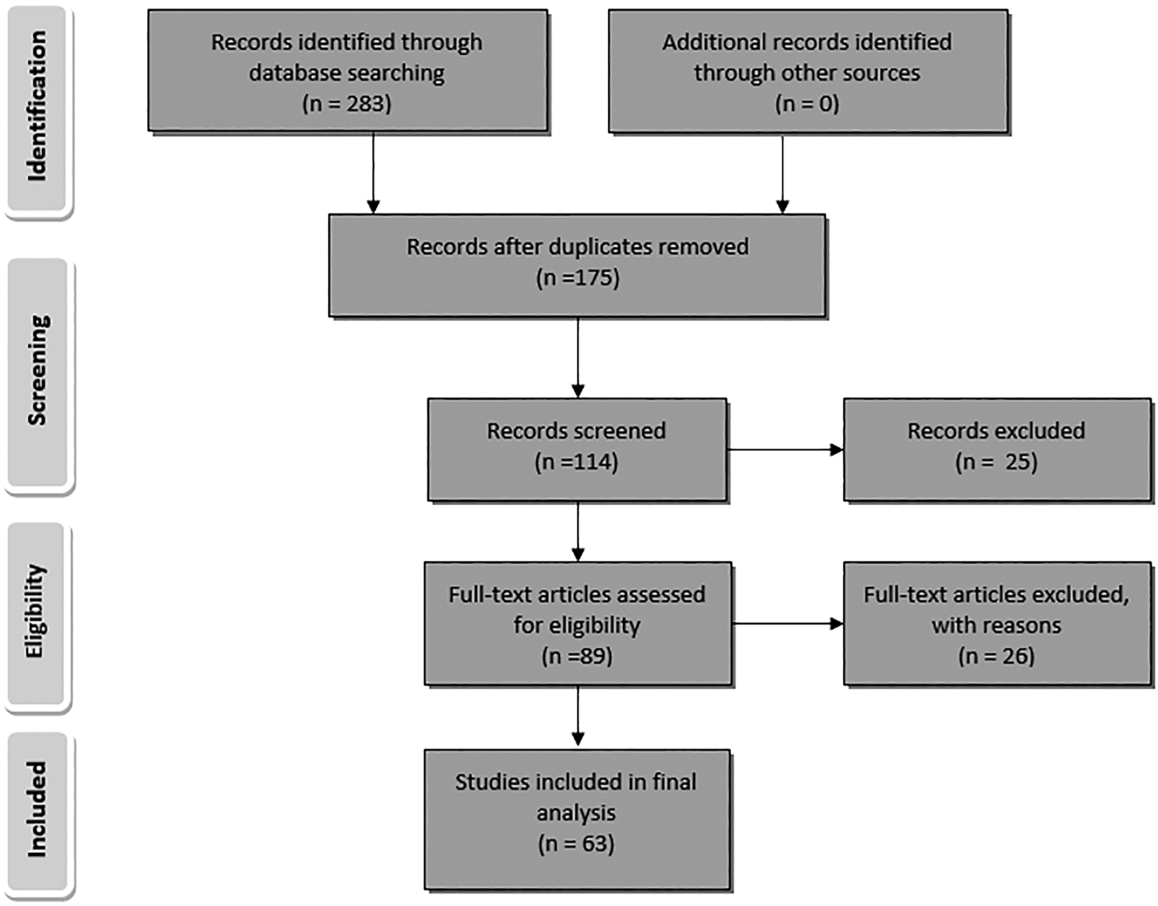

Figure 1. The flow of information through the different phases of the current review is shown

S. aureus (Table 1). The antimicrobial properties the oil of *Thymus* species is due to phenol content. The oil of *Thymus* has been traditionally used as anthelmintic, bacteriostatic, antiseptic and spasmolytic agents (14, 15). *Achillea* species also contain a complex of different antimicrobial agents such as monoterpens, sesquiterpene lactones, flavonoids, and phenolic acids that are found most often in their oils (16-18). Therefore, displaying acceptable inhibitory effect against *S. aureus* was predictable in these plants. It seems the best antimicrobial effect of *T. caucasicus*, may be due to more phenol concentration in this species.

Flower extract of *H. scabrum*, collected from Charmahal va Bakhtiari was more potent than that collected from Isfahan due to its more thymol and carvacrol content (41). It is consistent with other studies that variation in environmental parameters, such as irradiance, climate, nutrients, and soil-water availability can influence plant compositions, and thus cause variation in the antimicrobial activity (73). In some herbs, variation in the antimicrobial activity was due to the plant parts used for extract preparation. For example, methanolic extract of the root from *P. harmala* has the best effect rather than other parts of this plant. Moreover, different extracts of herbs showed significant different antimicrobial effects in most cases. In addition, some plants showed different antimicrobial effects at different stages of their growth. In this case, *Thymus pubescens*, *Thymus serpyllum* (44), and *Tanacetum parthenium* (64) should be noted that during flowering stage, they had a better anti-staphylococcal effect than the pre-flowering stage. Unripe seeds of *Terminalia chebula* was also more active against *S. aureus* than ripe seeds (22).

The antimicrobial effect of methanolic extract of aerial parts of *Salvia sahendica* (27) and essential oil and methanolic extract from aerial parts of *Salvia eremophila* (29) were the same as Gentamicin on *S. aureus*. Moreover, the antimicrobial effect of hydroalcholic extract of *Teucrium polium*

Figure 2. Geographical position of provinces in Iran is shown

was higher compared to Amoxicillin, Ciprofloxacin, Vancomycin, and Imipenem (58). Surprisingly, essential oil of *M. pulegium* (48), *Tanacetum parthenium* (11), and *Tanacetum pinnatum* (74) showed better anti-staphylococcal effects than standard antibiotics.

Bahrami et al. determined that the antimicrobial activity of ethanolic extract from *S. striata* leaves is lower than Doxycyclin and Ofloxacin against *S. aureus*. However, these antibiotics have synergistic effects in combination with ethanolic extract of *S. striata* leaves (42).

Among all of the evaluated medical herbs, antimicrobial effect of 12 species, including *S. tomentosa*, *Cuminum cyminum*, *Artemisia dracunulus*, *Artemisia herbalba*, *Artemisia absinthium*, *Thymus vulgaris*, *Thymus caramanicus*, *Mentha piperita*, *Peganum harmala*, *Achillea wilhelmsii*, *Berberis vulgaris*, and *Eucalyptus globules* are also studied against MRSA. In comparison to antibacterial assays against MRSA we found that ethanolic extract of *S. tomentosa*, seeds of *C. cyminum*, *A. dracunulus*, *A. herbalba*, *A. absinthium*, *T. caramanicus*, *A. wilhelmsii*, ethanolic, and aqueous extract of *M. piperita*, root of *B. vulgaris*, essential oil and ethanolic extract of *T. vulgaris*, methanolic extract of seed, leaves, stem, root, flower and ethanolic extract of *P. harmala*, ethanolic extract, aqueous extract and essential oil of leaves of *E. globulus* have effective inhibitory effects against MRSA.

It is noteworthy that *S. multicaulis* (methanolic extract) was the only plant active against penicillin-resistant *S. aureus*. More studies concerning the molecular basis of every active extract against clinical *S. aureus*, especially MRSA must be performed in the future. A limitation was trouble finding the full text of some articles. We had to email the authors. Lack of response or late response of some of them caused to waste a lot of time.

6. Conclusions

Most of the evaluated Iranian plants with acceptable MIC or inhibition zone have the potency of antimicrobial activity, especially against *S. aureus* and its most frequent resistant strains, MRSA. So the intended natural extract, especially essential oil of *Thymus caucasicus* can be a candidate for drug design for replacement of conventional antibiotics with the intention treatment of *S. aureus* infections. However, further clinical and analytical trials of these data are necessary to finding new knowledge such as *in vivo* effects and side effects of using herbal extracts as antibiotics. It was also understood that extracts derived from the same species can show significant differences in antimicrobial potency when collected at different sites, owing to the influence of soil, climate, and other factors. These differences may also relate to the type of extract, using plant parts, and the stage of plant growth.

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Footnotes

Authors' Contribution: Study design, collection of data, analysis and interpretation of data, drafting of the manuscript: Masoumeh Baradaran; study concept, critical revision of the manuscript for important intellectual content: Amir Jalali.

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Table 1. The Name of the Plant Species with Their Related Characterization are Listed in the

Plant	References	Using Part	Extraction	Inhibition Zone (IZ)	MIC
Dicyclophora persica	(19)	Aerial part	Essential oil	20 mm	1.2 mg/mL
Nepeta cripsa	(20)	Aerial part	Essential oil	19.5 mm (15 μL/disc)	
Nepeta menthoid	(21)	Aerial part	Essential oil	21 mm (10 μL/disc)	3.6 mg/mL
Terminalia chebula	(22)	Ripe and unripe seed	Methanolic extract		5 mg/mL for ripe seed 2.5 mg/mL for unripe seed
Myrtus communis	(23)	Leaves and seeds	Methanolic extract	26 mm (20 mg/mL), 10 mm (5 mg/mL) for leaves 16 mm(20 mg/mL), 9 mm (0.62 mg/mL) for seeds	5 mg/mL (leaves) 0.62 mg/mL (for seed)
Salvia multicaulis	(24)	Aerial parts	Essential oil		7.5 mg/mL
Salvia multicaulis	(25)		Methanolic extract	10 mm (*S. aureus* penicillin-resistant)	
Salvia sclarea	(24)	Aerial parts	Essential oil		15 mg/mL
Salvia verticillata	(24)	Aerial parts	Essential oil		7.5 mg/mL
Salvia limbata	(26)		Essential oil		15 mg/mL
Salvia choloroleuca	(26)		Essential oil		7.5 mg/mL
Salvia officinalis	(22)	Whole plant	Methanolic extract	16 mm	
Salvia sahendica	(27)	Aerial parts	Methanolic extract	14 mm	1.2 mg/mL
Salvia reuterana	(28)	Flower and leaves	Methanolic extract		0.5 mg/mL for flower, 0.25 mg/mL for leaves
Salvia eremophila	(29)	Aerial parts	Methanolic extract and essential oil		7.8 mg/mL for essential oil, 0.5 mg/mL for methanolic extract
Salvia eremophila	(30)	Aerial parts	Methanolic extract	10 mm (4 mg/disc)	1 mg/mL
Salvia reuterana	(30)	Aerial parts	Methanolic extract	8 mm (4 mg/disc)	1 mg/mL
Salvia mirzayanii	(30)	Aerial parts	Methanolic extract	12.2 mm (4 mg/disc)	1 mg/mL
Salvia santolinifolia	(30)	Aerial parts	Methanolic extract	12.2mm (4 mg/disc)	1 mg/mL
Salvia microsiphon	(30)	Aerial parts	Methanolic extract	14.2 mm (4 mg/disc)	1 mg/mL
Salvia urmiensis	(31)		Ethyl acetate extract		21.3 μg/mL
Salvia urmiensis	(31)		Essential oil		85.3 μg/mL
Salvia urmiensis	(31)		Ether extracts		37.3 μg/mL
Salvia tomentosa	(32)	Mature plant	Aqueous extract	NA for MRSA[a] & *S. aureus* strains	
Salvia tomentosa	(32)	Mature plant	Ethanolic extract	8.4 mm (4 mg/disc for MRSA[a]) 6.8 mm(4 mg/disc for S.aureus)	
Alhagi maurorum	(22)	Stem gum	Methanolic extract	15 mm	
Heracleum rechingeri	(22)	Fruit	Methanolic extract	20 mm	
Heracleum transcaucasicum	(33)	Aerial parts	Essential oil	NA	
Heracleum anisactis	(33)	Aerial parts	Essential oil	NA	
Foeniculum vulgare	(34)	Fennel seeds	Essential oil		2%
Foeniculum vulgare	(22)	Fennel root	Methanolic extract	12 mm	
Cuminum cyminum	(35)		Essential oil	10 mm (10 μL/disc)	1/8 oil dilution
Cuminum cyminum	(22)	Fruit	Methanolic extract	12 mm	
Cuminum cyminum	(23)	Seeds	Methanolic extract	15 mm	
Cuminum cyminum	(32)	Seeds	Aqueous extract	NA for MRSA[a] and *S. aureus*	
Cuminum cyminum	(32)	Seeds	Ethanolic extract	11.5 mm (4 mg/disc for MRSA[a]) 8.5 mm(4 mg/disc for *S. aureus*)	
Artemisia diffusa	(36)	Aerial parts	Methanolic extract	18.4 mm (16 mg/cup)	10 mg/mL
Artemisia oliveria	(36)	Aerial parts	Methanolic extract	12.2 mm (16 mg/cup)	10 mg/mL
Artemisia scorpia	(36)	Aerial parts	Methanolic extract	13.6 mm (16 mg/cup)	10 mg/mL

Artemisia turanica	(36)	Aerial parts	Methanolic extract	11.9 mm (16 mg/cup)	10 mg/mL
Artemisia dracunulus	(34)		Essential oil		7.0%
Artemisia dracunulus	(32)	Mature plant	Ethanolic extract	8 mm(4 mg/disc) (for MRSA[a]) 7 mm(4 mg/disc for *S. aureus*)	
Artemisia dracunulus	(32)	Mature plant	Aqueous extract	NA (for MRSA[a] & *S. aureus*)	
Artemisia herbalba	(32)	Mature plant	Ethanolic extract	22.5 mm(4 mg/disc) (for MRSA[a]) 11 mm (4 mg/disc for *S. aureus*)	0.39 mg/mL (for clinical MRSA[a] and *S. aureus* strains) 0.04 mg/mL (for standard MRSA[a] strain) 0.02 mg/mL(for standard *S. aureus* strain)
Artemisia herbalba	(32)	Mature plant	Aqueous extract	12 mm(4 mg/disc) (for MRSA[a]) 9 mm(4 mg/disc for *S. aureus*)	
Artemisia absinthium	(32)	Mature plant	Ethanolic extract	9 mm(4 mg/disc) (for MRSA[a]) 8 mm(4 mg/disc for *S. aureus*)	
Artemisia absinthium	(32)	Mature plant	Aqueous extract	NA (for MRSA[a] & *S. aureus*)	
Pistacia vera	(37)	Fruit	Extract	32 mm	
Pistacia mutica	(37)	Fruit	Extract	18 mm	
Pistacia vera	(37)	Leaves	Extract	22 mm	
Pistacia mutica	(37)	Leaves	Extract	22 mm	
P. khinjuk	(38)	Leaves	Chloroform		0.04 mg/mL
P. khinjuk	(38)	Leaves	Ethyl acetate		0.13 mg/mL
P. khinjuk	(38)	Leaves	Ethyl alcohol		0.09 mg/mL
P. khinjuk	(38)	Leaves	Diethyl ether		0.42 mg/mL
P. atlantica	(39)	Mastic gum	Essential oil	11 mm (10 μL/disc) 13 mm (20 μL/disc)	
Helichrysum armenium	(40)	Flower, leaf and stem	Oil	12.4 mm, 11.22 mm and 10.8 mm (50 μL/cup)	
Helichrysum scabrum	(41)	Flower	Extract	9mm to 19mm	MIC value varied from lower than 19 μg/mL to 5000 μg/mL
Scrophulari astriata	(42)	Leaves	Ethanolic extract		50.6 μg/mL
Thymus persicus	(43)	Leaves	Essential oil		0.5 μL/mL
Thymus eriocalyx	(43)	Leaves	Essential oil		0.5 μL/mL
Thymus pubescens	(44)	Pre and flowering stages	Essential oil	29 mm for pre and 34 mm for flowering	dilution of 1/8
Thymus serpyllum	(44)	Pre and flowering stages	Essential oil	14 mm for pre and 22 mm for flowering	dilution of 1/4
Thymus pubescens	(45)	Aerial parts	Methanolic extract	8 to 16 mm	
Thymus vulgaris	(34)	Leaves	Essential oil		0.1%
Thymus vulgaris	(22)	Whole plant	Methanolic extract	10 mm	5 mg/mL
Thymus vulgaris	(46)		Essential oil	20 - 35 mm (for 14 clinical MRSA[a] strains) 19 mm (for *S. aureus*)	18.5 μg/ml -37 μg/mL (for 14 clinical MRSA[a] strains) 18.5 μg/mL (for *S. aureus*)
Thymus vulgaris	(32)	Mature plant	Ethanolic extract	10.5 mm (4 mg/disc for MRSA[a]) 9.4 mg/disc for *S. aureus*	
Thymus vulgaris	(32)	Mature plant	Aqueous extract	NA (for MRSA[a] & *S. aureus*)	
Thymus caramanicus	(32)	Mature plant	Ethanolic extract	11.2 mm (4 mg/disc for MRSA[a]) 9 (4 mg/disc for *S. aureus*	
Thymus caramanicus	(32)	Mature plant	Aqueous extract	NA (for MRSA[a] & *S. aureus*)	
Thymus caucasicus	(47)		Essential oil		0.31 μg/mL for *S. aureus* 2.5 μg/mL for MRSA[a]
Mentha pulegium	(48)	Flowering aerial parts	Essential oil	21 mm (1 μL of oil)	0.5 μL/mL
Mentha pulegium	(34)	Leaves	Essential oil		0.5%
Menth apiperita	(49)		Essential oil		2 μL/mL

Mentha piperita	(34)	Leaves	Essential oil		0.4%
Mentha piperita	(32)	Leaves	Ethanolic extract	7.5 mm (4 mg/disc for MRSA[a]) 8.5 (4 mg/disc for *S. aureus*	
Mentha piperita	(32)	Leaves	Aqueous extract	7 mm (4 mg/disc for MRSA[a]) 7.5 mm (4 mg/disc for *S. aureus*)	
Peganum harmala	(50)	Seed smoke	Dichloromethane extract	15.7 mm(5 mg of smoke condensate)	
Peganum harmala	(32)	Mature plant	Aqueous extract	7.4 mm(4 mg/disc) (for MRSA[a]) NA (4 mg/disc)	
Peganum harmala	(32)	Mature plant	Ethanolic extract	18 mm(4 mg/disc) (for MRSA[a]) 20 mm(4 mg/disc)	0.02 mg/mL (for clinical and standard MRSA[a] strains) 0.02 mg/mL(for standard and clinical *S. aureus* strains)
Peganum harmala	(51)	Seed	Methanolic extract	22 mm (in concentration of 400 mg/mL for MRSA[a])	0.625 mg/mL
Peganum harmala	(51)	Leaves	Methanolic extract	10 mm (in concentration of 400 mg/mL for MRSA[a])	
Peganum harmala	(51)	Stem	Methanolic extract	11 mm (in concentration of 400 mg/mL for MRSA[a])	
Peganum harmala	(51)	Root	Methanolic extract	24.5 mm (in concentration of 400 mg/mL for MRSA[a])	0.625 mg/mL
Peganum harmala	(51)	Flower	Methanolic extract	5.5 mm (in concentration of 400 mg/mL for MRSA[a])	
Grammosciadium platycarpum	(52)	Aerial parts	Essential oil	18 mm	1.9 mg/mL
Grammosciadium scabridum	(53)	Aerial parts	Essential oil	14 mm (10 μg/disc)	1.2 mg/mL
Onosmadi chroanthum	(54)	Root	Methanolic and ethanolic extract	15 mm (50 μL/well), 15 mm (50 μL/well)	0.156 mg/mL for methanolic extract and 0.312 mg/mL for ethanolic extract
Scutellaria litwinowii	(55)	Aerial parts	Methanolic extract		6.25 mg/mL
Scutellaria lindbergii	(55)	Aerial parts	Methanolic extract		6.25 mg/mL
Oliveria decumbens	(56)	Aerial parts	Ethanolic and methanolic exracts		20 mg/mL, 20 mg/mL
Teucrium polium	(57)	Aerial parts	Alcoholic extracts		40 mg/mL
Teucrium polium	(58)		Hydroalcholic	20 mm	
Stachys fruticulosa	(27)	Aerial parts	Methanolic extract	12 mm	2.5 mg/mL
Stachys schtschegleevii	(27)	Aerial parts	Methanolic extract	13 mm	1.25 mg/mL
Stachys byzantia	(59)		Methanolic extract	8.4 mm	100 μg/mL
Stachys inflate	(59)		Methanolic extract	8.3 mm	250 μg/mL
Stachys lavandulifolia	(59)		Methanolic extract	8.6 mm	500 μg/mL
Stachys laxa	(59)		Methanolic extract	8.6 mm	100 μg/mL
Stachys grandiflora	(60)	Aerial parts	Essential oil	12 mm	
Stachys obtusicrena	(30)	Aerial parts	Methanolic extract	9.2 mm (4 mg/disc)	
Hymenocrater longiflorus	(61)	Polar sub-fraction	Essential oil	31 mm	40 μg/mL
Pistachia vera	(62)	Green hull	Purified extract	11.7 mm (at 1200 μg/plate)	
Phlomis caucasica	(27)	Aerial parts	Methanolic extract		1.25 mg/mL
Phlomis buruguieri	(59)	Aerial parts	Mehanolic extract	16.7 mm	10 mg/mL
Phlomis herbaventi	(59)	Aerial parts	Mehanolic extract	12.2 mm	10 mg/mL
Phlomis oliveri	(59)	Aerial parts	Mehanolic extract	13.1 mm	25 mg/mL
Torilis leptophyla	(63)	Aerial parts	Ethanolic extract	10 mm	0.4 g/mL
Tanacetum balsamita	(27)	Aerial parts	Dichloromethane extract		2.5 mg/mL
Tanacetum parthenium	(11)	Whole plant	Essential oil	18.5 mm (2.5 μL), 34mm (5 μL), 39mm (7.5 μL) and 42 mm (15 μL)	1 μg/mL
Tanacetum parthenium	(64)	Flowering stage	Essential oil	24 mm	8 μg/mL

Tanacetum parthenium	(64)	Pre-flowering stage	Essential oil	18 mm	8 μg/mL
Tanacetum parthenium	(64)	Post-flowering stage	Essential oil	22 mm	8 μg/mL
T. pinnatumboiss	(65)	Aerial parts	Essential oil	24.2 mm	
Achillea millefollum	(27)		Methanolic extract		0.625 mg/mL
Achillea millefollum	(66)		Essential oil	31.4 mm (region 1) 19.8 mm(region 2)	15.4 μg/mL (region 1) 27.5 μg/mL (region 2)
Achillea pachycephala	(67)	Flowers	Essential oil	12 mm	
Achillea pachycephala	(67)	Leaves	Essential oil	10.5 mm	
Achillea pachycephala	(67)	Stems	Essential oil	8 mm	
Achillea pachycephala	(67)	Aerial parts	Hexan-ether	14 mm	6.25 mg/mL
Achillea pachycephala	(67)	Aerial parts	Methanolic extract	6 mm	12.5 mg/mL
Achillea santolina	(67)	Flowers	Essential oil	9 mm	
Achillea santolina	(67)	Leaves	Essential oil	7.5 mm	
Achillea santolina	(67)	Stems	Essential oil	6.5 mm	
Achillea santolina	(67)	Arial parts	Hexan-ether	7 mm	6.25 mg/mL
Achilleas antolina	(67)	Aerial parts	Methanolic extract	5 mm	12.5 mg/mL
Achillea tenuifolia	(68)	Flower	Volatile oils	14 mm	
Achillea tenuifolia	(68)	Leaves	Volatile oils	9 mm	
Achillea tenuifolia	(68)	Stems	Volatile oils	8 mm	
Achillea wilhelmsii	(69)		Essential oil	27 mm (200 μL) (for MRSA[a]) 19 mm (200 μL)(for MRSA[a])	
Achillea wilhelmsii	(70)		Methanolic extract	19mm(400 mg/mL)	
Otostegia persica	(71)	Aerial parts	Hexane extract	11.4 mm	10 mg/mL
Otostegia persica	(71)	Aerial parts	Chloroform extract	15.4 mm	1.25 mg/mL
Otostegia persica	(71)	Aerial parts	Methanolic extract	15.6 mm	3.12 mg/mL
Otostegia persica	(30)	Aerial parts	Methanolic extract	9.7 mm (4 mg/disc)	
Berberis vulgaris	(32)	Root	Aqueous extract	8.4 mm (4 mg/disc) (for MRSA[a]) 7 mm (4 mg/disc)	
Berberis vulgaris	(32)	Root	Ethanolic extract	12.5 mm (4 mg/disc) (for MRSA[a]) 15.5 mm (4 mg/disc)	0.39 mg/mL (for clinical strain *S. aureus* & MRSA[a]) 0.04 mg/mL (for standard strain *S. aureus* & MRSA[a])
Berberis vulgaris	(22)	Fruit	Methanolic extract		17 mm
Ferulago angulata	(38)	Aerial parts	Essential oil		15 μg/mL
Ferula goangulata	(38)	Seeds	Essential oil		$> 4 \times 10^3$ μg/mL
Ferulago Bernardii	(72)	Aerial parts	Essential oil		250 μg/mL
Eucalyptus globulus	(32)	Leaves	Aqueous extract	14 mm (4 mg/disc) (for MRSA[a]) 11 mm (4 mg/disc)	
Eucalyptus globulus	(32)	Leaves	Ethanolic extract	17 mm(4 mg/disc) (for MRSA[a]) 15.5 mm(4 mg/disc)	0.18 mg/mL (for clinical strain MRSA[a]) 0.09 mg/mL (for standard MRSA[a] strain) 0.39 mg/mL(for standard and clinical *S. aureus* strains)
Eucalyptus globulus	(46)		Essential oil	10 to 30 mm (for 14 clinical MRSA[a] strains) 17 mm (for *S. aureus*)	34.24 to 85.6 μg/mL (for 14 clinical MRSA[a] strains) 51.36 μg/mL (for *S. aureus*)

Abbreviation: NA, no activity.
[a]Plants that were also evaluated against MRSA.