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 bacteria 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. millefolium, 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 dis-
eases 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 widespread 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 medicinal 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. millefolium*, 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...
The flow of information through the different phases of the current review is shown in Figure 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 spasmyloytic 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 hydroalcoholic extract of *Teucrium polium*
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 absinthium*, *Thymus vulgaris*, *Artemisia herbalba*, *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

![Image](77x280 to 531x697)

**Figure 2.** Geographical position of provinces in Iran is shown

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oil of leaves of *E. globulus* have effective inhibitory effects against MRSA.

It is noteworthy that *S. multicaulis* (methylamatic 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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**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 crispia*         | (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 |             |
| *Salvia multicaulis*     | (24)       | Aerial parts        | Essential oil     |                      | 7.5 mg/mL    |
| *Salvia scabra*          | (24)       | Aerial parts        | Essential oil     |                      | 15 mg/mL     |
| *Salvia verticillata*    | (24)       | Aerial parts        | Essential oil     |                      | 7.5 mg/mL     |
| *Salvia limbata*         | (25)       | Aerial parts        | Essential oil     |                      | 10 mg/mL     |
| *Salvia chloroleuca*     | (26)       | Aerial parts        | Essential oil     |                      | 7.5 mg/mL     |
| *Salvia officinalis*     | (22)       | Whole plant         | Methanolic extract| 16 mm                |             |
| *Salvia suhendica*       | (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 mirzayani*       | (30)       | Aerial parts        | Methanolic extract| 12.2 mm (4 mg/disc)  | 1 mg/mL      |
| *Salvia santolinifolia*  | (30)       | Aerial parts        | Methanolic extract| 12.2 mm (4 mg/disc)  | 1 mg/mL      |
| *Salvia microsiphon*     | (30)       | Aerial parts        | Methanolic extract| 14.2 mm (4 mg/disc)  | 1 mg/mL      |
| *Salvia armieszii*       | (31)       | Essential oil       | Ethyl acetate extract |                      | 21.3 µg/mL   |
| *Salvia armieszii*       | (31)       | Ethanol extract      | Ethanol extract    | 8.4 mm (4 mg/disc for MRSA<sup>a</sup> 6.8 mm/4 mg/disc for S.aureus) |             |
| *Salvia armieszii*       | (31)       | Ethanol extract      | Ethanol extract    | 8.4 mm (4 mg/disc for MRSA<sup>a</sup> 6.8 mm/4 mg/disc for S.aureus) |             |
| *Salvia tomentosa*       | (32)       | Mature plant        | Aqueous extract    | NA for MRSA<sup>a</sup> & S. aureus strains |             |
| *Salvia tomentosa*       | (32)       | Mature plant        | Ethanol extract    | 8.4 mm (4 mg/disc for MRSA<sup>a</sup> 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%                   |             |
| *Cuminum cyminum*        | (22)       | Fennel root         | Methanolic extract| 12 mm                |             |
| *Cuminum cyminum*        | (35)       | Fennel root         | Methanolic extract| 12 mm                |             |
| *Cuminum cyminum*        | (23)       | Seeds               | Methanolic extract| 15 mm                |             |
| *Cuminum cyminum*        | (32)       | Seeds               | Aqueous extract    | NA for MRSA<sup>a</sup> & S. aureus strains |             |
| *Cuminum cyminum*        | (32)       | Seeds               | Ethanol extract    | 11.5 mm (4 mg/disc for MRSA<sup>a</sup> 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 oligerria*    | (36)       | Aerial parts        | Methanolic extract| 12.2 mm (16 mg/cup)  | 10 mg/mL     |
| *Artemisia scoparia*     | (36)       | Aerial parts        | Methanolic extract| 13.6 mm (16 mg/cup)  | 10 mg/mL     |
| Plant                          | Type               | Extract/Component          | Concentration/Clinical Effect                                                                 |
|-------------------------------|--------------------|----------------------------|------------------------------------------------------------------------------------------------|
| Artemisia turanica           | Aerial parts       | Methanolic extract         | 11.9 mm (4 mg/disc) (for MRSA<sup>a</sup>) 7 mm (4 mg/disc for S. aureus)                        |
| Artemisia dracunculus        | Mature plant       | Ethanollic extract         | 8 mm (4 mg/disc) (for MRSA<sup>a</sup>) 7 mm (4 mg/disc for S. aureus)                         |
| Artemisia dracunculus        | Mature plant       | Aqueous extract            | NA (for MRSA<sup>a</sup> & S. aureus)                                                         |
| Artemisia herbalba           | Mature plant       | Ethanollic extract         | 22.5 mm (4 mg/disc) (for MRSA<sup>a</sup>) 11 mm (4 mg/disc for S. aureus)                    |
| Artemisia herbalba           | Mature plant       | Aqueous extract            | 12 mm (4 mg/disc) (for MRSA<sup>a</sup>) 9 mm (4 mg/disc for S. aureus)                       |
| Artemisia absinthium         | Mature plant       | Ethanollic extract         | 9 mm (4 mg/disc) (for MRSA<sup>a</sup>) 8 mm (4 mg/disc for S. aureus)                        |
| Pistacia vera                | Fruit              | Extract                    | 32 mm                                                                                           |
| Pistacia mutica              | Fruit              | Extract                    | 18 mm                                                                                           |
| Pistacia vera                | Leaves             | Extract                    | 22 mm                                                                                           |
| Pistacia mutica              | Leaves             | Extract                    | 22 mm                                                                                           |
| P. khinjuk                   | Leaves             | Chloroform                 | 0.04 mg/ml                                                                                        |
| P. khinjuk                   | Leaves             | Ethyl acetate              | 0.13 mg/ml                                                                                      |
| P. khinjuk                   | Leaves             | Ethyl alcohol              | 0.09 mg/ml                                                                                      |
| P. khinjuk                   | Leaves             | Diethyl ether              | 0.42 mg/ml                                                                                      |
| P. atlantica                 | Mastic gum         | Essential oil              | 11 mm (10 µL/disc) 13 mm (20 µL/disc)                                                           |
| Helichrysum armenium         | Flower, leaf and stem | Oil                       | 12.4 mm, 11.22 mm and 10.8 mm (50 µL/cup)                                                        |
| Helichrysum scabrum          | Flower             | Extract                    | 9 mm to 19 mm (MIC value varied from lower than 19 µg/mL to 5000 µg/mL)                         |
| Scrophulari astriata         | Leaves             | Ethanollic extract         | 50.6 µg/mL                                                                                      |
| Thymus persicus             | Leaves             | Essential oil              | 0.5 µL/mL                                                                                        |
| Thymus ericoclyx             | Leaves             | Essential oil              | 0.5 µL/mL                                                                                        |
| Thymus pubescens            | Pre and flowering stages | Essential oil             | 29 mm for pre and 34 mm for flowering (dilution of 1/8)                                         |
| Thymus serpyllum             | Pre and flowering stages | Essential oil             | 14 mm for pre and 22 mm for flowering (dilution of 1/4)                                         |
| Thymus pubescens            | Aerial parts       | Methanolic extract         | 8 to 16 mm                                                                                      |
| Thymus vulgaris             | Leaves             | Essential oil              | 0.1%                                                                                             |
| Thymus vulgaris             | Whole plant        | Methanolic extract         | 10 mm                                                                                           |
| Thymus vulgaris             | Essential oil      | 20 - 35 mm (for 14 clinical MRSA<sup>a</sup> strains) 19 mm (for S. aureus) 18.5 µg/mL (for 14 clinical MRSA<sup>a</sup> strains) 18.5 µg/mL (for S. aureus) |
| Thymus vulgaris             | Mature plant       | Ethanollic extract         | 10.5 mm (4 mg/disc for MRSA<sup>a</sup>) 9.4 mg/disc for S. aureus                              |
| Thymus vulgaris             | Mature plant       | Aqueous extract            | NA (for MRSA<sup>a</sup> & S. aureus)                                                           |
| Thymus vulgaris             | Mature plant       | Ethanollic extract         | 11.2 mm (4 mg/disc for MRSA<sup>a</sup>) 9 (4 mg/disc for S. aureus)                           |
| Thymus caraminicus          | Mature plant       | Aqueous extract            | NA (for MRSA<sup>a</sup> & S. aureus)                                                           |
| Thymus caucasicus           | Mature plant       | Essential oil              | 0.31 µg/mL (for S. aureus 2.5 µg/mL for MRSA<sup>a</sup>)                                     |
| Mentha pulegium             | Flowering aerial parts | Essential oil             | 21 mm (1 µL of oil)                                                                             |
| Mentha pulegium             | Leaves             | Essential oil              | 0.5%                                                                                             |
| Mentha apipera              | Essential oil      | 2 µL/mL.                                                               |
| Plant Name                  | Part                  | Type                  | Diameter (mm) | 
|----------------------------|-----------------------|-----------------------|---------------|
| Mentha piperita            | Leaves                | Essential oil         | 7.5 (4 mg/disc) | 0.4%          |
|                            |                      | Ethanolic extract     | 7.5 mm (4 mg/disc) for MRSA^a, 8.5 mm (4 mg/disc) for S. aureus |
| Peganum harmala            | Seed smoke            | Dichloromethane extract | 15.7 mm (5 mg of smoke condensate) |
| Peganum harmala            | Mature plant          | Aqueous extract       | 7.4 mm (4 mg/disc) for MRSA^a, NA (4 mg/disc) |
|                           |                      | 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            | Seed                  | Methanolic extract    | 22 mm (in concentration of 400 mg/mL for MRSA^a) |
|                           |                      |                      |               | 0.625 mg/mL |
|                           | Leaves                | Methanolic extract    | 10 mm (in concentration of 400 mg/mL for MRSA^a) |
|                           |                      |                      |               | 0.625 mg/mL |
|                           | Stem                  | Methanolic extract    | 18 mm (in concentration of 400 mg/mL for MRSA^a) |
|                           | Root                  | Methanolic extract    | 24.5 mm (in concentration of 400 mg/mL for MRSA^a) |
|                           |                      |                      |               | 0.625 mg/mL |
| Grammosciadium platycarpum| Aerial parts          | Essential oil         | 18 mm         |
|                           |                      |                      |               | 1.9 mg/mL |
| Grammosciadium scabridum   | Aerial parts          | Essential oil         | 14 mm (10 µg/disc) |
|                           |                      |                      |               | 1.2 mg/mL |
| Onosma chroanthum          | Root                  | Methanolic and ethanolic extract | 15 mm (50 µL/well), 15 mm (50 µL/well) |
|                           |                      |                      |               | 0.36 mg/mL for methanolic extract and 0.32 mg/mL for ethanolic extract |
| Scutellaria litwinowii     | Aerial parts          | Methanolic extract    | 6.25 mg/mL |
| Scutellaria lindbergii     | Aerial parts          | Methanolic extract    | 6.25 mg/mL |
| Oliveria decumbens        | Aerial parts          | Ethanol and methanolic extracts | 20 mg/mL, 20 mg/mL |
| Teucrium polium            | Aerial parts          | Alcoholic extracts    | 40 mg/mL |
| Stachys fruticulosa       | Aerial parts          | Methanolic extract    | 12 mm         |
|                           |                      |                      |               | 2.5 mg/mL |
| Stachys schtschegleevii   | Aerial parts          | Methanolic extract    | 13 mm         |
|                           |                      |                      |               | 1.25 mg/mL |
| Stachys byzantia           | Aerial parts          | Methanolic extract    | 8.4 mm        |
|                           |                      |                      |               | 100 µg/mL |
| Stachys inflata            | Aerial parts          | Methanolic extract    | 8.3 mm        |
|                           |                      |                      |               | 250 µg/mL |
| Stachys lavandulifolia     | Aerial parts          | Methanolic extract    | 8.6 mm        |
|                           |                      |                      |               | 500 µg/mL |
| Stachys laxa               | Aerial parts          | Methanolic extract    | 8.6 mm        |
|                           |                      |                      |               | 100 µg/mL |
| Stachys grandiflora        | Aerial parts          | Essential oil         | 12 mm         |
| Stachys obtusiflora        | Aerial parts          | Methanolic extract    | 9.2 mm (4 mg/disc) |
| Hyoscyamus longiflorus     | Polar sub-fraction    | Essential oil         | 31 mm         |
|                           |                      |                      |               | 40 µg/mL |
| Pistacia vera              | Green hull            | Purified extract      | 11.7 mm (at 1200 µg/plate) |
| Phlomis caucasia           | Aerial parts          | Methanolic extract    | 12 mm         |
|                           |                      |                      |               | 1.25 mg/mL |
| Phlomis buruguieri         | Aerial parts          | Methanolic extract    | 16.7 mm       |
|                           |                      |                      |               | 10 mg/mL |
| Phlomis herbaeenti         | Aerial parts          | Methanolic extract    | 12.2 mm       |
|                           |                      |                      |               | 10 mg/mL |
| Phlomis oliveri            | Aerial parts          | Methanolic extract    | 13.1 mm       |
|                           |                      |                      |               | 25 mg/mL |
| Tornilis leptophylla       | Aerial parts          | Ethanol extract       | 10 mm         |
|                           |                      |                      |               | 0.4 g/mL |
| Tanacetum balsamita        | Aerial parts          | Dichloromethane extract | 18.5 mm (2.5 µL), 34 mm (5 µL), 39 mm (7.5 µL) and 42 mm (15 µL) |
|                           |                      |                      |               | 2.5 mg/mL |
| Tanacetum parthenium       | Whole plant           | Essential oil         | 24 mm         |
|                           |                      |                      |               | 8 µg/mL |

^a MRSA: Methicillin Resistant Staphylococcus aureus

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| Plant Name                  | Stage            | Type                | Extract/Concentration          | Diameter (mm) | 
|-----------------------------|------------------|---------------------|--------------------------------|---------------|
| Tanacetum parthenium        | Pre-flowering    | Essential oil       | 8 µg/mL                        | 18            |
| T. parthenium               | Post-flowering   | Essential oil       | 8 µg/mL                        | 22            |
| T. pinnatumboiss            | Aerial parts     | Essential oil       |                                | 24.2          |
| Achillea millefolium        |                 | Methanolic extract  | 0.625 mg/mL                    |               |
| Achillea pachycephala       | Flowers          | Essential oil       | 12 mm                          |               |
| Achillea pachycephala       | Leaves           | Essential oil       | 10.5 mm                        |               |
| Achillea pachycephala       | Stems            | Essential oil       | 8 mm                           |               |
| Achillea santolina          | Aerial parts     | Methanolic extract  | 12.5 mg/mL                     |               |
| Achillea santolina          | Flowers          | Essential oil       | 9 mm                           |               |
| Achillea santolina          | Leaves           | Essential oil       | 7.5 mm                         |               |
| Achillea santolina          | Stems            | Essential oil       | 6.5 mm                         |               |
| Achillea santolina          | Aerial parts     | Hexan-ether         | 6.25 mg/mL                     |               |
| Achillea tenuifolia         | Flowers          | Volatile oils       | 14 mm                          |               |
| Achillea tenuifolia         | Leaves           | Volatile oils       | 9 mm                           |               |
| Achillea tenuifolia         | Stems            | Volatile oils       | 8 mm                           |               |
| Achillea wilhelmsii         | Essential oil    | 27 mm (200 µL) (for MRSA<sup>a</sup>) |               |
| Otostegia persica           | Aerial parts     | Hexane extract      | 10 mg/mL                       |               |
| Otostegia persica           | Aerial parts     | Chloroform extract  | 1.25 mg/mL                     |               |
| Otostegia persica           | Aerial parts     | Methanolic extract  | 3.12 mg/mL                     |               |
| Berberis vulgaris           | Root             | Aqueous extract     | 0.39 mg/mL (for clinical strain S. aureus & MRSA<sup>a</sup>) 0.04 mg/mL (for standard S. aureus strains) 0.39 mg/mL (for standard and clinical S. aureus strains) | 17 mm |
| Berberis vulgaris           | Root             | Ethanol extract     | 0.39 mg/mL (for clinical strain S. aureus & MRSA<sup>a</sup>) 0.04 mg/mL (for standard S. aureus strains) 0.39 mg/mL (for standard and clinical S. aureus strains) | 17 mm |
| Ferula angulata             | Aerial parts     | Essential oil       | 15 µg/mL                       |               |
| Ferula angulata             | Seeds            | Essential oil       | > 4 × 10<sup>3</sup> µg/mL     |               |
| Eucalyptus globulus         | Aerial parts     | Essential oil       | 51.36 µg/mL                    |               |
| Eucalyptus globulus         | Leaves           | Aqueous extract     | 34.24 to 85.6 µg/mL (for 14 clinical MRSA<sup>a</sup> strains) 37 mm (for S. aureus) | 10 to 30 mm (for 14 clinical MRSA<sup>a</sup> strains) 17 mm (for S. aureus) | 11 mm |
| Eucalyptus globulus         | Leaves           | Ethanol extract     | 0.18 mg/mL (for clinical strain MRSA<sup>a</sup>) 0.09 mg/mL (for standard MRSA<sup>a</sup> strain) 0.39 mg/mL (for standard and clinical S. aureus strains) | 17 mm |

Abbreviation: NA, no activity.
<sup>a</sup>Plants that were also evaluated against MRSA.