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A review on medical plants affecting *Staphylococcus aureus*

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ABSTRACT

Background and aims: Infectious diseases are among the most important causes of mortality around the world and according to the WHO report 10.5 million cases of death were happened due to infections. *Staphylococcus aureus* is one of the most important pathogen that its infections are varied from local infections to life threatening infections. With regard to high antibiotic resistance of this agent its control and treatment is a challenge in medicine. The aim of this study was to review the effective medicinal plants against *S. aureus* with special attention of native plants of Iran.
Methods: A comprehensive literature review was performed on papers that have been published from 2004 till 2016 in data resources such as NCBI, Sciencedirect, Springer, Web of science and as well as local databases such as Irandoc, Islamic science citation (ISC) and magiran with special focus on those that have been reported native medicinal plants in Iran. The selected keywords were *Staphylococcus aureus*, medicinal plant, natural antibiotic, antibacterial plant and medicinal herbs.
Results: Different studies were found that have reported effective medicinal plants against *S. aureus* and were able to significantly inhibit bacterial growth. As well as different parts of these plants have been investigated for antibacterial activity and found that considerable differences are present among these parts of plants.
Conclusion: Based on the reported studies, there are different medicinal plants in Iran that can be regarded as effective source for discovery new antibacterial agents against *S. aureus* and treatment of resistant strains.

Keywords: *Staphylococcus aureus*, Antibiotic resistance, Medical plants.

Review article

INTRODUCTION

Methicillin resistant *Staphylococcus aureus* (MRSA) had been emerged at 1980s as a major obstacle in medicine and infection control.[1] *S. aureus* is a community and also hospital acquired pathogen that cause different infections such as scalded skin syndrome, toxic shock syndrome, urinary tract infections, bacteremia, etc.[2,3] This agent can be found as normal flora of human and animal skin and in specific situations can cause local or systemic infections.[4] The severity of infections caused by this agent is varied from self-limiting infections to bacteremia that can lead to 80% mortality without antibiotic treatment.[4,5]

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During recent decades *S. aureus* bacteremia has been increased significantly which cause difficulties in infection control.[6] Before antibiotic era, infectious diseases were regarded as a life threatening problem in human life. Fortunately with penicillin discovery, infections control was successful and the infectious diseases mortality was reduced significantly but with frequent use of antibiotics, resistant bacterial strains were found as a result of acquiring resistance genetic elements, genetic drift, genetic shift and also expressing new metabolic pathways.[7] So, presently antibiotic resistance is a worldwide problem especially in developing countries. It causes mortality following infectious diseases e.g. in tropical countries near half of mortalities is due to infectious diseases.[8] *S. aureus* is one of the most antibiotic resistant pathogen as more than 90% of its infections don't respond to penicillin or ampicillin.[9] This agent can quickly acquire resistance factor to newly discovered antibiotics and as a result treatment of infections due to this pathogen is difficult. One example is the emergence of methicillin resistant *S. aureus* (MRSA) strains following to application of these antibiotics in treatment of *S. aureus* infections.[4,9] During past decades MRSA infections has been increased and even these strains developed resistance to cefixime and vancomycin.[1] These strains cause treatment failure and increase mortality of patients.[10] Furthermore, multi-drug resistant (MDR) stains cause more compliance in treatment of infectious diseases especially *S. aureus* infections. With respect to these facts searching for new and effective antibacterial agents is in great importance.[4,11] One possible and potential for finding such antibiotics is medicinal plants. These natural antibiotics in comparison with synthetics antibiotics have less side effects and undesirable properties and hence are good candidates for substituting of chemical antibiotics. These sources are usually broad spectrum agents with minimal side effects and in some cases are less expensive than the chemical antibiotics.[12,13]

Medicinal plants have been used for long time in traditional medicine around the world. These plants have active biological substances including terpenses, flavonoids, benzophonones, xanthenes, tannins, saponin, cyanates and oxalate.[14] These constituents have the least toxicity for host cells and while have potent antibacterial, antifungal and antiviral activity and hence considered as good candidates for development of new antibiotics.[7,14] In traditional medicine, plant extracts have been used as hygienic coatings in more than 80% of human population around the world.[15,16] These plants have been mostly used in Asia, Latin America and Africa.[17] In recent years, more interest have been expressed for antibacterial agents originated from medicinal plants and governments and pharmaceutical companies have focused on trading such antimicrobial agents.[7,18] Hence this, several different researches have been planned around the world to discover and introduce new antimicrobial agents from plants, especially native plants that are mainly restricted to a distinct regions. The aim of present manuscript is to review the effective medicinal plants against *S. aureus*. With regarded to the importance of this pathogen and its life threatening infections, such reviews can provide new insights for researchers to conduct their studies toward finding new antimicrobial agents. The aim of this study was to review the effective medicinal plants against *S. aureus* with special attention of native plants of Iran.

METHODS

In this review a comprehensive literature review was performed on papers that have been published from 2004 till 2016

with special focus on those that have been reported native medicinal plants in Iran. For this purpose, the most related data resources such as NCBI, Sciencedirect, Springer, Web of science and as well as local databases such as Irandoc, Islamic science citation (ISC) and Magiran were searched for desired papers. These papers were selected based on the following keywords: *Staphylococcus aureus*, medicinal plant, natural antibiotic, antibacterial plant and medicinal herbs.

RESULTS

The reported MIC and MBC indices for the mentioned plants against *S. aureus* were summarized in Table 1. As it can be found majority of studied plants had bacteriostatic activity and some of had both bacteriostatic and as well as bactericidal activity.

Table 1: MIC and MBC values of effective medicinal plants against *S. aureus*

Antimicrobial plants	Family	MIC	MBC	Reference
Prunus mahaleb	Rosaceae	400*	NR*	13
Torilis leptophylla	Apiaceae	400*	NR	19
Teucrium polium	Lamiaceae	40*	>200*	12
Euphorbia granulata Forssk	Euphorbiaceae	5*	10*	14
Oliveria decumbens	Umbliferae	20*	20*	8
Plantago ovata	Plantaginaceae	20*	>200*	8
Peganum harmala	Zygophyllaceae	0.625*	0.625*	11
Eucalyptus microtheca	Myrtaceae	24*	NR	21
Arum maculatum	Araceae	2.5**	NR	22
Mentha pulegium	Lamiaceae	8*	8*	18
Teucrium polium L.	Lamiaceae	4*	NR	23
Zatoria multiflora Biss	Labiatae	0.839 to 12.50*	1.601 to 25.00*	24
Cistus salvifolius	Cistaceae	25*	NR	26
Salvia officinalis	Labiatae	50*	NR	26
Arbutus pavarii	Ericaceae	50*	NR	26
Pistacia atantica	Anacardiaceae	50*	NR	26
Myrtus communis	Myrtaceae	50*	NR	26
Salvia officinalis	Labiatae	150**	NR	27
Eucalyptus globulus	Myrtaceae	120**	NR	27
Coleus forskohlii	Lamiaceae	160**	NR	27
Arctostaphylos uvaursi	Ericaceae	90**	NR	27
Coptis chinensis	Ranunculaceae	120**	NR	27
Larrea tridentata	Zygophyllaceae	60**	NR	27
Turnera diffusa	Turneraceae	300**	NR	27
Anemopsis californica	Saururaceae	360**	NR	27
Allium sativum	Alliaceae	400**	NR	27
Hypericum Japonicum	Clusiaceae	16**	64**	25
Withania somnifera (leaf extracts in aqueous)	Solanaceae	0.946**	NR	30
Withania somnifera (leaf extracts in methanol)	Solanaceae	0.812**	NR	30
Withania somnifera (leaf extracts in ethanol)	Solanaceae	0.832**	NR	30
Cinnamomum iners (stem bark, volatile oil extract)	Lauraceae	625**	1250**	28
Cinnamomum altissimum (stem bark, volatile oil extract)	Lauraceae	156.25**	312.5**	28
Cinnamomum porrectum (stem bark, volatile oil extract)	Lauraceae	2500**	5000**	28
Cinnamomum impressicostatum (stem bark, volatile oil extract)	Lauraceae	156.25**	312.5**	28

*MIC: Minimum Inhibitory Concentration; MBC: Minimum Bactericidal Concentration; *: mg/ml; **: µg/ml.*

DISCUSSION

Seyyednejad et al. have studied the antibacterial effect of ethanol extract of Parsley and *Prunus mahaleb* against 11 pathogenic bacteria including clinical isolates of *S. aureus*. Their results showed that the 0.4 gr/ml concentration of extract obtained from *Prunus mahaleb* inhibited the growth of *S. aureus* while the extract of Parsley was unable to inhibit *S. aureus*.[13]

Torilis leptophylla is a native plant in Iran that the antibacterial effect of methanol extract from this plant was studied by Maleki et al. The results of this research revealed that this plant have inhibitory effect against all tested bacterial strains including *S. aureus* except *Bacillus subtilis*. The MIC of this extract against *S. aureus* was reported as 0.4 gr/ml.[19]

Darabpour et al. have studied the antibacterial activity of alcoholic extracts prepared from different aerial parts of *Teucrium polium*, a native plant of Iran against pathogenic bacteria. The results of this study showed that these extracts have more antibacterial activity against gram positive bacteria than gram negative species. The methanol extract of this plant had synergistic activity with methicillin against *S. aureus*. The MIC of ethanol extract of this plant against *S. aureus* was 40 mg/ml and this extract was more potential than methanol extract against *S. aureus*. These finding provide new hopes for treatment of MRSA infections and prevent their spread.[12]

Hibiscus rosa-sinensis, *Alcea rosea* L. and *Malva neglecta* wallr are medicinal plants that their antibacterial activity was studied by Seyyednejad et al. Their results suggest that hydroalcoholic extracts of all plants had inhibitory effects against all bacterial strains. The ethanol extract of *H. rosea* had the most inhibitory effect against *S. aureus* and *Staphylococcus epidermidis*. The results of mentioned study explain that these native plants have suitable antibacterial potential and can be considered as new and local source for antibiotic exploration.[15]

Shojaei Moghadam et al. investigated the anti-staphylococcal potency of 8 native medicinal plants of Iran. The tested bacterial strains were clinical isolates with resistance to methicillin and cefixime. As a result, the extracts of *Peganum harmala*, *Quercus brantii*, *Oliveria decumbens* and *Ziziphus spina-Christ* among the studied plants had high inhibitory effect against MRSA and their effects were related to their concentrations. *Quercus brantii* that is a native plant in Iran was the most potent plant for inhibition of *S. aureus*. So, it can be suggested that these plants can be considered for further studies and finding the active constituents of these plants.[1]

Beta vulgaris, *Polygonum patulum*, *Rumex obtusifolius* and *Amaranthus graecizans* are four plants that grow in Iran and anti *S. aureus* activity of their ethanol extract has been proven in the study of Koochak et al.[20] In another study by Koochak et al. it was found that the ethanol extract from aerial parts of *Euphorbia granulata Forssk* has been more effective against gram positive bacteria than gram negative species especially against *S. aureus*. The MIC and MBC values of this extract against *S. aureus* were 5 and 10 mg/ml, respectively. So this plant species is a native and available source for antimicrobial agent extraction.[14]

In the research of Motamedi et al. ethanol and methanol extracts of *Oliveria decumbens* and *Plantago ovata* were examined for antibacterial activity against different pathogenic bacterial species. Both extracts showed broad spectrum activity against gram positive and gram negative species. *S. aureus* showed most sensitivity to methanol extract of *O. decumbens*, with MIC=MBC as 20 mg/ml. Furthermore, *S. aureus* was the most sensitive

species to ethanol extract of *P. ovata* with MIC= 20 mg/ml.[8]

Darabpour et al. found that methanol extract of root and seed of *Peganum harmala* have high antibacterial activity even in least concentration and root extract was more effective against gram positive species than seed extract. Both extracts were bactericidal agents against MRSA species with MIC=MBC as 0.625 mg/ml. Furthermore, the root extract of this plant showed synergistic activity against MRSA. So, it can be used alone or in combination with synthetic antibiotics for treatment of MRSA infections.[11]

The antibacterial activity of *Eucalyptus microtheca* was reported by Seyyednejad et al. The ethanol and methanol extracts of this plant were efficiently inhibited *S. aureus* and it has suggested that this plant can be regarded as a possible source of antibiotic discovery.[21]

In the research of Safari et al, *Allium hirtifolium* has been introduced as an effective remedy for control of hospital acquired-MRSA. Furthermore, *Arum maculatum* and *Teucrium polium* were able to inhibit HA-MRSA but were less effective than *Allium hirtifolium*.[22]

Motamedi et al. have surveyed the antibacterial activity of *Mentha pulegium*. As a result it was found that this plant has considerable inhibitory effect against different bacterial pathogens especially against *S. aureus* with MIC=MBC as 8 mg/ml. So, this plant can be suggested for further study and finding new antibacterial agents.[18]

The methanol extract of *Teucrium polium* efficiently inhibited the MRSA even in the least used concentration (4 mg/ml) in the study of Motamedi et al.[23]

Antibacterial effects of hydroalcoholic extract of *Zatoria multiflora Biss* against community-acquired MRSA (CA-MRSA) was assessed by Ur-rahman et al. The results showed that all extracts of this plant, i.e. ethanol, methanol, chloroform and hexane extracts were effective against CA-MRSA and the most inhibition was related to the chloroform extract. The MIC and MBC values for individual extracts and their combinations were in the range of 0.839 to 12.50 mg/ml and 1.601 to 25.00 mg/ml, respectively.[24]

The *Hypericum japonicum* in the study of Zuo et al. was found as an efficient anti-MRSA compound and it showed strong synergistic activity with ampicillin, ceftazidime and levofloxacin, so it can be used as single antibacterial agent or in combination with such synthetic antibiotics for treatment of MRSA infections.[25]

Abouzeed et al. investigated the potential of 8 medicinal plants for control of MRSA strains. Their results revealed that all tested plants were effective against MRSA with MIC values between 25-50 mg/ml and *Cistus salvifolius*, *Salvia officinalis*, *Pistacia atantica*, *Arbutus pavarii*, and *Myrtus communis* had the highest anti-MRSA activity while *Teucrium polium*, *Thymus capitellatus*, and *Euphorbia dendroides* had less activity against MRSA.[26]

Snowden et al. have also found that *Salvia officinalis*, *Eucalyptus globulus*, *Coleus forskohlii*, *Coptis chinensis*, *Turnera diffusa* and *Larrea tridentate* are potent sources for inhibition of *S. aureus* with MIC value between 30-600 μg/ml and while *Baptisia tinctoria*, *Baptisia vulgaris* and *Glycyrrhiza glabra* had less antibacterial activity against *S. aureus*.[27]

Three species of Cinnamomum, including *C. impressicostatum*, *C. altissimum* and *C. porrectum* were investigated for anti- MRSA activity in the study of Sunday Buru et al. Among these plants, *C. impressicostatum* had the most inhibitory effect against MRSA. The findings of this study confirmed the traditional use of Cinnamomum for wound infection treatment.[28]

Fensterseifer et al reported that the cyclotides extracted from *Viola odorata* and *Oldenlandia affinis* are efficient anti *S. aureus* substances and have reduced the bacterial load at *in vivo* experiment.[29]

Different parts of *Withania somnifera* in the study of Kaur et al. were tested against various bacterial pathogens including *S. aureus*. Their results revealed that ethanol, methanol and aqueous extracts have antibacterial activity and methanol and ethanol extracts of leaf of this plant had the highest activity against *S. aureus*.[30]

CONCLUSION

Based on the mentioned reports in this review it can be concluded that medicinal plants especially native plants in Iran are good resources for finding new and effective anti *S. aureus* agents. With regard to this fact that the majority of *S. aureus* strains are resistant to present antibiotics, it is necessary to find new antibiotics in order to control MRSA infections and prevention of life threatening infections.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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