



Iranian Native Medicinal Plants Affecting *Staphylococcus aureus* as Septic Pathogens: An updated Review

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Staphylococcus aureus is the second leading pathogenic cause of nosocomial infections and plays an important role in the development of food poisoning and purulent, systemic and nosocomial infections. This bacterium is responsible for infections such as abscess, food poisoning, third grade burns, traumatic ulcers, surgical incisions, bed sores or atrophic ulcers. Long-term use of antibiotics has led to the emergence of multi-drug resistant strains in infectious diseases. Due to increased resistance of bacteria to chemical drugs and the few side effects of medicinal plants, medicinal plants have nowadays attracted much more attention of researchers. In this regard, studies have been done on the effectiveness of medicinal plants against infectious agents such as *S. aureus* and methicillin-resistant *S. aureus*. Therefore, in this review study, native Iranian herbs that are effective on *S. aureus* were reported. In this review study, search terms including *Staphylococcus aureus*, herbs, extracts and essential oils were used to retrieve articles indexed in databases such as the *Institute for Scientific Information*, *PubMed*, *Scopus*, *Scientific Information Database*, *Magiran*, and *Google Scholar*. Garlic, pomegranate, *Anethum graveolens*, coriander, eucalyptus, *Lawsonia inermis*, *Descurainia sophia*, Figworts, artemisia, thyme, etc. are some of the most important anti-staphylococcal herbs.

Keywords: Herbal medicine, Infection, Toxic shock syndrome, Toxic sepsis, Antibiotic, Drug resistance.

Introduction

Infectious diseases kill thousands each day around the world [1]. *Staphylococcus aureus* is the second leading pathogenic cause of nosocomial infections [2]. *S. aureus* is a pathogenic bacterium that produces catalase. This bacterium plays an important role in the development of food poisoning and purulent, respiratory, and nosocomial infections [3]. This bacterium is a major contributor to infections such as toxic

shock syndrome, toxic sepsis, abscess, food poisoning, third grade burns, traumatic ulceration, surgical incision, bed sores or atrophic ulcers [4, 5]. Reports have indicated that 25-30% of people in different communities are nasal carriers of the bacterium [6]. The increasing incidence of bacterial resistance to antibiotics as well as the side effects of these drugs have been among the factors that have led to the spread of research on medicinal plants in recent years [7]. Long-term use

of antibiotics has led to the emergence of multidrug resistant strains in infectious diseases [8]. The increasing spread of resistance of *S. aureus* strains to antibiotics is one of the problems that today's medicine faces; and due to the emergence of semi-resistant and resistant strains to common antibiotics and even the last-line drugs such as vancomycin, the future of the treatment of these infectious species has become tentative [9]. Today, *S. aureus* has been identified as the most important cause of nosocomial infection. Currently, over 90% of patients with staphylococcal infections do not respond to penicillin or ampicillin [10,11]. The antibiotic methicillin is the first semi-synthetic penicillin resistant to β -lactamase [12]. Methicillin resistance represents resistance to all penicillinase and cephalosporin-resistant penicillins [13]. Recently, due to the side effects of the used drugs and antibiotics and antibiotic resistance to *S. aureus*, the use of natural antimicrobial compounds and plant compounds has drawn great attention [14]. *S. aureus* is one of the most important infectious agents in humans, and on the other hand, due to the increased resistance of bacteria to chemical drugs and the few side effects of medicinal plants, medicinal

plants are nowadays have attracted much more attention of the researchers. In this regard, studies have been done on the effectiveness of medicinal plants against infectious agents such as *S. aureus* and methicillin-resistant *S. aureus*. Therefore, in this review study, native Iranian herbs that were effective on this bacterium were reported.

Methods

To conduct this review, search terms including *Staphylococcus aureus*, herbs, extracts and essential oils were used to retrieve articles indexed in databases such as the *Institute for Scientific Information, PubMed, Scopus, Scientific Information Database, Magiran*, and *Google Scholar*.

Results

Garlic, pomegranate, *Anethum graveolens*, coriander, eucalyptus, *Lawsonia inermis*, *Descurainia sophia*, Figworts, artemisia, thyme, etc. are some of the most important anti-staphylococcal herbs. Additional information is shown in Table 1.

TABLE 1. The most important anti-*Staphylococcus aureus* herbs

Scientific Name	Part of plant	Family Name	Type affect	Common name	Origin of plant	Year/ Type of study	Result
<i>Allium Sativum</i>	Bulb	Alliaceae	Aqueous and chloroform extracts	Garlic	Between the Mediterranean and China and common seasoning worldwide	In-vitro 2013	To investigate the effect of extracts, <i>Staphylococcus aureus</i> bacteria cultured in a liquid culture medium were transferred to plates containing Mullerinton agar medium. Then, the disks impregnated with pure dilutions, 12/, containing zinc enzymes, were placed on 12.18, 1/64, 1/32, 16.1, 8.1, and 1/4 <i>Staphylococcus aureus</i> , this test One time for aqueous extract and once for chloroform extract. After incubation, the diameter of the bacterial growth holes was measured. The chloroform extract with a mean diameter of 27 ± 3 without an antimicrobial effect had a stronger antimicrobial effect on <i>Staphylococcus aureus</i> , but the aqueous extract showed a weaker antimicrobial effect with a mean diameter of 17 ± 2 without dilution and by dilution The extract was reduced, antimicrobial effect decreased, so that at dilution of 32: 1 chloroform extract with mean diameter of the non-growth hole of 1 ± 2 and the aqueous extract with the mean diameter of the no-growth zone was almost zero and in dilutions of 64: 1 and 128 : 1 No bacterial[15].
<i>Punica granatum</i>	Peel	Lythraceae	Peel extract (ethanol)	Pomegranate	It is widely Cultivated throughout the Middle East and Caucasus region + north Asia and mediterranean.	In vitro 2017	Many previous studies evaluated the antimicrobial potential of <i>P. granatum</i> extracts.in a study the water soluble alkaline fractions contain the highest number of phenolic acids and they were most effective against Gram positive bacteria [16].

<i>Anethum graveolens</i>	Seed	Umbelliferae	An emulsion of water is essential oil	Shevid	_ grown in Eurasia	In vitro 2016	The antimicrobial activity of the essential oil from seeds was evaluated on three pathogenic microorganisms: <i>Staphylococcus aureus</i> (1431 PTCC, Escherichia coli (H7: O157) 35218 ATCC) and <i>Salmonella typhimurium</i> (14028 ATCC), and the lowest inhibitory concentration (MIC) The lowest lethal concentration (MBC) was also determined for this purpose. Six concentrations of each essential oil including 250ppm, 4000.2000,1000,500,125 were selected for this purpose. The seeds of the seed had the lowest inhibitory concentration (MIC) (equivalent to 500 ppm and lowest) The bactericidal concentration (MBC) was 1000 ppm against the bacterium <i>Staphylococcus</i>
<i>Coriandrum sativum</i>	Seed	Apiaceae	Coriander oil water emulsion	Geshniz	Native to Southwest Asia and North Africa	Invitro 2016	In this research, the antimicrobial activity of essential oil from coriander seeds on three pathogenic microorganisms: <i>Staphylococcus aureus</i> (1431 PTCC, Escherichia coli (H7: O157) 35218 ATCC) and <i>Salmonella typhimurium</i> (14028 ATCC) were evaluated and the lowest inhibitory concentration MIC and the least lethal concentration (MBC) were determined for this purpose, six levels of concentration of each essential oil including 250 ppm, 4000, 2000, 1000, 500, 125. The essential oil of coriander seeds compared to the essential oil of the seeds was more inhibitory to bacteria Gram negative. The essential oil of coriander seed had MIC and MBC equal to 1000 ppm against the <i>Staphylococcus aureus</i> [17].
<i>Eucalyptus</i>	Leaf	<u>Myrtaceae</u>	Vjvshandh aqueous extract of Eucalyptus	Gum trees	<u>Australia</u> And cultivated in Americas, Europe, Africa, the Middle East, China, and the Indian subcontinent.	Invitro 2007	In this study, the antimicrobial activity of Eucalyptus aquatic extract and decoction extract was carried out using agar disc diffusion method. Each test was repeated three times and the mean diameter of the growth hole on the Muller Hinton Agar environment was measured and recorded. Eucalyptus dilutions of 1.2, 1.4, and 1.8 were prepared from aqueous and boiled water extracts. Due to the lack of growth of the bacteria and stomach, Dordish disc diffusion was observed that inhibited the growth of 64% of the bacteria [18].
<i>Lawsonia inermis</i>	Leaf	<u>Lythraceae</u>	Water and ethanol extracts of Henna	Lawsonia Or hina	Native to North Africa, South and West Asia, and Australia	Invitro 2009	A wide range of aqueous and ethanolic extracts of henna were used against <i>Staphylococcus aureus</i> So that with a MIC of 50 for this bacterium in aqueous extract is 2.5 mg/ml and ethanol extract is 3 mg / ml. The aqueous extract at a concentration of 7.5 mg/ml could prevent the isolation of 25 isolates of <i>Staphylococcus aureus</i> . Ethanol concentration of 7.5 mg/ml prevents the growth of all isolates of <i>Staphylococcus aureus</i> [19].
<i>Descurainia sophia</i>	Seed	Brassicaceae	Ethanol extract	Hherb-Sophia	The hills in the plains and mountains are in most mountainous regions of the world.	In vitro 2005	In the study of the effect of extracts obtained from husker with distillation in vacuum at a concentration of 5.8, 3.1, 8.8 g / 100 cc distilled water and standard <i>Staphylococcus aureus</i> , no inhibition zone was observed around the wells. In fact, the extracts were not able to inhibit the growth or kill of the bacteria and did not have bactericidal or bacteriostatic effects on bacteria [20].

<i>Scrophularia</i>	Aerial part	Scrophulariaceae	Aqueous and Alcoholic Extract	Figworts	A plant that grows in the mountainous areas of Zagros, and its name is local in the province of Ilam, thirsty.	In vitro 2007	The results showed the inhibitory effect of the aqueous and alcoholic extract of the thirsty plant on <i>Staphylococcus aureus</i> bacteria. The diameter of the aqueous inhibition of the aqueous extract of this plant on 14 mm <i>Staphylococcus aureus</i> bacteria and the ethanolic and methanolic anesthetics of the ethanolic and methanolic extract of the <i>Staphylococcus aureus</i> were 10 and 12 mm M. The results of MIC and MBC determination (the lowest inhibitory concentration (MIC) and the lowest effective killer concentration (MBC) for this bacterium were 5 and 10 µg / ml respectively [21].
<i>Artemisia</i>	Aerial part	<u>Asteraceae</u>	Ethanolic extract	Mugwort		Invitro 2006	Antimicrobial effect of <i>Artemisia</i> ethanolic extract had an excellent antibacterial effect against <i>Staphylococcus aureus</i> resistant and motilcin susceptible strains. The results of F-test showed that value-P value of F-test was in all investigated values of the extract of <i>Artemisia</i> seedlings (P <0.05). MIC results also showed that the ethanolic extract of this plant, even at very low concentrations, inhibited good growth [22].
<i>Thymes</i>	Aerial part	<u>Lamiaceae</u>	Thyme essential oil	<u>Thymus vulgaris</u>	Iran and europe and Romans	Invitro 2012	The results of quantitative testing of MIC from the tested essential oils for antibiotic resistant <i>Staphylococcus aureus</i> were as follows. The lowest MIC value for tetracycline-resistant tetanus essential oil was 3.163 µg/ml [23].
<i>Mentha longifolia</i>	Aerial part	Lamiaceae	Ethanolic extract	Wild mint	PALESTINE	In vitro 2006	Antibacterial properties of the ethanolic extract of the plant with a diameter of 14 mm inhibition zone for MRSA has been proved. MIC and MBC were also 3.125 and 12.5 mg/ml respectively [24].
<i>Melissa officinalis</i>	Aerial part	Lamiaceae	Ethanolic extract	Lemon balm	PALESTINE	In vitro 2006	Antibacterial properties of ethanolic extract of the plant with a diameter of 15 mm inhibition zone for MRSA has been proven. MIC and MBC were also 3.125 and 12.5 mg/ml respectively [25].
<i>Rosa damascena</i>	Flower	Rosaceae	Ethanolic extract	Damask rose	PALESTINE	In vitro 2006	Antibacterial properties of ethanolic extract of the plant with a diameter of 34 mm inhibition zone for MRSA have been proven. MIC and MBC were 0.39 and 0.78 mg/ml, respectively [24].
<i>Scutellaria barbata</i>	Leaves	Lamiaceae	Ethereal Extract	Barbed skullcap	Asia	In vitro 2000	The ether extract of this plant with an MIC of 125-250 has antibacterial properties [25].
<i>Camellia sinensis</i>	Leaves	Theaceae	Alcoholic Extract	Tea plan	Chinese	In vitro 2005	Antibacterial effect of ethanolic extract with MIC = 1.8-7.5 mg/ml was proved [26].
<i>Delonix regia</i>	Flowers	Fabaceae	Alcoholic Extract	<u>Flame tree</u>	Madagascar	In vitro 2005	Antibacterial properties of ethanolic extract with MIC = 5-7.5 mg/ml have been proven [27].
<i>Holarrhena antidysenterica</i>	Bark	Apocynaceae	Alcoholic Extract	White angel	Indian	In vitro 2005	Antibacterial effect of ethanolic extract with MIC = 2.8-5.6 mg/ml has been proved [26].
<i>Lawsonia inermis</i>	Leaves	Lythraceae	Alcoholic Extract	Hina	northern Africa, western and <u>southern Asia</u> , and northern <u>Australasia</u>	In vitro 2005	Antibacterial properties of ethanolic extract with MIC = 1.3-7.5 mg/ml have been proven [26].

<i>Punica granatum</i>	Rind	Lythraceae	Alcoholic Extract	Punica granatum	Iran and <u>Mediterranean</u> region and northern <u>India</u>	In vitro 2005	Antibacterial properties of ethanolic extract with MIC = 1.8-5.3 mg/ml have been proven [26].
<i>Terminalia chebula</i>	Fruits	Combretaceae	Alcoholic Extract	Chebulic myrobalan	South East Asia.	In vitro 2005	Antibacterial properties of ethanolic extract with MIC = 1.5-8.2 mg/ml have been proven [26].
<i>Terminalia belerica</i>	Fruits	Combretaceae	Alcoholic Extract	Bastard myrobalan	Southeast Asia	In vitro 2005	Antibacterial properties of ethanolic extract with MIC = 1.8-7.8 mg/ml have been proven [26].
<i>Acorus calamus</i>	Rhizome	Acoraceae	Alcoholic Extract	Sweet flag	South Asia Indian	In vitro 2006	Antibacterial properties of ethanolic extract with MIC = 1.5-3 mg/ml have been proven [27].
<i>Hemidesmus Indicus</i>	Stem	Apocynaceae	Alcoholic Extract	Sarsaparilla	South Asia Indian	In vitro 2006	Antibacterial properties of ethanolic extract with MIC = 1.5-2.8 mg/ml have been proven [27].
<i>Holarrhena Antidysenterica</i>	Bark	Apocynaceae	Alcoholic Extract	White angel	Indian	In vitro 2006	Antibacterial properties of ethanolic extract with MIC = 2.5-3 mg/ml have been proven [28].
<i>Plumbago zeylanica</i>	Root	Plumbaginaceae	Alcoholic Extract	Ceylon leadwort	India	In vitro 2006	Antibacterial properties of ethanolic extract with MIC = 0.75-1.8 mg/ml have been proven [27].
<i>Terminalia avicennioides</i>	Bark	<u>Combretaceae</u>	water and ethanol extracts	-	West Africa.	In vitro 2005	MIC of the extracts was determined by dilution of Terminalia avicennioides Water extract: 20.8 Ethanol extract: 18.2 [28].
<i>Ocimum gratissimum</i>	Leaf	<u>Lamiaceae</u>	water and ethanol extracts	Clove basil	Africa, Madagascar, southern Asia	In vitro 2005	MIC of the extracts was determined by dilution of <i>Ocimum gratissimum</i> - Water extract: 25.0 and Ethanol extract :22.3 [28].
<i>Acalypha wilkesiana</i>	Leaf	<u>Euphorbiaceae</u>	water and ethanol extracts	-	In South Florida and tropical America.	In vitro 2005	MIC of the extracts was determined by dilution of <i>Acalypha wilkesiana</i> Water extract: 24.5 Ethanol extract : 24.0 [28].
<i>Melaleuca alternifolia</i>	leaves	<u>Myrtaceae</u>	oil	Tea tree	Endemic To Australia	In Vitro 1997	The MIC was defined as the lowest concentration of each oil that inhibited visible growth after overnight incubation in air at 37°C. MIC : 0.25 mg/ml [28].
<i>R. repens</i>	leaves		oil	-	Iran	In-vitro 2020	MIC: 50 µl [47].
<i>P. harmala fruit</i>	Leaves, fruit		oil	-	Iran	In-vitro 2020	MIC: 50 µl [47].
<i>J. conglomeratus</i>	Fruit		oil		Iran	In-vitro 2020	MIC: 50 µl [47].
<i>Eremurus persicus</i>			Ethanol Extract			In-vitro 2020	MIC: 2.55 ppm [48].

Discussion

The effect of medicinal plants on infectious and bacterial agents has been investigated in different studies. Native herbs of Iran and their effects on infectious agents such as *S. aureus* have been addressed in this review. Many of the herbs also have anti-inflammatory and antimicrobial effects due to the above-mentioned active ingredients and possibly inflammatory and microbial processes. The effects of medicinal plants on infectious diseases are undeniable, and it is a common practice to use them either traditionally, or to prepare processed, nature-based products used to control and treat infections and microbial diseases. According to several studies on numerous plants, their effects have been scientifically proven. This information can be used to produce effective pharmaceutical products. In herbs, there are drug combinations and antioxidants that are responsible for the therapeutic effects [45-47]. The active ingredients of these plants, which include anthocyanins, phenolic compounds, flavonoids and flavones, tannins and other bioactive substances, can be used to produce antibacterial products.

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Conflict of Interest

This is a review article, no conflict of interest.

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