

# Sumac (*Rhus coriaria* L.) Represents a Considerable Antibacterial Activity Against Meticillin Susceptible and Meticillin Resistant *Staphylococcus aureus*



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## Abstract

**Background:** *Staphylococcus aureus* is one of the most important pathogens and the cause of suppuration, abscess formation, a variety of pyogenic infections, and even fatal septicemia in human beings. Isolation of resistant strains of *S. aureus* especially meticillin-resistant one has elucidated the importance of finding new antibacterial agents. Sumac is one of the important medicinal herbs of Iranian traditional medicine (ITM). Sumac has been traditionally prescribed for some ailments with infectious etiology and therefore, it probably contains antibacterial compounds. Recently, antibacterial activities of sumac against some bacteria were studied by our team.

**Objective:** In this article, we aimed to compare the antibacterial activities of sumac against meticillin susceptible (MSSA) and meticillin resistant *S. aureus* (MRSA) via minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC) determination.

**Materials and Methods:** Antibacterial activity of sumac water extract was studied on 19 clinical and 1 standard strain of *S. aureus* via MIC and MBC determination. Based on their sensitivity to cloxacillin, these bacteria were classified as meticillin-susceptible, intermediate meticillin-resistant, and meticillin-resistant. MICs and MBCs of the extracts in these 3 groups were statistically compared via one-way analysis of variance (ANOVA) followed by a post hoc analysis (Tukey HSD test) using SPSS for Windows (version 15).

**Results:** The results showed that in spite of different susceptibilities to cloxacillin, susceptibility to sumac extract was not different and MICs and MBCs of sumac for all clinical isolates including MSSA and MRSA were similar ( $P > 0.05$ ).

**Conclusion:** Based on previous studies, sumac extract acts against *S. aureus* probably through changing the cell wall properties. This activity is similar for both MRSA and MSSA. More investigation on the precise mechanism of action of this extract would be fruitful.

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## Background

Meticillin-resistant *Staphylococcus aureus* (MRSA), which its resistance is due to the production of penicillin-binding protein (PBP) 2, has been recently emerged as one of the most important nosocomial and community pathogens. According to a European report, MRSA population-weighted mean in European Union is 17.8%, highlighting that MRSA remains a public health priority.<sup>1</sup> MRSA is resistant to not only meticillin and other  $\beta$ -lactams but also to many other antimicrobials. This has now resulted in multidrug resistance of MRSA. Today, some glycopeptides such as vancomycin are widely prescribed for serious MRSA infections; however, the

emergence of vancomycin tolerance and resistance has complicated treatment and highlighted the clinical need for new antibiotics which can work against MRSA and other Gram-positive bacteria.<sup>2</sup>

Sumac (*Rhus coriaria* L.) is a shrub, inhabiting the regions from Mediterranean Sea to Iran and Afghanistan. Its fruit is widely used in Middle Eastern cuisine especially in Iran and Turkey.<sup>3</sup> Sumac fruit has also been mentioned in Iranian traditional medicine (ITM) as a herb with some therapeutic potentials. Traditionally, the powdered fruits have been prescribed as astringent, anti-diarrhea, anti-trachoma, and anti-pus in infectious wounds.<sup>4</sup>

Inspired from ITM, we previously planned a series

of investigations on sumac antibacterial activities.<sup>5-8</sup> In these studies, we showed that sumac has considerable antimicrobial activities against some standard and susceptible strains of gram-positive bacteria such as *Bacillus cereus*, *Corynebacterium xerosis*, *Staphylococcus epidermidis*, and *S. aureus*.

### Objectives

The present study was aimed to compare the antibacterial activities of sumac against both methicillin-susceptible *S. aureus* (MSSA) and MRSA via minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC) determination.

### Materials and Methods

#### Plant Material and Extraction

*Rhus coriaria* L. was obtained from local botanical market and confirmed by Dr. Gholamreza Amin, at Herbarium of the School of Pharmacy, Tehran University of Medical Sciences. One hundred grams of the powder of *R. coriaria* L. epicarp was soaked in 1000 mL of distilled water at 45°C for 5 days. The extract was concentrated in a rotary evaporator (Heidolph, Germany) and was left to dry in a desiccator. The yield of extract (calculated as weight of dry extract/weight of dry starting material × 100) was 43.6 (w/w). The extract was diluted at desirable concentrations in distilled water and was filter sterilized prior to antibacterial assays.

#### Bacterial Strains

Staphylococcal strains listed in Table 1 were 19 clinical strains isolated from Shariati and Bouali University

hospitals and Danesh Pathobiology Laboratory and identified by conventional morphological and biochemical tests. The standard strain of *S. aureus* ATCC 6539-P, which was methicillin-sensitive, was stock of the Department of Pharmaceutical and Food Control, School of Pharmacy, Tehran University of Medical Sciences, used in assessing the development of antibacterial resistance induced by the extract. Antibiotic susceptibility was determined by the amount of MIC of cloxacillin, in accordance with guidelines of the National Committee for Clinical Laboratory Standards (NCCLS, 1997). After culture on Mueller–Hinton agar (Merck, Germany), the bacteria were suspended in Mueller–Hinton broth (Merck, Germany) and used for inoculation.

#### Determination of MICs and MBCs

The concentrations of the extract were prepared in the range of 0.25 to 56.7 (mg/mL) in Muller-Hinton broth containing 10<sup>8</sup> CFU/mL of the bacteria. After incubation at 37°C overnight, the test tubes were examined for possible growth and MICs of the extract were determined as the lowest concentration that ended with no growth. Tubes containing concentrations above the MICs were streaked onto Muller-Hinton agar plates to achieve MBCs of the extract against the bacteria. Vancomycin antibiotic was also used as a positive control.

#### Statistical Analysis

According to the sensitivity of the bacteria to cloxacillin, the bacteria were divided into 3 groups: methicillin-susceptible *S. aureus*, Intermediate methicillin-resistant *S. aureus*, and methicillin-resistant *S. aureus*. To evaluate

**Table 1.** MICs and MBCs of Sumac, Cloxacillin, and Vancomycin Against Susceptible, Intermediate Resistant, and Resistant *Staphylococcus aureus*

Clinical Isolates	<i>Rhus coriaria</i> L. (mg/mL)	Cloxacillin (µg/mL)	Vancomycin (µg/mL)
Methicillin-susceptible <i>S. aureus</i>	2.04 <sup>a</sup>	1.5 (3.1)	0.8 (1.6)
	8.15 (16.35) <sup>b</sup>	1.5 (3.1)	3.1 (3.1)
	4.07 (16.35)	1.5 (3.1)	3.1 (6.2)
	0.25 (8.15)	1.5 (3.1)	1.5 (6.2)
	4.07 (16.35)	0.8 (1.6)	3.1 (3.1)
<i>S. aureus</i> ATCC 6539-P	1.02 (4.07)	1.5 (3.1)	1.5 (6.2)
	2.04	3.1 (12.5)	1.5 (3.1)
Intermediate methicillin-resistant <i>S. aureus</i>	4.07	3.1 (12.5)	0.8 (1.6)
	2.04 (16.35)	3.1 (6.2)	1.5 (3.1)
	2.04 (16.35)	3.1 (12.5)	6.2 (6.2)
	2.04	3.1 (25)	3.1 (6.2)
	0.25 (16.35)	3.1 (6.2)	3.1 (6.2)
	4.07 (28.35)	25 (50)	1.5 (3.1)
Methicillin-resistant <i>S. aureus</i>	2.04 (16.35)	12.5 (12.5)	3.1 (6.2)
	8.15 (16.35)	25 (50)	1.5 (3.1)
	0.25 (16.35)	25 (50)	3.1 (6.2)
	4.07 (16.35)	12.5 (25)	1.5 (3.1)
	0.25 (28.35)	50 (50)	3.1 (6.2)
	4.07 (16.35)	12.5 (25)	3.1 (6.2)
	1.02 (8.15)	25 (50)	3.1 (6.2)

the effectiveness of sumac, MICs and MBCs of the extract in these 3 groups were statistically compared via one-way analysis of variance (ANOVA) followed by a post hoc analysis (Tukey HSD test) using SPSS for Windows (version 15.0).

## Results

According to the sensitivity to cloxacillin, the clinical isolates were divided into 3 subgroups: methicillin-susceptible *S. aureus*, intermediate-methicillin resistant *S. aureus*, and methicillin-resistant *S. aureus* (Table 1). The statistical analysis showed that in spite of different susceptibilities to cloxacillin, susceptibility to sumac extract was not different and MICs and MBCs of sumac for all clinical isolates including MSSA and MRSA were similar ( $P > 0.05$ ). The effect of vancomycin against all strains of *S. aureus* was also similar (Figure 1A and 1B).

## Discussion

Sumac as an herb with a traditional anti-infective background of use has been recently considered in ethnopharmacological studies. Based on a series of investigations, we published several studies on antibacterial activities of sumac. In these studies, sumac antibacterial activities against both gram-positive and gram-negative bacteria including *B. cereus*, *C. xerosis*, *S.*

*epidermidis*, *S. aureus*, *Escherichia coli*, *Salmonella typhi*, *Pseudomonas aeruginosa*, and *Shigella flexneri* were well presented.<sup>5,6</sup> Other studies completed this list and showed that antibacterial activities of sumac are beyond these bacteria.<sup>9</sup> It has also been shown that the total extract of sumac can be sterilized by autoclaving without any changes in its antibacterial activities.<sup>8</sup> In another article published recently, our team showed the major active compounds of sumac extract against bacteria specifically *S. aureus*.<sup>10</sup> These activities present sumac as a good candidate to be developed as a final product in pharmaceutical dosage form.

To complete the above-mentioned studies and due to the increasing importance of bacterial resistance, this study aimed to evaluate the behavior of sumac extract in the presence of different MSSA and MRSA strains. The results showed that resistance to methicillin family does not affect antibacterial activity of sumac, as their mechanisms of action probably completely differ from each other.

Gallic acid was recently introduced as one of the active compounds of sumac.<sup>10</sup> Based on the work of Borges and colleagues on the mechanism of action of gallic acid against different bacteria, gallic acid caused irreversible changes in membrane properties through hydrophobicity changes, decrease of surface negative charge, and occurrence of local rupture or pore formation in the cell membranes resulting in consequent leakage of essential intracellular constituents.<sup>11</sup>

The other active compound of sumac, 1,2-dioxo-6-hydroxycyclohexadiene-4-carboxylic acid, belongs to quinones. This class of compounds provides a source of stable free radicals and can form irreversible complexes with nucleophilic amino acids in proteins that often cause their function loss and subsequent cell death. Surface-exposed adhesions, cell wall polypeptides, and membrane-bound enzymes are probable targets of quinone oxidation.<sup>12</sup>

As a conclusion, sumac extract acts against *S. aureus* probably through changing the cell wall properties. This activity is similar for both MRSA and MSSA. More investigation on the precise mechanism of action of this extract would be fruitful.

### Authors' Contributions

Study concept and design: MRF and HJ; Data acquisition: MK and MMAA; Analysis and interpretation of data: MMAA and MK; Drafting of the manuscript: MMAA; Study supervision: MRF and HJ.

### Ethical Approval

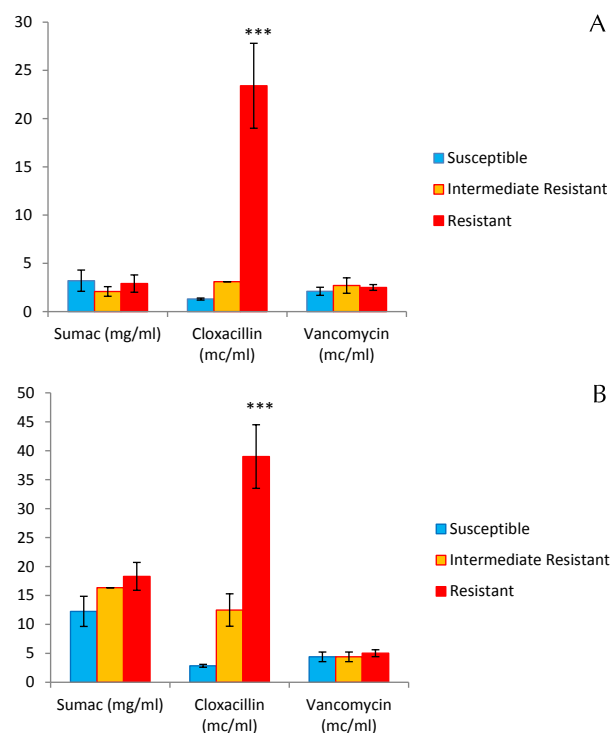
The research followed the principles of Basel Declaration.

### Conflict of Interest Disclosures

The authors declare that they have no conflict of interests.

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**Figure 1.** (A) Mean MICs of Sumac, Cloxacillin, and Vancomycin Against Susceptible, Intermediate Resistant, and Resistant *Staphylococcus aureus*. (B) Mean MBCs of Sumac, Cloxacillin, and Vancomycin Against Susceptible, Intermediate Resistant, and Resistant *Staphylococcus aureus*. The meaningful differences were only seen in cloxacillin subgroups (\*\*\*)  $P < 0.001$ .

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**References**

1. European Centre for Disease Prevention and Control. Antimicrobial resistance surveillance in Europe 2012. Stockholm: 2013:62.
2. French GL. Bactericidal agents in the treatment of MRSA infections--the potential role of daptomycin. J Antimicrob Chemother. 2006;58(6):1107-1117.
3. Amin G. Popular Medicinal Plants of Iran. Tehran: Tehran University of Medical Sciences Publication; 2004:178.
4. Aghili-Khorasani MH (18th century). Makhzan ul-Advia. Tehran: Enqelab-e Eslami Publishing and Educational Organization; 1992.
5. Fazeli MR, Amin G, Ahmadian-Attari MM, Ashtiani H, Jamalifar H, Samadi N. Antimicrobial activities of Iranian sumac and avishan-e shirazi (*Zataria multiflora*) against some food-borne bacteria. Food Control. 2007;18:646-649. doi:10.1016/j.foodcont.2006.03.002.
6. Fazeli MR, Ashtiani H, Ahmadian-Attari MM, Jamalifar H, Zaheri A. Antimicrobial effect of *Rhus coriaria* L. (Sumac) total extract on skin isolates *Staphylococcus epidermidis* and *Corynebacterium xerosis*. J Med Plant. 2006;17(1):27-31.
7. Ahmadian Atari MM, Monsef Esfahani HR, Amin GR, et al. The ethnopharmacological study on antibacterial activity of some selected plants used in Iranian traditional medicine. J Med Plant. 2009;8(31):50-57.
8. Amin GH, Ahmadian-Attari MM, Fazeli MR, et al. The effects of autoclaving, salt and protein on antimicrobial activities of Iranian sumac. J Med Plant. 2008;25(1):49-53.
9. Ahmadian-Attari MM, Amin G, Fazeli M, Jamalifar H. A review on antimicrobial activities of sumac fruit (*Rhus coriaria* L.). J Med Plant. 2008;1(25):1-11.
10. Ahmadian-Attari MM, Amini M, Farsam H, et al. Isolation of major active antibacterial compounds of sumac fruit (*Rhus coriaria* L.). Int J Enteric Pathog. 2016;4(4):e37101. doi:10.15171/ijep.2016.11.
11. Borges A, Ferreira C, Saavedra MJ, Simões M. Antibacterial activity and mode of action of ferulic and gallic acids against pathogenic bacteria. Microb Drug Resist. 2013;19(4):256-265. doi:10.1089/mdr.2012.0244.
12. Cowan MM. Plant products as antimicrobial agents. Clin Microbiol Rev. 1999;12:564-582.