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Research Article

Salvia cadmica as a potential agent in biofilm-related infection prevention

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Abstract: This study investigates the antibiofilm activity of *Salvia cadmica (S. cadmica)* aqueous-ethanol extract against *Staphylococcus aureus (S. aureus)* ATCC 25923, a well-known biofilm-forming bacterium. The antibiofilm efficacy of the extract on both planktonic and biofilm forms of *S. aureus* ATCC 25923 was assessed using the MTT reduction assay, while morphological alterations were examined by scanning electron microscopy. A dose-dependent increase in biofilm inhibition was observed, with biofilm inhibition and eradication rates reaching 34.07±0.44% and 35.71±0.4%, respectively, at 2× MIC concentration of plant extract. Microbiological analyses confirmed the antibiofilm potential of *S. cadmica* extract against *S. aureus* ATCC 25923. These findings highlight the promising antibiofilm properties of *Salvia cadmica* extract, suggesting its potential application in the treatment of infections associated with biofilm-forming *S. aureus* ATCC 25923. Future research should aim to isolate and characterize individual bioactive compounds from *S. cadmica* to better understand their mechanisms of action and potential synergistic effects.

1. INTRODUCTION

Antibiotic resistance presents a major challenge in the treatment of infections, with biofilm formation playing a pivotal role in the development of this resistance. This has led to an urgent need for the discovery of novel compounds capable of inhibiting biofilm formation to effectively combat persistent, antibiotic-resistant pathogens (Stewart & Costerton, 2001). Biofilms are microbial communities that adhere to surfaces, embedded in a self-produced, gel-like matrix. The extracellular matrix, composed of exopolysaccharides and proteins, forms a crucial attachment surface that facilitates biofilm formation (Ciftci & Aksoy, 2015). Biofilms are largely composed mainly of water (approximately 97%), with smaller amounts of microorganisms (2-5%), polysaccharides (1-2%), proteins (1-2%), DNA (1-2%), and various ions. This matrix serves as a protective barrier, shielding the bacteria from harsh environmental conditions and antimicrobial agents, resulting in a significant increase in bacterial resistance within biofilms compared to their planktonic counterparts (Donlan & Costerton, 2002). Studies indicate that biofilm-forming bacteria can exhibit antibiotic resistance up to 100 to 10,000 times greater than planktonic bacteria. Furthermore, bacteria initially susceptible to antimicrobial agents may develop resistance upon biofilm formation, although they can regain susceptibility

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once they detach from the biofilm (Szczuka & Kaznowski, 2014). The process of biofilm formation is complex, involving multiple genes that regulate cell physiology, including adhesion, quorum sensing, cell wall structure, metabolism, stress responses, and plasmid attachment (Zhao *et al.*, 2005; Boles & Horswill, 2011). The increased resistance of biofilm-embedded bacteria is largely attributed to the enhanced horizontal transfer of antibiotic resistance genes among bacterial cells within the biofilm (Savage *et al.*, 2013).

Biofilm-associated microorganisms are implicated in various human diseases, such as native valve endocarditis and cystic fibrosis, and commonly colonize medical devices. Although epidemiological evidence links biofilms to these infections, the exact mechanisms by which they cause disease remain poorly understood (Donlan & Costerton, 2002). Processes such as detachment of cells or aggregates, production of endotoxins, and increased resistance to the host immune system contribute to pathogenesis (Hall-Stoodley *et al.*, 2004; Gebreyohannes *et al.*, 2019). Notably, pathogens such as *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Escherichia coli*, and *Candida albicans* utilize biofilm formation to cause serious nosocomial infections (Del Pozo, 2018).

S. aureus is a major pathogen causing infections in both humans and animals. As a commensal organism on the skin and mucosal surfaces, *S. aureus* is responsible for a range of skin and soft tissue infections. Due to its virulence factors, it can also lead to severe infections, including bacteremia, toxic shock syndrome, osteomyelitis, and meningitis. The rapid emergence and spread of multidrug-resistant strains, particularly methicillin-resistant *S. aureus* (MRSA), present significant challenges in treating these infections (Kiedrowski & Horswill, 2011).

Plants are rich in antibiotics and other pharmacological compounds, with some having the ability to inhibit biofilm formation in *S. aureus* (Zhao *et al.*, 2005; Li *et al.*, 2011). Compounds such as diterpenoids (Kuźma *et al.*, 2007), oleic acid (Stenz *et al.*, 2008), ellagic acid (Quave *et al.*, 2012), esculetin and fisetin (Ebbensgaard *et al.*, 2010), 1,2,3,4,6-penta-O-galloyl-ß-D-glucopyranose (Lin *et al.*, 2011), and tannic acid (Payne *et al.*, 2013) have been reported to inhibit biofilm formation in *S. aureus*. These plants provide a wide range of substances with multidirectional actions, low side effect risks, and a low potential to induce drug resistance due to their complex compositions. One such group of compounds, polyphenols, is known for its antioxidant, antimicrobial, anti-inflammatory, and antitumor activities, offering broad applications. The antioxidant capacity of polyphenols plays a crucial role in alleviating the adverse effects of oxidative stress, which is associated with the development of various contemporary diseases (Ma *et al.*, 2020).

The *Salvia* (Lamiaceae) genus, which contains 95 species in the Turkish flora, includes a group of plants with an endemism rate of approximately 50% (Baser *et al.*, 2009; Behçet & Avlamaz, 2009). Many *Salvia* species are rich in essential oils, which are economically significant in industries such as food, cosmetics, and perfumery, and these plants are also used in the pharmaceutical industry due to the biologically active phytochemicals they contain. In addition, *Salvia* species are frequently used as herbal teas, food flavorings, and sources of essential oils. The *Salvia* genus, with nearly 1000 species worldwide, provides a variety of herbal substances used globally in medical plants, dietary supplements, food additives, and cosmetics (Bahadori *et al.*, 2015; Bahadori *et al.*, 2017). The aerial parts of *Salvia* (leaves and flowering tops) are the most common sources of secondary metabolites, but the roots also offer valuable compounds. For example, the root of *Salvia miltiorrhiza* is widely used in phytotherapy as a traditional medicine and is included in both Chinese and European pharmacopoeias (Ożarowski *et al.*, 2017). Many endemic *Salvia* species hold potential medicinal importance, although they remain insufficiently studied and are widely used in ethnobotany in their regions of occurrence. In this study, *S. cadmica* Boiss., an endemic species to Turkey, which grows in Central and Western Anatolia, was selected to evaluate its biofilm-inhibiting properties.

The primary objective of this study was to investigate, for the first time, the potential biofilm-inhibiting effects of the aqueous ethanol extract of *S. cadmica* on *S. aureus* ATCC 25923, a

well-known biofilm-forming strain. This research aims to contribute to the identification of novel plant-derived compounds that could be used as effective strategies to combat biofilm-related infections, particularly those caused by antibiotic-resistant strains such as *S. aureus*.

2. METHOD

2.1. Preparation of Plant Extract

The *S. cadmica* Boiss. plant was collected on May 2023, from the rocky mountains along the road, located 3-5 km between Uluborlu and Keçiborlu area (1080 m, 38°04'06"N 30°25'03"E, Herbarium No: MUH 2112). This specimen was identified by Dr. Olcay Ceylan, a Lecturer at the Faculty of Science, Muğla Sıtkı Koçman University. The aerial parts of *S. cadmica* were dried and ground into a fine powder. The ethanol-distilled water (1:1) extract of *S. cadmica* was prepared using the ultrasonic extraction method, following the protocol described by (Latiff *et al.*, 2021). Specifically, 30 g of powdered sample was mixed with 400 mL of solvent and subjected to ultrasonic extraction at a temperature of 35–40°C for 1 hour. To prevent the degradation of bioactive compounds due to heat, the temperature was carefully maintained below 40°C throughout the process. The extract was subsequently filtered through Whatman No.1 filter paper. The solvents were then evaporated under reduced pressure at temperatures below 40°C using a rotary evaporator (Heidolph). After solvent removal, the plant extract was further dried and concentrated in a lyophilizer (Labconco) at -110°C under low pressure to eliminate any remaining liquid residues. The resulting powdered extract was stored at +4°C until further use.

2.2. Minimum Inhibition Concentration

To determine the MIC value of the plant extract, the Clinical Laboratory Standards Institute (CLSI) M7-A8 protocol was modified and applied (CLSI, 2009; Sandasi *et al.*, 2010; Bazargani & Rohloff, 2016). For the broth microdilution assay, sterile U-bottom 96-well microplates were used. *S. aureus* ATCC 25923 was incubated overnight at 37 °C in Mueller Hinton Broth (MHB). The bacterial suspension was prepared at a final concentration of 1×10^6 cells/mL. To achieve this, the bacterial liquid culture was diluted 1:100 with fresh sterile medium, and its optical density (OD_{590} nm) was measured using a spectrophotometer (Sandasi *et al.*, 2010; Bazargani & Rohloff, 2016). A 100 µL aliquot of the prepared bacterial suspension (1×10^6 cells/mL) was added to each well. Subsequently, 100 µL of plant extract at different concentrations (0.024-100 mg/mL, in two-fold serial dilutions) was added to the wells and incubated overnight at 37 °C. After incubation, absorbance was measured at 545 nm using a microplate reader. Ciprofloxacin (1 mg/mL, 100 µL) was used as the positive control, while the medium served as the negative control (Bazargani & Rohloff, 2016). The MIC value was determined as the lowest concentration at which no visible microbial growth was observed compared to the control groups. All analyses were performed in at least three independent replicates.

2.3. Determination of the Antibiofilm Effect by MTT Reduction Test

MTT (3-[4, 5- dimethyl-2-thiazolyl]-2, 5-diphenyl-2H-tetrazolium-bromide) reduction test was used to determine the antibiofilm effect at ½ x MIC, MIC, 2 x MIC concentrations of plant extract (Teanpaisan *et al.*, 2014a; Erdoğmuş *et al.*, 2022). *S. aureus* ATCC 25923 was incubated in Triptic Soy Broth (TSB) medium containing 1% glucose for 24 hours at 37°C. 100 µL of bacterial suspension ($1x10^6$ cells/mL) was added to 96-well plates. Then 100 µL of each treatment group was added to 96-well plates and incubated at 37°C for 24 hours. 100 µL ciprofloxacin (1 mg/mL) was used as a positive control. Medium was used as negative control (Bazargani & Rohloff, 2016). After incubation, the supernatants were discarded and the wells were washed three times with phosphate buffered saline (PBS). 150 µL PBS and 50 µL MTT (0.3%) were added and incubated at 37 °C for 2 hours. MTT solution was removed from the wells and 150 µL dimethyl sulfoxide (DMSO), 25 µL 0.1 M glycine buffer (pH 10.2) was added to the wells to dissolve the formazan crystals and incubated for 15 min at room temperature. The optical density was then measured with a microplate reader at a wavelength of 570 nm. All

analyses were performed with at least three replicates. To calculate the percentage of biofilm inhibition, the following Equation 1 was used:

$$\text{Inhibition (\%)} = \left[1 - \left(\frac{A_{570}\text{of the test}}{A_{570}\text{of none teated control}}\right)\right] \times 100 \quad \text{Eq (1)}$$

2.4. Determination of the Biofilm Eradication

Minimum biofilm eradication concentration (MBEC) was determined to determine the antibiofilm effect of ½ x MIC, MIC, 2 x MIC concentrations of plant extract on the biofilm structure formed by *S. aureus* ATCC 25923 (Teanpaisan *et al.*, 2014b). 200 µL of bacterial suspension (1x10^6 cells/mL) was transferred to 96-well plates and incubated at 37 °C for 24 hours to allow biofilm formation. After biofilm formation, the wells were carefully washed three times with PBS to remove bacterial cells that did not adhere to the wells. Then 200 µL of each treatment group was added to the wells and incubated at 37 °C for 24 hours. The MTT reduction assay was then performed as described above. 100 µL ciprofloxacin (1 mg/mL) was used as a positive control. The medium was used as a negative control (Bazargani & Rohloff, 2016). All experiments were repeated three times. The percentage of eradication was calculated using Equation 2.

$$\text{Biofilm eradiction (\%)} = \left[1 - \left(\frac{A_{570}\text{of the test}}{A_{570}\text{of none teated control}}\right)\right] \times 100 \quad \text{Eq (2)}$$

2.5. Evaluation of Antibiofilm Effect by Microscopic Methods

Antibiofilm effect of plant extract on *S. aureus* ATCC 25923 was determined by SEM. In a previous study, it was determined that *S. aureus* ATCC 25923 is a strong biofilm producer (Erdoğmuş *et al.*, 2022). For microscopic analyses, the surface area of each piece of positively charged slides (Marienfeld C980501) was cut to 1 cm^2 and cleaned with 70% ethanol for 10 min. The blocks will be washed with sterile distilled water and sterilised in an autoclave at 121 °C under 1.5 atm pressure for 15 min. These blocks were individually placed in 24-well plates. Treatment groups were formed with ½ x MIC, MIC, 2 x MIC concentrations of plant extract. 200 µL of these concentrations prepared in TSB was added to each well. 200 µL of bacterial suspension (1x10^6 cells/mL) was added to each well. TSB medium was added as a positive control for biofilm formation. The plates were incubated at 37 °C for 24 hours. The samples were then prepared for SEM analysis. For this purpose, the samples were placed in a solution containing 2.5% glutaraldehyde (0.1 M phosphate buffer, pH 7.4) at 4 °C for 24 hours for primary fixation. At the end of the time, the samples were washed 3 times with PBS. They were then placed in osmium tetroxide for 2 hours in the dark. After this step, the samples were dehydrated with increasing concentrations of ethyl alcohol (30%, 50%, 70%, 90%, 96%), dried and coated with gold (Polaron SC7620 Sputter Coater) (Yılmaz Öztürk *et al.*, 2022). All analyses were performed in at least three replicates.

3. RESULTS

3.1. The Minimum Inhibition Concentration of *Salvia cadmica* Extract on *S. aureus*

The minimum inhibitory concentration (MIC) of *S. cadmica* extract (SC) against *S. aureus* ATCC 25923 was determined to be 250 µg/mL. The MTT reduction assay was employed to evaluate the antibiofilm activity of SC at concentrations of ½ × MIC, MIC, and 2 × MIC against *S. aureus* ATCC 25923. The results indicated a concentration-dependent increase in the percentage of biofilm inhibition. The antibiofilm effect of different SC concentrations on *S. aureus* ATCC 25923 is presented in Figure 1. At a concentration of 2 × MIC, SC resulted in a biofilm inhibition of 34.07 ± 0.44%. At the MIC concentration, the inhibition was determined to be 26.06 ± 0.79%. However, no biofilm inhibition was observed at the ½ × MIC concentration.

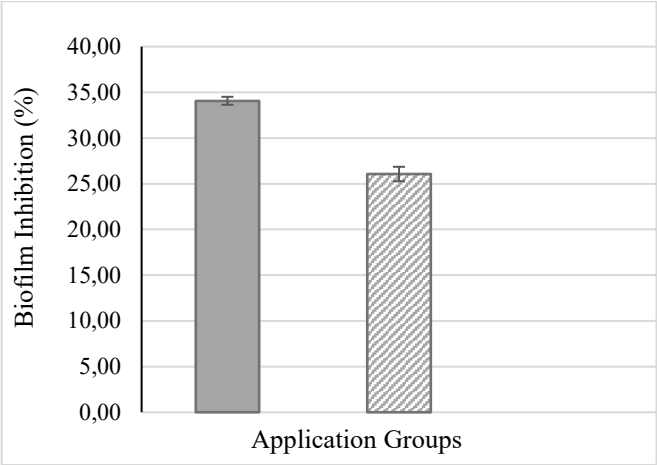

Figure 1. The effect of plant extract on biofilm inhibition of *S. aureus* ATCC 25923.

3.2. The Biofilm Eradiction of *S. cadmica* Extract on *S. aureus*

The biofilm eradication effect of ½ × MIC, MIC, and 2 × MIC concentrations on the biofilm structure formed by *S. aureus* ATCC 25923 was determined and is presented in Figure 2. The results demonstrated a concentration-dependent increase in the percentage of biofilm eradication. At a concentration of 2 × MIC, SC resulted in a biofilm eradication rate of 35.71 ± 0.35%. At the MIC concentration, the eradication rate was determined to be 33.93 ± 1.36%, while at the ½ × MIC concentration, it was 28.05 ± 0.64%.

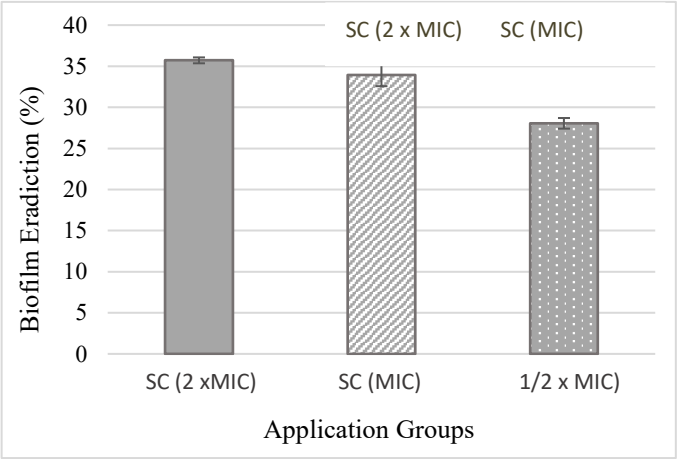

Figure 2. Effect of plant extract on biofilm eradication of *S. aureus* ATCC 25923.

3.3. The Antibiofilm Effect of *S. cadmica* Extract on *S. aureus*

The antibiofilm effect of SC extract on *S. aureus* ATCC 25923 was determined using Scanning Electron Microscopy (SEM). Treatment groups were established with SC at concentrations of ½ × MIC, MIC, and 2 × MIC. The antibiofilm effect of the plant extract on *S. aureus* ATCC 25923 was evaluated by SEM and is shown in Figure 3. According to the SEM analysis results, the group treated with ½ × MIC SC concentration exhibited an increase in biofilm structure and cell count compared to the control group. A dense extracellular polymeric substance (EPS) layer was observed. This indicated that the ½ × MIC SC concentration did not have an antibiofilm effect but, on the contrary, supported biofilm formation. In the group treated with MIC SC concentration, a reduction in cell count and biofilm formation was observed compared to the control group. Morphological disruptions, cell aggregation, and cell lysis were detected. In the group treated with 2 × MIC SC concentration, more biofilm formation and a greater reduction in cell count were observed compared to the MIC-treated group. Morphological degradation of cells, cellular aggregation, and cell lysis were also noted. The SEM analysis

demonstrated that SC concentrations at MIC and above exhibited antibiofilm activity against *S. aureus* ATCC 25923.

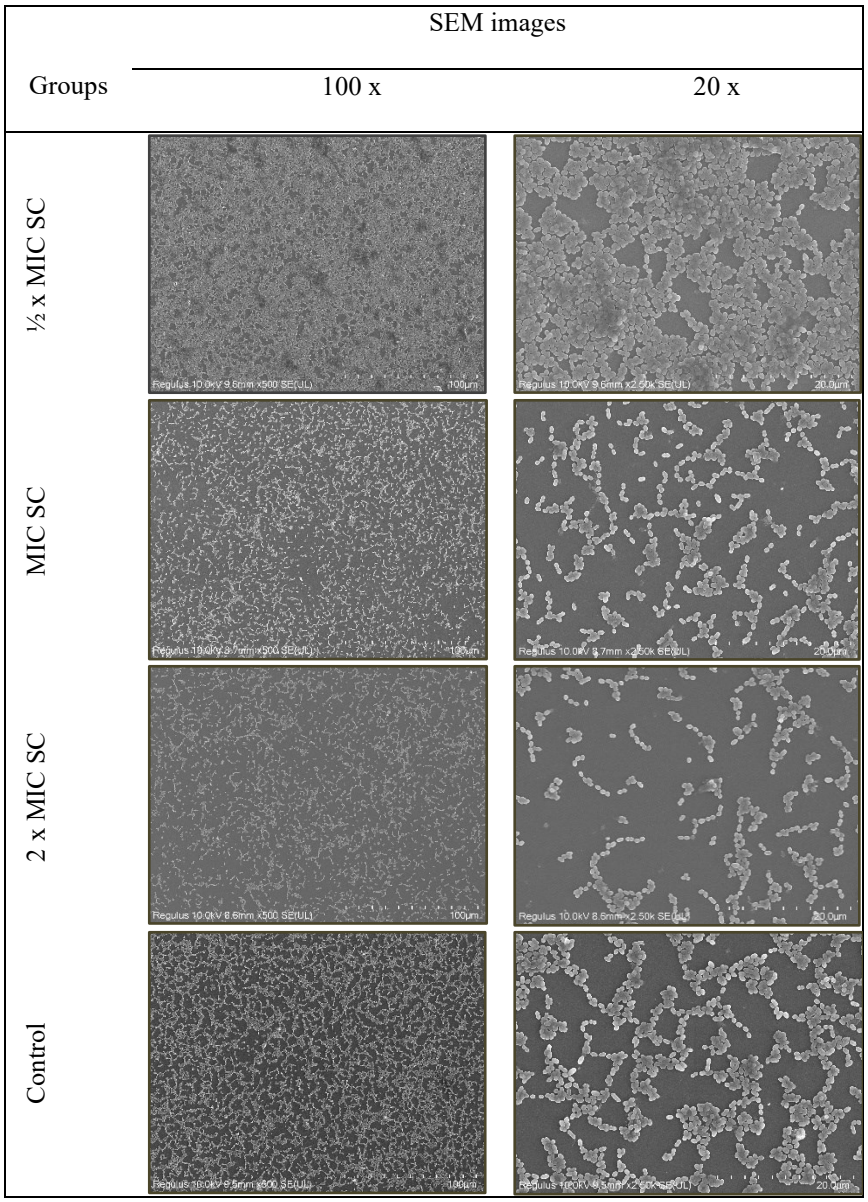

Figure 3. Antibiofilm effect of *S. cadmica* extract on *S. aureus* ATCC 25923.

4. DISCUSSION and CONCLUSION

Medicinal and aromatic plants have been used for centuries in the treatment of diseases due to their bioactive compounds. Natural phenolic compounds exhibit various beneficial effects in humans, including antioxidant, anti-aging, anti-inflammatory, and antimicrobial activities. Due to the significant side effects of synthetic drugs, there has been a growing interest in medicinal and aromatic plants for the discovery and development of new pharmaceutical raw materials. Furthermore, the emergence of microbial resistance to existing antibiotics has led researchers to investigate the antimicrobial activities of medicinal and aromatic plants.

In this study, potential use of *S. cadmica* extract was evaluated for the first time for treatment of biofilm-associated infections using microbiological, and microscopic methods. The findings revealed a proportional increase in biofilm inhibition with increasing SC concentration. Biofilm inhibition was determined as 34.07% ± 0.44 at 2 × MIC SC concentration, while biofilm eradication was determined a 35.71% ± 0.35. Microbiological analysis demonstrated that the plant extract exhibited antibiofilm effect against *S. aureus* ATCC 25923.

Kocak *et al.* (2016) evaluated the phenolic content and biological activity of *S. cadmica* extracts. The results revealed that the methanol extract contained significant amounts of apigenin, caffeic acid, chlorogenic acid, ferulic acid, hesperidin, kaempferol, luteolin, *p*-coumaric acid, protocatechuic acid, and rosmarinic acid. In another study, various phytochemicals such as chlorogenic acid, hesperidin, and rosmarinic acid were determined in *S. cadmica* extract. Chlorogenic acid is well-documented for its diverse pharmacological properties, including antioxidant, antibacterial, hepatoprotective, cardioprotective, anti-inflammatory, antipyretic, neuroprotective, and antiviral effects. Additionally, it has been reported to modulate lipid metabolism and glucose levels, suggesting its potential role in managing metabolic disorders (Naveed *et al.*, 2018). Hesperidin, a flavonoid glycoside, is another key compound known for its antibacterial, antioxidant, and anticancer activities. Its mechanism of action includes disrupting bacterial cell walls and promoting the leakage of intracellular macromolecules through reactive oxygen species generation. Moreover, hesperidin has been shown to alleviate motor dysfunction associated with neuropathological degeneration and spinal cord injuries due to its antioxidant and anti-inflammatory properties (Bahadori *et al.*, 2023). Similarly, rosmarinic acid, a naturally occurring polyphenol, plays a crucial role in plant defense and growth regulation. It is biosynthesized from tyrosine and phenylalanine and serves as a precursor to various derivatives, including melitric acid, salvianolic acid, lithospermic acid, and yunnaneic acid. Studies have highlighted the broad pharmacological potential of rosmarinic acid and its derivatives, encompassing anti-carcinogenic, anti-angiogenic, anti-inflammatory, antioxidant, and antimicrobial activities (Swamy *et al.*, 2018). The presence of these bioactive constituents in *S. cadmica* extract may contribute to its observed antimicrobial and antibiofilm effects, reinforcing its potential as a natural therapeutic agent.

In line with previous studies, Piątczak *et al.* (2021) investigated the phenolic composition, antioxidant, antibacterial, and antifungal activities of *S. cadmica* aerial parts and roots. Using UPLC-DAD/ESI-MS/MS analysis, they identified 14 phenolic compounds. Among these compounds, rosmarinic acid and salvianolic acid K were found to be the dominant components in the aerial parts and roots, respectively. Both the aerial parts and root extracts exhibited significant antioxidant potential, as demonstrated by DPPH and O_2•− radical scavenging assays. Furthermore, the plant extracts showed antimicrobial activity against various Gram-positive bacteria, including *Bacillus cereus*, and *Staphylococcus* spp. Notably, while the aerial parts exhibited stronger antioxidant potential, the roots demonstrated more potent antimicrobial activity. The extracts also showed low cytotoxicity in the MTT assay against mouse L929 fibroblast cells.

Recent findings on the antimicrobial properties of natural plant extracts highlight their potential role as alternative or adjunctive strategies in combating biofilm-associated infections. In this context, a study by Al-Bakri et al. (year) demonstrated that *Salvia triloba*, among seven *Salvia* species tested, exhibited notable antimicrobial effects against *S. aureus*, including methicillin-resistant strains (MRSA). The results of this study demonstrated that *Salvia triloba* stood out for its significant activity against *S. aureus*, including methicillin-resistant strains (MRSA). Both the extract and its volatile oil showed strong bactericidal effects, with the extract achieving ≥4 log reduction in planktonic *S. aureus* and MRSA. Notably, *S. triloba* also demonstrated clear antiadhesion and antibiofilm effects, indicating its potential as a natural agent for preventing and managing *S. aureus*-associated biofilm infections. While other *Salvia* species showed minimal antimicrobial activity, *S. triloba*'s dual action suggests it could be considered in the development of antiseptic or prophylactic formulations targeting resistant staphylococcal strains. These findings align with present study, *S. cadmica* specifically inhibited biofilm formation and structure in a dose-dependent manner, as confirmed by MTT assay and SEM imaging. Compared to the more extensive spectrum of *S. triloba*, the moderate but significant activity of *S. cadmica* still supports its potential use in managing *S. aureus*-related biofilm

infections, particularly in settings where resistance and biofilm formation complicate treatment outcomes.

In another study by Herbert-Doctor *et al.* (2025), the antibacterial and antibiofilm activities of *Salvia hispanica (S. hispanica)* seed extracts against drug-resistant *S. aureus* reference strains and clinical isolates were investigated. The nonpolar seed extract demonstrated significant antibiofilm activity with IC_{50} values of 93.9 ± 5.4 µg/mL and 146.2 ± 2.4 µg/mL against *S. aureus* ATCC 43300 and clinical strain SAU-UIMY-31, respectively. Additionally, both nonpolar and polar extracts showed antihemolytic effects. Chemometric analyses suggested that fatty acid methyl esters contribute to the biological activity. These findings provide a promising basis for the use of *S. hispanica* seeds as natural agents in combating resistant *S. aureus* infections. This aligns with our study and other research on *Salvia* species, supporting the potential of plant-derived compounds in antibiofilm therapies.

Similarly, Gonciarz *et al.* (2022) evaluated the antibacterial activity of *S. cadmica* extracts, specifically examining their ability to neutralize harmful effects caused by *Helicobacter pylori (H. pylori)* lipopolysaccharide (LPS), such as oxidative stress and apoptosis, as well as promoting *in vitro* cell regeneration in gastric epithelial cells or fibroblasts. The minimum inhibitory concentration (MIC) of the root extract for reference *H. pylori* strains ranged from 39 to 78 µg/mL, while the minimum bactericidal concentration (MBC) was between 78 and 310 µg/mL. For clinical *H. pylori* isolates, MIC values ranged from 195 to 1560 µg/mL, with MBC values ranging from 390 to 1560 µg/mL. In contrast, the aerial parts of *S. cadmica* showed weaker inhibitory and bactericidal effects against *H. pylori* reference strains (MIC/MBC range: 78–156 µg/mL) and clinical isolates (MIC/MBC range: 390–1560 µg/mL). Additionally, the *S. cadmica* extracts effectively reduced oxidative stress, apoptosis rates, and phosphorylated extracellular signal-regulated kinase (pErk) levels induced by *H. pylori* LPS.

Moreover, Doğan *et al.* (2021) examined the total phenolic, flavonoid, and protein contents, radical scavenging capacities, antibacterial, and cytotoxic properties of five different *Salvia* species. The radical scavenging capacities of the *Salvia* species ranged from 84.1±4.5% to 96.8±0.1%. The extracts exhibited strong antibacterial activity against *Escherichia coli* and *Staphylococcus aureus*. The highest rutin hydrate content was found in *S. kronenburgii* and *S. euphratica* var. *euphratica*, while the highest luteolin-7-glucoside content was detected in *S. huberi* and *S. kronenburgii* extracts. Additionally, vanillic acid was only found in the extracts of *S. huberi* and *S. kurdica*.

In conclusion, *S. cadmica* extract demonstrates significant bioactive potential, making them promising candidate for therapeutic applications. Our study aligns with previous research highlighting the diverse pharmacological properties of *S. cadmica*, including its ability to inhibit biofilm formation and its antimicrobial effects against *S. aureus.* Based on the promising findings from this study, further research is needed to explore the full pharmacological potential of *S. cadmica* extracts, particularly in clinical settings. Also, *in vivo* studies are essential to evaluate the safety, efficacy, and potential side effects of *S. cadmica* extracts. Considering the antimicrobial resistance problems, *S. cadmica* could provide a viable alternative for developing new, natural antimicrobial agents. Investigating the plant's effects on multidrug-resistant bacteria and biofilm-associated infections could offer valuable insights into its potential therapeutic applications. The environmental sustainability and economic feasibility of cultivating *S. cadmica* on a larger scale for pharmaceutical purposes should be assessed, as this could provide a sustainable source of bioactive compounds for the development of new drugs.

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Declaration of Conflicting Interests and Ethics

The authors declare no conflict of interest. This research study complies with research and publishing ethics. The scientific and legal responsibility for manuscripts published in IJSM belongs to the authors.

Ethics Committee Number: Afyonkarahisar Health Sciences University Non-Intervention Scientific Research Ethics Committee, 19/04/2024 - 2024/2.

Authorship Contribution Statement

Nilay Isitez: Investigation, Methodology, Resources, Visualization, Formal Analysis, and Writing – review & editing. **Sevim Feyza Erdoğmuş:** Project administration, Investigation, Methodology, Writing-original draft, and Validation. **Cengiz Sarikurkcu**: Investigation, Conceptualization, and Supervision.

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