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(REVIEW ARTICLE)

ACTIVE COMPOUNDS OF GARLIC AND ONION (*ALLIUM* SPECIES) AGAINST METHICILLIN-RESISTANT *STAPHYLOCOCCUS AUREUS* (MRSA): A NARRATIVE REVIEW

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ABSTRACT

Methicillin-resistant *Staphylococcus aureus* (MRSA) is a leading contributor to antimicrobial-resistance-related mortality, and its limited treatment options have renewed interest in plant-derived antibacterial compounds. Garlic (*Allium sativum*) and onion (*Allium cepa*) are widely consumed *Allium* species whose bioactive constituents are of particular interest. This narrative review summarises evidence published between 2020 and 2026 on the active compounds of *Allium* species against MRSA and their proposed mechanisms of action. Twenty-five peer-reviewed publications from indexed journals were selected through PubMed/PMC and publisher platforms. Two main groups of constituents emerge: organosulfur compounds from garlic, mainly allicin, ajoene and diallyl polysulfides, and flavonoids from onion, mainly quercetin and its derivatives. Allicin reacts with thiol groups of proteins and low-molecular-weight thiols such as bacillithiol, and molecular docking suggests an interaction with penicillin-binding protein 3. Quercetin has been associated with antibiofilm activity and with potentiation of β-lactam antibiotics. Garlic and onion peel extracts showed activity in vitro, and a red onion scale extract reduced MRSA load in a rat colonisation model. Important gaps remain: allicin is unstable, extracts are rarely standardised, MRSA-specific mechanistic evidence is limited, and no clinical studies were identified in the reviewed literature. Standardised extracts, stable formulations, and in vivo and clinical studies are needed before *Allium* compounds can be considered adjuncts to conventional MRSA therapy.

Keywords: MRSA; *Allium Sativum*; *Allium Cepa*; Allicin; Quercetin; Antibiofilm

1 INTRODUCTION

Staphylococcus aureus is a Gram-positive opportunistic pathogen, and its methicillin-resistant lineage (MRSA) is a major cause of healthcare- and community-associated infections. In a global analysis of bacterial antimicrobial resistance for 2019, MRSA was the single pathogen-drug combination associated with more than 100,000 attributable deaths [1].

Resistance to β-lactams in MRSA is mainly due to the *mecA* gene, carried on the staphylococcal cassette chromosome *mec* (SCC*mec*), which encodes penicillin-binding protein 2a (PBP2a); further mechanisms include β-lactamase production, efflux pumps, target modification and biofilm formation [2]. A study published in *Nature* concluded that methicillin resistance emerged before the clinical use of antibiotics [3].

Treatment options for MRSA are limited, and alternatives such as bacteriophages, immunotherapy, nanobiotics and antimicrobial peptides are being explored [2]. Plant-derived compounds are another source of candidate agents. Garlic (*Allium sativum* L.) and onion (*Allium cepa* L.) are among the most widely consumed *Allium* species. The antimicrobial activity of garlic was attributed in the 1940s to allicin, a volatile compound obtained from raw garlic [4], and garlic contains a broader set of antibacterial organosulfur compounds, including ajoene and diallyl sulfides [5]. Onion is the most abundant dietary source of the flavonol quercetin [6], and its outer scales contain higher flavonoid levels than the edible part [7].

Recent studies have examined *Allium* preparations against MRSA, but the findings are scattered across microbiological, phytochemical and formulation studies. This review therefore summarises evidence from 2020 to 2026 on (i) the active compounds of garlic and onion, (ii) their proposed mechanisms of action against MRSA and *S. aureus*, and (iii) the gaps that remain before these compounds can be developed further.

2 MATERIALS AND METHODS

This work is a narrative literature review. Literature was identified through web-based searches of PubMed/PMC and the platforms of indexed journal publishers, using combinations of the terms "MRSA", "methicillin-resistant *Staphylococcus aureus*", "*Allium sativum*", "*Allium cepa*", "garlic", "onion", "allicin", "quercetin", "biofilm" and "synergy". Publications from 2020 to 2026 were considered. Peer-reviewed articles from internationally indexed journals and from one Indonesian national journal were included; theses, preprints and repository documents were excluded.

Twenty-five publications were selected according to their relevance to MRSA or *S. aureus*, to the active compounds of garlic and onion, or to the resistance background. For each publication, the compounds studied, the test system and the main findings were extracted and summarised narratively. Because the review is narrative, no meta-analysis or formal risk-of-bias assessment was performed.

3 RESULTS AND DISCUSSION

3.1 MRSA resistance mechanisms as targets for natural compounds

The central determinant of methicillin resistance is PBP2a, encoded by *mecA* on the SCC*mec* element, which has low affinity for most β-lactam antibiotics and allows cell wall synthesis to continue in their presence [2]. Beyond this, *S. aureus* depends on thiol-based redox systems to protect itself against redox-active antimicrobials; the low-molecular-weight thiol bacillithiol and associated redox switches contribute to protection against compounds such as allicin [8]. These features give natural compounds several possible points of attack: the cell wall synthesis machinery, the thiol redox balance, biofilm formation and virulence regulation, and the activity of conventional antibiotics.

3.2 Active compounds of garlic and onion

Intact garlic cloves mainly contain non-volatile sulfur precursors, whereas crushed garlic yields highly reactive, unstable and volatile allicin, which decomposes into sulfides such as diallyl sulfide, disulfide and trisulfide [5]. The antibacterial organosulfur compounds of garlic include allicin, ajoene and the aliphatic sulfides, with additional vinyldithiins [5,9]. Among the hydrophobic compounds, antimicrobial activity has been reported to depend on the number of sulfur atoms, in the order diallyl tetrasulfide > trisulfide > disulfide > sulfide [9].

In onion, the main antibacterial candidates are flavonoids. Flavonoid and total phenol contents of onion skin were compared across fifteen Indian cultivars [10], and polyphenolic extracts of onion skin from the same number of cultivars were assessed for antimicrobial activity [11]. Peel extracts of *A. cepa* varieties have also been characterised for flavonols and anthocyanins together with antioxidant, antimicrobial and antiproliferative properties [12]. In a study that tested both plants against bacterial isolates from the wounds of diabetic patients, aqueous and ethanolic extracts of *A. cepa* had higher phenolic content than those of *A. sativum* [13]. Table 1 summarises the compound groups discussed in this review.

Table 1: Main active compound groups of garlic and onion and their reported activities

Compound(s)	Source	Reported activity relevant to MRSA/*S. aureus*	Ref.
Allicin	Garlic	Thiol-reactive compound that modifies cysteine residues and low-molecular-weight thiols including bacillithiol; dose-dependent antimicrobial activity; combination with antibiotics may enhance activity; docking to PBP3 predicted strong interaction	[4,14,15]
Ajoene	Garlic	Hydrophobic garlic compound reported to inhibit biofilm formation and quorum sensing	[9]
Diallyl polysulfides (DAS, DADS, DATS, DATTS)	Garlic	Antibacterial, antibiofilm and anti-quorum-sensing activity; activity increases with sulfur chain length	[5,9]
Quercetin	Onion (outer scales)	Antibacterial activity against MRSA and MSSA; antibiofilm activity; potentiation of penicillin G	[6,16,17]
Flavonoid-rich fraction (quercetin-standardised)	Red onion scales	MBC 0.33 mg/mL against MRSA USA300; biofilm eradication in vitro	[7]
Anthocyanin-rich fraction	Red onion scales	Bactericidal against MRSA USA300 (MBC 4.17 mg/mL), less potent than flavonoid-rich fraction	[7]

3.3 Organosulfur compounds: allicin, ajoene and diallyl polysulfides

Allicin is a reactive thiol-trapping sulfur compound that S-thioallylates accessible cysteine residues in proteins and in low-molecular-weight thiols, including bacillithiol in Gram-positive bacteria, and shows dose-dependent antimicrobial activity [14]. Consistent with this, allicin has been reported to preferentially target thiol-containing proteins and enzymes in microorganisms and to regulate genes essential for virulence [4]. Reactive organosulfur compounds from garlic are also described as forming disulfide bonds with free sulfhydryl groups of enzymes and compromising membrane integrity [5]. Since *S. aureus* relies on bacillithiol-based redox buffering [8], thiol depletion is a plausible route to its inhibition, although most mechanistic work on allicin was not performed specifically in MRSA.

MRSA-specific evidence comes from a clinical isolate study in which a garlic extract (prepared for allicin) produced a wide inhibition zone against MRSA, and molecular docking indicated a strong interaction between allicin and PBP3 of *S. aureus* [15]. The extract also augmented the activity of a cefoxitin disc [15]. Docking is a predictive method, and the finding should be confirmed by binding or enzymatic assays before PBP inhibition is accepted as a mechanism.

Ajoene and diallyl polysulfides add antivirulence effects: garlic-derived sulfur compounds such as diallyl disulfide and ajoene have been reported to inhibit biofilm formation and quorum sensing, although their direct antimicrobial activity is lower than that of antibiotics used clinically [9]. A review of garlic organosulfur compounds likewise lists bactericidal, antibiofilm, antitoxin and anti-quorum-sensing activity against multidrug-resistant strains [5].

3.4 Flavonoids: quercetin and onion extracts

Quercetin has been reported to be active against Gram-positive bacteria including MRSA and methicillin-sensitive *S. aureus* [6]. In a study of 40 clinical MRSA isolates, the minimum inhibitory concentration of quercetin and its antibiofilm effect at sub-inhibitory concentrations were evaluated [16]. A red onion scale extract and its flavonoid-rich fraction were bactericidal against MRSA USA300, and the flavonoid-rich fraction was the most active; the authors attributed this mainly to quercetin, which was quantified by HPLC at 0.0478 mg per mg of total extract and 0.2188 mg per mg of the flavonoid-rich fraction [7]. Onion peel extract also showed promising antimicrobial activity, especially against MRSA, in a study of vegetable by-products [18].

Table 2 summarises the experimental studies on garlic, onion and quercetin that directly involve MRSA or *S. aureus*. The studies differ in extract type, test strain and endpoint, which limits direct comparison of potency.

Table 2: Selected experimental studies on garlic, onion and quercetin against MRSA/S. aureus

Study	Material	Test system	Main finding	Ref.
Indira et al., 2024	Garlic crude extract (allicin)	Clinical MRSA isolates; docking with PBP3	Wide inhibition zone; augmented cefoxitin activity; strong allicin-PBP3 interaction predicted	[15]
Ali et al., 2023	Red onion scale extract and fractions	MRSA USA300 in vitro; rat vaginal colonisation model (hydrogel)	Flavonoid-rich fraction MBC 0.33 mg/mL; total extract lowered MRSA load by 2.998 log versus 3.358 log for vancomycin	[7]
Magryś et al., 2021	Fresh garlic extract	Drug-sensitive and multidrug-resistant isolates including *S. aureus*	Broad inhibition; combinations with gentamicin and ciprofloxacin mostly synergistic or insignificant	[19]
Elsayed et al., 2024	Quercetin	40 clinical MRSA isolates	MIC and sub-MIC antibiofilm effect evaluated	[16]
Sari et al., 2024	Red onion peel ethanol extract	*S. aureus* biofilm	Biofilm degradation, highest at 25% and 48 h	[20]
Salem et al., 2023	Onion peel extract	In vitro antimicrobial assays	Promising activity, especially against MRSA	[18]
Tiwana and Cock, 2026	Quercetin with penicillin G	*S. aureus*, MRSA and other resistant bacteria	Quercetin synergised penicillin G against S. aureus; beta-lactamase inhibition and cytotoxicity assessed	[17]

3.5 Antibiofilm and antivirulence activity

Biofilm formation contributes to the resistance and persistence of MRSA [2], which makes antibiofilm activity an important property of candidate compounds. The red onion scale extracts significantly inhibited MRSA USA300 biofilm formation and eradicated established biofilm, with the flavonoid-rich fraction the most effective [7]. A red onion peel ethanol extract degraded *S. aureus* biofilm, with the highest activity at a concentration of 25% and an incubation time of 48 hours [20]. Outside onion, flavonoids were reported to act on staphylococcal biofilms by targeting BAP amyloids [21], and quercetin decreased the production and altered the composition of extracellular polymeric substances in *Staphylococcus epidermidis* biofilm [22]. These two studies were not performed in MRSA, and their relevance to MRSA remains to be tested. Extracts of other plants, such as *Ginkgo biloba* exocarp, have likewise been reported to disrupt biofilms and affect gene expression in *S. aureus* and MRSA [23], which suggests that antibiofilm activity is a general feature of several plant products rather than a property unique to *Allium*.

3.6 Combination with conventional antibiotics

Allicin has been reported to enhance the activity of antibiotics and antifungals when used in combination [4]. For MRSA, the garlic extract augmented the cefoxitin disc [15]. In a broader panel of drug-sensitive and multidrug-resistant bacteria that included *S. aureus*, fresh garlic extract combined with gentamicin and ciprofloxacin was in most cases synergistic or showed an insignificant interaction [19]. For onion-derived quercetin, a recent study found synergy with penicillin G against *S. aureus* and examined β-lactamase inhibition as a possible mechanism, together with cytotoxicity against human dermal fibroblasts [17]. These findings support the idea of using *Allium* compounds as adjuncts rather than replacements, but the MRSA-specific data are still limited to a few studies and to in vitro systems.

3.7 In vivo evidence and formulation approaches

In vivo evidence for *Allium* against MRSA is scarce. The red onion scale extract, formulated as a hydrogel, significantly reduced MRSA load in a rat vaginal colonisation model, and the effect of the total extract was not significantly different from that of vancomycin [7]. Topical allicin has been reported to improve MRSA skin infection [9]. For comparison, an extract of another plant, star anise, was tested in a murine MRSA skin infection model in relation to its metabolite profile [24], illustrating the type of model that could be applied to garlic and onion preparations.

Formulation work on onion by-products is progressing. Red onion skin extract has been formulated into bioadhesive polymeric films for wound treatment [25], and an onion peel extract loaded into a lipid capsule-based hydrogel showed enhanced cellular viability [18]. Such delivery systems could address the instability of allicin and the poor retention of extracts at the infection site, but they have not yet been evaluated against MRSA in the reviewed studies.

Limitations and research gaps

Several gaps were evident across the reviewed literature. First, allicin is unstable and garlic organosulfur compounds have low bioavailability, and their composition depends on how the garlic is processed [5]. Second, extracts are rarely standardised; the red onion scale study, which standardised quercetin content by HPLC [7], is an exception, and because onion skin composition was compared across fifteen cultivars [10], reporting of cultivar, plant part and extraction method is essential. Third, mechanistic claims such as PBP3 inhibition rest on docking [15] and need experimental confirmation. Fourth, many antibiofilm and mechanistic studies were done in other staphylococci or in non-MRSA strains [21,22]. Fifth, safety data are limited, with only one of the reviewed studies assessing cytotoxicity [17]. Finally, no clinical studies on *Allium* compounds against MRSA were identified in the reviewed literature.

Future work should therefore (i) use standardised, chemically characterised extracts or isolated compounds, (ii) test MRSA panels that include clinical isolates, (iii) confirm mechanisms experimentally, (iv) include cytotoxicity and in vivo infection models, and (v) develop stable topical formulations before clinical evaluation.

4 CONCLUSION

The reviewed evidence indicates that the activity of garlic and onion against MRSA is attributable mainly to organosulfur compounds (allicin, ajoene and diallyl polysulfides) and to flavonoids, particularly quercetin. Reported mechanisms include thiol modification, a predicted interaction with PBP3, antibiofilm activity and potentiation of antibiotics, but most of the evidence comes from in vitro or computational studies. Standardised extracts, stable formulations, in vivo models and clinical studies are needed to determine whether *Allium* compounds can serve as adjuncts to MRSA therapy.

STATEMENTS ON COMPLIANCE WITH ETHICAL STANDARDS

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Disclosure of conflict of interest

The authors declare that there is no conflict of interest.

Statement of Informed Consent

Informed consent was not required for this study, as it was a narrative review that relied exclusively on previously published data and did not involve human participants in data collection.

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