

**Natural Products Enhancing Antibiotic-Sensitivity of Methicillin-Resistant
*Staphylococcus aureus***

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The bacterium *Staphylococcus aureus* has been found to be the most prevalent cause of bloodstream infection, skin and soft-tissue infection and pneumonia. The effectiveness of β -lactam antibiotics such as penicillin and methicillin in the control of this bacterium is fading because of the rapid emergence of penicillin- and methicillin-resistant strains of *S. aureus* (MRSA). Although vancomycin, a glycopeptide antibiotic, has been used to control such strains of *S. aureus*, vancomycin-resistant strains have now emerged. Alternative strategies are required to control emergence and spread of antibiotic-resistant staphylococci. One approach is to use antibiotics together with compounds that inhibit resistance mechanisms.

The resistance mechanisms employed by bacteria are drug-specific and include the following: degradation of the antibiotic drug by enzymes of the bacteria, modification of the receptor site in the bacteria such that the efficiency of drug-binding is reduced, extrusion of the drug by multidrug-resistance (MDR) efflux pumps of the bacteria, and quorum sensing by way of biofilms produced by bacteria.

In their defense against microbes, plants produce antimicrobials and, over time, must have experienced antimicrobial-resistance as well. Consequently, plants have developed compounds that interfere with drug-resistance mechanisms, and enhance the potency of the antimicrobials through synergistic combinations. Antimicrobial activity of berberine, which is formed in Barberry plant, is, for example, enhanced by another constituent of the same plant, 5'-methoxyhydrnocarpin-D, which is a potent inhibitor of MDR efflux pumps.

Plants provide a range of compounds - alkaloids, flavonoids, polyphenols, terpenoids, etc. - that can effectively modify the drug-resistance of MRSA. Epigallocatechin gallate (EGCg), a major polyphenol found in tea plant (*Camellia sinensis*), for example, acts by inhibiting β -lactamases that degrade methicillin and penicillin, blocking MDR efflux pumps, and binds to peptidoglycan and inhibiting cell wall synthesis. Incubation of MRSA with EGCg remarkably improves the potency of oxacillin against MRSA through time- and dose-dependent synergistic effects.