Hybrid molecule: combination between sulfonamides and trimethoprim to inhibit growth of methicillin-resistant Staphylococcus aureus (MRSA)

Taechin Nowwarat, Napon Nilchan, Chutima Jiarpinitnun*
Department of Chemistry and Center for Innovation in Chemistry (PERCH-CIC), Faculty of Science, Mahidol University, Rama VI Road, Bangkok 10400, Thailand
*E-mail: chutima.jia@mahidol.ac.th

Abstract: The pathogenic Gram-positive bacteria Staphylococcus aureus (S. aureus) causes global health concerns due to its rapid development of resistance towards antibiotics used. The emergence of antibiotic resistance has complicated the treatment of S. aureus infections, especially, methicillin-resistant S. aureus (MRSA) that acquired resistance to beta-lactam antibiotics such as penicillin. Sulfonamide antibiotics have been used to treat S. aureus and MRSA infections. Sulfa-drug can be used as single-entity drug or in combination with trimethoprim. However, the rise of sulfa-resistance and trimethoprim-resistance has led to a decrease in clinical uses. Several studies have exploited the dimerization concept to enhance efficacy and to overcome bacterial resistance. Here in, we reported the rationally design and synthesis of a sulfonamide-trimethoprim hybrid. The hybrid ligand was simply designed to covalently linked trimethoprim and sulfonamide adducts via C-C bond formation. The hybrid molecule was evaluated for their efficacy against S. aureus control strains, bovine mastitis-causing S. aureus strain RF122, and globally epidemic MRSA strain SF8300. Based on Kirby-Bauer disk diffusion assay, our results promisingly indicated that the hybrid molecule could successfully inhibit growth of all S. aureus strains, suggesting that the hybrid compound was effective against antibiotic resistant strains of S. aureus.

Keywords: Antibiotic resistance; Methicillin-resistant Staphylococcus aureus; Sulfa-drugs, Hybridization