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Antimicrobial effects of sulfonyl derivative of 2(5H)-furanone against planktonic and biofilm associated methicillin-resistant and -susceptible *Staphylococcus aureus*

Sharafutdinov I., Trizna E., Baidamshina D., Ryzhikova M., Sibgatullina R., Khabibrakhmanova A., Latypova L., Kurbangalieva A., Rozhina E., Klinger-Strobel M., Fakhrullin R., Pletz M., Bogachev M., Kayumov A., Makarewicz O.

Kazan Federal University, 420008, Kremlevskaya 18, Kazan, Russia

Abstract

© 2017 Sharafutdinov, Trizna, Baidamshina, Ryzhikova, Sibgatullina, Khabibrakhmanova, Latypova, Kurbangalieva, Rozhina, Klinger-Strobel, Fakhrullin, Pletz, Bogachev, Kayumov and Makarewicz. The gram-positive opportunistic bacterium *Staphylococcus aureus* is one of the most common causatives of a variety of diseases including skin and skin structure infection or nosocomial catheter-associated infections. The biofilm formation that is an important virulence factor of this microorganism renders the antibiotic therapy ineffective, because biofilm-embedded bacteria exhibit strongly increased tolerance to antimicrobials. Here, we describe a novel 3-chloro-5(S)-[(1R,2S,5R)-2-isopropyl-5-methylcyclohexyloxy]-4-[4-methylphenylsulfonyl]-2(5H)-furanone (F105), possessing a sulfonyl group and l-menthol moiety. Minimal inhibitory and bactericidal concentration values (MIC and MBC) of F105 were 10 and 40 mg/L, respectively, suggesting F105 biocidal properties. F105 exhibits pronounced activity against biofilm-embedded *S. aureus* and increases the efficacy of aminoglycosides (amikacin, gentamicin, and kanamycin) and benzalkonium chloride with fractional inhibitory concentration index values of 0.33-0.44 and 0.29, respectively, suggesting an alternative external treatment option, e.g., for wound infections. Moreover, low concentrations (0.5-1.3 mg/L) of F105 reduced the MICs of these antimicrobials twofold. By using confocal laser scanning microscopy and CFU counting, we show explicitly that F105 also restores the antimicrobial activity of gentamicin and ampicillin against *S. aureus* biofilms by several orders of magnitude. Biofilm structures were not destroyed but sterilized, with embedded cells being almost completely killed at twofold MBC. While F105 is quite toxic (CC₅₀/MBC ratio 0.2), our data suggest that the F105 chemotype might be a promising starting point for the development of complex topical agents for combined anti-staphylococcal biofilm-therapies restoring the efficacy of some antibiotics against difficult to treat *S. aureus* biofilm.

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Keywords

2(5H)-furanones, Antimicrobials synergism, Biofilm, MRSA, *Staphylococcus aureus*, Sulfones

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