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Increasing Susceptibility of Drug-Resistant Candida albicans to Fluconazole and Terbinafine by 2(5H)-Furanone Derivative

Sharafutdinov I.S., Ozhegov G.D., Sabirova A.E., Novikova V.V., Lisovskaya S.A., Khabibrakhmanova A.M., Kurbangalieva A.R., Bogachev M.I., Kayumov A.R.
Kazan Federal University, 420008, Kremlevskaya 18, Kazan, Russia

Abstract

© 2020 by the authors The frequency of mycoses caused by drug-resistant fungal pathogen Candida albicans has increased drastically over the last two decades. The spread of drug-resistant strains, along with the limitations of currently available antifungals, complicates the management of fungal infections, thereby representing great challenges for clinical healthcare. Among various antimicrobial pharmacophores, 2(5H)-furanone derivatives have demonstrated antimicrobial, antifungal, and antibiofilm activities. In this study, we report the antifungal activity of the 2(5H)-furanone derivative F105, consisting of three pharmacophores, namely chlorinated 2(5H)-furanone, sulfonyl group, and l-menthol moiety. Although exhibiting moderate antifungal activity alone with the minimum inhibitory concentration (MIC) values of 32–256 μg/mL, F105 potentiates the activity of fluconazole and terbinafine with fractional inhibitory concentration index (FICI) values of 0.27–0.50. Thus, 16 μg/mL of F105 reduced the MICs of these antifungals against fluconazole-resistant C. albicans isolates four-fold, achieving similar values as for the intermediately susceptible phenotype. Confocal laser scanning microscopy revealed that the fluorescent 2(5H)-furanone derivative F145 was also able to penetrate through biofilms formed by C. albicans. Indeed, in the presence of F105, even sub-MIC concentrations of both fluconazole and terbinafine led to significant reduction of C. albicans CFUs in the mature biofilm. Thus, F105 appears to be a promising candidate for the development of novel antifungal agents as well as enhancers of current antifungal agents, particularly for the treatment of drug-resistant C. albicans infections.

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Keywords

2(5H)-furanones, Biofilm, Candida albicans, Drug resistance, Synergy

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