Abstract

Charles University in Prague
Faculty of Pharmacy in Hradec Kralové
Department of Biological and Medical Sciences
Candidate: Pavla Pešková
Supervisor: Ing. Lucie Křivčíková

Diploma Thesis: Susceptibility profile of biofilms of non-albicans Candida spp. to echinocandins

Yeasts of the genus Candida are one of the most frequent human fungal pathogens. Infections caused by them are related to a specific form of growth – biofilm (BF), which has increased their resistance to antifungal treatment. Since bloodstream infections caused by non-albicans Candida species are increasing, it is important to focus on their susceptibility characteristics.

The main aim of our experiment was to examine the susceptibility profiles of BF produced by rare non-albicans Candida species to echinocandins. We tested 3 species of the genus Candida – C. lusitaniae, C. guilliermondii and C. krusei and 3 different echinocandins – anidulafungin (AND), caspofungin (CAS) and micafungin (MFG). Echinocandins have unique mechanisms of action. They inhibit the function of the enzyme β-1,3-glucan synthase. Disruption of its function leads to inhibition of β-1,3-glucan production, damage of fungal cell wall and loss of viability of the cell.

In experimental part we used YNB medium and RPMI 1640 medium to grow Candida species BF and planktonic cells (PL). We incubated both BF and PL in 96-well microtiter polystyrene plates. Antifungal activity was assessed by the 2,3-bis[2-methoxy-4-nitro-5-sulfophenyl]2H-tetrazolium-5-carboxanilide (XTT) metabolic assay. Each drug concentration was processed in pentaplicate for each isolate.

Results indicate that MFG have the lowest MIC \( \text{MIC}_{50} \) and that it is the most
efficient drug to all tested species. MFG to BF formed by C. krusei (MIC\textsubscript{50} 0.125 mg/L) was most efficient, followed by C. guilliermondii (MIC\textsubscript{50} 2 mg/L) and less susceptible C. lusitaniae BF (MIC\textsubscript{50} 16 mg/L). AND was most efficient against C. krusei BF (MIC\textsubscript{50} 0.125 mg/L), then C. guilliermondii (MIC\textsubscript{50} 4 mg/L) and C. lusitaniae (MIC\textsubscript{50} >256 mg/L). CAS was most efficient against C. krusei BF (MIC\textsubscript{50} 1 mg/L), then against C. guilliermondii (MIC\textsubscript{50} 32 mg/L) and C. lusitaniae (MIC\textsubscript{50} 32 mg/L).

In the conclusion of our project we pronounced our findings stating that echinocandins seem to be efficient against non-\textit{albicans} Candida biofilms in vitro. Biofilm was more resistant to echinocandins than planktonic cells.

Key words: echinocandins, biofilm, Candida, resistance, XTT