# SYNERGISTIC EFFECT ON *CANDIDA* GENUS YEAST OF A MIXTURE OF ANTIFUNGAL DRUGS AND SURFACTANTS, SYNTHESIZED BY *ACINETOBACTER CALCOACETICUS* IMV B-7241

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**Introduction.** The number of publications devoted to the study of *Candida* genus representatives causative agents of nosocomial infectious diseases is increasing every year [1, 2]. This is due, first of all, to the spread of their resistant forms, arising against the background of prolonged use of broad-spectrum antibiotics, immunosuppressive therapy, and prolonged catheterization of patients [3].

Compared to antibacterial agents, the number of antifungal agents is much smaller, and most clinical isolates of the genus *Candida* (in particular *C. albicans, C. tropicalis* and *C. glabrata*) are resistant to azoles, which are currently the most common to fungal infections treated. One of the approaches to increasing the efficiency of using antifungal compounds is their combination with natural substances that can be microbial surfactants [4, 5].

But under different cultivation conditions, the biological activity of microbial surfactants can change. Previously was shown the possibility to regulate the biological activity of *Acinetobacter calcoaceticus* IMV B-7241 surfactants by cultivating the IMV B-7241 strain in a medium with an increased concentration of calcium and magnesium cations - activators of $NADP^+$-dependent glutamate dehydrogenase, and a key enzyme in the biosynthesis of lipopeptides (main antimicrobial agents) and potassium and sodium cations.

These monovalent cations in high concentrations inhibit $NADP^+$-dependent glutamate dehydrogenase, which ultimately leads to a low antimicrobial and antifungal activity of the synthesized surfactants. It was suggested that it is possible to enhance the antifungal activity of surfactants synthesized by IMV B-7241 in the presence of potassium and sodium cations in a mixture with antifungal agents.

The **aim** of this work is to investigate the possibility of a synergistic effect on *Candida* genus yeast of a mixture of *A. calcoaceticus* IMV B-7241 surfactants with clotrimazole and fluconazole.

**Materials and methods.** Strain *A. calcoaceticus* IMV B-7241 was grown in a liquid mineral medium (g/l): $(NH_2)_2CO$ – 0,35, NaCl – 1,0, $Na_2HPO_4 \cdot 12H_2O$ – 0,6, $KH_2PO_4$ – 0,14, $MgSO_4 \cdot 7H_2O$ – 0,1, yeast autolysate – 0,5 % (v/v), trace elements a solution – 0.1%, (v/v) (base medium). Cultivation of strain IMV B-7241 was also carried out in a basic medium that did not contain NaCl (medium 1), in which the concentration of NaCl was 2.0 g/l (medium 2), in which 1.0 g/l KCl was additionally added (medium 3 ).

Spent after frying potatoes sunflower oil 2% (v/v) was used of carbon source. The amount of synthesized surfactants (g/l) was determined by weighting method after extraction from a supernatant of culture fluid with a modified Folch mixture. Antimicrobial properties of the surfactants and antifungal drugs were determined by index of the minimum inhibitory concentration (MIC). To assess the synergistic effect of a mixture of surfactants with antifungal drugs, the fractional inhibitory concentration

(FIC) index was used.

**Results.** It was found that the surfactants synthesized by IMV B-7241 on base medium proved to be effective antifungal agents, the MIC value against *Candida albicans* D-6, *Candida tropicalis* PE-2 and *Candida utilis* BMS-65 was 22.5-45 μg/ml, and were lower than the MIC of surfactants obtained on modified media 1-3. Nevertheless, regardless of *A. calcoaceticus* IMV B-7241 cultivation conditions of and the MIC values, all synthesized surfactants in a mixture with clotrimazole reduced the minimum inhibitory concentrations of this drug against test cultures in 4-32 times.

At the same time, the FIC value did not exceed 0.5, which indicates synergy between compounds. Surfactants synthesized by IMV B-7241 in various cultivation conditions also showed synergistic antifungal activity in a mixture with fluconazole. Thus, in a mixture with surfactants, the MIC values of fluconazole in against *C. albicans* D-6, *C. tropicalis* PE-2, and *C. utilis* BMS-65 were reduced from 35.5 μg/ml to 1.1-9.3 μg/ml. Despite the high FIC values of the mixture of surfactants synthesized on medium 3 with fluconazole (FIC 0.51-0.76), the MIC of the latter were reduced by almost 4 times (from 35.5 to 9.3 μg/ml).

**Conclusions.** The possibility to using a mixture of *A. calcoaceticus* IMV B-7241 surfactants and antifungal drugs to reduce the MIC of the latter against *Candida* genus representatives was showed.

**References:**

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