

**THE SELECTION OF RESISTANCE TO ERYTHROMYCIN IN CLINICAL STRAINS OF
STAPHYLOCOCCUS EPIDERMIDIS AND THE INFLUENCE OF 50% ETHANOLIC
RUTA GRAVEOLENS L. EXTRACT ON THE RATE OF ITS DEVELOPMENT**

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Skin pathogens are characterized by a high level of antibiotic resistance, especially to antimicrobials of MLS-group. Usually, it happens due to the frequent use of erythromycin (ERY) as a treatment for skin diseases.

In our study, six clinical isolates of *S. epidermidis* with different susceptibility to ERY were used: 3 strains with intermediate susceptibility (MIC 62,5-125 µg/mL) and 3 susceptible strains (MIC 0,5-1 µg/mL). The study of the rate of ERY-resistance development for staphylococcal strains alone and in combination with 1/4 MIC of 50% ruta herb extract was performed by serial dilutions in MH broth. Selection of resistance was performed in two rows of test tubes: the first row included tubes with 3 double dilutions below and 3 double dilutions above the MIC of ERY, to the second row - 1/4 MIC of the investigated extract was added. After incubation at 37°C for 24 hours, the aliquots from the last tubes with the highest antibiotic concentration, where visible bacterial growth was observed, were taken, diluted 1:100, and inoculated into the second set of serial dilutions. Such procedure was repeated for 30 days. After every fifth passage test strains were identified and the MIC of ERY was determined.

Susceptible strains of staphylococci quickly developed resistance to ERY and its MICs after the last passage were 4000-8000 µg/mL. Investigated extract slowed rates of antibiotic resistance development in all susceptible strains and after the last passage MICs of ERY were 250-500 µg/mL. MICs of ERY after the last passage for strains with intermediate susceptibility were 2000 µg/mL and MICs of ERY from tubes with extract were 1000-2000 µg/mL.

All *S. epidermidis* isolates have developed resistance to ERY after 30 passages. The rate of antibiotic resistance differed between investigated strains. In susceptible strains, MICs of ERY were increased 31-62 times after 10 passages, 2000-4000 times after 20 passages, and 4000-8000 times after 30 passages. To compare, MICs of ERY for the same strains incubated with 50% of ruta herb extract were increased 31, 125-250, and 250 times after 10, 20, and 30 passages, respectively. For strains with moderate susceptibility to ERY, drug MICs increased 8-16 times after 10 passages and stopped at that rate until the end of the experiment. Besides, there was no difference between the results for samples with investigated extract and without.

There is a dependence between the initial susceptibility of tested microbial isolates to ERY and the rate of resistance development to it. Ethanolic ruta extract decreased the rate of resistance development only in strains that were susceptible to ERY.