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DETERMINATION OF PHYSICOCHEMICAL PROPERTIES OF GENTAMICIN, VANCOMYCIN AND RIFAMPIN SUITABLE TO PENETRATION IN BIOFILM OF *Staphylococcus* spp.

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Introduction: Coagulase-negative staphylococci (CNS) are the leading cause of foreign-body-associated infections and nosocomial bacteremia. Besides, catheter-related infections are among the most common nosocomial infections, and CNS are the major cause of device-related infections. The ability of CNS to colonize and subsequently form biofilms on the surfaces of medical devices is the primary contributing factor in the pathogenesis of such infections. The biofilms often show inherent resistance to high levels of antimicrobial agents, what makes treatment of biofilm-related infections a difficult and costly endeavor. This resistance can be caused by antibiotics' diffusion problems through the bacterial biofilm layer, possibly due a variety of physicochemical properties inherent to each antimicrobial agent, that can facilitate or difficult the penetration through the exopolysaccharide layer. These properties could be related to the molecule's polarity in physiological pH. One of the main physicochemical properties of a molecule that could alter its pharmacological behavior are the partition coefficient (log P), which express the molecular lipophilicity.
Objectives: determinate which physicochemical properties are directly related to the antimicrobial agent penetration in the biofim matrix and which antimicrobial agents are suitable for clinical treatment of biofilm-related infections.
Methods: The staphylococcal strains were obtained from a hospital from Porto Alegre. The antibiotics were selected according to the partition coefficient (log P) that should form a gradient. Biofim formation was evaluated using colorimetric method with crystal violet that uses a flat-bottomed microtiter plate 96-well polystyrene. The penetration of the antimicrobial agents was evaluated with increasing concentrations of different antimicrobial agents. Afterwards, the microtiter plates were incubated at the same conditions as previously described. After treatment with crystal violet, the optical density of bacterial biofilm that was colored will be measured using a microtiter-plate reader.
Results and Discussion: Rifampin MICB (minimum inhibitory concentration in biofilm) tested were lower than others antibiotics, with the highest MIC/MICB ratio, showing rifampin's effectiveness microbial inhibition in biofilm and planctonics cells. This was not observed for gentamicin and vancomycin, which showed poor or none penetration in biofilm exopolysacaride matrix, which became more evident with a much larger MIC/MICB ratio than the ripampin ratio (10-100 x higher).
Conclusions: The MIC/MICB ratio seems to be closely related to antimicrobials log P, meaning that the higher the log P, the higher the MIC/MICB ratio. This suggests that the lipophilicity facilitates penetration of the molecule in biofilm.

	Vancomycin	Gentamicin	Rifampin
MIC/MICB (n=12)	$9{,}4x10^{-4}$	$4{,}7x10^{-3}$	$1{,}3x10^{-2}$
Log P	-2,60	-1,90	4,20