TITLE: ACTIVITY OF MOLECULES PRODUCED *BY STAPHYLOCOCCUS EPIDERMIDIS* AGAINST MULTI-RESISTANT PATHOGENS.

AUTHORS: CAMPOS, J. C. M.¹; GLATTHARDT, T.¹; LIMA, R. D.¹; ANTUNES, L. C. M.²; FERREIRA, R. B. R.¹

INSTITUTION: ¹INSTITUTO DE MICROBIOLOGIA PAULO DE GÓES, UNIVERSIDADE FEDERAL DO RIO DE JANEIRO (AV. CARLOS CHAGAS FILHO, 373, CCS, SALA I2-028, CEP 21941-902, RIO DE JANEIRO – RJ, BRAZIL). ²CENTRO DE REFERÊNCIA PROF. HÉLIO FRAGA, FUNDAÇÃO OSWALDO CRUZ, RIO DE JANEIRO, BRASIL (ESTRADA DA CURICICA, 2000, CEP:22780-194, RIO DE JANEIRO – RJ, BRASIL).

ABSTRACT:

Enterococcus faecium, Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa, Enterobacter spp. and Salmonella spp. are part of a group of pathogens that pose a major threat to human health due to its association with health care-related infections and the emergence of antimicrobial multi-resistant strains. They cause increasing mortality and morbidity rates and there is an urgent need to develop new strategies for the treatment and control of these infections. Staphylococcus epidermidis, found in the skin microbiome, secretes compounds that inhibit colonization by pathogens, such as S. aureus, and could be a possible source for the discovery of novel therapeutic alternatives. Recently, we have shown that an S. epidermidis commensal strain produces compounds capable of inhibiting Staphylococcus spp. biofilm formation, including S. aureus, without inhibiting its growth. Thus, in this work we aimed to evaluate the impact of molecules secreted by S. epidermidis isolated from the human skin (RF1) on the growth and virulence of strains from this group of pathogens. For this, the supernatant of commensal S. epidermidis was obtained after growth in TSB medium for 24 h at 37°C, filtered and concentrated by evaporation. In the pilot study, the impact of the molecules produced by RF1 on the growth of E. faecium, S. aureus, K. pneumoniae, A. baumannii, P. aeruginosa, Enterobacter spp. and Salmonella spp. was evaluated through growth curve and agar diffusion test, where we observed growth inhibition only for Salmonella. We then evaluated the effect of these molecules on the biofilm production of the isolates by polystyrene microplate assay. The results showed significant reduction in S. aureus, K. pneumoniae, Enterobacter spp. and Salmonella spp. biofilm production. Besides that, the molecules produced by RF1 decreased motility of A. baumannii and P. aeruginosa, and increased Salmonella spp. motility. The discovery of new antimicrobial and anti-virulence compounds against highly resistant pathogens is extremely relevant and, the latter might be an interesting option to treat infections caused by these microorganisms, since these compounds may not exercise the same selective pressure for drug resistance. Additional work might reveal new therapeutic options from human commensal bacteria for the control of infections caused by S. aureus, K. pneumoniae, A. baumannii, P. aeruginosa, Enterobacter spp. and Salmonella spp.

Keywords: *Enterococcus, Staphylococcus, Klebsiella, Acinetobacter, Pseudomonas, Enterobacter, Salmonella*, biofilm, antimicrobial activity, motility, microbiota.

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