TITLE: ACTIVITY OF SMALL MOLECULES SECRETED BY THE INTESTINAL MICROBIOME AGAINST *Staphylococcus* spp.

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ABSTRACT:

The human gut microbiota encompasses a large variety of microorganisms. These organisms can have a significant impact on the health status of the host. The intestinal bacteria play a crucial role in maintaining homeostasis and protecting against pathogens, and microbes within this community can communicate through the production and sensing of small molecules. Previous studies from our group showed that the gut microbiome contains molecules with strong antivirulence activity against *Salmonella enterica* serovar Typhimurium. *Staphylococcus* spp. causes diverse types of infections, ranging from localized skin infections to systemic infections. Two important virulence factors of *Staphylococcus* spp. are the ability to develop antimicrobial resistance and to produce biofilms, both of which can jeopardize the treatment of these infections. Therefore, there is a demand for new therapeutic options against these pathogens. The long-term goal of this study is to find new molecules produced by the intestinal microbiome that are involved in interspecies interactions and could be used as therapeutics. The present work aimed to evaluate the antimicrobial and antibiofilm activity of molecules present in the intestinal microbiota from healthy individuals against clinical *Staphylococcus* spp. strains. The preparation of the fecal extract was carried out using ethyl acetate to extract small apolar molecules contained in the microbiota. The analysis of the antimicrobial effect of the fecal extract was then performed by disk diffusion of the extract and growth curves of the *Staphylococcus* spp. strains in the absence or presence of different concentrations of the extract. The antimicrobial activity of the fecal extract was observed through the formation of an inhibition halo on the two *S. lugdunensis* strains tested. In addition, a significant inhibition of growth on all the species assessed (*S. aureus*, *S. lugdunensis*, *S. warneri*, *S. haemolyticus* and *S. epidermidis*) was observed by performing growth curves with and without the fecal extract. Our results show that small molecules present in our intestinal microbiome have a strong antimicrobial activity against several species of *Staphylococcus*, including multidrug-resistant clinical isolates. Further studies are needed to determine the activity of these molecules against biofilms. We also plan to purify and characterize the bioactive molecules responsible for this phenotype.

Keywords: microbiota, gut metabolome, *Staphylococcus*

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