TITLE: CHARACTERIZATION OF MOLECULES SECRETED BY COMMENSAL *Staphylococcus epidermidis* WITH ANTI-VIRULENCE ACTIVITY AGAINST *S. aureus* CLINICAL STRAINS

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ABSTRACT:
The human microbiota is considered a crucial factor that influences the state of health and disease of the host by protecting it from colonization by pathogens. Among the skin microbiota commensals, *Staphylococcus epidermidis* is one of the most frequently found species, and considered ubiquitous in the human skin microbiota. It has been shown that *S. epidermidis* can limit the development of some pathogens by producing proteases and bacteriocins, including skin pathogens such as *S. aureus*. *S. aureus* causes diverse types of infections, ranging from skin abscesses to life-threatening bloodstream infections. Resistance to several antibiotics is a common virulence trait of *S. aureus*, and methicillin-resistant isolates have been a major public health concern. Therefore, the development of new strategies such as the use of anti-virulence compounds against this pathogen is urgent. Previous studies from our group demonstrated the presence of anti-biofilm molecules secreted by *S. epidermidis* isolated from the skin microbiota with no effect on *S. aureus* growth. Thus, this study aimed to investigate the nature of the molecules secreted by *S. epidermidis* that affect the virulence of clinical *S. aureus* strains . The supernatant of *S. epidermidis* cultures was fractionated by molecular size and the fractions tested on *S. aureus* biofilm production. Results showed that the active compound have a molecular weight between 3 kDa and 10 kDa. As a preliminary characterization of the nature of the active compound, the supernatant was treated with proteinase K and heat (boiling for 30 minutes). After these treatments, the anti-biofilm activity persisted, indicating that the active compound is resistant to both treatments. Furthermore, ethyl acetate was used to extract the supernatant, and the organic phase of the extraction retained the anti-biofilm activity. These preliminary results showed that the active compound is a small molecule that is protease and heat resistant and partitions to the organic phase during an ethyl acetate extraction. This suggests that the nature of the active molecule is not proteinaceous but rather lipidic. The identification of compounds with anti-virulence activity can help in the search for new strategies against *S. aureus* infections, besides helping understand the interactions between the microbiota and pathogens.

KEYWORDS: Microbiota, anti-virulence, *S. epidermidis*, *S. aureus*, biofilm

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