TITLE: BLOCKING EXTRACELLULAR COMMUNICATION TO PREVENT URINARY TRACT INFECTIONS

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ABSTRACT: Urogenital infections are a serious public health problem, affecting millions of people worldwide, especially women. Treatment has become increasingly difficult because of the spread of multidrug resistance. Ideal therapies should not allow the development of resistance and, unquestionably, should not alter the individual's healthy resident microbiota. Therefore, the present study aimed to contribute to the development of alternative therapies against the main microbial species involved in urogenital infections (*Escherichia coli*, *Candida albicans*, *Streptococcus agalactiae*, *Enterococcus faecalis*, *Klebsiella pneumoniae*, and *Staphylococcus aureus*) based on the interference of extracellular communication by Quorum Sensing, using low molecular weight (less than 3 kDa) fractions of biological extracts obtained from the algae *Prototheca zopfii* (LMPZ) and from the venom of the scorpion *Tityus serrulatusI* (LMTS). Fractions were obtained by ultrafiltration with a 3 kDa molecular weight cut-off membrane. The effect of LMPZ and LMTS was evaluated on biofilm formation, performed on polystyrene microtiter plates for quantitative analysis (Crystal Violet assay) or on glass coverslips for qualitative analysis (Confocal Laser Scanning Microscopy), and on *Galleria mellonella* infection/protection assay. Regarding biofilm formation, LMPZ practically abolished the ability of *E. coli* to form biofilm. Both fractions decreased the biofilm mass of *E. faecalis* and *S. aureus*, and increased *K. pneumoniae* biofilm mass. No change was observed in *S. agalactiae* and *C. albicans* biofilm formation. In the *G. mellonella* protection/infection assay, LMPZ was able to protect 100% of individuals infected with *C. albicans* and 60% of individuals infected with *S. agalactiae*, even after 96h post-infection. No protector effect was observed when larvae were infected with *E. coli*, *E. faecalis*, *S. aureus* or *K. pneumoniae*. In the final analysis, the results highlight the complex nature of the extracellular signaling systems of microorganisms and allow us to conclude that their effects on the pathogenesis of urinary tract infections strains depend on the species and on the evaluated phenotype. Nevertheless, this approach represents a promising technological innovation in the development of new products for clinical use that would potentially replace the use of antimicrobials in infection control.

Keywords: urinary tract infection, extracellular communication, biofilm, *Galleria mellonella*, biological extracts

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