Evaluation of the Peptide p-BthTX-I and Its Dimer $(p\text{-BthTX-I})_2$ for Activity Against Multiresistant Bacteria and Biofilm

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Introduction: The emergence of bacteria resistance to conventional antibiotics is the greatest challenge to microbial infection control. In this context, antimicrobial peptides represent a promising alternative group to be used as antibiotics. **Objectives:** Evaluate the antimicrobial activity of the peptide p-BthTX-I (KKYRYHLKPFCKK) and its disulfide-linked dimeric form, obtained via air oxidation $(p\text{-BthTX-I})_2$ against a variety of bacteria, including resistant and clinical. Furthermore, the use of latex membrane from *Hevea brasiliensis* on its controlled release was analyzed. **Material and Methods:** Solid phase peptide synthesis was performed manually using the Fmoc protocol. MIC was determined by the technique described in the CLSI (CLSI, 2013) and MBC was performed according Qin and co-workers (2014). Peptide serum stability was assayed as previously described by Nguyen et al. (2010). For peptide latex release experiments (Herculano et al., 2009), the $(p\text{-BthTX-I})_2$ was incorporated into the latex solution and monitored by LC/MS in different times. **Results and Discussion:** p-BthTX-I and its dimer presented bactericidal activity against strains including *S. aureus* SA16, *S. aureus* SA33, *S. aureus* SA88, *S. aureus* SA90, *S. epidermidis* ATCC35984, *E. faecium* VRE16, *E. faecium* HSJRP8, *K. pneumoniae* NDM-1 and *E. coli* ATCC 35218. $(p\text{-BthTX-I})_2$ showed bactericidal activity against all these strains plus *S. aureus* ATCC25923, *E. faecalis* ATCC29212, *K. pneumoniae* ATCC700603, *K. pneumoniae* ATCC BAA1705, *E. coli* ATCC 25922 and *E. coli* CA4, moreover degraded biofilm formed by *S. epidermidis* ATCC35984. Peptide serum stability activity showed that $(p\text{-BthTX-I})_2$ was degraded after 10 min of incubation. The main degradation product was the peptide without four lysine residues, which maintain stable since after 48h of incubation. Interestingly, this peptide conserves antibacterial activity. Furthermore, $(p\text{-BthTX-I})_2$ was efficiently liberated by rubber latex since after 12h. **Conclusions:** These peptides are promising prototypes for new drugs aiming the treatment of multidrug resistant infection.

Acknowledgments: Fapesp, Capes and CNPq.

Keywords: $(p\text{-BthTX-I})_2$, multiresistant bacteria, Biofilm