Potent antibacterial and antifungal synthetic peptides derived of LyeTx I, a toxin from the venom of the spider Lycosa erythrognatha (Lucas, 1836)

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Introduction and objectives: The rise of many bacteria and fungi strains resistant to many drugs used against infectious disease it is essential to develop new antimicrobial medicines. Antimicrobial peptides (AMPs) could be new candidates to deal with these dangerous strains. One AMP is LyeTxI, purified from the venom of the spider (L. erythrognatha), with activity against bacteria, fungi and having poor hemolytic effects. Trying to improve its activity it was truncated and some modifications were performed.

Material and methods: LyeTxI and their derivatives were synthesized by Fmoc method and purified by HPLC. Minimal inhibitory concentrations (MICs) of the peptides were determined against five bacteria and three fungi strains, and performed according to CLSI protocols. Hemolytic assays were performed to evaluate the toxicity of the synthetic peptides and their concentrations able to lyse 50% of erythrocyte (EC50) calculated. Circular dichroism profiles (CD) were performed in different percentages of 2,2,2 trifluorethanol. Therapeutic index were calculated to compare the ratio between EC50 and MIC values.

Results and discussion: Four pure synthetic peptides were obtained, LyeTxI and three derivatives: LyeTxImn, LyeTxImnΔK and LyeTxImnΔKAc. All these synthetic peptides were actives against fungi and bacteria, but LyeTxImn was less active than LyeTxI and than LyeTxImnΔK. The strains tested were: Escherichia coli, Pseudomonas aeruginosa, Acinetobacter baumannii, Staphylococcus aureus, Staphylococcus epidermidis, Cryptococcus neoformans, Cryptococcus gattii and Candida krusei. LyeTxImnΔK was more active than LyeTxI against E. coli and Cryptococcus spp. On the hemolytic assays, LyeTxImnΔK and LyeTxImn were the less hemolytic of the set. Comparing the therapeutic index LyeTxImnΔK showed the best value among the peptides. CD analysis revealed that all peptides derivated from LyeTxI adopted an α-helix conformation, depending on the medium. Conclusion: Based in those results LyeTxImnΔK seems to be the best candidate to perform in vivo tests to search a new candidate to antimicrobial drug.

Keywords: Antimicrobial drugs, MIC, Spider Venom

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