TITLE: BIOINSPIRED ANTIBACTERIAL AND ANTIBIOFILM PEPTIDES FROM *HYLARANA PICTURATA* CUTANEOUS SECRETION

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ABSTRACT:

In recent years bacterial resistance to antibiotics has proven to be a worldwide problem. The synthetic antibacterial peptides (AMPs) bioinspired in toxins have high potential to become alternatives for this problematic. AMPs might be found in several sources as bacteria, fungi, plants, insects and vertebrates as example the cutaneous secretion of anuran. Therefore, this work proposes two new analogues of temporin-PTa from *Hylarana picturata* cutaneus secretion against bacteria forming biofilm. The methodologies for the rational design of the new sequences were carried out according to the main physicochemical characteristics of AMPs, the *in vitro* tests minimum inhibitory concentration (MIC), minimal bactericidal concentration (MBC), minimum inhibitory concentration of biofilm (MICB) and hemolytic were realized. The *in silico* studies were performed by molecular dynamics on 1,2-dipalmitoyl-sn-lycero-3-phosphatidylethanolamine and 1,2-dipalmitoylsn-glycero-3-phosphatidylglycerol mimetic membranes. Temporin-PTa, T-1 and T-2 analogs showed 43.4 and 2.8 μM MICs against *Escherichia coli* and 43.4, 23 and 21.8 *Staphylococcus aureus* were bactericidal In the biofilm assays, the temporin-TPa showed no inhibition against *E. coli and K. pneumoniae* resistant, the T-1 and T-2 analogues had MICB at the concentration of 46.6 and 23 μM. Peptides do not show hemolysis against red blood cells. *In silico* studies of molecular dynamics temporin-TPa and T-2 demonstrated affinity for Gram-positive membrane and T-1 for Gram-negative through of hydrogen bounds. T-2 was promising in the results shipped to MIC and MBC in the bacteria tested. In the biofilm formation, T-1 peptide has been shown to be a good candidate for the elimination of biofilm formation. Conclusion the rational design of the new bioinspired peptides from anuran skin secretion led to the improvement of activity lower citotoxicity for erytrocites became candidates for the development of biotechnological tools as alternative conventional antibiotics.

Keywords: Rational design; Antimicrobial peptides; *In silico* study.

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