TITLE: DEVELOPMENT OF BIOATIVE PEPTIDES AGAINST MULTIDRUG-RESISTANT BACTERIA

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ABSTRACT:

Multidrug resistant bacteria are a global health care concern and it is increasingly evident that new therapeutic strategies are needed against these microorganisms. To make this situation even worse, biofilm formation represents a rising clinical threat, since bacteria are in biofilm resilient to most of the treatments available. As alternative against this scenario, antimicrobial peptides (AMPs) are very interesting molecules to be explored in the search for new antimicrobial agents because they are relatively easy to produce while exhibiting broad-spectrum antimicrobial activity, with a distinct mode of action that means that they are less prone to developing resistance. This study aimed to evaluate biofilm and antimicrobial activities of rational designed peptides against multidrug resistant strains. At first, six peptides were tested, in two concentrations (1 and 10 μM) using crystal violet assay. The peptide identified as P5, in the higher concentration, showed antimicrobial and antibiofilm activities against KPC (*Klebsiella pneumoniae* carbapenemase) producing *K. pneumoniae* (30 % and > 95 %), KPC producing *Enterobacter cloacae* (50 % and > 95 %), NDM (New Delhi metalo beta lactamase) producing *Escherichia coli* (30 % and > 95 %); P5 showed antibiofilm activity against MRSA Methicillin-resistant *Staphylococcus aureus* (MRSA) ATCC® 43300 (90 %), OXA-48-producing *K. pneumoniae* (90 %) and, antimicrobial activity was observed against OXA-23-producing *Acinetobacter* spp. (> 95 %). Secondly, more five peptides, analogous to P5 sequence, were designed and synthetized. Two of these peptides, identified as P7 and P8, showed similar results to P5. The next step of our study is to evaluate infection model using *Galleria mellonella* larvae. We are facing a post-antibiotic era, where antibiotics are no longer effective against all bacterial threats. In this regard, antimicrobial peptides represent a promising alternative strategy in the development of new antimicrobial agents.

Keywords: peptides, multidrug resistance, antimicrobial and antibiofilm activity

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