Structural and Functional Analyses of a Palindrome Poly-Alanine Antibacterial Peptide from *Pleuronectes americanus*

Migliolo, L.¹, Silva, O.N.², Teixeira, L.D.¹, Fensterseifer, I.C.M.¹, Franco, O.L.¹

¹Centro de Analises Proteômicas e Bioquímicas, Programa de Pós-Graduação em Ciências Genômicas e Biotecnologia; UCB, Brasília, Brazil; ²Programa de Pós-Graduação em Genética e Biotecnologia, Universidade Federal de Juiz de Fora, Juiz de Fora-MG, Brazil

In last decades several peptides have been screened showing activity against pathogenic microorganism, being able to act against different targets. This ability allows the development of novel strategies for rational design of unusual bioactive compounds. The present work focus on structural and functional evaluation of a palindrome analogue peptide named *Pa-MAP* 1.5 with 28 amino acids residues length designed from original peptide *Pa-MAP* previously synthesized as a multifunctional peptide. After chemical synthesis, *Pa-MAP* 1.5 showed a strong activity against *Escherichia coli* ATCC 8739 with a MIC value of 3.2 µM. Moreover none cytotoxicity against erythrocytes was observed. *Pa-MAP* 1.5 at standard concentrations of 1 mg.kg⁻¹ was also evaluated *in vivo* through intraperitoneally *E. coli* infected mice with a sub-lethal concentration. *Pa-MAP* 1.5 was able to prevent *E. coli* infection and further improve mice survival with total weight gain of 2.5%. In contrast mice treated with ampicillin concentration 2 mg.kg⁻¹ lost 5.6% of their weight. In addition, for a better understanding of functional-structure relations *Pa-MAP* 1.5 was *in silico* modeled showing 100% of amino acid residues in favorable regions. The final structural model showed a well-defined amphipathic α-helix favored by Ala residues and with six amino acid residues (Lys², Lys⁹, Lys¹³, Lys¹⁶, Lys²⁰ and Lys²⁷) that might contribute for electrostatic interaction with anionic bacterial membranes phospholipids. Otherwise four hydrophobic amino acid residues (Leu¹, Leu¹⁰, Leu¹⁸ and Leu²⁶) are encountered in oppose side which might interact with membranes phospholipids carbon by Van der Walls forces probably helping on membrane disruption. In conclusion our data here report that *Pa-MAP* 1.5 could be utilized as a potent candidate for *E. coli* infections control.

Keyword: *Pleuronectes americanus*, synthetic peptide, antibacterial, secondary structure

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