BIOCONJUGATE CONTAINING HECATE PEPTIDE AND GALLIC ACID: STRUCTURE, ANTICANCER ACTIVITY AND TOXICITY

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Bioconjugate constitute a class of molecules of important biological interest mainly for the treatment of diseases. In addition, the N-terminus position of cationic peptides has been described as important for their biological activity. The aim of this study was to evaluate the structure and biological activity of the lytic peptide Hecate (FALALKALKKALKKLKKAL) and the effect of conjugating this macromolecule with gallic acid (C₇H₆O₅). Hecate peptide and GA-Hecate peptide conjugate were synthesized by SPPS. The anti-cancer activity in HeLa cancer cells using MTT assay indicated that Hecate (IC₅₀=5.9 µmol/L) is more active than AG-Hecate (IC₅₀=10.1 µmol/L). Micrograph images after treatment of the cells with these compounds demonstrates cavity formation and loss of microvilli and membrane integrity. This mode of action supports previous studies using lytic peptides in cancer cells that indicated that these compounds cause cell necrosis. GA-Hecate showed lower activity in non-tumor keratinocyte cells but higher hemolytic activity. However, lower concentrations of the Hecate peptide caused cancer cells death but did not promoted substantial damage to membranes, suggesting another action mechanism - apoptosis. The CD measurements showed that the Hecate peptide showed α-helical structures in the presence of SDS and LPC, while GA-Hecate presented lower incidence of α-helical structures in the same chemical environment. These data were used to provide information regarding the relationship between the amino-terminal region and its charge and the secondary structure and biological activity of the peptides. Our findings suggest that the N-terminus of Hecate plays an important role in its activity against cervical cancer by affecting it secondary structure, toxicity, and hemolytic activity. This study demonstrated activity against cervical cancer for the lytic peptide Hecate and showed that N-terminal modification could be used as a strategy for altering the specificity and toxicity of lytic peptides. Supported by: FAPESP, CNPq, and CAPES.¹ Amino acids, 2015, in press.