Lunatin 1 From The Venom Of The Peruvian Scorpion *Hadruroides Lunatus* As Cytotoxic And Pro-Apoptotic Peptide

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INTRODUCTION: Lunatin 1 was previously isolated by our group and described as an antimicrobial peptide (AMP). We also verified that Lunatin 1 has both cytotoxic and anti-tumor activities, as observed for other AMPs. **OBJECTIVES:** The aim of this study was to evaluate the cytotoxicity of the Lunatin 1 in HL60 leukemic cells and to identify the mechanism that leads to cell death. **MATERIAL AND METHODS:** The peptide was synthetized by Fmoc in solid phase, and purified by reversed-phase liquid chromatography. Cell viability was evaluated by MTT method and LDH assay. DNA fragmentation was evaluated by cytometry and agarose gel. Caspase-3 and Annexin V/Propidium Iodide Apoptosis Assay were accomplished by flow cytometry. Confocal microscopy was used to check nuclear morphological changes. **RESULTS AND DISCUSSION:** Lunatin 1 showed an important antitumor activity against HL60 cell line (IC_{50}=43,42µM). Lunatin 1 induced DNA fragmentation, phosphatidylserine exposure, nuclear morphological changes as condensation, fragmentation and reduction of nucleus size. The LDH release was partial with 3 hours of treatment (14% cell lysis), gradually increased to total lysis with 24 of treatment. Caspase 3 was also activated with 3 hours of treatment, suggesting that the death cell is caused by induction of apoptosis. **CONCLUSIONS:** We have identified a new cytotoxic and pro-apoptotic activity of Lunatin 1 against leukemia cells. Furthermore, Lunatin 1 can be good model for the development of new antitumor peptides.

Keywords: *Hadruroides lunatus,* Lunatin 1, antitumor peptides, death cell, apoptosis.
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