Spermicidal Activity of Fragments of a Protein Extracted From Spider Venom.

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From the venom of the Chilean spider Latrodectus mactans was isolated a protein, denoted Arachnotoxin (ATx), containing 69 amino acid residues. The molecule showed to be a potent human spermicide [Romero, F. et al. Fertil Steril, 87, 1345, 2007 and Parodi et al. B.B.R.C., 375, 571, 2008]. In order to obtain smaller active molecules, in this study we synthesized and tested tree ATx fragments {Ac-[Ala⁴³]-ATx⁴¹-⁶⁰-NH₂; Ac-ATx⁴⁶-⁶⁰-NH₂ and Ac-ATx⁴¹-⁵⁷-NH₂}. After a degradation resistances evaluation in different biological fluids, we decide to use the most stable compound, Ac-[Ala⁴³]-ATx⁴¹-⁶⁰-NH₂, and its linear counterpart, Ac-[Ala⁴³, Ser⁴⁷,⁵⁶]-ATx⁴¹-⁶⁰-NH₂. The effect of these compounds in the motility and viability of human spermatozoids were then evaluated. The experiments were conducted in the presence and in the absence of the seminal liquid. Spermatozoids were incubated for 5, 15, 30, 45 and 60 minutes. In order to evaluated the Ca²⁺ release fluorescence experiments were also performed for 3 and 15 minutes. From our results we could observe that both peptides caused a decrease in the spermatozoid mobility. The viability data showed that both peptides were not able to kill the spermatozoids, but they caused a drastic reduction in the spermatozoid movement. Fluorescence evaluation demonstrated a significative increase in the Ca²⁺ release caused by both compounds in a time depend way. We could conclude that both peptides could be good lead compounds to be used in the development of contraceptive drugs.

Word Keys: Degradation resistance; motility; peptide synthesis; sperm viability; spermicidal properties; spider venom

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