PNPP-19, A SYNTHETIC AND NON TOXIC PEPTIDE DESIGNED FROM A PHONEUTRIA NIGRIVENTER TOXIN, POTENTIATES ERECTILE FUNCTION VIA NO/CGMP

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Introduction and Objectives: Erectile dysfunction (ED) is a common medical disorder that seriously impacts life quality. The current treatment involves the use of phosphodiesterase-5 inhibitors. However, 30-35% of patients fail to respond to it, indicating the need for alternative treatments. In the present work, we designed a synthetic peptide, PnPP-19 (P. nigriventer potentiating peptide, containing 19 amino acid residues) comprising the potential active core of PnTx2-6 native toxin from the venom of the spider Phoneutria nigriventer and investigated its role in erectile function (EF).

Material and methods: EF was evaluated in vivo by measuring intracavernous pressure/ mean arterial pressure ratio during electrical field stimulation (EFS) of the pelvic ganglion of rats. In vitro studies, corpus cavernosum strips were phenylephrine-contracted and relaxation induced by EFS with or without PnPP-19. The possible activity of PnPP-19 on sodium channels was evaluated by electrophysiological screening of transfected channels on oocyte of Xenopus. Immunogenicity was evaluated on mice, and the presence of antibodies against the peptide was determined by indirect ELISA. To check the toxicity, mice were intraperitoneal injected with different doses of PnPP-19, for posterior histopathological studies of some organs. Results and conclusions: PnPP-19 was able to potentiate erection even at low doses, both in in vitro and in vivo assays. It showed no apparent toxicity or immunogenicity to mice even at extremely high doses and did not affect sodium channels or isolated rat hearts. PnPP-19 increased cGMP levels at 8 Hz and this effect was inhibited by L-NAME (10⁻⁴M). EF was partially inhibited by 7-nitroindazole (10⁻⁵M), a selective inhibitor of nNOS. Finally, PnPP-19 can easily be obtained by chemical synthesis. Therefore, our results suggested that this new synthetic peptide has the potential to emerge as a new pharmacological tool and be a promising alternative drug model for the treatment of ED.

Keywords: Erection, bioactive peptides, PnPP-19.

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