

Pnpp-19 Potentiates Erection By Increasing Nitric Oxide, In Rat Cavernosal Tissue.

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INTRODUCTION: The synthetic peptide named PnPP-19 comprises the supposed potential active core of the *Phoneutria nigriventer* native toxin PnTx2-6. We have previously shown that PnPP-19 potentiates erection *in vivo* and *ex vivo* in rats showing promising features for erectile dysfunction treatment. **OBJECTIVES:** To understand the mechanism by which PnPP-19 evokes relaxation in rat *corpus cavernosum* (CC). **MATERIAL AND METHODS:** cavernosal strips from Sprague Dawley rats were incubated with guanethidine monosulfate (5×10^{-6} M) and contracted with phenylephrine (10^{-5} M). Relaxation responses were evoked by electrical field stimulation (EFS), before and after 10 minutes of incubation with PnPP-19 (10^{-8} M). The effect of PnPP-19 on relaxation induced by EFS was also tested in the presence of atropine (10^{-6} M), a muscarinic receptor antagonist, N-type Ca^{2+} channel blockers (w-conotoxin GVIA, 10^{-5} M) and sildenafil (3×10^{-9} M). Nitric oxide (NO) release was detected in *cavernosum* slices with fluorescent dye (DAF-FM) and confocal microscopy. The effect of PnPP-19 was also characterized after use of a non-selective nitric oxide synthase (NOS) inhibitor, L-NAME. **RESULTS AND DISCUSSION:** EFS-induced relaxation of CC was significantly potentiated by PnPP-19. This potentiating effect was further increased by sildenafil, but it was neither altered by atropine, nor by blockage of N-type Ca^{2+} channels. L-NAME inhibited penile erection and treatment with PnPP-19 was unable to reverse this inhibition. PnPP-19 treatment induced a significant increase of NO release in *cavernosum* tissue. Attenuated erectile function of SHR hypertensive rats was fully restored after peptide injection. **CONCLUSIONS:** We showed that PnPP-19 promotes increased NO production in CC. In addition, the relaxation effect of CC seems to be independent of phosphodiesterase enzyme type 5 inhibition and the depressed erectile function of SHR hypertensive rats was normalized by PnPP-19 administration. Our data displays PnPP-19 as a possible pharmacological tool to study alternative treatments for erectile dysfunction.

Keywords: Erection, bioactive peptides, PnPP-19.
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