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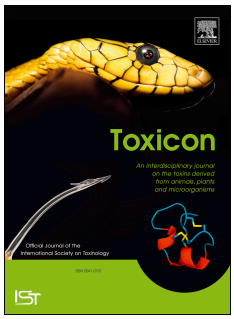

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BotAF, a new *Buthus occitanus tunetanus* scorpion toxin, produces potent analgesia in rodents

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Abstract

This work reports the purification of new potent scorpion neuropeptide, named BotAF, by an activity-guided screening approach. BotAF is a 64-residue long-chain peptide that shares very high similarity with the original β-like scorpion toxin group, in which several peptides have been characterized to be anti-nociceptive in rodents. BotAF administration to rodents does not produce any toxicity or motor impairment, including at high doses. In all models investigated, BotAF turned out to be an efficient peptide in abolishing acute and inflammatory (both somatic and visceral) pain in rodents. It performs with high potency compared to standard analgesics tested in the same conditions. The anti-nociceptive activity of BotAF depends on the route of injection: it is inactive when tested by i.c.v. or i.v. routes but gains in potency when pre-injected locally (in the same compartment than the irritant itself) or by i.t. root 40 to 60 min before pain induction, respectively. BotAF is not an AINS-like compound as it fails to reduce inflammatory edema. Also, it does not activate the opoidergic system as its activity is not affected by naloxone. BotAF does also not bind onto RyR and has low activity towards DRG ion channels (particularly TTX sensitive Na^+ channels) and does not bind onto rat brain synaptosome receptors. In somatic and visceral pain models, BotAF dose-dependently inhibited lumbar spinal cord c-fos/c-jun mRNA up regulation. Altogether, our data favor a spinal or peripheral anti-nociceptive mode of action of BotAF.