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Cv6 And Cv7: Two New Peptides Toxins from the Mexican Scorpion Centruroides Villegasi Which Inhibit Voltage-gated Potassium Channel Kv1.2

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Scorpion venom contains a diverse array of peptides that effectively block potassium ion channels. In this study, two new peptides designated Cv6 and Cv7, were isolated from the venom of Centruroides villegasi and their primary structures were determined. The MW of Cv6 and Cv7 peptides is 4277 and 4287 Da, consisting of 38 and 39 amino acid residues including 6 cysteines with three putative disulfide bridges, respectively. Comparison of the primary sequences with known potassium scorpion toxins (KTx) indicated that Cv6 and Cv7 has high similarity with α-KTx2 subfamily of potassium channel toxins. Electrophysiological characterization revealed that Cv7 inhibited Kv1.2 ion channel with high affinity than the Cv6 with Kd values of 23 pM and 4 nM, respectively. In addition to Kv1.2, Cv7 was active on KCa3.1, Kv1.1 and Kv1.3 with 18%, 34% and 84% inhibition at 100nM concentration, however, Cv6 blocked only 10% of Kv1.3 and 35% of KCa3.1 currents at this concentration. Both peptides did not show any activity on Kv11.1 and KCa1.1 ion channels. Our results showed that Cv7 is a high affinity blocker of Kv1.2 with high selectivity over Kv1.1 (8000-fold) and Kv1.3 (300-fold). These pharmacological properties of Cv7 make it a potential candidate to target Kv1.2 gain of function related channelopathies such as epilepsy.