Purification and characterization of three inhibitors of voltage-dependent K+ channels from Leiurus quinquestriatus var. hebraeus venom.

Garcia ML, Garcia-Calvo M, Hidalgo P, Lee A, MacKinnon R.

Department of Membrane Biochemistry and Biophysics, Merck Research Laboratories, Rahway, New Jersey 07065.

Three new toxins from the venom of the scorpion Leiurus quinquestriatus var. hebraeus have been identified on the basis of their ability to block the Shaker K+ channel. These toxins have been purified using HPLC techniques and characterized as 38 amino acid peptides by mass spectroscopy, amino acid analysis, and sequence determination. Their chemical identity was confirmed by producing fully functional synthetic toxins using recombinant methods. These peptides are potent inhibitors of the Shaker K+ channel (Kd < 1 nM) as well as the mammalian homologues of Shaker. They are related to other previously described K+ channel toxins, but form a new subclass within the larger family of K+ channel inhibitors derived from scorpion venom. We have named these toxins agitoxin 1, 2, and 3, respectively.