RESUMO DE TRABALHO

Neurochemical characterization of a novel neuroprotective and anticonvulsant component from \emph{Parawixia bistriata} spider venom that inhibits synaptosomal uptake of GABA and glycine.

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The major contribution of this work is the isolation of a novel neuroprotective and anticonvulsant component referred to as FrPbAII, from \emph{P. bistriata} spider venom, and a detailed investigation of its mode of action. This component, which is chemically similar to GABA, is also homogeneous and has a molecular weight of 174. FrPbAII inhibits synaptosomal GABAergic uptake in a dose- and time-dependent manner acting as a competitive inhibitor that does not act on Na$^+$, K$^+$, Ca^{2+} channels, GABA_B$ receptors or GABA-T enzyme, and therefore, is not directly dependent on these neural structures for its action. Direct increase of GABA release and reverse transport are also ruled out as constitutive mechanisms of FrPbAII activities, as well as unspecific actions on pore membrane formation. Moreover, FrPbAII is selective for GABA and glycine transporters, having slight or no effect on homologue (monoamines) or glutamate transporters. According to our experimental glaucoma data in rat retina, FrPbAII is able to cross the blood retina barrier and promotes effective protection of retinal layers submitted to ischemic conditions. Also, intracerebroventricular injection of FrPbAII abolishes rat convulsive tonic clonic seizures induced by convulsive agents, as bicuculline and picrotoxin. These studies are of relevance by providing a better understanding of neurochemical mechanisms involved in brain function, and for possible development of new neuropharmacological and therapeutic tools.