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Ultrastructural aspects of Bbil-TX (Asp49 PLA_2) from *Bothriopsis bilineata smargadina* snake venom (forest viper) in the skeletal muscle

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Snakebite envenoming is considered a neglected tropical disease and an important public health problem in many tropical and subtropical countries. In Brazil, there are 26 species of *Bothrops* which are responsible for ~70% of snakebites per year [1]. The venoms of these species consist of a complex mixture of toxins with various properties including proteolytic, coagulant, hemorrhagic and myotoxic activities [2,3,4]. In addition, these venoms have shown to induce *in vitro* postsynaptic and/or presynaptic neuromuscular blockade which can potentially cause tissue damage [5,6,7]. In this study, we analyzed the myotoxic effect of Bbil-TX toxin, an Asp49 PLA_2 isolated from *Bothriopsis bilineata smargadina* snake venom [8], on mammalian and avian isolated neuromuscular preparations at concentrations of 10 µg/ml and 30 µg/ml, respectively, under transmission electron microscopy (TEM). Results show that the muscle fibers affected were presented with necrotic aspects such as structural disorganization of myofibrils with severe mitochondrial damage and empty-looking sarcoplasmic reticulum which indicates loss of regular actin-myosin myofilaments pattern. The sarcoplasmic reticulum showed dilated cisterns and swollen mitochondria devoid of cristae. Schwann cells exhibited mitochondrial damage and infiltrated processes between pre- and postsynaptic compartments. Previously, we have shown that Bbil-TX has an unusual neurotoxic effect in which it produced marked neuromuscular facilitation followed by complete blockade in mammalian preparations and potent blockade at a very low concentration in avian preparations [9,10]. Experimental evidence suggests that this venom causes neuromuscular blockade by a presynaptic mechanism involving phospholipase A_2 (PLA_2). Together, these results indicate that Bbil-TX exerts a variety of *in vitro* neuromuscular effects causing muscle damage.

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