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PHARMACOLOGY OF CROTAMINE

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Crotamine is a basic polypeptide toxin present in the venom of a variety of *Crotalus durissus terrificus* (*C.d. terrificus* var. *crotaminicus)*. The LD50 of this toxin i.v. in mice and its 95% confidence intervals are 1,500 (1,010-2,230) μg/kg. Crotamine is considerably (about 18 times) less toxic than crotoxin (LD50 82 μg/kg), the main toxin from the South American rattlesnake venom. Crotamine activates the sodium channel exclusively or mainly in the skeletal muscle fibre membrane. All effects produced by it are assigned to this action. They are in isolated or *in situ* neuromuscular preparations of mammals:[6,4] i. fibrillation and/or a sustained contraction of short duration usually only observed immediately after the injection or addition of the toxin to the bath; ii. a delay of relaxation of the muscle and/or an aftercontraction following the muscle response to direct or indirect stimulation with single or high frequency shocks; iii. an increase of the twitch tension in muscles stimulated directly or indirectly with maximal shocks. These effects, also evoked in curarized muscle are accompanied either (effects referred to in i. and ii.) by discharges of potentials of high frequencies (over 200-300 per sec.) and small amplitude (50-150 μV), or (effect referred to in iii.) by more than one action potential. Ca^{++}, Mg^{++} and quinine or quinidine antagonize these effects. Crotamine may also depress the responses to direct or indirect stimulation, and in large doses, to render the muscles inexcitable. Dilatation of the sarcoplasmic reticulum and myonecrosis, effects evoked by all toxins that activate the sodium channel, are induced by crotamine.[1] They are explained by an increase in Na^+ influx leading to increased water influx, cell swelling, and eventually cell death[3].

The action of crotamine in the sodium channel was demonstrated in the rat diaphragm.[4,5] The depolarization produced by crotamine in curarized or noncurarized muscles was prevented by tetrodotoxin or low sodium in the bathing fluid.

Crotamine produces in nonanesthetized animals, especially in goats, myotonia-like symptoms.[4,6] Myotonia may be caused either by an increase in muscle fibre membrane resistance due to a decrease in its conductance to Cl^- or to an increase in the membrane conductance to Na^+. The selectivity of action of crotamine in producing activation of the sodium channel in skeletal muscles is responsible for inducing myotonia-like effects in animals.

The participation of crotamine in the genesis of the myonecrosis observed in *C.d. terrificus* snake-bite accidents[2] is doubtful owing to its low activity and concentration in the venom.

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