EFFECTS OF CROTAMINE, CROTOXIN AND L-AMINOACID-OXIDASE ON VIABILITY OF INSULIN-PRODUCING RINm5F CELLS

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Crotamine and crotoxin are the main components found in the *Crotalus durissus* venom. Crotamine display many interesting biological actions on targeting cells. Crotoxin is a heterodimeric PLA2 and the main responsible for the toxic effects of the venom. Additionally to toxins, several other proteins possessing enzymatic activities can be isolated from snake venoms, like L-aminoacid-oxidase. It was the aim of this study to determine whether these purified compounds could affect the viability of insulin-producing cells.

Crotamine, crotoxin, and L-aminoacid-oxidase were purified from *C. durissus ruiruna* venom by chromatography and reverse phase HPLC. Viability was determined using MTS assay. Crotamine decreased the viability of RINm5F cells in a dose dependent manner (5-500 µg/ml, 48 h). RINm5F cells overexpressing the enzyme catalase were also affected by the compound. Surprisingly, crotoxin (5-500 µg/ml) and L-aminoacid-oxidase (0.25-25 µg/ml) did not affect RINm5F cells viability in either control or catalase-overexpressing cells.

Crotamine is cytotoxic to insulin-producing beta-cells, contrasting to crotoxin and purified L-aminoacid-oxidase. Interestingly, the effect of crotamine on insulin-producing cells appears not to be driven by oxidative stress and/or intracellular peroxides formation, as catalase-overexpressing cells are also sensitive to the compound. It will be of great interest to search for the mechanism of action and also for the component(s) of crotamine responsible for the cytotoxicity.