ON THE PHARMACOLOGY OF CONVULXIN AND GYROXIN

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The venom of the South American rattlesnake *C.d. terrificus* is known to contain several neurotoxins: crotoxin[10], crotamine[5], gyroxin[2] and convulxin[6]. Crotoxin is the main neurotoxin of this venom and is the component responsible for its very high toxicity[12].

Crotamine is a basic polypetide which, unlike crotoxin, is present only in the venom from certain regions[3]. However, the injection of crotoxin or of crotamine into experimental animals does not reproduce all the effects of *C.d. terrificus*-induced envenomation such as early respiratory and circulatory effects, convulsions or the symptomatology resembling a labyrinthic lesion. This latter effect could be attributed to gyroxin[2], a non-lethal neurotoxin.

The most characteristic effect observed following injection of purified gyroxin consists of rolling movements in one direction for 5 to 20 minutes, after a lag time of some minutes. This syndrome gradually disappears and there is complete recovery. Purified gyroxin demonstrates TAME-esterase activity[1].

In 1967 we described a neurotoxic fraction responsible for the convulsions and early respiratory and circulatory disturbances[13]. From this fraction we isolated convulxin (Cx), a high molecular weight toxin which behaves as a homogeneous protein when examined by gel filtration chromatography and immunoelectrophoresis[6,7].

When administered i.v. into conscious mice, Cx evokes within 20 seconds a brief phase of apnea, followed by loss of equilibrium, including tonic-clonic convulsions. In the cat, we also observed autonomic disturbances such as salivation, flaccid paralysis, abdominal cramps and nistagmus.

Intravenous administration of Cx into anesthetized dogs causes intense respiratory stimulation followed by apnea of short duration as well as circulatory disturbances characterized by an immediate and abrupt fall in blood pressure followed by a transient hypertension.

Cx produces a rapid thrombocytopenia "in vivo" associated with respiratory and circulatory changes, suggesting that they are produced by pharmacologically active substances which Cx liberates from platelets.

In studying the Cx activated guinea-pig platelets we have verified that this Cx concentration-dependent aggregation is followed by the release of ATP and by the formation of thromboxanes[11], Cx-induced platelet aggregation was inhibited by EDTA and by prostacyclin. As Cx also induces leukopenia[8], the participation of leukocytes or of any substance that they may produce, is not excluded.

Cx is extremely feeble when administered by the i.m. or s.c. route. This could be related to poor absorption due to its high molecular weight. The significance of Cx in the symptoms caused by South American rattlesnake bite is still not clear. The high content of Cx in *C.d. cascavella* venom could be relevant. The appearance of convulsive movements in some victims[4,9] strongly suggests that this toxin may participate in envenomation.

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