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47. PHARMACOLOGICAL PROPERTIES OF CARDIOTOXIN ISOLATED FROM THE VENOM OF *NAJA NAJA ATRA* *

C. Y. LEE, C. C. CHANG, T. H. CHIU, T. C. TSENG and S. Y. LEE

Pharmacological Institute, College of Medicine, National Taiwan University, Taipei, Taiwan, China.

Lyophylized venom of *Naja naja atra* was fractionated on columns of CM-Sephadex (G-50) into 13 fractions by gradient elution with ammonium acetate buffer at pH 5-7. Among them five fractions (V-IX) were found to be neurotoxic and three (X, XII, XIII) were cardiotoxic. Intraperitoneal LD_{50} in mice was 0.074 $\mu g/g$ for Fr. VIII — the major neurotoxic component (NT) and 1.48 $\mu g/g$ for Fr. XIII — the major cardiotoxic one (CT). CT caused contracture, as well as reduction of resting membrane potentials, of the frog's sartorius, chick's biventer cervicis, and rat's diaphragm. In the absence of calcium, the contracture was markedly reduced, although the depolarizing effect remained unchanged. Neither contracture nor depolarization was caused by NT. The terminal nerve spikes of the frog sartorius were abolished by CT but unaffected by NT. CT caused systolic arrest of isolated frog hearts and rat's atria by reducing the membrane potentials, whereas NT was almost without effect up to 10^{-4} g/ml. CT caused a slow contraction of the guinea pig ileum, which was partially antagonized by either atropine or procaine but not by hexamethonium or antihistaminics. In the presence of CT (10^{-6} — 10^{-5} g/ml), the responses to nicotine and 5-hydroxytryptamine were greatly inhibited, usually preceded by an initial and transient facilitation. The responses to histamine and acetylcholine were not, or only slightly, reduced by CT. The vessels of the rabbit ear were constricted by CT. In cats, CT caused a fall in systolic pressure more than diastolic pressure, accompanied by various ECG changes, such as P-R interval prolongation, inverted T waves, S-T segment depression, ventricular premature beats, A-V interference, complete A-V block, idioventricular rhythm etc. It is concluded that cardiotoxin isolated from cobra venom acts on various excitable cells, predominantly, if not entirely, by reducing the membrane potentials.

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