Functional reserve of the hepatic mass to be made out as shown by the clearance constant should show a parallel relationship between the various functional parameters of the liver, during regeneration.

**INTRODUCTION**

It has been reported that some fractions of *Naja mossambica*, *N. nivea*, *N. melanoleuca* and *N. naja* have a cardio-depressant effect on the rat heart (1,3). In the course of our experiments, it was found that the venom of *Dendroaspis angusticeps* reduced the rate and force of contraction of the rabbit heart. This paper deals with the mechanism of this cardio-depressant effect on the heart and the identification of the myocardial depressant factor.

**MATERIALS AND METHODS**

The isolated rabbit heart was set up according to the method of Langendorff. The contractions were recorded on a Microdynamometer (Ugo Basile 7050) coupled to an isometric transducer (Ugo Basile DY1). The venom was fractionated by column chromatography on a CM-Sephadex C25 and fractions eluted by sodium phosphate buffer (unpublished communications). The protein content of the fractions as determined by the method of Lowry et al. (2).

**Drug used** :- Atropine sulphate (Sigma, London), hexamethonium bromide (Sigma, London). Disscated whole venom was obtained from Mr. J.H. Leakey, Baringo Snake Farm, P.O. Box 1141, Nakuru, Kenya.

*The work reported here was undertaken in partial fulfilment of the requirements for the degree of Ph.D of the University of Nairobi.*
RESULTS

The isolated rabbit heart was considerably slowed after administration of small doses of the venom (10, 20, 50 and 100 μg in 0.1 ml); the force of contraction was also diminished. After perfusion of the heart with Ringer solution containing atropine (100 μg/ml) for 20 min, no reduction in the heart rate was noted, although there was a slight reduction in the force of contraction (Fig. 1). Column chromatography of the venom led to isolation of a cardiac depressant factor, which was designated as T₃₉ fraction. Administration of T₃₉ fraction (200 μg in 0.1 ml) to the isolated rabbit heart slowed the heart rate and reduced the force of contraction. Recovery of heart rate and force of contraction occurred in about 3 min (Fig. 2A). After perfusion of the isolated rabbit heart with solution containing atropine (100 μg/ml: Fig. 2B) or hexamethonium (100 μg/ml: Fig. 2C) for 20 min, no effect on the heart rate was noted but there was a reduction in the force of contraction with the same dose of T₃₉ fraction.
slowed after administration of small doses; the force of contraction was also reduced. When the solution containing atropine (100 µg/ml) was added, although there was a slight increase in heart rate, the force of contraction was also reduced. This fraction, designated as T39 fraction, had a cardio-depressant effect on the isolated rabbit heart. The heart rate and force of contraction of the isolated rabbit heart were slowed after perfusion of the venom. Slight decrease in heart rate and force of contraction was noted during the administration of atropine (Atr; 100 µg/ml) or hexamethonium (Hex; 100 µg/ml). The administration of T39 fraction (200 µg/0.1 ml) caused a decrease in heart rate and force of contraction. Recovery (b) after 3 min.

Fig. 2: Effect of administration of T39 fraction obtained by column chromatography on the force of contraction and heart rate (HR) of the isolated rabbit heart.

(A) Changes in the force of contraction and heart rate (a) 1 min after administration of T39 fraction (200 µg/0.1 ml). Recovery (b) after 3 min.

(B and C) No effect on the heart rate with the same dose of T39 fraction after perfusion with atropinized (Atr) Ringer solution (100 µg/ml) or hexamethonium (Hex; 100 µg/ml). Note the decrease in the force of contraction.

HR128 (beats/min) 120 96 88 128
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(A) Changes in the force of contraction and heart rate (a) 1 min after administration of T39 fraction (200 µg/0.1 ml). Recovery (b) after 3 min.

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DISCUSSION

The present investigation shows that the administration of whole venom of D. angusticeps causes bradycardia and reduced force of contraction of the heart. After perfusion of the heart with atropine, there was no effect on the heart rate with the same dose of the venom but the reduction in the force of contraction was not completely blocked. The bradycardia produced by the venom may be due to large amount of acetylcholine present in the venom (4). Administration of T39 fraction produced the same effect on the heart rate and force of contraction; on perfusion with atropine or hexamethonium, there was no effect on the heart rate but the force of contraction was reduced. Thus the T39 fraction seems to have two components of action; a cholinergic component and a direct depressant effect on the myocardium.

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