

PHYSIOLOGICAL AND PHARMACOLOGICAL STUDIES
ON THE CERASTES CERASTES VENOM

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GENERAL INTRODUCTION

Venomous Snakes :

Snakes belong to the reptilian order Ophidra. They are limbless creatures found all over the world. Most of the Venomous snakes are found in five families:

- Crotalidae.
- Viperidae.
- Elapidae.
- Hydrophidae.
- Colubridae.

Elapidae and Viperidae are numerous through out Africa.

Actively poisoness snakes are usually defined as, those that possess Venom glands and specialized Venom conducting fangs, which enable them to inflict bites of utmost severity upon their Victims .

Venom Apparatus :

The Venom app. of the snakes consists of :

- (a) Venom gland.
- (b) Duct.
- (c) One or more fangs (teeth localized at sides of head).

In most species the venom glands are homologous with the mammalian salivary parotids. Their size and structure depend on the size and species of the snake. Each gland is enclosed by a layer of connective tissue sheath which is invaded by muscles supplied by many nerve fibres.

The innervation of these muscles, is different from that controlling the biting mechanisms, thus the snake can control the amount of venom to be ejected.

The venom is produced by the tubules of the venom gland and stored in the lumen of different collecting ducts.

The main duct of the gland bends downwards and penetrates the fang sheath terminating opposite the upper fang opening.

The fang is a specialized tooth, usually larger than the other teeth, possessing a deep groove running along its rostral edge, a closed groove or a tube like canal that penetrates the tooth from its base to the tip.

EGYPTIAN VENOMOUS SNAKES

Snakes are classified into five families that contain venomous members. Of these two families : Elapidae and Viperidae are represented throughout Africa.

The Elapidae family is represented in Egypt by the Egyptian Cobra (*Naja haje*), the spitting cobra (*Naja nigricollis*) and the Egyptian black snake (*Walterinnesia aegyptia*).

The Viperidae family is represented in Egypt by the Cerastes viper, *Cerastes cerastes* (Cornutus or horned viper), *Echiscarinatus* and *Echis coloratus*.

CERASTES CERASTES VIPER

This viper is also known as *C. cornutus* or *cornutus*.

Morphology :

It is sandy yellow in colour with 30-36 rows or dark brown spots. It is characterized by the presence of 2 conical eminences (horns) on the upper surface of its head. Its body is cylindrical, its tail is short. The head is markedly distinct from the neck.

Distribution :

This species is common in :

- Margin of the desert along the Nile.
- The Red Sea.
- North Africa.

Habits :

Its habit is to conceal itself in the sand of the desert only its eyes and the upper part of its head being visible, including its horns. It lays eggs. It feeds on Rodents. When disturbed, it attacks with great energy, throwing itself forward by a bound for some distance.

Mechanism of Intoxication by Venoms is through Action on:

- (1) Striated muscle.
- (2) Smooth muscle.
- (3) Cardiac muscle.
- (4) CHO metabolism.
- (5) Alkali Reserve.
- (6) RBCs or WBCs.
- (7) Any cell or organ.
- (8) Producing histological & cytological changes.

VENOM COMPOSITION

Snake venoms are complex mixtures composed of:

- (A) Protein component (chief component).
- (B) Non-protein component.

Protein Component :

The protein component of snake venoms can be classified into:-

- (a) Proteins with toxic properties.
- (b) Proteins with enzymatic activities.
- (c) Proteins with unknown biological activities.

Nerve Growth Factor:

This is a protein found in many viperidae which is non-toxic.

It enhances outgrowth of nervous filaments.

Enzymes:

Phospholipases
Proteinases
Cholinesterase
Anticholine esterase
Phosphotases
Amino oxidase
Phosphodiesterases
Nucleotidases
Adenosine tryphosphatases
Hyalouronidases.

Non Protein Component:

This includes :

(A) Cu

Zn

Sulphur.

(B) Lipids:

Cholesterol

Lecithin.

Lethal Effects of Venoms are due to :

(A) Enzymes:

These lead to:

- 1) Local capillary damage & tissue necrosis
Eg.: Proteases
Phospholipase A.
Hyaluronidase.
- 2) Coagulant & anticoagulant effects.
- 3) Release of kinins from their precursors by
arginine ester hydrolase.
- (B) Toxic Proteins or Polypeptides (Non-Enzymatic)
Eg.: Crotamine.

They also reported that a lethal dose of same venoms produces an initial increase in blood K and decrease in blood Na in same animal.

- (7) Freire -Maia et al (1959) have shown the hyperglycaemic effect in experimental scorpion poisoning of the dog.
- (8) Mohamed and Zaki (1961) studied the effect resulting from bee venom on blood glucose and liver glycogen in rabbits.
- (9) Freire-Maia and Ferreira (1961) studied the mechanism of hyperglycaemia and arterial hypertension produced by the venom of the scorpion in the dog.
- (10) Mohamed et al studied the effect of scorpion toxin on serum Na and K and effect of Egyptian black snake on serum Na and K. 5-4-64.
- (11) Chang (1963) reported an inhibitory action of Bitis multicinctus viper venom on the rat phrenic nerve diaphragm preparation.
- (12) Russel and Bohr (1962) studied the effects of intraventricular injection of five venoms of different species of snakes, 2 species of scorpions, one spider and one stingray, on their work in cats, they

reported motor changes, parasympathetic dysfunction and behavioural changes.

- (13) Mohamed et al (1963) studied the effects of the viper *Echis carinatus* venom on the blood glucose level and liver and muscle glycogen.
- (14) Ivanevic et al (1963) tested the effect of *Vipera ammodytes* venom on Straub (frog) and Langendorff (Guinea Pig) heart.
- (15) Mohamed et al (1963) have shown the effect of *Echis carinatus* venom on blood glucose, liver and muscle glycogen concentrations.
- (16) Condrea et al (1964) found that Viperidae venoms contain phospholipase A but no lytic factor.
- (17) Meldrum (1965) described the presence of a nerve growth factor in the venoms of snakes specially venoms of Viperidae Eg. *V. Russellii* and *V. aspis*. This factor is neither an enzyme nor a toxin.
- (18) Mohamed and Khalid (1965) studied the effect of *Cerastes cerastes* venom at the myoneural junction.
- (19) Mohamed et al (1968) studied the effect of *Echis carinatus* viper venom on tissue and blood histamine and their relation to local tissue reactions and eosinophil changes.

- (20) Mohamed et al (1969) studied the effect of Cerastes cerastes venom on rat diaphragm tissue cells.
- (21) Mohamed and Khaled (1969) studied the effect of Cerastes cerastes venom on blood pressure
- (22) Changeux, Kasai and Lee (1970) described the use of a bungaratoxin to characterise the cholinergic receptor protein of electric organs, changeux et al found that bungaratoxin blocked the responses of cells in the intact electroplaques of electrophorous electricus to the acetyl choline analogue carbamyl choline, and that this effect was irreversible. They also showed the same effects of bungaratoxin in an in vitro system, in which carbamyl choline normally increased the Na permeability of isolated membrane fragments prepared from the electroplaques.
- (23) Mohamed et al (1971) had isolated a nerve growth factor from the venoms of Naja nigricolis and Echis carinatus venom which could be abolished by anti venom.
- (24) Mohamed et al (1974) had prepared a highly potent Cerastes cerastes antivenom from horses.

- (25) Mohamed et al (1977) had isolated and identified toxic fractions from *Cerastes cerastes* venom on Sephadex G 100 gel.
- (26) F. Hassan and M.S. El Hawary (1977) stated that electrophoretic analysis classified *cerastes cerastes* venom and *Cerastes viper* venoms, on an intermediate type between cationic moving elapid venoms and anionic viperid venom.
- (27) D. Petkovic et al (1979) stated that the whole venom of *Vipera ammodytes viper* increased the amplitude of perfused rat heart beats and appearance of extrasystoles, then the heart beat rate was diminished together with the amplitude of contraction until heart stopped in a contracted state, an irreversible effect. The E.C.G. showed heart block.

AIM OF THE WORK

In Egypt, there are about 7 species of dangerous snakes which belong to the following 2 families:

(1) Viperidae family, represented by:

- (a) *Cerastes vipera*.
- (b) *Cerastes cerastes* (*Cornutus*).
- (c) *Echis carinatus*.
- (d) *Echis coloratus*.

(2) Elapidae family, represented by :

Naja haja (Egyptian cobra)

Naja nigrecolis.

Walterinnesia aegyptea (Egyptian black snake).

Of these 7 species *Cerastes* forms 63.93 % (Hymen 1968). These poisonous animals are fatal to both man and animals. The solution of this problem depends, in part on the preparation of antisera (antidotes) to neutralize and thus antagonize their venom as soon as it is injected through the victim, which in turn depends on intensive physiopharmacological & metabolic studies.

Consequently, the present work as embodied in this thesis deals mainly with the haemodynamic & metabolic actions of *cerastes cerastes* venom.