THE EGYPTIAN SNAKES AND SOCOTRAN VENOMS IN RELATION TO CARBOHYDRATE METABOLISM.

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By

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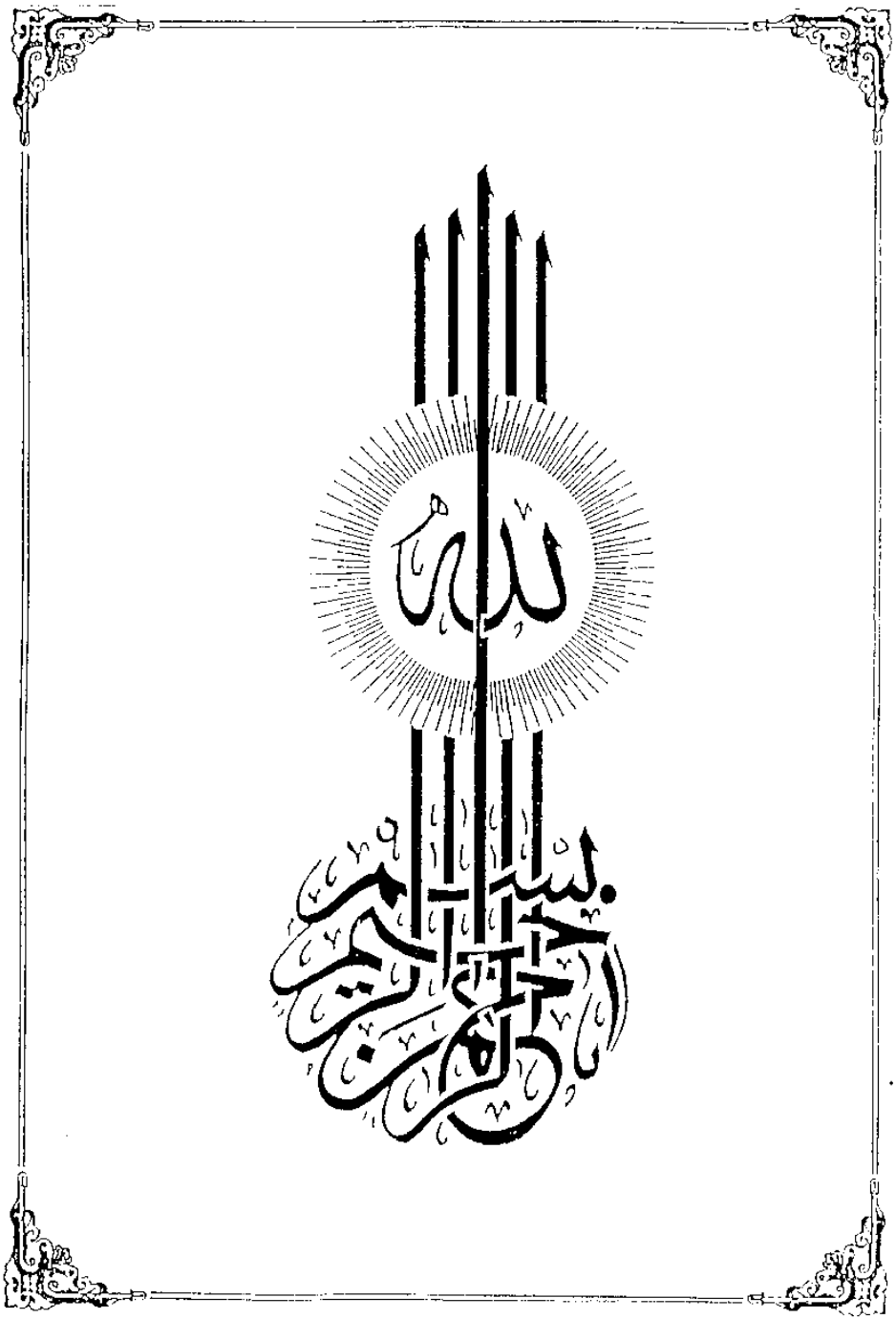

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ARABIC SUMMARY.

INTRODUCTION

Partial disorders of carbohydrate metabolism are known to accompany envenomation by snakes and scorpions. The disturbances so far described include: hyperglycaemic and hypoglycaemic responses, glycogenolysis and some enzymatic blocks in pathways of glucose metabolism at cellular levels.

Similar metabolic defects have been described in cases of hepatic tumours, certain fibrosarcomata and other malignant neoplasms in man. These were recently ascribed to ectopic production of hormones or hormone-like polypeptides by the tumour cells. The possibility arises, therefore, that the biological effects of poisonous snake bites and scorpion stings are due to ectopic hormones or hormone-like polypeptides in the venoms. In fact, accumulated evidence shows that certain venoms contain local hormones or hormone-like substances e.g. serotonin and kallikreins, which suggest that these venoms could be a source of ectopic hormones.

Nevertheless, a study of the structural aspects of these toxins and of the underlying mechanisms, is a primary step to unveil the exact similarities or dissimilarities between these toxins and conventional hormones. This is an essential prerequisite before drawing final conclusions on the fascinating and complex relationship between snake venoms and ectopic hormones or hormone-like polypeptides.

REVIEW OF LITERATURE

Glycaemic responses to snake venoms:

Clinical and physiological experience has amply shown that snake venoms act on a large number of metabolic processes. Of these, changes in carbohydrate metabolism were the first metabolic abnormalities to be described. This preoccupation with carbohydrate metabolism may be traced back to as early as 1921 when Houssay et al reported hyperglycaemia as a result of snake envenomation (cited by Mebs, 1968). Later, Epstein (1930) noticed hyperglycaemic responses to injection of Naja flava venom. This finding was later confirmed by other investigators (Bertrand and Vladesco, 1939,a,b; 1940a,b; RI,1939a-f; To and Chin, 1941; Grasset and Goldstein, 1947).

Since that time, there has been a lot of speculation about the mechanism(s) of this hyperglycaemic effect.

RI (1939,a-f) in a series of publications showed that the hyperglycaemic responses to snake venoms were associated with a decrease of liver and muscle glycogen. He attributed these effects to the liberation of adrenaline from the suprarenal medulla, as he was able to demonstrate

[illegible] increased blood levels of this hormone after venom poisoning. Further, he showed that these effects disappeared after immunization with specific antisera.

To and Chin (1941) drew the same conclusions regarding the mechanism of the hyperglycaemic responses to snake envenomation. They further demonstrated that bilateral splanchnicotomy or bilateral adrenalectomy halfed this hyperglycaemic effect, while bilateral abdominal vagotomy had no effect, and that the adrenergic response to the venom resulted in liver and muscle glycogenolysis and hyperlactacidaemia.

Master et al(1960) reported wide glycaemic excursions following injections of sublethal doses of Russell's viper venom in rabbits. In some cases there was a rise and in others a depression in the values. In most of these cases an increase of blood inorganic phosphorus was noticed.

Recently, Mebs (1968) reported no change in the levels of blood glucose, blood lactate and liver and muscle glycogen after injection of a lethal dose of cobra venom (Naja naja) in rats.

Studies of the effects of [illegible] cellular levels, have shown inhibition of glycolysis in cancerous tissue slices in vitro (Mellanby, 1934, 1935, 1936) an effect which was attributed to a non-specific lytic action of the venoms. Similar inhibition of glycolysis in muscle extracts by various venoms, coupled with inactivation of different dehydrogenases was demonstrated by Chain (1937, 1939). Also inhibition of glucose oxidation in Krebs cycle by brain homogenates, to which small quantities of heated cobra venom were added, was demonstrated by Braganca and Quastel (1953).

During a series of studies of blood sugar responses to snake envenomation carried out in this laboratory since a number of years, it has been shown by Mohamed and Zaki (1959) that injection of Walterinnesia toxin in rats produced a hypoglycaemic response without noticeable changes in liver glycogen content and that the hypoglycaemic action of a sublethal dose of the venom was abolished by bellafoline; while the lethal dose required the injection of cortisone as well. They ~~con~~ concluded that the hypoglycaemic response may be due to either an increased outpouring of insulin or

an inhibition of the diabetogenic factors of the anterior pituitary and suprarenal cortex.

In further studies on Cerastes aegyptia venom, Mohamed et al (1965), proved a definite direct effect of the venom on the pancreas in the production of this hypoglycaemic response. It was found that the hypoglycaemic response disappeared in diabetic, pancreatectomized and alloxan treated, animals.

On the other hand, hyperglycaemic responses to other Egyptian snake venoms were reported.

Mohamed et al (1963) demonstrated that injection of Echis carinatus venom in rabbits produced hyperglycaemia and a fall in liver and muscle glycogen. They suggested that this effect is due to inhibition of glucokinase enzyme, directly by the venom or indirectly through the release of catecholamines.

Similar findings were reported by Khaled (1967) using Cerastes cerastes venom.

Hamed (1967) obtained similar hyperglycaemic responses to Naja nigricollis venom accompanied by mobilization of liver and muscle glycogen. The author also

demonstrated a rise in blood catecholamines, in dogs, following the injection of the venom.

In 1968 Hamza showed that injection of cobra venom (Naja haje) in rabbits produced hyperglycaemia and liver and muscle glycogenolysis and suggested that these effects are probably due to phospholipase A enzyme and to a dializable fraction of the venom (Neurotoxin).

In attempting to gain further insight into the mechanism of action of snake venoms on blood sugar, Mohamed (1970) studied the effects of Naja nigricollis venom on blood sugar and insulin responses in dogs, and on glucose metabolism by rat muscle and found that the venom inhibited plasma insulin activity and antagonized the insulin action on muscle. She concluded that the venom effects were due to insulin deficiency and/or insulin inefficiency. In further studies the author emphasized the role of free fatty acid release in the venom-induced carbohydrate intolerance.

From this brief summary of the literature describing the effects of snake venoms on carbohydrate metabolism, it is clear that the glycaemic responses differ with the