

Pharmacology of some Arthropod Venoms of Sri Lanka

by

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SUMMARY The Ceylon Hunting Spider, *Poecilothermia fasciata* and the Giant Ceylon Centipede, *Scolopendra moristans* are two arthropods of Sri Lanka which can cause poisonous effects in man. Pharmacologically active substances common to the venom of both were 5HT and histamine. The venom of the spider contained a neuromuscular stimulant. On the basis of these findings, the treatment of envenomation is discussed.

INTRODUCTION

Among the common arthropods of Sri Lanka, three which may cause poisonous effects in man are the Ceylon Hunting Spider, *Poecilothermia fasciata*, the Giant Ceylon Centipede, *Scolopendra moristans* and the Large Ceylon Scorpion, *Palamneus indicus*.

This paper describes the identification of some of the active pharmacological constituents of the venom of the Hunting Spider and of the Giant Centipede and discusses the possible lines of treatment of envenomation. There are no recorded instances of a fatal outcome of envenomation by these arthropods. Preliminary communications on these findings have been made earlier (Kottegoda, 1963; Kottegoda, 1969).

The Ceylon Hunting Spider, *Poecilothermia fasciata*, is a hairy arthropod 15 — 20 cms in length (Plate I). It resembles the tarantulas of South America: *Lycosa raptor* of Brazil and *Glyptocranium gasteracanthoides* of Peru. It is a quick mover, dwelling in the trees of the dry regions of Sri Lanka. When stakes are used for coconut plucking this spider has been known to descend along these, bite the hand of the plucker and return rapidly to the crown of the tree. In the villages its bite is feared as much as that of the venomous snakes. The natural enemy of *Poecilothermia* is the wasp. The relationship between the spider and the wasp is analogous to that between the cobra and the mongoose.

The common effects of envenomation by *Poecilothermia* are :

- (1) Intense local pain which spreads along the bitten site which is usually on a limb,
- (2) Muscle spasms.

The victim of the bite has been described to take up a spider-like stance. "Jumping of the flesh" is an expression used by villagers to describe the symptoms in the muscle. This description could be interpreted to signify fasciculation and spasm of the voluntary muscles.

It is known that spider venom, in common with other animal venoms, contains proteolytic enzymes (Kaiser, 1956; Mebs, 1970). Very rarely acute pancreatitis has developed after the bite of this spider; this has also been reported after scorpion stings (Bartholomew, 1970). Local necrosis has also been described after spider bite. This could be due to the action of the enzymes or the result of excessive local treatment or of infection.

The other systemic effects which have been seen after arachnoid envenomation, namely, burning of soles of feet (Essex, 1945) and haemolysis and haemoglobinuria, (Gotton and McGowan, 1940) have not so far been described after the bite of the Ceylon Hunting Spider.

MATERIALS, METHODS AND RESULTS

The venom of *Poecilothermia fasciata* was extracted, without killing the spider, by the application of small induction shocks to the mouth parts after immobilizing the spider in its cage.

Paper chromatography of the venom revealed the presence of 5HT (serotonin) and histamine. The solvent used was butanol : acetic acid : water (4 : 1 : 5) on Whatman No. 3 paper; 5HT was identified by Ehrlich's reagent and histamine by ninhydrin. These substances could account for the pain experienced after the bite (Armstrong, Dry, Keele and Markham, 1953).

Since, in addition to the pain, the characteristic symptoms appear in the skeletal muscle, the venom was tested on the guinea-pig phrenic nerve diaphragm preparation. In this preparation, the venom in a concentration of 1 $\mu\text{g}/\text{ml}$ caused a marked increase in the response of the muscle to indirect stimulation. The effect was well sustained. This observation could explain some of the muscular symptoms seen after the bite. The effect of the venom on the preparation was antagonized by the competitive neuromuscular blocking drug, gallamine (Plate 2).

Intravenous calcium salts (e.g. calcium gluconate) have been reported to be effective in relaxing the muscle spasm produced by the bite of the black widow spider, *Latrodectus spp.* (Bogan, 1956). The mechanism of benefit of calcium in such a situation could well be non-specific. Activity of cells depends on the movement of sodium and potassium across cell membranes. Excess of calcium diminishes, and a decrease of calcium augments, permeability changes. The muscular symptoms seen after spider bite could be due to hypocalcaemia caused by the venom chelating serum calcium. Addition of calcium gluconate to the phrenic nerve preparation did not reverse or prevent the effects produced by spider venom. The calcium chelating agent, EDTA, did not produce any effects on the preparation.

DISCUSSION

From these findings it would appear that the common symptoms seen after the bite of the Ceylon Hunting Spider could be attributable to —

- (a) 5HT and histamine which could account for the pain. Antihistamine drugs could prove useful in counteracting these effects. Since cyproheptadine ("Periactin") has both antihistamine and anti-5HT effects, this drug may have an advantage over other antihistamines. However, there is no parental preparation of cyproheptadine; the drug may cause marked drowsiness in some subjects. In addition, analgesics such as pethidine or pentazocine may be needed to relieve the pain.
- (b) Some substance or substances which increase the activity of skeletal muscle by acting peripherally. The finding that, *in vitro*, this action is antagonized by gallamine does not, by itself, indicate the exact mechanism of action of the venom.

Bogan (1956) has advocated, but not described the effectiveness of, tubocurarine and mephenesin in spider bite. While the use of competitive muscle relaxants such as gallamine and tubocurarine may be beneficial in spider bite, such drugs should, perhaps, be avoided in the first instance because of the problems which may arise as a result of their use. The histamine-releasing action of tubocurarine may also be significant in this situation. Intravenous diazepam would appear to be the most appropriate drug to relieve the effects produced in the muscles; this drug has the additional advantage of possessing an anxiolytic action. The doses employed could be analogous to those used in tetanus e.g. 10 mg i.v. in the adult, repeated after 90 min (Karnes, 1968). In cases not responding to this drug, gallamine might have to be tried.

There does not appear to be a place for the use of intravenous calcium in poisoning caused by the Ceylon Hunting Spider. Essex (1945) has stated that the use of calcium gluconate in spider bite is not universally satisfactory while Sampayo (1943) found calcium gluconate ineffective in experimental animals bitten by some species of black widow spider.

The Giant Ceylon Centipede *Scolopendra moristans*, (Plate 2) is the biggest of the Ceylon centipedes. There are two varieties, *Scolopendra crassa* and *S. moristans*; the former is the more attractive. Tennent (1861) found specimens as long as 30 cms; *Scolopendra spp.* is found in Egypt as well. The Giant Ceylon Centipede lives mostly at bases of coconut leaves, under stones or in the roofs of thatched houses; it feeds on small insects such as cockroaches.

In man, the characteristic symptoms of the bite are severe pain radiating markedly if a bite, as it often is, takes place on a limb; swelling and tenderness follow within half an hour or so and may persist for 5 — 7 days with treatment. There may be local necrosis. The above description is from personal experience. Similar effects have been described by

Remington (1950). According to Coffin (1919), the effects can be more severe, with vomiting local bullae and vesicular eruption on other parts of the body; lymphangitis and lymphadenitis have been reported (Castellani and Chalmers, 1910). Haneveld (1957) has asserted that even contractures and paralysis of extremities as well as irregularities of the heart occur after centipede bite in humans.

MATERIALS, METHODS AND RESULTS

The venom apparatus of the centipede consist of two curved fusiform structures which lie in the curvature of each venom claw (Cornwall, 1916). The venom claws are really chitinous mouth parts. The poison claw of the centipede can be cut and a glairy opalescent liquid can then be scooped out. Examination of the venom using paper chromatography as well as biological methods (Fernando and Kottegoda, 1966) revealed the presence of both 5HT (serotonin) and histamine (Kottegoda, 1963). The presence of 5HT in centipede venom has been confirmed (Welsh and Batty, 1963). The venom, when tested on the guinea-pig phrenic nerve preparation, up to a concentration of $1\mu\text{g/ml}$ did not reveal any action at the neuromuscular junction. Centipede venom, like that of other similar animals, is used by the centipede for the purpose of immobilizing its prey as well as for the extra corporeal digestion of its food.

DISCUSSION

The pain of centipede bite could be accounted for at least in part to its histamine and 5HT content (Armstrong, Dry, Keele and Markham, 1953); the swelling and the tissue damage could be due to the histamine as well as the digestive peptidases and other enzymes which have been found in *Scolopendra* venom (Said, 1959).

As far as the pharmacological agents which may be effective in relieving the clinical effects of centipede bite are concerned, local anaesthetics with adrenaline, local applications of ammonia and analgesics such as morphine have been advocated (Blay, 1955).

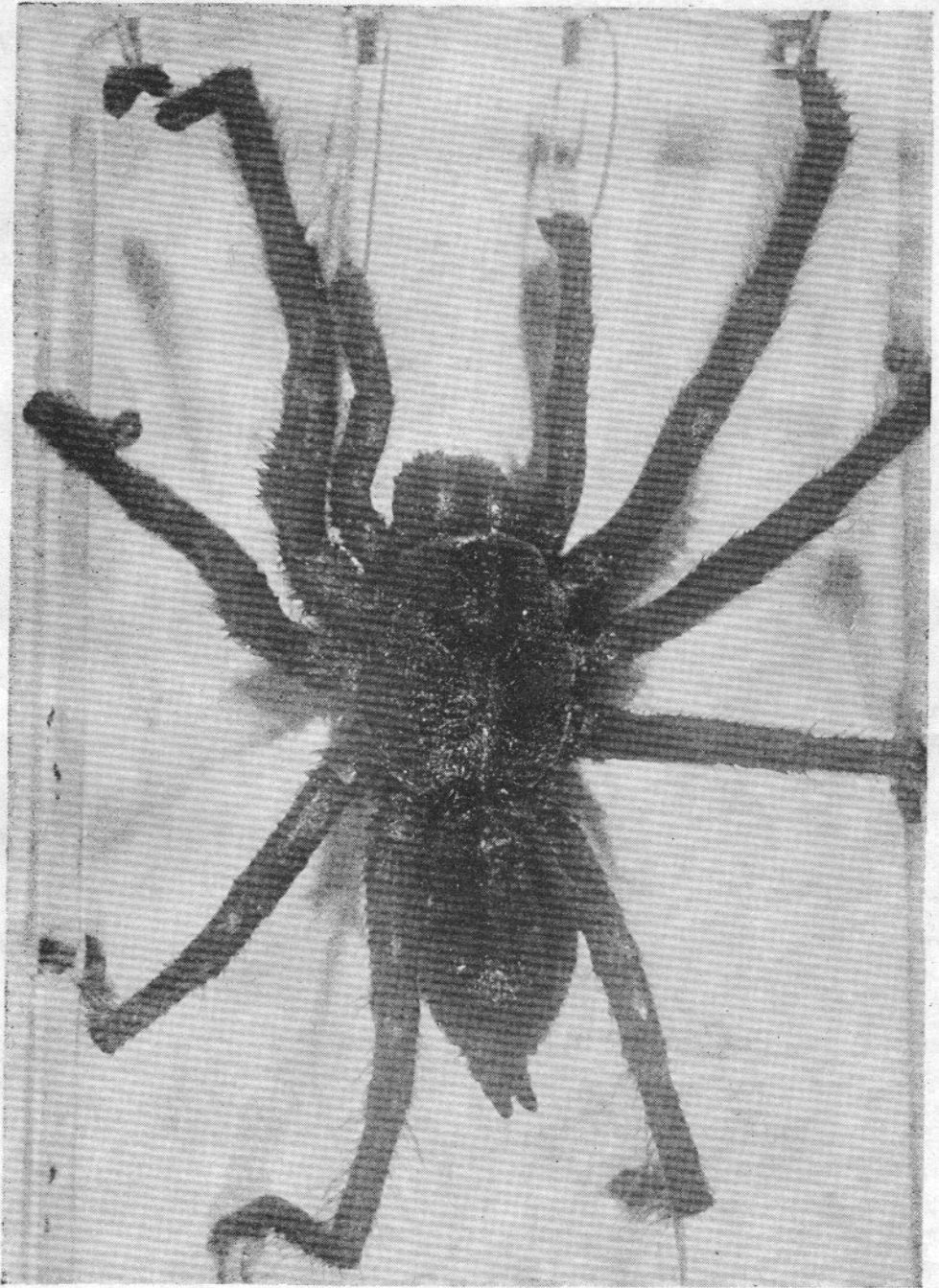
The general antistress actions of corticosteroids have also been useful (Haneveld, 1957). However, in addition to analgesics the oral use of a drug such as cyproheptadine ("Periactin") seems rational since the latter has both antihistamine as well as anti 5HT-properties (Goodman and Gilman, 1970).

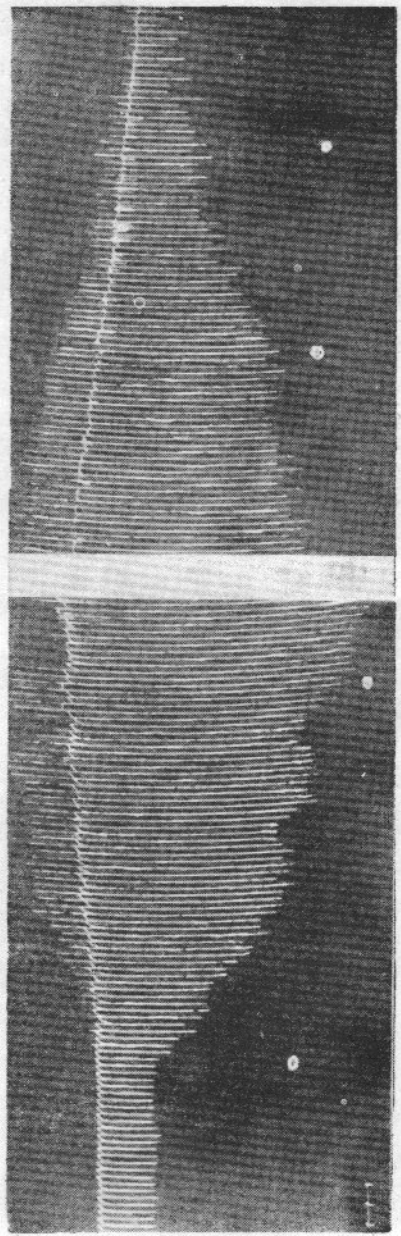
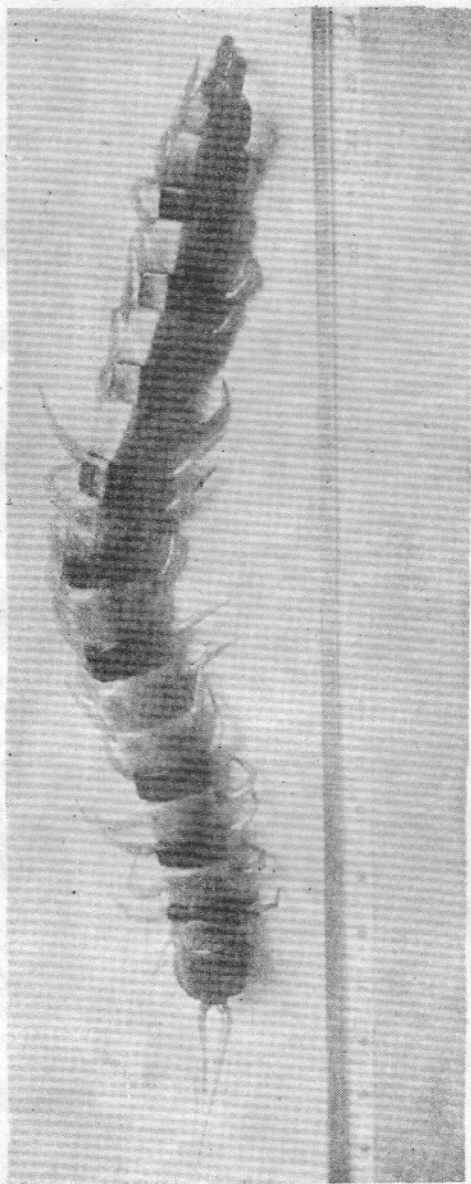
It has been suggested that some degree of immunity may be conferred after the first bite (Mackie, Hunter and Worth, 1954).

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Venom 10⁻⁶ Wash 5 min Gallamine 2x10⁻⁶ Gallamine 2x10⁻⁶

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