SUMMARY
Effects of scorpion venom (Buthus tamulus) have been studied in intact animals (dogs, rabbits, guinea pigs, rats and mice) and in isolated tissue preparations.

1. Intravenous injection of scorpion venom in anaesthetized animals (50 μg/kg in rats, 100 μg/kg in guinea pigs, 100-250 μg/kg in rabbits and dogs) produced generally rise in blood pressure with bradycardia and repetition of doses produced tachyphylaxis. The hypertensive effect was prolonged for 5-20 min in different species, which was not affected by hexamethonium. It was blocked by phenoxybenzamine or was prevented by reserpinization in dogs, rabbits, guinea pigs and rats. Guanethidine decreased the pressor effect in rats and guinea pigs. The pressor effect was not seen in guanethidine treated adrenalectomized rats. These observations show that the hypertensive response was due to the release of catecholamines from postganglionic sympathetic nerve endings and from adrenal glands.

Bradycardia usually associated with the pressor response, was blocked by atropine. It was possibly due to reflex stimulation of the vagus as well as due to local release of acetylcholine in the heart.

In some animals initial brief hypotensive effect was
observed. The hypotensive effect was blocked by atropine.

2. Smaller doses of the venom (50-100 ug/kg in rats and
guinea pigs, 100-250 ug/kg in rabbits and dogs) injected intra-
venously produced sinus bradycardia, cardiac arrhythmias and
transient tachycardia, followed by bradycardia, in which
recovery usually set in 1-2 hr. Larger doses of the venom
(250-500 ug/kg in rats and guinea pigs, 1-2 mg/kg in rabbits
and 0.5 - 1.5 mg/kg in dogs) given intravenously produced
death within 2-5 hr. In these animals changes in the ECG showed
sinus arrest, arrhythmias, prolongation of P-R interval,
decrease in the amplitude of QRS complex, ST depression and
T wave inversion. The changes of myocarditis were irreversible,
it is possible that these effects involve not only the release
of acetylcholine and catecholamines but also involve ionic
changes in the myocardium due to direct myocardial injury.

3. In isolated perfused rabbit heart preparations the venom
(5-50 ug) produced dose dependent negative chronotropic and
inotropic effects followed by positive chronotropic and inotropic
effects. These effects were blocked by atropine and propranolol
respectively. The venom (25-50 ug) decreased coronary flow. In
similar preparation obtained from reserpinized rabbits, only
negative chronotropic and inotropic effect with temporary
stoppage of the heart was seen. In isolated perfused heart of frog the venom (10-100 µg) produced dose dependent cardiac stimulation which was blocked by propranolol.

In rabbits, the venom produced elevation of SGOT and SGPT. Blood clotting time was increased. In frog blood vessel perfusion experiments, the venom (5-20 µg) produced vasoconstriction, which was not affected by atropine but was blocked by phenoxybenzamine.

4. The venom had prominent effects on the skeletal muscles and neuromuscular junction. The venom (10-20 µg/ml) produced contracture of the frog rectus abdominis muscles which was potentiated by physostigmine and was blocked by d-tubocurarine.

In phrenic nerve diaphragm preparation of rat and gastrocnemius sciatic nerve preparation of frog the venom (5 µg/ml) produced augmentation of responses to nerve stimulation followed by marked irreversible depression. The venom antagonized the d-tubocurarine blockade (decurarization). In calcium free perfusion fluid the blockade, produced by the venom was quick and in perfusion fluid, containing double the amount of calcium the venom produced delayed block. The blockade produced by the venom was not antagonized by physostigmine or calcium and was not reversible by wash.
In mice, the spontaneous motor activity was reduced by larger doses of the venom (0.5 mg/kg i.p.).

The effect of subthreshold doses of paraldehyde or barbiturates in mice and rats was potentiated by the venom (0.1 - 0.4 mg/kg i.p.).

5. Depending upon the dose, the venom produced either stimulation or paralysis of the respiratory movements in rats and guinea pigs. Immediate apnoea or respiratory paralysis was not prevented by bilateral vagotomy. After a brief period of artificial respiration or administration of nikethamide, gasping and ataxic breathing pattern occurred and at times respiration became normal. Respiratory arrest occurring in inspiratory position may suggest stimulation of inspiratory centre. Dogs and rabbits showed less respiratory irregularities.

6. In intestinal smooth muscles stimulation produced by the venom was not affected by hexamethonium, but was blocked by atropine. In rat duodenum, the contractile response was followed by marked relaxation. The relaxant response was prevented or blocked by bretylium or phenoxybenzamine. Contraction of isolated vas deferens by the venom was blocked by bretylium.

7. In rabbits, intravenous injection of the venom (0.5 mg/kg) produced rise of rectal temperature which could be influenced
by paracetamol.

8. The venom in lower doses (i.p. or i.v.) produced salivation, lachrymation, bronchial secretion, passing of urine and stool in experimental animals (dogs, rabbits, guinea pigs, rats and mice). With higher doses animals had profuse salivation and lachrymation, bronchial secretion, froth in the trachea, dilatation of pupils, frequent passing of urine and stool with or without blood, respiratory distress, jerking of head, muscular spasms, twitchings, tremor, convulsions, cyanosis, respiratory arrest and death.

9. In acute toxicity studies the following values of LD50 for the venom were obtained.

<table>
<thead>
<tr>
<th>Animal</th>
<th>Route</th>
<th>Dose LD50(± SD)mg/kg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mice</td>
<td>i.p.</td>
<td>0.89 ± 0.22</td>
</tr>
<tr>
<td>Rats</td>
<td>i.p.</td>
<td>0.79 ± 0.18</td>
</tr>
<tr>
<td>Guinea pigs</td>
<td>i.p.</td>
<td>0.67 ± 0.15</td>
</tr>
<tr>
<td>Rabbits</td>
<td>i.v.</td>
<td>1.15 ± 0.18</td>
</tr>
</tbody>
</table>

Autopsy studies revealed general changes like myocardial congestion, focal myocarditis, cerebral and pulmonary oedema, haemorrhages, hepatic necrosis and tubular necrosis in the kidney.
10. Pretreatment with dexamethasone, calcium gluconate, atropine and phenoxybenzamine increased the MLD of venom and increased the survival time in rats, guinea pigs and rabbits. Respiratory depression was prevented or could be treated by nikethamide, however, these drugs could not afford protection against the delayed cardiac and neurological complications.