SOME PHARMACOLOGICAL ACTIONS OF AN EXTRACT OF OCIMUM SANCTUM (PRELIMINARY OBSERVATIONS)

By

T. R. KRISHNAMURTHY.

Department of Pharmacology, Stanley Medical College, Madras.

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The numerous and widely used drugs of indigenous origin have stimulated pharmacologists and physicians to ponder over their actions and therapeutic usefulness. Clinical evaluation of liquid extracts of some drugs has been undertaken by physicians sporadically, with varying reports on their efficacy. Chemists and pharmacologists have been engaged in their respective spheres, the former to isolate and assign a chemical structure to active principle, if any, and the latter to demonstrate one useful action at least, with varying results. However, from the available literature, the pharmacological actions of a liquid extract of Ocimum Sanctum does not seem to have been studied so far, though marvellous properties are ascribed to different parts of the plant, ranging from cure of snake bite to mania. These formed the necessary stimulus to undertake the present study wherein an attempt is made to elucidate the actions of a liquid extract on the cardiovascular, intestinal and respiratory systems. A few preliminary observations and possible deductions from such are reported in this communication. The extract seems to possess anthelmentic and local anaesthetic actions also. These are under investigation separately.

MATERIALS AND METHODS

(1) *Preparation of the Extract.*—The leaves were collected and allowed to dry in shade, (which takes about two to three weeks), when they were powdered well and stored in an amber coloured bottle. 1000 ml. of distilled water was added to 100 G. of the powder, in a wide mouthed bottle with an air-tight cork and set aside for a week, shaking the contents thoroughly at intervals. The brown supernatent liquid was syphoned off at the end of this period, the marc pressed in a piece of gauze, and the extract added to the original liquid. The volume was made upto 1000 ml. with fresh distilled water, 0.3 percent phenol was added as a preservative. The extract was sterilised for ½ hour under 15 pounds pressure, before use in some experiments. Sterilisation was not found to alter the responses significantly.

(2) (A) Healthy dogs weighing between 4 - 10 kg. were anaesthetised with paraldehyde (2 ml./kg. weight) intramuscularly or in some instances, chloralose intravenously (80-100 mg./kg.). Blood pressure and respiration

were recorded from a carotid artery and tracheal canula in the conventional manner. A femoral vein was canulated for administration of drugs. Peripheral arterial pressure in an intact limb recorded by Rawolf's technique, reflects the response of the vascular bed to drugs similar to measuring limb volume. This method was adopted to observe the effects of the extract on peripheral vessels. Jackson's enterograph was used to record intestinal movements. Doses of other drugs used in the investigation are mentioned in appropriate places in the graphs.

(B) Isolated Tissues.—Pieces of rat's ileum suspended in Tyrode's solution, oxygenated continuously and kept at constant temperature were used to study the effects on smooth muscles. The capacity of the bath was 100 ml. and doses ranging from 0.5 to 1 ml. of the extract were added to the bath directly.

(C) Graded doses of the sterilised and unsterilised extracts ranging from 0.5 ml./kg. to 2 ml /kg. were administrated by slow intravenous injection to batches of six rabbits, twice daily at an interval of 6 hours for one week. They were observed for two weeks, for evidence of local or systemic reactions. Similarly, rats were given intraperitoneally, graded doses, ranging from 0.125 to 0.5 ml./gm. and observed for a similar period. The animals were not sacrificed to see for any pathological changes in the organs at this stage of investigation.

RESULTS

(1) Intravenous and intraperitoneal injections did not exhibit either local or systemic toxic effects, judged from the fact that the animals were healthy and normal throughout the period of observation. Further experiments are in progress to confirm these preliminary observations.

(2) Intravenous administration of the extract in dogs in doses of 0.5 ml./kg. and 1 ml./kg. produced a transient fall in blood pressure, both systemic and peripheral. The duration and depth of hypotension was proportional to dose. Slight increase in the rate and depth of respiratory movements were seen attributable to hypotension. (Fig. 1) Local injection of the extract into the femoral artery, exhibited a marked drop in peripheral pressure, indicating peripheral vascular dilatation. (Fig. 2) Intra-carotid injection did not produce significant effects on blood pressure or respiration (Fig. 3) Next both vagi were cut and the extract was injected in a dose of 0.5 ml./kg. The hypotensive response was still observed. (Fig. 4) But after T.E.A.B. the effects on blood pressure were found to have been abolished. (Fig. 5) The hypotensive action was not annulled by the prior administration of Phenergan in a suitable dose (1 mg./kg.) (Fig. 5A). Diminution in amplitude of auricular contraction was prominent, in the myocardiogram (Fig. 6). A short period of cardiac arrest and

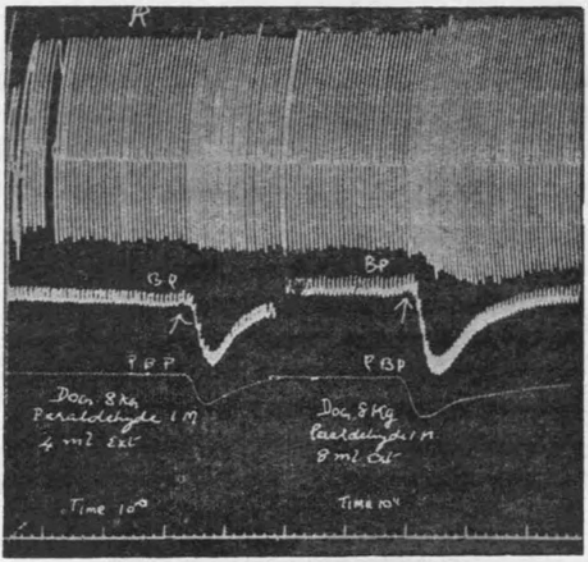

Fig. 1. Effects of 1 and 2 ml./kg. of extract of Ocimum sanctum. Respiration, B. P., and Peripheral pressure from above downwards. Drop in systemic and peripheral pressures are evident. Slight stimulation of respiration during hypotension is evident.

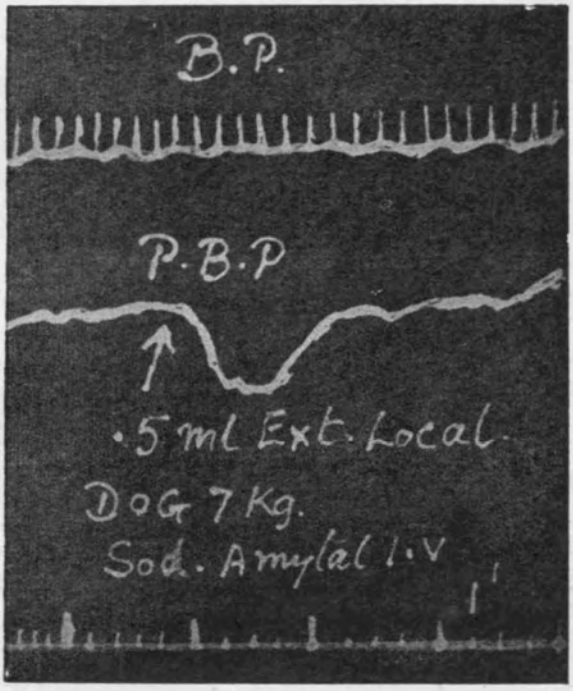

Fig. 2. Injection of 0·5 ml. of extract locally, exhibited a fall in peripheral pressure, indicating peripheral vascular dilatation.

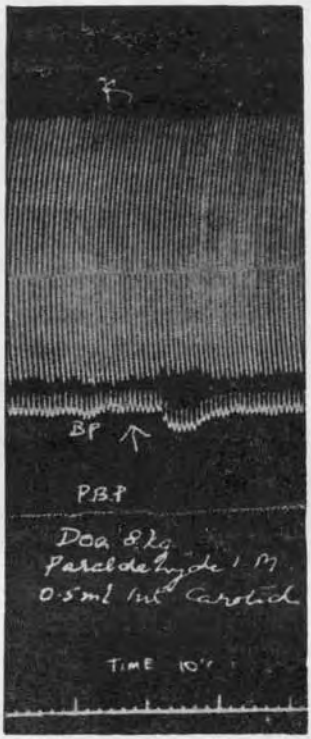

Fig. 3. Intra-carotid administration did not show significant effects on respiration or blood pressure.

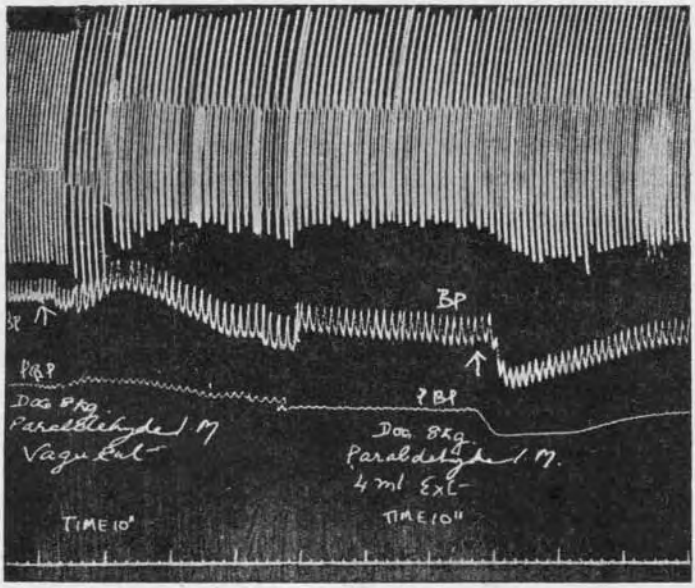

Fig. 4. 0·5 ml./kg. of extract administered after section of vagi. Drop in blood pressure is not abolished. Slight stimulation respiration as in Fig. I.

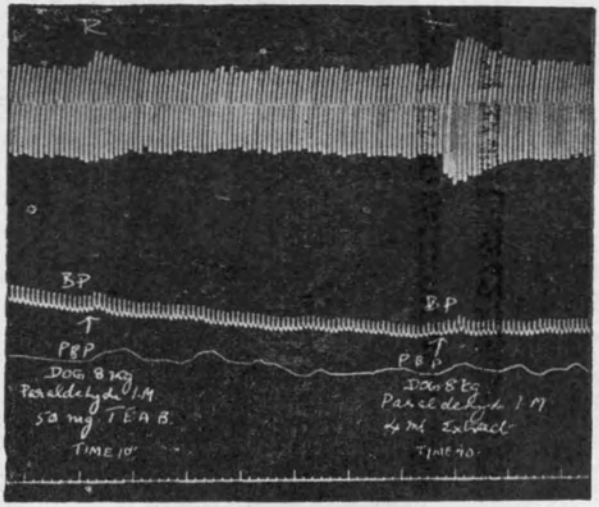

Fig. 5. After T. E. A. B. the effects on blood pressure are annulled. Transient respiratory stimulation is seen.

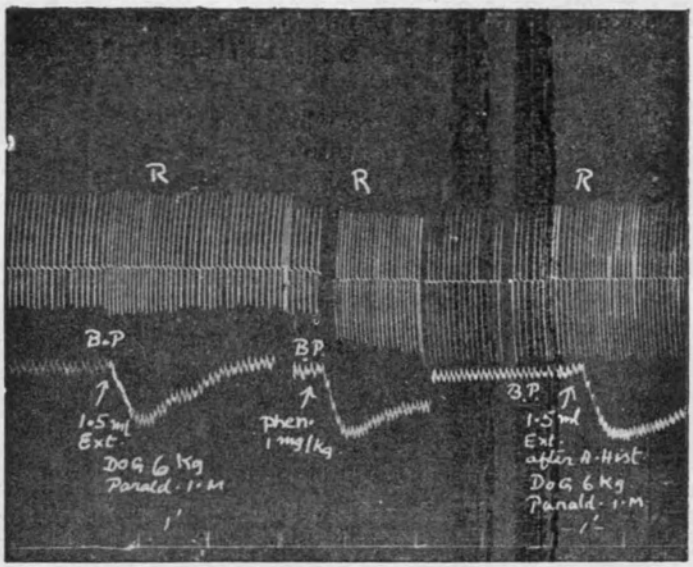

Fig. 5A. Hypotensive action is not abolished by prior administration of an antihistamine Phenergan. (1 mg./kg.)

Fig. 6. Myocardiogram: Diminished amplitude of auricular contractions is prominent. Ventricular contractions are not significantly altered.

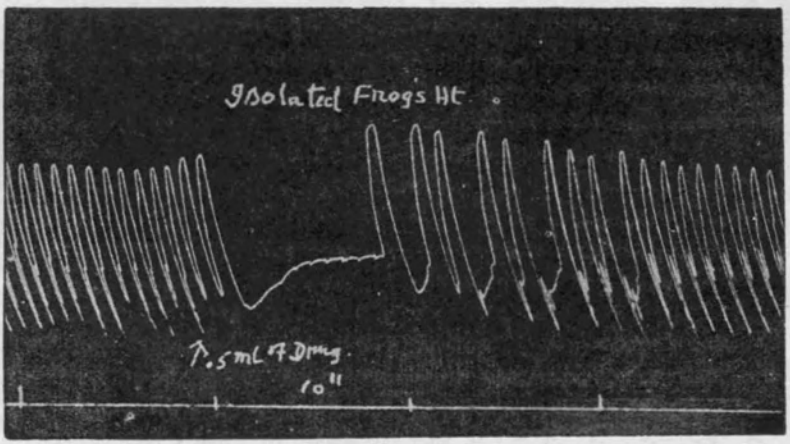

Fig. 7. Isolated Frog's heart: A short period of cardiac arrest and slow recovery is seen.

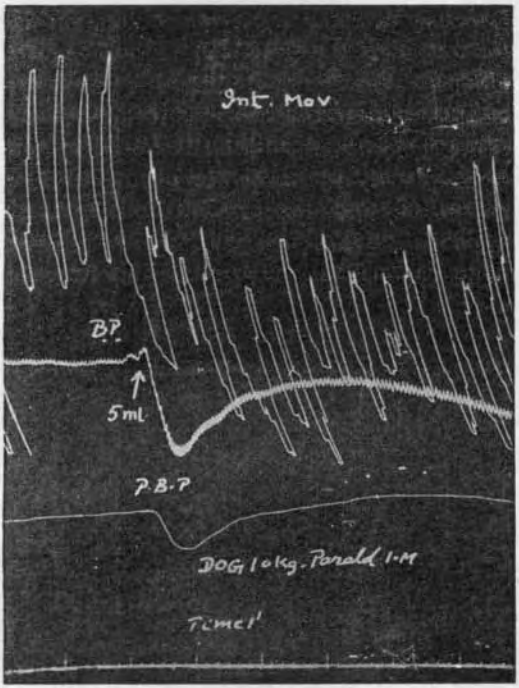

Fig. 8. Intestinal movements: The tone of intact intestines is considerably reduced. Movements are not abolished: Effects on B. P. same as before. (Hypotensive action).

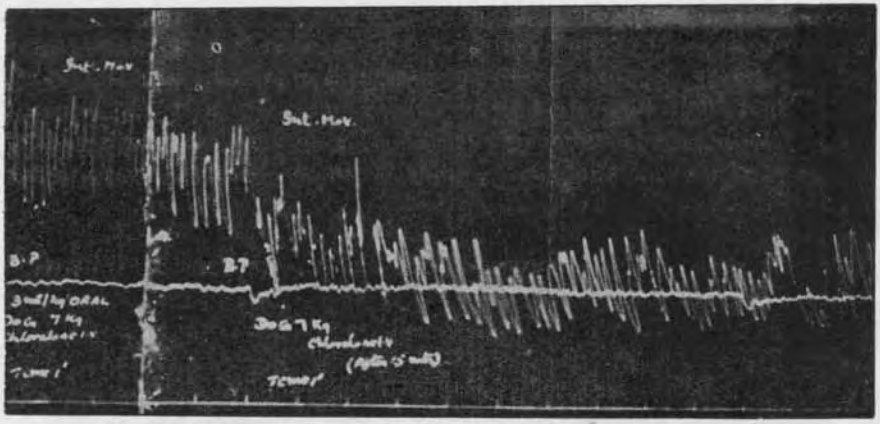

Fig. 9. Relaxation of tone 15 mts. after oral administration in a dose of 3 ml./kg. and lasting for considerable time is note-worthy.

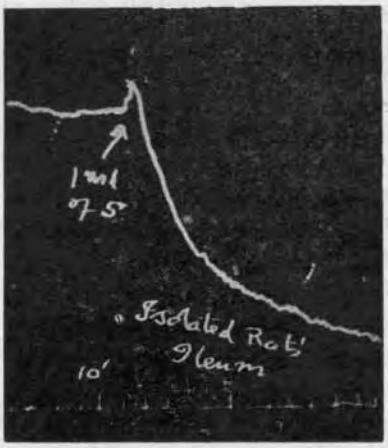

Fig. 10. Isolated Rat's Ileum: Significant relaxation is evident. 1 ml. of extract in 100 c. c. of the bath.

gradual recovery was seen in isolated perfused frog's heart. (Fig. 7) The tone of the intact intestines was considerably reduced and the duration was in proportion to dose; on an average the relaxed state continued for more than half an hour, though the movements were not completely abolished. (Fig. 8) The extract was next administered orally in a dose of 3 ml./kg. (provisionally chosen) through a stomach tube. Relaxation was evident 15 minutes after administration, which lasted for more than an hour, but the movements were not abolished. (Fig. 9) Marked relaxation of isolated rat's ileum was observed. (Fig. 10)

DISCUSSION

The factors responsible for the maintenance of blood pressure, and the tone and motility of intestines are many and complex. Even under identical and controlled experimental conditions, it is not uncommon to observe variations in degree or depth of response to the same dose of a drug or to a higher dose. Keeping such possibilities in view, from the above observations, it is seen that the extract produces a drop in blood pressure fairly proportional to dose, the hypotensive state lasting for a significant length of time. Peripheral vascular dilatation seems to contribute much to the overall effect. Since the response to intracarotid injection of the drug was not significant the chances of central effects are reduced. Section of both vagi did not abolish the hypotensive effect but after T.E.A.B. it was abolished. Since antihistamine did not prevent a drop in blood pressure, it is reasonable to presume that the effect was not due to histamine release, by the extract. A depressant effect on the cardiac muscle was also noticed. From the data so far, having excluded vagal effects and histamine release as probable contributory

causes, it may be reasonable to presume that the drop in blood pressure is due to peripheral vascular dilatation and a direct action on the heart probably mediated at ganglionic level. Further experiments to accurately locate the site and mode of action are indicated. A possible use as an anti-hypertensive, if cardiac effects can be excluded, is suggested.

Another important and perhaps more useful property is the marked relaxation of intestines on oral administration of the extract. An added desirable feature is that the cardiovascular effects are absent. The duration of relaxation is encouraging enough to anticipate it to be more in higher doses, thereby increasing the therapeutic usefulness. The adequate relaxation of isolated ileum tends to point towards a direct action on the muscles. This property may also be a contributory factor in vascular dilatation observed, resulting in hypotension.

SUMMARY

From the above preliminary observations, the extract of Ocimum sanctum shows: 1) a hypotensive action brought about by peripheral vascular dilatation and a direct cardiac effect. Interference with ganglionic transmission seems possible. A possible use as an antihypertensive agent is suggested. This obviously requires more experimental data. 2) Under normal conditions, the extract has not exhibited significant effects on respiration. A transient stimulant effect noted with 1 mg./kg. can be correlated to drop in blood pressure. Increase in rate and depth are only seen after blocking the ganglia, for experimental purposes. 3) A prominent smooth muscle relaxing property on the intestinal tract on parenteral and oral administration. This may be deemed as a useful therapeutic property, specially as no cardiovascular effects are seen on oral administration. A direct action on the smooth muscles seems to be a permissible inference.

In all probability relief from colic may be easily obtained with less cost compared to other antispasmodics, commonly used. The extract retains its properties on sterilisation which is noteworthy.

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