PRELIMINARY STUDY OF PHARMACOLOGIC PROPERTIES OF *ANANTMUL (HEMIDESMUS INDICUS)*

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The following extracts from crushed roots of Anantmul were investigated for their diuretic and other pharmacological actions: aqueous, cold alcoholic, hot alcoholic and steam distilled fraction. It was observed that none of these extracts has significant diuretic activity. Watery extract showed a slight increase in urinary flow in rats, but not in dogs. However, watery extract produced a rise in blood pressure and contraction of spleen in dogs and contraction of isolated guineapig's ileum. Rise in blood pressure was observed even in spinal cats treated with ganlionic blocking agent. The contraction of guineapig's ileum could be blocked by atropine and antistine, only partially. These effects were not seen with alcoholic extract in dosage used. Watery extract also produced some increase in cardiac rate.

The plant *Hemidismus indicus*, also known as *Anantmul* or Indian *Sarsaparilla* has a vague reputation in the treatment of nutritional disorders and syphillis for ages (Chopra, 1958). This climber plant is predominently found in Bengal and South Konkan. It has been recommended as tonic, diaphoretic and diuretic. Infusion or decoction from powdered roots mixed with milk and sugar is generally employed (Nadkarni, 1927). The aroma and taste of the drug is attributed to the presence of coumarin and other volatile substances (Chopra, 1958; Desai, 1927). In addition, the roots contain two sterols and a little amount of glycosides besides some other unknown snbstances (Chopra, 1958). Because of its reputation as a powerful diuretic and almost non-toxic in nature, present investigation was undertaken to study some of its pharmacological properties.

METHODS

Watery extract from crushed roots.—Crushed roots(fresh)200 g were extracted with 500 ml of distilled water by boiling for six hours. The extract was filtered and the volume made up to 200 ml to get a strength of 1 ml equivalent of 1 g crude plant. In some cases double the concentration was used in order to keep down the total volume of injection.

Alcoholic extracts.—Crushed roots (fresh) 500 g were soaked in absolute alcohol for three days at room temperature. The process was repeated thrice. The extract was filtered and excess solvent distilled under reduced pressure.

Similarly, hot alcoholic extract was prepared by soxlating the roots.

Steam distilled fractions.—This was prepared from the roots (fresh) by the method as described by Desai (1927).

Studies on urinary output.—Diuretic studies on male albino rats weighing between 150-200 g were carried out according to the method described previously (Mehta *et al.*, 1960). Experiments were also carried out in healthy mongrel dogs where ureters were canulated under anaesthesia. The drug was also studied in trained unanesthetized female dogs, urine being collected from the bladder through a self retaining catheter in the urethra.

Studies on blood pressure and respiration.—Healthy mongrel dogs weighing between 10-12 kg and cats between 2.4 kg were used. Dogs were anesthetized with sodium pentobarbital given intraperitoneally while the cats received ether. Injections were made through the canulated femoral vein. Arterial blood pressure and the respiration were recorded on the kymograph by standard techniques. Spleen volume was recorded by oncometer. In some animals, simultaneous EGG recordings were also obtained.

Experiments in vitro.—The isolated guineapig ileum was employed in the usual way while the isolated perfused rabbit's heart, as described by Langendorff, was used.

The potassium content of the extracts, urinary content of sodium and potassium were estimated by flamephotometer.

RESULTS

Table I shows the diuretic response in rats in groups of four, following the oral administration of watery extract. Results following the use of equivalent quantity of distilled water and hydrochlorothiazide, a known potent diuretic in control animals are given for comparision. The watery extract in the doses equivalent to 5–15 g/kg of crude drug increased the urinary output along with the increase in the sodium and potassium excretion. The excretion of potassium was relatively more. The response was however much less as compared to hydrochlorothiazide. The potassium content of the extract was 0.08-0.12 m. equiv/ml. Administration of equivalent amount of potassium in control group also produced similar response.

TABLE I

Effect of Anantmul-watery extract on urinary output in rats, in groups of four each

Drug	Urine ml/5 hr	pH	Total sodium m. equiv.	Total potassium m. equiv.
Distilled Water				
5 ml/kg	3.0	6.9	0.047	0.165
10 ml/kg	3.7	6.9	0 123	0.398
15 ml/kg	3.0	6.9	0.167	0.223
Anantmul Watery Extract				
5 ml/kg	6.0	6.8	0.473	0.563
10 ml/kg	7.1	6.9	0.481	0.784
15 ml/kg	5.2	6.8	0.450	0.732
Potassium				
5 ml/kg	6.2	6.8	0.412	0.720
10 ml/kg	4.0	6.8	0.362	0.652
15 ml/kg	7.3	6.9	0.490	0.784
Hydrochlorothiazide				
30 ml/kg	10.0	7.0	0.560	1.700
60 ml/kg	13.2	7.0	0.495	1.456
120 ml/kg	14.1	7.0	1.231	1·890

1 ml extract = 1 g of crude drug. * 1 ml = 0.1 m. equiv. of potassium.

Alcoholic extracts were emulsified with Tween-80, for oral administration while equivalent amounts of Tween-80 alone was used as control. Both cold and hot alcoholic extracts (Table II) in doses equivalent to 5, 10 and 15 g/kg showed no significant diuretic effect as compared to the control figures. In fact, the urine output in three groups administered *Anantmul* extract was little less than that seen in normal groups.

Since no significant diuretic activity was observed after oral administration of the drug, the extracts were used intravenously in dogs. For the purpose of injection, the alcoholic extract was suspended with acacia mucilage since Tween-80 produces fall in blood pressure when given intravenously. Animals were hydrated with normal saline half an hour prior to the experiment. Acacia mucilage alone was used as control. Both the alcoholic extracts in doses equivalent to 0.18-0.22 g/kg of crude drug failed

to produce significant diuretic response, Use of similar doses of the extracts given intravenouly in trained female dogs did not produce any significant diuresis. Oral administration in doses of 1-2 g/kg in dogs also produced no response. Steam distilled fraction given orally and intravenously in dogs was found to be devoid of any significant diuretic action.

TABLE II

Effect of Anantmul-alcoholic extract on urinary output in rats, in groups of four each

Drug	Urine ml/5 hr.	pH	Total sodium m. equiv.	Total potassium m. equiv.
Tween 80 Solution				
5 ml/kg	1.5	6.8	0.134	0.137
10 ml/kg	2.0	6.8	0 043	0.104
15 ml/kg	2.5	6.8	0.085	0.146
Anantmul Alcoholic extract (cold)*				
5 ml/kg	2.0	6.9	0.081	0.146
10 ml/kg	1.0	6.8	0.065	0.112
15 ml/kg	1.2	6.7	0.068	0.159
Anantmul Alcoholic extract (Soxhalation)*				
5 ml/kg	1.5	6.8	0.023	0.024
10 ml/kg	1.0	6.9	0.026	0.099
15 ml/kg	4.0	6.8	0.535	0.733

* 1 ml extract = 1 g of crude *Anantmul* root.

Effect on blood pressure, respiration and spleen volume.—Intravenous administration of water extract in dogs in doses equivalent to 1-6 g (0.1-0.5 g/kg) of crude drug produced rise in blood pressure and transient respiratory stimulation in all the animals studied. Associated with this, there was a contraction of spleen (*Figs* 1 *and* 2). On comparision with adrenaline, it was noticed that the rise in blood pressure was slower in onset and more prolonged. The contraction of the spleen showed a double hump. The response varied with the different batches of extract.

Administration of watery extract in doses equivalent to 0.04 g/kg of crude drug in spinal cats produced a similar rise in blood pressure. Previous intravenous use of pentolenium tartrate did not prevent this effect (*Fig. 3*). These

results were confirmed in subsequent animals. Alcoholic extract showed a similar effect while volatile extract had none.

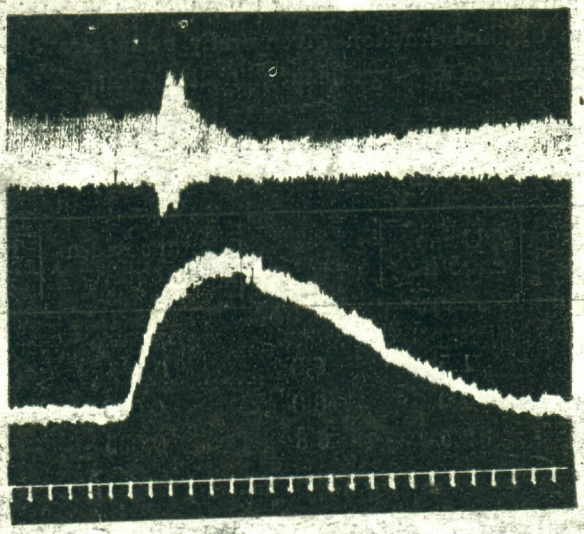

Fig. 1. The effect of *Anantmul* extract on blood pressure and respiration in anesthetised dog (wt 11 kg) Dose 2.5 ml of watery extract. (Time 10 sec).

Effect on guineapig's ileum.—The effect of watery extract in the doses equivalent to 50 to 100 mg of crude drug in 30 ml bath, on guineapig's ileum are shown in *Fig. 4.* The drug elicited a prolonged contraction of the muscle in comparision with acetylcholine or histamine. Equivalent amount of potassium did not produce any such respone. Alcoholic extract in doses upto 200 mg added to 30 ml bath produced no significant effect.

The effect of 10 μg acetylcholine could be blocked by atropine; however 50 μg of atropine only modified the intestinal response of 100 mg of the extract (*Fig. 5*).

Administration of 2 mg of antistine could block the effect of 10 μg of histamine while it only reduced the height of contraction following *Anantmul* extract.

Effect on isolated rabbit's hearts and on ECG in dogs.—Doses equivalent to 10-20 mg of crude preparation, produced initial acceleration in heart rate. Higher doses produced some co nduction disturbances (*Fig. 6*). This effect was inconsistent and found to vary from batch to batch. In order to study the possible effect on mycocardium, ECG recordings were made in anaes-

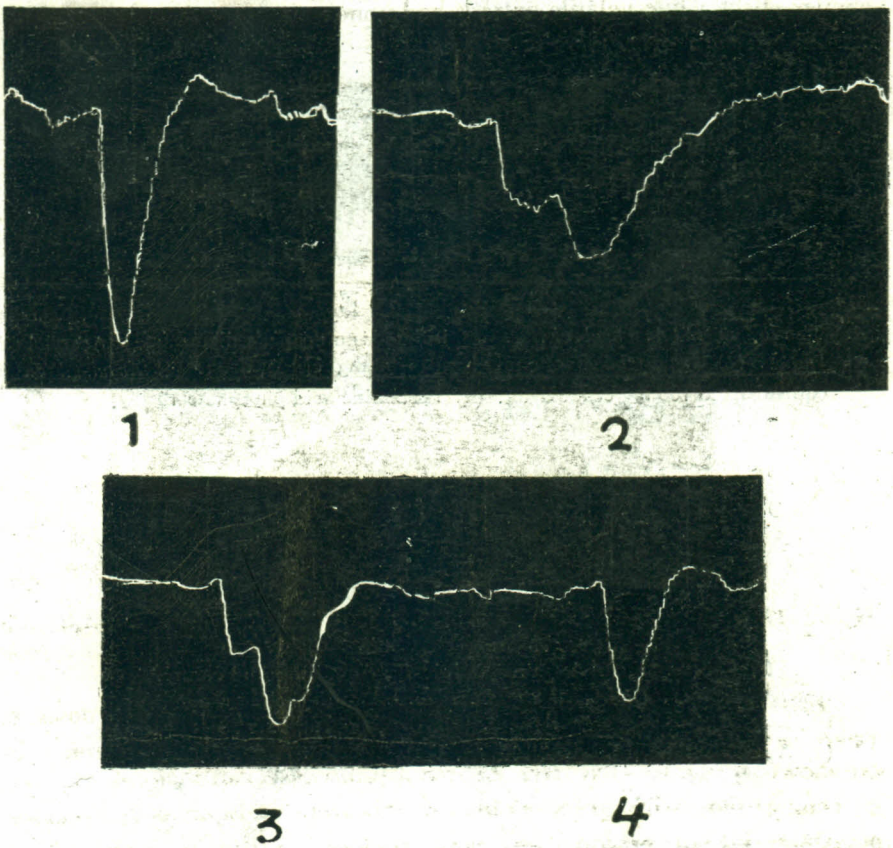

Fig. 2. The effect of *Anantmul* on spleen volume in a dog (12.0 kg). (1) Adrenaline hydrochloride, 0.004 mg (2) *Anantmul* extract equivalent to 1.5 g crude drug. (3) *Anantmul* extract equivalent to 1.0 g after atropine. (4) Adrenaline hydrochloride, 0.002 mg.

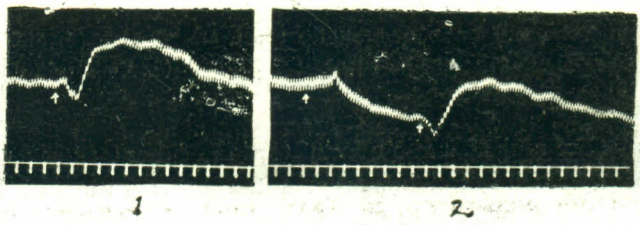

Fig. 3. The effect of *Anantmul* watery extract on blood pressure in spinal cat (2.5 kg) Dose 0.5 ml. (1) Before injection of pentolinium tartarate. (2) After injection of pentolinium tartarate, 2.5 mg.

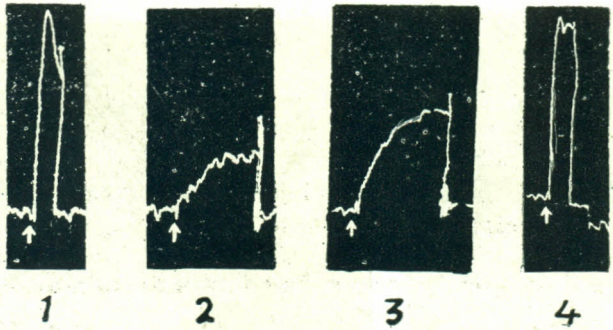

Fig. 4. The effect of *Anantmul* extract on isolated guineapig's ileum. (1) Acetylcholine 10 μg. (2) *Anantmul* extract equivalent to 50 mg crude drug. (3) *Anantmul* extract equivalent to 100 mg crude drug. (4) Histamine acid phosphate 10 μg.

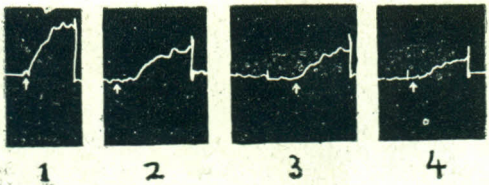

Fig. 5. The effect of atropine and antihistaminic drug on intestinal contraction produced by *Anantmul* extract. (1) *Anantmul* extract equivalent to 100 mg crude drug. (2) Atropine sulphate 25 μg+*Anantmul* 100 mg. (3) Atropine sulphate 50 μg+*Anantmul* 100 mg. (4) Antistine 2 mg+*Anantmul* 100 mg.

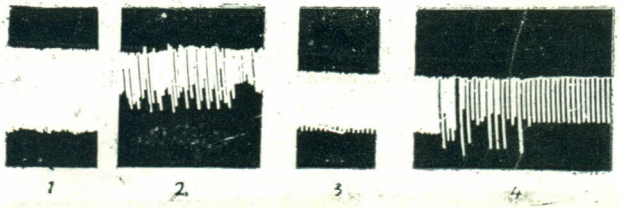

Fig. 6. The effect of *Anantmul* on isolated rabbit's heart. (1) Normal. (2) Following *Anantmul* extract equivalent to 10 mg crude drug. (3) Normal. (4) Following *Anantmul* extract equivalent to 20 mg crude drug.

thetized dogs before and after the administration of these extracts. Majority of the batches produced initial increase in the heart rate and large doses failed to induce any significant cardiac irregularities except in animals where ventricular abnormalities could be observed (*Fig. 7*). However, extract prepared from two batches of roots showed distinct effect on conduction resulting into production of various types of heart block and abnormal ventri-

cular rhythm (*Fig. 8*). These effect were more marked with alcoholic extract.

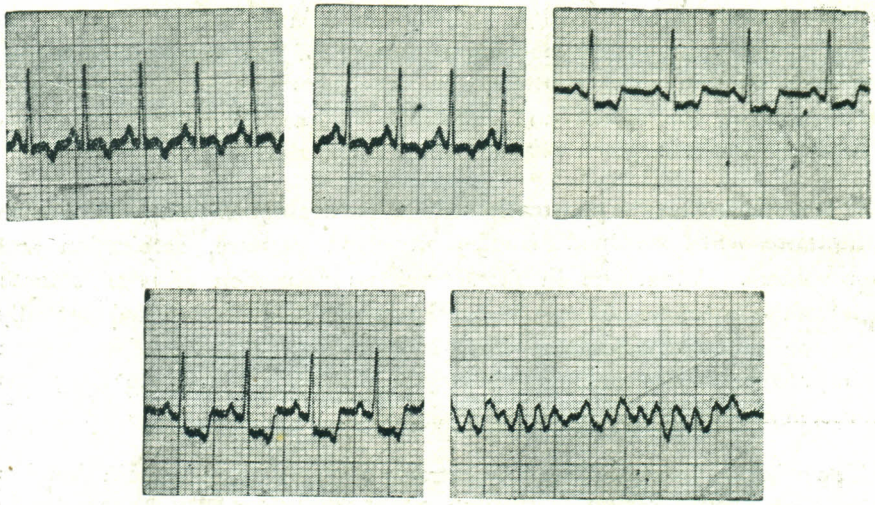

Fig. 7. The effect of *Anantmul* (alcoholic extract) on E. C. G. (Lead II) in normal anaesthetized dog. (Dog wt 12.3 kg). Serial changes following repeated doses of 2, 3, 5 and 7 ml over a period of 2 hr. Initial heart rate 186 per min. The first panel shows the normal tracing.

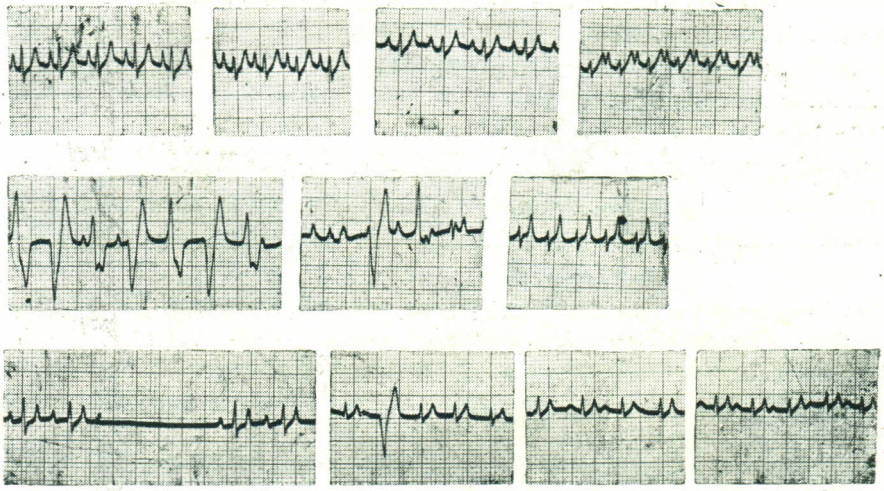

Fig. 8. Serial changes in the E. C. G, (Lead II) of anaesthetised dog following repeated injections of *Anantmul* (alcoholic extract). Dog wt 13.0 kg. The first panel shows normal tracing.
Repeated dose of 2.5 ml were given. Total dose administered over a period of 6 hr. was 20 ml. Initial heart rate 180 per min.

DISCUSSION

Judging from these results, it seems that various *Anantmul* extracts have very little diuretic activity. Slight increase in urinary output observed in rats was probably due to the potassium content of the extract. However, the extracts contain some substance or substances which raise the blood pressure, contract the spleen and intestine. Unlike adrenaline, its action on blood pressure and spleen volume was of longer duration.

It is unlikely that the contraction of the guineapig's ileum was due to the substance which produced the effect on blood pressure, respiration and spleen volume. Adrenaline in fact, produces relaxation of the smooth muscles of the intestine. The action of the extract could be blocked partially by atropine and antihistaminics whereas equivalent amount of potassium did not produce similar response. It may be pointed out that the drug has been recommended in the treatment of diarrhoea.

The effect on heart produced by extracts prepared from certain batches was interesting. The initial acceleration in all the animals and ventricular fibrilation in a few dogs could be due to the same substance which produced effect on blood pressure and respiration. However, extract from a few batches of roots produced certain conduction irregularities of the heart. Previously, it has been mentioned that *Anantmul* contains a glycoside, but the yield is extremely small. No more information is available about the nature of the glycoside. It is likely that the contents of this small amount of glycoside might vary from batch to batch and this may be the cause of inconsistant effect on the heart.

The steam distilled fraction which possessed distinct aroma was found to be almost inactive pharmacologically with respect to it's actions on heart, respiration or urinary output. The fraction may be useful as a flavouring agent.

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