THE PHARMACOLOGICAL ACTIONS OF *ERYTHRÆA SPICATA*

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ERYTHRÆA SPICATA is an annual herb belonging to the family Gentianaceæ. It grows wild in damp places specially in rice fields. Muschler[1] described this plant and other species growing in Egypt, where the public has used extracts as an antidote for scorpion sting, but one of us[2] has shown that it has no practical effect for this purpose. Gaston Bonnier[3] (1886) examined the European species *Erythræa Centaurium*. He found that it contains two glycosides and stated that it was antipyretic. Washburn[4] stated that it contained a bitter principle similar to that in gentian and stated that it was a diaphoretic and febrifuge. Gathercoal[5] said that it contained a glycoside, erythrocentaurin, and a resin.

Recently, attention was drawn to *Erythræa spicata* as it is believed to be efficacious in hypertension. The present work was therefore undertaken.

Experimental

Preparation of solutions.—An alcoholic extract of the plant was concentrated to a semi-solid consistency so that 0·3 g. of concentrated extract corresponded to 1 g. of the powdered plant. This concentrated extract (alcohol free) was dissolved in Ringer's or Locke's solution to the required concentration and the *p*H of the solution was adjusted before the experiment to *p*H 7·6.

Toad's Heart.—The method used was a modification of Syme's method of perfusion. The drug produced depression in the force of

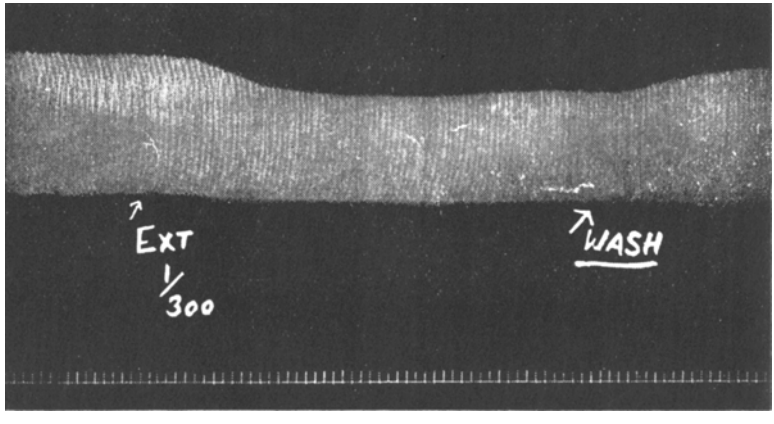

Fig. 1. Effect of extract of *Erythræa spicata* extract (1 in 300) on toad's heart.

contraction of the heart (Fig. 1). The lowest concentration which just produced depression of the heart was 1 in 600 of the extract. The same effect was produced by the drug after atropinising the heart.

Rabbit's Heart.—A modification of Gunn's method was used. No change in the amplitude or rate of the heart was demonstrated by 1 in 1000 but there was an increase in the coronary outflow varying from 30 to 40 per cent.

Blood Vessels.—Trendelenberg's method was used for perfusion of toad's vessels. The drug produced definite dilatation of blood vessels in dilutions between 1 in 100 and 1 in 5000 of the extracts. Solutions of 1 in 100 produced an increase of the flow varying from 68 per cent. to 100 per cent. averaging 86 per cent. and 1 in 1000 produced an increase varying from 39 per cent. to 73 per cent. with an average of 58 per cent. and 1 in 5000 produced an average increase of 19 per cent.

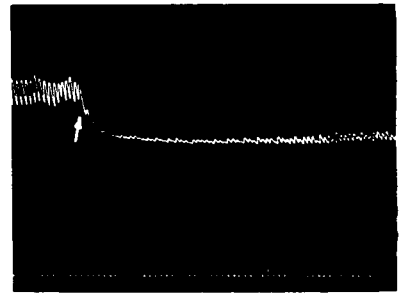

FIG. 2. Effect of *Erythræa spicata* extract (1 in 4500) on rabbit's intestine.

Intestine.—A modified Magnus technique was employed. The drug produced definite relaxation of the intestine of the rabbit (Fig. 2). Dilutions of 1 in 1000 produced in some cases very strong inhibition of the contractions, while 1 in 10,000 produced just noticeable depression.

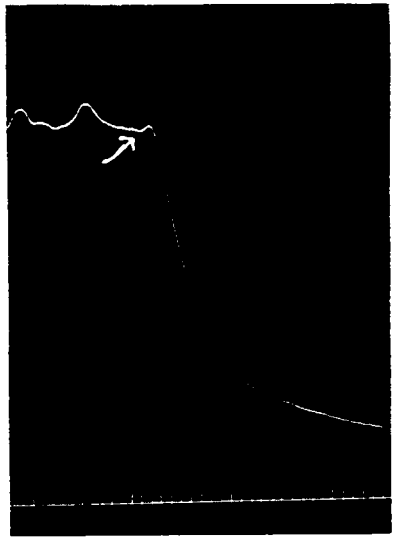

FIG. 3. Effect of *Erythræa spicata* extract (1 in 1000) on guinea-pig's uterus.

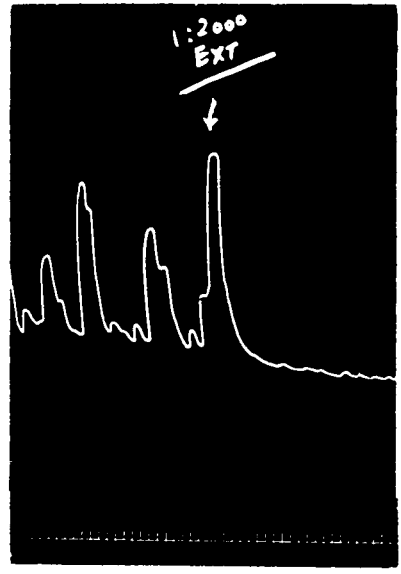

FIG. 4. Effect of *Erythræa spicata* extract (1 in 2000) on rabbit's uterus.

Uterus.—The drug produced definite relaxation of the rabbit's and guinea-pig's uteri whether pregnant or not, in all dilutions tested which ranged from 1 in 8000 to 1 in 1000 (Figures 3 and 4).

Action on Blood Pressure.—Dogs anæsthetised by chloralose intravenously after preliminary ether anæsthesia were used. The blood pressure was recorded from the carotid artery by mercury manometer on smoked paper in the ordinary way. The drug was injected intravenously through a cannula into the jugular vein. The drug produced a definite fall of blood pressure; the greater the dose injected, the greater the fall of blood pressure and the longer the duration of the fall. Experimental results in two animals may be quoted. (a) In a dog of 15 kg. body weight injected with 0·3 g. of extract, the blood pressure reading was reduced from 185 mm. Hg to 155; 1·5 g. reduced it to 115 mm. Hg and 3 g. to 95 mm. Hg.

(b) In a dog of 7 kg. body weight 3 g. of extract reduced the blood pressure reading from 155 to 65 mm. Hg. The reading returned to 100 mm. in 10 minutes then to 138 mm. in 70 minutes and to 142 mm. in 100 minutes.

The fall of blood pressure produced by the drug was not affected by atropine, indicating that the fall was not due to stimulation of the cholinergic nerve endings. After each injection of the drug there was acceleration of the heart beats and of the respiration, probably as a result of the fall in blood pressure (Fig. 5).

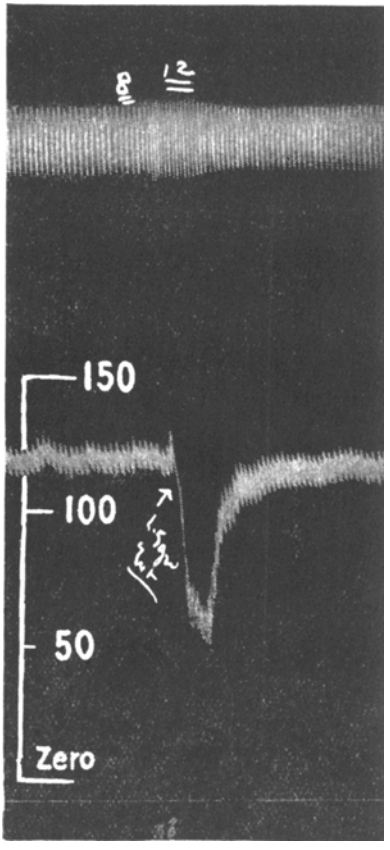

FIG. 5. Dog 7·5 kg. Effect of 1·5 g. of extract on respiration (upper tracing) and blood pressure (lower tracing).

Toxicity.—Groups of experimental animals i.e. toads, rats and dogs were injected with relatively large doses of the extract without any toxic effects. The following doses were injected without toxic manifestation. (1) Up to 1·2 g. of extract per 100 g. in the ventral lymph sac of toad. (2) Up to 2 g. of extract intramuscularly per kg. of rat. (3) Up to 0·6 g. of extract intravenously per kg. of dog.

Moreover, intramuscular injections of the extract in rabbits in doses of 0·25 g./kg. every day for 15 days produced no apparent toxic manifestations and no pathological changes in the internal organs on killing the animals.

The Active Principle

An attempt to isolate the active principle by purifying the extract with lead acetate, and precipitating it from alcoholic solution by ether resulted in an amorphous hygroscopic light brownish powder. This powder was proved to be a glycoside, readily soluble in water or dilute alcohol but insoluble in ether, chloroform, ethyl acetate and absolute alcohol. It had the pharmacological activities of the extract and it formed about 1·6 per cent. of the powdered plant. It did not lose its effects after treatment with hydrochloric acid.

Discussion

Erythræa spicata produces some depression of the force of contraction of the heart in dilutions of 1 in 600 to 1 in 100 of extract. This was not due to vagus stimulation as it occurred after administration of atropine. Dilutions weaker than 1 in 600 of the extract produce practically no depression. In rabbits it produces a definite increase in the coronary flow. It produces definite relaxation of the plain muscle in general. This was shown in: (a) The dilatation of the blood vessels of the toad when perfused with solutions of the drug. The percentage increase in the flow varies from an average of 86 per cent. which was produced by 1 in 100 of the extract, to 19 per cent. which was produced by 1 in 5000 concentration. A moderately good increase in the flow of average 58 per cent. was produced by 1 in 1000. This last concentration did not depress the perfused heart. (b) The powerful relaxation of the rabbits' intestine, in dilutions of 1 in 1000, diminishing both tone and contractions. (c) Definite relaxation of the rabbits' and guinea-pigs' uteri whether pregnant or not.

The drug produces a definite fall of blood pressure; 0·2 g. of the extract per kg. of body weight given intravenously produces an average fall of blood pressure of 46 per cent. of the normal, and 0·04 g. of the extract per kg. of body weight produced an average fall of blood pressure 19 per cent. of the normal. This last dose will make a concentration in the blood of nearly 1 in 2000. This concentration did not depress the perfused heart, so the fall in blood pressure is presumably due to the effect on the blood vessels. The drug is not toxic even if given in relatively large doses. Hydrolysis did not destroy the activity of the drug.

The experiments recorded show that this drug may be of value for reducing blood pressure. At the same time it dilates the coronaries and has a low toxicity, while the effect on the heart in the usual doses is slight. It seems to be worthy of clinical trial as an anti-spasmodic and in cases of hypertension, possibly also in angina pectoris.

SUMMARY

1. The drug produced depression of the toad's heart at a concentration of 1 in 600 of the extract; below this concentration there was practically no depression.

2. It produced increase in coronary flow in the rabbit's heart.

3. It produced fall of blood pressure in dogs and dilatation of vessels in toads.

4. It depressed plain muscle.

5. The active principle is glycosidal in nature.

6. It has a very low toxicity.

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