

PRELIMINARY PHYTOCHEMICAL AND PHARMACOLOGICAL STUDY OF SYMPLOCOS RACEMOSA (ROXB.)

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Fraction C, acetone soluble fraction of *Symplocos Racemosa* (Roxb.) has been investigated. It is a powerful depressant of blood pressure and intestinal movements. This latter effect seems to be the basis of the use of this drug in various gastrointestinal disorders in Ayurvedic practice.

Symplocos Racemosa (Roxb.) known in Hindi as Lodhra, is a common indigenous drug used by Ayurvedic practitioners for the treatment of diarrhoea, dysentery, liver diseases etc. (Chopra, 1958, Nadkarni, 1954). Although it is a popular drug, no scientific investigation has been done to elucidate its pharmacological actions. This communication embodies the findings of a preliminary phytochemical and pharmacodynamic study of the drug.

HABITAT

The plant belongs to N. O. "Symplocaceae" which is distributed throughout Northern India. The most important part of the plant is its dark-grey, rough, acrid stem bark which is used for medicinal purposes (Chopra, 1956). For the present study the bark was procured from the Himalaya Drug Co., Dehradun and subjected to chemical analysis after pharmacognostic identification.

METHODS

A. *Chemical Analysis* :—A preliminary chemical examination of the stem bark revealed the presence of a white substance, a mixture of three coloured compounds, besides reducing sugars, oxalic acid and a phytosterol.

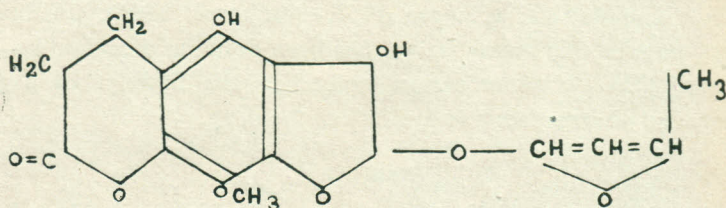
A number of solvents were tried for the extraction of the constituents from the air dried finely powdered stem bark. A comparative study of the extractives of the bark showed that 95% ethanol was the most suitable solvent for the purpose of extraction of compounds. Large scale solvent extraction of the powdered stem bark was, therefore, carried out with ethanol and from the ethanolic extract, the following four compounds A, B, C and D were isolated in pure form :—

- (i) Compound A, $C_{20}H_{38}O_2$, white deposit, m.p. $82^\circ C$ sharp.
- (ii) Compound B, $C_{25}H_{42}O_{11}$, coloured compound m.p. $310^\circ C$ sharp.
- (iii) Compound C, $C_{16}H_{14}O_8$, coloured compound m.p. $245^\circ C$ sharp.
- (iv) Compound D, $C_{24}H_{28}O_{10}$, coloured compound m.p. $190^\circ C$ sharp.

Of all these fractions which were isolated, compound C, which is soluble in acetone, was found to be most potent, and was, therefore, studied in detail.

B. Chemical Nature of Compound 'C' :—The coloured compound 'C' was dark red in colour. It was found to dissolve in methanol, ethanol, acetone and pyridine, but was insoluble in petroleum, ether, benzene, chloroform, ethyl acetate and carbon tetra chloride. It gave red colour with dilute alkali in cold from which the original compound could be precipitated back by the addition of mineral acids. It decolourised alkaline potassium permanganate solution and bromine water. It gave dirty green colouration with ferric chloride, but gave no effervescence with sodium bicarbonate solution. It did not reduce Fehling's solution even after hydrolysis with mineral acids.

As a result of the study of various reactions of the compound the following structural formula has been tentatively suggested to the compound 'C' :—



Compound C

Pharmacological Investigations :

Amphibian Heart in Situ:—50 experiments were performed on hearts of *Rana tigrina* perfused through the sinus venosus with a Ringer's solution (NaCl, 0.65 per cent; KCl, 0.014 per cent; CaCl₂, 0.012 per cent; NaHCO₃, 0.02 per cent; NaH₂PO₄; 0.001 per cent). Venus pressure was maintained at a constant level. The amplitude of cardiac contractions was recorded on a smoked drum by a Starling heart lever. The effect of various fractions given in various doses is given in Table I.

Intact Circulation:—Experiments were performed on 20 mongrel dogs, weighing between 4 to 10 kg., anaesthetized with pentobarbitone sodium (35 mg/kg.). In addition, experiments were performed on five spinal cats prepared by the technique of Burn (1952). Blood pressure was recorded from the common carotid artery by using mercury manometer. Respiration was recorded by connecting the trachea with Mary's tambour. All injections were made through the cannulated femoral vein.

Nictitating Membrane:—A preparation of nictitating membrane of cats was set up in five animals after the method of Burn (1952). The action of the drug was seen on electrically induced contractions.

Smooth Muscle :—Contractions of rabbit ileum were recorded in ten preparations. The freshly removed segments were suspended in a bath containing Tyrode solution. Action was also seen on isolated rat uterus suspended in a bath containing Dale's solution and freely oxygenated.

Action of drug was seen on movements of intestines in situ by using modified Jackson's enterograph and recording the movements by a frontal writing point.

Amphibian blood vessel perfusion :—Blood vessels of frog were perfused with the Ringer's solution by introducing a cannula in the innominate artery and counting the drops of perfusate. Injections of drug were made in the ventral lymph sac.

Diuretic Studies :—Studies regarding diuretic activity were made on rats and diuretic potency calculated after the method of Lipschitz, Hadidian, and Kerpcsar as modified by van Arman.

Toxicity studies :—Acute toxicity studies were made on rats and LD 50 of the drug calculated by plotting a log dose response curve.

OBSERVATIONS AND RESULTS

Action on amphibian heart :—The actions of the drug in various dosage are given in Table I.

TABLE I

Dose of the drug	Action on amplitude	Action on heart rate
1 mg.	Insignificant reduction	No effect
2 mg.	Slight reduction	No effect
3 mg.	Marked reduction but transient	No effect
10 mg.	Marked reduction long lasting	Slight diminution

The action is not blocked by giving 1.1 mg. (1/60 gr.) of atropine (Fig. 1, 2 and 3).

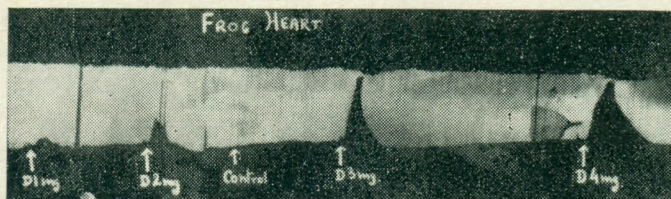


Fig. 1. Showing the action of the drug on frog heart.

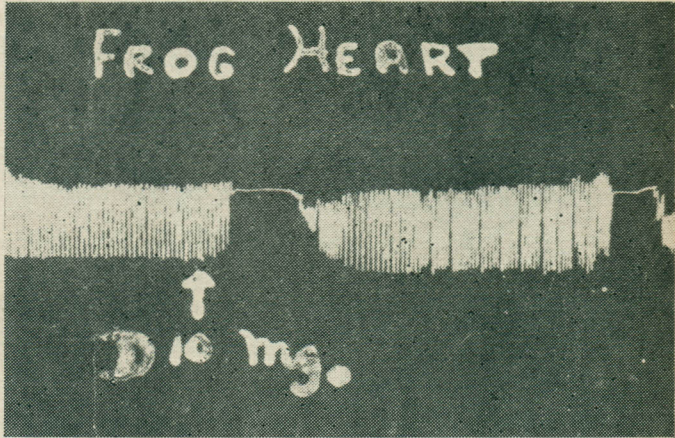


Fig. 2. Showing the action of the drug on frog heart.

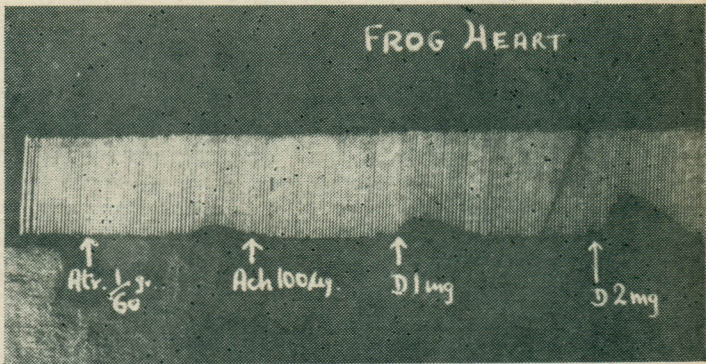


Fig. 3. Showing the action of the drug on frog heart after blockade.

On intact circulation:—On intact circulation seen in anaesthetized dogs, the effects of the drug in dosage from 3 to 5 mg. per kilogram body weight, are typically depressor. The typical response produced by administration of two doses of 4 mg/Kg. and 5 mg/Kg. are shown in Fig. 4. This effect too is not abolished by blockade with atropine (Fig. 5). This dosage of 5 mg/Kg. produces a fall of about 80 mm. of mercury.

In spinal dogs, small doses (2-5 mg per Kg.) had no effect on blood pressure but larger doses (10 mg/Kg.) produced a fall, after which the animal could not survive (Fig. 6).

Respiration:—A dose of 5 mg/Kg. produced a transient diminution of respiratory rate. This soon returned to normal (Fig. 5).

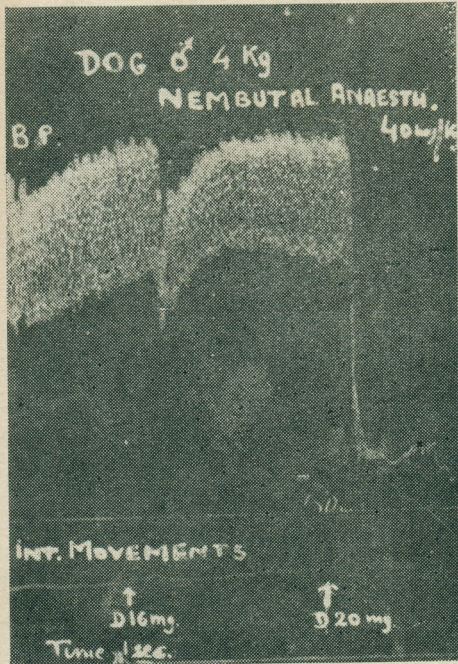


Fig. 4. Showing the action of the drug on dog B.P. and intestinal movements.

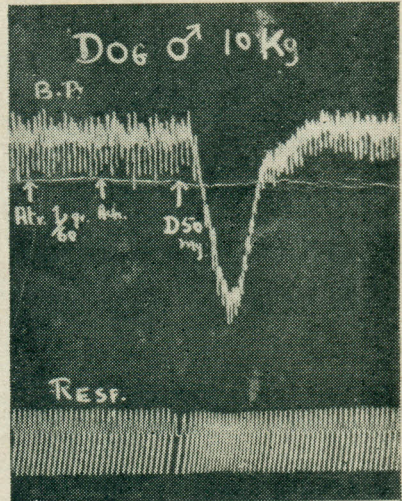


Fig. 5. Showing the action of the drug on B.P. and respiration.

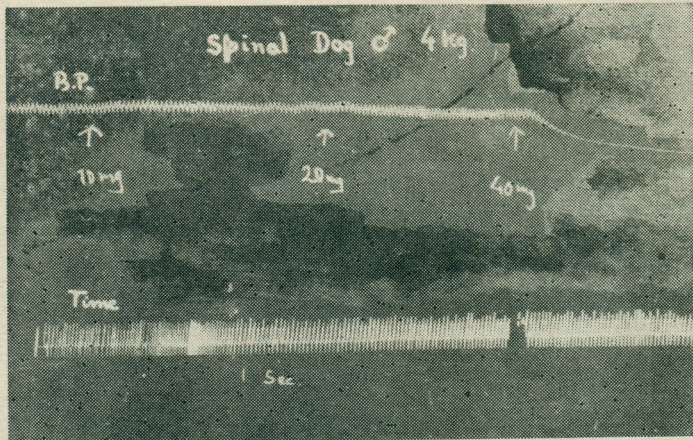


Fig. 6. Showing the action of the drug on B.P. of spinal dog.

Action of drug on nictitating membrane :—The drug did not abolish the electrically induced contractions of the nictitating membrane when preganglionic fibres were stimulated by an electronic stimulator (Fig. 7).

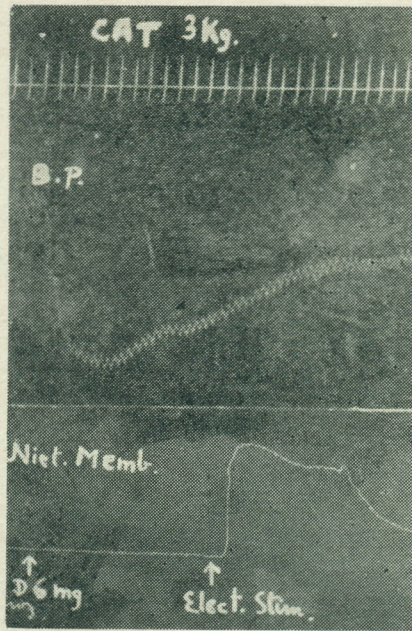


Fig. 7. Showing the action of the drug on nictitating membrane.

Smooth Muscle : Ileum :—5 and 10 mg. doses of the drug put in the bath produced a relaxation of the gut which increased in the increasing doses (Fig. 8).

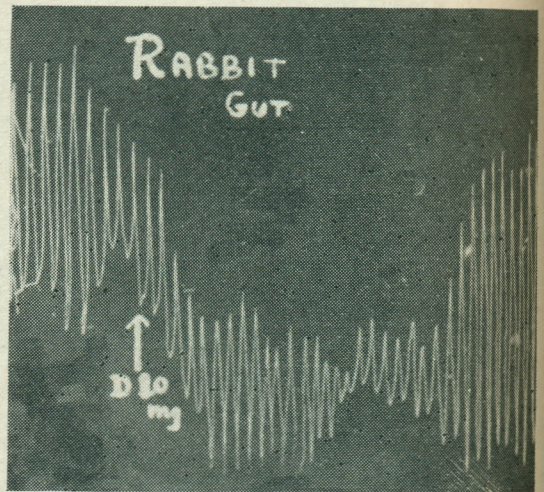
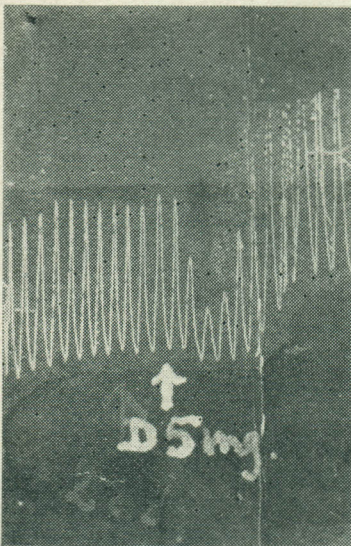


Fig. 8. Showing the action of the drug on rabbit ileum.

The drug also abolished spasm induced by acetyl-choline but failed to do so when the spasm was induced by either posterior pituitary or histamine (Fig. 9).

Rat Uterus :—The drug did not show significant effect on isolated rat uterus. It also did not antagonise the spasm of the uterus induced by posterior pituitary (Fig. 10).

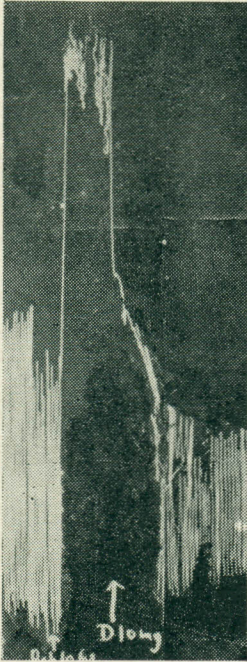


Fig. 9. Showing the action of the drug on the spasm induced by Acetyl Choline in rabbit intestine.

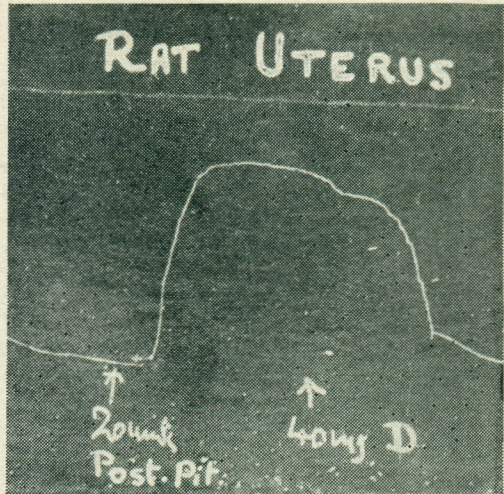


Fig. 10. Showing the action of the drug on rat uterus.

The drug did not show any effect on isolated frog rectus preparation.

Amphibian blood vessel perfusion :—This study showed that the drug has a vasoconstrictor effect in this species. Priscoline in the dose of 20 mg. was used as an adrenergic blocker. The vasoconstrictor effect persisted after adrenergic blockade.

Diuretic studies in rats :—The diuretic studies in rats showed that the drug has a diuretic potency of .132 with urea as a standard.

Toxicity studies :—The toxicity studies made on rats showed the LD 50 dose to be 77.49 mg./100gm.

DISCUSSION

Preliminary observations on the pharmacodynamic effects of a lactone isolated from the bark of *Symplocos racemosa* Roxb. have been presented in

the present communication. Action worthy of notice shown by this active principle are the depressant effect on the amphibian heart, depressor effect on the blood pressure of dogs and relaxant effect on the rabbit gut. These effects warrant a more detailed study which is in progress and will be communicated separately.

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