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PHARMACOLOGICAL STUDIES OF PLUMERIA ACUTIFOLIA

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The aquous portion of the alcoholic extracts of plumeria acutifolia, is a strong relaxant of smooth muscles of the intestine. Its action on isolated atria and heart are like those of acetylcholine. Its action on rat uterus are interesting in the way that it relaxes the uterine muscle and antagonises the action of syntocinon and oxytocin. The drug is not toxic and can be given in high doses.

Introduction

Plumeria acutifolia is a very widely grown garden plant of this subcontinent. Popularly known as "Champa", its white and yellow flowers give a very pleasant fragrance. In folk medicine, its use ranges far and wide. It has been used as purgative, rubefacient, antiherpetic and antidote to snake poison (Nadkarni[1]). However this plant has not been studied scientifically so far. This paper deals with the pharmacology of the extract of the leaves of this plant.

In folk medicine the therapeutic activity of this plant in attributed to its crude extract. The pharmacological studies were therefore carried out on extracts obtained by simple proceedures thus ensuring the presence of all the possible active ingredients.

Extraction

Fresh undried leaves of plumeria acutifolia were collected and cut in small pieces. Four kilograms of the cut leaves were soaked in ethyl alcohol for 15 days. Alcohol was removed from the extract at 40°C *in vacuo* leaving a dark brown coloured sticky mass, which weighed 211.25 g. This material was thoroughly shaken in a separating funnel with 500 ml of distilled water and 500 ml of petroleum ether (b.p. 60–80°C) and left overnight. The lower aqueous layer was collected from below and heated on a water bath at 60°C *in vacuo*. The dark brown sticky material left in the flask weighed 95.19 g. This material was used in the pharmacological experiments.

Pharmacology

The pharmacological properties of the extract were studied on the following preparations:

Isolated Rabbit Duodenum.—A piece of rabbit duodenum was suspended in oxygenated Tyrode's solution at 37°C. Contractions were recorded on a smoked drum by a frontal writing lever.

Isolated Guinea-pig Ileum.—A small piece of terminal ileum was perfused with oxygenated Tyrode's solution at 37°C in a small organ bath. The contractions were recorded on smoked-drum by a frontal writing lever.

Isolated Rabbit Atria.—The preparation was set up according to the method of Burn.[2] The tissue was perfused in oxygenated McEwen's solution at 28°C. The contraction was recorded by spring loaded lever.

Isolated Rabbit Heart.—Langendorff isolated heart preparations was set up according to the method of Burn.[3] McEwen's solution was used for perfusion.

Isolated Rat Uterus.—Adult virgin female rats in oestrus were selected by studying their vaginal smears under the microscope. The tissue was perfused in oxygenated de Jalon's solution warmed upto 27–28°C.

Rat Phrenic Nerve-diaphragm Preparation.—The preparation was set up according to the method of Bulbring.[4] The nerve was stimulted electrically using square wave pulses of 6–8 volts strength, having a duration of 0.5 msec and a frequency of 6 per minute.

Guinea-Pig Lungs in vivo.—Preparation was set up to study the resistence of the guinea-pig lungs to inflation *in vivo* by the method of Konzet and Rossler.[5]

Dog Blood Pressure.—Femoral artery was canulated in an anaesthetised dog and blood pressure recorded by a mercury mano-meter. Respiration was recorded by canulating trachea. Injections were given *via* femoral vein. Carotid arteries were isolated and were clamped periodically for 30 secs.

Toxicity.—Adult male albino mice weighing 20–25 g were used. Increasing doses of the extract were injected intraperitoneally in different groups of mice. The animals were observed for

signs of acute toxicity and the mortality was noted after 24 hours.

Results

Isolated Rabbit Duodenum.—The extract when added to the bath markedly relaxed the duodenum.

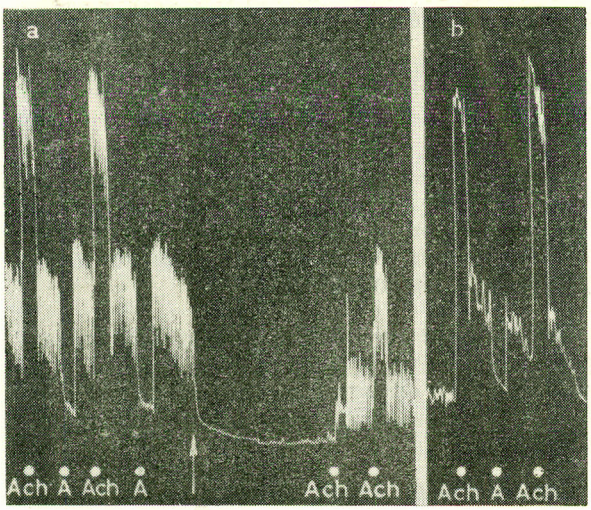

Fig. 1.—Rabbit duodenum: At Ach 2 μg acetylcholine was added to the bath. At A. 0.5 μg adrenaline was added. A dose of 0.5 mg of the extract was added at ↑.

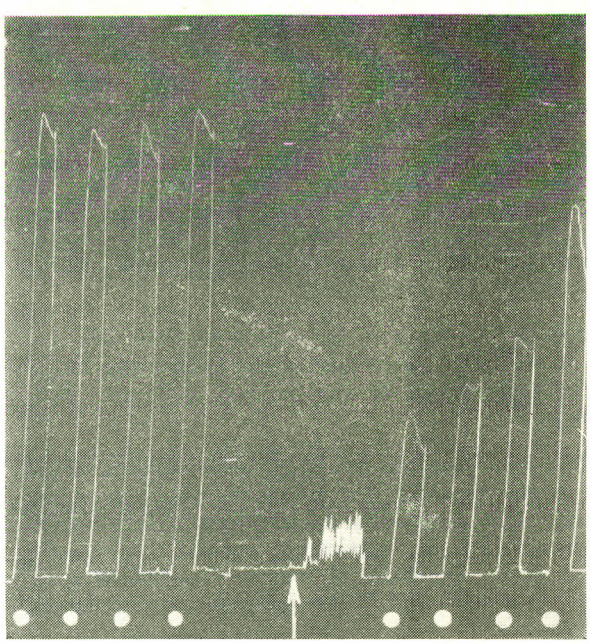

Fig. 2.—Guinea-pig ileum: Contractions produced by adding 1 μg acetylcholine to the bath. At ↑ a dose of 0.5 gm of the extract was added. The preparation was washed and acetylcholine repeated.

(Fig. 1a). Both tone and spontaneous movements of the duodenum were reduced. The response was similar to that produced by adding adrenaline to the bath. The normal response of the tissue to acetylcholine were also reduced significantly. These responses returned to normal when the preparation was left for half an hour (Fig. 1b).

Isolated Guinea-pig Ileum.—The extract when added to the bath did not reduce the tone of the preparation. Acetylcholine was now added in presence of the extract. The normal contraction of the ileum was now replaced by increase in spontaneous activity only (Fig. 2). Subsequent contractions of the ileum in response to the same dose of acetylcholine were also smaller than the control response. The contractions returned to normal after sometime.

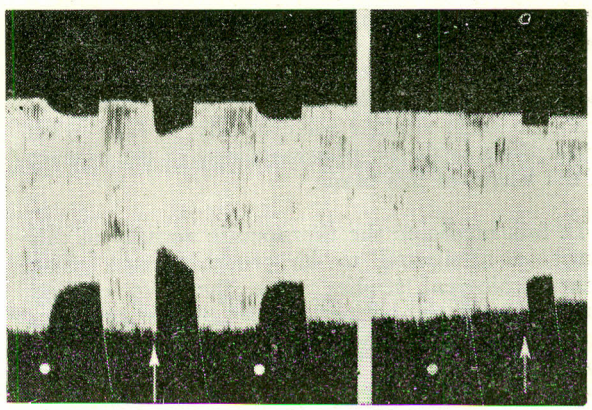

Fig. 3.—Rabbit atria: 0.5 μg acetylcholine added to the preparation, reduced the force of the contractions. At ↑ 0.5 mg of the extract added. Contractions reduced. Thirty minutes after atropine, acetylcholine and the extract repeated. Action of actylcholine abolished but that of extract reduced.

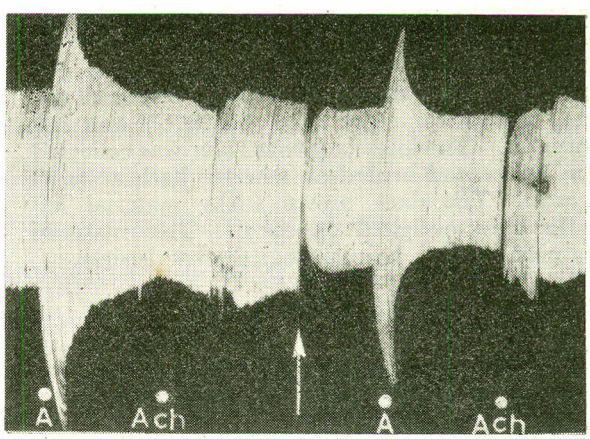

Fig. 4.—Isolated rabbit heart (Langendorff): At A 1 μg adrenaline was injected while at Ach 0.25 μg acetylcholine was added. At ↑ a dose of 0.25 mg of the extract was injected.

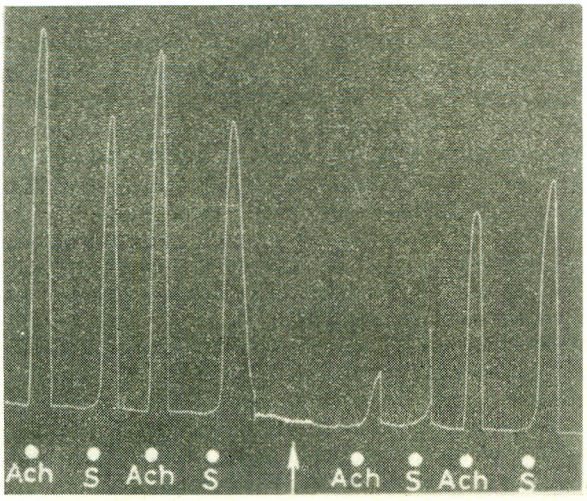

Fig. 5.—Isolated rat uterus: At Ach 5 μg of acetylcholine added to the bath. At S a dose of 1 mu oxytocin (syntocinon) was added to the bath. At ↑ a dose of 0.25 mg of the extract added to the bath and left there for 3 minutes.

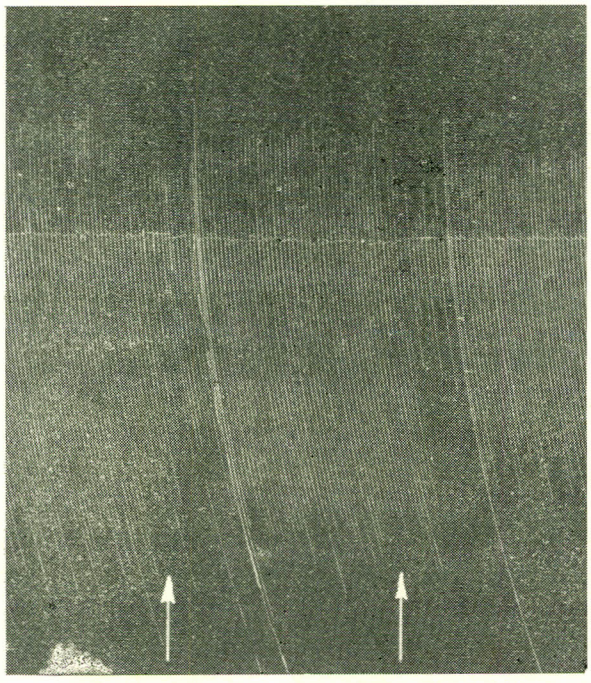

Fig. 6.—Rat phrenic nerve-diaphragm preparation: At the first ↑ a dose of 0.25 mg of the extract added to the bath while at the second ↑, the dose was increased to 0.5 mg.

Isolated Rabbit Atria.—Acetylcholine added to the bath reduced the amplitude of contractions of the atria (Fig. 3a). When a dose of the extract was added to the bath, the contractions of atria were reduced significantly. They returned to normal when the drug was washed away. Atropine, in a dose of 100 was now added and left in the bath for half an hour. After atropinization, acetylcholine was ineffective (Fig. 3b). The original dose of the extract was also less effective.

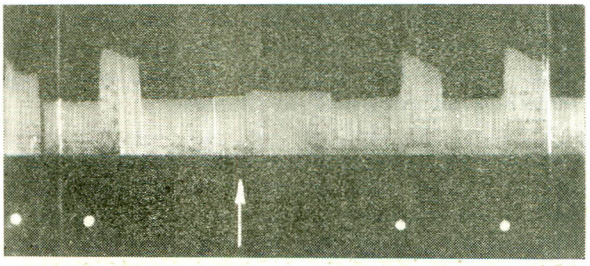

Fig. 7.—Guinea-pig lung *in vivo*. At ● histamine was injected in a dose of 1 μg i.v. This resulted in construction of the bronchiols. At ↑ 0.5 mg extract was injected.

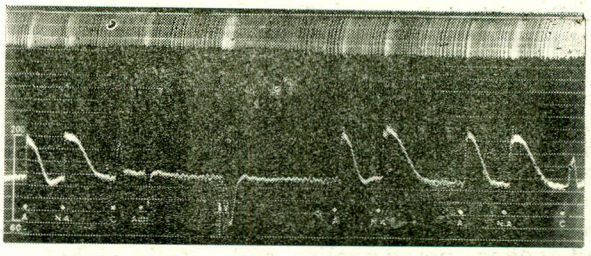

Fig. 8.—Dog blood pressure and respiration: The upper tracing records the respiration while the lower one the blood pressure. At A, 10 μg adrenaline was given, at NA, 10 μg noradrenaline was injected and at Ach, acetylcholine was given in a dose of 10 μg. The extract was injected at ↑ and carotid arteries were clamped at C.

Isolated Rabbit Heart.—Adrenaline applied to the Langendorff heart preparation produced marked increases in the amplitude of the contractions (Fig. 4). Acetylcholine on the other hand reduced the contractions. Plumeria extract was now applied to the heart. It reduced the contractions of the heart significantly. The subsequent responses of the heart to adrenaline and acetylcholine were not affected.

Isolated Rat Uterus.—Rat uterus showed contractile response to application of acetylcholine and oxytocin (Fig. 5). Plumeria extract was now added to the bath. The response of the uterus to both acetylcholine and oxytocin were depressed. The contractions increased in size after several washings of the preparation.

Rat Phrenic Nerve-diaphragm Preparation.—Electrical stimulation of the phrenic nerve caused a contraction of the diaphragm musculature (Fig. 6). Addition of the extract to the bath reduced the

amplitude of this contraction. When a higher dose was added to the bath, the contractions were further reduced, showing a dose-response relationship. When the drug was washed away, the contractions returned to normal.

Guinea-pig Lungs in vivo.—Injections of histamine in the jugular vein produced contraction of the bronchiols resulting in increase of the volume of escaped air. This was registered on the drum as upward swing of the pointer (Fig. 7). Plumeria extract did not produce any bronchioconstriction. When histamine was repeated again, the response was the same as the control one.

Dog Blood Pressure.—Intravenous injections of adrenaline produced sharp rise in the blood pressure of the dog (Fig. 8). Occlusion of the carotid arteries also caused elevation of blood pressure. Pleumeria extract given intravenously produced a sharp fall in the blood pressure. This fall was of short duration and the blood pressure returned to normal level in a few minutes. The responses of the blood pressure to injections of adrenaline, noradrenaline and carotid occlusion were not altered.

Toxicity.—Increasing doses were given to mice till a dose of 800 mg/kg body weight was reached. The animals did not show any sign of acute toxicity. No deaths were noted after 24 hours.

Discussion

The extract proved to be a strong relaxant of smooth muscles of the duodenum and ileum (Fig. 1 and 2). This activity was very much like that of adrenaline. However, its actions on isolated atria (Fig. 3), isolated heart (Fig. 4) as well as blood pressure (Fig. 8) resembled the actions of acetylcholine more than those of adrenaline. The actions of the extract on rat uterus are very interesting. It relaxed the rat uterus and antagonised the uterine contractile response to oxytocin and acetylcholine (Fig. 5). This action of the drug might be of use in dysmenorhoea and other clinical conditions induced by painful uterine contractions. The drug does not appear to be toxic and can be given in high doses. Further studies of its uterine actions are under way and will form the topic of the next communication.

References

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