PHARMACOLOGICAL STUDY OF MORINGA PTERYGOSPERMA

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Moringa pterygosperma, commonly known as 'Sanjna', is a well-known medicinal plant. The aqueous extract of the leaves was found to be an active hypotensive agent on intravenous injection in anaesthetised dogs. It stimulated the isolated rabbit heart, had neuromuscular blocking action on phrenic nerve-diaphragm preparation and produced sedation in conscious animals. The alcoholic extract had similar properties. The toxicity of the compound was very low.

Introduction

Moringa pterygosperma is a large tree and grows wild in the sub-Himalyan tract of the Indo-Pakistan subcontinent. It is locally known as 'Sanjna'. The leaves, flowers and fruits are all eaten as vegetables. The medicinal value of this plant has long been recognised in indigenous system of medicine.[7] The seeds of this tree have been used in cases of ascitis resulting from enlargement of liver. The oil from the seeds is applied externally for relieving pain of joints in rheumatism and gout. The decoction of the roots is used internally for a variety of conditions such as fever, epilepsy, hysteria, palsy, dropsy, tetanus, paralysis leprosy and high blood pressure.

Chemical studies of the plant have been made by Rangaswami *et al.*[2] They obtained a wax from the flowers. Rao and George[3] obtained an oily fraction from the root extract. They called it "ptergospermin".

Chopra[1] reported some pharmacological work done with the vegetable bases obtained from the plant. According to him the amorphous base closely resembles adrenaline and ephedrine in its effect. It raises the blood pressure, constricts the blood vessels and accelerates the heart. It also relaxes the smooth muscles of the intestine.

The present study describes in detail the pharmacological properties of the aqueous and the alcoholic extracts of the leaves of the plant.

Materials and Methods

Aquous Extract.—Fresh leaves were plucked from the branches, weighed (100 g) and washed first with tap water and then with glass-distilled water. After thorough crushing in a porcelain mortar with a porcelain pestle the leaves and the juice were transferred to a 2-l. conical flask. After adding 1 l. of distilled water the leaves were boiled for 75 min. The extract thus obtained was filtered (184 ml) and the filtrate allowed to cool to 37°C and used the same day.

Alcoholic Extract.—Fresh leaves were plucked from the branches, weighed (100 g) and washed first with tap water and then with glass-distilled water. After thorough crushing by a porcelain mortar and pestle the leaves and the juice were transferred to a 2-l. conical flask. Ethyl alcohol (2 l) was added to it and the flask was tightly closed.

After 49-day percolation the leaves were separated out by filtration and the alcohol was completely removed in vaccum at 40°C. The extract was treated with petroleum ether and distilled water in a separating funnel. The aqueous layer was collected and the water was removed under reduced pressure at 60°C. A 10% solution was prepared from the material thus obtained and used for pharmacological studies.

Pharmacological Studies of the Extracts

(i) *Blood Pressure of Dog.*—Dogs were anaesthetised with an intravenous injection of sodium pentothal 15 mg/kg and phenobarbitone 25 mg/kg. This injection was followed by an intraperitoneal injection of phenobarbitone 75 mg/kg. Blood pressure was recorded from a femoral artery by a mercury manometer. Both carotid arteries were exposed and occluded by clamps at regular intervals for short durations.

(2) *Isolated Rabbit Heart.*—Langendorff isolated heart preparation was set up according to the method of Burn.[4] McEven's solution was used for perfusion.

(3) *Isolated Guinea Pig Ileum.*—Terminal ileum segment from a guinea pig starved overnight was suspended in a 10-ml bath containing oxygenated Tyrode's solution at 37°C. The drugs were repeated after every 3 min.

(4) *Frog's Rectus Abdominis Muscle Preparation.*—Frog's rectus abdominis muscle was set up according to the method of Burn.[4] An aerated 5-ml bath containing Ringer's solution at room temperature was used for perfusion.

(5) *Rat Phrenic-diaphragm Preparation.*—The preparation was set up according to the method of Bulbring.[5] The diaphragm was suspended in oxygenated Tyrode's solution in a 50-ml bath and its contractions recorded by a spring-loaded lever on a drum. The nerve was stimulated every 10 sec by square wave pulses of 6 volts and 5 milisec duration.

(6) *Spontaneous Motion of Mice.*—Spontaneous motion of mice were recorded on a smoked drum by using a modification of commonly used actograph. Two circular Perspex cages were made in such a way that it consisted of an inner cage and an outer cage quite separate from each other. The inner cage was mounted on a spring mechanism and its movements were recorded on a paper by a pointer. Six to eight mice were put in the outer cage and two in the inner cage. The presence of mice in the outer cage prevented the mice in the inner cage from retiring in a corner and going off to sleep. The drug was given by intraperitoneal injection to the mice placed in the inner cage.

(7) *Isolated Rat Uterus.*—One horn of a female rat uterus in oestrus was set up in an isolated organ bath of 30 ml capacity at 28°C. de Jalon's solution was used for perfusion. Movements of the muscle were recorded on smoked drum by frontal writing lever.

(8) *Bronchial Musculature of Guinea Pig.*—The method of Konzett and Rassler[6] was used for this study. Guinea pigs were anaesthetised with urethane (150 mg/100 g i.p.), and closed circuit artificial respiration was started. The air that escaped after inflating the bronchial system moved the piston recorder and this movement was recorded on the drum. Drugs which constricted the bronchi reduced the volume of the bronchial system and more air thus escaped from the system. This caused the piston recorder to move further up and record an upward swing on the paper. All drugs were injected intravenously.

(9) *Toxicity.*—Experiments were performed on dogs. Increasing doses were given intravenously to groups of animals and the mortality noted after 24 hr.

Results

(1) *Blood Pressure of Dog.*—Fresh aqueous extract of the leaves produced marked hypotensive effect in dogs (Fig. 1). A dose of 5 ml given intravenously produced a marked fall in the blood pressure which returned to original level after 10 min. Pressor responses of 15 μg adrenaline and carotid arterial occlusion for 30 sec were not altered.

The water-soluble fraction of the alcoholic extract also produced a hypotensive response (Fig. 2). This response was however not marked. The responses to acetylcholine injection and carotid arterial occlusion were not affected. The fall in the blood pressure was accompanied with stimulation of respiration.

In some experiments injections of the extract were repeated after intravenous injection of 2 mg atropine. As shown in (Fig. 3) there was no significant change in the blood pressure response.

(2) *Isolated Rabbit Heart.*—The aqueous extract in doses of 0.5 ml to 1 ml slightly enhanced the cardiac action both in rate and force (Fig. 4a). It did not affect the stimulatory response of adrenaline. On the other hand, the alcoholic extract produced a reverse action. In doses of 0.5 ml to 1 ml the extract markedly reduced the amplitude of the heart (Fig. 4b). The amplitude returned to normal after a short while. The action of adrenaline remained unaffected.

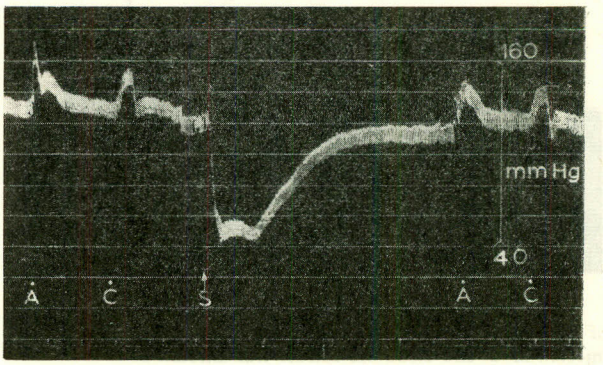

Fig. 1.—Blood Pressure of dog. At A 10 μg adrenaline was injected while at C carotid arteries were occluded for 30 sec, and at S 5 ml fresh aqueous extract of the leaves was injected.

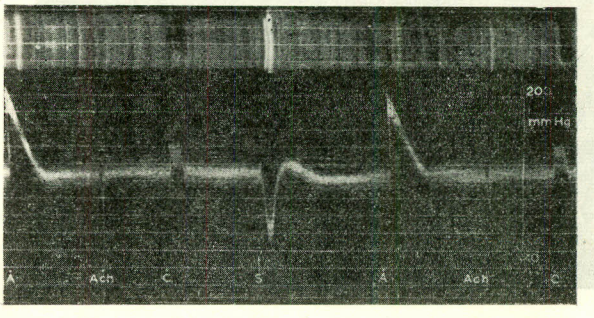

Fig. 2.—Blood pressure of dog. Upper record shows respiration and lower record shows blood pressure. At A10 μg adrenaline was injected while at Ach 10 μg acetylcholine was injected, at C carotid arteries were occluded and at S 5 ml water-soluble fraction of alcoholic extract was injected.

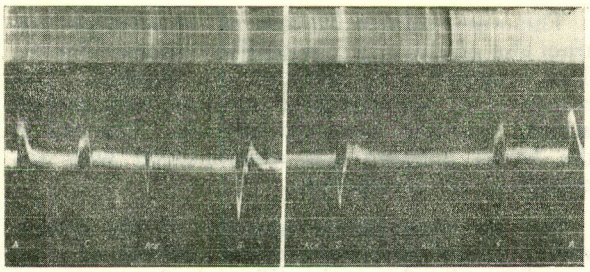

Fig. 3.—Dog blood pressure and respiration before (left) and after (right) atropinisation (2 mg). At A adrenaline 10 μg was injected while at C carotid arteries were occluded, at Ach 10 μg acetylcholine was injected and at S 5 ml aqueous fraction was injected.

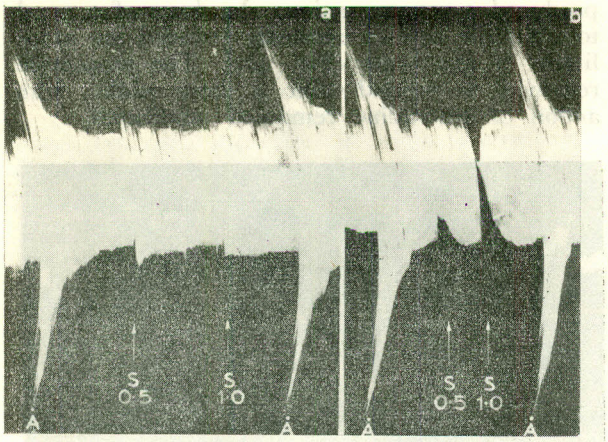

Fig. 4.—Isolated rabbit heart (Langendorff). At A 1 μg of adrenaline was injected while at S aqueous extract was injected in 'a' and alcoholic extract was injected in b.

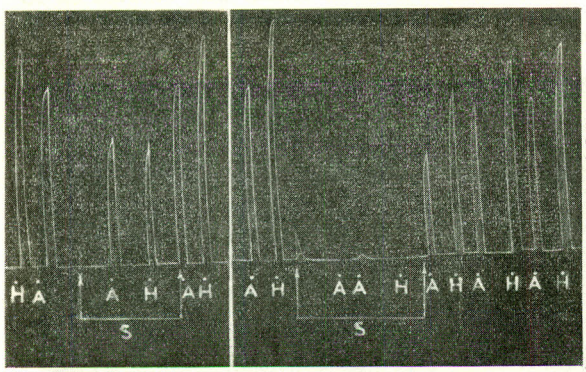

Fig. 5.—Guinea pig ileum. At H 10 μ of histamine was added in the bath and at A 5μ of acetylcoholine was added. At S on the left 1 ml of aqueous extract was added and at S on the right 1 ml of alcoholic extract was added.

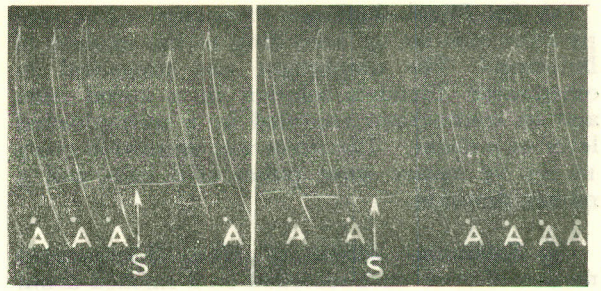

Fig. 6.—Frog rectus abdominis. At A 20 μg acetylcholine was added to the bath and at S on the left 1 ml of aqueous extract and on right 1 ml alcoholic extract was added.

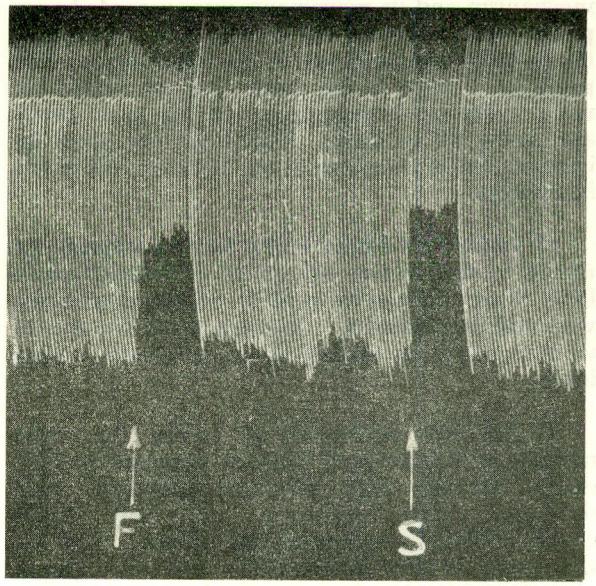

Fig. 7.—Rat's phrenic nerve-diaphragm record. At F4 mg of Flaxedil was added to the bath and at S 3 ml of alcoholic extract was added.

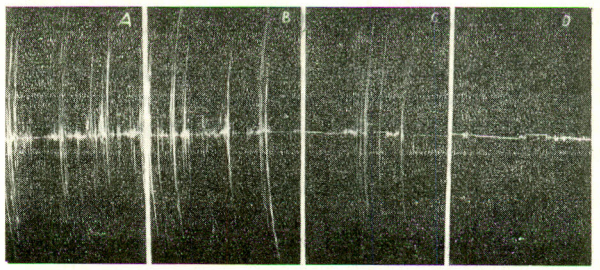

Fig. 8.—Actographic recording of the spontaneous activity of mice. A control reading. B 1 hr after intraperitioneal injection of 0.2 ml of the aqueous extract. C and D are recordings after 1 hr and 1½ hr respectively.

(3) *Isolated Guinea Pig Ileum.*—The aqueous extract has no stimulatory effect on this preparation. However, the responses of the tissue to standard doses of acetylcholine and histamine were depressed in the presence of the extract. When the solution was washed, the contraction returned to normal (Fig. 5).

A dose of 1 ml of the alcoholic extract completely abolished the contractions produced by acetylcholine and histamine (Fig. 5). These contractions returned to normal when the solution was washed away.

(4) *Frog's Rectus Abdominis.*—A dose of 20 μg of acetylcholine produced constant contractions of the muscle. When 1 ml of the aqueous extract was added to the bath, the response of the tissue to the same dose of acetylcholine was slightly reduced. On washing the solution out, the recovery was prompt (Fig. 6). The alcoholic extract had a similar but much more pronounced action.

(5) *Rat's Phrenic-diaphragm Preparation.*—The electrical stimulation of the phrenic nerve produced contractions of the diaphragm. These contractions remained constant over a long period. When a dose of 4 mg of Gallamine (Flaxedil) was added to the bath, the contractions decreased in size significantly. The solution was washed out and the preparation given a rest of 10 min. On restarting the drum the contraction returned to control size (Fig. 7).

The alcoholic extract in a dose of 3 ml produced similar reduction in the size of the contractions (Fig. 7). The preparation recovered completely when the drug was washed out.

(6) *Spontaneous Movement of Mice.*—The extract produced sedation and reduction in the movements in mice. A dose of 0.2 ml i.p. reduced the normal movements of mice considerably (Fig. 8). When the animals were returned to the cage after 24 hr, the normal movements returned.

Similar experiments were performed on dogs also. Five ml of the extract was injected intravenously in conscious animals. It resulted in marked sedative effect. The animal remained quiet and drowsy for several hours.

(7) *Isolated Rat Uterus.*—The extract did not produce any significant effect on this preparation. Doses upto 2 ml failed to produce a contraction. The response of the tissue to oxytocin were not affected.

(8) *Bronchial Musculature of Guinea Pig.*—Injections of the extract failed to affect the bronchi. There was no constriction, neither were the constrictory responses to injections of histamine reduced.

(9) *Toxicity.*—No death was noted in the 12 animals even after injecting 50 ml of either the alcoholic or aqueous extract. The only toxic symptoms noticed were marked prostration, nausea and vomiting.

Discussion

The extract of the leaves of *Moringa pterygosperma* were found to produce marked fall in the blood pressure of anaesthetised dogs. This response appears to be pripheral in origin since the pressor response to carotid arterial occlusion was not depressed. It has no adrenolytic activity since injected adrenaline produced the same response before and after injection of the drug. There appears to be a minimal cholinergic component in this response as atropinisation had no effect on the fall of blood pressure. It has an antispasmodic action inhibiting the contractile effects of acetycholine and histamine on guinea pig ileum. A similar inhibitory action was noticed on rabbit's heart and frog's rectus abdominis muscle. The effect was non-specific and probably due to a direct action on the musculature. The hypotensive action also might be partly due to a direct inhibiting effect on cardiac musculature since central and peripheral mechanisms of action as shown by carotid occlusion and adrenaline administration were not interfered with, to any extent.

The neuromuscular blocking action seen on phrenic nerve diaphragm preparation is significant. It appears to be due to an antiacetylcholine action of this drug.

As the aqueous extract is more potent hypotensive agent than the alcoholic extract, the active principle appears to be readily soluble in water. This hypotensive property probably explains the clinical usefulness of the plant in cases of high blood pressure.

The pharmacological findings reported here appear to be at variance with those reported for vegetable bases by Chopra.[1] According to him these bases have strong sympathomimetic properties. Such activity was not found in the aqueous or alcoholic extract of the leaves. It appears that there are more than one active principles in the plant which are only separable by elaborate chemical procedures.

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