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Research Article

STUDIES ON THE EFFECTS OF *KOPSIA FRUTICOSA* ON MEAN ARTERIAL BLOOD PRESSURE OF ANAESTHETIZED CATS

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ABSTRACT

Introduction: *Kopsia fruticosa,*a member of the Apocynaceae family contains four indole alkaloids whose pharmacological effects have not been extensively studied (Fig. 1-3). Drugs bearing indole alkaloids are known to produce important pharmacological effects. It has been reported that most of the indigenous plant having indole alkaloids exhibit varieties of pharmacological actions on the CVS like hypotension, dilatation of both peripheral and coronary vessels and antileukaemic effect etc. **Materials and methods:** Hence it was conceived that the compounds of *Kopsia fruticosa* (KF) may produce some interesting pharmacological actions especially on the cardio-vascular system. The crude extract was prepared from the dried leaves in laboratory and the chief objective of this study was to evaluate the possible effects of both the propylene glycolic (KF1) and the aqueous solution (KF2) of the crude extract of dried leaves of *Kopsia fruticosa.* **Results:** Kopsine, one of the alkaloids obtained from the plant Kopsia fruticosa, possesses cholinergic action. This study on the mean arterial blood pressure and respiration of anaesthetized cats consistently revealed that both KF1 and KF2 induce a dose dependent fall in blood pressure, with slight bradycardia and little stimulatory effect on the respiration. **Conclusion:** Both the solutions, KF1 and KF2 had potent depressor effect on the mean arterial blood pressure of anaesthetized cats.

KEYWORDS: *Kopsia fruticosa*, Kopsine, Fruticosine, cardiovascular effects, mean arterial blood pressure, anaesthetized cat.

INTRODUCTION

It has been reported that most of the indigenous plants having indole alkaloids exhibit a variety of pharmacological actions like hypotension, central nervous system depression, local anaesthesia, dilatation of both peripheral and coronary vessels, antileukaemic effect etc. *Rauwolfia serpentina* is the most potent member of the genus Apocynaceae and the rauwolfia alkaloids have proved to be the most potent hypotensive agent. Also Strophanthin, glycoside derived from the plant Stropanthus kobe produces digitalis like activity on the heart and causes increased force of myocardial contraction and slowing of heart (Kroneberg,1963). It is interesting to note that natives of Africa, long ago used the extract of the seeds of *Stropanthus kombe* as an arrow poison.

Kopsia fruticosa, another member of the Apocynaceae family contains four indole alkaloids. Its pharmacological effects have not been extensively studied Hence it was conceived that the compounds of *Kopsia fruticosa* may produce some interesting pharmacological actions. Although some chemical studies on *Kopsia fruticosa* (KF) have been reported in literature but observation on pharmacological effect either with the chemical substance or of crude extract obtained from the plant could not be traced. Therefore, it was thought worthwhile to study the effect of the crude extract obtained from the leaves of *Kopsia fruticosa,* as described before and designated as KF1 and KF2, on the mean arterial blood pressure and parameters of respiration on anesthetized cats with an idea to obtain preliminary report on the nature of the action of the drug.

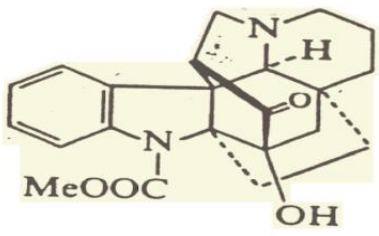

Fig. 1
Showing the chemical structure of Kopsine an alkaloid derived from the leaves of *Kopsia fruticosa*

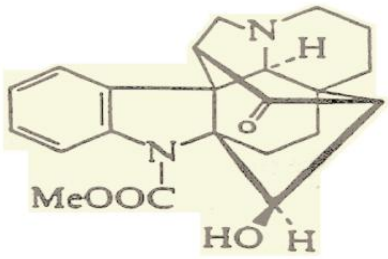

Fig. 2
Showing the chemical structure of Fruticosine another alkaloid derived from the leaves of *Kopsia fruticosa*

Fig. 3 - *Kopsia fruticosa* (KF) plant

MATERIALS AND METHODS

Ethics Clearance

The present work was MD Thesis dissertation work of SM during 1992-94 at the department of Pharmacology, Institute of Post-Graduate Education and Research (IPGMER) and Seth Sukhlal Karnani Memorial Hospital (SSKM), Kolkata. At that time Institutional Animal Ethics Committee (IAEC) was not in vogue and the permission to initiate and continue this research work was granted by the guide Professor Dipankar Bhattacharyya, Head, department of Pharmacology.

Test Drug

Solutions were made from dried total extract of leaves of *Kopsia fruticosa* (fig. 3). The propylene glycolic solution of *K. fruticosa* was designated as KF1 and the aqueous solution of *K. fruticosa* as KF2.

I. Preparation of the extract from the leaves of *Kopsia fruticosa*

Since very few plants are available in our country, the study was carried out mainly with the shed leaves causing no harm to the mother plant. The leaves were dried in open air and crushed by grinders and the total extract was prepared.

The leaves of *Kopsia fruticosa* were provided by the Central Council for Research in Ayurvedic Sciences (CCRS), Kolkata, West Bengal. Solutions for the present study were prepared from the dried total extract of leaves of KF using the Soxhlet apparatus and the propylene glycolic solution of KF was designated as KF1 while the aqueous solution of KF designated as KF2. The crude extract was prepared from the dried leaves in our laboratory. Leaves (1000 g) were first defatted in petrol ether, the petrol ether discarded and the leaves left was soaked in ethanol and acetic acid mixture for 30 days, extracted, evaporated, crushed with 5% citric acid solution and then filtered. The filtrate was washed with petrol ether and benzene, basified with liquid ammonia and extracted with benzene. The benzene extract of free base (alkaloids, fig.1&2) washed with water and dried over anhydrous sodium sulphate and then concentrated and evaporated to dryness under reduced pressure. Total alkaloids (8 g.) were thus extracted.

II. Study on the effect of *Kopsia fruticosa* on the mean arterial blood pressure of anaesthetized cat

This was done following the method of Jackson (1939). Healthy mongrel cats of either sex weighing between 2.5 to 3 kg were used in this study. The animals were starved overnight but water was allowed ad libitum. They were anaesthetized first by placing them in the anaesthesia box and exposed to ether soaked in cotton ball. When it lost its righting reflex it was placed on its back on the operation table. The limbs were stretched and secured by string. The neck was extended by passing a string through the tooth and the head was fixed.

Cannulation of the femoral vein

The femoral vein of right side was exposed. The distal end was tied first and then a transverse cut was made on the vein. A polythene cannula was inserted towards the heart and tied properly so that it could not slip. Normal saline was injected into the cannula to confirm that it is within the vein. The anaesthetic proper (i.e.-chloralose 80 mg/kg body wt. in 2% aqueous solution) was given intravenously. A hypodermic needle was fitted with the cannula for injecting drugs. A constant volume (2 ml) of normal saline was introduced after each injection of drug so that it can push in the drug from the polythene tube.

Tracheal cannulation

A mid line vertical incision was made on the neck muscles, separated and the trachea was exposed. Tracheostomy was done and then a glass tracheal cannula was introduced into the opening points towards the lung and was hold firmly in position by thread passed around it. The purpose of the tracheal cannulation is to allow free breathing without obstruction by secretions which can be cleared up when necessary. Also, artificial respiration can easily be provided when required and by tracheal cannulation we can note the respiratory movements by connecting one end of the glass tracheal cannula to a Marey's tambour.

Cannulation of the Carotid artery

Right common carotid artery in the neck was identified, and separated from its fascia, internal jugular vein and the vago-sysmpathetic trunk. A ligature was given high up in the neck in the common carotid artery. A bull dog clamp was applied and pulled to a place about 3 cm nearer to the heart and the thread was passed round the artery. A small cut was made carefully close to the first ligature and a carotid cannula was introduced through an opening pointing towards the heart and secured tightly in position by thread. The carotid cannula was previously treated with 2 to 3 drops of heparin solution and dried. The cannula was connected to rubber tubing to a Anderson's glass capsule mercury manometer. The spare between the mercury and the artery was made air free and filled with 3.8% sodium citrate solution which served as an anticoagulant. A base line was then taken on a smoked paper and recorded.

RESULTS

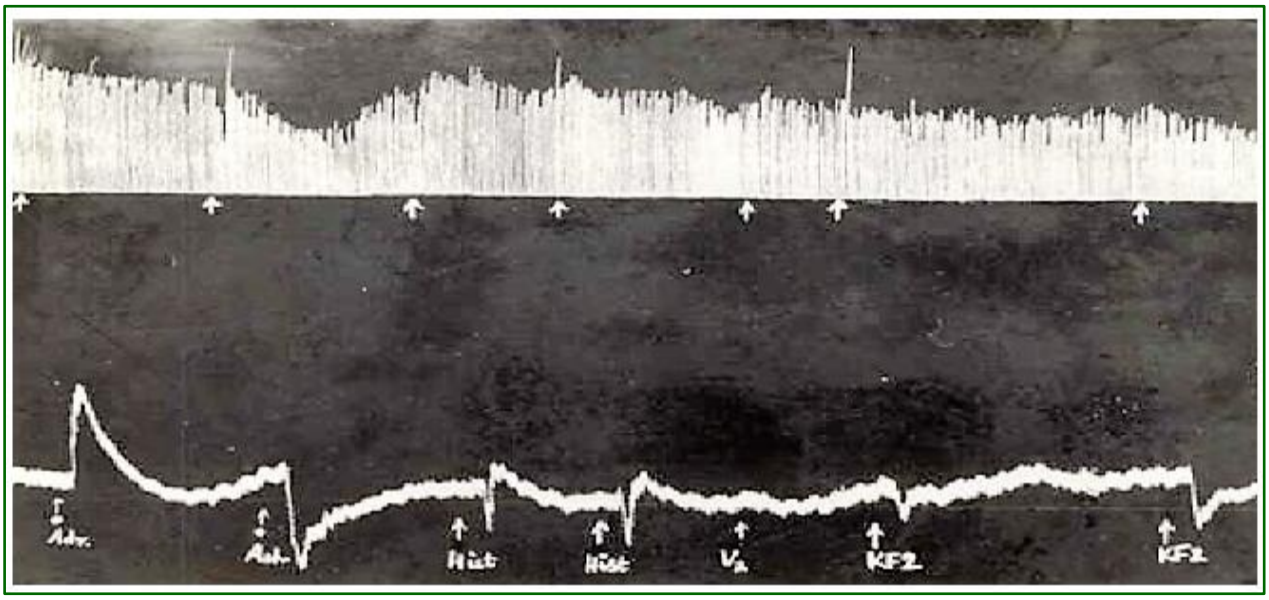

Fig. 4: Showing the effect of KF2 on the mean arterial blood pressure & respiration in anaesthetized cats
Note the dose dependent fall in blood pressure.
N.B. Adr-Adrenaline, Ach-Acetylcholine, Hist-Histamine, V_2-Vehicle (Distilled water, 1 c. c)
KF2- KF2 in dose of 4 &then 8 mg/kg. body wt. I.V.

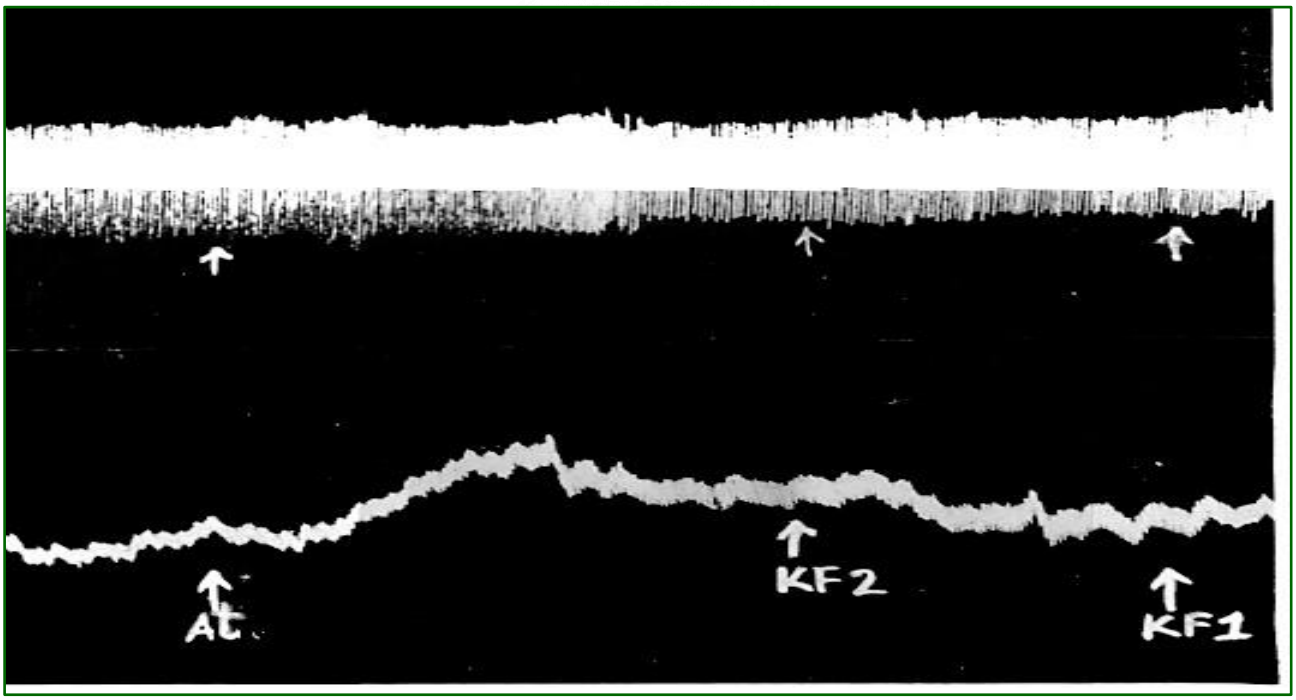

Fig. 5 Showing the blocking effect of Atropine sulphate on Ach and KF2
N.B. At - Atropine sulphate 2 mg/kg. body wt
KF1 & KF2 in doses of 8 mg/kg body weight. I.V.

Observation with crude extract in aqueous solution

It was observed that in 4 out of 5 animals, the acqueous extract KF2 produced a sharp fall in mean arterial blood pressure with gradual return to normal pressure. This depressor effect of the drug is dose related and was blocked by Atropine 2mg/kg body weight I.V. as depicted in Fig.5. There is no significant effect on the respiration after I.V. injection with the drug.

Observation with crude extract in glycolic solution

Prior to the administration of the drug, an equivalent dose of propylene glycol which was used as a vehicle was given through intravenous route. Controlled administration of 0.5 ml of propylene glycol IV produced no change of blood pressure and no change in respiratory movement. KF1 (Glycolic solution of the crude extract) in doses 4, 8, 16 mg/kg body weight produced dose dependent fall in blood pressure but no change in

respiration shown in Fig.4. This depressor effect was blocked by IV Atropine 2mg/kg body weight shown in Fig.5.

DISCUSSION

Although the literature on Kopsia genus is very scanty but from the above review it may be noted that many plants under the Apocynaceae family produce distinct and important pharmacological effects. For example, *Rauwolfia serpentina* is the most potent member of the genus and Muller, Schlittler and Bien in 1952 extracted and isolated reserpine from the *Rauwolfia* alkaloids.[2] It was found to be the most potent hypotensive agent. The antihypertensive effect of reserpine was attributed to reduction in the central sympathetic outflow.[2,3] Studies reported the loss of catecholamine from adrenergic neurons, and the reduction of 5HT content of brain by reserpine.[5-6]

The plant being investigated, i.e. *Kopsia fruticosa,* reported to yield four different alkaloids, isolated from different parts of the plant, all of which have *indole* moiety as basic nucleus. In the field of studies of indigenous plants, several potent pharmacological actions have been attributed to the presence of the indole alkaloids in the extracts of plants. Though reports about pharmacological actions of *K. fruticosa* are scanty, they have been reported to induce cholinergic actions. Paucity in the previous literature regarding *K. fruticosa* alkaloids prompted us to investigate the effects of the extracts of this plant on cardiovascular and respiratory system, as other members of Apocynaceae family have been reported to induce varieties of pharmacological effects like depression of the CNS and CVS, vasodilatation, local anaesthesia and others. [7-8]

Kopsine, one of the alkaloids obtained from the plant *Kopsia fruticosa*, possesses cholinergic action. Studies on the mean arterial blood pressure and respiration of anaesthetized cats consistently revealed that both KF1 and KF2 induce a dose dependent fall in blood pressure, with slight bradycardia and little stimulatory effect on the respiration. This effect on the respiration was not in a dose dependant manner whereas the effect on blood pressure was dose dependant. Moreover, the effect on respiration was not modified when the animal was kept on artificial respiration. Hypotension and bradycardia were both antagonized by atropine and not by anti-histaminic. So the effect may be a cholinergic action which corroborates with earlier report of *K. fruticosa* having cholinergic effect.[7]

CONCLUSION

Both the solutions, KF1 and KF2, produced a significant dose dependant depressor effect on the mean arterial blood pressure, without any significant effect on the respiratory system. Further studies with both the solutions may reveal some interesting pharmacological effects on central nervous system as well to obtain preliminary report on the nature of the action of the drug. In future, further extensive work on *K. fruticosa* may reveal pharmacologically effective and therapeutically useful drugs.

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