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Screening of folklore claim of *Scaevola frutescens* Krause

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In post GATT WTO era, it is essential for every country to develop own drug molecules for self-reliance in drugs and medicine. India has rich biodiversity. Many of the traditionally used medicinal plants have not been exploited / investigated scientifically. The paper presents the pharmacological, phytochemical and pharmacognostical characters of *Scaevola frutescens* Krause leaves, used in traditional and folk medicine.

Keywords: Analgesic activity, Antipyretic activity, Antiinflammatory activity, Cardiovascular activity, CNS depressant activity, Diarrhoea, Dysentery, Hepatoprotective activity, Medicinal plants, Muscle relaxant activity, *Scaevola frutescens* Krause, Traditional knowledge

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In recent times, focus on plant research has increased all over the world and immense potential of medicinal plants used in various traditional systems has been highlighted[1]. Despite its existence and continued use over many centuries, and its popularity and extensive use during the last decade, traditional medicine has not been officially recognized in most countries. Consequently, education, training and research in this area have not received due attention and support. Though data on research in traditional medicine in various countries is available, further research in safety and efficacy is needed. Traditional procedure-based therapies are relatively safe, if they are performed properly[2]. Serious adverse effects of therapies are rare, but supportive data on adverse effects are not readily available. The technological advancements and expanding knowledge in the fields of chemistry, botany and biology have helped in substantiating the value of the medicinal plants. These folklore and traditional claims need to be corroborated by experimental and clinical evidences.

The combinations of biological and chemical screenings provide important information about plant constituents but will not be a sufficient condition for the discovery of potent new drugs, if suitable pharmacological models are not available. It is thus essential to adopt a multidisciplinary approach when working in this field. Efficient collaborations with pharmacologists, medical doctors, plant pathologists and biologists are crucial for the complete development of an interesting lead compound into an exploitable product. The organized research based on traditional and folklore claims has resulted in the discovery of many therapeutically useful products. *Scaevola frutescens* Krause (Goodeniaceae) has been selected to investigate the therapeutically useful product.

In vernacular (Tamil) language, it is known as *Vella muttagam*. Bark, leaves and roots of the plant possess several medicinal and therapeutic properties, but have not been fully investigated. Decoction of the leaves and bark is reported to combat tachycardia, one of the principal symptoms of beriberi, but the plant has not been analyzed for vitamin B1. The drug reduces the frequency of heartbeat, slows down pulse rate and stimulates the heart to normal contraction. Tests with animals and human beings have shown that *Scaevola frutescens* Krause dose not possess the cumulative action of *Digitalis* and can be safely administered in heart conditions in preferences to *Digitalis*. The drug acts as a diuretic by increasing the tension in the renal arteries without causing irritation of the kidney parenchyma. It is reported to be an excellent remedy for dropsy.

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Leaves are bitter and are eaten to relieve indigestion. A poultice made from the leaves is applied to cure headache, tumours and swollen legs. The juice of the berries is used to cure sore eyes. A fruit in the form of a cataplasm are applied to tumours and is taken internally to induce menstruation. Root decoction is used in certain syphilitic affections and dysentery. The pith of the stem is taken to cure diarrhoea. Wood from the basal part is hard and durable in salt water. It is used for making wooden nails or pegs for boats in Malaysia. The pith from stem and thick branches takes dyes well and can easily be made into fancy articles. It is also used for preparing sun-hats and floats and can be pressed flat to make a kind of rice paper[3]. Juice of berries is instilled into the eyes to clear off opacities and take away dimness of vision[4]. No information about ethnomedicinal and biological activities was found[4]. Two species are reported to occur in India[3-4].

Methodology

Scaevola frutescens Krause leaves were extracted separately with methanol by cold maceration method and the extract was suspended in 2% Gum Acacia and used for the experiments. Rats of Wistar strain (100-200 gm) and Swiss albino mice (15-25 gm) of either sex maintained in the Central Animal House, Raja Muthiah Medical College and Hospital at room temperature (25±2ºC), relative humidity 75±5% for 12 hrs, dark light cycle, were used for the experiments. They were allowed to feed on standard diet and water *ad libitum*. The Institutional Animal Ethical Committee approved the experimental protocols.

For anatomical analysis of the vegetative parts of the species, the macroscopy and microscopy of different parts of the plants, location of active constituents by histochemical test (Figs. 1-9) and preliminary phytochemical screening of the leaves were undertaken[6-10]. It is generally believed that each taxon as a biological entity is endowed with specific structure and organization that distinguish it from the other. Acute toxic study and LD_{50} of plant extract was determined by the OECD guidelines. The gross behavioural changes in mice were studied and the effect of drug in skeletal muscle and cardiac muscle was studied in frog rectus and frog's heart, respectively[11-13]. Carrageenan induced antiinflammatory study and antipyretic study was carried out in rats[14-16]. Analgesic effect of the drug was determined by the tail flick method, while the skeletal muscle relaxant activity in mice was studied using Rota-rod apparatus[11,17]. The effect of drug in gastrointestinal tract, anticoagulant, antidiabetic and antimicrobial screening were also carried out[13,16,18-21]. The extract was chromatographed over silica gel (100-200 mesh) and eluted with solvents of increasing polarity, collecting 100 ml each. The corresponding eluates were combined depending on TLC profiles. The identities of the compounds were confirmed by the physical and spectroscopic data and by comparison with authentic samples.

Results and discussion

The oral and intraperitoneal administration of the test extract of *Scaevola frutescens* Krause to the mice up to 2 gm/kg dose neither showed the mortality nor any visible clinical signs of general weakness. But more than 300 mg/kg *Scaevola frutescens* Krause treated groups showed muscle twitching. According to the neuropharmacological profile toxicity was developed at the dose level of 2000 mg/kg. So, the standard dose level was fixed as 300 mg/kg. Behavioural profile of *Scaevola frutescens* Krause indicates skeletal muscle relaxant activity of the plant, but it did not show any central nervous system stimulant or depressant effect. In skeletal muscle of frog, the drug had acetylcholine potentiating effect, but the drug alone had no effect on skeletal muscle. In cardiac muscle, the *Scaevola frutescens* Krause increased the force of contraction but reduced the heart rate. Thus, the drug in cardiovascular system acts as a positive ionotropic and negative chronotropic agent.

Scaevola frutescens Krause at doses of 100 and 300 mg/kg showed a significant reduction in the oedema and the effect was dose-related and comparable with that of indomethacin (10 mg/kg). The plant showed antiinflammatory activity but no analgesic activity was observed. The yeast induced hyperthermia reached a maximum of 38.6ºC in rats. SF at 100-mg/kg dose reached normal body temperature after 3 hrs and the percentage reduction of pyrexia was found to be 72.94%. But, 300-mg/kg dose showed normal temperature at 2 hrs after administration of drug. The maximum percentage reduction was 84.37 and 91.58 after 3 hrs for *Scaevola frutescens* Krause (300 mg/kg) and Paracetamol (100 mg/kg), respectively. So, the comparable antipyretic effect was observed with the standard drug. Presence of alkaloid may be responsible for the antipyretic activity[3, 22]. In *Scaevola*

frutescens Krause treated group (300 mg/kg dose), the fall off time of the animals from Rotarod was 14 and 12 sec at 30 and 60 min, respectively. But at 10 and 100-mg/kg dose level, it was more than 30 sec. SF at 300-mg/kg dose level acts like CNS depressant drug and the effect were comparable to the standard drug Diazepam. The plant drug has been found to be a good skeletal muscle relaxant. During the study of effect of drugs on cilliary movements of frog buccal cavity, SF showed anticholinergic like effect. In 1-1000 µg concentration of *Scaevola frutescens* Krause, the anticoagulant effect of this plant was observed, but at more than 1 mg/ml concentration, it developed clotting immediately after addition of calcium chloride. The anticoagulant activity of the plant may be due to coumarins present in the plant (Table 1).

In streptozotocin-induced diabetic rats, the blood glucose levels were in the range of 400 to 500 mg/kg, which can be considered as severe diabetes. In untreated control group, out of 8 animals, 2 died of diabetes on 2nd day. Among the animals, which survived, blood glucose level was found to be more than 400 mg/dl. In SF treated group, one of the animals died on the 3rd day. In SF (300 mg/kg) treated group, the blood glucose level was 227 mg/dl on the 15th day. In Glibenclamide treated group, the blood glucose level was 131 mg/dl on 15th day and it reached normal range on 18th day. But in the case of SF treated group, it took more than 30 days. The plant drug was found to be less effective compared to Glibenclamide in streptozotocin-induced diabetic model in lowering blood glucose level. The analysis of the results showed that hexane and ethyl acetate extracts showed inhibitory action against *Bacillus subtilis.* Ethyl acetate extract showed activity against *Klebsiella pneumonia*. The extracts were not effective

Table 1—Pharmacolgical screening of *Scaevola frutescens* Krause leaf

Activity	Standard drug	Dose (mg/kg)	Observation	Time in hrs							Time in Days		
				0.3	1	2	3	4	5	6	2	14	30
Acute toxicity	-	5	Mortality								-	-	
		50									-	-	
		300									-	-	
		2000									-	-	
Antiinflamma	Indomethacin	10	Odema		1.2	1.4	1.1	0.9	0.9	0.8			
tory		100	volume		1	1.1	0.9	0.8	0.7	0.6			
		300	(ml)		0.8	0.7	0.6	0.4	0.4	0.2			
		10			0.7	0.7	0.5	0.4	0.2	0.2			
Antipyretic	Paracetamol	10	Rectal		37.9	37.8	37.5						
		100	temperature		38.4	38.1	37.8						
		300	(C)		37.9	37.8	37.5						
		100			37.9	37.8	37.5						
Analgesic	Diclofenac	300	Response time	2	2	2	2.5						
		10	(sec)	7	10	10	10						
Diabetic	Glibenclamide	300	Glucose								491		
		0.6	(mg/dl)								442		
												227	
Skeletal	Diazepam	10	Fall of time	34	37	34						131	
muscle		100	(sec)	31	21	17							
relaxant		300		20	14	12							
		4		9	7	8							
Anticoagulant		1 µg/ml	Clotting		-								
		10	time		-								
		100			-								
		1000											
Cilliary	Neostigmine	1 µg/ml	Cilliary	59	65	76	57	72					
movement		10	movement	55	60	72	58	65					
		0.001	(sec)	32	35	40	36	43					
Antibacterial	Erythromycin	100 µg/ml	Zone of	B. substilis,				K.pneumonia					
		10 µg/disc	inhibition (mm)	8				9					

- No response

Fig .1 *Scaevola frutescens* Krause

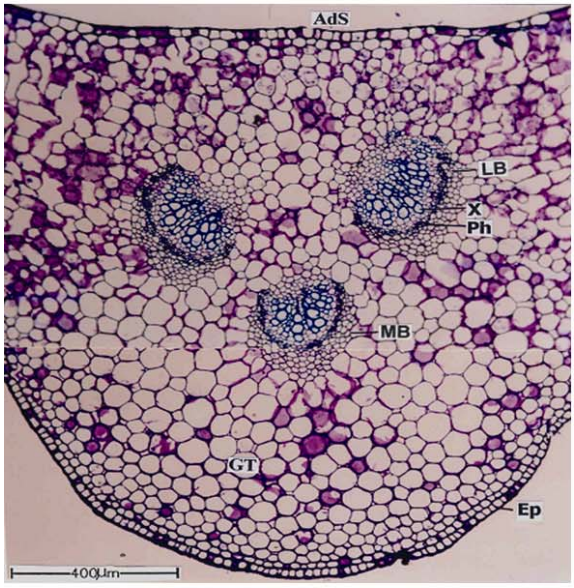


Fig. 3 Anatomy of leaf midrib

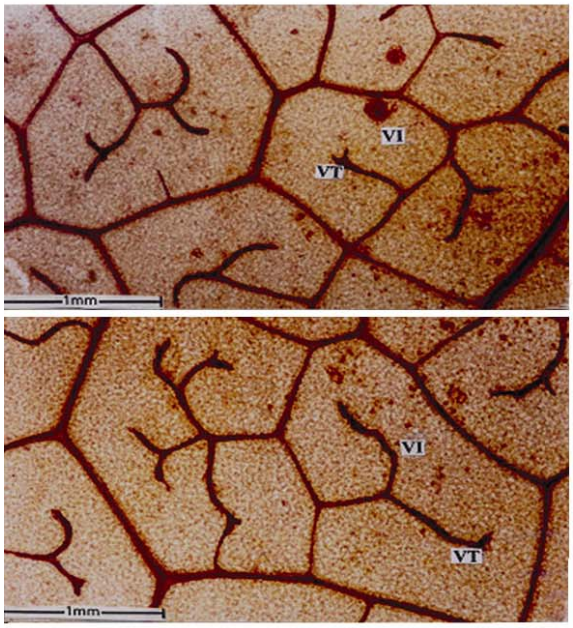


Fig. 4 Venation pattern of the lamina

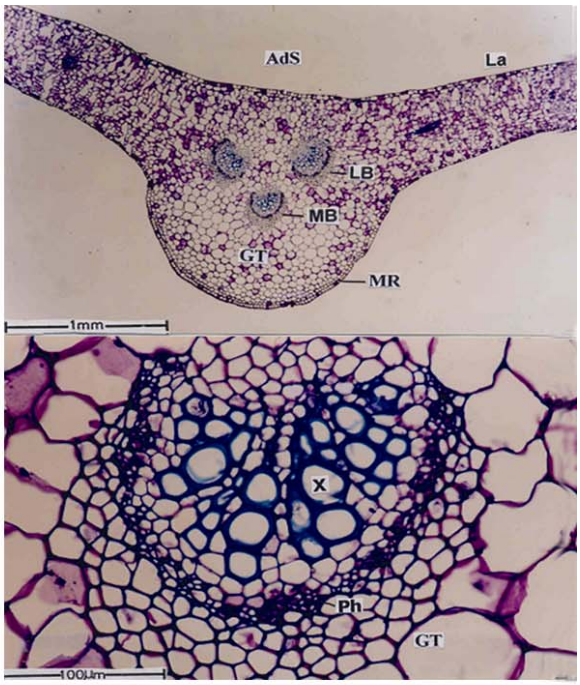


Fig. 2 TS of leaf through midrib

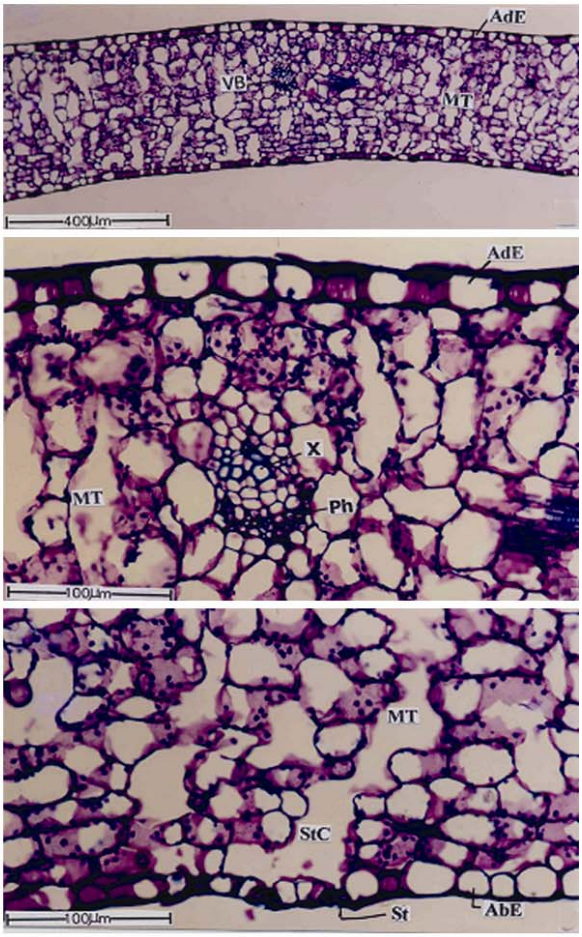


Fig. 5 Anatomy of lamina

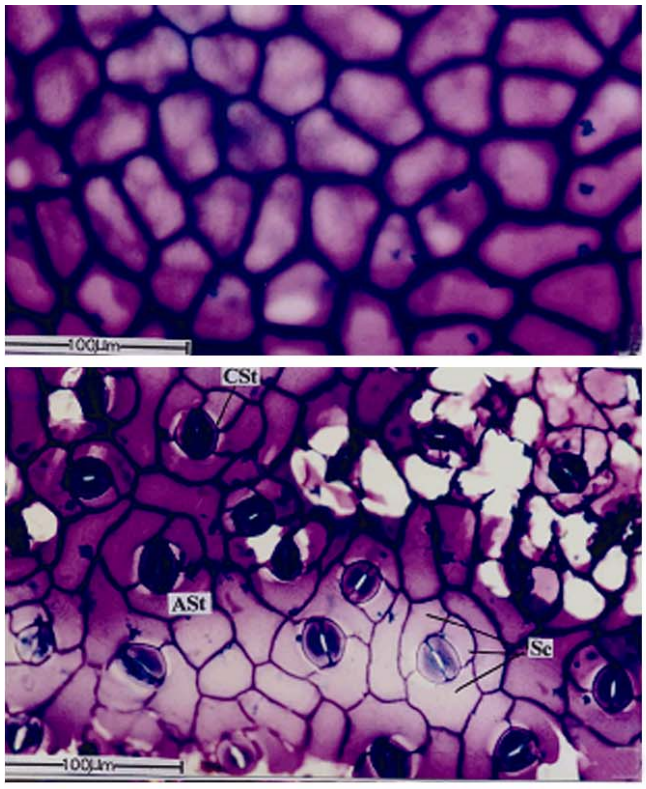


Fig. 6 Epidermal cells and stomatal morphology

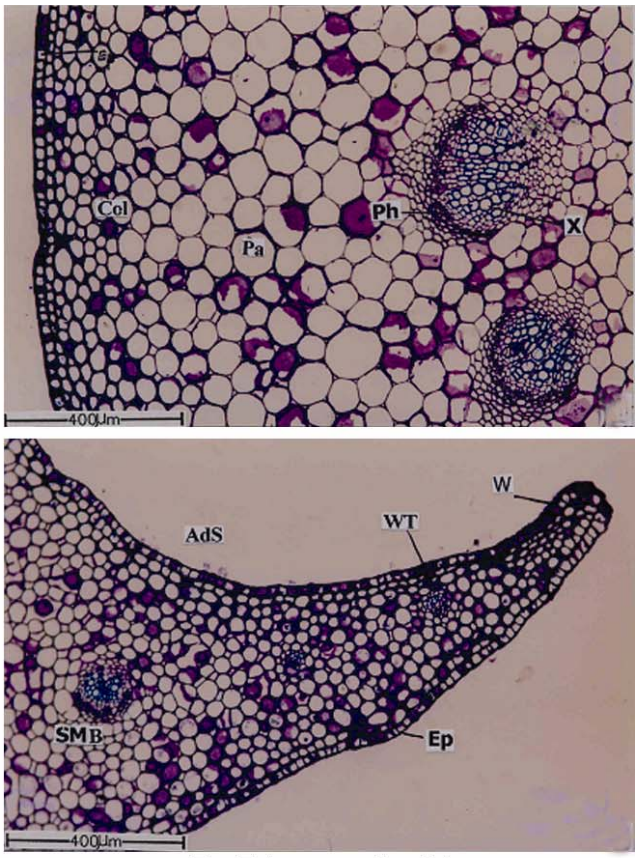
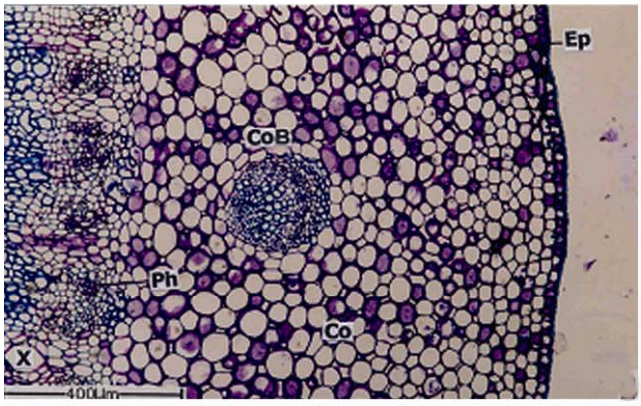


Fig. 7 Anatomy of petiole



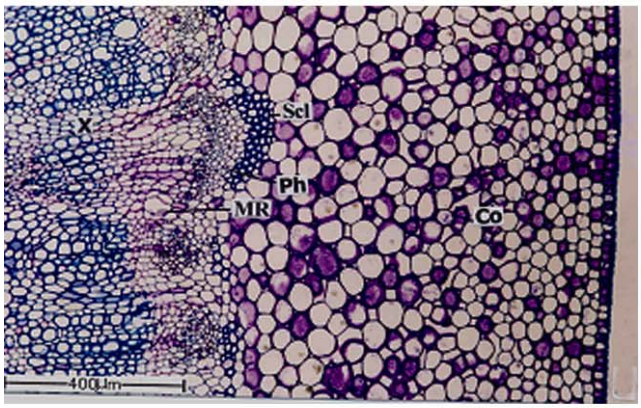
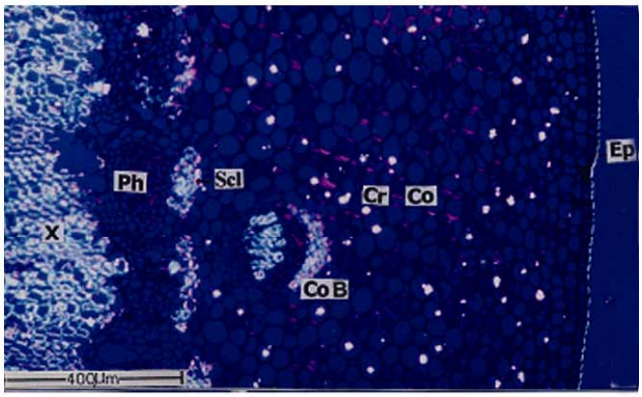


Fig. 8 TS of Stem



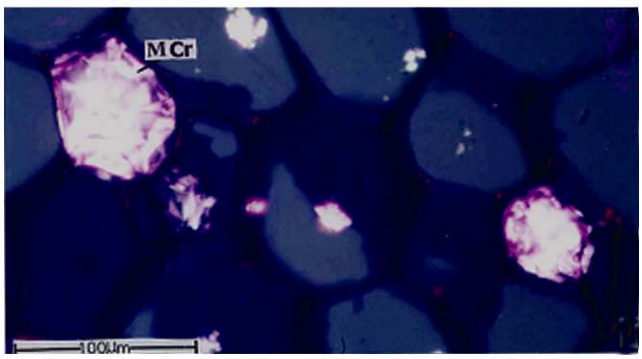


Fig. 9 Crystal distribution of stem

against other organisms tested. The methanolic extract did not show any antibacterial effect against tested organisms. Ethyl acetate extract (100 µg/ml) exhibited inhibitory action against *Candida albicans* and the zone of inhibition was similar to the standard drug Clotrimazole (100 µg/disc) and it did not have inhibitory action against other organisms tested. Thus, *Scaevola frutescens* Krause exhibited both antibacterial and antifungal activity.

Diagnostic features from pharmacognostic study were recorded. Midrib was planoconvex with prominently projecting abaxial side. Three vascular bundles of the midrib were noticed. Lamina was even and glabrous; thick and succulent; epidermal layers were unistratose; hypostomatic. Adaxial epidermal cells were polygonal, thick and straight walled. Abaxial epidermal cells were thin walled, straight and stomatiferous. Stomatal type anisocytic were found; occasionally cyclocytic. Mesophyll tissue not sharply differentiated into palisade cells and spongy mesophyll cells. Stem cortex broad and parenchymatous; pith wide, homogeneous and parenchymatous. Vascular cylinder consisted of wedge - shaped discrete vascular bundles separated from each other by narrow medullary rays. Vascular bundles were collateral with sclerenchymatous bundle cap. Inverted cortical bundles were seen in the stem. Petiole was thick with an arc of several vascular bundles extending up to the margins of the wings; two accessory adaxial bundles were present on the upper part of the petiole. Calcium oxalate crystals of druses and sphaeroidal types were fairly abundant in the ground cells of the stem. Histochemical studies revealed the presence of protein, alkaloid and phenolic compounds in leaf.

β-Sitosterol-β-D-glucoside, mannitol was isolated and has been reported for the first time from the plant. Imperatorin, marmesin coumarins were also isolated from this plant[23].

Conclusion

Based on findings of the study, the indigenous knowledge of the traditional and folklore claims has resulted in the discovery of many therapeutically useful products. This plant has been proved as an excellent remedy as antidiabetic, antipyretic, antiinflammatory, anticoagulant and as skeletal muscle relaxant. Hence, such indigenous knowledge can be gainfully blended with the modern scientific knowledge to evolve therapeutically useful product, without any adverse reactions.

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