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EVALUATION OF ANTIHYPERTENSIVE ACTIVITY ON AQUEOUS LEAVES EXTRACT OF *MURRAYA EXOTICA* LINN. IN RENAL ARTERY OCCLUDED HYPERTENSIVE RATS

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ABSTRACT

Aqueous extract of *Murraya exotica* Linn. (Family: Rutaceae) was evaluated for its antihypertensive activity in renal artery occluded hypertensive rats. Male Wistar rats (180-200g) were pretreated with aqueous extract of *Murraya exotica* for 6 weeks. Hypertension was induced in animals by clamping the renal artery with renal bulldog clamp for 4 h. Ischemia of the kidneys causes elevation of blood pressure by activation of the renin-angiotensin system. Elevated blood pressure of the animals was significantly (p<0.05) decreased by the aqueous extract of *Murraya exotica* at the dose levels of 25, 50 and 100mg/kg, *i.v.* Captopril, angiotensin converting enzyme inhibitor (ACE-I) at the dose of 1 mg/kg, *i.v.* showed significantly (p<0.05) reduced in the elevated blood pressure. The antihypertensive activity of aqueous leaf extract of *Murraya exotica* may be due to the action on rennin-angiotensin system.

KEYWORDS: *Murraya exotica*, antihypertensive activity, rennin-angiotensin system.

INTRODUCTION

Cardiovascular diseases account for 12 million deaths, annually worldwide and are known to be number one group of 'killer disease'. Hypertension is one of the leading causes of disability, mortality and morbality along the populance. It is the most common chronic illness among the world faces.[1,2] Hypertension is the most common cardiovascular diseases and

constituents a major factor for several cardiovascular pathologies including atherosclerosis, coronary artery disease, myocardium infract, heart failure, renal insufficiency, stroke and dissecting aneurysm of aorta.[3] An elevated arterial pressure is an important public health issue in developed countries. Although it is common, asymptomatic and readily detectable but it can often lead to lethal complication, if left untreated. Because of high incidence and morbidity, various drugs and regimes have been advocated for the control of hypertension. Many new drugs have been introduced which may demonstrate better efficacy but posses side effects. Recently attention has been focused towards herbal and mineral preparations which are traditionally used as potential therapeutic agents in the prevention and management of cardiovascular diseases.[4] *Murraya exotica* Folkloric Decoction of dried material (3 - 9 gms) or 0.3 - 0.9 gm of pulverized material by mouth with water: Used for gas pains. swelling pain due to sprain and contusions, rheumatic bone pain and poisonous snake bites, Poultice of fresh leaves used for swelling due to sprain and contusions; poisonous snake bites, infusion of leaves used as tonic; also used for diarrhea and dysentery, Decoction of leaves also used as mouthwash for toothaches, Infusion of leaves and flowers is tonic and stomachic, Leaves and root bark used for rheumatism, cough and hysteria, Used for abscesses, cellulitis, tapeworm disease, rheumatic fever, coughs, giddiness, hysteria, thirst and burning of the skin. Reported activities are Antiplatelet Aggregation.[5] Antiamoebic Activity.[6] Anti-Giardial Activity.[7] Insecticidal Activity, Essential Oil Composition.[8] Antinociceptive.[9] Antidiabetic/Antioxidant.[10] Antifungal12, Antibacterial.[11] Analgesic.[13] Antifertility.[15] Hypoglycemic.[16] 2′-O-ethylmurrangatin/Lipoxygenase and Respiratory Burst Inhibition.[14] Constituents - Leaves yield a volatile oil, 0.01%, with cadinene and sesquiterpene. Flowers yield murrayin (glucoside), murrayetin, and indol, Study yielded alkaloids, tannins, cardiac glycosides and saponins, Study yielded eight highly oxygenated flavones, identified as gardenin A, gardenin C, gardenin E, 5-O-desmethylnobiletin, umhengerin, 5,3--dihydroxy-6,7,4'5'--tetramethoxyflavone and new compound, 5,3',5'-trihydroxy-6,7,4'-trimethoxyflavone, Study reported nine coumarins from the aerial parts of the plant. of these three – murrmeranzin, 1'2'-O-isopropylidene murrangatin and murralonginal are new; one, pranferin was reported for the first time from the plant, Study yielded flavonoids, indole alkaloids, coumarins.[17]

MATERIALS AND METHOD

Plant Material and reagents

The fresh leaves of *Murraya exotica* were collected from in local area of warangal and identified by Dr. Raju, Department of Botany, Kakatiya university warangal, telangana, India.

Preparation of plant extract

Air dried coarsely powdered plant material was extracted with water for 48 hours by maceration. Thus obtained water extract were filtered and vacuum dried using vacuum flash evaporator to yield the solid residue of 8.8% respectively to the starting dry powder.

Experimental animals

Male Wistar rats (180–200g) and Swiss albino mice (20- 22g) of either sex were purchased from mahavir enterprises Hyderabad. They were housed in polypropylene cages in a controlled room temperature 22±1°C and relative humidity of 60–70%. They were kept under standard conditions of 12/12 h light and dark cycle. The animals were maintained with standard pellet diet and water *ad libitum*. The animals were acclimatized to laboratory condition for even days before commencement of experiment. All studies were carried out using 6 rats in each group. Ethical clearance was obtained from Institutional Animal Ethical Committee (IAEC).

Chemicals and instrument

Urethane was purchased from Hi media Pvt. Ltd. India. Captopril (ACETEN, WOCKHARDT), 12.5mg tablet as procured from local market. All the chemicals used for the study were of analytical grade. Eight-channel recorder powerlab (AD Instruments) system was used for the measurement of blood pressure.

Acute oral toxicity study

Acute oral toxicity study of aqueous extract *Murraya exotica* was carried out in Swiss albino mice of either sex (20-22 g) according to OECD guidelines no 423. Extract at different doses up to 2000 mg/kg, *p.o.* was administered and animals were observed for behavioural changes, toxicity and mortality up to 48 h.[18-19]

Antihypertensive activity[20-21]

Male wistar rats were divided into the 6 groups each group had six animals. Animals in normal control and negative control groups received distilled water. Aqueous leaf extract of *Murraya exotica* was administered orally at the dose levels of 250, 500 and 1000mg/kg to the treatment groups for six week. At the end day of treatment, animals were anaesthetized by intraperitoneal injection of 1.25 gm/kg of Urethane. A small incision was given on the left side of peritoneal cavity of the animal to expose left kidney. The renal artery was occluded for the 4 h by using renal bulldog clamp. The jugular vein was cannulated for the administration of test drug. The carotid artery was cannulated to measure the blood pressure and connected to the blood pressure transducer of power lab eight channel recorder power lab. After stabilization blood pressure, the renal bulldog clip was removed. Then $1/10^{th}$ of the administered dose of the *Murraya exotica leaf* aqueous extract, i.e. 25, 50, and 100 mg/kg was given respectively through jugular vein and mean arterial blood pressure (MABP) was measured at different time intervals (5,15,30,60 min). MABP of normal control groups were recorded without clamping the renal artery. Captopril mg/kg, *i.v.* was used as a standard. Changes in blood pressure of treated groups were compared with negative control.

Statistical Analysis

The results are expressed as the mean± SEM for each group. Statistical differences were evaluated using a oneway analysis of variance (ANOVA) followed by Dunnett´s test. Results were considered to be statistically significant at $p<0.05$.

RESULTS

The evaluation of aqueous leaf extract of *Murraya exotica* Animals treated with aqueous extract *Murraya exotica* didn't showed any behavioural changes, toxic reaction or mortality. The extract was found to be safe at the dose of 2000mg/kg. Removal of renal bulldog clip in the negative control group resulted in significant ($p<0.05$) increase in MABP (Table 1). Pre-treatment of animals with *Murraya exotica* aqueous leaf extract 25, 50 and 100 mg/kg *i.v.* showed significant decrease ($p<0.05$) in the MABP at different time intervals (Table 1). Captopril (1mg/kg *i.v.*) produced significant reduction in MABP. The hypotensive effect was maximum after 60min.

Table No.1: Effect of aqueous leaf extract of *Murraya exotica* on renal artery-occluded hypertensive rats.

Groups	Mean Arterial Blood Pressure Groups (MABP) in mmHg at different time interval Treatment					
	Treatment (mg/kg)	MABP after removing clip	5 min	15 min	30min	60min
Normal control	Distilled water, *p.o.*		83.33±5.92	85.83±4.89	84.83±6.31	86.83±5.89
Negative control	Distilled water, *p.o.*	126.45±6.35	116.16±4.57@	118.83±2.79@	105.33±4.65@	102.33±6.10@
Murraya exotica	25, *i.v.*	122.56±5.20	74.00±5.75*	76.33±4.44*	70.33±5.91*	69.00±4.81*
Murraya exotica	50, *i.v.*	115.76±6.53	71.66±4.35*	69.50±4.66*	67.50±4.86*	71.33±6.64*
Murraya exotica	100, *i.v.*	117.53±3.56	62.50±6.62*	62.50±7.59*	60.16±6.21*	60.50±6.97*
Captopril	1, *i.v.*	121.89±4.80	50.66±2.34*	39.16±4.08*	34.50±3.86*	26.83±3.50*

Values in the results are expressed as mean± SEM, (n=6), @ $p<0.05$ significantly different in comparison with Normal control, *$p<0.05$ significantly different in comparison with Negative control.

DISCUSSION

Present study revealed the significant antihypertensive activity of aqueous leaf extract of *Murraya exotica* in renal artery occluded hypertensive rats. The occlusion of renal artery upto 4 hour, leads to cause kidney ischemia. Ischemia of the kidneys causes elevation of blood pressure by activation of the renin-angiotensin system. The procedure can be used for acute and chronic hypertension. Acute renal hypertension can be induced in rats, by clamping the left renal artery for 4 h. After reopening of the vessel, accumulated renin is released into circulation.[20] Renin acts on angiotensinogen (renin substrate), an α2-globulin to release the decapeptide angiotensin I. This decapeptide is cleaved by angiotensin converting enzyme (ACE) to yield the active angiotensin II (octapeptide) which is a potent vasoconstrictor leading to hypertension. Angiotensin II undergoes hydrolysis by an aminopeptidase to yield the heptapeptide angiotensin III which is also active. Further cleavage yields to peptides with little activity.[22] The protease renin catalyzes the first and rate-limiting step in the formation of angiotensin II leading to acute hypertension. The test is used to evaluate antihypertensive activities of drugs. The results showed that, intravenous injection of aqueous extract of *E. ganitrus* seeds significantly ($p<0.05$) decreased the elevated blood pressure in dose dependent manner. Captopril, ACE-I at the dose of 1 mg/kg, *i.v.* showed the significant ($p<0.05$) decrease in the elevated blood pressure. The extract differed from captopril in respect of the

potency. After a sharp fall in MABP at 5 minute a stable baseline was observed whereas progressive decrease in MABP was shown by captopril. The drastic fall in MABP after 1 hour may precipitate reflex tachycardia and compensatory increase in sympathetic tone. The extract appears to be free from such hypertensive effect. The antihypertensive activity of aqueous leaf extract of *Murraya exotica* may be resulted through the action on rennin-angiotensin system.

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