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AN EXPERIMENTAL EVALUATION OF THE EFFECT OF RUDRAKSHA (*ELAEOCARPUS GANITRUS* ROXB) IN ADRENALINE AND NICOTINE INDUCED HYPERTENSION.

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***ABSTRACT* :** This study highlights the effect of Rudraksha (*Elaeocarpus ganitrus* Roxb) in experimentally induced acute hypertension by adrenaline and nicotine. Study was done in 6 anaesthetised cats having similar body weight and age. 90 % Ethanol extracts of *Elaeocarpus ganitrus* Roxb was given intravenously to cats. Blood pressure was measured by using **Pressure transducer** and Polyrite (INCO). *Elaeocarpus ganitrus* (Roxb) reduces adrenaline induced hypertension and also normal blood pressure; but it is not effective in nicotine induced hypertension. The effect of the drug was found when the water soluble portion of the extract was given to cats in a dose of 15mg / kg body weight.

INTRODUCTION

In the 19th and 20th centuries the inert sciences have been advancing rapidly. But the biological sciences have been progressing slowly. However more scientific instruments and new technologies for diagnosis and assessment have been invented in this period. In this new era, evaluation of efficacy of Ayurvedic drugs on a scientific basis is very important. Here in this study, Rudraksha has been taken for experimental study in hypertension. Ayurvedic physicians claim to have used decoction made from fruit of Rudraksha successfully in mental diseases, epilepsy, asthma, arthritis, fainting collapse, dropsy and in clinical conditions simulating the modern concepts of high blood pressure (Chopra et. Al.1956, Nadkarni 1954, Sharma1978). Blood pressure is the result of cardiac output and peripheral resistance. Hypertension is a universal health problem. In modern pharmacopeia, though there are so many potent antihypertensive drugs, it is still necessary to evaluate the antihypertensive efficacy of herbal drugs experimentally. For this experimental study, alcoholic extract has been isolated and used in animals induced with hypertension. Hypertension runs a chronic course in human beings. But in this experimental study, chronic hypertension could not be induced in experimental animals. This experimental study was done by inducing acute hypertension with some hypertensive agents. To induce acute hypertension, nicotine (BDH, UK) and adrenaline (Vulcan lab, Kolkata) has been used.

Nicotine (C_{10} $H_{14}N_2$) is a natural alkaloid isolated from tobacco. [1-methyl 1-2-(3-Pyridyl]. It is seen that when nicotine is administered through I/V route, there was immediate transcient fall of blood pressure followed by tachycardia and sustained hypertension. (Armitage & Hall, 1969, Zapata et. Al 1976, Koleyet 1987). Nicotine stimulates the sympathetic ganglia and adrenal medulla causing release of chemoreceptors of aortic and carotid bodies which reflexly results in vasoconstriction, tachycardia and elevation of blood pressure. Though some scientists (Hall & Reit 1996) suggested the cause of hypertension in anaesthetized cat was due to peripheral action of nicotine. pharmacological and cardiovascular effect of nicotine is very complex and wide spread. (Armitage et.al 1969).

Adrenaline synthesized and secreted by adrenal medulla is a tyrosine derivative. Its secretion is initiated by acetylcholine, released from preganglionic neurons that innervate the secretory cells. The acetylcholine increases the permeability of the cells and Ca++ enters from extra cellular fluid triggering exocytosis. It acts on α– receptors and *ß* – receptors of the effectors organ. Due to *a* – receptors, activity of adrenaline and blood pressure are raised, and cardiac muscle becomes excited. The total peripheral resistance is increased due to vasoconstriction in the skin and splanchnic area, causing decrease in total vascular capacity of the body.

MATERIALS & METHODS

1. Animal preparation or application and maintenance of anaesthesia

Cats were chosen as experimental animals. Six adult cats of either sex having body wt. 2-3 kg were collected. After induction with ether, the animal was placed on the operation table in supine position and was secured to the table by means of strings. *a* – chloralose at dose of 60mg/Kg body weight was used as anaesthetizing agent. A maintenance dose of 10mg/kg body weight of a chloralose was given when required to maintain anaesthesia.

Surgical Procedure

A polyethylene catheter fitted with a three way stop cork was introduced into the femoral vein to administer drug, saline and anaesthetics. Glucose saline (5%) was administered into the femoral vein slowly to maintain body fluid and electrolyte balance.

A low tracheostomy was performed by giving midline incision on the ventral surface of the neck and a 'T' shaped polyethylene or glass cannula was inserted into the trachea in order to allow free breathing and also for artificial ventilation (if required) with Starling's ideal respiratory pump.

A polyethylene catheter as fitted with a pressure transducer was introduced into the femoral artery in order to record blood pressure.

1.2 Recording of blood pressure ; extract preparation, and drug administration.

Recording of blood pressure

Blood pressure was recorded on an INCO polyrite through "Bell & Howell" transducer. The pressure transducer was connected to the INCO polyrite. All care was taken that animals could breathe normally. The body temperature was maintained at $37^{o}\pm 0.5^{o}C$ throughout.

Preparation of Extract

Dried fruit of Rudraksha (Elaeocarpus ganitrus Roxb) was identified pharmacognostically and authenticated. The shade dried fruits of Elaeocarpus ganitrus, Roxb were powdered. 200 gms of the drug was soaked in 90% ethanol for 48 hours. Percolation was done through suction by Sauxlet apparatus. Filtration was repeated through Whatman filter paper No-4 and the filtrate was air dried. The dried extracts were stored in screw cap vials at 4°C until further use. The yield of the drug was 05.83% (W/W interms of dried starting material), here after the drug is referred to as E.g.-90.

Drug Administration

The extract E.g – 90 was taken for I/V use. The water soluble portion of the ethanol of E.g. – 90 was injected in dose of 15mg/kg body wt. The control drug nicotine (BDH,UK) and adrenaline (Vulcan lab, Kolkata) was diluted in normal saline (0.9 gm % Nacl) and injected I/V in a dose of 10µg/kg body wt. through femoral venous cannula, effects were recorded on and also in pretreated animal by E.g. -90. The effect of drug was taken by pen recorder on INCO polyrite.

1.3 Statistical Analysis of Data :

Results are expressed as **MEAN ± SEM.** Significance test was performed by using students 'T' test.

Results

I/V administration of water soluble portion of 90% ethanol extract of Elaeocarpus gantitrus Roxb in a dose of 15mg/kg body wt. in anesthetized cat causes fall of blood pressure. Initial average mean blood pressure was 86.94 ± 0.95 mmHg, which decreases to 73.43 ± 2.56 mmHg. The fall of B.P was statistically significant at ($p<0.001$) (Table - 1).

Sl. No. of Observation n=6	MEAN BLOOD PRESSURE	
	Initial Control A	With E.g. 90 15 mg/kg B.WI/V B
AVERAGE ± SEM	86.94 ± 0.95	73.43 ± 2.56 a ***

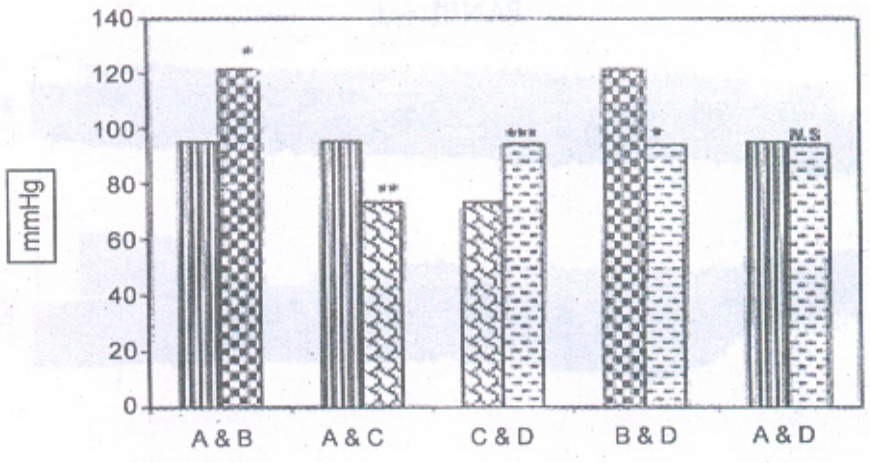
*** indicates $p<0.001$
a = compared in between A & B

Table - 2 Mean blood pressure in anaesthetised cat before and after treatment with adrenaline and with E.g - 90.

Sl. No. of Observation n=6	MEAN BLOOD PRESSURE			
	Initial Control A	With adrenaline 10µg/kg B.WI/V B	With E.g. 90 administration 15 mg/kg BW I/V C	Adernaline in E.g. 90 pretreated animal D
AVERAGE ± SEM	95.27 ± 5.49	121.44 ± 9.44 a*	73.43 ± 2.56 b**	94.22 ± 3.59 c ***d*e**

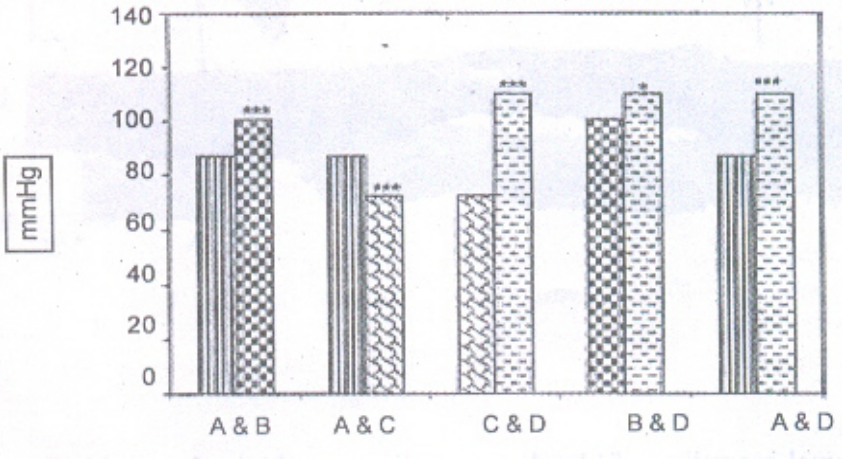
* indicates $p<0.05$
** indicates $p<0.01$
*** indicates $p<0.001$
ns - not significant
a = compared in between A & B
b = compared in between A & C
c = compared in between C & D
d = compared in between A & D

I/V administration of Adrenaline 10µg/kg B.W induces hypertension. The initial average mean blood pressure was 95.27± 5.49 mm Hg which increases to 121.44± 9.44. The increase of blood pressure ($p<0.05$) is statistically significant. I/V administration of aqeuous solution of E.g-90, 15mg/kg B.W causes fall of B.P, initial average mean blood pressure 95.27 ± 5.49 mm Hg decreases to 73.43±2.56 mm Hg. The fall of blood pressure is statistically significant ($p<0.001$). But I/V administration of a drenaline 10µg/kg B.W in pretreated cat with E.g-90 causes significant increase of mean B.P. The mean BP after E.g-90 administration was 73.43 ± 2.56 and increased to 94.22±3.59 which was statistically significant ($p<0.001$). (Table - 2); and does not cross the initial control mean B.P.



A = Initial (control) C = E. ganitrus (15mg/kg.) * $p<0.05$ *** $p<0.001$
B = Adrenaline (10µg/kg.) D = E. ganitrus + Adrenaline ** $p<0.01$

Fig - 1 Effect of E. ganitrus Roxb on mean blood pressure in anaesthestised cat before & after treatment with Adrenaline and E.ganitrus Roxb.



A = Initial (control) C = E. ganitrus (15mg/kg.) * $p<0.05$
B = Nicotine (10µg/kg.) D = E. ganitrus + Nicotine ** $p<0.001$

Fig - 2 Effect of E. ganitrus Roxb on mean blood pressure in anaesthetised cat before & after treatment with adrenaline and E.ganitrus Roxb.

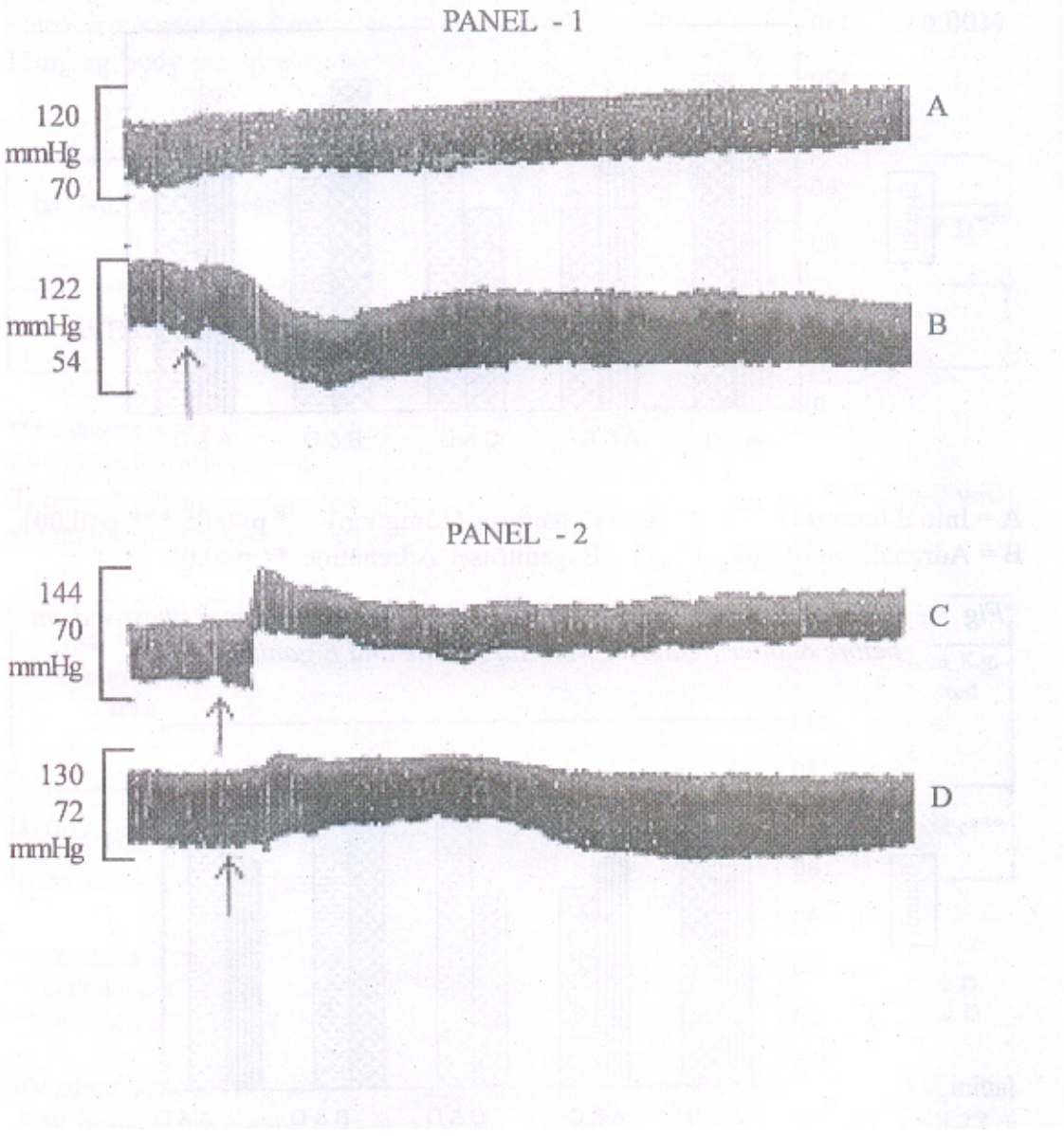


Fig : 3 Typical recording of blood pressure in anaesthetized cat with E. ganitrus. Panel – 1 shows the resting normal B.P (A), pressure on application of E. ganitrus (15 mg/kg B.W) (B). Panel II shows the effect of adrenaline 10µg/kg B.W in anaesthetized cat (C), after pretreatment with E. ganitrus (D) Arrow indicates the point of application of drug.

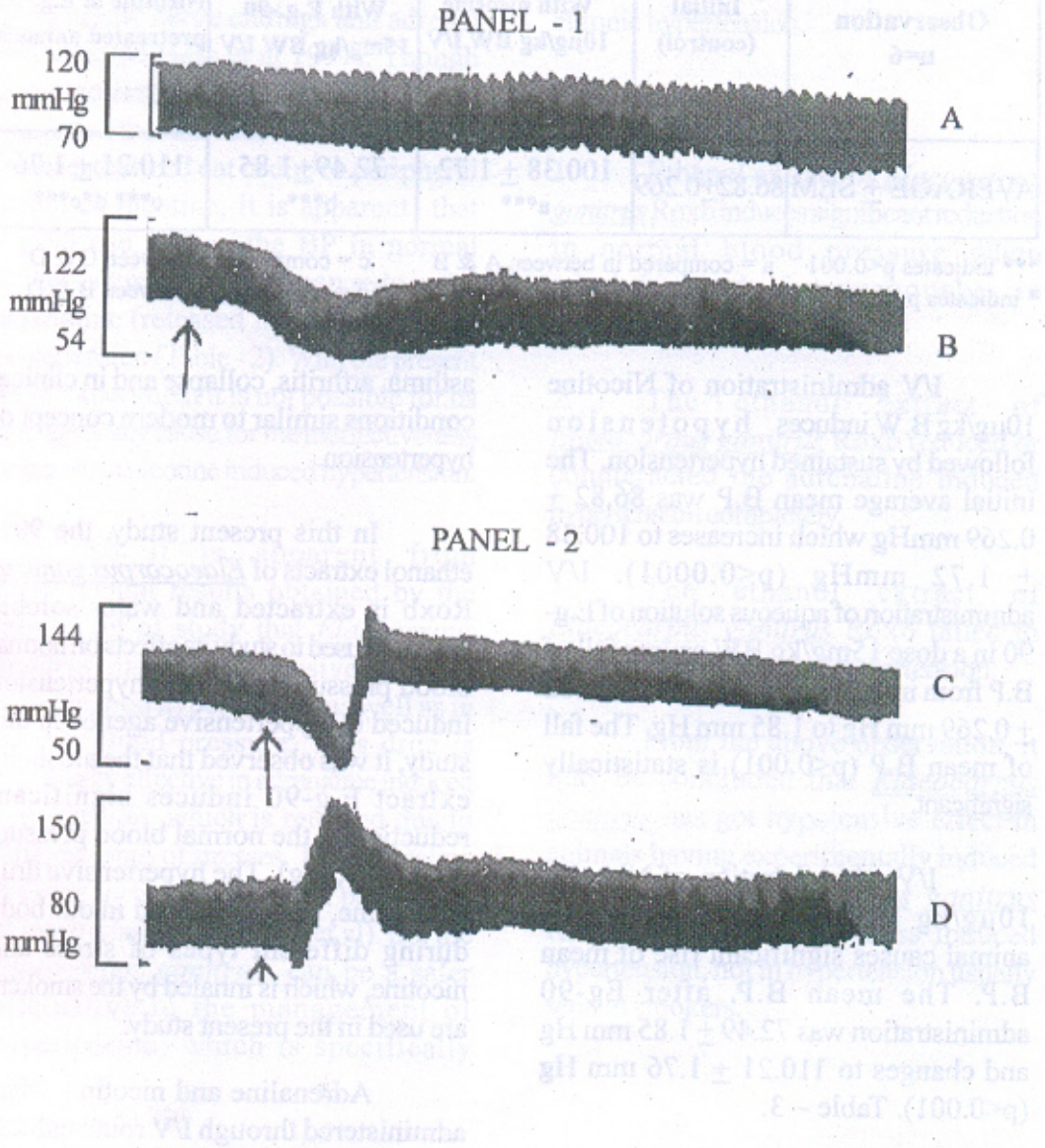


Fig : 4 Typical recording of blood pressure in anaesthetised cat with E. ganitrus. Panel – I shows the resting normal B.P(A), pressure on application of E.ganitrus (15mg/kg B.W) (B).Panel II shows the effect of nicotine 10µg/kg B.W in anathesthetised cat (C), after pretreatment with E. ganitrus (D). Arrow indicates the point of application of drug.

Table - 3:- Mean Blood Pressure in anaesthetised cat before and after treatment with nicotine & E.g-90

Sl. No. of Observation n=6	MEAN BLOOD PRESSURE			
	Initial (control)	**With nicotine 10µg/kg BW I/V**	**With E.g.90 15 mg/kg BW I/V**	**Nicotine in E.g.-90 pretreated animals**
AVERAGE ± SEM	86.82 ± 0.269	100.38 ± 1.72 a***	72.49 ± 1.85 b***	110.21 ± 1.76 c ***d*e**

*** indicates p<0.001
* indicates p<0.05

a = compared in between A & B
b = compared in between A & C
e = compared in between A & D

c = compared in between C & D
d = compared in between B & D

I/V administration of Nicotine 10µg/kg B.W induces hypotension followed by sustained hypertension. The initial average mean B.P was 86.82 $\pm$ 0.269 mmHg which increases to 100.38 $\pm$ 1.72 mmHg ($p<0.0001$). I/V administration of aqueous solution of E.g-90 in a dose 15mg/kg BW causes fall of B.P from initial average mean B.P 86.82 $\pm$ 0.269 mm Hg to 1.85 mm Hg. The fall of mean B.P ($p<0.001$) is statistically significant.

I/V administration of Nicotine 10µg/kg BW in E.g-90 pretreated animal causes significant rise of mean B.P. The mean B.P. after Eg-90 administration was 72.49 $\pm$ 1.85 mm Hg and changes to 110.21 $\pm$ 1.76 mm Hg ($p<0.001$). Table – 3.

DISCUSSION

Elaeocarpus ganitrus Roxb (Rudraksha) used by Ayurvedic physicians claims to have effects in the treatment of mental diseases, epilepsy, asthma, arthritis, collapse and in clinical conditions similar to modern concept of hypertension.

In this present study, the 90% ethanol extracts of *Elaeocarpus ganitrus* Roxb is extracted and water soluble portion is used to study its effects on normal blood pressure as well as hypertension induced by hypertensive agents. In this study, it was observed that the alcoholic extract E.g-90 induces significant reduction in the normal blood pressure (Table – 1, Fig). The hypertensive drug adrenaline, that is released in our body during different types of stress and nicotine, which is inhaled by the smokers are used in the present study.

Adrenaline and nicotine, when administered through I/V route induces significant increase of BP in normal control animals (cats). Adernaline failed to induce any hypertension in animals pretreated with E.g-90. But nicotine induces even more hypertension (statistically significant) in E.g-90 pretreated animals. (Table – 2 Fig)

Nicotine is a natural alkaloid isolated from tobacco and stimulates sympathetic ganglia and adrenal medulla causing release of catecholamine from sympathetic nerve endings and adrenal medulla. (M.Hass et.al 1997). Though some scientists (Hall & Reit 1966) suggested that the cause of hypertension in anaesthetized cat is due to peripheral action of nicotine, it is apparent that E.g-90 can reduce the BP in normal control animals and also can reduce the adrenaline (released in stress) induced Hypertension (Table - 2). With the present set of experiment it is not possible for us to

suggest any cause for the ineffectiveness of E.g-90 in nicotine induced hypertension.

So it is apparent from experimental results obtained by the present set of study that *Elaeocarpus ganitrus* has got hypotensive effect on experimental hypertension as well as in normal blood pressure. This drug is specifically effective in adrenaline induced hypertension, which is released due to different types of stresses. The adrenaline is a primary in vivo factor for production of hypertension. (Robert J.et.al). So, the *Elaeocarpus ganitrus* can be a safer alternative in the management of hypertension, which is specifically developed due to different types of mental stress.

In this present study, there was no scope for studying the effect of the drug in chronic hypertension.

Conclusion

1. Ethanol extract of *Elaeocarpus ganitrus* Roxb induces significant reduction in normal blood pressure when administrated intravenously in anaesthetized cats.

2. The ethanol extract of *Elaeocarpus ganitrus* Roxb reduced or counteracted the adrenaline induced hypertension completely.

3. The ethanol extract of *Elaeocarpus ganitrus* Roxb failed to reduce nicotine induced hypertension.

From the above observation, it may be concluded that *Elaeocarpus ganitrus* has got hypotensive effect in animals having experimentally induced hypertension. *Elaeocarpus ganitrus* Roxb. can be used in stress induced hypertension, not in hypertension usually seen in smokers.

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