Study of the Hypotensive Action of Garlic Extract Experimental Animals

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Abstract

Watersoluble extract of garlic when given intravenously to normal anaesthetized dogs, produced a significant fall in their mean blood pressure. The effect was not antagonized by atropine but it was antagonized partially but significantly by dimetane maleate. Same hypotensive responses were obtained before and after bilateral vagotomy. In cross circulation experiments the extract produced hypotensive effect in the donor animal but did not affect the blood pressure of recipient animal. Respiratory stimulant response of garlic extract was markedly reduced by dimetane. The extract increased the amplitude of cardiac contractions (in cat) very slightly. The extract produced vasoconstriction in rat hind quarter preparation. In view of the above findings some of the hypotensive action of extract is attributed to histamine release which produces decrease in total"peripheral resistance (JPMA 32:237, 1982).

Introduction

Garlic is extensively used in indigenous system of medicine in our country. In the form of oil, liniment, poultice and powder it has been extensively used in Indo-Pak subcontinent in indigenous system of medicine in following ailments (Nadkarni, 1954).

1. Acts as vermifuge especially for round worms.
2. Oil is a powerful antiseptic.
3. Atonic dyspepsia, flatulance and colic.
4. Antispasmodic.
5. Bronchial asthma.
6. Rheumatism.
7. Hypertension.
8. Atherosclerosis.

It has got hypocholesteraemic effect in man and animals (Bordia et al., 1975). It produces significant fall in blood pressure in normal anaesthetized dogs (Malik and Siddiqui, 1981). Present work has been planned to explore the mechanism responsible for the hypotensive action of garlic.

Material and Methods

Seventy dogs of either sex (weighing 10-15 kg) were used. They were divided in groups, each group comprising of six animals. Six cats were used for heart in situ experiment. Six rats were sacrificed to see the effect on the blood vessels.

Garlic extract was supplied by Institute of Chemistry, University of Karachi. Peeled, uncrushed cloves of garlic were extracted out thrice with alcohol at an interval of 48 hours. The combined alcoholic extract was freed of solvent and the residue was partitioned between ethyl acetate and distilled water. The water soluble portion was freed of solvent and residue was divided into alcohol soluble and alcohol insoluble portions. Water soluble, but alcohol insoluble fraction has been used in this study. The yield of this fraction is 0.9 percent. Stock solution (7% w/v) was prepared in distilled water and kept at 4°C.

Further dilutions were made with normal saline before use. Extract was given intravenously (after bringing it to room temperature). Dogs were anaesthetized with Nembutal (30 mg/kg B.W.) intravenously (Quilliam, 1959). Blood pressure, respiratory movements were recorded on a kymograph. Drugs were injected through a cannula fitted in femoral vein. The trachea was cut open, cannulated and attached to an artificial respirator to prevent respiratory obstruction (Chai and Wong, 1966). A common carotid artery was cannulated and attached to the mercury manometer for recording blood pressure. Sodium citrate solution 9% was used in the intervening tubings separating mercury from blood. Manometer was adjusted so that a 5 cm rise of writing pen was equal to 100 mm of mercury. Force of cardiac contractions of cats was also recorded on kymograph.

Resuls

Doses ranging between 12.7 and 101.6mg/kg B.W. produced a significant fall in systolic, diastolic and mean blood pressure. 25.1 mg (a dose producing 50 percent maximum response) doses produced 24.3±1.2 (S.E.) percent fall in mean blood pressure (Table I).

Table I

Hypotensive Effect of 25.1 mg/kg* Doses of Garlic Extract

	Blood pressure in mm Hg ± S.E.**			
	Control responses	*After the extract*	*Percent fall*	*P value*
Systolic	155.00 ±3.66 (6)	120.50 ±1.61 (6)	23.70 ±0.97 (6)	0.01
Diastolic	138.30 ±2.48	90.50 ±4.16	28.90 ±0.97	0.01
Mean	143.60 ±5.60 (6)	98.50 ±5.20 (6)	24.30 ±1.20 (6)	0.01

* Doses producing 50 percent of maximum response.

** Standard error

Figures in parentheses indicate number of animals.

The fall in blood pressure started within about 12 seconds of the injection and reached to maximum in 30.5±2.9 seconds after 25.1 mg/kg dose of garlic extract. Time required for complete recovery was 1.6±0.8 minutes. Inderal in doses of 1.5, 3,6 and 12 mg/kg produced 10.0±0.9, 23.0±2.1, 46.0±3.7 percent fall in mean blood pressure. ED50 of inderal, as calculated from the curve is 42.8 mg/kg, whereas that of garlic extract is 25.1 mg/kg. The relative potency of inderal to garlic extract is 1; 0.11. The fall in mean blood pressure before the administration of dimetane (10 mg/kg, with 25.1 mg/kg dose of extract) was 24.4±2.9 while after the administration of dimetane fall in blood pressure was8.7±2.1.

The difference was significant (P<0.01) (Table III).

Table III

Effects on Mean Blood Pressure after Bilateral Vagotomy, Atropinization and Dimetane Maleate

	Dose mg/kg	*Percent fall in mean blood pressure*		*P value*
		Before	*After*	
Atropine	25.1	24.5±2.3 (6)	23.9±2.2 (6)	0.01
Bilateral vagotomy	25.1	24.2±3.2 (6)	25.1±3.0 (6)	0.01
Dimetane maleate	25.1	24.4±2.9 (6)	8.7±2.1 (6)	0.01

Figures in parentheses indicate number of animals

In four cross circulation experiments the injection of 25.1 mg/kg doses of garlic extract in common carotid artery of recipient animal did not produce any hypotensive effect. A well marked hypotensive effect was however obtained in the donor animal. With 25.1 mg/kg doses of the extract the percent increase in rate and tidal value was 51.6±2.11 and 26.3±2.34 before and 23.3+-0.85 and 15.1 ±0.84 after the administration of dimetane maleate (10 mg/kg). Therefore dimetane maleate could significantly reduce the effects of garlic extract on respiration (P<0.01) (Table II).

Table II

Effect of Garlic Extract (25.1 mg/kg Doses) on Respiration before and after Dimetane Maleate (10 mg/kg).

	Before dimetane	*After dimetane*	*P value*
Percent increase in rate	51.6±2.11 (6)	23.3±0.85 (6)	0.01
Percent increase in tidal volume	26.3±2.34 (6)	15.1±0.84 (6)	0.01

Figures in parentheses indicate number of animals.

With 25.1 mg doses of the extract the volume of fluid (in mls) collected in 30 minute's duration was significantly decreased. Total volume of fluid collected in 30 minute's duration before the administration of extract was 49.0±2.3, while it was 25.0±2.1 after the administration of the extract. The difference was significant ($P<0.01$) (Table IV).

Table IV

Times for Onset of Hypotensive Action, Maximum Fall and Complete Recovery of Garlic Extract

S. No.	Dose (mg/kg)	Latent period (seconds)	Time required for maximum fall (seconds)	Time required for complete recovery (minutes)
1.	12.7	12.5±0.9 (6)	32.0±3.2 (6)	1.2±0.4 (6)
2.	25.1	13.4±1.2 (6)	30.5±2.9 (6)	1.6±0.8 (6)
3.	101.6	12.5±1.3 (6)	33.5±2.3 (6)	2.5±0.9 (6)

Figures in parentheses indicate number of animals.

Discussion

Present investigations have shown that garlic extract produ;es a significant fall in systolic, diastolic and mean blood pressure in dogs. As cross circulation experiments have shown that extract could not produce its hypotensive effect in the recipient animals, the hypotensive effect in dog could not be due to depression of vasomotor centre. Similarly the possibility of hypotensive effect of garlic extract due to stimulation of muscarinic receptors also has been excluded by the administration of atropine. Partial antagonism of the hypotensive effects of various histamine liberators like morphine sulphate by mepyramine maleate (Kayaalp and Kaymakcalan, 1966) has been well established. The observation that the previous administration of dimetane maleate could partially (but significantly) antagonize the hypotensive effect of garlic extract therefore indicates that some of its hypotensive effect is due to liberation of histamine.

Moran et al. (1959) observed that temporary increase in rate and depth of breath and bronchoconstriction following administration of oxypanamine could consistently be blocked by antihistaminic drugs in pentobarbitone anaesthetized dogs. The effects of garlic extract on respiration closely resemble these observations.

The observation that dimetane maleate has markedly reduced the respiratory stimulant response of garlic extract therefore indicates that the extract causes liberation of histamine.

The hypotensive action of garlic extract cannot be attributed to cardiac depression, as the extract could not produce decrease in the amplitude of cardiac contraction in cat.

Feldberg and Paton (1951) while carrying out perfusion experiments or isolated skin of cat observed that arterial injections of histamine liberators like morphine (10 mg) cause intense vasoconstriction. They consider this vasoconstriction to be either wholly or to a great extent due to release of histamine. The vasoconstriction produced by 25.1mg garlic extract can be explained on the basis of these observations.

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