

Blood pressure lowering, fibrinolysis enhancing and antioxidant activities of Cardamom (*Elettaria cardamomum*)

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Elettaria cardamomum (L.) Maton. (Small cardamom) fruit powder was evaluated for its antihypertensive potential and its effect on some of the cardiovascular risk factors in individuals with stage 1 hypertension. Twenty, newly diagnosed individuals with primary hypertension of stage 1 were administered 3 g of cardamom powder in two divided doses for 12 weeks. Blood pressure was recorded initially and at 4 weeks interval for 3 months. Blood samples were also collected initially and at 4 weeks interval for estimation of lipid profile, fibrinogen and fibrinolysis. Total antioxidant status, however, was assessed initially and at the end of the study. Administration of 3 g cardamom powder significantly ($p < 0.001$) decreased systolic, diastolic and mean blood pressure and significantly ($p < 0.05$) increased fibrinolytic activity at the end of 12th week. Total antioxidant status was also significantly ($p < 0.05$) increased by 90% at the end of 3 months. However, fibrinogen and lipid levels were not significantly altered. All study subjects experienced a feeling of well being without any side-effects. Thus, the present study demonstrates that small cardamom effectively reduces blood pressure, enhances fibrinolysis and improves antioxidant status, without significantly altering blood lipids and fibrinogen levels in stage 1 hypertensive individuals.

Keywords: Hypertension, Small cardamom, Fibrinolysis, Antioxidant, *Elettaria cardamomum* (L.) Maton

The hypertension is a multi-factorial disease prevalent the world over, and is a common cardiovascular risk factor for ischemic heart disease (IHD) and cerebrovascular accidents (CVA). It is usually associated with an abnormal level of antioxidant status and reduced fibrinolysis^{1,2}. The drug treatment of mild hypertension has been associated with metabolic alterations that increase the risk of cardiovascular diseases, resulting in stand off or even a negative overall effect³. In this regard dietary spices and various plant products have been evaluated². The small cardamom (*Elettaria cardamomum* Maton), the “Queen of Spices”, is one such common spice which has shown some promise⁴.

The cardamom is a popular food additive and flavoring agent used by people all over the world. Its medicinal properties have been described in Ayurveda and Unani system of medicine against gastrointestinal disorders, cardiac disorders, renal and vesicular calculi, dyspepsia, debility, anorexia, asthma, bronchitis and halitosis⁵. It has been recommended

that one teaspoonful of cardamom powder if taken with little honey twice a day is beneficial in high blood pressure and heart disease⁶. The various animal studies have shown its antioxidant⁷, antihypertensive⁸, gastroprotective⁹, antispasmodic¹⁰, antibacterial¹¹, antiplatelet aggregation¹² and anticancer¹³ properties.

The cardamom crude extract has demonstrated blood pressure reduction in anaesthetized rats⁸ and 1,8-cineole, the pharmacologically active constituent of its seeds has also demonstrated vasodilator activity in normotensive rats¹⁴. However, no long-term clinical studies have so far been carried out with respect to its effect on blood pressure, lipid profile, fibrinolysis, fibrinogen and total antioxidant status. Thus, in the present study, the long-term effect of cardamom on the above-mentioned parameters has been investigated in a single blinded study.

Materials and Methods

Preparation of drug

Best quality fruits of *Elettaria cardamomum* were collected from the local market and grinded well with their outer shells to make a fine homogenous powder and filled in gelatin capsules. Each capsule contained 0.75 g of the drug.

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Study protocol, subject distribution and drug administration

After approval from Institutional Ethical Committee, the study was conducted on 20 newly diagnosed patients of essential hypertension (Primary hypertension) between the ages of 35 to 50 yrs (BMI<25), who attended medical Out Patient Department of Maharana Bhopal General Hospital attached to RNT Medical College, Udaipur.

All the patients selected were of stage 1 ($\geq 140/90$ to $159/99$ mm Hg) hypertension of Joint National Committee (JNC) VII¹⁵. The patients with stage 2 ($\geq 160/100$ mm Hg) hypertension of JNC VII, secondary hypertension, diabetes, IHD, renal and endocrine diseases were excluded. Similarly, the patients who were smokers, alcoholics, on oral contraceptives, lipid lowering drugs, dietary restrictions or weight reduction program were excluded from the study. All the selected patients were not taking any anti-hypertensive medication and unwilling to take allopathic medicine for hypertension. They opted for herbal medicine for treatment of hypertension. After informed consent, two capsules of cardamom powder were administered twice daily. The dose of 1.5 g twice a day was decided based on ethnomedicinal recommendations and as observed in the preliminary study^{4,6}. During the study period, the patients were advised not to alter their dietary and exercise habits. They were also instructed not to take any medication without prior consultation.

Blood pressure measurement

The blood pressure was measured with a mercury sphygmomanometer with a standard size cuff in accordance with recommendations of JNC VII¹⁵. Average of two or more readings with the gap of 5 min was taken at each time of blood pressure recording. The blood pressure was recorded in sitting position, initially and at every 4th week and the mean blood pressure was determined by the formula: Diastolic blood pressure + $1/3^{\text{rd}}$ of pulse pressure.

Blood chemistry

The blood samples were collected in a fasting state, initially and at the end of 4th, 8th and 12th week for the analysis of fibrinolytic activity¹⁶, fibrinogen¹⁷, lipid profile¹⁸⁻²¹. Fibrinolytic activity (units) was assessed as euglobulin lysis time (ELT) in min and expressed in units by dividing 10000 by ELT. Fibrinogen was measured by chemical method as described by Nath and associates¹⁷.

The serum cholesterol¹⁸, triglycerides¹⁹ and HDL-C²⁰ were estimated colorimetrically by enzymatic methods employing test kits supplied by Reckon Diagnostics P. Ltd., Baroda, India. VLDL cholesterol and LDL cholesterol were calculated by Friedwald formula²¹ as follows:

$$\text{VLDL-C} = \text{Triglycerides}/5 \text{ and}$$

$$\text{LDL-C} = \text{Total cholesterol} - (\text{HDL-C} + \text{VLDL-C})$$

Total antioxidant status was assessed initially and at the end of the study using test kit supplied by Randox, UK, where the color produced by ABTS (2,2'-azino-di-[3-ethylbenzthiazoline sulphonate]) radicals is measured at 600 nm which is proportional to concentration of antioxidants present in the sample²².

Statistical analysis

Data were expressed as mean \pm standard error (SE). Results were statistically analyzed with student's t-test for paired data and a 'p' value less than or equal to 0.05 was considered as significant.

Results and Discussion

Administration of cardamom in a dose of 1.5 g twice daily significantly decreased systolic ($p < 0.01$), diastolic ($p < 0.01$) and mean ($p = 0.001$) blood pressure in stage 1 hypertensive individuals at the end of 1 month (Table 1). Although the reduction in blood pressure was statistically significant at the end of 4th week, the levels did not reach up to the normal values of less than 140/90 mm Hg. At the end of 8 weeks,

Table 1—Effect of *Elettaria cardamomum* (3 g) on blood pressure in stage 1 hypertensive individuals (n = 20)

Blood pressure (mm Hg)	[Values expressed as mean \pm SE]			
	Initial (I)	4 Weeks (II)	8 Weeks (III)	12 Weeks (IV)
Systolic	154.2 \pm 3.14	143.4 \pm 2.07 ^a	139.4 \pm 3.15 ^{b,c}	134.8 \pm 3.32 ^{d,e}
Diastolic	91.8 \pm 2.19	87.6 \pm 1.43 ^a	83.4 \pm 2.54 ^{f,g}	79.6 \pm 1.92 ^{d,h}
Mean	112.59 \pm 1.77	106.19 \pm 0.87 [*]	101.86 \pm 1.96 ^{f,p}	97.99 \pm 2.00 ^{d,k}

p values: <0.01- a II vs I, b III vs I, k IV vs III; <0.001 - d IV vs I, f III vs I; = 0.05- e IV vs III; <0.05- g III vs II, h IV vs III; = 0.001 - * II vs I; <0.02- p III vs II; NS -c III vs II (NS- Not significant)

further decrease was observed in systolic ($p < 0.01$), diastolic ($p < 0.001$) and mean ($p < 0.001$) blood pressure and systolic blood pressure lowered to 139.4 ± 3.15 from 143.4 ± 2.07 mm Hg. At the end of 3 months, the systolic (134.8 ± 3.32 mm Hg) and diastolic (79.6 ± 1.92 mm Hg) blood pressure reached within the range of normal level ($>140/90$ mm Hg), as defined by JNC VII criteria (Table 1).

On an average, there was a fall of 19 mm Hg in systolic and 12 mm Hg in diastolic blood pressure at the end of 12 weeks (Fig. 1). This statistically significant decrease in blood pressure is important in terms of its long-term morbidity and mortality from cardiovascular diseases. Randomized controlled trials have shown that in patients with mild hypertension, lowering of 5-6 mm Hg in diastolic and 10 mm Hg in systolic blood pressure reduces stroke risk by about one-third and risk of coronary events by about one-sixth^{23,24}.

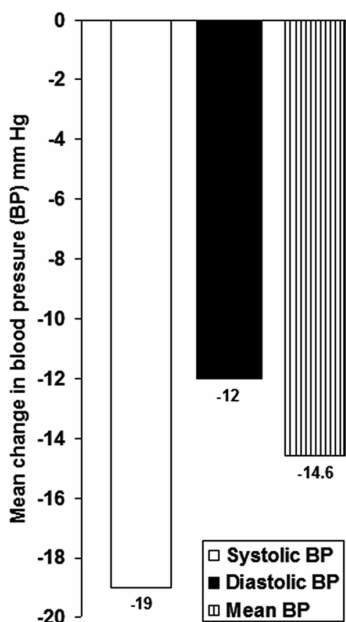


Fig. 1—Fall in systolic, diastolic and mean blood pressure (mm Hg) after 3 months administration of cardamom (3 g)

The significant ($p < 0.05$) enhancement of fibrinolysis by cardamom at the end of 4, 8 and 12 weeks is worth noting (Table 2). In health, there exists a dynamic equilibrium between fibrin deposition and its cleaning by fibrinolytic process. This fibrinolytic activity is influenced by drug, diet and diseases like diabetes, IHD and hypertension²⁵. Fibrinolysis enhancement along with blood pressure lowering effect is, therefore, a boon in disguise for patients with stage 1 hypertension treated with cardamom.

Besides its blood pressure lowering and fibrinolysis enhancement properties, cardamom significantly ($p < 0.05$) improved total antioxidant status by 90% after 12 weeks of its administration in stage 1 hypertensive individuals (Fig. 2). Furthermore, favorable reductions were also observed in total cholesterol (19%), triglycerides (15%), VLDL-C (15%) and LDL-C (25%) levels at the end of 3 months of cardamom administration (Fig. 3). However, the changes were statistically not significant. Similarly, fibrinogen levels were remained significantly unaltered throughout the study (Table 2).

The essential oil of cardamom contains around 25 identified compounds, of which 1,8-cineole and terpinyl acetate are the major chemical constituents.

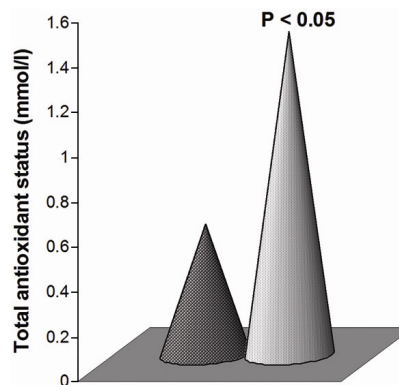


Fig.2—Effect of *Elettaria cardamomum* (3 g) on total antioxidant status in stage 1 hypertensive individuals (n = 20)

Table 2—Effect of *Elettaria cardamomum* (3 g) on fibrinolytic activity (FA) and fibrinogen (FB) in hypertensive individuals (n = 20)

Parameter	[Values expressed as mean \pm SE]			
	Initial (I)	4 Weeks (II)	8 Weeks (III)	12 Weeks (IV)
FA (Units)	70.81 \pm 11.94	113.2 \pm 19.92 ^a	104.09 \pm 12.28 ^{b,d}	113.84 \pm 12.34 ^{c,e}
FB (mg %)	249.7 \pm 23.46	238.36 \pm 15.27*	237.53 \pm 9.24* ^d	247.61 \pm 11.75* ^e

p values: <0.05 : a II vs I, b III vs I, c IV vs I; NS: d III vs II, e IV vs III, * as compared to I. (NS: Not significant)

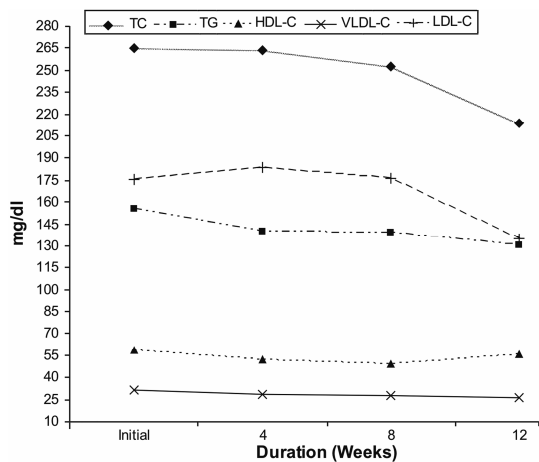


Fig. 3—Pattern of mean values of lipid profile during 12 weeks administration of 3 g cardamom in hypertensive individuals (n = 20) [P is not significant for all the parameters at all the levels]

Recently, cardiovascular effects of 1,8-cineole, a mono-terpene oxide have been evaluated in animal experimental studies. Interestingly, i.v. bolus injections of 1,8-cineole (0.3-10 mg/kg) has elicited dose-dependent decrease in mean aortic pressure. This effect is related to an active vascular relaxation rather than withdrawal of sympathetic tone¹⁴. In the present study, the dose of 1,8-cineole administered was 1.44 mg/kg as mentioned in our previous study⁴. However, other constituents such as limonene, terpinolene and myrcene may add to its pharmacological activity²⁶. Recently, crude extract of cardamom has also shown blood pressure lowering activity along with diuretic and sedative effects in animals⁸.

Moreover, in the present study not only cardamom seeds, but the fruit shell containing flavanoids was also used which might have some role in lowering blood pressure and improving antioxidant status²⁷. Furthermore, the role of central neurogenic effect of cardamom should also be considered in lowering the blood pressure, as most of the patients had a feeling of well being and tranquility. However, further investigations are warranted to unmask the mechanism of action.

In conclusion, the present study suggests that long-term administration of cardamom has significant blood pressure lowering effect along with fibrinolysis and antioxidant enhancing properties in patients with stage 1 hypertension. Thus, it may prove beneficial as a dietary supplement to such patients. However, further long-term placebo controlled study with a large number of patients is warranted to further establish its multiple therapeutic potential.

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