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# Effect of Greater cardamom (*Amomum subulatum* Roxb.) on blood lipids, fibrinolysis and total antioxidant status in patients with ischemic heart disease

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## ABSTRACT

**Objective:** Greater cardamom (*Amomum subulatum* Roxb.) fruit powder (seeds with pericarp) was evaluated for its effect on some of the cardiovascular risk factors in patients with ischemic heart disease. **Methods:** Thirty male individuals (50–70 years) with ischemic heart disease (old MI>6 months) were selected for the study and divided into two groups of fifteen each. Group I (Treated) received 3 g cardamom powder in two divided doses while Group II (Placebo) received matched placebo capsules for 12 weeks. Blood samples were collected initially and at 6 and 12 weeks for analysis of lipid profile, fibrinolytic activity and total antioxidant status. **Results:** Administration of Greater cardamom significantly ( $P<0.001$ ) reduced atherogenic lipids without significant alteration in HDL–cholesterol. Plasma fibrinolytic activity and serum total antioxidant status were also enhanced significantly ( $P<0.05$ ) at the end of the study. The placebo group however did not show significant alteration in any of these parameters. It was tolerated well without any untoward effects. **Conclusions:** Dietary supplementation of Greater cardamom favorably modifies lipid profile and significantly enhances fibrinolytic activity and total antioxidant status in patients with ischemic heart disease.

## 1. Introduction

Spices have been consumed in many cultures over centuries. They were primarily consumed because of their taste and aroma. However, the recent scientific studies have proved their biological activities beyond their taste and smell. Spices are now known to possess anti–thrombotic, anti–atherosclerotic, hypolipidemic, hypoglycemic, hypotensive, anti–inflammatory, anti–arthritic and platelet aggregation inhibition activities. Few of the spices also possess adaptogenic property against physical stress. Interestingly, they do have antioxidant component. In this context, Garlic, Onion, Ginger, Curcumin, Small cardamom, etc. have been extensively studied [1–3].

Greater cardamom or Large cardamom (*Amomum subulatum* Roxb.) member of Zingiberaceae family is a well known flavoring spice, used to treat various ailments in different medical systems world over. In Ayurveda, it

is commonly used for dyspepsia, nausea, cough, vomiting and itching. It is also used as preventive as well as curative for throat troubles, lung congestion, mouth infections and digestive disorders. Its seeds are cardiac tonic, expectorant, appetizer and diuretic [4,5]. Sarkar [6], after observing its ethnomedicinal properties from the Ra`rh civilization described Greater cardamom for its cardiovascular beneficial properties. He recommended that one teaspoonful of cardamom powder including seeds and pericarp, if taken twice a day, will benefit the patients with heart disease. However, its beneficial properties are enhanced if dietary alterations and some yoga postures are practiced along with it. A recent report also documented its cardio–adaptogenic property against physical stress in an animal experimental study [2].

In view of the ethnomedicinal recommendations and its cardiogenic, antioxidant and antistress properties, the present placebo controlled study was carried out to evaluate the effect of Greater cardamom on some of the cardiac risk parameters in patients with ischemic heart disease.

## 2. Materials and methods

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## 2.1. Preparation of plant material

Fruits of *Amomum subulatum* were collected from the local market. Fruits were identified and authenticated by Prof. S. S. Katewa, at Department of Botany, Mohanlal Sukhadia University where a voucher specimen no. (EA–623) was kept for future reference. The fruits were grinded well along with their outer shells to make a fine homogenous powder and filled in gelatin capsules. Each capsule contained 0.75 g of the cardamom powder. Matched placebo was prepared by filling the capsules with lactose powder.

## 2.2. Study protocol

After approval from institutional ethical committee, the study was conducted on 30, male non-obese (BMI<24) individuals with ischemic heart disease (IHD) between the ages of 50 to 70 years. It was a single blinded, placebo controlled study in accordance with the guidelines of the Declaration of Helsinki and Tokyo, 2004. The study subjects were selected from the medical Out Patient Department of Maharana Bhopal General Hospital attached to RNT Medical College, Udaipur.

All the patients selected were of established coronary artery disease (healed MI > 6 months), stable in their symptoms and were receiving isosorbide 5–mononitrate and aspirin. The patients with hypertension, diabetes, renal and endocrine diseases were not included in the study. Similarly, the patients who were smokers, alcoholics, on lipid lowering drugs, dietary restrictions or weight reduction program were excluded from this study.

After obtaining written consent, they were randomly divided in two groups of 15 each. Group I (treated group)

received 3 g of cardamom powder in two divided doses while Group II (placebo group) received matched placebo for a period of 12 weeks. The dose of cardamom was decided based on the ethnomedicinal recommendations. During the entire study period the patients were not allowed to take any medication without prior consultation except isosorbide 5–mononitrate and aspirin. Also, they were not allowed to alter their dietary and exercise schedule which they were following preceding six months of study period.

## 2.3. Blood chemistry

Blood samples were collected in a fasting state, initially and at the end of 6th and 12th week for the analysis of fibrinolytic activity, fibrinogen, lipid profile and total antioxidant status by the methods as described earlier<sup>2,7</sup>.

## 2.4. Statistical analysis

All the data were expressed as mean±SE. Results were statistically analyzed with student's *t*-test and *P* value less than 0.05 was considered as significant difference in analysis.

## 3. Results

Administration of Greater cardamom in a dose of 1.5 g twice daily did not alter any lipid fraction at the end of six weeks. The reduction, however in all the atherogenic lipid fractions was significant ( $P<0.001$ ) at the end of 12 weeks without significant alteration in HDL–Cholesterol (Table 1). This favorable alteration in blood lipids led to significant ( $P<0.01$ ) decrease in atherogenic index (Figure

**Table 1**  
Effect of Greater cardamom (3 g) on lipid profile in patients with ischemic heart disease.

Parameters(mg/dL)	Treated group(n=15)			Placebo group(n=15)		
	Initial	6 weeks	12 weeks	Initial	6 weeks	12 weeks
Total cholesterol	248.59 ± 9.15	240.23±8.23 a	221.79±7.58 b	247.54±11.06	245.44±11.23a	244.16±11.99a
Triglycerides	197.47±11.01	192.14±10.51a	176.63±10.22 b	177.44±11.12	177.23±10.54a	175.76 ± 9.98a
HDL–C	43.91 ± 2.04	44.21±2.10a	45.50 ± 2.2 a	44.56 ± 4.72	44.02± 3.98a	44.42 ± 4.41a
LDL–C	165.18 ± 8.44	160.79±7.68a	140.56±7.22 b	167.48±14.71	166 ± 14.54a	164.58±15.70a
VLDL–C	39.49 ± 2.20	38.48±2.12a	35.32±2.04 b	35.48 ± 2.2	35.44±2.02a	35.15 ± 1.99a

Values are expressed as mean±SE. *P* is compared to initial. a : NS (Not significant); b:<0.001. HDL–C: High density lipoprotein cholesterol; LDL–C: Low density lipoprotein cholesterol; VLDL–C: Very low density lipoprotein cholesterol.

**Table 2**  
Effect of Greater cardamom (3g) on fibrinolytic activity and fibrinogen in patients with ischemic heart disease.

Group(n=15)	Fibrinolytic Activity(Units)			Fibrinogen(mg %)		
	Initial	6 weeks	12 weeks	Initial	6 weeks	12 weeks
Treated	60.06 ± 1.71	70.12 ± 1.51b	81.65 ± 3.3 a	233.42 ± 8.68	232.79 ± 8.23b	235.59 ± 8.35 b
Placebo	71.59 ± 2.74	71.65 ± 1.94b	72.94 ± 3.12b	240.9 ± 16.31	239.12 ± 15.74b	239.14 ± 15.32b

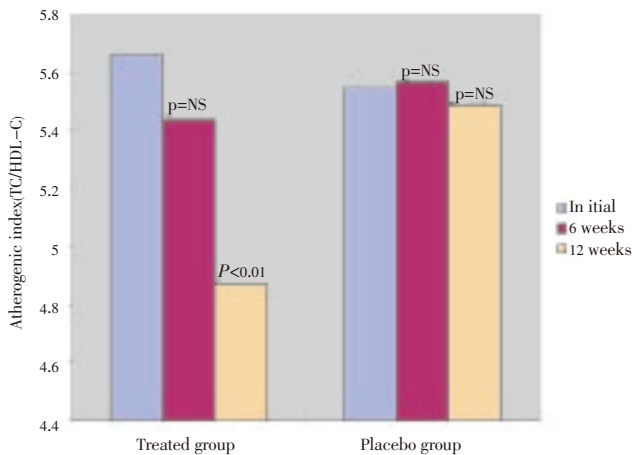
Values are expressed as mean ± SE, *P* is compared to initial, a:  $P<0.05$ . b: NS (Not significant).

**Table 3**  
Effect of Greater Cardamom (3 g) on total antioxidant status (mM/L) in patients with ischemic heart disease.

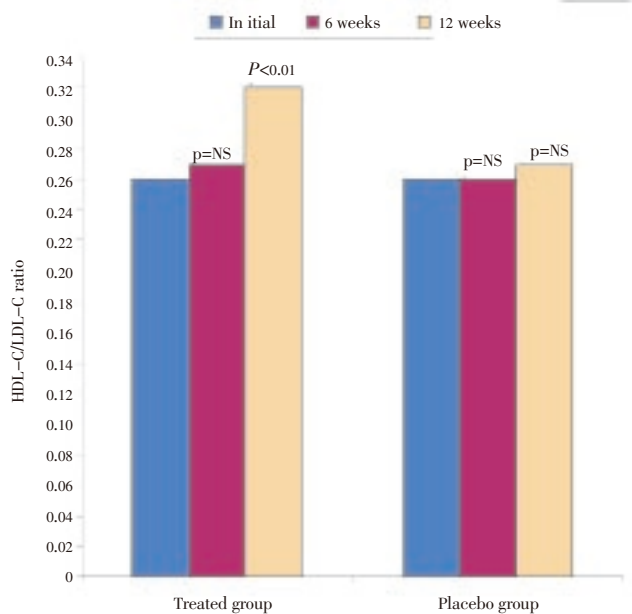
	Treated group(n=15)			Placebo group(n=15)		
	Initial	6 weeks	12 weeks	Initial	6 weeks	12 weeks
	0.63 ± 0.03	0.65 ± 0.02b	0.76 ± 0.22a	0.68 ± 0.03	0.67 ± 0.20b	0.69 ± 0.03b

Values are expressed as mean ± SE. *P* is compared to initial, a:  $P<0.05$ . b: NS (Not significant).

1) and improvement in the ratio between HDL–C/LDL–C (Figure 2). Plasma fibrinolytic activity was also increased significantly ( $P<0.05$ ) along with a significant rise in serum total antioxidant status at the end of 12 weeks without causing significant changes in fibrinogen levels (Table 2 and 3). The placebo group on the other hand, did not show any significant alteration in all these parameters (Table 1–3).



**Figure 1.** Effect of 3 g Greater cardamom on atherogenic index in patients with ischemic heart disease. TC: Total cholesterol; HDL–C: High density lipoprotein cholesterol; NS: Not significant.



**Figure 2.** Effect of Greater cardamom (3 g) on HDL–C/LDL–C ratio in patients with ischemic heart disease. HDL–C: High density lipoprotein cholesterol; LDL–C: Low density lipoprotein cholesterol; NS: Not significant.

#### 4. Discussion

Greater cardamom significantly reduced total cholesterol (10.78%), Triglycerides and VLDL–C (10.55%), LDL–C (14.90%) without significant effect on HDL–cholesterol. This favorable change was good enough to decrease the ratio of TC/HDL–C

to a significant extent ( $P<0.01$ ) which is detrimental to atherogenesis and therefore aptly called atherogenic index. Along with the decrease in atherogenic index, there was also significant ( $P<0.01$ ) improvement in the ratio between HDL–C and LDL–C.

The modest decrease of 12% in atherogenic lipids is in accordance with the pattern of hypolipidemic activity demonstrated by other plant products and spices [1,8]. However, it is worth noting that in spite of significant and favorable alterations in lipid profile by Greater cardamom; the values of total cholesterol, triglycerides and LDL–cholesterol were still in the higher range and undesirable for patients with IHD. If the present dose which is 60 mg/kg is increased further for a longer duration of time, it might be possible to further reduce the atherogenic lipids; as has been observed recently in an animal experimental study when 100 mg/kg chloroform:methanol (50:50) extract of Greater cardamom seeds for a period of 4 months have demonstrated significant decrease in atherogenic lipids, lipid peroxidation along with increase in HDL–C, glutathione and catalase activities in cholesterol fed rabbits [9].

It was interesting to note that plasma fibrinolytic activity was also significant ( $P<0.05$ ) increased by 36% at the end of 12 weeks. The placebo group however, did not show any significant alteration in fibrinolytic activity. On the other hand, fibrinogen an independent risk factor for cardiovascular disease [10] has not been favorably modified by administration of Greater cardamom in patients with IHD. Interestingly, serum total antioxidant status was significantly ( $P<0.05$ ) increased by 21% after 12 weeks of Greater cardamom administration.

Greater cardamom mediated hypolipidemic activity along with significant enhancement of fibrinolysis needs further attention. The lipids and fibrin deposition are the two important components of atheroma formation. The dynamic equilibrium between fibrin deposition and its clearance by fibrinolytic activity determines the healthy status of coronary arteries. On the contrary, if fibrin is not removed properly by body’s own clearing system, then its organization and fatty deposition on the artery involved will result in atheroma formation [11]. It is interesting that most of the spices used in oriental dishes have been demonstrated to have fibrinolysis enhancing properties in healthy individuals and in patients with IHD and hypertension [1]. Greater cardamom is further addition to this list.

Further the evidence of dietary antioxidants in prevention of diseases has been escalating [8], and in this context, the antioxidant effect of Greater cardamom is a further addition to its cardio–beneficial properties. In a nutshell, the combination of its hypolipidemic, fibrinolysis enhancing and antioxidant improving properties may prove favorable in patients with athero–thrombotic coronary artery disease.

Looking into the chemical composition, fruits of Greater cardamom contain steroids, terpenoids, flavanoids, tannins, glycosides, volatile oil and saponins and have shown to possess antioxidant, antifungal and anti–ulcerogenic activities [12–15]. The methanolic extract of seeds possesses hepato–protective property and was found to be non–toxic up to a dose of 3000 mg/kg [16].

The seeds of Greater cardamom have been reported to contain about 2.5% essential oil with 1,8-cineole (72.77%) and  $\alpha$ -terpineol (4.6%) as the two major constituents of the oil besides 23 other components. The other major components reported are  $\alpha$ -pinene (1.7%),  $\beta$ -pinene (3.2%), spathulenol (0.1%), 4-terpineol (1.4%), Germacrene D (0.1%) and cardamonin, alpinetin, protocatechuic acid and many glycosides [12,17]. The pericarp of fruits contains steroids, flavanoids, tannins and saponins along with 0.18 % volatile oil having total 37 components constituting >98% of total oil. Major compounds of the oil is 1,8-cineole (38.7%),  $\alpha$ -terpineol (12.6%),  $\beta$ -pinene (13.6%), Spathulenol (8.3%), 4-terpineol (4.5%), Germacrene D (3%),  $\alpha$ -pinene (2.8%) and  $\beta$ -selinene (2.7%). Although, the concentration of 1,8-cineole in pericarp oil, was less than 50 % when compared with seed oil; the concentration of other compounds isolated was more in volatile oil of pericarp as compared with seed oil [12,13].

On an average, seeds yield 2.5 % volatile oil which when included with 0.18 % volatile oil of pericarp gives a total yield of 2.68 % oil. In the present study, incorporation of both pericarp and seeds of Greater cardamom, as recommended in ethnomedicine have been employed which may have its basis by increasing the total concentration of 1,8-cineole, which is an important cardio-beneficial compound. This incorporation, which has increased the total concentration of 1,8-cineole (> 73%) might have resulted in its significant hypolipidemic activity which was not observed with the Small cardamom containing less than 40% of 1, 8-cineole [3].

Cardiovascular effects of 1, 8 -cineole, a monoterpene oxide have been evaluated in various experimental studies and demonstrated to possess vascular relaxant, anti-inflammatory and antioxidant properties [18–21]. The other major components isolated from Greater cardamom are Cardamonin and Alpinetin which have also shown significant anti-inflammatory, vasodilatory and platelet aggregation inhibitory activities in various animal studies [22–24]. These compounds might be responsible for the observed hypolipidemic and fibrinolysis enhancing activities of Greater cardamom in the present study.

Seeds also possess antioxidant activity as studied on hepatic and cardiac antioxidant enzymes, glutathione content and lipid conjugated dienes in rats fed high fat diet and in vitro DPPH radical scavenging activity. The antioxidant activity was attributed to their ability to activate antioxidant enzymes that catalyze the reduction of antioxidants [14]. It is therefore; clear that cardamom contains components which enhance TAS. Moreover, in the present study, not only cardamom seeds but the pericarp was also incorporated containing flavanoids and tannins which also possess antioxidant activities [25].

The present study therefore, suggests that long term dietary supplementation of Greater cardamom favorably alters lipid profile and significantly enhances fibrinolytic activity and total antioxidant status in patients with IHD. It is safe, well tolerated dietary functional food without any untoward side effects. Furthermore, in view of its stress adaptogenic property, it may prove to be beneficial as a dietary supplement to patients with coronary artery disease.

However, further large scale, placebo controlled studies are warranted.

### Conflict of interest statement

We declare that we have no conflict of interest.

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