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Research Article

Effect of Cinnamon (*Cinnamommum verum* J. Presl.) on Blood Lipids, Fibrinogen, Fibrinolysis, and Total Antioxidant Status in patients with Ischemic Heart Disease

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Abstract

Background: Spices and condiments are reported to possess many health-beneficial activities. Cinnamon (*Cinnamommum verum* J. Presl.) is a well-known spice used in preparation of many cuisines and sweet dishes. Several scientific studies have reported its protective role in modification of risk factors associated with cardio-vascular diseases. Traditional medicine also recommends its use for treatment of heart disease. In view of all this, its bark powder was evaluated for its effect on blood lipids, fibrinolysis, fibrinogen and total antioxidant status in patients with ischemic heart disease.

Methods: Forty individuals (50-70 years) with ischemic heart disease were selected for the study and divided into two groups of twenty each. Group I (Treated) received 3 g Cinnamon powder in two divided doses while Group II (Placebo) received matched placebo capsules for four weeks. Blood samples were collected initially and at the end of four weeks for analysis of lipid profile, fibrinogen, fibrinolytic activity and total antioxidant status.

Results: Administration of Cinnamon significantly ($p < 0.001$) reduced atherogenic lipids without significant alteration in HDL-cholesterol. A statistically significant enhancement in Plasma fibrinolytic activity ($p < 0.001$) and serum total antioxidant status ($p < 0.05$) was observed at the end of the study. The placebo group however did not show significant alteration in these parameters. It was tolerated well without any untoward effects.

Conclusion: Four weeks supplementation of Cinnamon (1.5g twice daily) to patients having ischemic heart disease favorably affects various lipid parameters, fibrinolytic activity and total antioxidant status in a statistically significant manner.

Keywords: Non-HDL-Cholesterol; Atherogenic Index; Cinnamaldehyde; Cholesterol; Atherosclerosis

Introduction

Spices have been consumed in many cultures primarily because of their taste or aroma and to treat various ailments in different medical systems world over. Recent scientific researches have proved their biological activities and validated their medicinal use. Spices are known to possess anti-thrombotic, anti-atherosclerotic, anti-hyperglycemic, hypolipidemic, anti-inflammatory, antihypertensive, antioxidant, adaptogenic and platelet aggregation inhibition activities [1-5].

Cinnamommum verum J. Presl. syn. *C. zeylanicum* Bl. (Family-Lauraceae); commonly referred as Cinnamon, is one of the most important spice used world over for its characteristic flavor and aroma. The plant part which is used for cooking as well as medicine is its bark. The bark is acrid, aromatic, astringent, aphrodisiac, diuretic, stimulant, expectorant, febrifuge and carminative in nature. Its bark is recommended for treatment of cardiac diseases in Indian ethnomedicine [6]. Recent researches have shown its antioxidant, antihyperglycemic, antimicrobial, antiparasitic, antitumor, antiulcerogenic and antihyperlipidemic properties [7-14].

Sarkar [15], after observing its ethnomedicinal properties has described Cinnamon for its cardiovascular beneficial properties. He recommended use of Cinnamon bark powder in a dose of one teaspoonful (1.5 g) twice daily for patients with heart disease along with dietary alterations and practices of yoga postures.

Materials and Methods

Preparation of cinnamon bark powder

Stem bark of *C. verum* was purchased from local market, identified and authenticated at Department of Botany, Mohanlal Sukhadia University, Udaipur, Rajasthan and a voucher specimen (EA-791) was kept for future reference. The bark was cleaned and grinded well to make a fine homogenous powder which was filled in gelatin capsules. Each capsule contained 0.75g of the Cinnamon powder. Matched placebo was prepared by filling the capsules with lactose powder.

Subject selection

The study was approved by Institutional ethical committee and conducted on forty, male, non-obese (BMI < 24) individuals between the age of 40 to 60 years who were having ischemic heart disease (IHD) with old healed Myocardial Infarction more than six months. All patients were stable in symptoms and receiving aspirin and isosorbide-5-mononitrate. It was a single blinded, placebo controlled study in accordance with the guidelines of the Declaration of Helsinki and Tokyo, 2004. The selection of the study subjects was from Out Patient Department of Maharana Bhopal General Hospital attached to RNT Medical College, Udaipur. The patients with hypertension, diabetes, renal and endocrine disorders were not included in the study. Similarly, the individuals who were smokers, tobacco chewers, alcoholics, on lipid lowering drugs, dietary restrictions or weight reduction program were excluded from this study.

Study protocol

After obtaining written consent, they were randomly divided into two groups of twenty each. Group I (treated group) was administered 3 g of Cinnamon powder in two divided doses (two capsules twice daily) while Group II (placebo group) received matched placebo for a period of four weeks. The 3 g dose of Cinnamon bark powder was decided based on the ethnomedicinal recommendations of Sarkar [15].

During the entire study period, the study subjects were not allowed to take any medication without prior consultation. They were also not allowed to alter their daily dietary and exercise schedule which they were following preceding six months of study period.

Biochemical analysis

Blood samples were collected in a fasting state, initially and at the end of four weeks for the analysis of fibrinolytic activity, fibrinogen, lipid profile and total antioxidant status by the methods as described earlier [16-23]. Blood lipids were estimated by enzymatic methods using Reckon diagnostics P. Ltd Kits. Fibrinolytic activity (Units) was assessed as euglobulin lysis time (ELT) in minutes and calculated by the formula: 10000/ELT = Units [16]. Fibrinogen was measured by chemical method as described by Nath and associates [17]. Total antioxidant status [22] in mM/l was measured using kits provided by Randox diagnostics Pvt. Ltd., USA. Non-HDL-C was calculated by subtracting High Density Lipoprotein Cholesterol (HDL-C) values from Total Cholesterol (TC) in mg/dl [23]. Low Density Lipoprotein Cholesterol (LDL-C) and Very Low Density Lipoprotein Cholesterol (VLDL-C) were calculated by Friedwald formula [21] as follows:

VLDL – C = Triglycerides/5

LDL – C = Total Cholesterol - (HDL- C + VLDL - C)

Statistical analysis

All the data were expressed as mean ± standard error (SE). Results were statistically analyzed with Student's t-test and a 'p' value less than 0.05 was considered as significant difference in analysis.

Results

Administration of Cinnamon in a dose of 1.5 g twice a day decreased atherogeinc lipids significantly at the end of 4 weeks without significant alteration in HDL-Cholesterol (Table 1). This reduction in blood lipids led to significant ($p < 0.01$) decrease in atherogenic index and improvement in the ratio between HDL-C/LDL-C (Figure 1-2). Plasma fibrinolytic activity was also increased significantly ($p < 0.001$) without causing significant changes in fibrinogen levels (Table 2). The total antioxidant status was significantly improved by 22.1% (Figure 3). The placebo group, however, didn't show any significant alterations in all these parameters (Table 1-2, Figure 1-3).

Parameters	Treated group (n = 20)		Placebo group (n = 20)	
	Initial	4 Weeks	Initial	4 Weeks
CHOLESTEROL (mg/dl)	233.67 ± 16.53	202.04 ± 12.39[a]	240.50 ± 15.80	243.45 ± 13.72[c]
TRIGLYCERIDES (mg/dl)	175.11 ± 24.51	144.10 ± 20.35[b]	180.25 ± 22.25	175.77 ± 20.30[c]
HDL-C (mg/dl)	49.83 ± 2.50	50.82 ± 2.45[c]	50.90 ± 3.40	50.56 ± 3.89[c]
VLDL-C (mg/dl)	35.08 ± 4.15	28.82 ± 3.28[b]	36.05 ± 3.92	35.15 ± 3.26[c]
LDL-C (mg/dl)	148.27 ± 13.72	122.46 ± 10.21[a]	153.55 ± 13.57	157.74 ± 15.20[c]
Non-HDL-C (mg/dl)	183.84 ± 11.25	151.22 ± 10.75[a]	189.60 ± 10.75	192.89 ± 11.15[c]

Table 1: Effect of Cinnamon (3g) on lipid profile in patients with ischemic heart disease.

Values are expressed as Mean ± SE

p Value (As compared to initial):

a : <0.01

b: <0.05

c: NS (Not significant).

HDL-C: High density lipoprotein cholesterol; LDL-C: Low density lipoprotein cholesterol; VLDL-C: Very low density lipoprotein cholesterol.

Group	Fibrinolytic Activity (Units)		Fibrinogen (mg %)	
	Initial	4 weeks	Initial	4 weeks
Treated (n = 20)	60.60 ± 1.88	71.48 ± 2.44 p < 0.001	259.94 ± 9.26	249.61 ± 7.34 p = NS
Placebo (n = 20)	70.59 ± 2.55	71.65 ± 3.12 p = NS	240.90 ± 11.25	238.45 ± 12.50 p = NS

Values are expressed as Mean ± SE; p Value- As compared to initial; NS- Not significant.

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

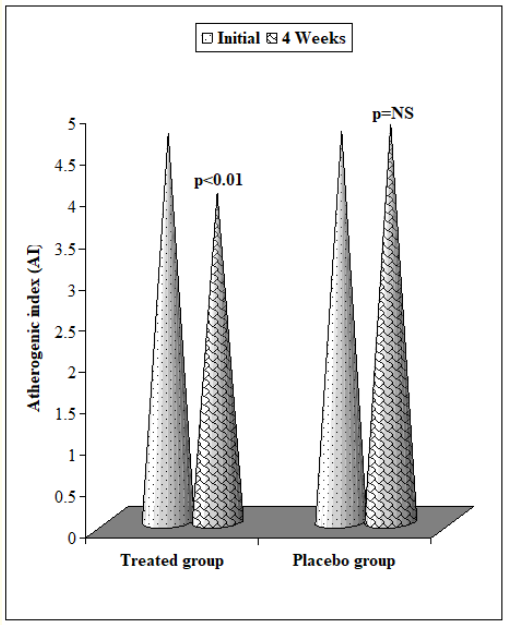

Figure 1: Effect of Cinnamon (3g) on Atherogenic index (Total cholesterol/HDL-C) in patients with IHD.

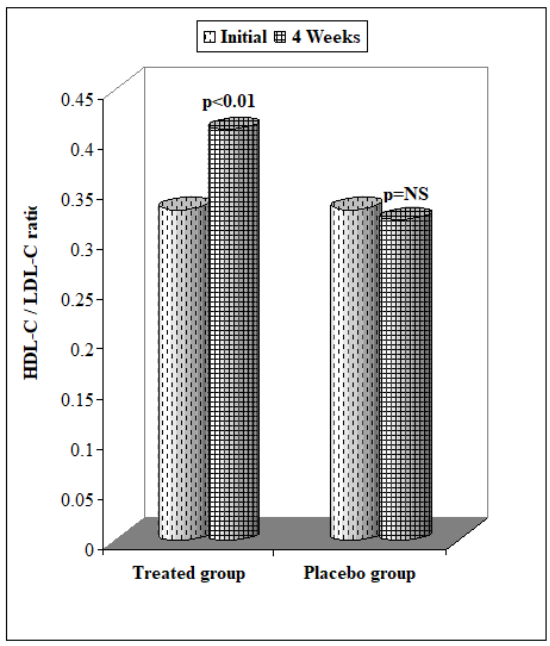

Figure 2: Effect of Cinnamon (3g) on HDL-C/LDL-C ratio in patients with IHD (n = 40).

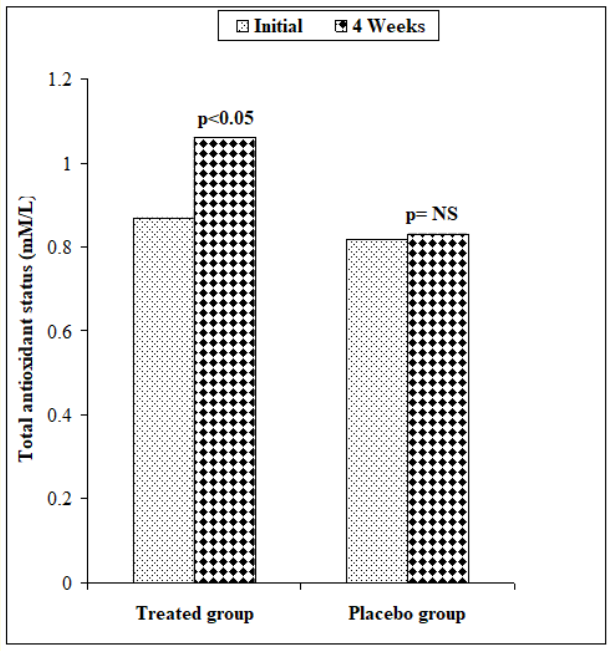

Figure 3: Effect of Cinnamon (3g) on total antioxidant status in patients with IHD.

Discussion

Cinnamon bark administration significantly reduced total cholesterol (13.1%), triglyceride and VLDL-C (17.84%), LDL-C (17.4%) and non-HDL-C (17.7%) without significant effect on HDL-C in patients with ischemic heart disease. These favorable changes in lipids also significantly ($p < 0.01$) decreased atherogenic index (TC/HDL-C) and non-HDL-C along with a significant ($p < 0.01$) rise in the ratio between HDL-C and LDL-C.

The atherogenic index and non HDL-C are the two parameters detrimental to the process of atherogenesis. Non-HDL-Cholesterol, the difference between total cholesterol and HDL-C, is a very sensitive measure of total atherogenic lipoprotein burden in serum. All component lipoproteins of non-HDL-C are known to be atherogenic and therefore, its reduction by whatever means would be a favorable approach for the prevention of atherogenesis. As the LDL-C is targeted in Coronary artery disease (CAD) patients as < 100 mg/dl; the non-HDL-C target is simply the risk stratified LDL-C target plus 30 mg/dl (< 130 mg/dl) [23]. Non-HDL-C reduction by Cinnamon, therefore, merits special attention and consideration.

The decrease in atherogenic lipids is not very drastic but modest, which is in accordance with the pattern of hypolipidemic activity demonstrated by other plant products and spices [3,24,25]. However, it is worth noting that in spite of significant decrease in atherogenic lipids by Cinnamon; the values of total cholesterol, triglycerides, LDL-C, non-HDL-C were still in the higher range and undesirable especially for individuals with Ischemic Heart Disease. The dose of Cinnamon administered, in the present study, is around 60 mg/kg. It is quite possible that by increasing the dose and duration of Cinnamon administration, further reduction in these atherogenic lipids may be achieved. Once the target is achieved, then the dose may again be lowered for maintenance phase. Hypolipidemic effect of Cinnamon has been demonstrated in many animal studies [26]. The mechanism behind this is reduction in lipogenesis by regulating genes or enzymes related with lipid metabolism [27]. Moreover, accumulation of lipids is also reduced by Cinnamon possibly due to regulating expression of cholesterol ester transfer proteins [28].

Notably, plasma fibrinolytic activity was also increased significantly ($p < 0.001$) at the end of the study. The placebo group, however, did not demonstrate any significant alteration in FA. On the contrary, fibrinogen, which is considered as an independent risk factor for cardiovascular diseases [29], has not been affected favorably by Cinnamon administration. Additionally, serum total antioxidant status was also significantly ($p < 0.05$) increased by 22% after Cinnamon supplementation.

Cinnamon mediated hypolipidemic activity along with significant enhancement of fibrinolysis, needs further elaboration. The lipids and fibrin deposition are the two important components of atheroma formation. In health, there exists a dynamic equilibrium between fibrin deposition and its clearance by fibrinolytic activity. If the fibrin is not removed properly by body's own clearing system, then its organization and fatty deposition on the artery involved will lead to atheroma formation [30]. It is an interesting observation that most of the spices have demonstrated fibrinolysis enhancing property in healthy individuals as well as in patients with IHD and hypertension [4,24]. Cinnamon is a further addition to the list.

The evidence of dietary antioxidants in prevention of diseases has been escalating [31]. In this context, the antioxidant effect of Cinnamon is a further addition to its cardio-beneficial properties. The aqueous and alcoholic extract of Cinnamon significantly inhibits fatty acid oxidation and lipid peroxidation *in vitro* [32]. Among 26 spices, Cinnamon has shown highest antioxidant activity [33]. In view of this, the combination of its hypolipidemic, fibrinolysis enhancing and antioxidant properties provide favorable substrate for patients with athero-thrombotic coronary artery disease.

Many phytochemicals are present in Cinnamon plant such as cinnamaldehyde, cinnamic acid, trans-cinnamaldehyde, cinnamyl acetate, eugenol, alpha-borneol, alpha-bornyl acetate, caryophyllene oxide, alpha-bergamotene, β-caryophyllene, caryophyllene, E-nerolidol, alpha-cubebene, alpha-terpineol, Trans-alpha-bergamotene, Gamma-eudesmol, terpinolene and alpha thujene has been reported [34]. The bark which has been employed in the present study, contain 65-80% of cinnamaldehyde which is highest among all plant parts and 5-10% eugenol. Both these compounds possess several cardio-vascular beneficial pharmacological activities besides many other activities [26,34-36].

The protective effects of cinnamaldehyde on the cardiovascular system have been demonstrated in several studies. For example, Cinnamaldehyde possesses potential activity against the production of nitric oxide as well as the expression of inducible nitric oxide. It can therefore, be interpreted as a dessert antioxidant in daily food. Cinnamaldehyde has also shown thrombaxane A2 (TxA2) receptor blocking activity as well as hypotensive effect due to peripheral vasodilatation [26]. Its platelet aggregation and vascular smooth muscle cell proliferation inhibitory and anti-thrombosis activities have also been demonstrated in animal studies [37,38]. Moreover, antioxidant potential of cinnamaldehyde has also been demonstrated in animal studies. For example, it has shown to reduce the production of intracellular reactive oxygen species, increased phosphorylated endothelial nitric oxide synthase, superoxide dismutase and aortic NO metabolite contents [39-41].

The present study is not comparable to any other human studies conducted so far [26]. In one human study, Cinnamon (3g) did not affect total cholesterol, HDL and LDL values in nine healthy subjects [42]. However, in the present study, the effect on hyperlipidemia has been observed in ischemic heart diseases individuals, without diabetes; while most of the other studies primarily selected type 2 diabetic patients [43-45]. In all of the above studies, the control

of sugar by Cinnamon will automatically modify the lipid levels; while in the present study, the effect of Cinnamon is primarily on blood lipids in non-diabetic individuals. Antihyperglycemic and hypolipidemic response have also been observed in type 2 diabetics when administered Cinnamon at 1,3 and 6 g doses daily for a period of 40 days. With the reduction of fasting blood glucose (18-29%), there was also a reduction in total cholesterol (12-26%), triglycerides (23-30%) and LDL-C (7-27%) with no significant change in HDL-C at all the three doses of Cinnamon [45].

Several scientific studies have shown safety profile of Cinnamon [46]. In some studies, long term administration of Cinnamon caused few side effects such as rashes, headache, nausea, diarrhea and menstrual cramps [47]. However, in the present study, the dose of 3 g daily intake was well tolerated by IHD individuals without any adverse effects.

Conclusion

Cinnamon has shown beneficial role in treatment of diabetes, hypertension, viral myocarditis, atherosclerosis, heart failure and myocardial ischaemia-reperfusion injury besides various pharmacological activities [26]. In view of its cardiovascular benefits, the present study further suggests its favorable effects on lipid profile, significant enhancement of fibrinolytic activity and total antioxidant status, making it a cardiovascular favorable food spice. Its administration is safe; tolerance is good and doesn't produce untoward side effects. It may prove to be beneficial as a "food spice" supplement to patients with coronary risk or disease. However, further long term, large scale; placebo-controlled double blind studies are needed.

Conflict of Interest

There is no conflict of interest.

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