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ANTIHYPERLIPIDEMIC EFFICACY OF CINNAMON IN ALBINO RATS

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ABSTRACT

The objective of this study was to assess the antihyperlipidemic efficacy of cinnamon powder in albino rats. For this purpose 180 adult albino rats (average weight 210 ± 11 grams) were purchased and divided into six groups. In rats blood lipid profile was raised using cholesterol @ 400mg/Kg body weight of rat which was mixed into rat feed for first 15 days of the study. Cinnamon bark powder equivalent to 1gm/kg, 2gm/kg, 4gm/kg and 6gm/kg was administered to the rats of treatment groups 15-60 days. Treatment control group was given Simvastatin at the dose rate of 0.6mg/Kg body weight. Blood samples were collected at 0, 15, 30, 45 and 60 days in sterilized gel tubes by direct heart puncturing. Serum was separated and analyzed for lipid profile parameters using reagent kits. Findings of present study revealed that various doses of *Cinnamomum cassiae* powder improved the serum lipid profile in albino rats by reducing Total Lipids, Total Cholesterol, Triglycerides and LDL cholesterol and increasing HDL cholesterol levels in cinnamon treated groups. Furthermore, the most significant effect was shown by 6 mg/kg dose level. From the results of the present study, it was concluded that Cinnamon powder has curative effect against hyperlipidemia.
Keywords: Cinnamon, Antihyperlipidemic efficacy, Albino rats, Lipid profile, Cholesterol

INTRODUCTION

Hyperlipidemia is considered as the biggest risk factor leading to occurrence and asperity of coronary artery diseases (CAD) (Grundy, 1986). It is also a primary cause of death besides stroke, coronary heart disease and atherosclerosis (Smith, 1993). Hyperlipidemia is mainly associated with increased serum total cholesterol (TC), low density lipoprotein (LDL), very low density lipoprotein (VLDL) and reduced high density lipoprotein (HDL) levels. Hyperlipidemia associated lipid diseases are considered to induce atherosclerosis and CAD (Saravanan *et al*., 2003). It mainly leads to manifestation and exploitation of atherosclerosis and CAD. Identified risk factors of CAD other than hypertension are smoking, age, gender, sedentary habits, dyslipidemia, obesity, family history, hypoestrogenemia and homocysteine (Beaglehole, 1990).

Statins are mostly used to reduce blood lipid level but the side effects of them are myopathy and asymptomatic increase in transaminase enzyme level (Alzira *et al*., 2004). Rarely occurring side effects of statins are nausea, dyspepsia, constipation or diarrhea, abdominal pain and flatulence (Ballantyne *et al*., 2003; Newman *et al*., 2003). It is reported that in comparison to synthetic drugs, herbal medications are safer (Murphy, 1999; Javed *et al*., 2009). According to WHO study 80% population of world believes in traditional methods of treatment that is the use of herbal treatment (Muller and Mechler, 2005), so researchers are interested in herbal remedies of cardiovascular ailments having lesser or fewer side effects.

Cinnamon is the inner stem bark of *Cinnamomum cassiae* family *Lauraceae*. It is being served as condiment in many cultures (Chaudhry and Tariq, 2006). Despite of its culinary benefits, it has also been employed to treat various health conditions and researchers have investigated cinnamon for its antimicrobial (Carmo *et al*., 2008), acaricidal (Fichi *et al*., 2007), insecticidal (Yang *et al*., 2005), antityrosinase (Marongiu *et al*., 2007), antimutagenic and antioxidant (Jayaprakasha *et al.*, 2007) activities and found it effective in these conditions. It was also found to be effective in hypertension (Preuss *et al*., 2006),) and in diabetes (Anderson, 2008; Khan *et al.*, 2003).

Although cinnamon was found to be very effective in various health conditions but its

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lipid lowering effect was not well explored so we hypothesized that Cinnamon has got antihyperlipidemic effect also. Therefore, the present study was conducted to evaluate the antihyperlipidemic efficacy of cinnamon powder in albino rats.

MATERIAL AND METHODS

Experimental animals

One hundred and eighty adult albino rats of either sex with average weight of 210 ± 11 grams were procured from and maintained in clean, spacious, and well aerated plastic cages at National Institute of Health (NIH), Islamabad, Pakistan under hygienic laboratory environment. Before the initiation of experiments, the rats were acclimatized for 7 days. After that, they were divided into six groups i.e. A (Untreated Control), B (Treated Control), C (Treated Group I), D (Treated Group II), E (Treated Group III) and F (Treated Group IV). Animals were kept in separated cage and were acclimatized for seven days. The rats had free access to routine rat feed and water.

Induction of hyperlipidemia and treatment plan

Hyperlipidemia was induced in albino rats with cholesterol (Cholesterol 90% E, AppliChem, Darmstadt, Germany) which was mixed at dose of 400mg/Kg body weight of rats in their daily routine feed. All the groups were fed on high cholesterol feed (Normal rat feed + Cholesterol) for first 15 days except Group A which was kept on high cholesterol feed throughout 60 days of experiment.

For experiment, cinnamon bark was procured from the local spice shop of Rawalpindi city, Pakistan. The bark was ground to powder form which was then fed at a dose of 1gm/kg, 2gm/kg, 4gm/kg and 6gm/kg respectively to the animals of treatment groups C, D, E and F for 15-60 days. In treatment control group (Group B) synthetic lipid lowering drug Simvastatin (10mg Tablet, OBS Pharmaceutical, Karachi, Pakistan) was given at dose of 0.6mg/Kg bodyweight for 15-60 days. Feed and drug administration protocol is shown in table 1.

Table – 1: Feeding and drugs administration schedule in albino rats during the experimental period of 0 to 60 days

Group A Normal control	High cholesterol feed (Normal rat feed + cholesterol 400mg/kg body weight) 0 to 60 days
Group B Treatment control	High cholesterol feed 0 to 15 days High cholesterol feed + simvastatin (0.6 mg/kg body weight) 15 to 60 days
Group C Treatment group I	High cholesterol feed 0 to 15 days High cholesterol feed + Cinnamon powder (1gm/kg body weight) 15 to 60 days
Group D Treatment group II	High cholesterol feed 0 to 15 days High cholesterol feed + Cinnamon powder (2gm/kg body weight) 15 to 60 days
Group E Treatment group III	High cholesterol feed 0 to 15 days High cholesterol feed + Cinnamon powder (4gm/kg body weight) 15 to 60 days
Group F Treatment group IV	High cholesterol feed 0 to 15 days High cholesterol feed + Cinnamon powder (6gm/kg body weight) 15 to 60 days

Determination of lipid profile

Blood samples were collected at 0, 15, 30, 45 and 60 days. On the sampling day, 6 albino rats from each group were anesthetized with chloroform. The blood of individual albino rat was taken into sterilized gel tube by direct heart puncturing using 3cc disposable syringe. Blood samples were centrifuged at 4000 rpm for 20 minutes. Serum was separated and transferred into small clean eppendorf tubes. These tubes were preserved at freezing temperature till laboratory analysis. Lipid profile was examined using Spin Lab, an Automated Chemistry Analyzer (manufactured by Spinreact, Girona, Spain). Total cholesterol (TC), Triglycerides (TG), Total lipids (TL) and High density

lipoprotein (HDL) were determined using reagent kits (Manufactured by Spinreact, Girona, Spain). The concentration of LDL in the sample was calculated using Friedewald formula (Friedewald *et al*., 1972).

Statistical Analysis

The data was subjected to t-test. The test was applied to check the significance for interpretation of results. The value of P< 0.05 was considered as significant while P> 0.05 as non-significant.

RESULTS

Antihyperlipidemic efficacy of *Cinnamomum cassiae* bark powder, equivalent to 1gm/kg, 2gm/kg, 4gm/kg and 6gm/kg body weight has been evaluated in hyperlipidemic albino rats. The results are presented below:

Hyperlipidemia in rats

Hyperlipidemia was induced in albino rats by feeding high cholesterol diet. Cholesterol powder at dose rate of 400 mg/kg of body weight was fed to the animals along with normal routine rat feed. The cholesterol substantially increased the serum cholesterol 68.75%, total lipids and triglycerides concentrations 29.75% and 55.38% respectively with decrease in the HDL level 33.61%. The serum lipid profile parameters have been shown in Fig 1.

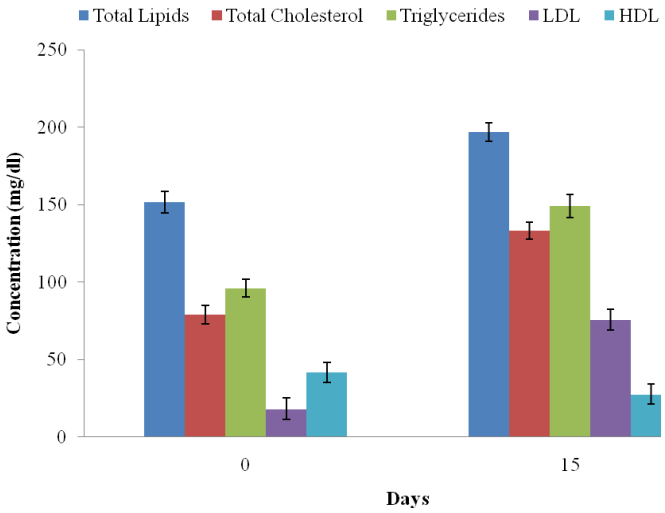

Fig – 1: Mean ± SD values of lipid profile parameters in albino rats fed with cholesterol 400 mg/kg body weight

Antihyperlipidemic efficacy of *C. cassiae* powder

Antihyperlipidemic efficacy of cinnamon powder equivalent to 1, 2, 4 and 6gm/kg body weight in induced hyperlipidemic rats has been presented in Tables 2-6. It is evident from these tables that cinnamon powder equivalent to 1gm/kg did not alter lipid profile parameters significantly altered at post medication days 30 and 45 but at 60 days, significant changes were observed in values of only LDL and HDL cholesterol. At post treatment day 60, the cinnamon powder equivalent to 2 gm/kg body weight lowered the total lipids levels by 11.83%, total cholesterol by 31.58%, triglycerides by 33.50% and LDL cholesterol by 63.40% while HDL cholesterol was raised by 56.36%. The change was most significant on final treatment day. Cinnamon powder equivalent to 4 gm/kg body weight decreased the lipid profile parameters; total lipid by 19.39%, total cholesterol by 37.64%., triglyceride by 37.58%, LDL cholesterol by 76.22 while HDL cholesterol was increased by 71.43% at post medication day 60. The change was significantly evident at this last day of experiment. The administration of cinnamon powder equivalent to 6 gm/kg of body weight reduced the lipid profile parameters in hyperlipidemic albino rats at posttreatment day 60; total lipids by 21.14%, total cholesterol by 35.88%, triglycerides by 41.81%, LDL cholesterol by 80.37% while the HDL cholesterol level was increased by 76.11% showing the most significant change in these parameters at the last day of the experiment.

From the results it was evident that the all parameters were most significantly altered by highest dose of the cinnamon powder in this study i.e., 06 mg/kg and its results were comparable to those with simvastatin (standard/treatment control group) as shown in Fig. 2.

Table – 2: Mean ± SD values of total lipids (mg/dl) and their percentage reduction in hyperlipidemic rats (n=30) after treatment with *Cinnamomum cassiae* powder equivalent to 1, 2, 4 and 6 gm/kg body weight and Simvastatin

Groups	Treatment days				Percentage reduction on treatment days		
	15	30	45	60	30	45	60
Untreated control	197 ± 4.81	211 ± 8.42	219.4 ± 9.01	227.8 ± 7.23	-	-	-
Treated control	203.1 ± 3.09	184 ± 7.40	171.5 ± 6.10	144 ± 8.33	9.40	15.56	29.10*
Treated Group I	201 ± 4.08	189.7 ± 8.21	183 ± 3.94	177.1 ± 5.62	5.62	8.96	11.89
Treated Group II	193 ± 6.08	180.7 ± 8.41	171.5 ± 4.93	164 ± 7.56	6.37	7.80	11.83
Treated Group III	196 ± 6.79	185.3 ± 7.93	169.4 ± 3.78	158 ± 7.43	5.46	13.57	19.39*
Treated Group IV	191 ± 3.94	180.7 ± 7.41	164 ± 6.27	150.1 ± 9.13	5.39	14.14	21.41*

n = number of animals in each group

***** = Significantly less (P≤0.05) than pretreatment value at 15th day

Table – 3: Mean ± SD values of total cholesterol (mg/dl) and their percentage reduction in hyperlipidemic rats (n=30) after treatment with *Cinnamomum cassiae* powder equivalent to 1, 2, 4 and 6 gm/kg body weight and Simvastatin

Groups	Treatment days				Percentage reduction on treatment days		
	15	30	45	60	30	45	60
Untreated control	118 ± 4.96	124.6 ± 9.03	138 ± 8.37	144.3 ± 5.52	-	-	-
Treated control	139 ± 6.15	112 ± 5.87	97 ± 8.23	80.4 ± 5.41	19.42	30.22	42.16*
Treated Group I	137 ± 4.67	122 ± 8.91	109 ± 5.73	98.6 ± 6.03	10.95	20.44	28.03
Treated Group II	133 ± 9.07	118 ± 3.89	106.7 ± 7.61	91 ± 5.82	11.28	19.77	31.58
Treated Group III	140 ± 7.63	113 ± 5.29	95.7 ± 6.83	87.3 ± 4.02	19.29	31.64	37.64*
Treated Group IV	131 ± 6.27	109.3 ± 3.75	93.6 ± 9.10	84 ± 6.43	16.56	28.55	35.88*

n = number of animals in each group

***** = Significantly less (P≤0.05) than pretreatment value at 15th day

Table – 4: Mean ± SD values of triglycerides (mg/dl) and their percentage reduction in hyperlipidemic rats (n=30) after treatment with *Cinnamomum cassiae* powder equivalent to 1, 2, 4 and 6 gm/kg body weight and Simvastatin

Groups	Treatment days				Percentage reduction on treatment days		
	15	30	45	60	30	45	60
Untreated control	143.1 ± 9.01	156 ± 7.83	163 ± 5.18	176.3 ± 8.29	-	-	-
Treated control	151.6 ± 3.97	127 ± 8.61	101.5 ± 5.86	81.7 ± 7.08	16.23	33.05*	46.11*
Treated Group I	146 ± 8.19	130.7 ± 3.78	119 ± 6.12	110 ± 7.33	10.48	18.49	24.66
Treated Group II	157 ± 4.38	140 ± 9.03	121.3 ± 5.22	104.4 ± 7.29	10.83	22.74	33.50*
Treated Group III	149 ± 8.52	128.8 ± 4.77	113.1 ± 7.63	93 ± 6.05	13.56	24.09	37.58*
Treated Group IV	147.8 ± 7.04	123.5 ± 9.18	101.7 ± 5.63	86 ± 7.34	16.44	31.19*	41.81*

n = number of animals in each group

***** = Significantly less (P≤0.05) than pretreatment value at 15th day

Table – 5: Mean values of LDL (mg/dl) and their percentage reduction in hyperlipidemic rats (n=30) after treatment with *Cinnamomum cassiae* powder equivalent to 1, 2, 4 and 6 gm/kg body weight and Simvastatin

Groups	Treatment days				Percentage reduction on treatment days		
	15	30	45	60	30	45	60
Untreated control	62.38 ± 5.76	69.60 ± 6.57	84.40 ± 4.07	92.84 ± 7.32	-	-	-
Treated control	80.38 ± 8.45	50.60 ± 3.78	33.70 ± 5.67	7.26 ± 7.29	37.05	58.07*	90.97*
Treated Group I	83.10 ± 6.91	66.76 ± 4.83	50.80 ± 7.40	38.60 ± 5.78	19.66	38.87	53.55*
Treated Group II	74.10 ± 5.80	57 ± 7.43	45.14 ± 8.39	27.12 ± 6.18	23.08	39.08	63.40*
Treated Group III	81.50 ± 7.45	52.24 ± 5.76	32.08 ± 8.51	19.50 ± 6.25	36.29	60.88*	76.22*
Treated Group IV	72.14 ± 3.97	46.60 ± 7.29	26.46 ± 4.75	15.20 ± 8.02	39.82	65.83*	80.37*

n = number of animals in each group

***** = Significantly less (P≤0.05) than pretreatment value at 15th day

Table – 6: Mean ± SD values of HDL (mg/dl) and their percentage increase in hyperlipidemic rats (n=30) after treatment with *Cinnamomum cassiae* powder equivalent to 1, 2, 4 and 6 gm/kg body weight and Simvastatin

Groups	Treatment days				Percentage increase on treatment days		
	15	30	45	60	30	45	60
Untreated control	27 ± 8.34	23.8 ± 7.08	21 ± 4.32	16.2 ± 6.79	-	-	-
Treated control	28.3 ± 5.43	36 ± 7.19	43 ± 4.78	56.8 ± 6.12	27.21	51.94*	100.71*
Treated Group I	24.7 ± 7.56	29.1 ± 5.81	34.4 ± 6.12	38 ± 8.27	17.81	39.27	53.85*
Treated Group II	27.5 ± 7.03	33 ± 5.67	37.3 ± 4.53	43 ± 6.11	20.00	35.64	56.36*
Treated Group III	28.7 ± 3.78	35 ± 6.25	41 ± 4.84	49.2 ± 5.63	21.95	42.86	71.43*
Treated Group IV	29.3 ± 8.25	38 ± 4.19	46.8 ± 7.82	51.6 ± 5.01	29.69	59.73*	76.11*

n = number of animals in each group

***** = Significantly higher (P≤0.05) than pretreatment value at 15th day

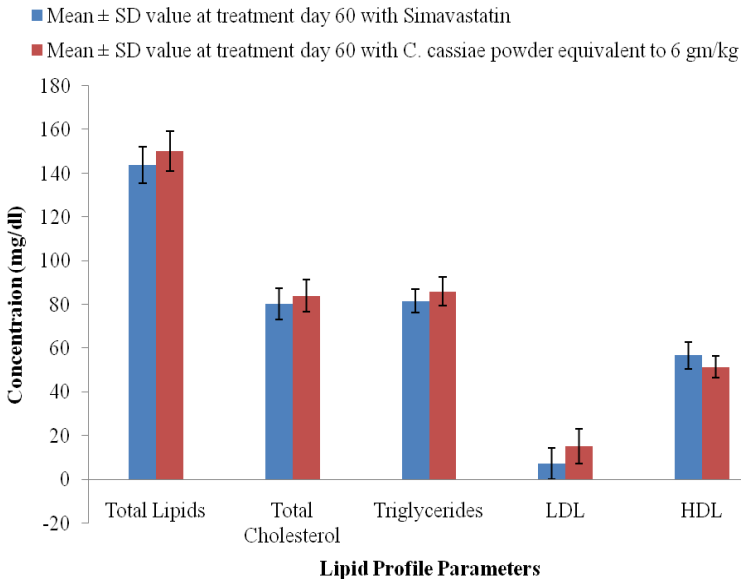

Fig – 2: Efficacy of *C. cassiae* powder equivalent to 6 gm/kg body weight and Simvastatin against lipid profile parameters in hyperlipidemic albino rats

DISCUSSION

Hyperlipidemia is considered well characterized risk factor for cardiovascular events, especially coronary artery disease (CAD). Various studies have revealed a very clear relationship between elevated cholesterol level and cardiovascular events (Bays *et al*., 2001). Cardiovascular events have been considered as major cause of death globally accounting 16.7 million deaths every year according to WHO. One out of every four middle aged persons is suffering from cardiovascular events in Pakistan (Raza *et al*., 2004). Many studies revealed that diet plays an important role in the development of hyperlipidemia and atherosclerosis. Several studies on animal and human have evaluated that the cholesterol and saturated fatty acids cause hypercholesterolemia by elevating total cholesterol and changing lipoprotein pattern and the mechanisms involved remain under study. Feeding of cholesterol has been often carried out to increase the cholesterol levels to induce hypercholesterolemia and related metabolic changes in various animal models (Zulet *et al*., 1999).

The present study indicated that supplementation of high cholesterol (400 mg/ kg body weight) diet was sufficient to induce hyperlipidemia. Similar findings were reported by Arafa (2005), Dhulasavant *et al.* (2010) and Iqbal *et al.* (2015) that rats and rabbits feeding with a high cholesterol diet elevated their serum lipid profile parameters. There was a substantial elevation in total cholesterol, total lipids, triglyceride and LDL levels at 15 days. Whereas the level of HDL in all groups was reduced due to administration of high cholesterol diet (Tables 2-6). When high cholesterol diet was co-supplemented with cinnamon powder, the increased levels of total lipids, total cholesterol, triglycerides and LDL demonstrated considerable decline. These findings correlated with the results of Dhulasavant *et al.* (2010) who reported that ethanolic and aqueous extracts of *Cinnamomum tamala* Nees leaves significantly reduced the levels of total cholesterol, triglyceride, LDL, VLDL and atherogenic index whereas the extracts significantly increased the HDL level. Javed *et al.* (2009) also reported similar findings which correlate with our finding in the current study.

Cinnamon powder at different doses lowered the total lipid, total cholesterol, triglyceride and LDL levels in serum of rats in our study and a remarkable increase was observed in HDL concentration in cinnamon treated groups (Tables 2-6) and it may be proposed that the cinnamon powder might have a direct role in the metabolism of lipids. These results correlate with the findings of Khan *et al.* (2003) who evaluated that the bark of cinnamon at various doses control total cholesterol and triglyceride levels and reduce free fatty acids level in type 2 diabetic subjects due to its strong activity of lipolysis. Hence it indicates the efficacy of cinnamon powder in preventing the increased levels of lipid profile in hyperlipidemia.

Biochemical studies indicate that triglycerides itself are considered independently related to cardiovascular disease (Bainton *et al*., 1992) and most of the drugs treating hypercholesterolemia do not reduce triglycerides concentration but the cinnamon powder equivalent to 6 gm/kg body weight reduced it by 41.81% at treatment day 60 in current study and a substantial reduction in triglycerides (41.81%) and LDL (80.37%) after supplementation of cinnamon powder equivalent to 6 gm/kg body weight demonstrates its importance in preventing cardiovascular diseases. These results also correlate with the findings of Zari and Allogmani (2009) who reported that there was a significant ($P < 0.05$) reduction in total cholesterol, triglycerides and LDL along with considerable increase ($P<0.05$) in HDL concentration after the supplementation of 5% *C. zeylanicum* oil in streptozotocin induced diabetic rats. Hence it may be inferred that the cinnamon powder may be useful in controlling the certain lipoproteins metabolism that results in considerable attenuation of LDL and HDL levels towards normal values thereby indicating the hypolipidemic effect of the cinnamon powder. Similar findings also reported by Khan *et al*. (2003) who evaluated that cinnamon lowered the concentration of glucose, triglyceride and LDL in type 2 diabetic people.

Ample studies exist in accordance to the fact that the level of HDL is inversely related to the total cholesterol in body and lower level of plasma HDL by impairing the cholesterol clearance from the arterial walls may lead to the development of atherosclerosis contributing to ischaemic heart disease (Kanungo *et al*., 2007). HDL acts an antiatherogenic lipoprotein.

HDL particles take up excess cell cholesterol and process then transport cholesterol for further delivery from peripheral tissues to liver for metabolism (Martinez *et al*., 2004), therefore, considered as protective agent against CAD. In our study, administration of cinnamon powder elevated the HDL levels in hyperlipidemic albino rats. These increased HDL levels, after the administration of cinnamon powder, may be due to the elevation in the lecithin cholesterol acyl transferase (LCAT) activity which may attribute to the blood lipids regulation (Patil *et al.,* 2004).

In this study efficacy of cinnamon powder was compared with simvastatin, a standard lipid lowering drug. A similar comparison was made by Javed *et al.* (2009) in albino rabbits. In present study, treatment with either cinnamon powder or simvastatin improved the lipid profile indicators. Cinnamon powder equivalent to 6 gm/ kg body weight substantially reduced the total lipids (21.41 %), total cholesterol (35.88 %), triglyceride (41.81 %) and LDL concentration (80.37 %) and substantially increase the HDL concentration (76.11 %) in serum at treatment day 60. The cinnamon treated groups showed hypolipidemic effect when compared with untreated control group. This may be due to the presence of some hypolipidemic compounds that may act as inhibitor for some enzymes such as HMG Co-A reductase, which inhibits the cholesterol production in liver of rats or decrease the cholesterol absorption form intestine and this has already been proposed by Sharma *et al.* (2003). Similar effects in lowering lipid profile parameters were also observed by Shepherd (2004) who found that the statin such as atoravastatin, rosuvastatin, fluvastatin and pravastatin administration to hypercholesterolemic rats inhibited the enzyme HMG Co-A reductase thus reducing the cholesterol production in liver of rats but did not attenuate the cholesterol absorption in intestine. There was also remarkable restoration in LDL levels near to normal (Tables 2-6) which may be attributed to the cholesterol depletion in hepatocytes, increased clearance of LDL from the blood by hepatic LDL receptors up regulation, and reduced LDL entry into the circulation (Steiner, 2003). Based on these findings it may safely be said that cinnamon powder and simvastatin are equi-efficacious in the treatment of hyperlipidemia.

CONCLUSION

It was concluded from present study that Cinnamon powder at a dose of 6 mg/kg body weight has significant antihyperlipidemic effect in albino rats.

AUTHORS' CONTRIBUTION

Zahid Iqbal developed the idea and methodology and implemented it and participated in article write up. Taseer Ashraf did sampling, analysis and results compilation and participated in write up also. Amir Ali Khan, Riaz Hussain and Mudassar Mohiuddin helped in write up of article and its refinement.

FINANCIAL DISCLOSURE

There is no conflict of interest amongst all authors and contributors of this study.

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