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ANTIHYPERLIPIDEMIC ACTIVITY OF ALCOHOLIC EXTRACT OF *CINNAMOMUM MALABATRUM* BURM. ON CHOLESTEROL DIET INDUCED RATS

Natarajan P[1]*, Sumi John[1], Thangathirupathi A[1], Kala R[1]

Department of Pharmacology[1], Sankaralingam Bhuvaneswari College of Pharmacy, Sivakasi-626130, Tamil Nadu, India

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***Correspondence for Author**
P. Natarajan
Department of Pharmacology, Sankaralingam Bhuvaneswari College of Pharmacy, Sivakasi-626130, Tamil Nadu, India.

ABSTRACT

Hyperlipidemia is an increase (hyper) in the lipids (lipi), which are a group of fats or fatlike substances in the blood (emia). The aim of the study was to reduce the elevated levels of lipids in the blood thus reduce the risk factors responsible for developing ischemic heart disease or the occurrence of further cardiovascular or cerebrovascular diseases using ethanolic extract of leavs of *Cinnamomum malabatrum* on hyperlipidemic rats. The plant extract showed significant decrease in levels of TC, TGs, LDL, VLDL and a significant increase in HDL cholesterol. They also reduced the atherogenic index (A.I) and LDL/HDL ratio when compared to hyperlipidemic control group. Atorvastatin and *Cinnamomum malabatrum* leaf extract resulted in significant increase in the antioxidant enzymes activities and GSH contents in liver and heart homogenate. Alcoholic extract of *Cinnamomum malabatrum* produced significant increase in HMG Co-A / mevalonate ratio in liver as compared to normal group shows that it blocks the HMG Co-A reductase activity. The phytochemical screening reveals the presence of many components responsible for its antioxidant and hypolipidemic activity which includes phenolics, flavinoids, saponins and the pharmacological effects may be due to its presence.

KEY WORDS: Hyperlidemia, *Cinnamomum malabatrum*, Atorvastatin, Lipid profile.

INTRODUCTION

The use of the plants, plant extracts and pure compounds isolated from natural sources provided the foundation to modern pharmaceutical compounds. The world Health Organization (WHO) has listed 21,000 plants, which are used for medicinal purposes around

the world. Among these 2500 species are in India, out of which 150 species are used commercially on a fairly large scale [1]. Spices were some of the most valuable items of trade in the ancient and medieval world Cardiovascular disease is the generic term that describes any disease that affects the cardiovascular system, including the heart and blood vessels. Coronary artery disease, stroke, hypertensive heart disease, rheumatic heart disease, congenital heart disease are some of the common cardiovascular diseases. In 2002, CVDs contributed to approximately a third of entire global deaths, whereas, by the year 2020, it is expected that CVDs will become the leading cause of death and disability worldwide [2]. Hyperlipidemia is an increase (hyper) in the lipids (lipi), which are a group of fats or fatlike substances in the blood (emia). In hyperlipidemia there is a presence of abnormally high amount of lipids (TG, cholesterol) and/or lipoproteins (LDL, VLDL) in the blood. Hyperlipidemia may be responsible for oxidative modification of LDL, protein glycation, glucose auto oxidation with excess production products; these all are the major risk factor for ischemic heart diseases. [3].

Cinnamomum malabatrum is a member of the family Lauraceae. The genus *Cinnamomum* comprises about 250 species, of which 20 occur in India. This species is a close relative of *Cinnamomum verum*. *C. malabatrum* is a moderately sized tree. The wild cinnamons are widely used to adulterate the cultivated cinnamon and also as an important raw material for the Agarbathy industry [4]. The plant has been known for their multiple pharmacological effects such as analgesic and anti-inflammatory [5], hepatoprotective [6], antioxidant [7], anticancer [8] e.t.c. Literature survey revealed that the anti-hyperlipidemic activity of *Cinnamomum malabatrum* has not been clinically evaluated so far. Hence the present study was aimed at evaluating the anti-hyperlipidemic activity of the alcoholic extract of *Cinnamomum malabatrum* in hyperlipidemic rat models.

MATERIALS AND METHODS

Preparation of leaf extract of *Cinnamomum malabatrum*

The leaves of *Cinnamomum malabatrum* collected from Trivandrum, Kerala were dried under shade thoroughly and powered. About 300g of powder was extracted with alcohol (95% ethanol) up to 800ml by a round bottom flask for 2 days, cooled, filtered and concentrated to obtain 3%w/w of extract and it was stored for further use [9]. During the study, the residual extract was suspended in tween-80 and orally administered to the hyperlipidemic rats [10].

Preliminary screening for secondary metabolites

The ethanolic extract of *Cinnamomum malabatrum* were tested for its different chemical groups such as alkaloids, flavinoids, tannins, saponins, glycosides, gums, mucilages, triterpinoids, carbohydrates, steroids and proteins [11,12].

Acute toxicity study

The acute oral toxicity study was carried out as per the OECD guidelines-423. Since upto 2000 mg/kg of ethanolic extract of *Cinnamomum malabatrum* did not produce any toxicity, 1/10th and 1/5th of the highest dose was fixed [13].

Treatment protocol

Healthy young wistar albino rats weighing 150-250 gm were selected for experimental study. The rats were kept in properly numbered large polypropylene cages, given a standard diet and water *ad libitum* throughout the experimental period. The animals were maintained in 12 hr. light and dark cycle at 22^{0}C (± 3^0 C) in a well ventilated animal house under natural conditions, they were acclimatized to laboratory conditions for 10 days prior to the commencements of the experiment. The experimental protocol has been approved by institutional animal ethics committee of the Pankajakasthuri Ayurveda Medical College and R&D section, Kerala (Reg no-PRC/expt/6/2012-2013 dated 30/07/13 and F.no.25/03/09-AWD, GOI). Animals were induced for hyperlipidemic by the oral administration cholesterol (400mg/kg) along with cholic acid for 15 days. The rats with elevated cholesterol level were divided into 5 groups of 6 animals and were given drug/vehicle for another 15 days. GroupI – Normal control and received tween 80 suspension (10 ml/kg b.w; p.o). Group II - Positive control. The animals were made hypercholestremic by supplying cholesterol diet at a dose of 400mg/kg b.w for 30 days. Group III received atorvastatin 1.3 mg/kg b.w; p.o to hypercholestremic rats from day 15 to day 30 Group IV- V received AECM 200 and 400 mg/kg b.w; p.o respectively to hypercholestremic rats from day 15 to day 30 After 30 days blood was collected by retro orbital sinus puncture, under mild ether anaesthesia. Blood samples were collected into non heparinized tubes then centrifuged at 3000 rpm for 10 minutes to obtain the serum for biochemical estimations(14).

Preparation of tissue homogenate

After blood collection, all the animals from each group were sacrificed by cervical dislocation under anaesthetic condition than remove the liver and heart,washed in ice cold normal saline and stored at ultra low deep freezer -86°C (Thermo Fisher Scientific, USA)

until they were processed for following biochemical estimation. 10% homogenate was prepared with ice cold 10% KCl and centrifuged at 1000 rpm for 15 min. The supernatant was used as the source of enzyme. Antioxidant profile such as GSH (reduced glutathione), LPO (Lipid peroxidation) [15] and HMG Co- A activity were measured using standard methods.

Indirect assessment of 3hydroxy3methyl glutaryl coenzyme A (HMG-CoA) reductase activity in liver tissue

A 10% w/v (10 g/dl) liver homogenate was prepared in saline arsenate solution. The homogenate was deproteinised using an equal volume of dilute perchloric acid and allowed to stand for 5 min, followed by centrifugation at 2000 rpm for 10 min. To 1 ml of the filtrate, 0.5 ml of freshly prepared alkaline hydroxylamine reagent (for estimation of HMG-CoA) and dilute hydroxylamine reagent (for estimation of mevalonate) was added. It was mixed and 1.5 ml of ferric chloride reagent was added after 5 min. The absorbance was read after 10 min at 540 nm versus a similarly treated saline arsenate blank. The ratio of HMG-CoA/ mevalonate was calculated [16].

Faecal bile acid estimation

Briefly, for estimation of faecal bile acids, wet faeces were mixed with 50 ml absolute ethanol, kept in a boiling water bath for 20‑30 min and the mixture was filtered into a round bottom flask, rinsed twice with about 5ml hot ethanol. Ethanol was evaporated using rotary evaporator at 60‑70°c at 180 rpm under vacuum. To the residue, 5 ml of 5% sodium hydroxide solution was added, boiled for 30 min, cooled to room temperature and 1 ml of conc. HCl was added drop wise along the sides of the flask. To this mixture, 10 ml of diethyl ether was added, mixed well, transferred into a separating funnel, lower layer (Congo red layer) and middle layer was discarded. The superficial layer (Bile acid layer) was collected. In a beaker containing a pinch of sodium sulphate salt and kept for overnight. Sodium sulphate salt was filtered and washed once with 5 ml diethyl ether. The residue obtained after evaporation of diethyl ether was dissolved in 10 ml acetone and mixed well. Acetone was evaporated after transferring 1 ml of aliquot into a clean beaker. To the residue, 5 ml of 65% sulphuric acid was added and kept for incubation at 60°C for 15 min in a water bath. The solution was allowed to cool at room temperature and was used for estimating Cholic acid by reading the absorbance at 320 nm and Deoxycholic acid at 385 nm using Ultraviolet‑Visible spectrophotometer [17].

Histopathological studies

Liver and Aorta collected from all the animals were preserved and fixed in 10% buffered neutral formalin.

Statistical analysis

Values are expressed as mean ± SEM. The mean differences in body weight and plasma biochemical analysis are analyzed using one way ANOVA followed by Dunnet 't' test. The difference between each groups are considered statistically significant at P<0.05. All statistical analysis was performed using Graph Pad prism statistical software (version 5.03).

RESULTS AND DISCUSSION

The weight gain in high cholesterol-diet group of rats was significantly higher than normal control rats reflecting the influence of high cholesterol diet. The vehicle treated group did not show any significant change in body weight. Drug treated groups (group III, IV &V) also showed a non significant change in body weight when compared to positive control group (hypercholestremic group). The percentage increase of body weight of Group I (negative control) was found to be 4.048% and that of group II (hypercholestremic) was found to be 19.7%. The body weight of drug treated groups (group III, IV, V) was increased by 0.73%, 3.86% and 1.84% respectively. The results of mean body weight of rats were shown in Table 1 The drug treated groups (group III, IV &V) were shown a significant decrease (p<0.001) in total cholesterol when compared to positive control group. The percentage reduction of total cholesterol (TC) of drug treated groups was found to be 28.69%, 17.89% and 31.9% respectively. The changes in total cholesterol were shown in table 2.

The percentage decrease of TG level in groups III, IV & V was found to be 36.97%, 11.0% and 29.51% respectively. The percentage decrease of VLDL level in groups III, IV & V was found to be 40.82%, 21.61% and 28.9% respectively. The percentage decrease of LDL level in groups III, IV & V was found to be 65.62%, 17.33% and 48.83% respectively. The percentage increase of HDL level in groups III, IV & V was found to be 58.94%, 0.64% and 52.62% respectively. The values of TG, LDL, VLDL & HDL and their percentage change were tabulated in table 3. The result in present study showed a decreased level of LDL-C by the administration of standard drug and AECM. This may be due to increased inhibition of intestinal absorption of intestinal cholesterol, interference with lipoprotein production, increased expression of hepatic LDL receptors and their protection etc. leading to an increased removal of LDL-C from the blood and its increased degradation and catabolism of

cholesterol from the body. All these events either individually or in combination lead to decreased serum LDL-C levels which may also have reduced serum TC levels during the treatment with the test extract. The alcoholic extract of *Cinnamomum malabatrum* induced an increase in serum HDL-C levels in the hyperlipidemic models. During blood circulation, HDL-C mediates the transfer of excess cholesterol from peripheral cells to the liver for its catabolism by a pathway termed as “reverse cholesterol transport” hence increased serum HDL-C levels may prove beneficial in lipid disorders and also serve as a cardio protective factor [21, 22].Atherogenic index (A.I) and LDL-C/HDL-C ratio are believed to be important risk factors for diagnosis of atherosclerosis [20]. The drug treated groups (group III, IV, V) demonstrated a decrease in A.I and LDL-C/HDL-C ratio when compared to positive control group. The values were shown in table 4. The study also suggests that cholesterol induction significantly affects the cardio vascular risk factors.

The results of renal and liver function test imply a significant change that was observed in experimental group when compared to hypercholestremic group, so the selected drug was found safe to liver. The positive treated group showed a significant change in all parameters (SGOT, SGPT, ALP, bilirubin, total protein, albumin and globulin) when compared to vehicle treated group. When compared to positive treated group, Atorvastatin treated group and AECM 400mg/kg treated group were showed a significant decrease ($p<0.001$) in SGOT, SGPT, ALP, bilirubin level. The protein level increased nonsignificantly whereas albumin level increased significantly ($p<0.001$) in both standard treated and AECM 400mg/kg treated group. AECM 200mg/kg treated group showed a non significant decrease in levels of SGOT and non significant increase in total protein and albumin level while SGPT, ALP and bilirubin levels were increased significantly($p<0.001$). A significant increase were observed in globulin level of both standard treated and AECM 400mg/kg ($p<0.05$) while a non significant increase were seen in AECM 200mg/kg. The values of biochemical parameters including SGOT, SGPT, ALP, bilirubin, total protein, albumin and globulin were tabulated in table 5a, 5b. The urea, creatinine and uric acid levels were significantly increased in hyperlipidemic models. The urea, creatinine and uric acid levels were significantly decreased in drug treated groups (atorvastatin and AECM 400mg/kg) but AECM 200mg/kg treated group showed a non significant decrease in creatinine and uric acid level and a significant decrease in urea level (table 6). Hyperlipidemic rats showed hyperlipidemia along with hyperglycemia. Studies showed the increased risk of coronary artery disease by the lipoprotein abnormalities associated with diabetes mellitus. AECM at a dose of 400mg/kg

exhibited a significant decrease in glucose level and this might be due to production of insulin by pancreatic β-cells in islets of langerhans or due to enhanced transport of blood glucose to peripheral tissue [21].

The current results revealed that atorvastatin and *Cinnamomum malabatrum* leaf extract resulted in significant increase in the antioxidant enzymes activities and GSH contents in liver and heart homogenate (table 7).

HMG Co-A reductase is the rate-limiting enzyme in the cholesterol biosynthetic pathway which converts HMG Co-A to mevalonate. In this study, HMG Co-A reductase activity was indirectly measured the ratio between HMG Co-A and mevalonate. The ratio was found to be inversely proportional to HMG Co-A reductase activity i.e. an increase in ratio indicating decreased enzyme activity [19]. The alcoholic extract of *Cinnamomum malabatrum* produced a significant increase in HMG Co-A / mevalonate ratio in liver as compared to normal group. The results were shown in table 8. Hypolipidemic activity of atorvastatin may be due to inhibition of HMG Co-A reductase enzyme.

Cholic acid, a component of HCD increases cholesterol absorption by its emulsifying property and decrease cholesterol excretion by concomitant suppression of cholesterol 7 α-hydroxylase [29]. In the present study there shown a slight increase in the fecal excretion of bile acids by drug treatment. The level of fecal cholic acid and deoxycholic acid decreased significantly ($p<0.001$) for positive control group in day 30 when compared to the level at day 1. Group III, IV and V (Atorvastatin, AECM 200mg/kg, and AECM400mg/kg treated) showed a non significant increase in the level of fecal cholic acid and deoxycholic acid after the treatment period. The values were shown in table 9. Fecal loss of cholesterol and its metabolite is the major pathway for sterol excretion; increasing the excretion of bile acids lead to decreased plasma cholesterol concentration [19]. Histopathological abnormalities seen in the liver and aorta of cholesterol control rats are also reversed showing almost normal appearance in standard and AECM 400mg/kg treated animals suggesting a good antihyperlipidemic activity.

Saponins are known to form complexes with cholesterol by binding plasma lipids, thereby altering lipid metabolism. *Cinnamomum malabatrum* contains saponins and tannins which inhibit lipid absorption [14]. Saponins and polyphenols bind with bile salt and cholesterol in the intestinal tract lead to reduction of blood cholesterol by preventing its reabsorption.

Evidences have shown that flavinoids have diverse beneficial effects, including antioxidant activity, decreasing LDL and increasing HDL [21]. Flavinoids and polyphenols are potent free radical scavengers and are known to modulate the activities of various systems. The results suggest that the phenolics are important component of these plants and most of these pharmacological effects may be due to its presence [19].

Table 1: Effect of alcoholic extract of *Cinnamomum malabatrum* Burm. on body weight of cholesterol diet induced hyperlipidemia

Groups	Treatments	Initial Body weight		% change in body weight
		Initial	Final	
I	Normal control (0.2% tween 80, p.o)	205±12.85	213.3±11.16	↑4.048%ns
II	Positive control (cholesterol diet, 400mg/kg b.w; p.o)	224.16±6.379	268.33±9.458	↑19.7%
III	Hypercholestremic albino rats + atorvastatin (1.3 mg/kg, b.w; p.o)	221.62±11.38	220±9.574	↓0.73% ns
IV	Hypercholestremic albino rats + AECM (200 mg/kg, b.w; p.o)	203±6.667	210.83±7.574	↑3.86% ns
V	Hypercholestremic albino rats +AECM(400 mg/kg, b.w; p.o)	224.16±9.347	228.3±9.458	↑1.84% ns

N=6, Data expressed as Mean± SEM. One way ANOVA followed by Dunnett's test.

Groups III, IV &V were compared with group II (Positive control). Group II compared with group I. *P<0.05, **P<0.01, P <0.001*** ns= Non Significant.

Table2: Effect of alcoholic extract of *Cinnamomum malabatrum* Burm. on total cholesterol (TC) of cholesterol -diet induced hyperlipidemic rats

Groups	Treatment	Cholesterol		% reduction
		Initial	Final	
I	Normal control (0.2% tween 80, p.o)	57.88±4.007	58.60±3.991	
II	Positive control (cholesterol diet, 400mg/kg b.w; p.o)	138.1±3.353	141.4±3.247	
III	Hypercholestremic albino rats + Atorvastatin (1.3 mg/kg, b.w; p.o)	139.0±4.202	78.07±5.008***	↓ 28.69 %
VI	Hypercholestremic albino rats + AECM (200 mg/kg, b.w; p.o)	154.2±3.239	116.1±2.879***	↓ 17.89 %
V	Hypercholestremic albino rats +AECM(400 mg/kg, b.w; p.o)	147.8±4.088	96.29±3.67***	↓ 31.9 %

N=6, Data expressed as Mean± SEM. One way ANOVA followed by Dunnett's test. *P<0.05, **P<0.01, P <0.001*** ns= Non Significant.

Table3: Effect Of Alcoholic Extract Of *Cinnamomum Malabatrum* Burm. On Lipid Profile Of Cholesterol - Diet Induced Hyperlipidemic Rats

Groups	Treatment	TG	HDL	VLDL	LDL
I	Normal control (0.2% tween 80, p.o)	54.6±3.991	25.11±1.114	15.02±1.639	19.86±3.445
II	Positive control (cholesterol diet, 400mg/kg b.w; p.o)	111.3±3.88***	18.66±1.804 ns	25.08±1.766***	97.66±4.037***
III	Hypercholestremic albino rats + atorvastatin (1.3 mg/kg, b.w; p.o)	70.15±3.941*** (36.97%) ↓	29.66±2.642** (58.94%) ↑	14.84±0.9492*** (40.82%) ↓	33.57±3.750*** (65.62%) ↓
IV	Hypercholestremic albino rats + AECM (200 mg/kg, b.w; p.o)	99.05±3.276ns (11.00%) ↓	18.54±1.293ns (0.64%) ↑	19.66±0.7243* (21.61%) ↓	80.73±5.500* (17.33%) ↓
V	Hypercholestremic albino rats +AECM(400 mg/kg, b.w; p.o)	78.45±.973*** (29.51%) ↓	28.48±2.112** (52.62%) ↑	17.83±0.7309** (28.9%) ↓	49.97±3.415*** (48.83%) ↓

N=6, Data expressed as Mean± SEM. One way ANOVA followed by Dunnett's test. *P<0.05, **P<0.01, P <0.001*** ns= Non Significant.

Table4: Effect Of Alcoholic Extract Of *Cinnamomum Malabatrum* Burm. On Cardiac Risk Factors Of Cholesterol - Diet Induced Hyperlipidemic Rats

Groups	Treatment	LDL/HDL	A.I
I	Normal control (0.2% tween 80, p.o)	0.8168±0.1638	1.376±0.2371
II	Positive control (cholesterol diet, 400mg/kg b.w; p.o)	5.632±0.8845	7.005±0.9543
III	Hypercholestremic albino rats + atorvastatin (1.3 mg/kg, b.w; p.o)	1.172±0.1587	1.697±0.2165
IV	Hypercholestremic albino rats + AECM (200 mg/kg, b.w; p.o)	4.448±0.4015	5.386±0.3709
V	Hypercholestremic albino rats +AECM(400 mg/kg, b.w; p.o)	1.828±0.2343	2.476±0.2917

N=6, Data expressed as Mean± SEM. One way ANOVA followed by Dunnett's test. *P<0.05, **P<0.01, P <0.001*** ns= Non Significant.

Table5a: Effect of alcoholic extract of *Cinnamomum malabatrum* Burm. on liver function test of cholesterol - diet induced hyperlipidemic rats

Groups	Treatments	SGOT	SGPT	ALP	Bilirubin
I	Normal control (0.2% tween 80, p.o)	59.88±3.99	24.15±1.84	94.42±7.96	0.3633±0.03
II	Positive control (cholesterol diet, 400mg/kg b.w; p.o)	91.69±1.94***	53.35±1.90***	298.7±11.54***	1.963±0.21***
III	Hypercholestremic albino rats + Atorvastatin (1.3 mg/kg, b.w; p.o)	72.58±2.82***	30.14±1.36***	92.07±7.17***	0.3650±0.35***
IV	Hypercholestremic albino rats + AECM (200 mg/kg, b.w; p.o)	85.95±1.920ns	39.63±2.56***	167.3±11.11***	0.47±0.34***
V	Hypercholestremic albino rats +AECM(400 mg/kg, b.w; p.o)	78.77±1.37**	27.28±1.23***	113.9±5.16***	0.49±0.61***

N=6, Data expressed as Mean± SEM. One way ANOVA followed by Dunnett's test. *P<0.05, **P<0.01, P <0.001*** ns= Non Significant.

Table5b: Effect Of Alcoholic Extract Of *Cinnamomum Malabatrum* Burm. On Total Protein, Albumin And Globulin Of Cholesterol - Diet Induced Hyperlipidemic Rats

Groups	Treatments	Total protein	Albumin	Globulin
I	Normal control (0.2% tween 80, p.o)	6.1252±0.49	4.37±0.22	1.755±0.23
II	Positive control (cholesterol diet, 400mg/kg b.w; p.o)	4.468±0.47***	2.835±0.23***	1.633±0.14***
III	Hypercholestremic albino rats + Atorvastatin (1.3 mg/kg, b.w; p.o)	6.05±0.43^{ns}	4.32±0.329***	1.73±0.19*
IV	Hypercholestremic albino rats + AECM (200 mg/kg, b.w; p.o)	5.427±0.57^{ns}	3.785±0.185^{ns}	1.642±0.342 ^{ns}
V	Hypercholestremic albino rats +AECM(400 mg/kg, b.w; p.o)	5.778±0.40^{ns}	4.078±0.168***	1.7±0.217*

N=6, Data expressed as Mean± SEM. One way ANOVA followed by Dunnett's test. *P<0.05, **P<0.01, P <0.001*** ns= Non Significant.

Table 6: Effect Of Alcoholic Extract Of *Cinnamomum Malabatrum* Burm. On Blood Glucose And Renal Function Test Of Cholesterol - Diet Induced Hyperlipidemic Rats

Groups	Treatment	Urea	Creatinine	Uric acid	Blood glucose
I	Normal control (0.2% tween 80, p.o)	21.01±1.572	1.022±0.1048	3.215±0.25	58.6±3.991
II	Positive control (cholesterol diet, 400mg/kg b.w; p.o)	60.59±2.955***	1.898±0.1320***	6.057±0.21***	141.4±3.25***
III	Hypercholestremic albino rats + Atorvastatin (1.3 mg/kg, b.w; p.o)	26.14±1.464***	1.127±0.1109***	3.59±0.48***	78.07±5.01***
IV	Hypercholestremic albino rats + AECM (200 mg/kg, b.w; p.o)	30.44±1.137***	1.878±0.074 ns	5.778±0.18 ns	116.1±2.88*
V	Hypercholestremic albino rats +AECM(400 mg/kg, b.w; p.o)	25.41±0.869***	1.228±0.0933***	4.658±0.28**	96.29±3.67**

N=6, Data expressed as Mean± SEM. One way ANOVA followed by Dunnett's test*P<0.05, **P<0.01, P <0.001*** ns= Non Significant.

Table7: Effect Of Alcoholic Extract Of *Cinnamomum Malabatrum* Burm. On Tissue Antioxidant Status Of Cholesterol - Diet Induced Hyperlipidemic Rats

Groups	Treatments	Lipid peroxide(mM/100g of tissue)		Glutathione (mg/100g of tissue)	
		Liver	Heart	Liver	Heart
I	Normal control (0.2% tween 80, p.o)	0.9983±0.06	1.117±0.01	93.88±1.97	154.2±3.44
II	Positive control (cholesterol diet, 400mg/kg b.w; p.o)	4.010±0.10***	2.02±0.0821***	59.78±2.607***	92.71±2.35***
III	Hypercholestremic albino rats + ATORVASTATIN (1.3 mg/kg, b.w; p.o)	1.115±0.037***	1.128±0.02***	214.8±2.46***	223.1±3.38***
IV	Hypercholestremic albino rats + AECM (200 mg/kg, b; p.o)	3.022±0.13***	1.407±0.07***	156.4±8.45***	176.3±6.80***
V	Hypercholestremic albino rats +AECM(400 mg/kg; p.o)	1.897±0.07***	1.202±0.016***	156.4±8.45***	206.6±1.85***

N=6, Data expressed as Mean± SEM. One way ANOVA followed by Dunnett's test. *P<0.05, **P<0.01, P <0.001*** ns= Non Significant.

Table8: Effect Of Alcoholic Extract Of *Cinnamomum Malabatrum* Burm. On HMG-Coa Reductase Enzyme Activity On Cholesterol - Diet Induced Hyperlipidemic Rats

Groups	Treatments	HMG-CoA/mevalonate ratio
I	Normal control (0.2% tween 80, p.o)	1.37±0.0362
III	Hypercholestremic albino rats + Atorvastatin (1.3 mg/kg, b.w; p.o)	2.170±0.1653***
IV	Hypercholestremic albino rats + AECM (200 mg/kg, b.w; p.o)	1.822±0.1145*
V	Hypercholestremic albino rats +AECM(400 mg/kg, b.w; p.o)	1.907±0.1205**

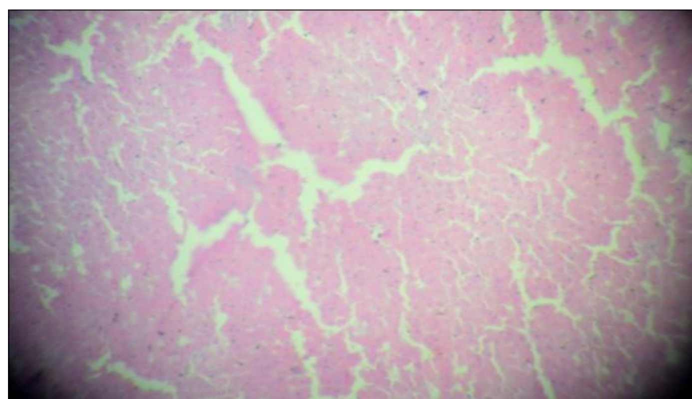
N=6, Data expressed as Mean± SEM. One way ANOVA followed by Dunnett's test. *P<0.05, **P<0.01, P <0.001*** ns= Non Significant.

Table9: Effect of alcoholic extract of *Cinnamomum malabatrum* Burm. on fecal cholic acid and deoxycholic acid of cholesterol - diet induced hyperlipidemic rats

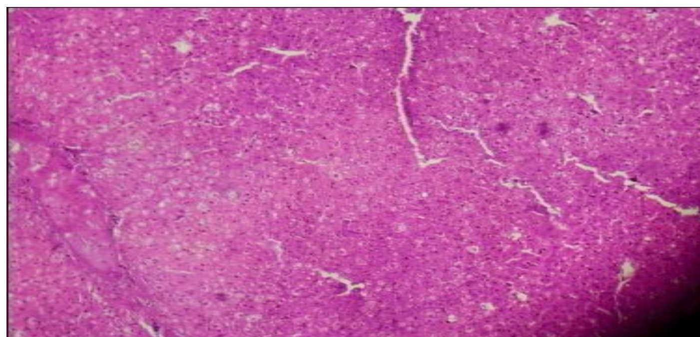
Groups	Treatments	Cholic acid		Deoxycholic acid	
		Day 0	Day 30	Day 0	Day 30
I	Normal control (0.2% tween 80, p.o)	30.83±0.30	30.83±0.30	21.17±0.30	21.17±0.30
II	Positive control (cholesterol diet, 400mg/kg b.w; p.o)	32.67±0.33	31.83±0.47**	22.83±0.30	20.50±0.34**
III	Hypercholestremic albino rats + Atorvastatin (1.3 mg/kg, b.w; p.o)	31.83±0.30	32.17±0.30 ns	20.83±0.30	21.33±0.33 ns
IV	Hypercholestremic albino rats + AECM (200 mg/kg, b.w; p.o)	31.50±0.22	31.50±0.22 ns	21.83±0.30	22.00±0.25 ns
V	Hypercholestremic albino rats +AECM(400 mg/kg, b.w; p.o)	32.00±0.25	32.03±0.30 ns	20.83±0.30	21.33±0.21 ns

N=6, Data expressed as Mean± SEM. One way ANOVA followed by Dunnett's test.*P<0.05, **P<0.01, P <0.001*** ns= Non Significant.

Histopathology for Liver



a



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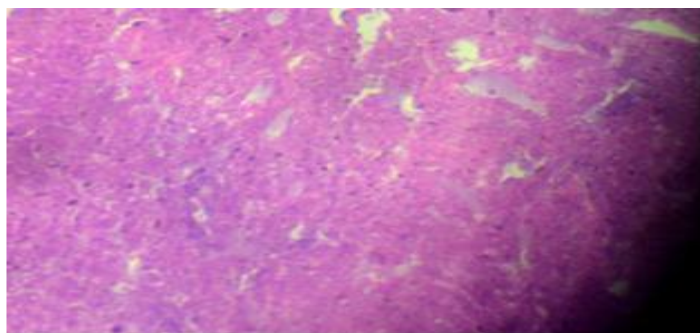

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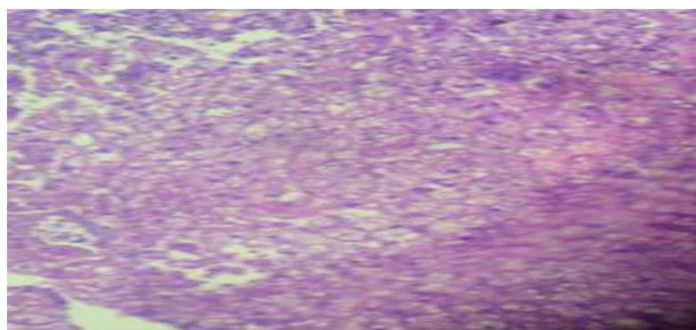

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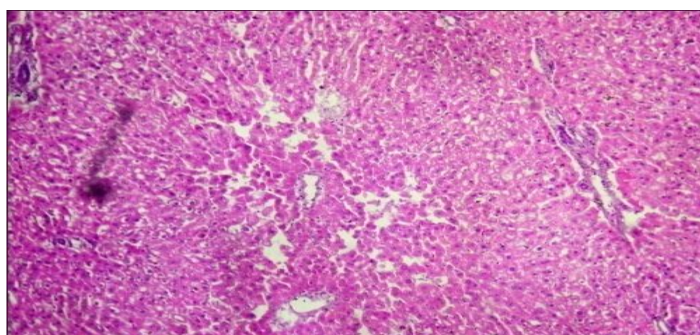
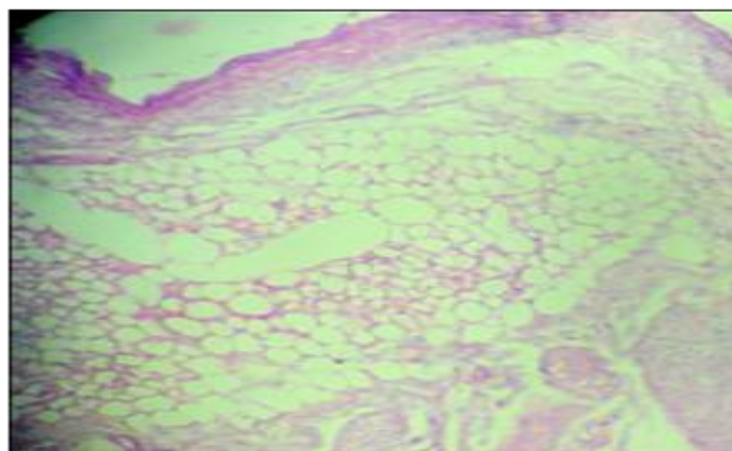


e

Fig.1: Light microscopic appearance of liver sections (haematoxylin-eosin, 400 x) - (a)Normal control group showing normal architecture; (b) Positive control group showing fatty infiltration and granular degeneration; (c) Standard treated group showing negligible degeneration; (d) AECM 200mg/kg treated group showing moderate fatty infiltration and granular degeneration; (e) AECM 400mg/kg treated group showing mild fatty infiltration and granular degeneration.

Histopathology for Heart

a



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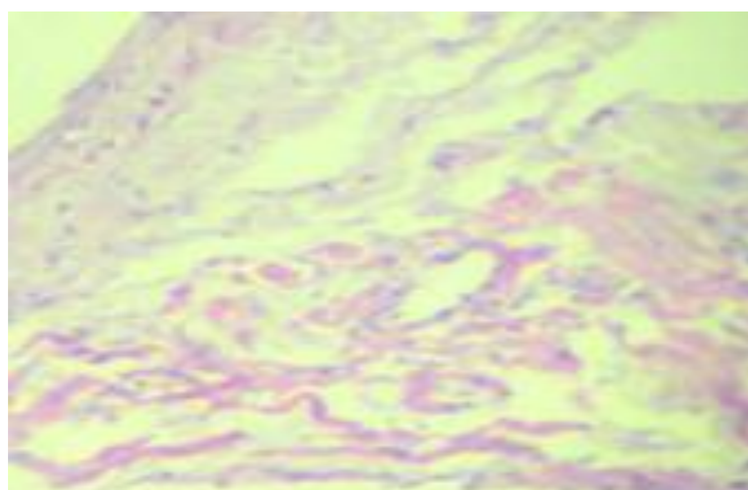

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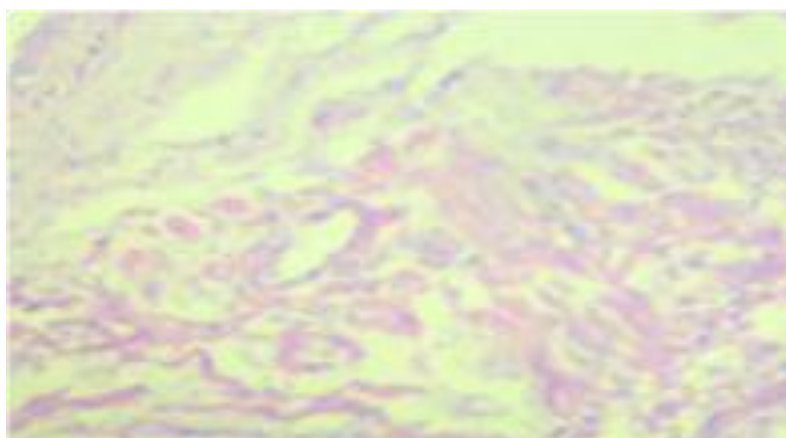

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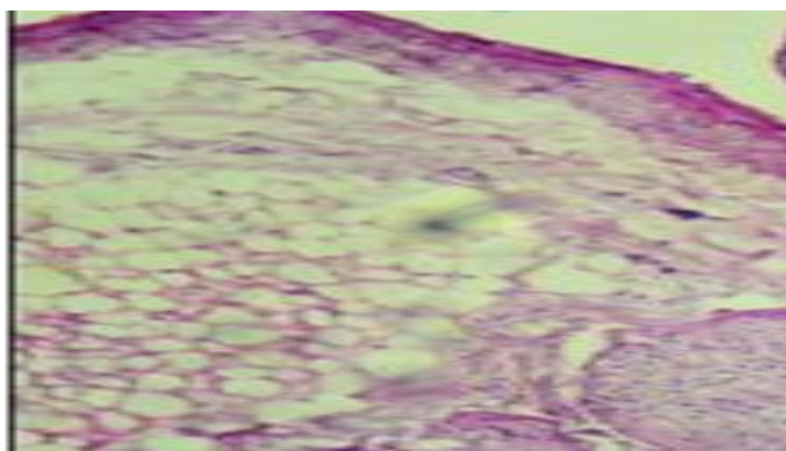

e

Fig.2: Light microscopic examination of heart sections (400 x) – (a) Structure of normal aorta consist of Intima-innermost layer lined by endothelial cell, Media-consist of elastic fibers and Adeventitia –fibrous outer covering; (b) Positive treated group showing lipid accumulation and deposits of mucopolysaccharide in the medial elastic tissue; (c) Standard treated group showing normal elastic fibers and no deposits of mucopolysaccharides. (d) AECM 200mg/kg treated group showing mild necrosis and accumulation of lipids; (e) AECM 400mg/kg treated group showing regeneration of necrosis and no deposits of lipids and mucopolysaccharide

CONCLUSION

The alcoholic extract of *Cinnamomum malabatrum* showed a significant antihyperlipidemic activity in cholesterol induced hyperlipidemic rat models, which was almost comparable to that of the standard atorvastatin drug used in the treatment. so it could be considered as a possible therapeutic value.

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