Anti-hyperlipidemic Activity of *Carissa carandas* (Auct.) Leaves Extract in Egg Yolk Induced Hyperlipidemic Rats

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Abstract: The Purpose of this study was to examine the lipid lowering activity of aqueous: ethanol (1:1) extract of *Carissa carandas* in Egg yolk induced hyperlipidemic rats. A highly significant increase in the weight of group ***C*** (High cholesterol diet) rats was observed when compared with control group ***N*** ($P<0.01$). The extract caused a significant reduction in body weight, Cholesterol, Triglycerides, HDL and LDL in hyperlipidemic rats. Histopathological changes induced by high cholesterol diet were also significantly reduced by the extract. The activity of ethanol and water extract of *C. carandas* was comparable to that of atorvastatin.

Keywords: *Carissa carandas,* hyperlipidemia, egg yolk, atorvastatin.

INTRODUCTION

Cardiovascular disease is a major problem worldwide. The World Health Organization estimates that this disease is responsible for the deaths of approximately 30,000 people each day [1]. The search for compounds that will prevent or retard progression of the disease and beneficially effect the impairment of patients with cardiac failure continues to attract much interest. There are a number of ways in which the heart can malfunction and, in many cases drugs, which alleviate these conditions are available [2, 3].

Cardiovascular diseases encompass an immense category of disorders, because many things can go wrong with the heart and blood vessels. Nevertheless, it is a rather common classification term for the primary cause of death in the U.S.A. and in most countries [4].

It is now established that hyperlipidemia represents a major risk factor for the premature development of atherosclerosis and its cardiovascular complications. A logical strategy to prevent or treat atherosclerosis and reduce the incidence of cardiovascular events is to target the hyperlipidemia by diet and /or lipid lowering drugs. [5, 6].

Carissa carandas belongs to family apocynaceae which consists of 300 genera and 1000 species. It is a large shrub with simple thorn and commonly cultivated throughout Pakistan for hedges and is called " Kakronda". The different parts of this plant have been used for various systems of medicine. Cardiotonic activity was found in root of this plant. This plant has been mentioned in the old chemical literature as purgative, stomachic, antihelmintics and antidote for snake-bite. The physical characteristics of oil from the fruits of Carissa carandas were determined by using standard methods. In addition to this a study of sugars and amino acids from the fruits of this plant was also undertaken by the present authors. Their studies in the chemical investigation on this plant had led to the isolation of two new triterpene carissol I a and carissic acid I b [7].

The unripe fruit is used medicinally as an astringent. The ripe fruit is taken as an antiscorbutic and remedy for biliousness. The leaf decoction is valued in cases of intermittent fever, diarrhea, oral inflammation and earache. The root is employed as a bitter stomachic and vermifuge and it is an ingredient in a remedy for itches. The roots contain salicylic acid and cardiac glycosides causing a slight decrease in blood pressure. Also reported are carissone; the D-glycoside of *B*-sitosterol; glucosides of odoroside H; carindone, a terpenoid; lupeol; ursolic acid and its methyl ester; also carinol, a phenolic lignan. Bark, leaves and fruit contain an unnamed alkaloid [7].

Alternative energy sources from plants of Western Ghats (Tamil Nadu, India) [8]. Twenty two taxa of Western Ghats plants were screened as potential alternative crops for renewable energy, oil, hydrocarbon and phytochemicals. The highest hydrocarbon yields were observed for Carissa carandas (1.7%), and Jatropha gossypifolia (1.7%).

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Volatile flavor constituents of Karanda (Carissa carandas L.) fruit [9]. The volatile flavor constituents of karanda fruits growing in Cuba were analyzed by GC and GC/MS. One hundred and fifty compounds were identified in the aroma concentration, of which isoamyl alcohol, isobutanol and **α**-caryophyllene were the major constituents.

Analgesic and anti-inflammatory activity of Carissa carandas linn fruits and Microstylis wallichii Lindl tubers [10]. The extracts of Carissa carandas and Microstylis wallichii resulted in an inhibition of stretching episodes and percentage protection was 16.05-17.58% respectively in acetic acid induced writhin.

MATERIAL AND METHODS

Plant Material

Carissa carandas (Auct.) was collected from the Herbal Garden of Hamdard University and Identified by Prof. Dr. M. Qaiser, Department of Botany, University of Karachi, where a voucher specimen GH no. 97998 has been deposited.

Extraction

Air dried leaves of *Carissa carandas* were crushed into coarse size in a mortor and pastle and soaked in a mixture of Ethanol and water (1:1) for six days then filtered. Solvents were evaporated by the help of a Rotary Evaporator (R-114- Buchi) and freeze dried by the help of Lyophilizer (Tokyo, Rikakikai CO. LTD.) [11]. This *Carissa carandas* leaves extract (C.C.L.E.) was used for the experiments related to cardiovascular studies.

Experimental Animals

Sprague- Dawley rats of either sex, weighing 220-250 g were purchased from animal house of *HEJ Research Institute of Chemistry, International Centre for Chemical and Biological Sciences (ICCBS), University of Karachi* and were given standard diet and water *ad-libitum* [12]. They were housed in a controlled room with a 12 h light-dark, at room temperature of 22±02^{o}C at *Dr. H. M. I. Institute of Pharmacology and Herbal Sciences, Hamdard University, Karachi, Pakistan.* The Institutional Animals Ethics Committee approved all the protocols of animal's maintenance and handling which were in accordance to internationally accepted standard guidelines for use of laboratory animals [13].

ANTI-HYPERLIPIDEMIC ACTIVITY ON RATS

Experimental Protocol

The hyperlipidemic condition was induced by addition of egg yolk (24%) of the whole feed (Table **1**). For the experiment, animals were divided into four groups of six rats in each group [14]. The rats were treated orally for eight weeks and their body weights were recorded every day [15].

Groups of Experimental Animals

Following groups of animals were made for the anti-hyperlipidemic activity [16].

Group (N) served as Control, received equivalent volume of distilled water as that of treated rats receiving drug through oral route.

Group (C) served as Control for rats taking test drug, as they received high cholesterol diet (24% egg yolk in total diet) [17].

Group (CS1) served as treated rats, receiving cholesterol diet and test drug i.e., ethanol: water (1:1) extract of *Carissa carandas* Leaves (C.C.L.E.). The doses were administered orally to rats once daily for eight weeks [18].

Table 1: Feed Formula for Cholesterol Control Group (Group C) Rats

S. No.	Ingredients	1 kg	S. No.	Ingredients	1 kg
1.	Wheat flour	300g	7.	Rovi mix	100g
2.	Gram flour	90g	8.	Yeast	20g
3.	Maize flour	50g	9.	Common Salt	5g
4.	**Egg Yolk**	240g	10.	CaCo3	3g
5.	Milk Powder	50g	11.	Mn So4	2g
6.	Fish meat	60g	12.	Fat	80g

Table 2: Change in the Weights of Rats After Eight Weeks Treatment

Groups	Duration Weeks	Initial Body Weight (gm)	Final Body Weight (gm)	% Gain in Body Weight	Ortality	Toxic Effect
Saline Control ***N***	8	244.05±12.31	270.44±20.13	10.64 ±5.534	Nil	Nil
Control(High cholesterol) ***C***	8	223.85±4.60	253.47±9.56	**13.00±2.292	Nil	Ni
Extract Treated 1000 mg/kg (***CS1)***	8	236.7 ±4.43	254.66±8.27	9.08±0.866	Nil	Nil
Atorvastatin Treated 0.2mg/kg (***CS2)***	8	240.2 ±4.28	256.52±9.05	8.25±1.228	Nil	Nil

n= 6

Mean value± SEM

**P<0.01

Group (CS2) served as treated rats, receive cholesterol diet and standard drug atorvastatin. The Standard drug was administered orally once daily for eight weeks [19].

All test drugs were compared with the control rats **(Group C).**

By the end of 8th week, rats were anaesthetized with Pentothal sodium 50 mg/kg i.p

24 hours after the last dose of treatment [20]. All animals were autopsied and their kidneys, heart and liver were dissected out and changes were observed.

Preparation of Dilutions of Drugs

The extract of leaves of plant C.C.L.E. was tested at the dose of 1000 mg/kg, p.o. by dissolving the extract in warm distilled water [21].

The standard hypolipdemic drug atorvastatin (10 mg) was administered at the dose of 0.2 mg/ kg p.o. dissolved in distilled water [22].

Biochemical Studies

At the end of eighth week, the blood samples from rats, approximately 4 to 6 ml from each rat, were drawn by cardiac puncture with sterile disposable syringe, before dissecting the animals. Serum was separated by centrifugation at 2000 rpm for 15 min by using BHG Hermle Z230 Centrifuge machine [18]. The Chemical Kits were used (Diagnostica Merck, Gernmany) for biochemical analysis. The serum level of Cholesterol, Triglyceride, High Density Lipoprotein, Low Density Lipoprotein, Alanine Amino Transferase, Aspartate Amino Transferase, Bilirubin (Total and direct), Gamma Glutatamyl Transferase, Alkaline Phosphatase, Creatinine kinase, Glucose, Albumin, Creatinine, Urea, and Uric acid were determined [23].

RESULTS

Behavioral Changes

Male and female rats treated with extract of C.C leaves (1000 mg / kg-body weight) for the period of eight weeks, did not show any mortality. Rats from ***C*** group (fed on high cholesterol diet) were compared with those of the ***N*** group (control) for the lipid profile. Rats from ***CS*** groups (fed on high cholesterol diet + treated drugs) were compared with those of ***C*** group for the effects of drugs. Rats from the ***C*** group spent most of the time in sleeping and resting. High cholesterol diet perhaps induced sluggishness [24] but some physical behavioral changes were observed in first hour after dosing like uncoordinated motor activity and corner sitting.

Body Weights

Rats of ***N, C, CS1*** and ***CS2*** groups showed an increase in the body weight. In groups ***N, CS1*** and ***CS2*** that increase was non significant (P>0.05) while highly significant increase was observed in the weight of group ***C*** rats when compared with control group ***N*** (P<0.01) (Table **2**).

Autopsy

Autopsy revealed that no gross changes were observed in organs like liver, spleen, heart and kidney among the animals of group **N,** and **CS** groups, while the animals of group **C** that were fed on 24% cholesterol diet for eight weeks showed **marked deposition** of fats on heart muscles, aorta and on the liver. (Figures **1**-**4**). **Brown spots** were observed on spleen causing a change in colour of spleen.

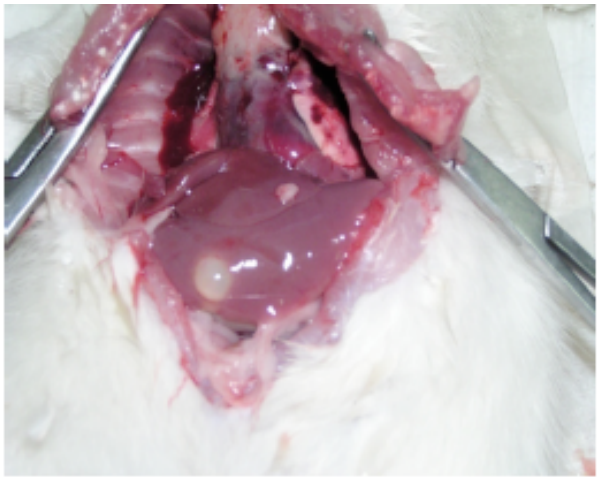


Figure 1: Deposition of fats on Aorta in rats.

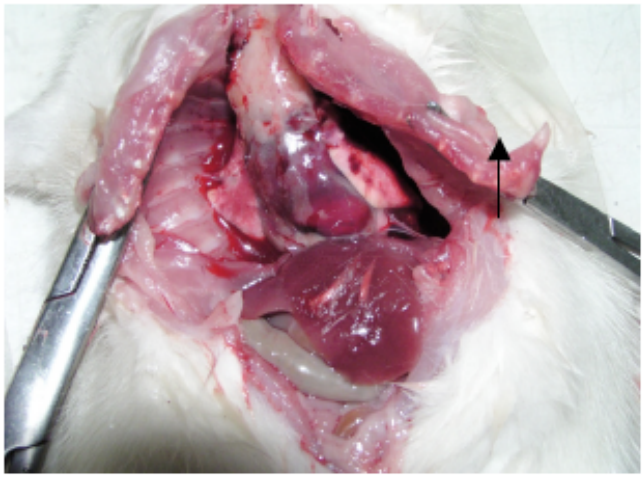


Figure 2: Deposition of fats on Aorta and liver tissues in rats after two weeks.

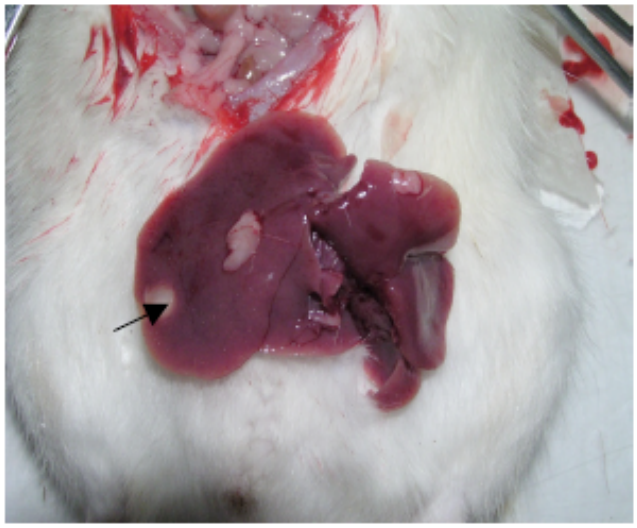


Figure 3: Deposition of fats in liver tissues of rats.

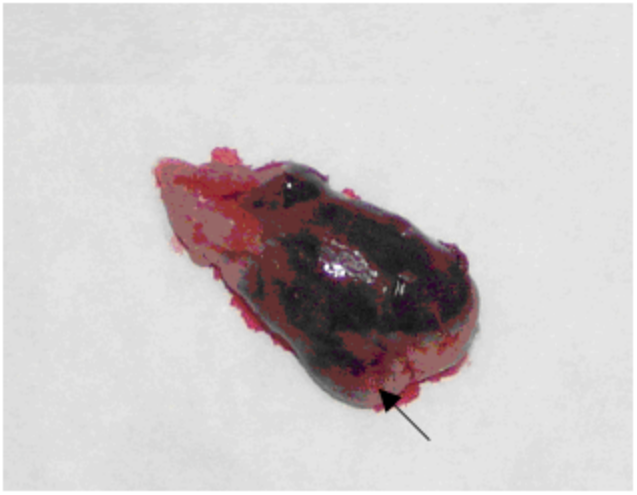


Figure 4: Deposition of fats on cardiac walls in rats.

Effects of Tested Drugs on Different Biochemical Parameters of Hyperlipidemic Rats

The effects of C.C.L.E. leaves extract on Rats' Blood chemistry were measured and presented in figures of Panel a and Panel b. The alterations in the concentration of, Cholesterol, Triglycerides, High Density Lipoprotein (HDL), Alanine amino transferase (ALAT), Aspartate Amino Transferase (ASAT), Creatinine, Creatinine Kinase (CK), Alkaline Phosphatase, Bilirubin Direct, Bilirubin Total, Albumin, and Glucose were recorded in all groups.

Group C

The rats fed with 24% egg yolk in their diet for eight weeks i.e**.,** Group **C** rats' serum were found to have highly significant increase in cholesterol i.e., 120.609 % ±12.05 ($P<0.005$), significant increase in Triglycerides i.e., 70.62 % ± 29.21 ($P<0.05$), highly significant increase in LDL i.e., 327.61% ± 97.73 ($P<0.005$), non significant increase in HDL i.e., 40.70% ± 23.77($P>0.05$). A non significant decrease in Creatinine i.e., 20.02%± 38.63 ($P>0.05$) was observed when compared with their controls **(N).** A non significant increase in ALAT, ASAT, GGT Alkaline Phosphatase, and Albumin, Bilirubin Direct ($P>0.05$), and highly significant increase in Bilirubin total i.e., 79.84% ± 36.52 ($P<0.01$) was observed when compared with their control. The level of Creatinine Kinase, Urea, and Glucose were non significantly increased ($P>0.05$) and no change in serum was observed when compared with their control group **(N)**. **(Panel a)**

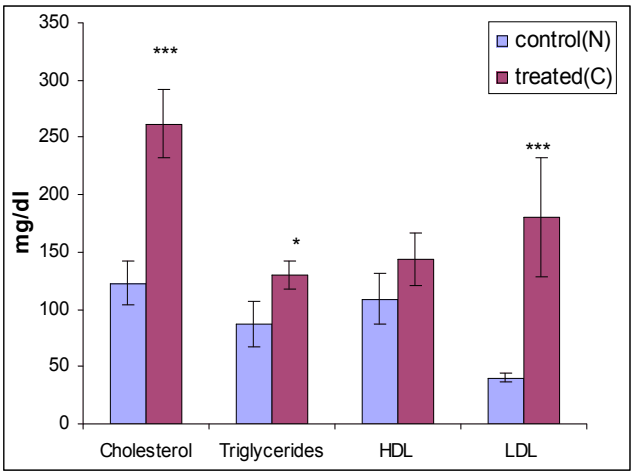
Group CS1:

Rats fed on 24% egg yolk in their diet as well as treated with extract C.C.L.E.(1000mg/kg) for eight weeks had significant decrease in cholesterol (P<0.025), Triglycerides, and HDL (P<0.05). A highly significant decrease in LDL (P<0.025) and Albumin (P<0.01). ALAT, ASAT, Alkaline Phosphatase, Bilirubin Direct, Bilirubin Total , CK, Creatinine, and Urea were decreased non significantly (P>0.05). GGT was significantly decreased (P<0.05). A significant increase in Serum Glucose (P<0.05) and highly significant decrease in Uric acid (P<0.01) was observed as compared to their respective control group **(C). (Panel b)**

Group CS2

Rats fed on 24% egg yolk in their diet as well as treated with Atorvastatin (0.2mg/kg) for eight weeks had a highly significant decrease in cholesterol and LDL (P<0.025) while Triglycerides, HDL, GGT, ALAT, CK and Creatinine were significantly decreased non significantly (P>0.05). ASAT, Alkaline Phosphatase, Bilirubin Direct, Bilirubin Total, Serum Glucose and Urea decreased non significantly (P>0.05) and Uric acid increased significantly (P<0.05) and a highly significant decrease in Albumin (P<0.01) and Uric acid (P<0.01) was observed as compared to their respective control group **(C). (Panel b)**

Panel a: Figures **5**-**12** Treated Group C (hyperlipidaemic) compared with Group N (control) for different biochemicals n=6, Mean ± SEM, P<0.05*, P<0.025**, P<0.01***, P<0.005*** *



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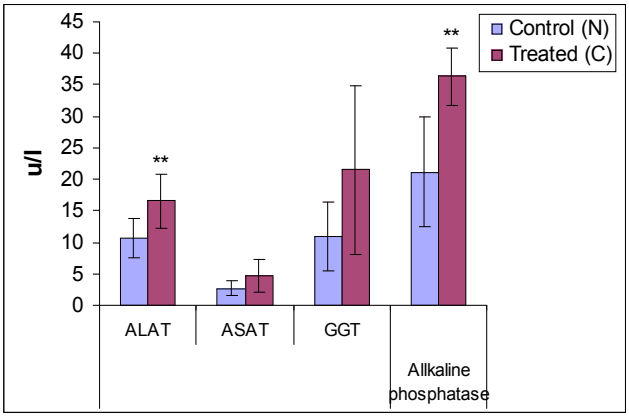

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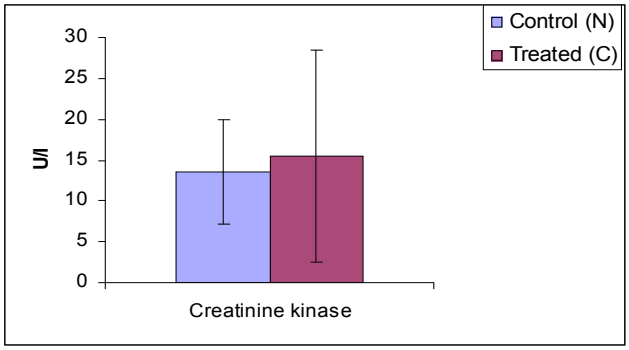

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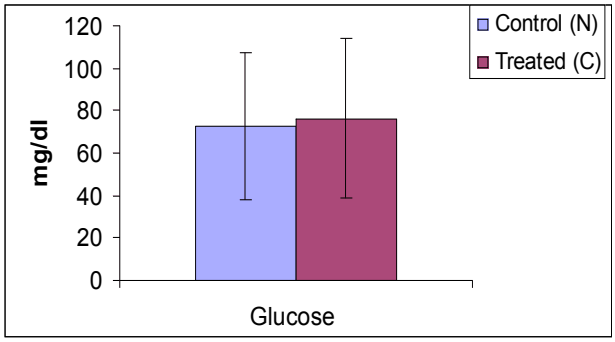

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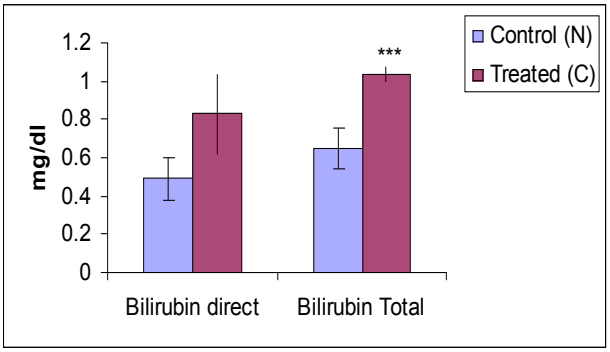

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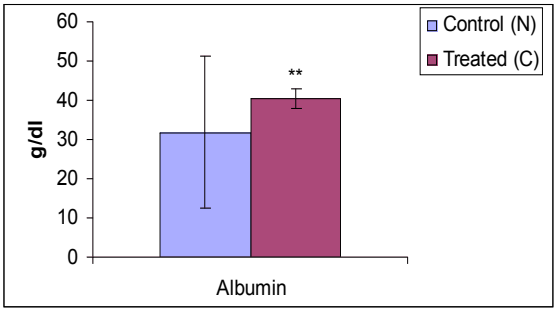

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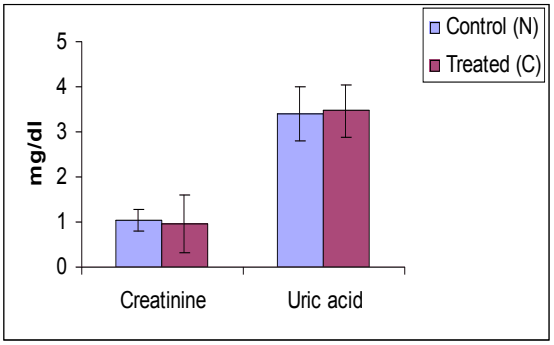

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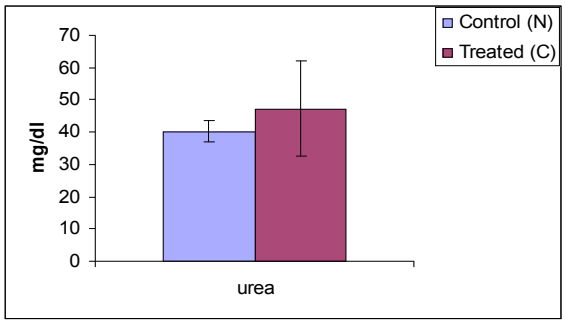
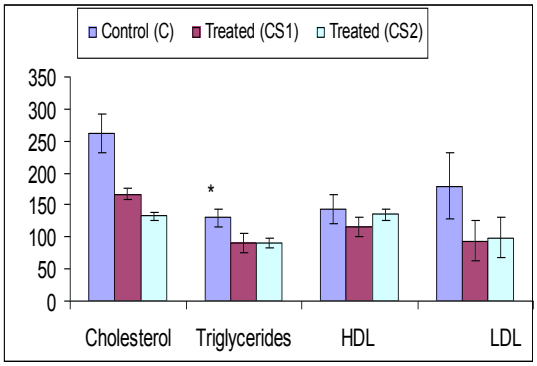


Figure 12:

Panel b: Fig.13-20 Treated Groups CS1= high cholesterol diet + C.C.L.E. 1000mg/kg and CS2= high cholesterol diet + Atorvastatin (0.2mg/kg) compared with hyperlipidaemic Group C (control) for different biochemicals n=6, Mean ± SEM, P<0.05*, P<0.025**, P<0.01***, P<0.005*** *



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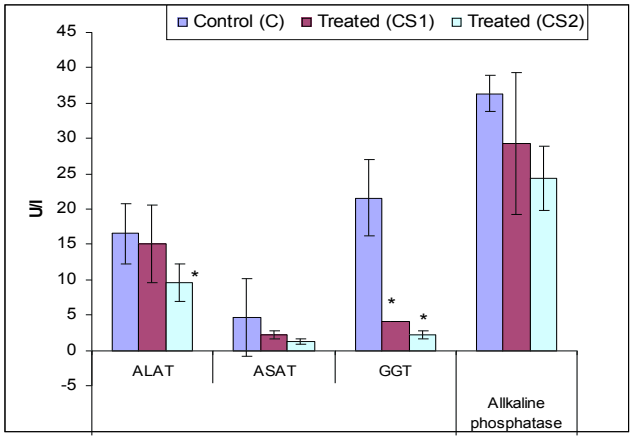

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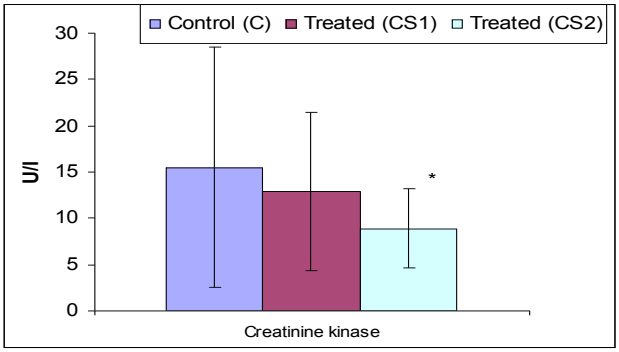

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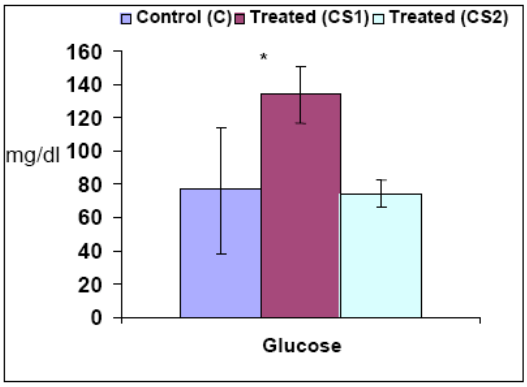

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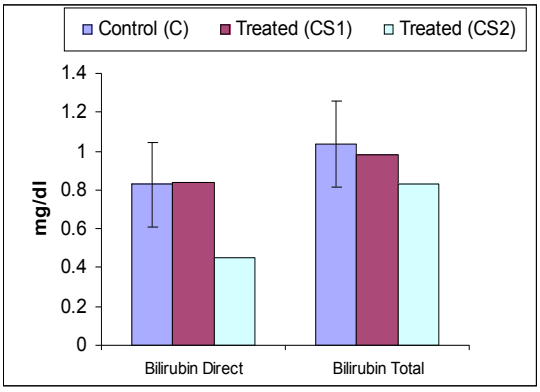

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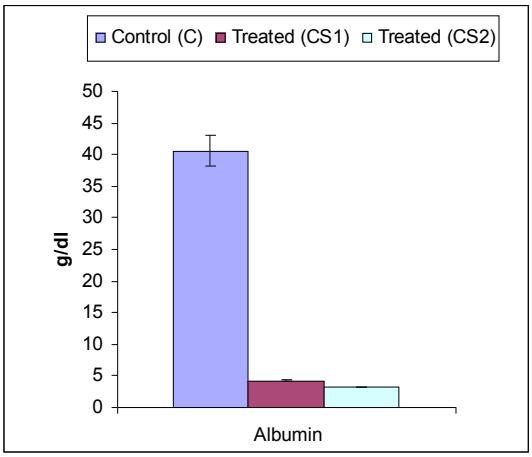

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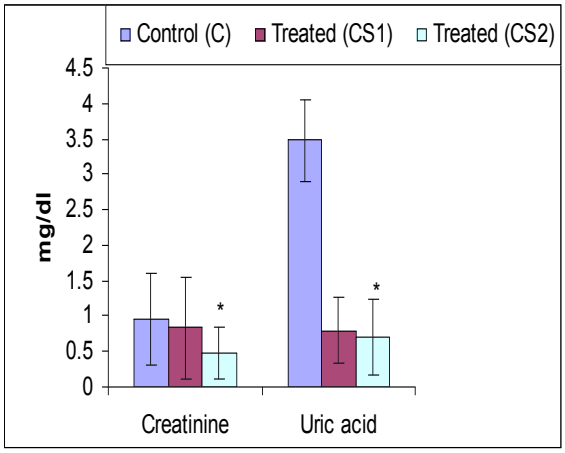

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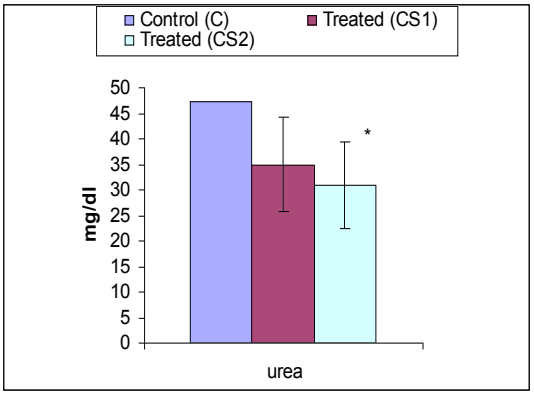

Figure 20:

DISCUSSION

Antihyperlipidemic Activity of C.C.L.E

Behavioral Changes

These changes like uncoordinated motor activity and corner sitting were observed only in one hour after dosing of tested drug and after one hour the rats **behaved** normally as compared with their controls group.

Body Weights

Body weight was reported to correlate well with serum cholesterol levels [25]. Long term intake of cholesterol in rats (C group) resulted in high blood cholesterol and caused accumulation of fats in tissues. It is possible that the gain in body weight of these rats was due to deposition of excess lipid that escaped the body's threshold metabolism [26]. **(Ohlogre et al., 1981)** Group **CS3** rats were lightest among four groups, while **CS1** and **CS2** were lighter than their controls group N, indicating that the weight gain was least in the group receiving Extract as tested drug.

Autopsy

Rats in group C were showing the changes in heart, liver, kidney and spleen in the form of fatty deposition on these tissues, while such depositions were not found in rats of tested drugs (Figures **1-4**).

Effect of Tested Drugs on different Biochemical Parameters of Hyperlipidemic Rats:

Serum Cholesterol

The high level of blood cholesterol observed in **Group C** (Figure **5**) rats surpassed those found in the other groups. This is due to the direct effect of high dietary cholesterol in increasing the total serum cholesterol levels and low density lipoprotiens (LDL)-cholesterol [27]. The high cholesterol absorbed is said to be transported to the liver via chylomicron remnants, which suppresses the synthesis of LDL receptors hence raises LDL concentration by decreasing the uptake of VLDL remnants, resulting in conversion of VLDL to LDL which delayed the clearance of circulating LDL [28].

Low Density Lipoprotein (LDL): was measured and it was reported that cholesterol feeding elevated LDL, and reduced HDL [29], due to the suppression of LDL receptor activity [30] **(Graundy and duke 1990)** or newly secreted lipoproteins enriched with cholesteryl ester at the expense of triglycerides (TG) [31, 32, 33, 34].

Liver regulates total body and plasma cholesterol level, by decreasing biliary cholesterol synthesis and absorption efficiency whereby excess cholesterol is converted to bile acid and eventually excreted through feces.

Although the serum cholesterol level of rats of **N** and **CS1 and CS2** groups were comparable i.e., 122.69 ± 19.1, 166.39 ± 8.96** and 132.22 ± 6.6** respectively (Table **2**), which were significantly lower ($p<0.025$) than rats on hypercholesterol diet i.e., 261.66 ± 29.72*** (Figure **5**).

The result showed that the extract (C.C.L.E) was able to reduce total blood cholesterol in rats on normal diet or high cholesterol diets and the effects were comparable to that produced by Reference Drug i.e., Atorvastatin (Figure **6**), (Table **2**).

Triglycerides Level

At the end of study, the drugs were found to cause a decrease in high level of TG. Among group C (129.70 ± 12.71*) and CS2 groups (90.23 ± 7.74**) highly significant decrease ($P< 0.025$) was seen (Figure **13**), while CS1 (190.63±15.53*) caused significant decrease i.e., ($P<0.05$) when compared with group C rats (Figure **13**).

Triglyceride metabolism is inversely related to the HDL concentration [35]. When the metabolism of TG is sluggish, the increased TG and decreased HDL levels are not associated with elevated LDL. The liver converts excess calories to TG, which is packed into VLDL and secreted into the circulation. In the fasting state, the VLDLs are the largest lipoproteins that carry a big load of buoyant TG through the blood stream. As the TG is removed by adipose tissue for storage of for muscle fuel, the VLDLs become successively smaller. They are converted first into intermediate lipoprotein (IDLs), and then LDLs, each lower in TG content and thus smaller and denser than its precursor. As VLDL is metabolized, HDL is formed in the circulation from the excess part of the VLDL, mainly cholesterol, phospholipid and certain lipoprotein [35].

High Density Lipoprotein (HDL)

This lipoprotein is the main cholesterol carrier from the body cells to the liver, including those from the arterial walls. In the liver, cholesterol is transformed into bile acids and then excreted through the intestine [24]. This would be the reason why the level of HDL is high in blood of rats fed with hypercholesterolaemic diets (C) (Figure **5**) than controls group (N). The drug of Groups CS1 was found to cause a significant decrease in HDL of C groups, while drug in CS2 group caused highly significant decrease (Figure **13**).

Blood HDL levels are dependent on alcohol intake, exercise, drugs such as clofibrate, nicotinic acids, dietary fat and cholesterol. Cholesterol feeding in several animals species resulted in the appearance of a HDL subfraction designated HDLc. In contrast to HDL, the HDLc is strongly bound by receptors at endothelial cells that have a high affinity for LDL. This suggests that HDL may protect against atherosclerosis by interfering with LDL binding to the endothelial cells, which would reduce the cholesterol uptake by arterial cells.

Creatine Kinase (Ck)

Creatine kinase was applied as a tool for diagnosing myocardial infraction in humans [36]. This is probably why the mean value of CK was non significantly higher in group C (Figure **7**) rats as compared to rats of group N ($P<0.05$). The drugs were found to cause a non significant decrease in CK value in group CS1 and CS2 rats ($P<0.025$) in the results reported here (Figure **15**).

Earlier investigators recorded higher values than normal range in the healthy population of men and women. Newborns generally have increased CK activities from skeletal muscle trauma during birth and the transient hypoxia that may cause the enzymes released [37].

Serum AST

Aspartate aminotransferase is one of several transaminases responsible for amino group transfer in gluconeogenesis. AST is responsible for transferring an amino group from aspartate to α, β- Glutaric acid, forming glutamate and oxaloacetate. The highest concentration of AST is located in cardiac and hepatic tissues. AST is the second enzyme to increase after an acute MI.

Rats of group C had non significant increase in AST serum level **(Fig. 6).** While rats of treated group CS2 showed some healing effect by non significantly decreasing the serum AST except that there was a significant decrease in serum AST in **Group CS1** as compared to there controls group **C** ($p<0.025$) (Figure **14**).

Serum ALT and GGT Levels

The levels of ALT and GGT were used to monitor possible adverse effect of hypercholesterolaemic diets on the liver and biliary tract functions [38]. The blood activity level of these enzymes is balance between the rates. It enters the circulation from changes in permeability of the hepatic cells and the rate at which it is inactivated or removed is changed. The ALT was a reliable indicator of liver necrosis in small animals [39].

On the other hand, GGT is an enzyme of the biliary tract, indicative of disorders/injury of the hepatobiliary system resulting in cholestasis [40] cholecystitis and hepatic necrosis [41, 42]. This enzyme was also released during treatments with certain drugs, medicaments and toxic agents [42, 43]. Changes in the rate of enzymes entering the circulation rates may result from (i) changes to the plasma membrane, (ii) altered rates of enzyme production, and (iii) proliferation of the enzyme producing cells.

There was no significant difference in the blood ALT levels between all experimental groups. Cholesterol fed animals had significant increase in ALT and non significant increase in GGT in their blood that might be due to hepatocellular damage and obstructive changes as observed by histopathology (Figure **20**) and the gross changes in liver. The drugs caused a non significant decrease in blood ALT of cholesterol fed rats, but drug produced a significant decrease in GGT in rats fed on high cholesterol diet. The cholesterol group receiving reference drug showed a highly significant decrease in serum GGT level (Figure **14**).

Bilirubin Direct and Total

Bilirubin is a metabolic end product of lysis of erythrocytes. The reticuloendothelial system catabolizes hemoglobin into free iron, globin, and biliverdin, which is rapidly converted to bilirubin. Unconjugated bilirubin is poorly soluble in serum; therefore it is transported to liver bound to albumin. Unconjugated formis known as indirect or prehepatic bilirubin. In liver, Glucuronyl transferase conjugates bilirubin with two molecules of glucuronic acid, forming bilirubin diglucuronide. This form of bilirubin is highly soluble in serum and is known as direct or hepatic bilirubin [44].

In our study the rats on high cholesterol diet showed a non significant increase in direct bilirubin and a highly significant increase in total bilirubin showing the hepatocellular injury (Figure **9**) as is also revealed by the histopathololgical study when compared with its controls. The extract (C.C.L.E) was found to decrease the bilirubin direct and total showing its healing property (Figure **17**).

Serum Albumin

Significant changes were seen in all groups of experimental animals. Non Significant change in serum Albumin was seen between rats of group **N** and **C**, **(Fig. 10)** while the extract caused a highly significant decrease in serum albumin as seen in groups **CS1 and CS2** suggesting that the drug is bound with serum albumin (Figure **18**)**.** Increased serum cholesterol raised LDL and VLDL levels which could alter the permeability of the glomerular basement membrane by neutralizing its negative charges [45], resulting in more albumin molecules being excreted. Same was observed in the study.

Serum Glucose

Glucose is one of the clinically important carbohydrates. Disorders of carbohydrate metabolism such as diabetes are evaluated in part by measurement of plasma glucose or after suppression or stimulation. Glucose is a major source of energy for brain, muscle and fat. The brain is only tissue not requiring insulin for glucose utilization. If glucose is not available exogenously (fasting state), the body through hormonal mechanisms (counter-regulatory hormones; glucagon, epinephrie, cortisol, and somatostatin), will form its own glucose by tissue and hepatic gluconeogenesis and hepatic glycogenolysis [44].

In our study serum glucose level was non significantly increased in rats fed on high cholesterol diet (group **C**) ($P>0.05$) (Figure **11**). The reason might be the liver cell damage. But the use of Extract (C.C.L.E) significantly increased the serum glucose level, suggesting that the presence of sugar as ingredient during the manufacturing of MUYM and high contents of Glucose and Glycosides in Extract may be responsible for increasing the blood sugar level. While the reference drug Atorvastatin did not produced any effect on blood sugar level when compared with their controls group (Figure **19**).

Serum Urea, Uric acid and Creatinine:

Non significant changes in the level of Creatinine, Urea and Uric acid were observed among groups C, (Figure **12**). While, the animals in Group of reference drug i.e., CS2 showed a signifant decrease in Creatinine, Urea and Uric acid when compared with their controls group C. (Figure **20**) while CS1 group showed significant decrease only in Uric acid. This result shows the healing property of tested drugs at the renal level, for biochemical alterations produced by hypercholesterolemia.

CONCLUSION

The extract (C.C.L.E) **group CS1** proved to be beneficial for treating the hazards produced by hypercholesterolemia. This plant has cardiotonic [3, 45,

46], (hypotensive [47], antioxidant, Radical scavenging [48] and anti-inflammatory properties [49]. In addition our studies have proven it to be an antihyperlipidemic extract. Histopathological screening also confirmed that the cellular damages caused by hyperlipidemia were healed by the tested extract. So the cardiovascular effects as seen during the above mentioned In-vivo Pharmacodynamic Studies are accompanied by the Antihyperlipidemic effects of the tested drugs, which prove this Extract to be effective to treat cardiovascular disorders.

The literature search for the pharmacologically active constituents shows the presence of Carbohydrates, Polyphenols and Gycosides leading to confirm the antihyperlipidemic activity of Carissa carandas leaves extract.

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