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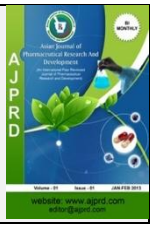

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Research Article

Evaluation of Anti-hyperlipidemic Activity of Red Onion In Experimental Animals

Pooja Kadam *[1], Vitthal Chaware [2], Vivek Redasani [3]

[1]Department of Pharmacology, YSPM's Yashoda Technical Campus Wadhe, Satara, India.

[2]Head of Department (Pharmacology), YSPM's Yashoda Technical Campus, Wadhe, Satara, India.

[3]Principal, YSPM's Yashoda Technical Campus, Wadhe, Satara, India.

A B S T R A C T

Objective: To evaluate antihyperlipidemic effect of red onion on poloxamer 407 induced hyperlipidemia in wistar albino rats.

Methods: Hyperlipidemia was induced by intraperitoneal injection of poloxamer-407 (P-407) at a dose of 1.0g/kg body weight in wistar albino rats. Drug treatments were done by oral gavage for 21 days. At the end of the study, animals were kept fasted over night and then blood samples were collected. The serum total cholesterol (TC), triglycerides (TG), and High density lipoprotein (HDL) were measured while low density lipoprotein (LDL) and very low density lipoprotein (VLDL) were calculated by Friedewald formula and atherogenic index was also calculated.

Results: From the present investigation, it was observed that ethanolic extract of red onion have shown significant reduction in serum cholesterol, triglyceride and lipoprotein levels and increase in HDL level in P-407 induced hyperlipidemia.

Conclusion: The findings in this study revealed the effectiveness of ethanolic extract of red onion against hyperlipidemic activity.

Key words: Hyperlipidemia, Poloxamer 407, red onion, Atorvastatin, Lipid Profile

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***Address for Correspondence:**

P. B. Kadam, Department of Pharmacology, YSPM's Yashoda Technical Campus Wadhe, Satara, India.

INTRODUCTION:

Hyperlipidemia is also termed as acquired hyperlipoproteinemia; high blood triglycerides; high blood cholesterol; high cholesterol; high triglycerides; hyperlipidemia etc. [1.] It is an elevation of one or more of the plasma lipids, including triglycerides, cholesterol, cholesterol esters and phospholipids etc. [2]. It is also described by elevation of serum total cholesterol and low density and very low-density lipoprotein cholesterol and decreased high-density lipoprotein levels [3–6]. Number of clinical trials have verified that increase in plasma total cholesterol (TC) and triglycerides (TG) levels are implicated in the development of atherosclerosis [2]. It is also one of the important risk factor for developing cardiovascular diseases (CVDs) [4,7,8]. Principal CVDs associated with hyperlipidemia are hypertension, ischemic heart diseases, stroke, coronary heart diseases (CHDs) and atherosclerosis. They account for almost 80% of the burden of CVD in both developed and developing countries. A 20% decrease in blood cholesterol level can reduce about 31% of CHD incidence, and 33% of its mortality rate [9]. Because of all these risks associated with hyperlipidemia, treatment is often recommended for people with hyperlipidemia [10].

Effective treatment of hyperlipidemia includes dietary modifications and medications. There are number of antihyperlipidemic agents available in the market but they show certain side-effects and contraindications [10]. Statins are the first-line drugs for treatment of hyperlipidemia which act by inhibiting 3-hydroxy-3-methyl-glutaryl-

coenzyme A (HMGCoA) reductase. However, statins have some adverse effects including rhabdomyolysis and derangements in hepatic function. Fibrates are used as second-line drugs for the treatment of dyslipidemia which acts by activating peroxisome proliferator-activated receptor alpha. However, fibrates shows adverse effects like allergic reactions, nausea, diarrhea etc. Nicotinic acid is also used to treat hyperlipidemia. However, it causes flushing, nausea, vomiting, diarrhea, anorexia like side-effects. Ezetimibe and bile acid sequestrants shows hypolipidemic effect by decreasing intestinal cholesterol absorption; but these drugs are associated with increased gastrointestinal adverse events and also affect the absorption of other biologically important substances [11]. An herbal treatment for hyperlipidemia has no side effects and is relatively less costly, locally available [4]. Hence, people are more interested towards traditional medicinal plants due to their natural origin, safe and non-toxic nature [12].

Red onion (*Allium cepa* L.) is the most widely cultivated species of the genus Allium. The portion of the plant commonly used is the bulb, utilized as a food ingredient to give flavour and aroma to a large variety of dishes [13]. Red onion has been reported to contain flavonoids, phenols, tannins, triterpenoids, cardiac glycosides, saponin and steroid phytochemicals [14]. It also contains Quercetin, cycloalliin, S-methyl-L-cysteine, S-propyl-L-cysteine sulfoxide, dimethyl trisulfide, S-methyl-L-cysteine sulfoxide etc. Literature survey indicates that red onion possesses anti-diabetic [15], Anti-Obesity [16], Hepatoprotective [17], Antidepressant [18], Analgesic [19], Anti-inflammatory [19] and antimicrobial activity etc [14]. Therefore, the present investigation was undertaken to evaluate hypolipidemic effect of ethanolic extract of red onion in poloxamer 407 induced hyperlipidemic rats which has not been previously reported. It is our belief that this investigation will take us another step forward in our quest to understand the mechanism of action of red onion in prevention and treatment of arteriosclerosis and heart related diseases.

MATERIALS AND METHODS:

Drugs & chemical

Poloxamer 407 was acquired from Emcure Pharmaceuticals Ltd Pune. Atorvastatin (Lipvas 20, cipla ltd.) was purchased in a tablet form at strength 20 mg. All other chemicals and reagents used were of analytical grade and procured from approved chemical suppliers. The total cholesterol (TC), triglycerides (TG) and high-density lipoprotein (HDL) were measured with the help of commercial kits.

Collection and extraction of plant material

Fresh red onions were purchased from a local market, satara and were identified by a botanist. They were washed with tap water and then cut into medium pieces. The chopped onions were then blended. The blended onion (200 g) then macerated in 2000 ml ethanol and allowed to stand for a period of 72 h. It was filtered using Whatman filter paper (No. 1). The filtrate was concentrated at 40°C in a water bath for complete dryness. Crude extract obtained was stored at 4°C for further use [20].

Experimental animals

The complete experiment was carried out using 36 wistar albino rats of either sex weighing 150 -200g. The study protocol was approved by Institutional Animal Ethics Committee (IAEC) of YSPM, Satara. The animals were procured from registered breeder and acquainted in the quarantine area for one week. Animals were housed in clean polypropylene cages in a controlled room temperature 22°C ± 2°C, relative humidity of 50 ± 15% and 12 hr dark/ 12 hr light cycle at our Institution's animal house and allowed to acclimatize for two weeks. The animals were fed with standard pellet diet and water *ad libitum*. Animals were maintained as per Committee for the Purpose of Control and Supervision of Experiments on Animals Guidelines.

Preparation of standard drug

Atorvastatin tablets were crushed into powder, dissolved in distilled water at dose 10mg/kg b. w. and administered orally *ad libitum* [9,21].

Induction of hyperlipidaemia

Poloxamer 407 dissolved in cold distilled water at dose 1.0g/kg b. w. and introduced intraperitoneally. All syringes were placed on ice prior to P-407 administration to maintain the polymer in a mobile viscous state during the injection [9,21].

Experimental design

A total 36 wistar albino rats of either sex were randomly divided into 6 groups containing 6 animals in each group. Group 1 (Normal control) did not receive any treatment apart from vehicle 10ml/kg b. w. /day for 21 days. Group 2 (Hyperlipidemic control) were induced with 1.0g/kg b. w. dose of P-407 without treatment [22]. Group 3 (Standard control) were induced with 1.0g/kg dose of P-407 and treated with atorvastatin at a dose of 10mg/kg b. w. /day for 21 days. Group 4, 5 and 6 were induced with 1.0g/kg dose of P-407 and treated with test drug at dose 200 (low), 300 (medium) and 400 (high) mg/kg b. w. /day for 21 days respectively [21].

Blood Sample Collection

At end of the experimental period, animals were kept fasted over night and anaesthetized with diethyl ether. Blood samples were collected serially by retro orbital puncture. The blood was allowed to clot for 30 min at room temperature then serum was separated by centrifugation and used for lipid analysis.

Evaluation parameters

Body weight

Body weight were recorded on the first day of treatment of all groups and final body weight were taken at the end of treatment of all groups to calculate changes between the initial and final body weight of animal throughout the study.

Biochemical parameters

The resulting serum was analyzed for serum TC and TG by Quinoneimine dye absorption method at 505 nm [23] and HDL by precipitation with phosphotungstic acid and Magnesium chloride [24].

Very low density lipoprotein cholesterol (VLDL-C) was calculated as [11,25,12]:

VLDL = TG/5.

Low density lipoprotein cholesterol (LDL-C) levels were calculated using Friedewald's formula [25]:

LDL = TC - HDL - TG/5

The atherogenic index (A.I.) was calculated using the following formula [26]:

(A.I.) = LOG (TG/HDL)

Liver histopathology

The fixed specimens of liver were processed by washing through running tap water, dehydration through ascending grades of alcohol, clearing through xylene and embedding completely with in paraffin into blocks. The serial sections of not exceeding 3 mm thickness were cut using microtome and were mounted on polylysine coated slides, deparaffinised using xylene, rehydrated and stained with hematoxylin and eosin, dehydrated, cleared and mounted on DPX under glass cover slips. The slides were then observed under light microscope which was connected to a camera to capture images.

Statistical analysis

The results were expressed as Mean ± SEM (n=6). The statistical analysis was carried out with Graph pad prism 5.0 software. The data was statistically analyzed using one-way ANOVA followed by Tukey's multiple comparison tests and $p< 0.05$ was considered to be statistically significant.

RESULTS & DISCUSSION

RESULTS

Yield of the extract

The yield of the extract was found to be 3.7%. Further preliminary phytochemical screening revealed the presence of flavonoids, saponins, phenol, diterpenes, triterpenes, alkaloids, phytosterol and proteins.

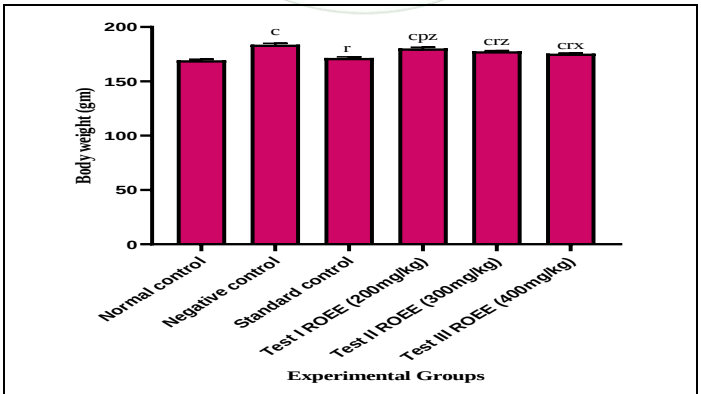
Body weight

Effect of administration of ethanolic extract of red onion on body weight of experimental animals has been shown in table 1. When compared with normal control group, negative control group and all test group animals showed significant ($p<0.001$) increase in body weight but standard control group animals do not show any significant changes in body weight. Furthermore, Standard control group and test II and III group animals showed significant ($p<0.001$) reduction in body weight, whereas test I group showed significant ($p<0.05$) reduction in body weight as compared to negative control group.

Table 1: Effect of ethanolic extract of red onion on body weight of P-407 induced hyperlipidemia in experimental animals.

Sr.	Experimental group	Initial body weight (gm)	Final body weight (gm)	Change in body weight (gm)
1	Normal control	166.6 ± 1.186	169.4 ± 1.622	4.642 ± 1.284
2	Negative control	170.30 ± 3.963	183.8 ± 1.126 ^{c}	13.45 ± 1.098
3	Standard control	168.9 ± 2.032	171.6 ± 1.287 ^{r}	5.33 ± 1.305
4	Test I (200mg/kg)	170.74 ± 2.889	180.3 ± 1.425^{cpz}	9.615 ± 1.491
5	Test II (300mg/kg)	168.75 ± 2.067	177.4 ± 0.689^{crz}	8.03 ± 1.56
6	Test III (400mg/kg)	169.15 ± 1.833	175.5 ± 0.872^{crx}	7.28 ± 1.046

Normal control: distilled water; Negative control: Poloxamer 407; Standard control: Atorvastatin; Test I: ROEE (200mg/kg); Test II: ROEE (300mg/kg); Test III: ROEE (400mg/kg).



Graph 1: Effect of ethanolic extract of Red Onion on body weight (gm)

Values represented mean ± SEM; n=6; Analysis was performed using one way ANOVA followed by Tukey's multiple comparison test; p value less than 0.05 was considered as statistically significant. a<0.05, b<0.01, c<0.001; Data compared with normal control; p<0.05, q<0.01, r<0.001 Data compared with negative control; x<0.05, y<0.01, z<0.001 Data compared with standard control (by one way ANOVA followed by Tukey's multiple comparison test)

Serum lipid profile

Poloxamer 407 administration developed acute hyperlipidemia in rats by significantly increasing the level of total cholesterol, triglycerides, lipoproteins and decreasing HDL level as compared to normal control group.

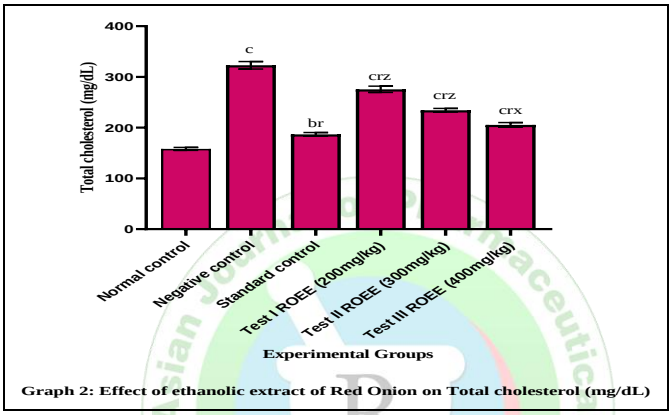
Table 2: Effect of ethanolic extract of red onion on serum lipid profile of P-407 induced hyperlipidemia in experimental animals.

Sr. No.	Experimental group	TC (mg/dL)	Triglyceride (mg/dL)	HDL (mg/dL)	LDL (mg/dL)	VLDL (mg/dL)	Atherogenic index
1	Normal control	158.3 ± 2.934	105.0 ± 2.061	45.00 ± 1.773	92.25 ± 3.382	21.00 ± 0.4522	0.3691 ± 0.01367
2	Negative control	323.0 ± 7.431 ^{c}	207.4 ± 5.259 ^{c}	23.08 ± 0.740 ^{c}	258.4 ± 6.506 ^{c}	41.48 ± 1.052 ^{c}	0.9541 ± 0.01793 ^{c}
3	Standard control	186.7 ± 3.669 ^{br}	128.80 ± 3.560 ^{ar}	38.02 ± 1.003 ^{br}	123.0 ± 3.420 ^{cr}	25.76 ± 0.7119 ^{ar}	0.5298 ± 0.02173 ^{cr}
4	Test I (200mg/kg)	275.6 ± 6.107 ^{crz}	185.7 ± 6.401 ^{cpz}	28.96 ± 0.879 ^{cpz}	209.5 ± 5.120 ^{crz}	37.15 ± 1.280 ^{cpz}	0.8067 ± 0.01864 ^{crz}
5	Test II (300mg/kg)	234.3 ± 3.614 ^{crz}	166.3 ± 5.921 ^{crz}	30.57 ± 1.386 ^{crz}	170.40 ± 2.324 ^{crz}	33.26 ± 1.184 ^{crz}	0.7364 ± 0.01412 ^{crz}
6	Test III (400mg/kg)	207.8 ± 4.021 ^{crx}	150.9 ± 3.912 ^{crx}	31.55 ± 1.218 ^{crx}	146.1 ± 4.276 ^{crx}	30.18 ± 0.782 ^{crx}	0.6805 ± 0.01656 ^{crz}

Normal control: distilled water; Negative control: Poloxamer 407; Standard control: Atorvastatin; Test I: ROEE (200mg/kg); Test II: ROEE (300mg/kg); Test III: ROEE (400mg/kg).

Effect of ethanolic extract of red onion on Total cholesterol

Table 2 shows that the ethanolic extract of red onion has significantly affected the level of total cholesterol in hyperlipidemic rats. The results found that the negative control group showed significant ($p<0.001$) increase in the level of TC as compared to normal control group. Whereas standard control, test I, test II and test III groups showed significant ($p<0.001$) reduction in TC level when compared with negative control group.

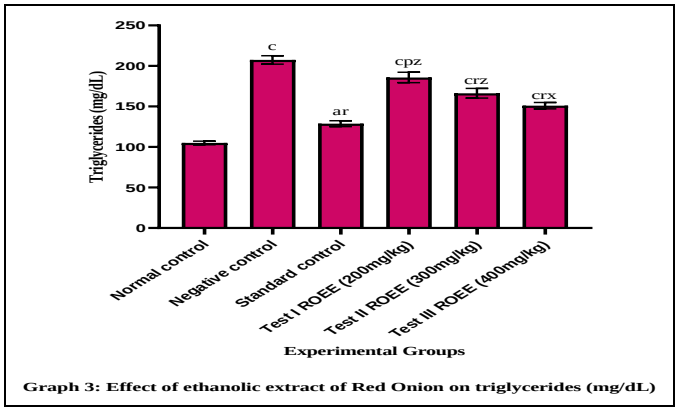


Graph 2: Effect of ethanolic extract of Red Onion on Total cholesterol (mg/dL)

Values represented mean ± SEM; n=6; Analysis was performed using one way ANOVA followed by Tukey's multiple comparison test; p value less than 0.05 was considered as statistically significant. a<0.05, b<0.01, c<0.001; Data compared with normal control; p<0.05, q<0.01, r<0.001 Data compared with negative control; x<0.05, y<0.01, z<0.001 Data compared with standard control (by one way ANOVA followed by Tukey's multiple comparison test).

Effect of ethanolic extract of red onion on Triglycerides

The mean values for triglyceride level are given in table 2. Negative control group showed significantly ($p<0.001$) increased level of triglycerides as compared to normal control group. Standard control, test II and test III group showed significant ($p<0.001$) reduction and test I group showed significant ($p<0.05$) reduction in the level of triglycerides as compared to negative control group.



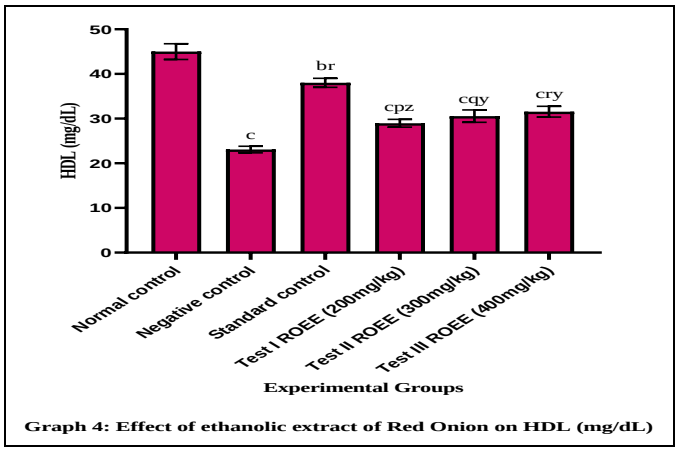
Graph 3: Effect of ethanolic extract of Red Onion on triglycerides (mg/dL)

Values represented mean ± SEM; n=6; Analysis was performed using one way ANOVA followed by Tukey's multiple comparison test; p value less than 0.05 was considered as statistically significant. a<0.05, b<0.01, c<0.001; Data compared with normal control; p<0.05, q<0.01, r<0.001 Data compared with negative control; x<0.05, y<0.01, z<0.001 Data compared with standard control (by one way ANOVA followed by Tukey's multiple comparison test).

Effect of ethanolic extract of red onion on HDL

According to the data presented in table 2, the negative control group showed significant ($p<0.001$) decrease in the level of HDL as compared to normal control group. Whereas significant increase in the level of HDL was observed in standard control ($p<0.001$), test I ($p<0.05$), test

II ($p<0.01$) and test III ($p<0.001$) group when compared with negative control group.

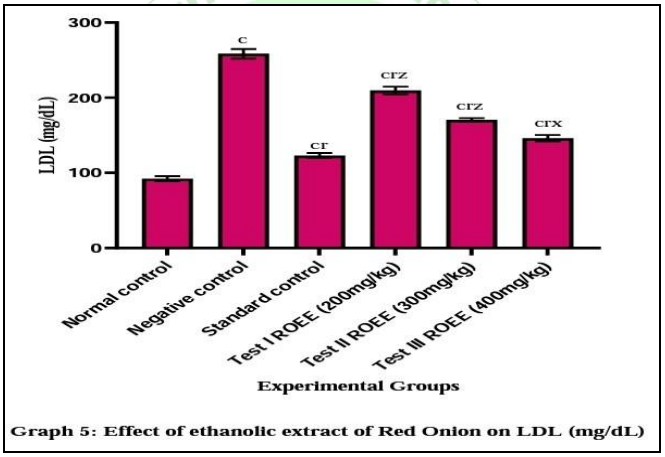


Graph 4: Effect of ethanolic extract of Red Onion on HDL (mg/dL)

Values represented mean ± SEM; n=6; Analysis was performed using one way ANOVA followed by Tukey's multiple comparison test; p value less than 0.05 was considered as statistically significant. a<0.05, b<0.01, c<0.001; Data compared with normal control; p<0.05, q<0.01, r<0.001 Data compared with negative control; x<0.05, y<0.01, z<0.001 Data compared with standard control (by one way ANOVA followed by Tukey's multiple comparison test).

Effect of ethanolic extract of red onion on LDL

The mean values for LDL levels in normal and hyperlipidemic groups are given in table 2. When compared with normal control group negative control group showed significant ($p<0.001$) increase in the LDL level. While as compared to negative control group the standard control, test I, II and III group showed significant ($p<0.001$) decrease in LDL level.

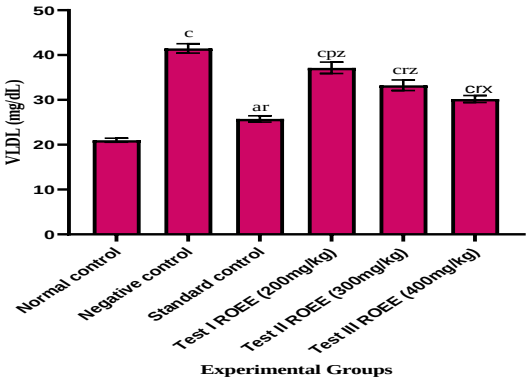


Graph 5: Effect of ethanolic extract of Red Onion on LDL (mg/dL)

Values represented mean ± SEM; n=6; Analysis was performed using one way ANOVA followed by Tukey's multiple comparison test; p value less than 0.05 was considered as statistically significant. a<0.05, b<0.01, c<0.001; Data compared with normal control; p<0.05, q<0.01, r<0.001 Data compared with negative control; x<0.05, y<0.01, z<0.001 Data compared with standard control (by one way ANOVA followed by Tukey's multiple comparison test).

Effect of ethanolic extract of red onion on VLDL

Table 2 illustrated that the level of VLDL in different treatment groups was considerably affected. The negative control group showed significant ($p<0.001$) increase in the level of VLDL as compared to normal control group. Whereas test I group showed ($p<0.05$) and standard control, test II and III showed ($p<0.001$) significant reduction in VLDL level as compared to negative control group.

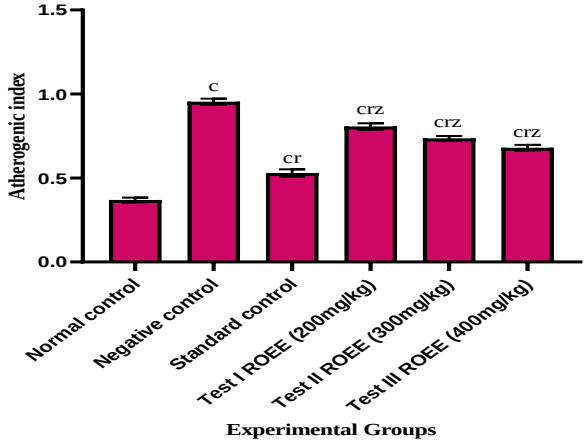


Graph 6: Effect of ethanolic extract of Red Onion on VLDL (mg/dL)

Values represented mean ± SEM; n=6; Analysis was performed using one way ANOVA followed by Tukey's multiple comparison test; p value less than 0.05 was considered as statistically significant. a<0.05, b<0.01, c<0.001; Data compared with normal control; p<0.05, q<0.01, r<0.001 Data compared with negative control; x<0.05, y<0.01, z<0.001 Data compared with standard control (by one way ANOVA followed by Tukey's multiple comparison test).

Effect of ethanolic extract of red onion on Atherogenic index

According to the data presented in table 2 the negative control group showed significant (p<0.001) increase in the atherogenic index as compared to normal control group. Whereas standard control and all test groups showed significant (p<0.001) reduction in atherogenic index as compared to negative control group.



Graph 7: Effect of ethanolic extract of Red Onion on atherogenic index

Values represented mean ± SEM; n=6; Analysis was performed using one way ANOVA followed by Tukey's multiple comparison test; p value less than 0.05 was considered as statistically significant. a<0.05, b<0.01, c<0.001; Data compared with normal control; p<0.05, q<0.01, r<0.001 Data compared with negative control; x<0.05, y<0.01, z<0.001 Data compared with standard control (by one way ANOVA followed by Tukey's multiple comparison test).

Histopathological changes

Histopathology of the liver for normal control, negative control and test III group were carried out

Histopathological observation of liver in normal control group

The normal control group animals showed normal hepatocyte architecture such as healthy nucleus and parenchymal structure [Fig.1 (a) & (b)].

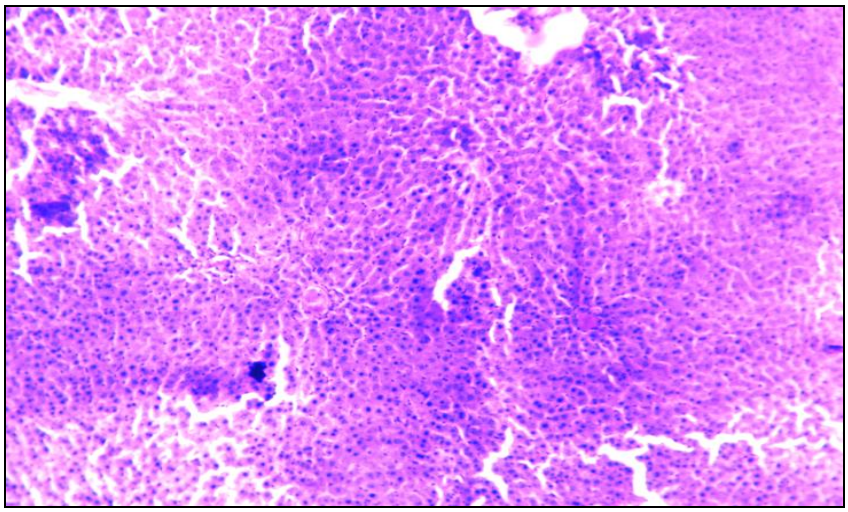


Figure 1 (a): Liver section (100X) of normal control group showing normal hepatocytes

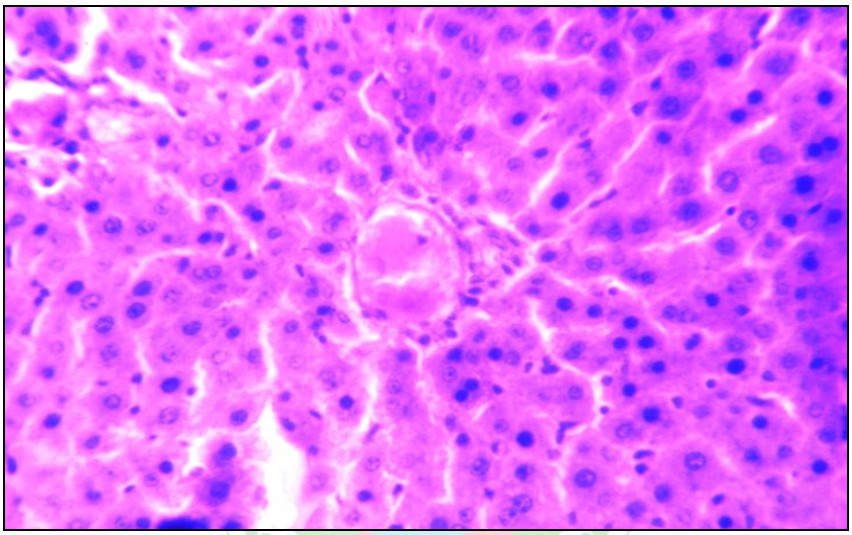


Figure 1 (b): Liver section (400X) of normal control group showing normal hepatocytes

Histopathological observation of liver in negative control group

As compared to normal control group the negative control group animals showed fatty changes, altered hepatocyte architecture along with necrosis, congestion and leucocytic infiltration [Fig.2 (a) & (b)].

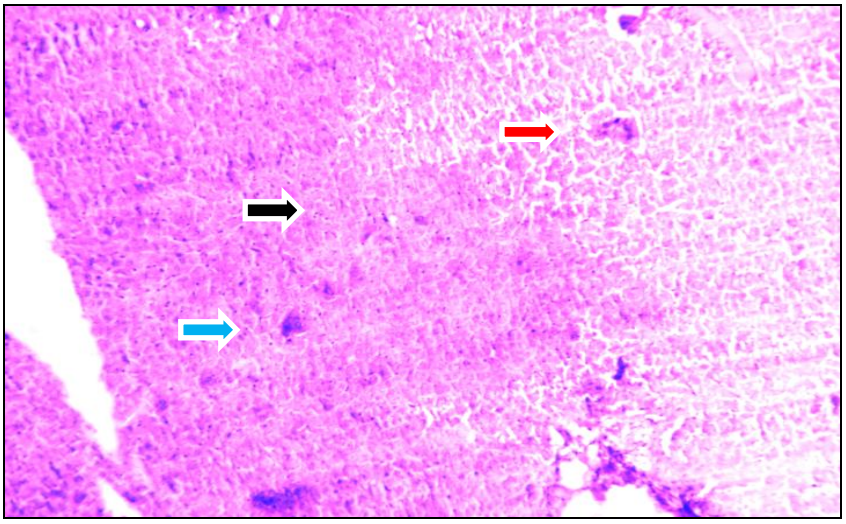


Fig 2 (a). Liver section (100X) of negative control group showing necrosis (Black arrow), congestion (red arrow) and leucocytic infiltration (blue arrow)

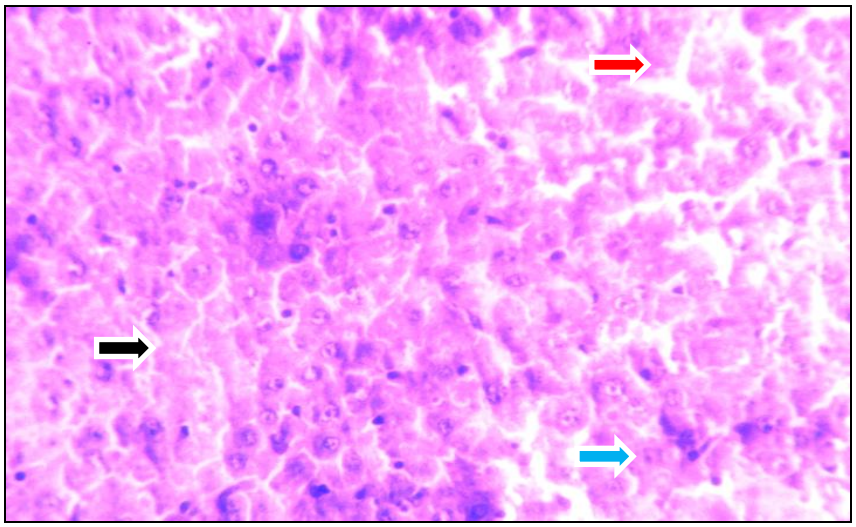


Figure 2 (b). Liver section (400X) of negative control group showing necrosis (Black arrow), congestion (red arrow) and leucocytic infiltration (blue arrow)

Histopathological observation of liver in test III group

When compared with negative control group the test III group animals has reduced fatty changes and restored the hepatocytes near to the normal group [Fig.3 (a) & (b)].

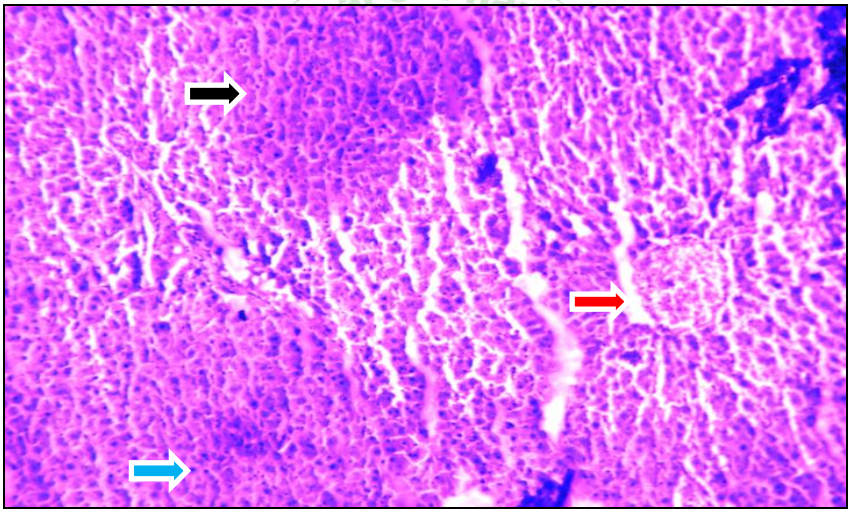


Figure 3 (a): Liver section (100X) of test III group showing necrosis (Black arrow), congestion (red arrow) and leucocytic infiltration (blue arrow)

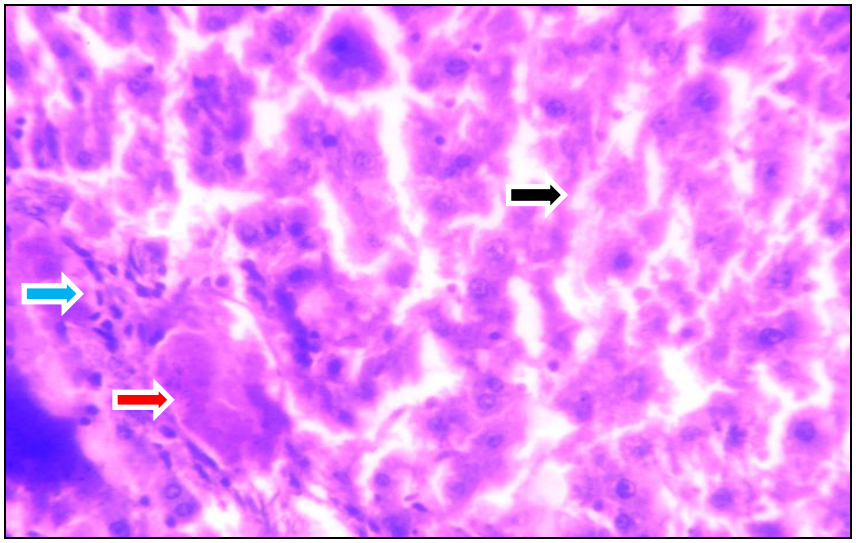


Figure 3 (b): Liver section (400X) of test III group showing necrosis (Black arrow), congestion (red arrow) and leucocytic infiltration (blue arrow)

DISCUSSION

Lipids are organic compounds which are water insoluble but soluble in organic solvents. Lipids perform number of functions such as chemical messengers, storage and provision of energy, maintenance of temperature and membrane lipid layer formation. Hyperlipidemia is nothing but abnormally elevated level of lipids such as total cholesterol (TC), triglyceride (TG) and lipoproteins [26]. Diseases associated with hyperlipidemia are major risk factors for development of cardiovascular diseases (CVD) [27]. Hyperlipidemia is risk factor for onset and progression of atherosclerosis [28,29] viz high risk factor in development of coronary heart diseases [26]. Hence prevention or treatment of such disorders can be achieved by targeting the causative hyperlipidemia [27].

P – 407 induced hyperlipidemia is one of the animal model used for the evaluation of antihyperlipidemic activity of drug. It was harmless to membranes of cells, in earlier studies it was used effectively to induce hyperlipidemia. Poloxamer 407, a non-ionic synthetic copolymer surfactant commonly known used to induce hyperlipidemia in small laboratory animals within 24 h through i. p. injection. Due to its rapid onset, convenience, reproducibility, and lack of undesirable toxicity, P-407 was used in this study to induce hyperlipidemia in animals [11,30]. A single injection of P-407 caused elevations of serum cholesterol and triglyceride levels in rats. P-407 induced hyperlipidemia via alterations in activity of 3-hydroxy-3- methylglutaryl-CoA (HMG-CoA) reductase, lipoprotein lipase (LPL), lecithin cholesterol acyltransferase (LCAT), cholesteryl ester transfer protein (CETP), hepatic lipase (HL) and lipoprotein lipase (LPL). P-407 directly inhibits the capillary (heparin releasable) LPL and HL, and it indirectly increases the biologic activity of CETP and LCAT [9,31].

In our analysis, there was marked increase in the level of total cholesterol, triglycerides, LDL,VLDL, AI and decrease in the level of HDL in negative control group as compared to normal control group (Table 2) confirming that i.p. injection of P-407 has induced hyperlipidemia experimentally [9]. Red Onion ethanolic extract (200mg/kg, 300mg/kg and 400mg/kg) significantly decreased the increased level of total cholesterol, triglycerides, LDL,VLDL, AI and increased the level of HDL after treatment suggest the ameliorative potential of Red Onion.

In our analysis the body weight gain of different groups of rats showed that negative control group animals showed the significant increase in the body weight as compared to normal control group animals. After treatment with standard and test drug the body weight decreased significantly.

In this study, the significant elevation of TC concentration was achieved by the indirect stimulation of HMG CoA reductase by an intraperitoneal (i.p) injection of P-407 [26]. Hence the hypocholesterolemic effect of red onion ethanolic extract could be due to decreased activity of hepatic HMG CoA reductase, stimulation of Cholesterol-7-alpha-hydroxylase, which converts cholesterol into bile acids. It could also be due to the presence of saponins, a phytochemical which forms insoluble complexes with cholesterol or their bile salt precursor, thus making them unavailable for absorption. The results obtained in our analysis conform to earlier report that polyphenols possesses antilipidemic activity [9,26]. Besides, the standard drug (Atorvastatin) used in this study inhibits HMG CoA reductase, viz a rate limiting enzyme in the biosynthesis of cholesterol [26].

In our analysis, elevation in TG concentration after P-407 i.p. injection results primarily from an inhibition of TG degradation, P-407 directly inhibits capillary lipoprotein lipase (LPL) enzyme which is responsible for plasma TG hydrolysis and its clearance from the circulation [11,26]. The Red Onion ethanolic extract could have reduced TG levels by either activating lipoprotein lipase enzyme which hydrolyses the triglyceride into fatty acid hence decreasing triglyceride levels or by inhibiting lipolysis so that fatty acids do not get converted to triglyceride [11, 12, 26].

HDL act as cholesterol scavengers, they transport excess cholesterol and cholesterol esters from the blood and peripheral tissues back to the liver where it is broken down to bile acids. It plays a crucial role in reducing blood and peripheral cholesterol concentrations and inhibits formation of atherosclerotic plaque in the aorta therefore known as the protective cholesterol or Good cholesterol [26]. The present study indicates significant elevation in HDL concentration by the standard drug and ROEE. This could possibly be due to increasing activity of lecithin-cholesterol acyl transferase (LCAT), an enzyme which is responsible for incorporating free cholesterol into HDL there by promoting reverse cholesterol transport and competitively inhibiting the uptake of LDL-c by endothelial cells.

LDL (low density lipoprotein) transports cholesterol to the body cells. It transports near 60-70% of total cholesterol to the body cells. Therefore, an increase in TC level accordingly increases LDL-c [26]. LDL is referred as the most dangerous among the serum lipids, and the oxidation of LDL-c leads to its increased penetration of arterial walls. The increased LDL-c levels play a vital role in the development of atherosclerotic lesions that progress from fatty streaks to ulcerated plaques. Therefore, serum LDL levels are used as the basis for initiating and monitoring the treatment of patients with elevated blood cholesterol levels [9]. In the present study, ROEE shows marked reduction in LDL levels (Table 2). This result could be due to the presence of phenolics, a phytochemical which may work by increasing LDL receptors densities in the liver binding to apolipoprotein B thereby making liver cells more efficient to remove LDL from circulation [26].

Very low density lipoproteins (VLDLs) are secreted from the liver. They contain large amount of triglycerides. As it eventually gets converted into LDL and causes buildup of cholesterol on the walls of arteries it is categorized as a type of bad cholesterol [32]. The present study indicates significant decrease in VLDL concentration by the ROEE. This effect could probably be due to the inhibition of triglyceride and possibly fatty acid synthesis by phenolic constituents of red onion. Atherogenic risk predictor index log (TG/HDL-c) has been considered as the most accurate in determining the extent of atherosclerosis and the risk of myocardial infarction. The present study showed that the Red Onion ethanolic extract has significantly reduced

atherogenic index as compared to negative control group. The results suggest the anti-atherogenic potential of Red Onion ethanolic extract and hence, reducing the development of coronary atherosclerosis [26].

Histopathology study of liver was also carried out to check fatty changes, necrosis of hepatocytes, congestion and leucocytic infiltration. The histopathological report of negative control group animals showed the development of fatty changes, necrosis of hepatocytes, congestion and leucocytic infiltration while the histopathological report of normal control group animals did not show any fatty changes. Whereas the group of animals treated with ROEE (400mg/kg) restored hepatocytes near to normal control group.

CONCLUSION

In conclusion, the present study has demonstrated that ethanolic extract of Red Onion has antihyperlipidemic effect in Poloxamer 407 induced hyperlipidemia. Red Onion ethanolic extract has showed dose dependent activities on body weight, various serum lipids and atherogenic index. Furthermore the better activities has revealed by the ROEE at dose of 400mg/kg. Utilizing this model, Red Onion ethanolic extract was shown to be effective in significantly lowering total cholesterol, triglycerides, LDL, VLDL and increasing HDL cholesterol levels; also decreasing atherogenic index; thus it can be used in the treatment and/or prevention of cardiovascular diseases.

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REFERENCES

1. Phogat P, Deep A, Sharma PC, Mittal SK, Goyal R, Thakral K. ewsletter Phogat et al . Introduction to Hyperlipidemia and Its Management : A Review ewsletter Phogat et al . 2010;266:251–66.
2. Al-hiari Y, Shattat G, Al-qirim T, El-huneidi W, Sheikha GA, Hikmat S. Antihyperlipidemic Properties of Novel. 2011;8292–304.
3. Asija R, Singh C. A Comprehensive Review on Antihyperlipidemic Activity of Various Medicinal Plants. 2016;7(6):407–15.
4. Mag P, A SK, Mazumder A, Saravanan VS. PHCOG MAG .: Research Article Antihyperlipidemic activity of Camellia sinensis leaves in Triton WR-1339 induced albino rats. 2008;4(13):60–4.
5. El-ghany A, Mahmoud FM. Performance of Hypolipidemic Activity of Persimmon Extracts on Triton-X Induced Hyperlipidemia in Male Rats. 2016;2:636–45.
6. Belagali Y, Ullal SD, Shoeb A, Bhagwath V, Ramya K, Maskeri R. Effect of Vanillin on lipid profile in a model of hyperlipidemia , a preliminary study. 2013;51(April):288–91. 57-63.pdf.
7. Edenta C, James DB, Owolabi OA. Hypolipidemic Effects of Aqueous Extract of Three Cultivars of Musa sapientum Fruit Peel on Poloxamer-407 Induced Hyperlipidemic Wistar Rats . 2014;5(12):1049–54.
8. Sutar G V, Das K, Einstein JW. Screening of different leaf extracts of Cassia fistula Linn for investigation of hypolipidemic activity in two different rat models. 2015;3:30–43.
9. Antihyperlipidemic activity of solvent fractions of Calotropis procera root bark extract in poloxamer-407 induced hyperlipidemic rats. 2018;12(1):1–8.
10. Ahmad U, Ahmad RS, Arshad MS, Mushtaq Z, Hussain SM. Antihyperlipidemic efficacy of aqueous extract of Stevia rebaudiana Bertoni in albino rats. 2018;1–8.
11. Airaodion AI, Ngwogu K, Ekenjoku J. Hypolipidaemic and Antidiabetic Potency of Allium cepa (Onions) Bulb in Alloxan-Induced Diabetic Rats Hypolipidaemic and Antidiabetic Potency of Allium cepa (Onions) Bulb in Alloxan-Induced Diabetic Rats. 2020;(February).
12. Efiong EE, Akumba LP, Chukwu EC, Olusesan AI, Obochi G. Comparative qualitative phytochemical analysis of oil , juice and dry forms of garlic (Allium sativum) and different varieties of onions (Allium cepa) consumed in Makurdi metropolis. 2020;12(June):9–16.
13. Ojieh AE, Adegor EC, Okolo AC, Lawrence EO, Njoku IP, Onyekpe CU. Hypoglycemic and Hypolipidaemic Effect of Allium Cepa in Streptozotocin-Induced Diabetes. 2015;6(10):23–9.
14. Yoshinari O, Shiojima Y, Igarashi K. Anti-Obesity Effects of Onion Extract in Zucker Diabetic Fatty Rats. 2012;1518–26.
15. Length F. Hepatoprotective effects of Allium cepa (onion) extracts against paracetamol-induced liver damage in rats. 2014;13(26):2679–88.
16. Publication O. Adv anc eV iew Pro ofs Adv anc eV iew Pro ofs. 2008;70454(013):1–7.
17. Sima Nasri. Evaluation of analgesic and anti-inflammatory effects of fresh onion juice in experimental animals. African J Pharm Pharmacol. 2012;6(23):1679–84.
18. Bamidele TO, Enemali MO, Ijeomah AU. Hepatoprotective Activity Of Ethanol Extract Of Purple Onion Bulb (Allium Cepa Linn) On Ccl 4 Induced Hepatotoxicity In Wistar Rats Titilayo O. Bamidele*, Michael Okey Enemali, Ann Ukamaka Ijeomah. 2018;3(1):149–52.
19. James DB, Sheneni VD. Antioxidant activity of Vitex doniana ethanol extracts in poloxamer-407-induced hyperlipidemic rats. 2014;
20. Megalli S, Aktan F, Davies NM, Roufogalis BD. Phytopreventative Effects Of Gynostemma Pentaphyllum In Rats. J Pharmacol Pharm Sci. 2005;8(3):507–15.
21. Prencipe L. zerum Triglycerides Determined Produces Hydrogen Peroxide Colorimetrically with an Enzyme That. 1982;28(10):2077–80.
22. Burstein M, Scholnick HR, Morfin R. Rapid method for the isolation of lipoproteins from human serum by precipitation with polyanions. J Lipid Res [Internet]. 1970;11(6):583–95. Available from: http://dx.doi.org/10.1016/S0022-2275(20)42943-8
23. Dalwadi PP, Patani P V. Anti hyperlipidemic activity of Tephrosia purpurea plant extracts in poloxomer 407 induced hyperlipidemic rats. 2014;4(4):186–93.
24. Sheneni VD, Odiba VA, Omede A, Idih FM. Anti-hyperlipidemic effect of Vitex doniana in poloxamer induced hyperlipidemia. 2018;3(4):168–73.
25. Jadeja RN, Thounaojam MC, Patel V, Devkar R V, Ramachandran A V. Antihyperlipidemic potential of a polyherbal preparation on triton WR 1339 (Tyloxapol) induced hyperlipidemia : A comparison with lovastatin. 2009;1339(June).
26. Im HYK, Eong MJ, Ung JJ, Ung JJ, Okozawa TY, Hoi JSC. Hypolipidemic Effects of Sophora flavescens and Its Constituents in Poloxamer 407-Induced Hyperlipidemic and Cholesterol-Fed Rats. 2008;31(January):73–8.
27. Mahmud ZA, Bachar SC, Qais N. (Roxb .) in Poloxamer-407 induced hyperlipidemic mice and rats Antihyperlipidemic activity of leaf and root extracts of Premna esculenta (Roxb .) in Poloxamer-407 induced hyperlipidemic mice and rats. 2011;(December).
28. Pyrazole N, Coumarin I, As D, Amylase A, Agents I. Evaluation of Antihyperlipidemic Activity of Ethanolic Root Extract of Carica Papaya in Poloxamer – 407 Induced Hyperlipidemia in Wistar Rats . 2017;(February 2018).
29. Sheneni VD, Shaibu IE, Okpe JM, Omada AA. In-vivo biological effect of Carica papaya leaf extracts on P-407 induced hyperlipidemic Wistar rats. 2020;(July).
30. Priya T, Maurya S, Khan KH. Cholesterol : Genetic , Clinical and Natural Implications Research Journal of Pharmaceutical , Biological and Chemical Sciences Cholesterol : Genetic , Clinical and Natural Implications July-September. 2014;(May).