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Effects of garlic oil on certain physiological and biochemical aspects in normal and experimentally induced hyperlipidemia in male albino rats.

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ABSTRACT

Garlic (*Allium sativum Linn.*) is ascribed with many therapeutic effects. For the present study, garlic oil was investigated for their hypolipidemic effect on hyperlipidemia induced by cholesterol containing diet in albino rats.Fourty; adult male albino rats were used in these experiments. The experimental induction of hyperlipidemia was performed by the feeding of diet rich in cholesterol, cholic acid and thiouracil for 45 days. Four groups of 10 rats each were studied. Group **I:** control rats were fed a normal diet. **Group II:** hyperlipidemic rats were continued fed a hyperlipidemic diet (hyperlipidemic control). **Group III:** hyperlipidemic rats administrated with garlic oil (28 mg/Kg. body wt. Orally). **Group IV:** control rats received garlic oil at a dose of (28mg/kg. body wt. Orally). Blood samples were collected from all animal groups two times along the duration of the experiment 2 and 4 weeks after administration of garlic oil. Serum was separated and used directly for estimation of lipid components [total lipids, total cholesterol, triacylglycerols, phospholipids, non-esterified fatty acids (NEFA)]; lipoprotein fractions as high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C) and very low- density lipoprotein cholesterol (VLDL-C) in addition to total protein and its components as well as immunoglobulins (IgG, IgA&IgM) concentrations. Also, serum lecithin-cholesterol acyltransferase (LCAT) and lipase activities were determined. The obtained results revealed that, there was a very highly significant increase in the value of serum total lipids, total cholesterol, triacylglycerols, phospholipids, NEFA, LDL-C and VLDL-C concentrations in rats fed a hyperlipidemic diet for 4 weeks, whereas serum HDL-C level showed a highly significant increase after two weeks, this increase became significant after 4 weeks .The activity of serum LCAT showed a very highly significant increase allover the experimental periods. However, the value of serum lipase activity showed a highly significant decrease after 2 weeks, this decrease became very highly significant after 4 weeks in hyperlipidemic rats, compared to rats fed on a normal diet. Administration of garlic oil to hyperlipidemic rats caused a very highly significant decrease in the value of serum total lipids, total cholesterol, triacylglycerols, phospholipids, LDL-C, VLDL-C concentrations and serum LCAT activity. On the other hand, serum NEFA level and lipase activity showed a very highly significant increase compared with hyperlipidemic control rats (group II). Administration of garlic oil to normal fed rats reduced the concentrations of serum total lipids, total cholesterol, triacylglycerols, and LDL-C and VLDL-C. However, serum NEFA and HDL-C levels showed a highly significant increase whereas, serum lipase activity was significantly increased. Feeding of hyperlipidemic diet caused a significant increase in serum albumin, alpha globulin and total globulin's concentrations. Administration of garlic oil to hyperlipidemic rats caused a significant increase in the value of serum total proteins and total globulin's concentrations. While, administration of garlic oil to normal fed rats caused a significant decrease in serum total proteins and significant decrease in serum albumin concentrations. The results of this study indicate that, garlic oil treatment almost nullified the lipid - increasing effects of the experimental hyperlipidemia and its hyperlipidemic therapy has potential benefits in treatment of hyperlipidemia.

INTRODUCTION

Garlic as a herbal remedy reduces a multitude of risk factors which play a decisive role in the genesis and progression of arteriosclerosis: decrease in total and LDL-cholesterol, increase in HDL-cholesterol, reduction of serum triglyceride and fibrinogen concentration, lowering of arterial blood pressure and promotion of organ perfusion, and,

finally, enhancement in fibrinolysis, inhibition of platelet aggregation, and diminution of plasma viscosity **Siegel et al. (1999).**

Ali et al. (2000) showed that, garlic is beneficial in reducing blood cholesterol, triglyceride levels and systolic blood pressure in hypercholesterolemic rats. Moreover, garlic may beneficially affect two risk factors for atherosclerosis--hyperlipidemia and hypertension.

S-allyl cysteine sulfoxide, isolated from garlic, Allium sativum, is more or less as active as gugulipid in controlling hypercholestermia, obesity and derangement of enzyme activities in cholesterol diet fed rats. The beneficial effects of the drugs are partly due to their inhibitory effects on transaminases, alkaline phosphatase, lipogenic enzymes and HMG CoA reductase and partly due to their stimulatory effects on plasma lecithin-cholesterol acyl transferase lipolytic enzymes and fecal excretion of sterols and bile acids, **Sheela and Augusti (1995).**

Furthermore, **Prasad et al. (1997)** suggested that, oxygen free radicals are involved in the genesis and maintenance of hypercholesterolemic atherosclerosis and that use of garlic can be useful in preventing the development of hypercholesterolemic atherosclerosis. However, **Berthold et al. (1998)** stated that, the commercial garlic oil preparation investigated had no influence on serum lipoproteins, cholesterol absorption, or cholesterol synthesis.

It is proposed that, the mechanism of the hypolipidemic effect of the oil involves the active principle, diallyl disulphide, inactivating enzymes and substrates containing thiol groups in an exchange reaction; increased hydrolysis of triacylglycerols as increased lipase activity is induced by the oil; and the reduction in the biosynthesis of triacylglycerols as NADPH is made unavailable for the process by the metabolism of the oil **Adoga (1987).**

AIM OF THE WORK

Accordingly, the present study was undertaken to elucidate the hypolipidemic effects of garlic oil on blood lipid profiles, lipoproteins, serum proteins and its components as well as certain immunoglobulins (IgG, IgA & IgM) concentrations in normal and experimentally induced hyperlipidemia of adult male albino rats.

MATERIAL AND METHODS

Fourty, Adult white male albino rats, 12-16 weeks old and weighing 200-250 grams were used in these experiments. Rats were kept at a constant environmental and nutritional condition throughout the period of the experiment. Water was supplied ad-libitum.

Induction of hyperlipidemia:

Hyperlipidemia was induced in rats according to the method of Fillios and Mann (1956). Experimental animals were kept on their normal food which has thoroughly mixed with o.5% cholesterol, o.5% cholic acid and o.o5% thiouracil for 45 days before garlic oil administration and the hyperlipidemi diet was continued overall the period of garlic oil administration.

Experimental Design:

The adult male rats were divided into four groups, each one consisting of 10 animals placed in individual cages and classified as follows: -

Group I: Control rats were fed a normal diet.

GroupII: Hperlipidemic rats, were continued fed a hyperlipidemic diet for 4 weeks, did not receive treatment and kept as hyperlipidemic control.

GroupIII: Hperlipidemic rats, were given hyperlipidemic diet andadministerated with garlic oil (28mg / Kg. body Wt.) orally and daily for a period of 4 weeks, according to **Paget and Barns (1964).** Garlic oil was obtained from El- Kahera Chemical Co. Egypt.
GroupIV: Control rats, were fed a normal diet, supplemented with garlic oil (28mg / Kg. body wt. orally and daily) for a duration of 4 weeks.

Sampling: -

Blood samples were collected from all animal groups two times along the duration of the experiment, 2 and 4 weeks after administration of garlic oil. The samples were collected in the morning following an overnight fast, from the medial canthus of the eyes using heparinized capillary glass tubes. Serum was separated by centrifugation, then kept in a deep freeze at –20C until used for subsequent biochemical analysis.

Analytical procedures: -

Serum total lipids, total cholesterol, triacylglycerols, phospholipids and non esterified fatty acids (NEFA) were assayed colorimeterically according to the methods described by **Frings and Dunn (1970), Meiattini et al. (1978), Bucolo and David (1973), Zilversmit and Davis (1950), and Duncombe (1964)**, respectively. Moreover, serum high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C) and very low- density lipoprotein cholesterol (VLDL-C) were estimated by the methods described by **Finley et al. (1978), Friedewald et al. (1972) and Bauer (1982)**, respectively. Serum lecithin-cholesterol acyltransferase (LCAT) and lipase activities were determined according to **Kostner and Dieplinger (1980) and Tietz (1976)**, respectively. Serum total protein level, separation of protein fractions electrophoretically and immunoglobulins concentration were down by the methods described by **Henry (1974), Koh (1968), and Macini et al. (1965)**, respectively.

Statistical analysis:

The obtained data were statistically analyzed and the significant difference between groups was evaluated by t-test as explained by **Snedecor and Cochran (1982).**

RESULTS

The obtained data (table 1) revealed that, the feeding of hyperlipidemic diet to normal rats allover the experimental periods showed a very highly significant increase in serum total lipids, total cholesterol, triacylglycerols, phospholipids , non esterified fatty acids (NEFA), low-density lipoprotein cholesterol (LDL-C) and very low- density lipoprotein cholesterol (VLDL-C) concentrations when compared to the normal control group of rats fed on a normal diet. Moreover, a highly significant increase in serum high-density lipoprotein cholesterol (HDL-C) concentration was reported after 2 weeks of hyperlipidemic diet feeding, this increase became significant after 4 weeks of experiments. The activity of lecithin-cholesterol acyltransferase (LCAT) had a very highly significant increase after 2 and 4 weeks of experiment. However, serum lipase activity showed a highly significant decrease after two weeks only, this decrease became very highly significant after 4 weeks in hyperlipidemic control rats compared to group of rats fed on a normal diet.

The obtained results (table 2) showed that, administration of garlic oil to hyperlipidemic rats (group III) caused a very highly significant decrease in serum total lipids, total cholesterol, triacylglycerols, phospholipids , LDL-C and VLDL-C concentrations after 2 and 4 weeks compared with the hyperlipidemic control rats (group II). However, a very highly significant increase in NEFA concentration was reported allover the experimental periods. Serum HDL-C level showed a non significant decrease, whereas , the

activity of serum LCAT showed a very highly significant increase in hyperlipidemic rats compared with hyperlipidemic control animals (group II).

The obtained data (table 3) showed that, administration of garlic oil in rats fed a normal control diet caused a significant decrease in serum total lipids, total cholesterol, triacylglycerols, LDL-C and VLDL-C concentrations. Meanwhile, the concentration of NEFA and HDL-C showed a highly significant increase after 2 weeks of garlic oil administration compared with control rats (group I). Moreover, the value of serum phospholipids concentration and serum LCAT and lipase activities showed a non-significant changes after garlic oil administration . After 4 weeks the obtained data showed a highly significant decrease in the concentrations of serum lipid profiles(total lipids, total cholesterol, triacylglycerols, LDL-C and VLDL-C) whereas, serum NEFA level showed a significant increase while HDL-C concentration and serum lipase activity showed a highly significant increase. However, serum phospholipids concentration and LCAT activity not affect by garlic oil administration in rats fed a control diet (group IV).

The effect of hyperlipidemia on serum proteins , its components and immunoglobulins concentrations were presented in table 4. The obtained results revealed that, a significant increase in serum albumin concentration was observed after 2 weeks of experiment. The value of serum total globulin levels showed a highly significant increase, while alpha-globulin level showed a significant increase in hyperlipidemic rats after 4 weeks when compared with control (group I). On the other hand, serum total protein, beta and gamma globulin fraction and immunoglobulins (IgG, IgA & IgM) concentrations did not show significant changes.

The effect of garlic oil administration to hyperlipidemic rats (group III) on serum total protein and its fractions was recorded in table (5). The obtained results showed a significant increase in serum total protein concentration after two weeks whereas, serum total globulin level showed a significant increase after 4 weeks. On the other hand, the concentrations of serum albumin, globulin fractions and immunoglobulins (IgG, IgA & IgM) showed no significant variations allover the experimental periods compared with group II.

The obtained data table (6) revealed that, serum total protein concentration showed a significant decrease and serum albumin level was highly significantly decrease after garlic oil administration in normal rats (group IV). However, serum total globulin, globulin fractions (alpha, Beta & gamma globulin) and immunoglobulins (IgG, IgA & IgM) concentrations did not show any significant changes after garlic oil administration when compared with control rats (group I) .

DISCUSSION

Triglycerides and cholesterol are important biological lipids, and their excessive intake in the diet is relevant to the development of two prevalent cardiovascular risk factors, obesity and hypercholesterolemia **Ros (2000).**

The obtained data revealed that, serum total lipids, total cholesterol, triacylglycerols, phospholipids , non-esterified fatty acids (NEFA), low-density lipoprotein cholesterol (LDL-C), high - density lipoprotein cholesterol (HDL-C) and very low- density lipoprotein cholesterol (VLDL-C) concentrations were markedly increased in normal rats fed hyperlipidemic diet. These results are nearly similar to those observed by **Okazaki (1998)** who reported that, a significant increase in plasma total cholesterol ,VLDL (very low-density lipoprotein) and LDL (low-density lipoprotein)-cholesterol was observed in mice fed on a high cholesterol diet for 3 months . Also, **Ismail et al. (1999**) demonstrated that, feeding the cholesterol- enriched diet in rabbits caused a significant increase in total-, LDL-

, and HDL- cholesterol levels. Moreover, **Ali et al. (2000) and Bennani et al. (2000)** reported that, rat receiving cholesterol- enriched diet showed sever hypercholesterolemia, elevated plasma LDL and VLDL- cholesterol compared to the control group of rats fed on a normal diet. Furthermore, **Vlad et al. (1995) and Lin and Ding (1996)** showed that, in rats fed a rich lipid diet there was a significant increase in plasma cholesterol, triglycerides and lipid concentrations. The increase in serum total cholesterol level in normal rats fed the hyperlipidemic diet may be due to the reduced catabolic rate of serum cholesterol or reduced activity of hepatic cholesterol 7 alpha - hydroxylase, the rate limiting enzyme in bile acid synthesis from cholesterol **(Szymanski et al.,1981).** As confirmed by **Osada et al. (1998)** who reported that, hepatic cholesterol 7 alpha -hydroxylase activity was lowered only when rats were given both 0.5% cholesterol and 0.5% oxidized cholesterol in diet. Also, **Zhao et al. (1998)** concluded that, the intake of high cholesterol diet with the passage of time, the decreased activity of LDL receptor of hepatocytes would reduced the synthesis of bile acid. Moreover, another suggestion for the dramatic rise in serum total cholesterol concentration observed in this study was due to increased uptake of exogenous cholesterol **(Emara,1999)** and/ or may be attributed to increase in 3-hydroxy-3-methylglutaryl-CoA reductase activity in the liver of animals fed the hypercholesterolemic diet **(Zulet et al., 1999).** Furthermore, reduced rates of clearance of LDL from circulation due to defective LDL receptors and is associated with increased plasma total cholesterol concentration.

Marked hypertriglyceridemia observed in normal rats fed on hyperlipidemic diet might be a consequence of either over production of VLDL by the liver or defective removal of triglyceride rich lipoproteins from the circulation, or both. The later possibility can be explained through lipoprotein lipase, an insulin dependent enzyme involved in triglyceride removal **(Yost et al., 1995).** It is known that, HDL apoA-I fractional catabolism is enhanced in hypertriglyceridemic subjects, possibly due to enhanced HDL cholesterol ester transfer to triglyceride rich lipoprotein **(Li et al., 1994).** Moreover, the increased serum triacylglycerols concentration might be attributed to increased hepatic triacylglycerol synthesis and very low density lipoprotein (VLDL) secretion **(Hussein and Azab 1998)**.

The marked increase in serum phospholipids concentration in rats fed on hyperlipidemic diet may be due to increased activity of choline phosphotransferase enzymes involved in phospholipid synthesis. This suggestion is confirmed by **Morisaki et al. (1983)** who reported that, in rats fed on high cholesterol diet, the activities of all enzymes involved in lipid synthesis were significantly increased (acyl-coA synthetase, acyl-coA : cholesterol acyltransferase and choline phosphotransferase). The marked decrease of serum non-esterified fatty acids (NEFA) level in rats fed on hyperlipidemia-induced diet may be due to decrease of the lipolytic effect of lipase activity reported in the present study which decrease the lipolysis of triacylglycerols into glycerol and free fatty acids **(Emara,1999).**

Rats receiving a hyperlipidemic diet showed elevated serum HDL-C, LDL-C and VLDL-C concentrations. Saturated fats mostly increase the concentration of cholesterol, LDL-C and to a less extent VLDL-C levels. The increase in LDL-C level produced by saturated fats seems to be related mainly to reduced catabolic rate (Shepherd et al., 1980). Also, when the cholesterol content of hepatocytes is raised by ingestion of diet high in saturated fat and cholesterol, LDL receptors fall and plasma LDl levels rise **(Goldstein and Brown 1987).** LDL is uptake by the LDL receptor in liver and extrahepatic tissues. The production of LDL exceeds the capacity of LDL receptors i.e. efflux of cholesterol from the liver is more than influx. This could be explaining the elevated serum LDL-C level observed in the present study. Moreover, the increased LDL-C level may be due to

degradation of IDL(intermediate density lipoprotein) to LDL by the action of hepatic lipase.

Lipoprotein lipase is also relevant to HDL-C production. Previous studies demonstrated that enhanced lipolysis of triglyceride-rich lipoproteins may lead to an increase in HDL-cholesterol **(Guillausseau, et al., 1992).** On the other hand, the subsequent reduction in intracellular cholesterol stimulates the synthesis of high affinity LDL-receptors on hepatocytes. The activity of increased number of LDL-receptors lead to increased uptake of LDL from plasma with increasing HDL levels, there is a beneficial reduction in the LDL : HDL cholesterol ratio **(Dugovne et al., 1984).** Moreover, the marked increase in VLDL-C in rat fed hyperlipidemic diet could be attributed to hepatic degradation of the chylomicron remnant to produce very low-density lipoproteins.

The activity of lecithin-cholesterol acyltransferase (LCAT) showed a marked increase. However, serum lipase activity was highly significantly decrease in hyperlipidemic control rats compared to group of rats fed on a normal diet. Similarly **Emara, (1999)** reported that, serum LCAT activity was highly significant increased and serum lipase activity showed a highly significant decrease in rats fed on a hyperlipidemic diet. Also, **Bennani et al.(2000)** observed that, rats receiving a. cholesterol-enriched diet for 54 days showed a rise of lecithin-cholesterol acyltransferase (LCAT) activity. The increase activity of LCAT may be due to increase of unesterified (free) cholesterol level E**mara, (1999).** So, the serum enzyme phosphatidylcholine:cholesterol acyltransferase (PCAT) removing free (unesterified) cholesterol from extrahepatic tissues and esterifying it. **Forsythe et al. (1980)** suggested that, increased esterified cholesterol level was responsible for decreased molar LCAT activity. Changes in molar LCAT activity in human positively correlate with change in unesterified cholesterol, triacylglycerol and phospholipid concentrations. On contrary, **Zulet et al.,(1999)** reported that, a significant reduction in plasma lecithin-cholesterol acyltransferase activity was found in the rat model of hypercholesterolemia. These results provide new evidence that a diet induced hyperlipidemia in rats is associated with several metabolic changes involving lipid and lipoprotein metabolism.

The hypolipidemic effects of garlic oil administration in rat fed a hyperlipidemic diet and normal control adult male rats were investigated in table(2&3). Garlic oil adminstraion produced a similar hypolipidemia in both hyperlipidemic and normal rats, their lipid levels were significantly reduced to levels near to those seen in untreated control rats. Similar results were recorded in rats by **Mathew et al. (1996)** who recorded that, both garlic protein (16% of diet) and garlic oil (100 mg/kg body weight/day) exhibited significant lipid lowering effects the hypolipidemic action is primarily due to a decrease in hepatic cholesterogenesis is the treated rats. Also, **Sodimu et al. (1984)** reported that, administration of garlic oil (100 mg/kg. b. wt/day) for 1 month together with high fat-high cholesterol diet to another group of rats almost nullified the lipid-increasing effects of that diet. The reduction of total lipids, cholesterol and triglycerides were highly significant in the garlic oil group. Moreover, **Gupta (1996)** indicated that, garlic oils prevented rapid increase in hepatic total lipids, triglycerides and phospholipids and decrease in free fatty acids induced by radiocalcium in adult male Swiss albino mice and the values reached normal levels earlier in garlic oil treated animals than in irradiated animals. Furthermore, **Ali et al. (2000)** observed that, when the rats were fed with a high cholesterol diet mixed with garlic powder, there was a significant reduction in their serum cholesterol and triglyceride levels when compared to control and high cholesterol diet group rats. The hypolipidemic action of garlic in rats f ed on hyperlipidemic diet is mainly due to an increase in cholesterol

degradation to bile acids and neutral sterols and mobilization of triacylglycerols in treated rats **Rajasree et al. (1999)**. Also, garlic oil enhances the catabolism of dietary cholesterol and fatty acids **(Shoetan et al., 1984)**. On the other hand, the lower serum cholesterol and triglyceride levels, which are major risk factors of cardiovascular diseases, may be attributed to inhibition of their biosynthesis in the liver, and to inhibit oxidation of low-density lipoprotein. **Sumiyoshi (1997)**, as confirmed b **(Gureshi et al., 1983)** who observed that, significant decrease in hepatic 3-hydroxy-3-methylglutaryl CoA reductase (79-83%), cholesterol 7 alpha-hydroxylase (45-51%), fatty acid synthetase (17-29%) and in representative pentose-phosphate pathway (23-39%) activates accompanied the feeding of commercial garlic oil in white leghorn pullets. Furthermore, **Yeh and Yeh (1994)** suggested that, the hypocholesterolemic effect of garlic stems, in part, from decreased hepatic cholesterogenesis, whereas, the triacylglycerol-lowering effect appears to be due to inhibition of fatty acid synthesis.

Regarding serum lipoproteins concentrations (HDL-C, LDL-C and VLDL-C) garlic oil administration caused a marked decrease in serum LDL-C and VLDL-C in both hy0erlipidemic and normal control rats. However, serum HDL-C level showed a highly significant increase in garlic oil treated normal rats. Similarly **Chi et al. (1982)** observed that, garlic supplementation decreased plasma cholesterol, very low-density lipoprotein cholesterol and increased high-density lipoprotein cholesterol in cholesterol- and lard-fed rats. Also, **Bordia et al. (1998)** reported that, garlic administration in a daily dose of 2 x2 capsules (each capsule containing ethyl acetate extract from 1 g peeled and crushed raw garlic), in patients with coronary artery disease, reduced significantly total serum cholesterol, and triglycerides, and increased significantly HDL- cholesterol and fibrinolytic activity the increase of HDL-C and decrease of LDL-C may be the visible reason of marked reduction of total cholesterol **(Adler and Holub, 1997)**. Reducing plasma concentration of tryglycerides and cholesterol by lowering the hepatic synthesis and secretion of VLDL- and also by increasing the activity of lipoprotein lipase, which in turn promotes the catabolism of the triglycerids-rich lipoproteins, VLDL- and LDL **(Grundy and Vega 1987)**. Moreover, lipoprotein lipase is also relevant to HDL-C production previous studies demonstrated that enhanced lipolysis of triglyceride-rich lipoprotein may lead to an increase in HDL-cholesterol **(Guillausseau, et al., 1992)**. Th obtained data regarding the hypolipidemic effects of garlic oil is disagree with that reported by **Berthold et al. (1998)** who observed that, using garlic oil preparation in hypercholesterolemic patients over 12 weeks had no influence on serum lipoproteins, cholesterol absorption, or cholesterol synthesis. Also, the hypolipidemic effects of garlic oil in normal control rats is disagree with that obtained by **Prasad et al. (1977)**, who reported that, supplementation of garlic powder (300 mg twice daily orally) in rabbits with control diet did not effect the levels of total cholesterol, low-density lipoprotein cholesterol, and high-density lipoprotein cholesterol and the ratio of LDL-cholesterol high –density lipoprotein cholesterol.

Regarding serum non-esterified fatty acids concentration garlic oil treatment caused a marked increase in some NEFA in both hyperlipidemic rat and in rat fed a normal control diet. The marked increase in serum NEFA concentration may be due to increased the lipolytic activity of lipase enzyme which increased the lipolysis of triacylglycerols to glycerol and free fatty acids **(Emara, 1999)**.

A very highly significant decrease in serum lecthin-cholesterol acyltransferase and a very highly significant increase in serum lipoprotein lipase activities was recorded accompanied the administration of garlic oil in hyperlipidemic rats. This increase in serum lipase activity become significant after garlic oil treatment in normal rat fed a control diet.

Similarly, **Adoga (1987)**, reported that, lipase activity was increase in rat treated with garlic oil. Also, **Sodima et al. (1984)**, recorded that, adipose tissue triglyceride lipase activity was significantly increase in rat feeding high-fat-high cholesterol diet for 1 month and much greater rise was reported in garlic oil treated rat. The decrease of serum lecithin cholesterol acyltransferase (LCAT) activity might be attributed to decreased the accumulation of unesterified cholesterol derived from the surface of chylomicrons and very low density lipoprotein **(Heller et al., 1981)**, as confirmed by **Forsythe et al. (1980)** who suggested that, increased esterified cholesterol levels were responsible for decreased molar LCAT activity. Changes in molar LCAT activity in humans positively correlate with changes in unesterified cholesterol, triacylglycerol and phospholipid blood levels. Moreover, **Larking and Sutherland (1977)** suggested that, increased esterified cholesterol levels were responsible for decreased molar LCAT activity.

Induction of hyperlipidemia produced a significant increase in serum albumin, total globulins and alpha globulin concentrations a long the time of the experiment. On the other hand, the values of serum total protein, beta and gamma globulin fractions as well as immunoglobulin, (IgG, IgA&IgM) concentrations did not show significant changes. The increase in serum albumin level in hyperlipidemic rats was nearly similar to the results reported by **Omnia (1993)**. She reported that, induction of hyperlipidemia in rats caused a significant increase in serum albumin and total protein concentrations. However, a significant reduction in the values of serum globulins level was observed. On contrary, **Sodimu et al. (1984)** reported that, the feeding of a high fat-high cholesterol diet to normal rats for 1 month decreased the serum albumin level very significantly. The increase of alpha-globulin level may be attributed to increased synthesis of beta and gamma globulin's.

The effects of garlic oil administration in rat fed a hyperlipidemic diet and normal control rat fed a normal diet were investigated in Table (5 and 6). Garlic oil administration produced a significant increase in serum total proteins and total globulins concentration in hyperlipidemic rats. However, in normal rats garlic oil treatment caused a significant decrease in serum total protein concentration and highly significant decrease in the value of serum albumin level. The increase in serum total proteins level in garlic oil treated hyperlipidemic rats could be attributed to the increase in the level of immunoglobulins and total globulins concentrations **(Hussein, 1996)**. Moreover, the decrease in the total protein levels in garlic oil treated normal rats was due to a decrease in albumin concentration and to a lesser degree to globulins. The synthesis of albumin and of many of the globulins take place in the animal's liver and chronic hepatic diseases hypoalbuminaemia occurs **(Kaneko, 1989)**. The obtained results were supported by the findings of **Joseph et al. (1989)** who reported that, garlic oil feeding (10 mg/100 g b. wt., intragastrically) has a toxic effect on liver and kidneys. However, similar feeding of garlic oil was well tolerated by rats in the fed state. Also, 24 hr. fasted rats could tolerate this dose of garlic oil, provided the were previously adapted to garlic oil feeding. In contrary **Shoetan et al. (1984)** reported that, garlic oil did not reduce the serum albumin or the total protein of liver, kidney or serum when fed along with ethanol to rats maintained on the high fat-high cholesterol diet. Furtherly, **Sodimu et al. (1984)** recorded that, administration of garlic oil (100 mg/kg b. wt/day) for 1 month together with high fat-high cholesterol diet to another group of rats almost nullified the albumin-decreasing effects of that diet. The restoration of serum albumin to normal level was highly significant in the garlic oil group. The differences in dose and duration of treatment may be the cause of inaccordance. On the other hand, the concentration of globulin fractions and immunoglobulins showed no significant variations

after garlic oil administration in both hyperlipidemic and normal control rats allover the experimental periods when compared with non treated animals groups.

From the obtained results it could be concluded that, garlic oil administration can mullified the lipid increasing effect of experimental induction of hyperlipidemia in adult male albino rats, and it is hypolipidemic agent which reduce serum lipids components and some lipoproteins fractions (LDL and VLDL)-cholesterol concentrations and increase the HDL-C without a significant effect on serum protein components and immunoglobulins levels. Thus garlic oil therapy may, therefore, be a possible coadjutor in the treatment and improving of hyperlipidemia (hypercholesterolemia).

Table (1) Changes of serum lipids and some lipoprotein concentrations(mg/dl), LCAT(nmol/ml/h) and lipase(Iu/L) activities in male hyperlipidemic rats and their control.

Durations	Parameters / Animal groups	Total lipids	Total cholesterol	Triacyl-glycerols	Phospho-lipids	Non-esterified fatty acids	HDL-cholesterol	LDL-cholesterol	VLDL-cholesterol	LCAT	Lipase
Two weeks	(Group I) Normal control	361.02 ± 7.21	72.90 ± 3.20	72.19 ± 4.35	96.13 ± 3.80	21.40 ± 0.56	35.18 ± 2.31	23.28 ± 0.94	14.69 ± 1.01	27.22 ± 1.88	108.87 ± 5.34
	(Group II) Hyperlipidemic control	642.77 ± 11.96***	125.58 ± 2.81***	164.87 ± 3.93***	197.37 ± 4.90***	15.14 ± 0.33***	45.39 ± 1.16**	56.46 ± 1.90***	32.97 ± 0.79***	42.35 ± 0.91***	85.39 ± 2.31**
Four weeks	(Group I) Normal control	398.42 ± 7.96	83.80 ± 1.88	85.30 ± 2.31	110.74 ± 3.26	24.15 ± 0.61	45.38 ± 1.81	28.79 ± 0.52	16.77 ± 0.67	33.58 ± 1.86	125.85 ± 2.74
	(Group II) Hyperlipidemic control	722.53 ± 14.21***	140.36 ± 2.90***	191.36 ± 3.68***	220.96 ± 5.37***	17.12 ± 0.33***	51.23 ± 1.35*	63.2 ± 1.28***	38.27 ± 0.73***	47.99 ± 0.96***	96.37 ± 1.20***

Results are presented as Mean ± S.E. S.E. = (standard error).
*: (P< 0.05) **: (P< 0.01) ***: (P< 0.001)

Table(2) Effect of Garlic oil administration (28 mg/kg B. wt. daily) on serum concentrations of lipids and some lipoproteins (mg/dl), LCAT (nmol/ml/h) and lipase (IU/L) activities in male hyperlipidemic rats.

Period after treatment	Parameters / Animal groups	Total lipids	Total cholesterol	Triacyl-glycerols	Phospho-lipids	Non-esterified fatty acids	HDL-cholesterol	LDL-cholesterol	VLDL-cholesterol	LCAT	Lipase
Two weeks	(Group II) Hyperlipidemic control	642.77 ± 11.96	125.58 ± 2.81	164.87 ± 3.93	197.37 ± 4.90	15.14 ± 0.33	45.39 ± 1.16	56.46 ± 1.90	32.97 ± 0.79	42.35 ± 0.91	85.39 ± 2.31
	(Group III) Hyperlipidemic + garlic oil	451.03 ± 9.83***	100.35 ± 2.24***	77.04 ± 1.64***	155.40 ± 3.27***	30.51 ± 0.69***	41.85 ± 1.24	37.86 ± 2.05***	15.37 ± 0.34***	25.39 ± 1.59***	132.43 ± 2.88***
Four weeks	(Group II) Hyperlipidemic control	722.53 ± 14.21	140.36 ± 2.90	191.36 ± 3.68	220.96 ± 5.37	17.12 ± 0.33	51.23 ± 1.35	63.2 ± 1.28	38.27 ± 0.73	47.99 ± 0.96	96.37 ± 1.20
	(Group III) Hyperlipidemic + garlic oil	500.71 ± 10.53***	116.97 ± 2.09***	89.81 ± 0.62***	173.80 ± 3.82***	34.12 ± 0.71***	49.63 ± 1.69	46.27 ± 2.35***	17.62 ± 0.32***	31.06 ± 1.38***	147.78 ± 3.05***

Results are presented as Mean ± S.E. S.E. = (standard error).
***: (P< 0.001)

Table (3) Effect of Garlic oil administration (28 mg/kg B. wt. daily) on serum concentrations of lipids and some lipoproteins (mg/dl), LCAT (nmol/ml/h) and lipase (IU/L) activities in normal male rats.

Period after treatment	Parameters / Animal groups	Total lipids	Total cholesterol	Triacyl-glycerols	Phospho-lipids	Non-esterified fatty acids	HDL-cholesterol	LDL-cholesterol	VLDL-cholesterol	LCAT	Lipase
Two weeks	(Group I) Normal control	361.02 ± 7.21	72.90 ± 3.20	72.19 ± 4.35	96.13 ± 3.80	21.40 ± 0.56	35.18 ± 2.31	23.28 ± 0.94	14.69 ± 1.01	27.22 ± 1.88	108.87 ± 5.34
	(Group IV) Normal + garlic oil	333.22 ± 5.22*	62.27 ± 1.61*	60.51 ± 2.35*	87.17 ± 3.15	24.73 ± 0.65**	43.64 ± 0.67**	19.99 ± 0.60*	11.29 ± 0.39*	23.90 ± 1.40	119.18 ± 1.40
Four weeks	(Group I) Normal control	398.42 ± 7.96	83.80 ± 1.88	85.30 ± 2.31	110.74 ± 3.26	24.15 ± 0.61	45.38 ± 1.81	28.79 ± 0.52	16.77 ± 0.67	33.58 ± 1.86	125.85 ± 2.74
	(Group IV) Normal + garlic oil	367.45 ± 2.81**	70.59 ± 2.31**	69.09 ± 2.52**	104.16 ± 2.11	26.34 ± 0.38*	53.28 ± 1.16**	21.68 ± 1.05***	14.12 ± 0.78*	32.89 ± 0.82	133.28 ± 1.28*

Results are presented as Mean ± S.E. S.E. = (standard error).
*: (P< 0.05) **: (P< 0.01) ***: (P< 0.001)

Table (4) Changes of electrophoretic pattern of serum proteins (g/dl), and immunoglobulins (mg/dl) concentrations in male hyperlipidemic rats and their control.

Durations	Parameters / Animal groups	Total Proteins	Albumin	Total globulins	Globulin fractions			Immunoglobulins (Ig)		
					α- globulin	β-globulin	γ-globulin	IgG	IgA	IgM
Two weeks	(Group I) Normal control	6.896 ± 0.02	3.994 ± 0.005	2.902 ± 0.01	0.978 ± 0.005	0.668 ± 0.006	1.256 ± 0.005	320.75 ± 9.91	78.15 ± 5.06	62.5 ± 8.09
	(Group II) Hyperlipidemic control	6.922 ± 0.03	4.044 ± 0.02*	2.878 ± 0.03	0.934 ± 0.06	0.686 ± 0.01	1.258 ± 0.01	305.75 ± 9.48	70.45 ± 4.94	62.83 ± 6.24
Four weeks	(Group I) Normal control	7.098 ± 0.06	4.144 ± 0.06	2.954 ± 0.01	0.996 ± 0.006	0.692 ± 0.009	1.266 ± 0.005	322.75 ± 10.14	80.91 ± 5.39	67.01 ± 6.43
	(Group II) Hyperlipidemic control	7.226 ± 0.07	4.146 ± 0.05	3.08 ± 0.03**	1.038 ± 0.01*	0.756 ± 0.02	1.286 ± 0.03	319.75 ± 9.54	77.87 ± 5.17	67.13 ± 6.58

Results are presented as Mean ± S.E. S.E. = (standard error).
*: (P< 0.05) **: (P< 0.01)

Table (5) Effect of Garlic oil administration (28 mg/kg. B. wt. daily) on electrophoretic pattern of serum proteins (g/dl), and immunoglobulins (mg/dl) concentrations in male hyperlipidemic rats.

Period after treatment	Parameters / Animal groups	Total Proteins	Albumin	Total globulins	Globulin fractions			Immunoglobulins (Ig)		
					α- globulin	β-globulin	γ-globulin	IgG	IgA	IgM
Two weeks	(Group II) Hyperlipidemic control	6.922 ± 0.03	4.044 ± 0.02	2.878 ± 0.03	0.934 ± 0.06	0.686 ± 0.01	1.258 ± 0.01	305.75 ± 9.48	70.45 ± 4.94	62.83 ± 6.24
	(Group III) Hyperlipidemic + garlic oil	7.07 ± 0.04*	4.056 ± 0.03	3.014 ± 0.02	1.024 ± 0.02	0.72 ± 0.01	1.27 ± 0.02	313.5 ± 13.85	82.49 ± 2.59	74.15 ± 9.26
Four weeks	(Group II) Hyperlipidemic control	7.226 ± 0.07	4.146 ± 0.05	3.08 ± 0.03**	1.038 ± 0.01*	0.756 ± 0.02	1.286 ± 0.03	319.75 ± 9.54	77.87 ± 5.17	67.13 ± 6.58
	(Group III) Hyperlipidemic + garlic oil	7.366 ± 0.08	4.142 ± 0.03	3.224 ± 0.06*	1.116 ± 0.04	0.808 ± 0.01	1.30 ± 0.03	321.25 ± 10.40	81.71 ± 5.14	68.84 ± 6.66

Results are presented as Mean ± S.E. S.E. = (standard error).
*: (P< 0.05)

Table (6) Effect of Garlic oil administration (28 mg/kg. B. wt. daily) on electrophoretic pattern of serum proteins (g/dl), and immunoglobulins (mg/dl) concentrations in normal male rats.

Period after treatment	Parameters / Animal groups	Total Protein	Albumin	Total globulins	Globulin fractions			Immunoglobulins (Ig)		
					α- globulin	β-globulin	γ-globulin	IgG	IgA	IgM
Two weeks	(Group I) Normal control	6.896 ± 0.02	3.994 ± 0.005	2.902 ± 0.01	0.978 ± 0.005	0.668 ± 0.006	1.256 ± 0.005	320.75 ± 9.91	78.15 ± 5.06	62.5 ± 8.09
	(Group IV) Normal + garlic oil	6.418 ± 0.06*	3.604 ± 0.03**	2.814 ± 0.04	0.94 ± 0.02	0.65 ± 0.01	1.224 ± 0.019	319.00 ± 9.40	73.63 ± 5.50	60.77 ± 8.19
Four weeks	(Group I) Normal control	7.098 ± 0.06	4.144 ± 0.06	2.954 ± 0.01	0.996 ± 0.006	0.692 ± 0.009	1.266 ± 0.005	322.75 ± 10.14	80.91 ± 5.39	67.01 ± 6.43
	(Group IV) Normal + garlic oil	6.978 ± 0.09	4.038 ± 0.04	2.940 ± 0.04	0.974 ± 0.03	0.716 ± 0.02	1.25 ± 0.02	321.00 ± 9.93	78.67 ± 5.22	65.50 ± 6.67

Results are presented as Mean ± S.E. S.E. = (standard error).
*: (P< 0.05) **: (P< 0.01)

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