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ANTIOXIDATIVE AND CARDIO-PROTECTIVE EFFECTS OF ETHANOLIC EXTRACT OF GINGER ON TRITON WR-1339 INDUCED HYPERLIPIDEMIA IN RATS

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Abstract- The present study aimed to clarify the protective effect of ethanolic extract of ginger on Triton WR-1339 induced hyperlipidemia in rats. Forty male rats were randomly divided into four groups: control, Triton WR-1339 treated group received 250 mg/kg b.wt intraperitoneally (3 times per week), ginger treated group received ethanolic extract of ginger 400 mg/kg b.wt orally and ginger pretreated Triton WR-1339 group received Triton WR-1339 and ethanolic extract of ginger at the same doses for three weeks. Hyperlipidemic rats exhibited significant increase in serum total lipids, cholesterol, triacylglycerol, low density lipoprotein and very low density lipoprotein levels with reduction in serum high density lipoprotein level. Also, serum testosterone, progesterone, estradiol, triiodothyronine and thyroxine hormones, and aspartate transaminase, lactate dehydrogenase, creatine kinase and creatine kinase-MB isoenzyme activities, and Troponin I level were significantly increased. Cardiac malondialdehyde level was increased while glutathione-S-transferase, glutathione peroxidase, and glutathione reductase activities, and reduced glutathione level were significantly decreased. Treatment with ethanolic extract of ginger significantly reduced serum lipid levels and normalized serum biomarkers of cardiac functions, increased serum endocrine hormones and antioxidant enzymatic activities with subsequent decrease of malondialdehyde level. We concluded that ethanolic extract of ginger has a protective role against cardiac damaging effect of hyperlipidemia.

Keywords- Ginger, testosterone, troponin, estradiol, hyperlipidemia

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Introduction

Hyperlipidemia, mainly increase level of total cholesterol (TC), triacylglycerol (TAG) and low-density lipoprotein (LDL) cholesterol along with decrease in high-density lipoprotein (HDL) cholesterol, is an important risk factor in the initiation and progression of atherosclerosis and coronary artery disease (CAD) [1]. Hyperlipidemia is typically due to a combination of environmental and/or genetic factors; in addition to secondary causes like diabetes mellitus type II, obesity, alcoholism, nephritic syndrome, hypothyroidism, Cushing's syndrome and some medications [2]. Disorders of lipid metabolism, hyperlipidemia, hypertension and obesity are associated with increased oxidative stress and over production of oxygen free radicals with decreased antioxidant activities which play an important role in the initiation and progression of atherosclerosis and related cardiovascular diseases [3].

Triton WR-1339 (tyloxapol) is a non-ionic surfactant being widely used to explore possible mechanism of lipid lowering drugs [4]. Triton causes drastic increase in serum TAG and TC levels due to increase in 3-hydroxy, 3-methyl-glutaryl CoA (HMG-CoA) reductase activity and by inhibition of lipoprotein lipase responsible for hydrolysis of plasma lipids [5,6]. A wide variety of therapeutic agents in modern medicine are available for the treatment of hyperlipidemia. However, most hypolipidemic drugs cause potentially serious side effects, and include digestive disturbances, nausea and vomiting. Herbal medical is a growing area of alternative medicines nowadays and regular usage of many herbs has been recommended in the management of hyperlipidemia [7]. Many active ingredients in manufactured drugs are derived from plant compounds and have a wide range of use. Plants and plant extracts more safe than chemical products whereas natural products is becoming more popular, since drugs of synthetic origin may have a negative impact on the environment and parasite resistance to poisonous chemicals can develop after repeated applications [8].

Ginger is an underground rhizome of plant *Zingiber officinale* belonging to the family *Zingibeaceae*, and now, it is considered a common constituent of diet worldwide [9]. Moreover, ginger is well known all over the world especially for its use in disorders of the gastrointestinal tract such as constipation, dyspepsia, nausea and vomiting [10]. It was reported that ginger has medicinal properties against digestive disorders, rheumatism, and diabetes [11]. Akhani, et al [12] reported that ginger treatment significantly decreased both serum cholesterol and triacylglycerol. In addition, Fuhrman, et al [13] reported that ginger decreased LDL-c, VLDL-c and triacylglycerol levels in apolipoprotein-E deficient mice. Furthermore,

Bhandari, et al [14] had reported that an ethanolic extract of ginger prevent hypercholesterolemia and development of atherosclerosis in cholesterol-fed rabbits. Bhandari, et al [15] found that the ethanolic extract of ginger significantly reduced serum total cholesterol and triacylglycerol and increased the HDL-cholesterol levels; also, the extract can protect tissues from lipid peroxidation and exhibit a significant lipid lowering activity in diabetic rats.

The present study aimed to evaluate the effect of ethanolic extract of ginger on hyperlipidemia with special reference to hormonal, cardiac functions, lipid peroxidation and antioxidant changes.

Material and Methods

Chemicals and Reagents

Triton WR-1339, cumene hydroperoxide, 1-chloro-2, 4-dinitrobenzene (CDNB), 5-5-dithiobis-2-nitrobenzoic acid (DTNB) were obtained from (Sigma chemical Co. St., Louis, MO, USA). Thiobarbituric acid (TBA) and reduced glutathione (GSH) were obtained from Fluka Chemical Co. Trichloroacetic acid (TCA) and tris base were obtained from Merk Chemical Co. Biochemical diagnostic kits for cholesterol, triacylglycerol, high density lipoprotein (HDL), total lipids, AST, LDH, CK, CK-MB obtained from vitro Scient Co. ELISA diagnostic kits for testosterone, progesterone, estradiol, triiodothyronine (T3) and thyroxine (T4) obtained from Dima Gesellschaft Fur Diagnostika [GmbH], Germany. All the reagents used were of analytical grade.

Preparation of Plant Ethanolic Extract

Dried roots of ginger (1 kg) were cut into small pieces and homogenized in a kitchen mixer then extracted by hydroalcoholic solvent (pure ethanol: distilled water, 80:20 v/v) for 3 hours using Soxhlet apparatus. The extracts were dried over anhydrous Na_2SO_4 then the solvent was completely evaporated using a rotary evaporator at 40°C and then, the extract was stored at 4°C [16].

Animals and Experimental Design

Forty adult male albino rats weighing 210 ± 18 g (obtained from medical research institute, Alexandria University, Egypt) were used in this study. They were fed standard diet pellets and allowed food and water *ad libitum* for an acclimation period of two weeks. Animals were handled with human care in accordance with the National Institutes of Health guidelines. The rats were randomly divided into four groups (10 rats each) as the following design: the control group fed on basal diet and distilled water *ad libitum*. The hyperlipidemic group was i.p treated with triton WR-1339 at dose of 250 mg/kg b.wt three times/week for three weeks. The 3rd group is ginger treated group, the rats fed with ethanolic extract of ginger 400 mg /kg b.wt dissolved in tween 20 for four weeks. Finally, the preventive group, the rats were i.p injected with triton WR-1339 and pretreated with ethanolic extract of ginger at the same doses mentioned before.

Samples for Biochemical Analysis

At the end of experiment, blood samples were withdrawn from the retro-orbital vein of each rat and each sample was collected into clean tubes. The blood samples were allowed to coagulate and then centrifuged at 3000 rpm for 5 min. The separated sera were kept at -20°C until used for the estimation of serum activity of AST, CK, CK-MB and LDH, testosterone, progesterone, estradiol, T3, T4 and Troponin I levels and lipid profile (total lipids, cholesterol, triacylglycerol, HDL-c, LDL-c and VLDL-c). Then, the rats were sacrificed by cervical dislocation under ether anesthesia, and the hearts were rapidly removed. One gm of each heart was weighed and homogenized, using glass homogenizer with ice-cooled saline to prepare 25% W/V homogenate. The homogenate was divided into two aliquots. The first one was deproteinized with equal volume of ice-cooled 12% trichloroacetic acid and the obtained supernatant, after centrifugation at 1000 xg was used for the estimation of reduced glutathione (GSH) content. The second aliquot was centrifuged at 1000 xg and the resultant supernatant was used for estimation of glutathione peroxidase (GPx), glutathione-S-transferase (GST) and glutathione reductase (GR) activities and level of malondialdehyde (MDA).

Biochemical Blood Analysis

Lipid profile (total lipid, cholesterol, triacylglycerol, LDL-c and HDL-c levels), AST, CK, CK-MB and LDH activities were determined using automated enzyme analyzers (Biochemical analyzer AE-600N, ERMA-INC-Japan) and commercial diagnostic kits. ELISA procedure was used for quantitative determination of serum total testosterone, progesterone, estradiol, T3, T4 and Troponin I levels according to manufacturer's instructions.

Oxidative Stress and Antioxidants

Tissue lipid peroxides (LP) level was determined as thiobarbituric acid-reactive substances, measured as malondialdhyde (MDA) [17]. GSH level in heart homogenate were estimated by spectrophotometer according to the method of Sedlak & Lindsay [18]. Heart glutathione peroxidase (GPx) activity was determined using reduced glutathione and cumene hydroperoxide as substrate by the modified method of Paglia & Valentine [19]. Glutathione reductase (GR) and glutathione-S-transferase (GST) activities were measured according to the method of Horn [20] & Habig, et al [21] respectively.

Statistical Analysis

Statistical analysis was performed by using computer of statistical package for social science (SPSS version 11.0). The results are presented as means ± SE. One way analysis of variance (ANOVA) was used to test the differences between groups [22].

Results

The present study revealed that triton WR-1339 induced significant hyperlipidemia represented by the elevation of serum total lipids, total cholesterol, triacylglycerol, LDL-c and VLDL-c levels while, decreased serum HDL-c level as compared to control group. However, administration of ginger extract alone significantly reduced serum total cholesterol and non-significantly decreased serum TAG, LDL-c, VLDL-c and total lipid levels with significant high level of HDL-c level as compared to control group. Also, treatment with ethanolic extract of ginger together with hyperlipidemia significantly reduced the severity of hyperlipidemia and corrected the serum lipid profile when compared to hyperlipidemic group ($P<0.05$), [Table-1]. Hyperlipidemic rats exhibited a perturbation in male sex gonads and endocrine glands indicated by significant increase in serum testosterone, progesterone, estradiol, T3 and T4 level when compared to control rats. Treatment with ethanolic extract of ginger significantly induced an elevation in the level of serum total testosterone and progesterone without any significant changes in serum estradiol, T3 and T4 levels when compared to control group ($P<0.05$), [Table-2]. Co-administration of ginger together with triton WR-1339 significantly increased the levels of all endocrine hormones as compared to

hyperlipidemic group.

As compared to control, hyperlipidemia caused damage to cardiac cells evident by significant increase in enzymatic biomarkers of cardiac functions; AST, LDH, CK and CK-MB activities and Troponin I level. Administration of ginger alone significantly decreased serum CK activity and troponin I level with non-significant decrease in serum activities of AST, LDH, CK-MB as compared to control rats. Ethanolic extract of ginger when given together with hyperlipidemia significantly decreased AST, CK, CK-MB activities and Troponin I level with non-significant decrease in LDH enzymatic activity when compared to hyperlipidemic group indicating cardioprotective effect ($P<0.05$), [Table-3]. Increased lipid content after triton treatment significantly affects the oxidative stress and antioxidant status; heart tissue has high level of MDA with depleted GST, GPX, GR activities and GSH level when compared to control group. However, administration of ginger ethanolic extract reduced cardiac MDA level with subsequently increased enzymatic antioxidant activities and reduced GSH level as compared to hyperlipidemic group ($P<0.05$), [Table-4].

Table 1- Effect of ethanolic extract of ginger on serum lipid profile in hyperlipidemic rats

	TC (mg/dl)	TAG (mg/dl)	HDL-c (mg/dl)	LDL-c (mg/dl)	VLDL-c (mg/dl)	Total lipid (mg/dl)
I	95.66±4.40^{c}	63.62±3.76^{c}	30.14±2.50^{b}	39.47±3.63^{c}	18.21±1.08^{b}	251.95±12.92^{c}
II	311.5±9.47^{a}	582.61±23.38^{a}	1.60±0.15^{c}	174.65±16.94^{a}	128.39±18.16^{a}	1234.50±150.94^{a}
III	72.01±2.41^{d}	52.02±2.22^{c}	37.11±1.76^{a}	26.42±0.25^{c}	16.06±0.50^{b}	213.66±15.70^{c}
IV	255.30±9.11^{b}	476.34±28.13^{b}	1.65±0.17^{c}	137.45±4.86^{b}	118.18±6.46^{a}	952.51±40.14^{b}

The values are mean ± S.E. Means with different superscript letter in the same column are significantly different at $P<0.05$. I; control group, II; hyperlipidemic group, III; ginger ethanolic extract group, IV; ginger pretreated hyperlipidemic group.

Table 2- Effect of ethanolic extract of ginger on testosterone, progesterone, estradiol, T3 and T4 in hyperlipidemic rats

	Testosterone (ng/ml)	Progesterone (ng/ml)	Estradiol (pg/ml)	T3 (ng/ml)	T4 (ug/ml)
I	0.25±0.05^{d}	0.04±0.00^{b}	7.17±1.16^{b}	1.01±0.06^{b}	2.90±0.29^{b}
II	3.06±0.03^{b}	0.36±0.01^{a}	52.15±0.17^{a}	6.71±0.04^{a}	8.06±0.11^{a}
III	2.57±0.54^{c}	0.35±0.04^{a}	10.37±1.81^{b}	0.91±0.03^{b}	2.60±0.12^{b}
IV	3.87±0.07^{a}	0.36±0.01^{a}	56.49±1.31^{a}	7.83±0.09^{a}	9.29±0.32^{a}

The values are mean ± S.E. Means with different superscript letter in the same column are significantly different at $P<0.05$. I; control group, II; hyperlipidemic group, III; ginger ethanolic extract group, IV; ginger pretreated hyperlipidemic group.

Table 3- Effect of ethanolic extract of ginger on enzymatic biomarkers and Troponin I level cardiac functions in hyperlipidemic rats

	AST (U/l)	LDH (U/l)	CK (U/l)	CK-MB (U/l)	Troponin I (ng/ml)
I	98.81±3.17^{c}	889.20±34.89^{b}	743.17±41.16^{b}	218.66±31.46^{b}	0.45±0.04^{c}
II	262.89±23.32^{a}	1707.22±158.48^{a}	1132.15±76.17^{a}	415.01±82.58^{a}	1.73±0.05^{a}
III	92.29±1.62^{c}	780.59±53.34^{b}	475±51.81^{c}	201.26±45.44^{b}	0.06±0.00^{d}
IV	186.23±16.05^{b}	1481.93±163.85^{a}	994±65.34^{b}	324.25±32.24^{c}	0.86±0.04^{b}

The values are mean ± S.E. Means with different superscript letter in the same column are significantly different at $P<0.05$. I; control group, II; hyperlipidemic group, III; ginger ethanolic extract group, IV; ginger pretreated hyperlipidemic group.

Table 4- Effect of ethanolic extract of ginger on cardiac lipid peroxidation and antioxidant indices in hyperlipidemic rats

	MDA (nmol/g tissue)	GSH (µmole/g tissue)	GST (µmole/min/g tissue)	GPX (U/g tissue)	GR (U/g tissue)
I	17.23±1.05^{c}	17.83±1.23^{b}	673.56±23.16^{a}	82.34±9.23^{a}	52.90±4.12^{a}
II	47.87±7.26^{a}	9.98±0.91^{d}	421.63±28.17^{c}	51.71±8.04^{c}	28.98±3.13^{c}
III	15.87±1.54^{c}	24.61±2.04^{a}	701.87±31.81^{a}	86.15±11.03^{a}	57.72±5.19^{a}
IV	39.54±6.09^{b}	14.62±1.01^{c}	587.34±21.31^{b}	77.83±6.09^{b}	41.64±3.37^{b}

The values are mean ± S.E. Means with different superscript letter in the same column are significantly different at $P<0.05$. I; control group, II; hyperlipidemic group, III; ginger ethanolic extract group, IV; ginger pretreated hyperlipidemic group.

Discussion

The main causative factor for atherosclerosis and cardiovascular diseases is the disturbances occurring in lipid metabolism. Though there is a large class of hypolipidemic drugs used in the treatment, none of the existing ones available worldwide is fully effective, absolutely safe and free from side effects [23]. In the present study, we examined whether the ginger ethanolic extract treatment might improve the lipid and hormonal profile as well as oxidative stress and antioxidant status in Triton WR-1339 induced hyperlipidemic model.

Triton WR-1339 is used for induction of sustained hyperlipidemia which may be attributed to stimulation of HMG-COA reductase and inhibition of lipoprotein lipase responsible for hydrolysis of plasma lipids [24]. Also, it could increase VLDL-c secretion by liver accompanied by reduction in VLDL-c and LDL-c catabolism through suppression of LDL receptor synthesis [25]. This result was in agreement with Al-Hiari, et al [26] who reported that single i.p injection of triton WR-1339 induced hyperlipidemia in rats.

The results regarding the effect of ginger on lipid profile are in the same line with Saeid, et al [27] who explored the usage of different

levels of aqueous extract of ginger at concentration of 0.4 and 0.6% respectively on the lipid profile of the broiler chickens. In this respect, Bhandari, et al [15] demonstrated that ethanolic extract of ginger produced significant decrease in serum total cholesterol and triacylglycerol levels and increased HDL-c level as compared to diabetic rats, and the extract exhibited a significant lipid lowering activity and protect the tissues from lipid peroxidation. It was found that (E)-8 beta, 17- epoxyllabed-12-ene-15, 16-dial, a compound isolated from ginger, interfered with cholesterol biosynthesis in liver homogenates of hypercholesterolaemic mice causing its reduction [28]. Furthermore, Lebda, et al [29] found that treatment with ginger significantly reduced serum triacylglycerol, VLDL-c and LDL-c levels with increased HDL-c level in paracetamol treated rats. These results are compatible with the results of previous research which applied ginger orally on high cholesterol fed rabbits to cause reduction in atherogenesis and lipid levels, by disruption of cholesterol absorption from gastrointestinal tract [14]. The hypocholesterolemic effect of ginger may also be due to the elevation of hepatic cholesterol-7α-hydroxylase activity which is the rate-limiting enzyme in the biosynthesis of bile acids and stimulates the conversion of cholesterol to bile acids [30], the inhibition of cellular cholesterol synthesis [31] which may be attributed to the presence of niacin in ginger [32] which increased clearance of VLDL-c, lowered TG levels, increased hepatic uptake of LDL-c, and inhibited cholesterogenesis [33].

Obesity is characterized by an imbalance between energy intake and expenditure that results in the enlargement of adipose tissue mass which is associated with many metabolic changes, mainly as a consequence of the altered secretion of several hormones and factors, such as increased leptin and serum free fatty acids (FFAs) and decreased adiponectin; hyperleptinemia is frequently associated with central leptin resistance with important consequences, such as hyperphagia and decreased energy expenditure [34]. Also, Nadeem, et al [35] reported that the fasting serum leptin level was significantly elevated in high fructose diet induced hyperlipidemia in rats. The hypothalamus pituitary thyroid (HPT) axis activity may be stimulated by leptin under physiological conditions [36]. Hyperleptinemia in obese humans [37] and rodents [38] is associated with high circulating thyroid hormones, suggesting that leptin still activates the HPT axis in these individuals even though they are resistant to the anorexigenic effect of leptin. Despite having high levels of thyroid hormones, the hyperlipidemic rats were markedly overweight, which seems counterintuitive because thyroid hormones increase the metabolic rate and energy expenditure [39]. However, in overweight animals, these effects may be counterbalanced by an increase in food intake induced by T3 [40] and possibly by an impairment of the metabolic actions of thyroid hormones, among other characteristics of obesity. Moreover, Harris, et al [41] favor the concept that leptin acts primarily on the hypothalamus, stimulating directly or indirectly thyrotrophin-releasing hormone (TRH) production and release and subsequent increased thyroid hormones. In rats, high fat food causes an increase in total and unbound plasma testosterone levels [42], a decrease in sex hormone binding globulin (SHBG) level [43] and inhibition of aromatase activity in testes [44]. Furthermore, Attyha, et al [45] found a significant elevation of estradiol level in atherosclerotic hyperlipidemic patient when compared with those of control group.

The positive effect of ginger extract on male sex hormone was in harmony with Khaki, et al [46] who reported that administration of ginger for twenty days significantly increased testosterone, FSH and LH levels in rats which could be attributed to the androgenic activity of ginger that increased the α-glycosidase enzyme in epididymis, and fructose sugar in seminal vesicle. Also, the increase in serum testosterone level agrees with the reports of Kamtchouing, et al [47] and Morakinyo, et al [48] which suggest a possible androgenic property of ginger. Furthermore, Sanavi & Afshar [49] reported that ginger has stimulating effect on thyroid gland and subsequent it is contraindicated in women with subacute thyroiditis. Talal and Al-Attar [50] found that treatment of diabetic rats with ginger significantly increased TSH, T3 and T4 as compared to control diabetic rats.

Free radical-induced lipid peroxidation or oxidative stress has been shown to participate in the pathogenesis of several diseases. Hypercholesterolemia induces not only atherosclerosis but also produces a lot of free radicals in blood and tissues [51]. MDA level is a good indicator of lipid peroxidation. The present study showed that the cardiac MDA level was significantly elevated with triton administration. It is widely known that both the liver and heart are primary organs at risk from hypercholesterolemia. Retention of hepatic lipid has been shown to induce steatosis, and finally impairs hepatic function. High cholesterol diet suppressed hepatic and cardiac functions as expressed by an augmentation of serum levels of AST, ALT, ALP, LDH, and CK-MB. Hepatic and cardiac lipid peroxidation also increased in HC rats. Moreover, antioxidant enzyme activities in both organs were depressed [52]. Also, Taha, et al [53] found that intraperitoneal injection of Triton WR-1339 at dose of (250 mg/kg/3 times/week) showed a significant increase in serum activities of AST, ALT and GGT enzymes as compared to control group.

The heart of hyperlipidemic/atherosclerotic patients adapts poorly to oxidative or other kinds of stress, suggesting that the endogenous adaptive mechanisms against myocardial stress are impaired [54]. Li, et al [55] showed that oxidized low density lipoprotein (oxLDL) is deposited in the myocardium which leads to expression of oxLDL receptor (LOX-1) and thereby induces apoptosis and cardiac dysfunction. Increased formation of free radicals is accompanied by perturbations in antioxidant status, resulting in oxidative damage to cellular components [56]. Hypercholesterolemia is reported to be associated with the oxidative stress that results from the increased production of ROS or impairment of the antioxidant system [57]. As enhanced lipid peroxidation leads to higher atherogenicity, it is plausible that antioxidant status should have a major impact not only on the rate of LDL oxidation but perhaps on development of atherosclerosis. A potential risk of atherosclerosis in individuals with high serum lipid levels may be associated with LDL oxidation as a result of increased levels of LDL-cholesterol and decreased antioxidant enzyme activity [58].

Liu, et al [59] reported the antioxidative effect of *Zingiber officinale Rosc* on hyperlipidemic rats that increased blood GSH-Px activity and decreased lipid peroxides (LPO) level. This result agreed with Blessy, et al [60] who found that *Zingiber officinale* significantly decrease lipid peroxidation level in rats. The observed reduction in the level of lipid peroxidation in *Zingiber officinale* treated animals was presumably due to its ability to scavenge the hydroxyl and peroxyl radicals. Moreover, Stoilova, et al [61] confirmed that the ginger extract is a powerful free hydroxyl (OH•) scavenger, resulting in inhibiting lipid peroxidation in linoleic acid model system. The antioxidant activity of the ginger extract plays a role on the inhibition of ROS generation, ROS neutralization, or the induction of endogenous antioxidants as obtained by Chakraborty, et al [62].

Conclusion

The current study showed that hyperlipidemia has adverse effect on cardiac functions, oxidative stress and antioxidant status. However, ethanolic extract of ginger has antioxidant, hypolipidemic and androgenic effect and cardio-protective activity in hyperlipidemic rats.

List of Abbreviations

AST: Aspartate Transaminase;
CAD: Coronary Artery Disease;
CDNB: 1-Chloro-2, 4-dinitrobenzene;
CK: Creatine Phosphokinase;
CK-MB: Creatine Phosphokinase MB Isoenzyme;
DTNB: 5-5-dithiobis-2-nitrobenzoic Acid;
FFAS: Free Fatty Acids;
GPX: Glutathione Peroxidase;
GR: Glutathione Reductase;
GSH: Reduced Glutathione;
GST: Glutathione Transferase;
HDL-c: High-density Lipoprotein cholesterol;
HMG-CoA: 3-hydroxy, 3-methyl-glutaryl CoA;
HPT: Hypothalamus Pituitary Thyroid;
LDH: Lactate Dehydrogenase;
LDL-c: Low-density Lipoprotein cholesterol;
LPO: Lipid Peroxides;
MDA: Malondialdehyde;
SHBG: Sex Hormone Binding Globulin;
TAG: Triacylglycerol;
TBA: Thiobarbituric Acid;
TC: Total Cholesterol;
TCA: Trichloroacetic Acid;
TRH: Thyrotrophin Releasing Hormone;
VLDL-c: Very Low Density Lipoprotein cholesterol.

Conflicts of Interest: None declared.

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