Antiatherogenic, hepatoprotective, and hypolipidemic effects of coenzyme Q10 in alloxan-induced type 1 diabetic rats

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Original Article

Abstract

BACKGROUND: Diabetes mellitus, one of the leading metabolic syndromes, accounts for highest morbidity and mortality worldwide. In this study, we examined possible protective effect of coenzyme Q10 on lipid profile, atherogenic index, and liver enzyme markers in alloxan-induced type 1 diabetic rats.

METHODS: A total of 30 male rats were randomly divided into three groups; group 1 as control, group 2 diabetic untreatment, and group 3 treatments with coenzyme Q10 by 15 mg/kg i.p. daily, respectively. Diabetes was induced in the second and third groups by alloxan injection subcutaneously. After 8 weeks, the levels of fasting blood glucose (FBG), triglyceride (TG), total cholesterol (TC), low density lipoprotein (LDL), very low-density lipoprotein (VLDL), high density lipoprotein (HDL), atherogenic index, atherogenic coefficient, cardiac risk ratio, and the activities of alanine aminotransferase (ALT), aspartate aminotransferase (AST), and alkaline phosphatase (ALP) of all groups were analyzed. Data were analyzed using non-parametric Mann-Whitney test (using SPSS) and $P < 0.05$ was considered as significant.

RESULTS: Coenzyme Q10 inhibited significantly the activities of ALT (11.17%), AST (19.35%) and ALP (36.67%) and decreased FBG (21.19%), TG (37.24%), TC (17.15%), LDL (30.44%), VLDL (37.24%), atherogenic index (44.24%), atherogenic coefficient (49.69%), and cardiac risk ratio (37.97%), HDL level was significantly (33.38%) increased when treated with coenzyme Q10.

CONCLUSION: The findings of this study suggest that coenzyme Q10 exert beneficial effects on the lipid profile, atherogenic index, and liver enzymes activity in alloxan-induced type 1 diabetic rats.

Keywords: Diabetes, Lipid Profile, Atherogenic Index, Rats, Liver Enzymes, Coenzyme Q10

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Introduction

Diabetes mellitus, one of the leading metabolic syndromes, accounts for highest morbidity and mortality worldwide.[1] Diabetes mellitus is characterized by abnormalities in carbohydrate, lipid and protein metabolism due to complete or relative insufficiency of insulin secretion from pancreatic β-cells and/or defect in insulin action.[2] Oxidative stresses is a state of imbalance between oxidant and antioxidant systems.[3]

In recent times, much attention has been focused on the central and key role of oxidative stress in the pathogenesis of different diabetic complications.[4] Several studies have shown that antioxidant treatment reduces diabetic complications.[5] Due to increasing demand of patients for the use of natural products with anti-diabetic activity, the general trend now is to use the natural products for medicinal application in their natural available form.[6] Polyphenols, well-known antioxidants, have also been showed to function as anti-diabetic by reducing blood glucose levels.[7,8] Researchers are recently interested in investigation and research into extraction of natural antioxidants to replace synthetic antioxidants.[9,10] Therefore, the research into the determination of the natural antioxidant source is very important to promote public health.

Coenzyme Q10 is a natural human ubiquinone, and it has fundamental role in mitochondrial energy (adenosine triphosphate) production in the respiratory chain.[11,12] It plays a role in extra-mitochondrial redox activity in the cell membrane. Coenzyme Q10 is also antioxidant, scavenging free

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radicals, and inhibiting lipid peroxidation.[13,14] The antioxidant effect of coenzyme Q10 is greater than vitamin E.[15] Coenzyme Q10 is also known to enhance the availability of other antioxidants such as vitamin C, vitamin E, and β-caroten.[16]

Since the hypolipidemic, antiatherogenic, and liver protective effects of coenzyme Q10 in alloxan-induced type 1 diabetic rats have not previously been reported; the objectives of the present study were to investigate antiatherogenic, hepatoprotective, and hypolipdemic effects of coenzyme Q10 in alloxan-induced type 1 diabetic rats.

Materials and Methods

Experimental design

Animals

Thirty male mature Sprague-Dawley rats (180-200 g) were obtained from Pasteur Institute of Tehran, Iran, and were allowed to adapt themselves with the new location for 1 week. This study was approved by the Animal Ethics Committee of Lorestan University of Medical Sciences, Iran, with accordance to the national health and medical research council guidelines. The rats were randomly divided into three groups (10 per each). The studied groups were as follows: group 1 as control, group 2 as diabetic without treatment, and group 3 as diabetic treatment with coenzyme Q10 (C9538, Sigma Chemical Co., St. Louis, MO, USA).

Diabetes induction

Diabetes was induced after overnight fasting in the second and third groups by injection of alloxan monohydrate (120 mg/kg) subcutaneously.[17] β-Cell degradation by alloxan leads to release of more insulin. Because of acute hypoglycemia, the rats received 10% sucrose solution for 48 h instead of drinking water. Five days after induction of diabetes, blood samples were gathered from the end part of tails. Blood glucose was measured by glucometer and the rats with blood glucose level of ≥ 300 mg/dl (16.7 mmol/l) were considered as diabetic.[18] During the first 5 days after diabetes induction, 1-3 rats per group died because of alloxan toxicity. The rats were kept at 12/12 dark-light period in 21 ± 3° C temperature. All animals were allowed free access to food and water *ad libitum* during the experiment. The third group was treated with coenzyme Q10 by 15 mg/kg i.p. daily.[19]

The treatment was begun at the 1st day of diabetes induction. After 8 weeks treatment, animals were anesthetized (nesdonal 50 mg/kg, i.p.), blood samples were obtained from hearts and allowed to clot for 20 min in laboratory temperature and then centrifuged at 3000 rpm for 10 min for serum separation.[20,21]

Biochemical study

The serum levels of fasting blood glucose (FBG), triglyceride (TG), total cholesterol (TC), low density lipoprotein (LDL), very low-density lipoprotein (VLDL), high density lipoprotein (HDL), atherogenic index and the activities of alanine aminotransferase (ALT), aspartate aminotransferase (AST), and alkaline phosphatase (ALP) of all groups were analyzed.

FBG, TC, and TG concentrations and ALT, AST, and ALP activity were measured by biochemical analyzer using commercial kits (Olympus AU-600, Tokyo, Japan). HDL was analyzed by a Pars Azmoon kit from Iran. LDL and VLDL were determined by calculation using the Freidewald equation.[22,23] The atherogenic index was determined by calculation using the Ikewuchi and Ikewuchi equation.[24]

Statistical analysis

All values are expressed as mean ± standard error of mean. The data were compared between groups by Mann-Whitney U test. Statistical analyses were performed using the SPSS for Windows (version 13, SPSS Inc., Chicago, IL, USA) software. P-value of < 0.05 was considered as statistically significant.

Results

The level of glucose in the untreated diabetic rats was significantly (4.48-fold) higher than that of control animals ($P < 0.05$). The treatment of diabetic animal with coenzyme Q10 could significantly (21.19%) inhibit the increase of glucose in comparison with the untreated diabetic animals (Table 1) ($P < 0.05$). The level of TC in the untreated diabetic rats was significantly (1.49-fold) higher than that of control animals ($P < 0.05$). The treatment of diabetic animal with coenzyme Q10 could significantly (17.15%) inhibit the increase of TC in comparison with the untreated diabetic animals (Table 1) ($P < 0.05$). The level of TG in the untreated diabetic rats was significantly (1.32-fold) higher than that of control animals ($P < 0.05$). The treatment of diabetic animal with coenzyme Q10 could significantly (37.24%) inhibit the increase of TG in comparison with the untreated diabetic animals (Table 1) ($P < 0.05$). The level of LDL in the untreated diabetic rats was significantly (2.72-fold) higher than that of control animals. The treatment of diabetic animal with coenzyme Q10 could significantly (30.44%) inhibit the increase of LDL in comparison with the untreated diabetic

animals (Table 1) (P < 0.05). The level of VLDL in the untreated diabetic rats was significantly (1.32-fold) higher than that of control animals (P < 0.05). The treatment of diabetic animal with coenzyme Q10 could significantly (37.24%) inhibit the increase of VLDL in comparison with the untreated diabetic animals (Table 1) (P < 0.05). The level of HDL in the untreated diabetic rats was significantly (1.23-fold) lower than that of control animals (P < 0.05). The treatment of diabetic animal with coenzyme Q10 could significantly (33.38%) increase of HDL in comparison with the untreated diabetic animals (Table 1) (P < 0.05).

The level of atherogenic index (units) [log (TG/HDL-C)] in the untreated diabetic rats was significantly (1.39-fold) higher than that of control animals (P < 0.05). The treatment of diabetic animal with coenzyme Q10 could significantly (44.24%) inhibit the increase of atherogenic index in comparison with the untreated diabetic animals (Table 2) (P < 0.05).

The level of atherogenic coefficient [(TC-HDL-C)/HDL-C] in the untreated diabetic rats was significantly (2.45-fold) higher than that of control animals (P < 0.05). The treatment of diabetic animal with coenzyme Q10 could significantly (49.69%) inhibit the increase of atherogenic coefficient in comparison with the untreated diabetic animals (Table 2) (P < 0.05). The level of cardiac risk ratio (TC/HDL-C) in the untreated diabetic rats was significantly (1.83-fold) higher than that of control animals (P < 0.05). The treatment of diabetic animal with coenzyme Q10 could significantly (37.97%) inhibit the increase of cardiac risk ratio (TC/HDL-C) in comparison with the untreated diabetic animals (Table 2) (P < 0.05). The level of cardiac risk ratio (LDL/HDL-C) in the untreated diabetic rats was significantly (3.45-fold) higher than that of control animals (P < 0.05). The treatment of diabetic animal with coenzyme Q10 could significantly (47.66%) inhibit the increase of cardiac risk ratio (LDL/HDL-C) in comparison with the untreated diabetic animals (Table 2) (P < 0.05).

The activity of ALP in the untreated diabetic rats was significantly (1.87-fold) higher than that of control animals. The treatment of diabetic animal with coenzyme Q10 could significantly (36.67%) inhibit the increase of ALP in comparison with the untreated diabetic animals (Figure 1) (P < 0.05). The activity of ALT in the untreated diabetic rats was significantly (1.30-fold) higher than that of control animals (P < 0.05). The treatment of diabetic animal with coenzyme Q10 could significantly (11.17%) inhibit the increase of ALT in comparison with the untreated diabetic animals (Figure 2) (P < 0.05). The activity of AST in the untreated diabetic rats was significantly (1.83-fold) higher than that of control animals (P < 0.05). The treatment of diabetic animal with coenzyme Q10 could significantly (19.35%) inhibit the increase of AST in comparison with the untreated diabetic animals (Figure 3) (P < 0.05).

Table 1. Effect of coenzyme Q10 on fasting blood glucose, triglyceride, total cholesterol, low density lipoprotein, very low density lipoprotein, and high density lipoprotein in diabetic rats

Parameter	Control	Diabetic	Diabetic + coenzyme Q10
FBG (mg/dl)	79.09 ± 27.66*	354.02 ± 58.32	279.07 ± 45.00*#
TG (mg/dl)	110.00 ± 29.66*	145.00 ± 28.01	91.00 ± 27.78*
TC (mg/dl)	75.32 ± 13.33*	112.05 ± 26.31	92.83 ± 21.14*#
HDL (mg/dl)	32.52 ± 7.75*	26.42 ± 12.49	35.24 ± 7.32*
LDL (mg/dl)	20.80 ± 3.87*	56.63 ± 6.94	39.39 ± 9.94*#
VLDL (mg/dl)	22.00 ± 4.89*	29.00 ± 4.78	18.20 ± 3.72*

Values are represented as mean ± SEM coenzyme Q10; * Significant change in comparison with diabetic without treatment at P < 0.05; # Significant change in comparison with control at P < 0.05; SEM: Standard error of mean; FBG: Fasting blood glucose; TG: Triglyceride; TC: Total cholesterol; HDL: High density lipoprotein; LDL: Low density lipoprotein; VLDL: Very low density lipoprotein

Table 2. Effect of coenzyme Q10 on atherogenic index, atherogenic coefficient, and cardiac risk ratio in diabetic rats

Parameter	Control	Diabetic	Diabetic + coenzyme Q10
Atherogenic index [(units) log (TG/HDL-C)]	0.53 ± 0.06*	0.74 ± 0.06	0.41 ± 0.02*#
Atherogenic coefficient [(TC-HDL-C)/HDL-C]	1.32 ± 0.72	3.24 ± 0.87	1.63 ± 0.21
Cardiac risk ratio (TC/HDL-C)	2.32 ± 0.54*	4.24 ± 0.75	2.63 ± 0.62*
Cardiac risk ratio (LDL/HDL-C)	0.62 ± 0.08*	2.14 ± 0.67	1.12 ± 0.27*#

Values are represented as mean ± SEM coenzyme Q10; * Significant change in comparison with diabetic without treatment at P < 0.05; # Significant change in comparison with control at P < 0.05; TG: Triglyceride; HDL-C: High density lipoprotein cholesterol; TC: Total cholesterol; LDL-C: Low density lipoprotein cholesterol

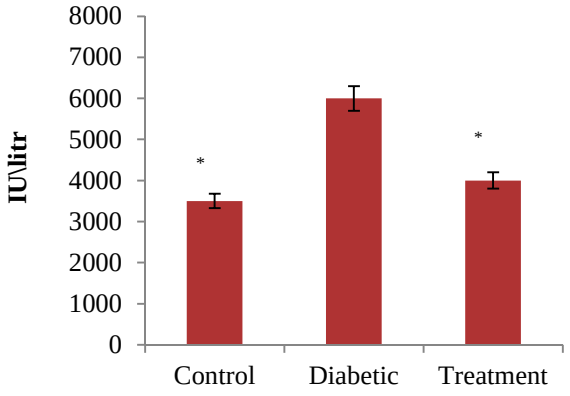

Figure 1. The effect of coenzyme Q10 on serum alkaline phosphatase activity in alloxan-induced diabetic rats
* Significant change in comparison with diabetic without treatment at P < 0.05

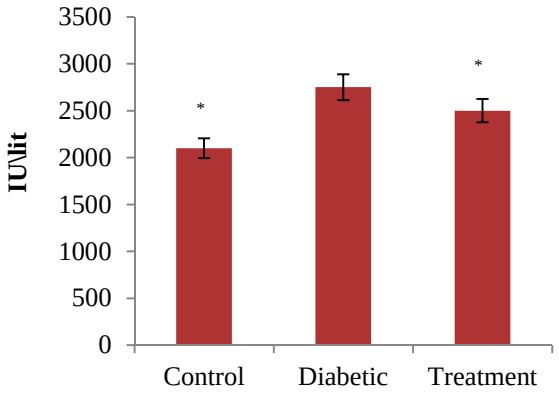

Figure 2. The effect of coenzyme Q10 on seruml alanine aminotransferase activity in alloxan-induced diabetic rats
* Significant change in comparison with diabetic without treatment at P < 0.05

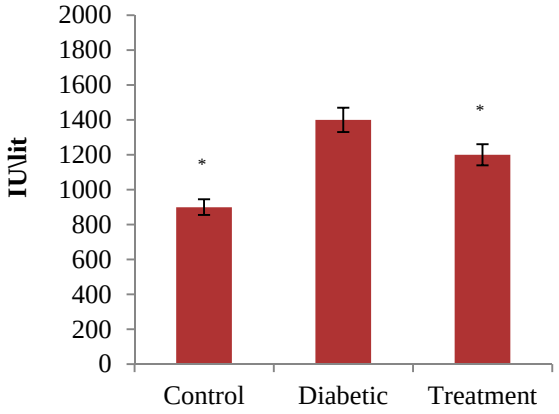

Figure 3. The effect of coenzyme Q10 on serum aspartate aminotransferase activity in alloxan-induced diabetic rats
* Significant change in comparison with diabetic without treatment at P < 0.05

Discussion

Effect of coenzyme Q10 on serum lipid profile and atherogenic index

Diabetes significantly increased serum FBG, TG, TC, VLDL, and LDL concentrations in comparison with the control group. Treatment of diabetic animals with coenzyme Q10 significantly inhibited inc rease of serum FBG, TG, TC, VLDL, and LDL concentrations, atherogenic index, atherogenic coefficient, and cardiac risk ratio in comparison with the untreated diabetic animals. Furthermore, treatment of diabetic animals with coenzyme Q10 significantly inhibited decrease of serum HDL concentrations in comparison with the untreated diabetic animals. There are reports that natural antioxidant such as lycopene and natural phenolic compounds have hypolipidemic effects.[25,26] Furthermore, there are reports that coenzyme Q10 have hypolipidemic effects. Cicero et al. showed coenzyme Q10 could reduce serum lipoprotein (a) level in patients with high serum triglyceride levels.[27] Moreover, Gao et al. showed coenzyme Q10 could reduce serum lipoprotein (a) level in patients with coronary artery diseases.[28] Also, Shojaei et al. showed coenzyme Q10 could reduce serum levels of lipoprotein (a) and lipids in Maintenance Hemodialysis Patients on Statin Therapy.[29]

Results of our study are in accordance with others researchers' study that showed coenzyme Q10 could reduce serum lipid and lipoprotein level. Therefore, natural antioxidant with hypolipidemic effects could prevent or be helpful in reducing the complications of lipid profile seen in diabetes patients. The mechanisms by which coenzyme Q10 can decrease high serum lipid level is not well known. The mechanism of hypolipedemic and antiatherogenic action of natural antioxidant may be due to the inhibition of dietary lipid absorption in the intestine or its production by liver or stimulation of the biliary secretion of cholesterol and cholesterol excretion in the faces.[30,31] Moreover, coenzyme Q10 is a lipid-solu ble molecule, and it is present in sufficient amounts in lipoprotein (a). Supplementation with coenzyme Q10 can inhibit expression of lipoprotein (a) receptor and result in decreased serum lipoprotein (a).[32] Also, the mechanism of hypolipedemic and antiatherogenic action of natural antioxidant may be due to the inhibition of glycation lipoproteins, enzymes and proteins that involve lipid and lipoprotein metabolism.[33]

Effect of coenzyme Q10 on serum ALP, ALT, and AST activity

Serum ALP, ALT, and AST activity as markers of liver function significantly were increased in the untreated diabetic animals in comparison with the control group. Treatment of the diabetic animals with coenzyme Q10 could significantly inhibit increase of serum ALP, ALT, and AST activity in comparison with the untreated diabetic animals. Treatment by coenzyme Q10 could maintain serum ALP, ALT, and AST activity of the treated animal at the same level as that of the control group. ALP, ALT, and AST are considered to be biochemical markers for assessing liver function. Hepatotoxicity is evidenced by an elevation of the serum marker enzymes.[34,35]

There are reports that natural antioxidant such as leptin and melatonin reduced these liver enzymes markers.[36,37] Also, there are reports that coenzyme Q10 have hepatoprotective effects.[38] Mabuchi et al. showed coenzyme Q10 could reduce serum ALT and AST activities.[38] Moreover, Ali et al. showed coenzyme Q10 could reduce serum ALT and AST activities on CCl_4-induced liver injury in rats.[39] Also, Amimoto et al. that is chemically damaged livers pretreated with coenzyme Q10 showed a decrease in the activity of serum ALT and AST.[40] Results of our study are in accordance with others researchers' study that showed coenzyme Q10 could reduce serum ALT, AST, and ALP activities. Therefore, natural antioxidant with hepatoprotective action could prevent or be helpful in reducing the complications of hepatic damage seen in diabetes patients.[41]

Researchers indicated that coenzyme Q10 is found to possess a good antioxidant activity.[15] Also researchers reported the role of oxidative stress as a central factor in onset and progression of diabetic complications such as hyperlipemia and hepatic damage.[4,42] Therefore, numerous reports and our results that showed efficacy of antioxidative supplements administration in the prevention of diabetic complications. Since antioxidant therapy is as one of the most important treatment strategies for diabetic patients for the prevention and slowing of diabetic complications progression such as hyperlipemia and hepatic damage.

This study has limitation in which we assumed the groups 2 diabetic without treatment with placebo.

Conclusion

This study showed that coenzyme Q10 has beneficial effects, in reducing the elevated serum lipid profile, atherogenic index and liver enzyme markers of alloxan-induced-diabetic rats. Hence, attenuation of lipid profile, atherogenic index and liver enzyme markers can decrease the risk of cardiovascular death and hepatic damage in diabetic patients.

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Conflict of Interests

Authors have no conflict of interests.

References

1. Najm W, Lie D. Herbals used for diabetes, obesity, and metabolic syndrome. Prim Care 2010; 37(2): 237-54.
2. Lin Y, Sun Z. Current views on type 2 diabetes. J Endocrinol 2010; 204(1): 1-11.
3. Koksal M, Eren MA, Turan MN, Sabuncu T. The effects of atorvastatin and rosuvastatin on oxidative stress in diabetic patients. Eur J Intern Med 2011; 22(3): 249-53.
4. Giacco F, Brownlee M. Oxidative stress and diabetic complications. Circ Res 2010; 107(9): 1058-70.
5. Golbidi S, Ebadi SA, Laher I. Antioxidants in the treatment of diabetes. Curr Diabetes Rev 2011; 7(2): 106-25.
6. Resmi CR, Venukumar MR, Latha MS. Antioxidant activity of Albizzia lebbeck (Linn.) Benth. in alloxan diabetic rats. Indian J Physiol Pharmacol 2006; 50(3): 297-302.
7. Hamden K, Allouche N, Damak M, Elfeki A. Hypoglycemic and antioxidant effects of phenolic extracts and purified hydroxytyrosol from olive mill waste in vitro and in rats. Chem Biol Interact 2009; 180(3): 421-32.
8. Kamalakkannan N, Prince PS. Antihyperglycaemic and antioxidant effect of rutin, a polyphenolic flavonoid, in streptozotocin-induced diabetic wistar rats. Basic Clin Pharmacol Toxicol 2006; 98(1): 97-103.
9. Wojcik M, Burzynska-Pedziwiatr I, Wozniak LA. A review of natural and synthetic antioxidants important for health and longevity. Curr Med Chem 2010; 17(28): 3262-88.
10. Zhang J, Yuan K, Zhou WL, Zhou J, Yang P. Studies on the active components and antioxidant activities of the extracts of Mimosa pudica Linn. from southern China. Pharmacogn Mag 2011; 7(25): 35-9.
11. Littarru GP, Tiano L. Bioenergetic and antioxidant properties of coenzyme Q10: recent developments.

Mol Biotechnol 2007; 37(1): 31-7.
12. Somayajulu M, McCarthy S, Hung M, Sikorska M, Borowy-Borowski H, Pandey S. Role of mitochondria in neuronal cell death induced by oxidative stress; neuroprotection by Coenzyme Q10. Neurobiol Dis 2005; 18(3): 618-27.
13. Belanger MC, Mirault ME, Dewailly E, Berthiaume L, Julien P. Environmental contaminants and redox status of coenzyme Q10 and vitamin E in Inuit from Nunavik. Metabolism 2008; 57(7): 927-33.
14. Mabuchi H, Higashikata T, Kawashiri M, Katsuda S, Mizuno M, Nohara A, et al. Reduction of serum ubiquinol-10 and ubiquinone-10 levels by atorvastatin in hypercholesterolemic patients. J Atheroscler Thromb 2005; 12(2): 111-9.
15. Niklowitz P, Menke T, Andler W, Okun JG. Simultaneous analysis of coenzyme Q10 in plasma, erythrocytes and platelets: comparison of the antioxidant level in blood cells and their environment in healthy children and after oral supplementation in adults. Clin Chim Acta 2004; 342(1-2): 219-26.
16. Shekelle P, Morton S, Hardy ML. Effect of supplemental antioxidants vitamin C, vitamin E, and coenzyme Q10 for the prevention and treatment of cardiovascular disease. Evid Rep Technol Assess (Summ) 2003; (83): 1-3.
17. Fernandes NP, Lagishetty CV, Panda VS, Naik SR. An experimental evaluation of the antidiabetic and antilipidemic properties of a standardized Momordica charantia fruit extract. BMC Complement Altern Med 2007; 7: 29.
18. Haidara MA, Mikhailidis DP, Rateb MA, Ahmed ZA, Yassin HZ, Ibrahim IM, et al. Evaluation of the effect of oxidative stress and vitamin E supplementation on renal function in rats with streptozotocin-induced Type 1 diabetes. J Diabetes Complications 2009; 23(2): 130-6.
19. Kim YH, Moon YI, Kang YH, Kang JS. Effect of Coenzyme Q10 and green tea on plasma and liver lipids, platelet aggregation, TBARS production and erythrocyte Na leak in simvastatin treated hypercholesterolmic rats. Nutr Res Pract 2007; 1(4): 298-304.
20. Tavafi M, Ahmadvand H, Tamjidipoor A, Delfan B, Khalatbari AR. Satureja khozestanica essential oil ameliorates progression of diabetic nephropathy in uninephrectomized diabetic rats. Tissue Cell 2011; 43(1): 45-51.
21. Ahmadvand H, Tavafi M, Khosrowbeygi A. Amelioration of altered antioxidant enzymes activity and glomerulosclerosis by coenzyme Q10 in alloxan-induced diabetic rats. J Diabetes Complications 2012; 26(6): 476-82.
22. Ahmadvand H, Ani M, Moshtaghie AA. Changes in Biochemical Parameters Related to Lipid Metabolism Following Titanium Treatment in Rat. Iran J Pharmacol Ther 2010; 9(2): 69-71.
23. Friedewald WT, Levy RI, Fredrickson DS. Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. Clin Chem 1972; 18(6): 499-502.
24. Ikewuch CJ, Ikewuchi CC. Alteration of Plasma Lipid Profiles and Atherogenic Indices by Stachytarpheta jamaicensis L. (Vahl). Biokemistri 2009; 21(2): 71-7.
25. Bose KS, Agrawal BK. Effect of lycopene from tomatoes (cooked) on plasma antioxidant enzymes, lipid peroxidation rate and lipid profile in grade-I hypertension. Ann Nutr Metab 2007; 51(5): 477-81.
26. Kaliora AC, Dedoussis GV. Natural antioxidant compounds in risk factors for CVD. Pharmacol Res 2007; 56(2): 99-109.
27. Cicero AF, Derosa G, Miconi A, Laghi L, Nascetti S, Gaddi A. Treatment of massive hypertriglyceridemia resistant to PUFA and fibrates: a possible role for the coenzyme Q10? Biofactors 2005; 23(1): 7-14.
28. Gao L, Mao Q, Cao J, Wang Y, Zhou X, Fan L. Effects of coenzyme Q10 on vascular endothelial function in humans: a meta-analysis of randomized controlled trials. Atherosclerosis 2012; 221(2): 311-6.
29. Shojaei M, Djalali M, Khatami M, Siassi F, Eshraghian M. Effects of carnitine and coenzyme Q10 on lipid profile and serum levels of lipoprotein(a) in maintenance hemodialysis patients on statin therapy. Iran J Kidney Dis 2011; 5(2): 114-8.
30. Garjani A, Fathiazad F, Zakheri A, Akbari NA, Azarmie Y, Fakhrjoo A, et al. The effect of total extract of Securigera securidaca L. seeds on serum lipid profiles, antioxidant status, and vascular function in hypercholesterolemic rats. J Ethnopharmacol 2009; 126(3): 525-32.
31. Jayasooriya AP, Sakono M, Yukizaki C, Kawano M, Yamamoto K, Fukuda N. Effects of Momordica charantia powder on serum glucose levels and various lipid parameters in rats fed with cholesterol-free and cholesterol-enriched diets. J Ethnopharmacol 2000; 72(1-2): 331-6.
32. Schmelzer C, Kubo H, Mori M, Sawashita J, Kitano M, Hosoe K, et al. Supplementation with the reduced form of Coenzyme Q10 decelerates phenotypic characteristics of senescence and induces a peroxisome proliferator-activated receptor-alpha gene expression signature in SAMP1 mice. Mol Nutr Food Res 2010; 54(6): 805-15.
33. Harris CS, Beaulieu LP, Fraser MH, McIntyre KL, Owen PL, Martineau LC, et al. Inhibition of advanced glycation end product formation by medicinal plant extracts correlates with phenolic metabolites and antioxidant activity. Planta Med 2011; 77(2): 196-204.

34. Murat BH, Atmaca M, Deniz OB, Ozekinci S, Tasdemir E, Ketani A. Protective effects of coumarin and coumarin derivatives against carbon tetrachloride-induced acute hepatotoxicity in rats. Exp Toxicol Pathol 2011; 63(4): 325-30.
35. Akande IS, Ebuehi OA, Samuel TA, Onubogu IC, Esin H. Effects of herbal remedies (Agyanom mixture, Bolex bitters and Remedia mixture) on hepatic and renal functions in male rats. Nig Q J Hosp Med 2010; 20(2): 70-6.
36. Murawska-Cialowicz E, Jethon Z, Magdalan J, Januszewska L, Podhorska-Okolow M, Zawadzki M, et al. Effects of melatonin on lipid peroxidation and antioxidative enzyme activities in the liver, kidneys and brain of rats administered with benzo(a) pyrene. Exp Toxicol Pathol 2011; 63(1-2): 97-103.
37. Carbone M, Campagnolo L, Angelico M, Tisone G, Almerighi C, Telesca C, et al. Leptin attenuates ischemia-reperfusion injury in the rat liver. Transpl Int 2012; 25(12): 1282-8.
38. Mabuchi H, Nohara A, Kobayashi J, Kawashiri MA, Katsuda S, Inazu A, et al. Effects of CoQ10 supplementation on plasma lipoprotein lipid, CoQ10 and liver and muscle enzyme levels in hypercholesterolemic patients treated with atorvastatin: a randomized double-blind study. Atherosclerosis 2007; 195(2): e182-e189.
39. Ali SA, Faddah L, Abdel-Baky A, Bayoumi A. Protective effect of L-carnitine and coenzyme Q10 on CCl(4)-induced liver injury in rats. Sci Pharm 2010; 78(4): 881-96.
40. Amimoto T, Matsura T, Koyama SY, Nakanishi T, Yamada K, Kajiyama G. Acetaminophen-induced hepatic injury in mice: the role of lipid peroxidation and effects of pretreatment with coenzyme Q10 and alpha-tocopherol. Free Radic Biol Med 1995; 19(2): 169-76.
41. Song HS, Kim HR, Park TW, Cho BJ, Choi MY, Kim CJ, et al. Antioxidant Effect of CoQ(10) on N-nitrosodiethylamine-induced Oxidative Stress in Mice. Korean J Physiol Pharmacol 2009; 13(4): 321-6.
42. Matough FA, Budin SB, Hamid ZA, Alwahaibi N, Mohamed J. The role of oxidative stress and antioxidants in diabetic complications. Sultan Qaboos Univ Med J 2012; 12(1): 5-18.

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