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Effect of Curcumin on Metabolism of Lipids in Streptozotocin induced Diabetic and normal Rats

Mahmood Najafian

Department of Biology, Jahrom Branch, Islamic Azad University, Jahrom, Iran.

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ABSTRACT

Background: Diabetes mellitus is one of the most common endocrine disorders characterized by hyperglycemia, hypercholesterolemia, and hypertriglyceridemia. A prudent strategy for preventing cardiovascular complications in patients with diabetes is treating dyslipidemia with lipid-lowering agents. ***Objective:*** We aimed to examinthe effect of curcumin on metabolism of lipids in diabetic and normal rats. ***Method:*** For this purpose in this research, doses of curcumin (0, 10, 20, 40 and 80 mg/kg-b.w) were given to diabetic and normal rats and blood sample of them were analyzed. ***Result:*** In diabetic group as compared to normal control group, the blood cholesterol, triglycerides,very low density lipoprotein-cholesterol(VLDL-C) and low density lipoprotein-cholesterol(LDL-C) levels, the water intake and urine volume were significantly increased while high density lipoprotein-cholesterol(HDL-C) was significantly decreased. In both groups diabetic and normal groups treated with curcumin; the levels of cholesterol, triglycerides, VLDL-C, and LDL-Cdecreased however only the level of HDL-C increased in diabetic groups. In diabetic groups treated with curcumin, the levels of water intake and urine volume decreased but in normal groups these changes were not significant. **Conclusion:** It may be concluded that curcumin as a lipid-lowering agents has beneficial effects in the treatment of diabetes and related disorders such as dyslipidemia.

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INTRODUCTION

Diabetes mellitus is one of the most challenging health problems in the 21st century. It is estimated that the diabetes affect nearly 10% of the population in the world[1- 3].Hyperglycemia, hypercholesterolemia and hypertriglyceridemia are the most common disorders of diabetes, resulting from defects in insulin secretion or reduced sensitivity of thetissue to insulin (insulin resistance) and/or combination of both[4-6].Patients with type1diabetes also present with lipiddisorders. Dyslipidemia plays an important role in the initiation and acceleration of the atherosclerotic process in individuals with diabetes. Hence, a prudent strategy for preventing cardiovascular complications in patients with diabetes would be treating dyslipidemia with lipid-lowering agents [7-9].There is a growing interest in herbal remedies because of their effectiveness and minimal side effects in clinical experience. Herbal drugs or their extracts are prescribed widely, even when their biological active compounds are unknown. The World Health Organization (WHO) also approves the use of plant drugs for different diseases, including diabetes mellitus. The potential role of the medicinal plants as anti-diabeticagents has been reviewed byseveral authors, supported by the ethnobotanicalsurveys and traditional medicines ofdifferent cultures [10-12].Polyphenolic compounds arewidely distributed in plants and fruits and are present innormal diets. These compounds have been shown to possessbeneficial effects in diabetes, cardiovascular diseases,atherosclerosis, allergy, inflammation, cancer, asthma andosteoporosis[13-16].Curcumin[1,7-bis(4-hydroxy-3-methoxyphenyl)-1,6-heptadiene-3,5-dione]a yellow colourpolyphenolic pigment ,was first isolated from the plant *Curcuma longa*aroundtwo centuries ago, and its structure as diferuloylmethane was determined in 1910. Curcumin has two isomers, the planar enolform(**fig-1**) and nonplanarketo form. The planar enol form is more stable than the nonplanardiketoform[17-19].

Corresponding Author: Mahmood Najafian, Department of Biology, Jahrom Branch, Islamic Azad University, Jahrom, Iran.
Tel: 00989171901742 E-mail: d.najafian@jia.ac.ir

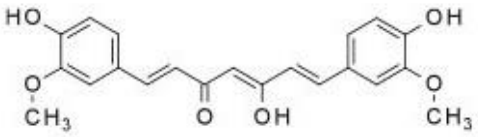

Fig. 1: The planar enol form of curcumin[17].

Turmeric (*Curcuma longa*) is extensively used as a spice, food preservative and colouring material. It has been used in traditional medicine as a household remedy for various diseases. It has been shown that curcumin has a wide spectrum of biological actions. These include its antiinflammatory, antioxidant, anticarcinogenic, antimutagenic, anticoagulant, antifertility, ant diabetes, antibacterial, antifungal, antiprotozoal, antiviral, antifibrotic, antivenom, antiulcer, hypotensive and hypocholesteremicactivities [20-22]. Based on this information, present study wasdesigned to investigate the association between diabetes and lipid levels and the effect of curcumin on lipids metabolism.

MATERIAL AND METHODS

Chemicals:

Curcumin[1,7-bis(4-hydroxy-3-methoxyphenyl)-1,6-heptadiene-3,5-dione] provided from Sigma Chemicals Company (St Louis, MO, USA) and Streptozotoc in provided from Pharmacia & Upjohn (Kalamazoo, MI, USA).

Animals:

Male adult Wistar rats (2.5 months) weighting 190 ± 10g were used in these experiments. The animals were housed as six rats per cage at room temperature (22–24 °C) with lights on from 08:00 to 20:00 h. They were fed with standard rodent diet. Food and water were *ad libitum*.

Diabetes induction:

Streptozotocin-induced hyperglycemia has been described as a useful experimentalmodel to study the activity of antidiabetic agents.Streptozotocin selectively destroys the pancreatic insulin secreting β cells[12].The animals were allowed to acclimatize 2 days before experiment in new environment. For two days prior to the experiment, diabetic state was induced by a single dose intraperitoneal injection of streptozotocin (STZ) (70 mg/kg body weight, dissolved in a citrate buffer 0.1 M, pH 4.5)[23]. The blood glucose levels were then measured after 2 days.

Treatment with curcumin:

Rats were divided into two classes of Normal rats (N) and diabetic rats(D) and each class divided into five groups (n = 6), as below: (I) Normal control group (NO): rats in this group received grape seed oil(solvent of curcumin) (O) orally for 30 days through a gastric cannula in a single dose (0.5 ml) at 8:30 pm. (II) Diabetic control group(DO): rats in this group received grape seed oil (O) as group I. (III) Normal groups receiving curcumin(NC): rats in these groups received curcumin at 10, 20, 40 and 80 mg/kg body weight (respectively, NC10, NC20, NC40, NC80) dissolved in grape seed oil, orally for 30 days through a gastric cannula in a single dose (0.5 ml) at 8:30 pm. (IV) Diabetic groups receiving curcumin (DC): rats in these groups received curcumin at 10, 20, 40, 80 mg/kg body weight (DC10, DC20, DC40, and DC80 respectively) as above.

Measured parameters:

The body weight of rats was measured in the first day of experiment. Ingestion of food and water and urine volume for 24h was measured every morning at 9:00 am with metabolic cage.Blood glucose levels were measured in blood samples extracted from the tail of the animalwith aglucometer (One Touch Profile, Life Scan) two days after injection of STZ.Body weight of the rats was measured after day30, and the animals were then sacrificed underlight ether anesthesia. Blood samples were collectedfrom rats hearts and were placed on ice,then` centrifuged at 3000g for five minutes. Serum was stored at -20°Cfor lessthan 1 week beforesubsequent analyses.Blood glucose, cholesterol,triacylglycerol, high-density lipoproteins(HDL) and low-density lipoproteins (LDL)concentrations weremeasured with standard biochemical kits.Estimates of Very Low Density Lipoprotein(VLDL) were calculated from the formula(VLDL-C = Triacylglycerol /5)[8].

Statistical analysis:

The data were analyzed by one-sample Kolmogrov-Smirnov test and then by the Levene's test. One way analysis of variance (ANOVA) followed by Tukey'spost hoctest for multiple comparisons were used to compare difference between experimental groups. The criterion for statistical significant was $P<0.0$

Results:

Blood glucose:

To make sure that diabetes state is happened, the blood glucose levels were measured 2 daysafteradministration ofSTZ.Administration of STZ resulted in high levels(408.4±39.8mg/dl) of blood glucose in thetreated groups in compare to the normal controlgroup in which blood glucose levels were in the range of106.4±11.2mg/dl.In the end of experimental period, the blood glucose levels were measured and the results are shown in fig. 2. In diabetic control group (DO) as compared to normal control group (NO) the blood glucose level significantly increased. In diabetic and normal groups treated with curcumin, the blood gluse levels reduced. For example this reduction in dose 40 mg/kg-B.W, in diabetic and normal rats were 34.3% and 35.1% respectively.

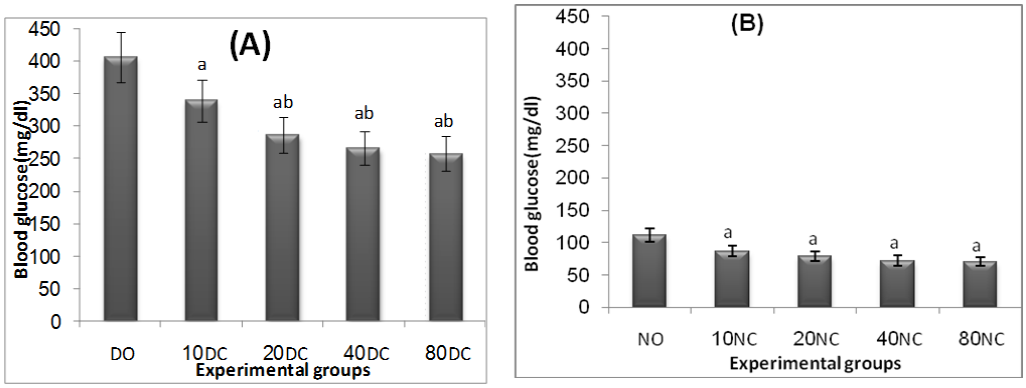

Fig. 2: Blood glucose levels in diabetic **(**D**)** and normal (N) rats treated with different doses of curcumin(10, 20, 40 and 80 mg/kg-B.W). (A): Blood glucose level in diabetic rats; a: significantly different from DO ($P<0.05$), b: significantly different from DC10 ($P<0.05$). (B): Blood glucose level in normal rats; a: significantly different from NO ($P<0.05$).

Lipids:

Cholesterol:

In diabetic control group(DO)as compared to normal control group(NO) the blood cholesterol level significantly increased(40.4%). In diabetic and normal groups treated with curcumin, the blood cholesterol levels reduced. For examplethis reduction indose 40mg/kg-B.W, in diabetic and normal rats were 35.4% and 22.1% respectively(As shown in fig-3).

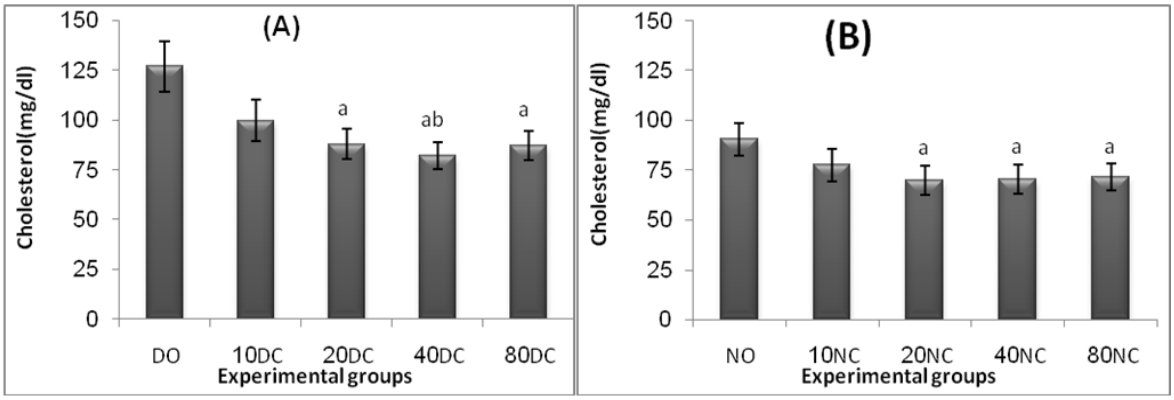

Fig. 3: Serum cholesterol levels in diabetic **(**D**)** and normal (N) rats treated with different doses of curcumin(10, 20, 40 and 80 mg/kg-B.W). (A): Serum cholesterol level in diabetic rats; a: significantly different from DO ($P<0.05$), b: significantly different from DC10 ($P<0.05$). (B): Serum cholesterol level in normal rats; a: significantly different from NO ($P<0.05$).

LDL:

The levels of LDLin rats with diabetes were found to be elevated (As shown in fig-4). In diabetic control group(DO) as compared to normal control group(NO), the LDL level was significantly increased(65.4%). In diabeticand normal groups with treated curcumin, the blood LDL levels were reduced.For example this reduction in dose 40 mg/kg-B.W, in diabetic and normal rats were 45.1% and 26.2% respectively.

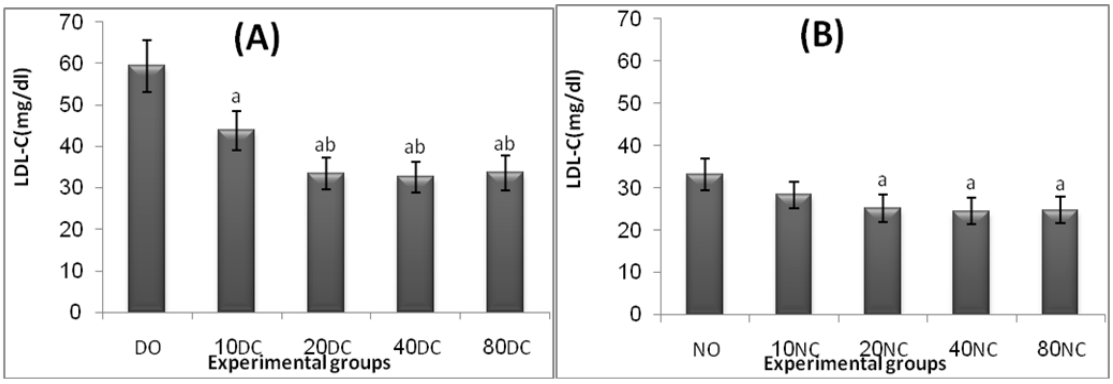

Fig. 4: Serum LDL-C levels in diabetic **(**D**)** and normal (N) rats treated with different doses of curcumin(10, 20, 40 and 80 mg/kg-B.W). (A): Serum LDL-C level in diabetic rats; a: significantly different from DO(P<0.05), b: significantly different from DC10(P<0.05). (B): Serum LDL-C level in normal rats; a: significantly different from NO (P<0.05).

HDL:

In diabetes state, the level of HDL is less than normal state[23, 24].In diabetic control group (DO) in comparison with normal control group(NO),HDL was significantly decreased(29.4±3.6 *v* 45.4±4.8(P<0.05). In diabetic groups thattreated with curcumin,HDL were found to be elevated. For example this enlargment in dose 40 mg/kg-B.W was49.8%. However changes were not significant in normal groups (fig-5).

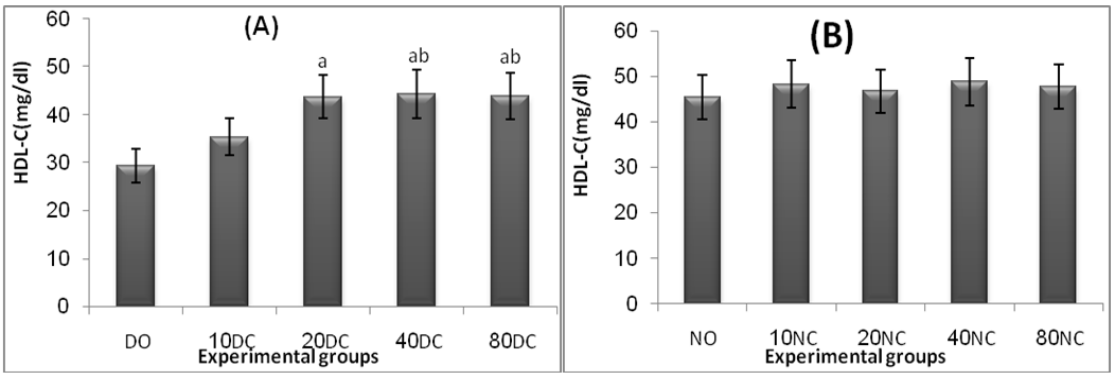

Fig. 5: Serum HDL-C levels in diabetic **(**D**)** and normal (N) rats treated with different doses of curcumin(10, 20, 40 and 80 mg/kg-B.W). (A): Serum HDL-C level in diabetic rats; a: significantly different from DO(P<0.05), b: significantly different from DC10(P<0.05). (B): Serum HDL-C level in normal rats.

Triglycerides:

In diabetic control group(DO) as compared to normal control group(NO), the blood triglycerides level was significantly increased (133.3±13.9 *v* 82.3±8.2) (P<0.05). In diabetic and normal groups treated with curcumin, the blood triglycerides levels were reduced.For example this reduction in dose 40 mg/kg-B.W, in diabetic and normal rats were 78.3±8.5 *v* 133.3±13.9(P<0.05) and 62.3±6.9*v* 82.3±8.2(P<0.05) respectively(fig-6).

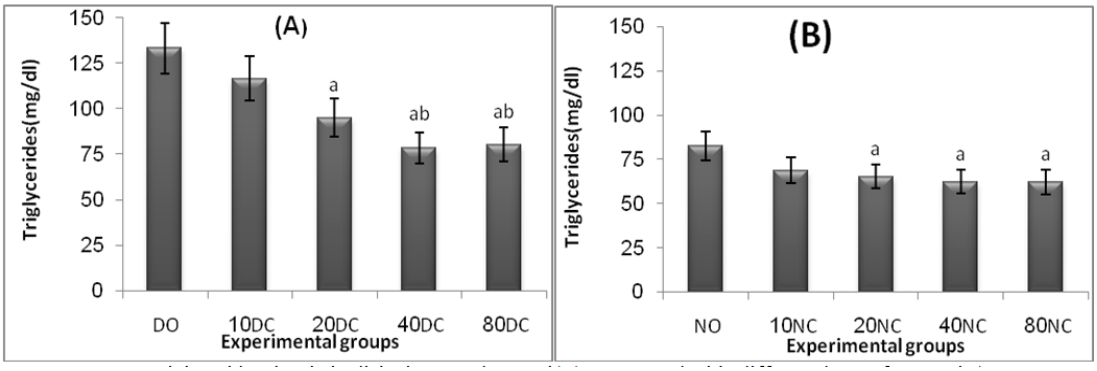

Fig. 6: Serum triglycerides levels in diabetic**(**D**)** and normal(N) rats treated with different doses of curcumin(10, 20, 40 and 80 mg/kg-B.W). (A): Serum triglycerides level in diabetic rats; a: significantly different from DO($P<0.05$), b: significantly different from DC10($P<0.05$). (B): Serum triglycerides level in normal rats; a: significantly different from NO($P<0.05$).

VLDL:

Following increasing triglycerids in rats with diabetes, VLDL were also increased. Level of VLDL was significantly increased(61.81%) in diabetic control group (DO) as compared to normal control group (NO). In diabetic groups and normal groups treated with curcuminVLDL levels were reduced.For example this reduction in dose 40 mg/kg-B.W, in diabetic and normal rats were 43.1% and 24.2% respectively(fig-7).

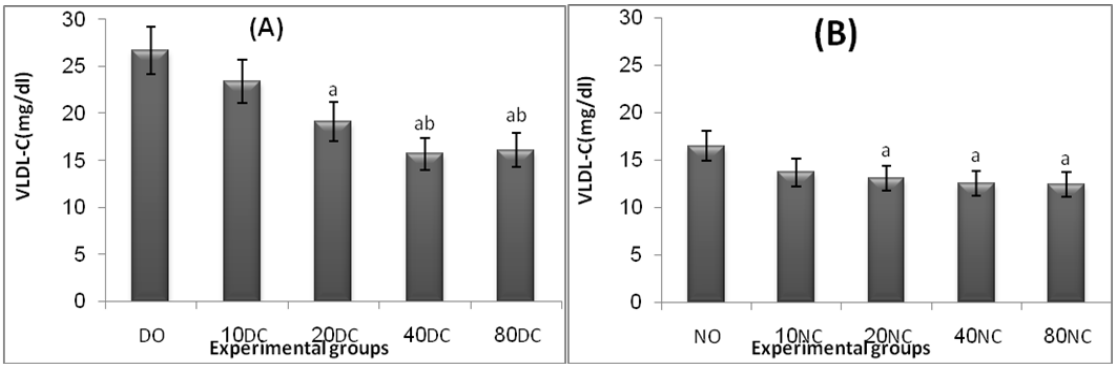

Fig. 7: Serum VLDL-C levels in diabetic **(**D**)** and normal (N) rats treated with different doses of curcumin (10, 20, 40 and 80 mg/kg-B.W). (A): Serum VLDL-C level in diabetic rats; a: significantly different from DO ($P<0.05$), b: significantly different from DC10 ($P<0.05$). (B): Serum VLDL-C level in normal rats; a: significantly different from NO($P<0.05$).

Food intake:

As shown in table 1, food intake was significantlyincreased in the diabetic control group (DO) compared withthe normal control group (NO) (34.1 ± 2.8g*v*22.2 ± 2.3g, $P<0.01$). Upon administration of curcumin, food intake was reduced in all groups receiving the treatment. However the three doses of C20, C40 and C80had almost the same effect in diabetic and normal groups.

Table 1: Effect of curcumin treatment on food intake and body weightinin diabetic and normal ra.

	Food intake(g/day)		Body weight(g)	
Groups	Diabetic rats	Normal rats	Diabetic rats	Normal rats
Control	34.1±2.8	22.2±2.3	201.2±14.1	249.2±16.8
Dose 10	26.9±2.9[a]	17.8±1.9	183.8±13.6	220.4±18.5
Dose 20	21.5±2.4[ab]	14.8±1.8[a]	172.4±14.4[a]	195.5±13.2[a]
Dose 40	21.8±2.6[ab]	15.1±1.9[a]	168.5±15.3[a]	192.4±13.8[a]
Dose 80	21.6±2.5[ab]	14.6±1.7[a]	163.2±15.8[a]	189.6±15.2[a]

Data are expressed as mean ±SD for six rats. In each case (a) is significantly different from control groups and (b) is significantly different from Dose 10 mg/kg-b.w, using one way ANOVA with Tukey's post hoc test for multiple comparisons were used to compare difference between experimental groups. The criterion for statistical significant was $P<0.05$.

Bodyweight:

Results of body weight measured at day 30 are shown intable 1. As a known consequence of type 1 diabetes, the body weight in the diabetic control groupwas significantly reduced in comparison with the normal control group (201.2 ± 14.1g *v*249.2 ± 16.8g, P<0.01). In diabetic and normal groups treated with curcumin, body weight were reduced, However the three doses of C20, C40 and C80 had almostthe same effect in diabetic and normal groups.

Water intake:

Water intake was observed to significantly increase in the diabetic control group (DO) compared with normal control group(NO)(110.3 ± 9.4ml *v* 37.8 ± 3.9ml, P<0.001) (fig-8). Curcumin administration nearly in a dose-dependent manner decreased the amount of water intakein diabetic groups. Howevercurcumin had no significant effect on the water intake in the normal groups.

Urine volume:

In diabetesstate, following increasing in water intake, the urine volume increase. In diabetic control group(DO), urine volume was significantly increased compare to the normal control group(NO) (92.7 ± 9.8ml *v*18.2 ± 1.7ml, P<0.001) (fig-8).Administration of curcuminin diabetic reduced urine volume nearly in a dose-dependent manner. However there was no significant difference between DC40 and DC80.Crcumin had no significant effect on the urine volume in the normal groups.

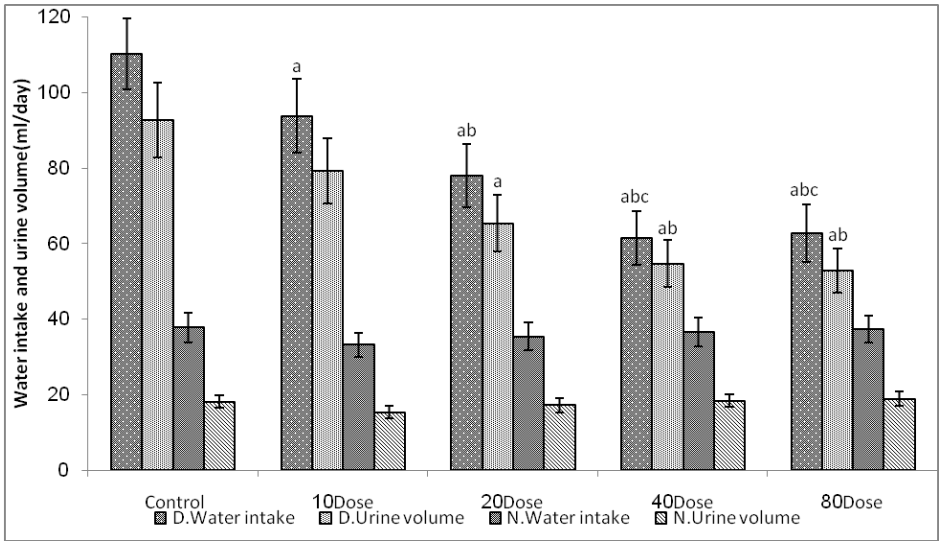

Fig. 8: Water intake and urine volume in diabetic and normal rats treatment with curcumin. In each part (set cloumns, control and doses 10, 20, 40 and 80mg/kg-B.W) the first columns are water intake in diabetic rats, the second columns are urine volume in diabetic rats, the third columns are water intake in normal rats, the fourth columns are urine volume in normal rats. a: significantly different from DO(P<0.05), b: significantly different from DC10(P<0.05), C: significantly different from DC20(P<0.05).

Discussion:

Diabetes mellitus is one of the most widespread diseases of world. According to the International Diabetes Federation(IDF), the global prevalence of diabetes is predicted to grow from 6.6% in 2010 to 7.8% in 2030 and it is fourth or fifth leading cause of death in the world[23].Diabetes is one of the most common endocrine disorders and is characterized by hyperglycemia, hypercholesterolemia, and hypertriglyceridemia[4-6].Dyslipidemia is observed as a consequence of both type 1and type 2 diabetes, and could contribute to an increased incidence of cardiovascular diseases if untreated[7, 9].Atherosclerosis is also a major cause of cardiovascular disease caused by high cholesterol.The World Health Organization (WHO) reported that Cardiovascular disease (CVD) is one of the main causes of mortality globally[25, 26].Hyperlipidemia is induced bysecondary effect of diabetes, therefore, the agent having some antioxidant and anti-diabetes effect also showed favorable effect to hyperlipidemia. Plants and phytochemicals have been shown to exert CVD protective effects. These effects could be due to plant polyphenolic compounds such as curcumin. It is yellow pigment of curcuma, exhibitsanticarcinogenic, antioxidative and hypocholesterolemicactivities[27-29].The aim of this research was to study the effect of curcuminon lipids metabolism diabetic and normal rats. Results of this study showed that curcumincause reduction of cholesterol and LDL level in diabetic and normal rats. These effects may be based on this fact that curcumin cause increase excretionbile acidvia increasing the amount mRNA of

cholesterol 7α-hydroxylase, a liver-specific enzyme that catalyzes the rate limiting step in the biosynthesis of bile acid from cholesterol[25 , 30].Curcumin reduced the level mRNA of HMG-CoA reductase, a liver-specific enzyme that catalyzes the rate limiting step in the biosynthesis of cholesterol[27].Curcumincause reduce the level of triglycerides and VLDL in diabetic and normal rats. These effects of curcuminmaybe based on thisactuality that curcumin causeincreasethe activity offatty acid β-oxidation, hepatic lipase and lipoprotein lipase but decreasefatty acid synthase activity[27, 31,].Curcumin as an antiatherosclerosisagent in rats with diabetes cause increase the level of HDL via increasing the serum level of apolipoprotein A and the level of plasma lecithin cholesterol acyltransferase(LCAT) activity[27, 32].Weight loss and decrease of food intake were also observed in diabetic and normal rats.It may be due to curcumin as a polyphenolic compound whichcould cause the reduction of calorie intake by inhibition of alpha amylase and decrease of carbohydrates digestion[23].It seems that curcumin is an effective agent for the treatment and even the prevention of obesity. Water intake and urine volume in diabeticrats is also showing a remarkable decrease nearly in a dose-dependent manner. It is in accordance with its effect on blood glucose, and interesting in terms of the therapeutically benefits that it could have on these discomforting consequences of diabetes in patients. Curcumin had no significantly effect on the water intake and urine volume in the normal groups.Between four doses, 40mg/kg body weight of curcumin had the best results of improving the lipids metabolism in diabetic and normal rats. It may be concluded thatcurcuminas a lipid-lowering agentshas beneficial effects in the treatment of diabetes and related disorders such as dyslipidemia.

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REFERENCES

[1] Prasad, S., A. Kulshreshtha, T.N. Qureshi, 2009. Antidiabetic activity of some herbal plants in streptozotocin induced diabetic albino rats, Pak. J. Nutr, 8: 551-557.
[2] Shah, H., S. Bodhankar, R. Bhonde, V. Mohan, 2006. Combinative therapeutic approach for better blood sugar levelcontrol in alloxan diabetic mice, Int. J. Diabetes & Metab, 14: 104-105.
[3] Sicree, B.R., J. Shaw, P. Zimmet, 2010. The Global Burden Diabetes and Impaired Glucose Tolerance, Diabetes, 27: 1-105.
[4] Kianbakht, S., R. Hajiaghaee, F.H. Dabaghian, H.F. Huseini, 2012. Anti-hyperglycemic and anti-hypercholesterolemic effects of Aloe vera leaf gel in hyperlipidemic type 2 diabetic patients: a randomized double-blind placebocontrolled clinical trial, Planta Med, 78: 311-316.
[5] Mahesh, T., M.M.S. Balasubashini, V. Menon, 2004. Photo-Irradiated Curcumin Supplementation in Streptozotocin-Induced Diabetic Rats: Effect on Lipid Peroxidation: Supplementation en curcumine photo-irradiee chez le rat rendu diabetiquepar la streptozotocine: effetssur la peroxydationlipidique, Therapie, 59: 639-644.
[6] Padhye, S., D. Chavan, S. Pandey, J. Deshpande, K.V. Swamy, F.H. Sarkar, 2010. Perspectives on chemopreventiveand therapeutic potential of curcumin analogs in medicinal chemistry, Mini. Rev. Med. Chem., 10: 372-387.
[7] Aparna, G., F. Gregory, G. David, 2006. Lipid management reduces cardiovascular complications in individuals with diabetes and prediabetes, Prev. cardiol, 9: 102-109.
[8] Najafian, M., M.Z. Jahromi, M.J. Nowroznejhad, P. Khajeaian, M.M. Kargar, M. Sadeghi, 2011. Phloridzin reduces blood glucose levels and improves lipids metabolism in streptozotocin-induced diabetic rats, Mol. Biol. Rep., 39: 1-8
[9] Verges, B., 2009. Lipid disorders in type 1 diabetes, Diabetes Metab, 35: 353-360.
[10] Biesalski, H.K., 2004. Diabetes preventive components in the Mediterranean diet, Eur. J. Nutr, 43: 26-30.
[11] Najafian, M., A. Ebrahim-Habibi, P. Yaghmaei, K. Parivar, B. Larijani, 2011. Citral as a potential antihyperlipidemic medicine in diabetes: a study on streptozotocin-induced diabetic rats, JDMD, 10: 1-8.
[12] Patil, A., S. Nirmal, S. Pattan, V. Tambe, M. Tare, 2012. Antidiabetic effect of polyherbal combinations in STZ induced diabetes involve inhibition of α-amylase and α-glucosidase with amelioration of lipid profile, Phytopharmacology, 2: 46-57.
[13] Linseisen, J., S. Rohrmann, A.B. Miller, H.B. Bueno, F.L. Buchner, P. Vineis, 2007. Fruit and vegetable consumption and lung cancer risk: updated information from the European Prospective Investigation into Cancer and Nutrition (EPIC), Int. j. cancer, 121: 1103-1114.
[14] Najafian, M., A. Ebrahim-Habibi, N. Hezareh, P. Yaghmaei, K. Parivar, B. Larijani, 2011. Trans-chalcone: a novel small molecule inhibitor of mammalian alpha-amylase, Mol. Biol. Rep., 38: 1617-1620.

[15] Russo, G.L., 2007. Ins and outs of dietary phytochemicals in cancer chemoprevention, Biochem. Pharmacol, 74: 533-544.
[16] Woods, R.K., E.H. Walters, J.M. Raven, R. Wolfe, P.D. Ireland, F.C. Thien, 2003. Food and nutrient intakes and asthma risk in young adults, Am. J. Clin. Nutr, 78: 414-421.
[17] Aggarwal, B.B., C. Sundaram, N. Malani, H. Ichikawa, 2007. Curcumin: the Indian solid gold,Adv. Exp. Med. Biol, 595: 1-75.
[18] Kolev, T.M., E.A. Velcheva, B.A. Stamboliyska, Spitller, 2005. DFT and experimental studies of the structure and vibrational spectra of curcumin, Int. J. Quantum Chem, 102: 1069-1079.
[19] Yu, W.G., G. Xu, G.J. Ren, X. Xu, H.Q. Yuan, X.L. Qi, 2011. Preventive action of curcumin in experimental acute pancreatitis in mouse, Indian J. Med. Res., 134: 717.
[20] Chattopadhyay, I., K. Biswas, U. Bandyopadhyay, R.K. Banerjee, 2004. Turmeric and curcumin: Biological actions and medicinal applications, Curr. Sci. India, 87: 44-53.
[21] Hatcher, H., R. Planalp, J. Cho, F.M. Torti, S.V. Torti, 2008. Curcumin: from ancient medicine to current clinical trials, Cell Mol. Life Sci., 65: 1631-1652.
[22] Maheshwari, R.K., A.K. Singh, J. Gaddipati, 2006. Srimal.,Multiple biological activities of curcumin: a short review, Life sci., 78: 2081-2087.
[23] Najafian, M., A. Ebrahim-Habibi, P. Yaghmaei, K. Parivar, B. Larijani, 2010. Core structure of flavonoids precursor as an antihyperglycemic and antihyperlipidemic agent: an in vivo study in rats, ActaBiochi. Pol., 57: 553-560.
[24] Arafa, H.M., 2005. Curcumin attenuates diet-induced hypercholesterolemia in rats, Med. Sci. Monit., 11: 228-234.
[25] Kim, M., Y. Kim, 2010. Hypocholesterolemic effects of curcumin via up-regulation of cholesterol 7a-hydroxylase in rats fed a high fat diet, Nutr. Res. Pract., 4: 191-195.
[26] Shin, S.K., T.Y. Ha, R.A. McGregor, M.S. Choi, 2011. Long-term curcumin administration protects againstatherosclerosis via hepatic regulation of lipoprotein cholesterol metabolism, Mol. Nutr. food Res., 55: 1829-1840.
[27] Jang, E.M., M.S. Choi, U.J. Jung, M.J. Kim, H.J. Kim, S.M. Jeon, 2008. Beneficial effects of curcumin on hyperlipidemia and insulin resistance in high-fat-fed hamsters, Metabolism, 57: 1576-1583.
[28] Peschel, D., R. Koerting, N. Nass, 2007. Curcumin induces changes in expression of genes involved in cholesterol homeostasis, J. Nutr.Bioch, 18: 113-119.
[29] Saxena, A., N.K. Vikram, 2004. Role of selected Indian plants in management of type 2 diabetes: a review, J. Altern. Complement. Med, 10: 369-378.
[30] Akram, M., S. Uddin, A. Ahmed, K. Usmanghani, A. Hanan, E. Mohiuddin, 2010. Curcumalonga and curcumin: a review article, Rom. J. Biol. Plant Biol., 55: 65-70.
[31] Asai, A., T. Miyazawa, 2001. Dietary curcuminoids prevent high-fat diet–induced lipid accumulation in rat liver and epididymal adipose tissue, J. Nutr, 131: 2932-2935.
[32] Wang, S., B. Chen, C. Sun, 2000. Regulation effect of curcumin on blood lipids and antioxidation in hyperlipidemia rats, Europe PMC., 29: 240-242.