Effect of Curcumin Supplementation on Fructosamine Level, Blood Lipids, Lipid Peroxidation and Hepatic Enzymes in Type 2 Diabetics

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Abstract

Objective: DM is a major medical problem in developing countries such as Iran. Blood sugar and lipids levels increase in diabetics exacerbates the onset of diabetes mellitus (DM) late complications. Researchers have focused on herbal medicines improve sugar and lipid levels against side decreasing effects and possible inefficacy of chemical drugs. This study has assessed the effect of curcumin on fructosamine, lipids profile and lipid peroxidation in patients with type 2 DM.

Materials and Methods: Sixty type II diabetics (40-60 years old) with history of diabetes above 10 years who had referred to diabetes center of Shahid Sadoughi medical university, were randomly divided in to two groups of case and control. The case group daily received two capsules of 250mg curcumin for 6 weeks and the control group took placebo over the trialperiod. Blood samples were collected in both groups at the beginning and end of the experiment .The cholesterol, Triglyceride, Low and high density lipoprotein were measured by auto analyzer (Auto lab). The rest of serums were frozen for measuring fructosamine and malondialdehyde by nitroblue tetrazolium and thiobarbituric acid tests in same condition. These tests were repeated after six weeks. Statistic alanalysis was done by SPSS 15, paired and independent T-tests.

Results Finally, 48 participants completed the study. After 6 weeks, the case group showed significant decrease in fructosamine, cholesterol, triglyceride, LDL-cholesterol, malondialdehyde and increase in HDL-cholesterol (P=0.001). At the end of study significant differences were observed between the meansfructosamine (P=0.023) and HDL-cholesterol (P=0.013) in two groups of case and control. No significant changes were observed for mean cholesterol, triglyceride, LDL-cholesterol and malondialdehyde between two groups.

Conclusion: Consumption of curcumin capsules improved the lipid profile and decreased the fructosamine and lipid peroxidation

Keywords: Curcumin, type 2 diabetes, Fructosamine, Lipid profile, Lipid peroxidation

Introduction

Type 2 DM (T2DM) is a metabolic disorder that is characterized by high blood glucose and insulin resistance and is associated with diseases of obesity including hypertension/ dyslipidemia and fatty liver disease (1). Long-term complications of

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increase in blood glucose including diabetic retinopathy and blindness, kidney failure requires to dialysis and impaired circulation of limbs leads to amputations. The causes of type 2 diabetes are complex but relate to over nutrition and the failure of tissues to store excess sugars and fatty acids. Insulin signaling via the insulin receptor induces phosphorylation of insulin-receptor substrate 1 (IRS-1) leading to export of the high affinity glucose transporter (Glut 4) molecules to the outer membrane of insulin responsive tissues, including muscle cells and adipose tissue. This leads to increase absorption of glucose from blood into these tissues. Insulin signaling also increases absorption of blood lipids, and their conversion to triglycerides (2).

The impacts of T2DM on global health care and economy are enormous (3). According to the World Health Organization, there are; 311 million people worldwide who live with T2DM. This number continues to rise, especially in the newly developing and poorer countries in Asia and elsewhere. The focus now is to identify new effective therapeutic agents, with relatively low cost and low toxicity. Natural products have received considerable attention for the management of diabetes and its complications (4-7)

Curcumin is found the principal curcuminoid in turmeric (Curcuma longa Linn.), a popular spice in Asian cuisine. It is widely consumed and generally believed to be beneficial for human health (8). Curcumin extract from rhizomes of turmeric has been shown to contain antiinflammation and antidiabetic properties. Curcumin interacts directly withcyclooxygenase-2 (COX-2), DNA polymerase, lipoxygenase (LOX), glycogen synthase kinase- 3b (GSK-3b), and cytokines (TNF-a) (9-16). Moreover, no dose-limiting toxicities were observed in healthy human volunteers consuming a single dose of curcumin ranging from 500 to 12000 mg/day. Few developed adverse reactions such as diarrhea, headache, skin rashes and yellow stool. (17). However ,the mechanism underlying the hypoglycemic effect of curcumin is unclear .This study aimed to determine the effectiveness of curcumin extracton fructosamine, blood lipid ,lipid peroxidation and hepatic enzymes in type2 diabetics

Materials and Methods

Study design and participants

This randomized, double-blinded, placebo controlled trial was conducted at diabetic research center of Yazd University of Medical Sciences in Iran, 2013. The research was approved by Medical Ethical Committee of the Yazd University with the identification code of 10206. Sixty patients were selected to participate in this study by inclusion and exclusion .Inclusion criteria for study were: 1) age range between 40-60 years 2) type 2diabetic individuals suffering over 10 years 3) Fasting blood glucose in range of 130-200 mg/dl 4) 2hours blood glucose between 160-250 mg/dl 5) using oral hypoglycemic agents containing Glyburide, Acarbose, Metformin and, which didn't change in the type and dose of drugs during the study 6) Having routine diet and physical activity levels until the end of the study. Exclusion criteria were: 1) patients that have Hepatic cirrhosis, Chronic Kidney Disease, active Proliferative Diabetic Retinopathy, Congestive Heart Failure, Myocardial Infarction in recent 6 month 2) pregnant and lactating women .The study participants were informed about the research status and only those who approved and verified the consent form were included .The diabetics were randomly divided into two groups; case and control (n=30 in each group). Case group received two curcumin capsules with curcuminoid content of 250 mg and control group daily received placebo for 6weeks.

Preparation of curcuminoids capsules

The turmeric powder was bought from the reliable local markets of Yazd. It was evaporated with ethanol at low pressure to obtain ethanol extract in the form of semisolid containing oleoresin and curcuminoids. The

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oleoresin was removed to yield curcuminoid extract (curcuminoids total content between 75 and 85%). The peak of curcumin: demethoxy curcumin and bisdemethoxy curcuminin the extract was determined by high performance thin-layer chromatography (HPTLC) of the extract (calculated for 250 mg of curcuminoids) was filled into capsules under good manufacturing procedures standard. Demographic information including weight, body mass index (BMI) were measured at the beginning and end of the study. At the beginning of the study and after 6 weeks, venous blood samples were taken from all patients and were centrifuged at 3500 rpm for20 min to obtain serum. Serum was kept in −80°C refrigerator until evaluation. Some biochemical factors including: Total cholesterol, Triglycerides, HDL, LDL, SGPT, SGOT were assessed by method of calorimetric enzymatic and with using commercial kits (Pars Azmoon, Iran), Fructosamine (using Diazyme kit, USA) and Malondialdehyde (MDA) levelsi.e. end product of lipid peroxidation, were measured by thiobarbituric acid reactive substances (TBARS) Method (18). Data are expressed by SPSS as mean ± SEM. we used Paired T-test method for assessment blood parameter from before and after consumption of curcumin and placebo capsules. On the other handdata analysis between two groups was method of independent T-test. $P<0.05$ was considered as statistically significant difference.

Results

50 percent of participants were male and 50 percent were female. The mean the patient's age was 54 ±5 and the mean body mass index (BMI) was 28 ± 5 kg/m^2. Table 1 and 2 illustrate the comparison between serum fructosamine, lipids, lipoproteins, malondialdehyde and hepatic enzymes in both the case and control groups, before and after the intervention.In the beginning of the study, there were not remarkable differences in means factors, as you noticed in blood between the case and control groups (Table 1 and 2). After 6 weeks consumption of curcumin capsules we observed significant increase in blood HDL level (P=0.001) and remarkable decrease in blood fructosamine, cholesterol, triglycerides, LDL, malondialdehyde (P=0.001) SGOT (P=0.001) and SGPT (P=0.001) levels of diabetics. In control group blood fructosamine and malondialdehyde levels showed a significantly decrease (P=0.001) and HDL level showed a

Table1. The comparison between means biochemical index in baseline and after intervention in case group

Variables	Baseline	After intervention	*P*-value
Fructosamine (µmol/L)	405.22 ± 1.15	384.01± 1.08	0.001
Cholesterol (mg/dl)	212.21 ± 38.28	171.29± 44.30	0.001
Triglyceride (mg/dl)	195.29 ± 53.33	152.71± 43.86	0.001
LDL (mg/dl)	134.71 ± 25.55	110.54 ± 21.93	0.001
HDL (mg/dl)	34.71 ± 7.74	45.46 ± 8.99	0.001
MDA(µM)	0.357± 0.052	0.30± 0.056	0.001
IU/L (SGOT(IU/L)	28.15 ± 3.21	17.81 ± 2.24	0.001
SGPT(IU/L)	33.5 ± 2 2.81	24.62 ± 1.75	0.001

Table 2. The comparison betweenmeans biochemical index in baseline and afterintervention in Control group

Variables	Baseline	After intervention	*P*-value
Fructosamine (µmol/L)	406.37 ± 1.52	397.42± 0.94	0.001
Cholesterol (mg/dl)	187.14± 37.11	172.64± 34.16	0.176
Triglyceride (mg/dl)	177.81 ± 47.19	166.32± 38.77	0.339
LDL (mg/dl	118 ± 32.80	106.05 ± 21.65	0.123
HDL (mg/dl)	34.59 ± 6.74	38.77 ± 8.54	0.041
MDA(µM)	0.317± 0.043	0.280± 0.049	0.001
IU/L (SGOT(IU/L)	32.45 ± 3.12	29.96 ± 3.15	0.304
SGPT(IU/L)	36.02 ± 4.45	31.23 ± 4.20	0.429

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significantly increase after 6 weeks (P<0.041). We have not observed other significant changes in blood variables at the end of study in control group (Table 2).Comparison between blood parameters of control and case groups after 6 weeks, showed a significant decrease in the levels of fructosamine (P=0.023), SGOT (P=0.038) and SGPT (P=0.056) and increase in HDL (P=0.013) (Table 3).

Discussion

Diabetes is a chronic metabolic disorder which needs prolonged treatment for maintenance of normal blood glucose level and control several induced complications by this disease like retinopathy, nephropathy, peripheral neuropathy, cardiomyopathy and an underlying high oxidant stress (18). Many plants have been used for the treatment of DM in the world. Out of these, only a few have been evaluated as per modern system of medicine. Extracts From many such plants only have been prepared and their usefulness were evaluated in experimental diabetes in animals. There are several treatments for type 2 diabetes but lack of definitive cure for it, more investigations need for treatment this disease (19). This study has evaluated the effect of curcumin supplementation on fructosamine, blood lipids, lipid peroxidation levels and hepatic enzymes in type 2 diabetics. Our study indicates that daily consumption of two curcumin capsules (250mg) for 6 weeks, significantly decreases blood total cholesterol, triglyceride, LDL, MDA, SGPT, SGOT and increases HDL in type 2 diabetics. Also in the present study fructosamine level significantly decreases. Fructosamine is a putative measurement of glycosylatedproteins and it has been suggested to measure blood value as a method for evaluating DM (20). It results in spontaneous no enzymatic condensation of excess of glucose available in blood and large number of proteins including; albumin and hemoglobin due to uncontrolled or poorly controlled diabetes. Fructosamine is more useful why it shows the decline and improvement diabetic conditions over a period of several days or weeks (21). Taniguchi et al showed that Curcumin inhibits advance glycation end product in diabetic rats (22). So treatment with curcumin in comparison with untreated diabetics significantly reduces fructosamine.

Pari et al showed that curcumin administration to diabetic rats for 45 days, results in a significant reduction in, cholesterol, triglycerides, low density lipoprotein (LDL) and serum high density lipoprotein (HDL) cholesterol in diabetic rats increases .They showed that curcumin has antidiabetic and antihyperlipidemic performance in control experimental diabetic rats (23). This researchis against our study which shows curcumin supplementation in diabetics causes a significant decrease in cholesterol, triglycerides, low density lipoprotein (LDL) and the increase in HDL. Researchers reported that probable mechanism of curcumin in decreasing lipid profile, may be due to cholesterol metabolism by increasing 7-cholesterol hydroxylase enzyme activity which inhibits cholesterol synthesis by inhibiting HMG-CoA reductase. Cholesterol 7α hydroxylase controls the first limit step in bile acid synthesis and indirectly regulates cholesterol biosynthesis and plasma LDL-C

Table 3. The comparison between means of biochemical index after intervention between groups

Variables	Baseline	After intervention	*P*-value
Fructosamine (µmol/L)	397.42 ± 0.94	384.01± 1.08	0.023
Cholesterol (mg/dl)	172.64 ± 34.16	171.29± 44.30	0.909
Triglyceride (mg/dl)	166.32 ± 38.77	152.71± 43.86	0.273
LDL (mg/dl)	106.05 ± 21.65	110.54 ± 21.93	0.488
HDL (mg/dl)	38.77 ± 8.54	45.46 ± 8.99	0.013
MDA(µM)	0.280 ± 0.049	0.30 ± 0.056	0.000
IU/L (SGOT(IU/L)	29.96 ± 3.15	17.81 ± 2.24	0.038
SGPT(IU/L)	31.23 ± 4.20	24.62 ± 1.75	0.056

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levels (23).Curcumin affects LDL receptors and inhibits cholesterol absorption (24). Idrus A et al demonstrated that curcumin is a cholesterol-potential decreasing agent and a decrease in levels of cholesterol and LDL-C and increase in HDL-C (25). Soni KB et al reported that oral administration of 0.5 g/day of curcumin for 1 week decrease serum total cholesterol 12% and increase HDL cholesterol 29% in human subjects. Therefore curcumin might serve as a cholesterol-decreasing drug (26). Many studies have demonstrated the antioxidant properties of curcumin both in vivo and in vitro (27). In the present study, we found a significant increase in plasma MDA in diabetics .A decrease in the antioxidant status exacerbates the species of oxygen O2− and H2O2production in return it causes peroxidation of membrane lipids that leads to the formation of lipid byproducts, MDA etc, thereby increasing the plasma MDA levels. Curcumin also inhibits the lipid peroxidation product, MDA. Our results are consistent with previous reports that curcumin decreases lipid peroxidation product (MDA). Curcumin takes its protective effect by modulating lipid peroxidation and augmenting the antioxidant defensive system, and its effects are attributed to the presence of the hydroxyl groups and methylene group of the β-diketone moiety (28). Previous reports have shown a significant decrease in MDA in diabetic rats upon curcumin treatment (29). Curcumin protect against oxidative stress by trapping ability typical of radical as chain breaking antioxidant .It also contains a number of polypeptides with antioxidant activities such as turmeric (30-31).
Curcumin decreases AST and ALT activities. The hepatoprotector effect might also be related toantioxidant effect of curcumin (32).In present study activities of serum AST and ALT (markers of hepatictissue damage) significantly increases. The increments of such markers may be due to the leakage of these enzymes from hepaticcytosol into blood stream (33). Treatment of diabetics with curcumin extract caused normalization in the activities of these enzymes and indicated their potential activities in inhibiting liver damage induced by diabetic status. Evaluation the adverse effects of normal products that was accepted as remedies, is important in implementing safety measures for public health. The present study proves that the antidiabetic therapeutic dose of curcumin has no adverse effect. So far Curcumin has had no known dose-limiting toxicities and is consumed by human in dosage of up to 12 g/d without any adverse effects (34).
In conclusion, the present study is demonstrated that curcumin has beneficial effects on lipid profile and lipid peroxidation as well as it has principal role in preventing the liver damage caused by hyperglycemia. Hence, with antilipidemic and antioxidant features, treatment with curcumin effective therapeutic dose used in current study, can be effective in the recovery of hepatic tissue from damage induced by diabetes and may be candidate as natural antidiabetic drug.

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References

1. Donath MY, Shoelson SE. Type 2 diabetes as an inflammatory disease. Nat. Rev. Immunol. 2011;11:98-107.
2. Piccinini AM, Midwood KS. Dampening inflammation by modulating TLR signalling. Mediators Inflamm. 2010.
3. Wild S, Roglic G, Green A, Sicree R, King H. Global prevalence of diabetes: estimates for the year 2000 and projections for 2030. Diabetes Care 2004;27:1047-53
4. Gobert CP Duncan AM. Consumption, perceptions and knowledge of soy among adults with type 2 diabetes, Journal of the American College of Nutrition 2009;28(2):203-18.

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5. Jiang CS, Liang LF, Guo YW. Natural products possessing protein tyrosine phosphatase 1B (PTP1B) inhibitory activity found in the last decades, Acta Pharmacologica Sinica 2012;33(10):1217-45
6. Nolan CJ, Damm P, Prentki M. Type 2 diabetes across generations: from pathophysiology to prevention and management, The Lancet 2011;378(9786):169-81.
7. Aggarwal BB, Sundaram C, Malani N, Ichikawa H. Curcumin: the Indian solid gold, Advancesin Experimental edicine and Biology 2007;595:1-75.
8. Kochhar KP. Dietary spices in health and disease. Indian JPhysiol Pharmacol 2008;354-52.
9, Aggarwal BB. Targeting inflammation induced obesity and metabolic diseases by curcumin and other nutraceuticals. Annu Rev Nutr 2010;30:173-99.
10.Weisberg SP ,Leibel R ,Tortoriello DV. Dietary curcumin significantly improves obesity-associated inflammation and diabetes in mouse models of diabesity. Endocrinology 2008;149:3549-58.
11. Shao W, Yu Z, Chiang Y. Curcumin prevents high fat diet induced insulin resistance and obesity via attenuating lipogenesis in liver and inflammatory pathway in adipocytes. PLoS ONE 2012;7:28784
12. Kuroda M, Mimaki Y, Nishiyama T. Hypoglycemic effects of turmeric (Curcuma longa L. rhizomes) on genetically diabetic KK-Ay mice. Biol Pharm Bull 2005;28:937-9
13. Nishiyama T, Mae T, Kishida H, Tsukagawa M,[1] Mimaki Y, Kuroda M, et al. Curcuminoids and sesquiterpenoids in turmeric (Curcuma longa L.) suppress an increase in blood glucose level in type 2 diabetic KK-Ay mice. J Agric Food Chem 2005;53:959-63
14. Jain SK, Rains J, Croad J, Larson B, Jones K. Curcumin supplementation lowers TNF-alpha, IL-6, IL-8, and MCP-1 secretion in high glucose-treated cultured monocytes and blood levels of TNFalpha, IL-6, MCP-1, glucose, and glycosylated hemoglobin in diabetic rats. Antioxid Redox Signal 2009;11:241-9.
15. Jacob A, Wu R, Zhou M, Wang P. Mechanism of the Anti-inflammatory Effect of Curcumin: PPAR-gamma Activation.PPAR Res 2007;2007:89369
16. Lao CD, Ruffin MT, Normolle D, Heath DD, Murray S, Bailey J, et al., Dose escalation of a curcuminoid formulation. BMC Complement Altern. Med. 2006;6:10.
17. Hodges DM, DeLong JM, Forney CF, Prange RK: Improving the thiobarbituric acidreactive-substances assay for estimating lipid peroxidation in plant tissues containing anthocyanin and other interfering compounds**.** Planta 1999;207(4):604-11.
18. Zeping HU, Xiaoxia Y, Paul CH, Sui YC, Shufeng Z. Herb-Drug interactions, A Literature Review. Drugs 2005;65:1265-7.
19. Russell-jones D, Cuddihy RM, Hanefeld M, Kumar A, Gonzalez JG, Chan M, et al. Efficacy and Safety of Exenatide Once Weekly Versus Metformin, Pioglitazone and Sitagliptin Used asMonotherapy in Drug-Naive PatientsWith Type 2 Diabetes (DURATION-4). Diabetes Care 2012;35:252-8.
20. Donnelly JG. Carbohydrates and alterations in lucose metabolism. In Clinical chemistry (principles, procedures, correlations). Edited by Bishop ML, Fody EP. Philadelphia: Lippincott; 1996:308-9.
21. Mohamed AO, Moneim AA, Yazid IA, Mahmoud AM. Antihyperglycemic, Antihyperlipidemic and Antioxidant effects and the probable mechanisms of action of Ruta Graveolens Infusion and Rutin in Nicotinamide-Streptozotocin Induced Diabetic Rats. Diabetol Croat 2010;39(1):15-35.
22. Taniguchi N, Kaneto N, Asahi M. 1996. Involvment of glycation and oxidative stress in diabetic macroangiopathy. Diabetes 1996;45:81-3.
23. Pari L, Murgan P. Anttihyperlipidemic effect of curcumin and tetrahydrocurcumin in experimental type 2 rats.Ren fail 2007;29(7):881-9.
24. Sunkandar E, Permana H, Adnyana I, Sigit J. Ilyas R, Hasimun P et al. Clinical study of turmeric(Curcuma longa L.) and garlic (Allium sativum L.) extracts as antihyperglycemicand antihyperlipidemic agent in type 2 diabetes dyslipidemic patients .Lnt Pharmacol 2010;6(4):456-63.
25. Alwi I, Santoso T, Suyono S, Sutrisna B, Suyatna FD, Kresno SB, et al. The Effect of Curcumin on Lipid Level in Patients withAcute Coronary Syndrome. Acta Med Indones-Indones J Intern Med 2008;40(4):201-10.
26. Soni KB, Kuttan R. Effect of oral curcumin administration on serum peroxides and cholesterol levels in human volunteers. Indian J Physiol Pharmacol 1992;36:273-5.
27. Deng SL, Chen WF, Yang BZL, Liu ZL. Protective effects of curcumin and its analogues free radical-induced oxidative haemolysis of human red blood cells. Food Chem. 2006;98:112-9.
28. Dinkova-Kostova AT, Talalay P. Relation of structure of curcumin analogs to their potencies as inducers of Phase 2 detoxification enzymes. Carcinogenesis 1999;20:911-4.
29. Khattab HAH, Al-Amoudi NS, Al-Faleh AA. Effect of Ginger, Curcumin and Their Mixture on Blood Glucose and Lipids in Diabetic Rats. Life Sci J 2013;10:428-42.
30. Zafir A, Banu N. Antioxidant potential of fluoxetine in composition to Curcuma Longa in restraint stressed rats.Eur.J.Pharmacol 2007;572:23-31.
31. Bayrak O, Uz E, Bayrak R, Turgut F, Atmaca AF. Curcumin protects aganist ischemia reperfusin injury in rat kidneys.World J.Urol 2008 26:285-291.

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32. Sajithlal GB, Chithra P, Chandrakasan G. Effect of curcumin on the advanced glycation and cross-linking of collagen in diabetic rats. Biochem Pharmacol 1998;56:1607-14.
33. Mansur HA, Newairy AA, Yousef MI, Sheweita SA. Biochemical study on the effect of some Egyptian herbs in alloxan induced diabetic rats.Toxicology 2002;170:221-7.
34. Manjunatha H, Srinivasan K. Protective effect of dietary curcumin and capsaicin on induced oxidation of low-density lipoprotein, ironinduced hepatotoxicity and carrageenan-induced inflammation inexperimental rats. FEBS J 2006;273:4528-37.
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