

Biochemical effect of curcumin on hyperlipidemia induced in rats

Efectul biochimic al curcuminului în hiperlipidemia indusă la șobolani

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Cuvinte cheie: hiperlipidemie, diabet zaharat, curcumin, profilului lipidic, inflamație, interleukina-

Abstract

This study was performed to investigate the effect of oral supplementation of curcumin, garlic extract and olive oil on lipid profile, nitric oxide, adiponectin, endothelin-1, blood glucose and some inflammatory markers in normal, diabetic and hyperlipidemic rats supplementing high fat and cholesterol-enriched diet. Forty female adult albino rats were divided into four equal groups of 10 rats each. Group (1): negative control received normal diet only, group (2): rats fed on normal diet and received curcumin orally, group (3): positive control received hyperlipidemic diet, group (4): rats fed on hyperlipidemic diet and received curcumin (350 mg/ 1 kg b.w.) orally. The obtained results revealed that, curcumin supplementations to hyperlipidemic rats showed a significant increase in serum HDL-cholesterol, nitric oxide, adiponectin and Endothelin-1 concentrations and significantly decrease in serum total cholesterol, triacylglycerols, LDL-cholesterol, Fasting blood glucose, Glycated Hemoglobin (HbA1C), high sensitive C-reactive protein and Interleukin-6 levels. These results suggest that, curcumin supplementations may have some benefits in patients suffering from dyslipidemia and diabetes.

Rezumat

Acest studiu a fost efectuat pentru a investiga efectul suplimentării orale de curcumin, extract de usturoi și ulei de măsline asupra profilul lipidic, oxidului nitric, adiponectinei, endotelinei-1, glicemiei și asupra unor marker inflamatori la șobolani sănătoși, diabetici și cu hiperlipidemie prin completarea dietei cu un conținut ridicat de grăsimi și colesterol. Patruzeci de femele adulte de șobolani albi au fost împărțiți în patru grupe egale a câte 10 șobolani fiecare. Grupul (1): control negativ cu dietă normală, grupul (2): șobolani hrăniți cu dieta normală și supliment oral de curcumin, grupul (3): control pozitiv cu dieta hiperlipidemică, grupul (4): șobolani hrăniți cu dietă hiperlipidemică și supliment de curcumin (350 mg / 1 kg greutate corporală) pe cale orală. Rezultatele obținute au relevat că suplimentul de curcumin la șobolani hiperlipidemică a produs o creștere semnificativă a colesterolului HDL, oxidului nitric, adiponectinei și a concentrației de endotelina-1 și o reducere semnificativă a colesterolului total seric, triacilglicerolilor, colesterolului LDL, glucozei, hemoglobinei glicate (HbA1c) și a nivelurilor de proteina C reactivă de înaltă sensibilitate și Interleukina-6. Aceste rezultate sugerează că suplimentul de curcumin poate avea unele beneficii pentru pacienții care suferă de dislipidemie și diabet.

Introduction

Hyperlipidemia is a common disorder caused by lifestyle habits in developed countries and is the major cause of coronary heart disease. It results from abnormalities in lipid metabolism or plasma lipid transport or a disorder in the synthesis and degradation of plasma lipoproteins (Jang *et al.*, 2008).

The consequence of hyperlipidemia can cause atherosclerosis, and thus the risk of coronary heart disease and stroke is increased.

Diabetes mellitus is associated with hyperlipidemia, which is a significant risk factor for cardiovascular diseases (El-Moselhy *et al.*,

2011).

The incidence of type 2 diabetes mellitus is rapidly increasing worldwide. Type 2 (formerly called non-insulin dependent) diabetes mellitus accounts for over 90% of the diagnosed cases of diabetes (Pillarsetti and Saxena 2004).

Diabetes is a well-recognized risk factor for atherosclerotic and cardiovascular disease that confers a markedly increased risk of coronary heart disease (CHD). The altered lipid profile characterized by elevated levels of circulating free fatty acids (FFAs) and triacylglycerols, as well as a reduction in high-density lipoprotein cholesterol (HDL-C) along with excess fat deposition in various tissues

including the liver (Banerjee *et al.*, 2004). An abnormal accumulation of fat in the liver and muscle elicits insulin resistances that culminate in beta cell reduction in type 2 diabetes (Seo *et al.*, 2008).

Curcumin has been widely used in traditional medicine in Southeast Asia. It prevents many diseases including biliary disorders, anorexia, cough, diabetes, hepatic disorders, rheumatism, sinusitis, cancer, and Alzheimer's (Aggarwal and Harikumar 2009). Several studies have indicated that curcumin plays a beneficial role in terms of being an antioxidant, anti-tumorigenic and anti-inflammatory agent (Suzuki *et al.*, 2005; Kurup *et al.*, 2007; Ansari *et al.*, 2007; Kurup and Barrios, 2008).

Accordingly, the aim of this work was to investigate the antihyperlipidemic effects of oral supplementation of curcumin, garlic extract and olive oil on some inflammatory markers, blood glucose, lipid profile, adiponectin and endothelin-1 in serum of female rats feeding high fat diet.

Materials and Method

Experimental animals.

A total number of (40) adult female albino rats of (4 – 6) weeks weighting (140-160) gm were used in the experimental investigation of this study.

Rats were obtained from the Research Institute of Ophthalmology, Giza, Egypt. Animals were housed in separated metal cages and kept at constant environmental and nutritional conditions and allowed free access to standard pellet diet and water was supplied ad-libitum.

Diet. Diets supplied to rats according to NRC (1995) (Table 1).

Induction of Diabetes.

Streptozotocin powder manufactured by Sigma chemical Co. (USA) was used for induction of diabetes. According to (Mrudula *et al.*, 2007).

Streptozotocin is an analogue of N-acetyl glucosamine which is readily transported into pancreatic beta cells by Glut2 and cause β -cell

toxicity, resulting in insulin deficiency (Mrudula *et al.*, 2007).

Table 1
Composition of the basal and fat-enriched diets for rats:

Feed Ingredients	Level (%) in basal diet	Level (%) in fat-enriched diet
Oil	15.00	13.00
Yellow corn	44.15	44.15
Soya bean meal (44%)	20.51	20.51
Wheat Bran	12.33	12.33
Cholesterol	0.00	1.00
Coconut Oil	0.00	2.00
Molasses	3.00	3.00
Common Salts	0.50	0.50
Lysine	0.18	0.18
DL-Methionine	0.74	0.74
Min.-Vit. Premix	2.00	1.50
Ground Limestone	1.59	1.09
Total	100.00	100.00

Curcumin was dissolved in (7%) of Dimethyl sulfoxide solution (DMSO) (Rong *et al.*, 2012) and administrated orally at a dose of (350 mg / kg bw/day) for 6 weeks (Aggarwal *et al.*, 2003).

Experimental design

Rats were randomly divided into 4 main equal groups, 10 rats each, placed in individual cages and classified as follow:

- group 1: negative control,
- group 2: rats fed on normal diet and receive curcumin orally,
- group 3: positive control,
- group 4: rats fed on hyperlipidemic diet and receive curcumin (350 mg/ 1 kg b.w.) orally.

Blood samples were collected from all animal groups after 2, 4 and 6 weeks from the onset of curcumin, garlic and olive oil administration. The samples were collected in the morning after overnight fasting from the retro-orbital plexus of eyes.

Serum was separated by centrifugation at 3000 rpm for 10 minutes. The clear serum was aspirated and transferred into sterile labeled tubes and kept in a deep freeze at (- 70°C) until used for subsequent biochemical analysis:

- total cholesterol according to (Schettler, 1975),
- triacylglycerols (Schettler, 1975),
- HDL-cholesterol (Gordon et al, 1977),
- LDL-cholesterol (Friedewald, 1972),
- blood glucose (Trinder, 1969),
- high sensitive C-reactive protein (Kimberly et al, 2003),
- nitric oxide (Montgomery and Dymock, 1961),
- endothelin-1 (Rolinski, 1994).
- glycated hemoglobin (Trivelli et al, 1971).
- adiponectin (Yamauchi et al, 2002) and
- interleukin-6 (Hirano, 1990).

The obtained data were statistically analyzed using one way analysis of variance (ANOVA) followed by the Duncan multiple test.

All analysis were performed using SPSS (statistical package for social sciences, 1999; ver.10.0), values of $P \leq 0.05$ were considered to be significant.

Results and Discussion

The obtained results presented in table (2) revealed that, hyperlipidemia and diabetes caused significant increase in serum total cholesterol, triacylglycerols, LDL-cholesterol, glucose, glycated hemoglobin, high sensitive C-reactive protein, interleukin-6 and endothelin-1 can confirm as compared with normal control group.

Meanwhile, Oral administration of curcumin, garlic extract and olive oil cause significant reduction in all of parameters as compared to that of positive control group.

Hyperlipidemia and diabetes induced significant decrease in serum HDL-cholesterol, adiponectin and nitric oxide can confirm as compared to that of normal control group.

The table represents the mean value of the obtained results for each parameter of the samples collected after 2, 4 and 6 weeks from the onset of curcumin, garlic extraction and olive oil

The obtained results demonstrated that curcumin supplementation have potential effects in preventing hyperlipidemia, diabetes

and on cardiovascular protection.

Table 2.

Effect of curcumin on serum total cholesterol, serum triglyceride, LDL-cholesterol, blood glucose, glycated hemoglobin, high sensitive C-reactive protein, interleukin-6, endothelin-1 HDL-cholesterol, adiponectin and nitric oxide level in the blood.

Parametru investigat	Grupul			
	G1	G2	G3	G4
FBS	92.79a ±0.63	93.89ab ±0.61	177.11c ±2.25	106.68d ±1.57
Adiponectin	5.93d ±0.05	4.52b ±0.06	2.77a ±0.08	8.42f ±0.06
hs-CRP (high sensitive C-reactive protein)	0.52b ±0.02	0.46ab ±0.02	1.22d ±0.04	0.91c ±0.04
IL-6 (interleukin-6)	67.26e ±0.69	61.16cd ±0.37	83.35f ±0.54	54.17a ±0.6
NO (nitric oxid)	76.24d ±0.47	94.48e ±0.46	66.63a ±0.47	111.70g ±0.41
Cholesterol	142.49c ±0.40	125.10b ±0.51	241.18g ±2.35	155.59d ±1.26
Triglyceride	99.27c ±0.38	89.94b ±0.47	199.48 ±1.55	135.27d ±1.27
HDL-C (cholesterol HDL)	40.72d ±0.48	43.36e ±0.45	27.71a ±0.55	34.85c ±0.54
LDL (cholesterol LDL)	130.31e ±0.71	114.12a ±0.81	195.81f ±0.80	114.07a ±1.47
HBA1C	5.02a ±0.11	5.05a ±0.08	7.02c ±0.11	5.63b ±0.07
Endothelin-1	0.96bc ±0.04	0.87ab ±0.04	1.67d ±0.05	1.02c ±0.04

Legend

S.E : Standard error

a, b, c: Average values ($p \leq 0.05$).

Interestingly, the results showed that curcumin supplementation significantly improved serum lipid profile, as revealed by marked increase in HDL level and decrease serum total Cholesterol, triacylglycerols and LDL-C level.

These results are nearly similar to these reported by (Karthikesan *et al.*, 2010), who investigate the effect of curcumin on serum glucose level and lipid profile in hyperlipidemic rats through the inhibition of the generation of superoxide radicals.

The obtained results also indicate that curcumin garlic extract and olive oil supplementation were increased the serum NO level.

This was matching with the study of (Patumraj *et al.*, 2006), who showed that curcumin can increase serum NO level in diabetic rats. Also curcumin could significantly increase sodium nitroprusside SNP-induced vasodilatation in diabetes and could enhance

smooth muscle cell relaxation when activated by NO donor.

Regarding serum adiponectin level similar results was reported by (Wongcharoen and Phrommintikul 2009), who showed that, curcumin improve serum adiponectin level in hyperlipidemic rats as curcumin inhibits the independent mitogen activated protein kinase (MAPK) pathways which are the pathways activated by most inflammatory stimulation.

It was confirmed that curcumin, garlic and olive oil to have anti-inflammatory effect and lower levels of hs-CRP and Interleukin-6 in obese rats and this suggestion was supported by the finding of (Juha *et al.*, 2007) who revealed that curcumin lowers serum hs-CRP and Interleukin-6 levels in obese individuals.

They explain the rule of curcumin that, down regulates the expression of the NF- κ B-regulated gene products such as tumor necrosis factor (TNF), interleukin-1 (IL-1), interleukin-6 (IL-6), interleukin-8 (IL-8), macrophage interferon protein-1 α (MIP-1 α), adhesion molecules, C-reactive protein (CRP).

Also (Diego *et al.*, 2013) showed that garlic lowers hs-CRP and Interleukin-6 levels in serum of patients with hyperlipidemia.

The obtained results revealed that curcumin supplementations increased serum level of endothelin-1 level and our results were similar to the study of (Chiu *et al.*, 2009), who showed that, curcumin could improve serum endothelin-1 level in diabetic rats as vasoactive factors such as ET-1 that may act as an upstream mediator of fibronectin (FN) expression in diabetes by transcription factor NF- κ B. It has been demonstrated that curcumin exerts one of its beneficial effects through the inhibition of NF- κ B.

Conclusions

The present study demonstrated that, curcumin supplementations showed positive effects on lipid profile, blood glucose level and serum inflammatory markers that may be developed by hyperlipidemia and diabetes.

The antioxidant effects of curcumin have been shown to attenuate Streptozotocin-induced diabetes and may prevent diabetic

cardiovascular complications.

Also, the present study demonstrated that curcumin is potent vasorelaxants as well as reduce the atherogenic properties of cholesterol.

So we recommended that, curcumin is useful in treatment of hyperlipidemia, cardiovascular disorders and insulin resistance. It must be used carefully and under medical supervision to get its therapeutic benefits and avoid their side effects.

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