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*El-Sayeda Ghandour Elsayed El-Sahar**

Abstract

Curcuma longa L. plant (known as curcum hence the name Curcuma, turmeric) is a member of the Curcuma botanical group, which is part of the ginger family of herbs, Turmeric is used worldwide as the main ingredient in curry, the spice, and as a source for curcumin or curcuminoids. it is used for medicinal purposes This study was conducted on sixty Sprague Dawley strain male rats and weighting 100±10 g. Six rats served as control (-ve) group (Co.(-)) while Twenty-four rats were fed high- containing basal diet+5% tallow+1% cholesterol+ 0.02% bile salt to induce Hypercholesterolemia. These rats were reclassified into control (+ ve) (Co.(+)), three treated rat groups that were 4, 6 and 8 g /kg diet turmeric. The treatment period was designed for six weeks. The obtained results revealed that the total cholesterol (TC), triglycerides (TG), HDL-C and LDL-C were determined, in addition to serum glucose, liver and kidney function. The histopathological changes of the heart, liver and kidney were evaluated. SPSS, one way ANOVA was used to analyze the results. The results indicated that dietary curcumin significantly blocked the effect of HFD on the body-weight gain, the best value was in G (3), The best treatment was turmeric (6g and 8g) which had the lowest values of total cholesterol, TG and LDL-C, and the best values of HDL-C. Also, the best improvement in glucose level in G (3), results clearly revealed that the best treatment was turmeric (8 g / Kg diet) which had the lowest values of ALK, ALT and ALP. uric acid and urea gave a significant decrease in groups G2 and G3. The moderate and higher dose from turmeric gave normal histological structure in the heart, liver and kidney in Morphologic changes. In conclusion, results showed that turmeric had a similar potential to

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attenuate CHD-related parameters in mild oxidative stress induced by a high-fat diet in rats.

KEYWORDS: Atherosclerosis turmeric, Liver, Heart, High-Fat Diets rats

INTRODUCTION

Hypertension, dyslipidemia, obesity, type 2 diabetes mellitus (T2DM), and metabolic syndrome, and insulin resistance, promote endothelial dysfunction and vascular inflammation leading to atherosclerosis—the main cause of CVD **(Srikanth and Deedwania 2016)**. The study showed that low circulating concentrations of triglycerides (TG) and low-density lipoprotein cholesterol (LDL-C) were associated with a low risk of CVD **(Musunuru, 2010).** Therefore, the treatment of dyslipidemia is critical for the prevention of CVD.

Turmeric (Curcuma longa), an Indian spice, is a yellow pigment that is used worldwide in cooking, cosmetics, dyes, and medicines **(Goel et al., 2008)**. It is worth noting that turmeric is a frequently used food additive in Southeast Asia, which mends the color and flavor of food preparations. Curcumin (chemical name: diferuloylmethane) is an effective component of turmeric **(Sahebkar,2013)** which has the ability to interact with hundreds of molecular targets. Many studies have confirmed the protective effects of curcumin against many chronic diseases, including pulmonary disorders, various cancers, and autoimmune diseases **(Kunnumakkara et al., 2016)**. It has been shown to attenuate oxidative stress **(Pulido et al., 2016)** and to exert a cardioprotective effect owing to its lipid-lowering properties **(Maithilikarpagaselvi et al., 2016; Li et al., 2015 and Shin et al., 2011)**. Also, most of the randomized trials have reported positive effects of curcumin on blood lipid levels. Nonetheless, conflicting reports exist in that some studies have reported promising effects **(Rahmani et al., 2016; Rahimi et al., 2016; Maithili et al., 2015; Amin et al., 2015; Yang et al., 2014 and Chuengsamarn et al., 2013).** Whereas others failed to demonstrate any significant effect **(Usharani et al., 2008).**

Turmeric is on the FDA's Generally Recognized as Safe list. No LD_{50} has been discovered for curcumin**(Bratman and Girman 2003). Cheng et al.,(2001)** found that curcumin is not toxic in oral human doses up to 8000 mg/day for 3 months. Curcumin has a wide range of therapeutic actions as the ability to halt or prevent certain types of cancer **(Aggarwal et al., 2003; Bharti et al., 2003 and Chan et al., 2003)**, anti-inflammation **(Ramsewak et al., 2000)**; improve cardiovascular health **(Ramirez-Tortosa et al., 1999; Quiles et al., 2002 and Mesa et al., 2003)**; prevent cataracts **(Suryanarayana et al., 2003)**.

Many naturally occurring dietary polyphenols possess antioxidant and anti-inflammatory properties **(Alappat and Awad, 2010)**. This could be achieved by modulating an inflammatory or oxidative signaling pathway, **(Alappat and Awad, 2010**; **Yu et al., 2010 and Bereswill et al., 2010).** Many dietary polyphenols, such as curcumin, also have anti-carcinogenic effects. One prospect mechanism of curcumin to suppress tumorigenesis**(Mukhopadhyay, 2002 and Jaiswal et al., 2002)**.Curcumin, a low-molecular-weight polyphenol obtained from the herbal medicine and dietary spice turmeric, was found to suppressed obesity and diabetes in rats models **(Weisberg et al., 2008)**.curcumin may do its beneficial effects decrease leptin and insulin resistance, speed fatty acid oxidation, weaken inflammatory cytokine, also enhancing antioxidant enzyme **(Alappat and Awad, 2010).**

In addition, curcumin could also function as an inhibitor of p300 histone acetyltransferase (HAT), a potential molecular mechanism for cancer prevention and cardiovascular improvement **(Morimoto et al., 2008 and Barnes, 2009). (Alappat and Awad, 2010)**. In addition, curcumin could also function as an inhibitor of p300 histone acetyltransferase (HAT), a potential molecular mechanism for cancer prevention and cardiovascular improvement **(Morimoto et al., 2008 and Barnes, 2009)**. It is to focus efforts toward improving the most effective drugs and exploring natural factors as alternatives to the treatments that are currently available.

This study aimed to investigate the effects of turmeric on blood lipids level and glucose in a rat model with mild oxidative stress induced by a high-fat diet.

MATERIALS AND METHODS:

Animals protocols:

Thirty male Sprague Dawley rats, weighing 100±10 g were used in this study. They were obtained from the National Research Center (NRC) Dokki Giza Egypt. Animals were clinically healthy and they randomized and housed in stainless steel wire bottom cages (3 rats /cage) and maintained in an air-conditioned room on a 12 h light/ dark cycle at 22+ 2 °C and given the basal diet for 10 days as an adaptation period before treatments.

Preparation of turmeric

Turmeric was purchased from the local market as roots, then grounded before mixing with the diet and added to the basal diet in 4 g, 6 g and 8 g /kg diet. During the feeding experiments, animals were daily inspected and food intake was recorded while body weights were recorded according to **(Chapman et al., 1959)**. The feeding experiment lasted for six weeks.

Tallow was purchased from the local market, then grounded before mixing with the diet and added to the basal diet in 50 g /kg diet.

Experimental design

The animals were distributed into two main groups: the first, negative control group Co. (-) (n=6), fed basal diet **(AIN, 1993)**. The second group (n=24) fed high- fat diet (containing basal diet + 5 % tallow + 1% cholesterol+ 0.02% bile salt). This group was divided into four subgroups: group positive control co. (+) (n=6) fed high-fat diet only, group 1 (G (1)) (n=6) fed high-fat diet plus 4 g /kg diet turmeric, group 2 (G (2) (n=6) fed high-fat diet plus 6 g /kg diet turmeric, and group 3 (G (3)) (n=6) fed high-fat diet plus 8 g /kg dietturmeric.

Used chemicals

Cholesterol as pure white crystalline powder and bile salts as a pure yellow powder were obtained from Elgamhoria Company for Med Preparations Chemicals and Medical Equipment's, Cairo –Egypt.

Biological evaluation

During the experimental period (6 weeks), the diet consumed was recorded every day. The body weight gain (B.W.G %) and feed efficiency ratio (F.E.R.) were determined according to **Chapman et al. (1959)**.

At the end of the experiment period, animals were sacrificed after 12 h of fasting then blood samples were collected with care to avoid hemolysis by receiving it on the wall of the tube. Blood samples were collected in clean dry labeled centrifuge tubes and left to clot at room temperature for a while, then centrifuged at 3000 rpm for 10 minutes. The clear supernatant serums were aspirated by means of Pasteur pipette and stored at -20˚C in Epindorff's tubes until used in the biochemical analysis **(Drury and Wallington, 1980)**.

Serum total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C) and low-density lipoprotein cholesterol (LDL-C) were determined by using enzymatic colorimetric method **(NIHP, 1987; Young and Pestaner, 1975; Fendewaid, 1972; Gordon and Amer, 1977; Lee and Nieman, 1996),** respectively. Very low-density lipoprotein cholesterol (VLDL-C) was carried out according to **Lee and Nieman (1996)** as follows VLDL-C =TC— (HDL-c) - (VLDL-c).

Serum activities of aspartate aminotransferase AST, alanine aminotransferase ALT Alkaline Phosphatase (ALP) activities were colorimetrically determined according to the method described by **Reitman and Frankel (1957)**. Uric acid**,** Serum urea nitrogen and creatinine were determined consistent with the methods described by **Fossati et al., (1980), Patton and Crouch, (1977) and Husdan and Rapoport, (1968)**. Serum total protein and creatinine were determined by **Henry (1964) and Reitman and Frankel (1957)** respectively. Albumin content was calculated from the

standard curve prepared by sub dilution preparation of the albumin stock and the corresponding absorbencies.

Sample preparation

The target organs were examined as follows: Organs such as heart, liver and kidney were excised and weighed. Then washed in cold saline (9 g/l NaCl), stored in formalin solution (10%) for 24r hours. Washing was wiped out the water then serial dilutions of alcohol (methyl, ethyl and absolute ethyl) were used for dehydration. Specimens were cleared in xylene and embedded in paraffin at 56 degrees in a hot air oven for 24 hours. Paraffin bees wax tissue blocks were prepared for sectioning at four microns by slide microtome. The obtained tissue sections were collected on glass slides, deparaffinized and stained by hematoxylin and eosin stains **(Bancraft et al., 1975)** for histopathological examination through the microscope.

Statistical Analysis

Statistical Analysis was performed by using the computer program, Statistical Package for Social Sciences **(SPSS, 1998)**. Values are given as means ± SD, and the differences between groups were determined by one way ANOVA. Values of $P< 0.05$ were considered significant.

RESULTS AND DISCUSSION:

Effect of turmeric:

1- Bodyweight gain, food intake and feed efficiency ratio.

As shown in Table .1, the mean values of initial body weight (IBW) of all experimental groups (G1, G2 and G3) showed no significant difference when compared with Co. (+). The mean value of final body weight (FBW) in group Co. (+) (154.80±18.67g) was significantly ($p<0.05$) higher compared to the corresponding mean values of groups Co. (-), G 1, G 2 and G3 (116.60 ±27,95.00 ± 16.87, 85.20±20, and 91.60±17.53 respectively). The mean values of body weight gain (BWG) and feed efficiency ratio (FIR) in groups Co. (-), G 1, G 2 and G3 had significant

decrease when compared with group co (+), while G (2) and G (3) showed highest significant decrease compared to group co (-) and co. (+).

This result agreed with, **Ghada and Soliman (2005)** who revealed that body weight gain (BWG) of curcumin in the treated groups showed a slightly non-significant decrease in their BWG than control. Also, FBW and BWG of cholesterol-fed rats were significantly higher than that of their respective control group. Which are in agreement with **Hulbron et al. (1982)** and disagree with **Sérougne et al. (1995).**

Also, **Shao et al. (2012)**confirmed that Long term dietary curcumin administration blocked HFD-induced body-weight gain and obesity in chronic HFD mouse model, body-weight increased significantly only after 16 weeks of HFD feeding. At the end of the 28th week, dietary curcumin significantly blocked the effect of HFD on body-weight gain. HFD also significantly increased a load of epididymal fat pads, while curcumin supplementation significantly blocked this stimulation. Oral curcumin supplementation was shown to stop the event of obesity-associated inflammation**(Weisberg et al., 2008)**.

Table (1): Body weight gain, food intake and feed efficiency ratio after 6 weeks feeding.

Groups	IBW(g)	FBW(g)	BWG (g)	FI(g)	FER%
Co.(-)	$106.20^{b} \pm 24.14$	$116.60^{c} \pm 27.37$	$10.40^{b} \pm 3.44$	$16.20^{c} \pm 1.10$	$0.64^{b} \pm 0.22$
Co.(+)	$97.60^{a} \pm 22.17$	$154.80^{b} \pm 18.67$	$57.20^{a} \pm 4.82$	$19.80^{ab} \pm 1.92$	$2.91^{a} \pm 0.41$
G1	$99.00^{a} \pm 17.90$	$95.00^{ab} \pm 16.87$	$-4.00^{c} \pm 1.87$	$21.00^{a} \pm 2.45$	$-0.19^{c} \pm 0.09$
G2	$98.20^{a} \pm 13.48$	$85.20^{b} \pm 20.00$	$-13.00^{c} \pm 14.44$	$18.00^{bc} \pm 2.00$	$-0.69^{c} \pm 0.71$
G3	$105.80^{a} \pm 19.95$	$91.60^{ab} \pm 17.53$	$-14.20^{c} \pm 5.97$	$21.40^{a} \pm 1.52$	$-0.66^{c} \pm 0.25$

Co (-), normal diet; Co (+) high-fat diet; G(1), high-fat diet plus turmeric (4g); G (2), high-fat diet plus turmeric (6g);G(3), high-fat diet plus turmeric (8 g); IBW, initial body weight; FBW, final body weight; BWG, body weight gain; FI, food intake; FER, feed efficiency ratio. Values with the same letters by column indicate no significant difference($p< 0.05$) and vice versa.

2- Relative weight of heart, liver and kidney:

The results showed that in groups (G1, G2 and G3) fed on a high-fat diet and turmeric the relative weight of the heart and liver had a significant increase when compared with control negative group. However kidney weight had no significant difference in G1 when compared with the control positive group, However, relative kidney weight showed a significant increase in G2 and G3 (0.79±0.09 and 0.87±0.14) when compared with group co.(+). (Table .2).This result agrees with **Ghada and Soliman (2005)** demonstrated that relative liver and heart weight of cholesterol-fed groups showed a significant increase when compared with the control group. The significant increase in liver and heart weight may be attributed to fat deposits. As recorded by several investigators, increased cholesterol level increases the fat accumulation in the liver **(Kahloneet al. 1997 and Murray et al. 2000).**

Table (2): Relative weight of heart, liver and kidney (g):

Groups	Heart (g)	Liver (g)	Kidney (g)
Co.(-)	$0.30^{c} \pm 0.07$	$2.56^{b} \pm 0.59$	$0.74^{b} \pm 0.21$
Co.(+)	$0.33^{b} \pm 0.06$	$2.92^{a} \pm 0.82$	$0.73^{a} \pm 0.11$
G1	$0.32^{ab} \pm 0.09$	$2.88^{a} \pm 0.72$	$0.73^{a} \pm 0.12$
G2	$0.31^{b} \pm 0.06$	$2.93^{a} \pm 0.32$	$0.79^{a} \pm 0.09$
G3	$0.33^{ab} \pm 0.04$	$2.78^{a} \pm 0.68$	$0.87^{a} \pm 0.14$

Co (-), normal diet; Co (+) high-fat diet; G(1), high-fat diet plus turmeric (4g); G (2), high-fat diet plus turmeric (6g);G (3), a high-fat diet plus turmeric (8 g). Values with the same letters by column indicate no significant difference ($p< 0.05$) and vice versa.

3- Serum lipid profile and glucose level:

Table (3) shows the effect of different levels of turmeric on serum total cholesterol (TC), triglyceride (TG), low-density lipoprotein cholesterol (LDL-C) and high-density lipoprotein cholesterol (HDL-C). It could be observed that group co. (+) had a significant increase in TC, TG and LDL-C compared with control negative rats. Also, all groups fed on high-fat diet containing different levels of turmeric (4, 6 and 8 g/ kg diet) had significant

decrease in TC, TG and LDL-C compared with control positive group of rats, also could be observed that G2 and G3 fed on high-fat diet containing levels of turmeric (6 and 8 g/ kg diet) had improved significantly in HDL-C (43.40±9.07 and 41.0±3.94 respectively) when compared with control positive group co. (+). The groups fed on turmeric give results similar to group co. (-). The best treatment was turmeric (6g and 8g) which had the lowest values of total lipid cholesterol, TG and LDL-C, and the best values of HDL-C. However, the results demonstrated that the mean values of glucose had a significant decrease in groups fed on a high-fat diet containing different levels of turmeric (4g, 6g and 8 g /kg diet)when compared with control positive group co. (+).

This result agreed with **Ghada and Soliman (2005)** who indicated that serum cholesterol (total, LDL, VLDL) of the groups of normal rats which fed on curcumin- or curcum was significantly lower than the control group. Also serum HDL-C of groups of curcumin- /or curcum- fed was significantly above the control group. An identical result's found in hypercholesterolemic rats which ate up different levels of curcumin- and/or curcum.

Also, founded this review which identified 7 trials of turmeric and curcumin in patients in danger for disorder evidence of their beneficial effects on serum levels of LDL-C and TG, although there was no significant difference in HDL levels within the blood. A beneficial effect of turmeric and curcumin on serum TC levels has been observed in people with metabolic syndrome; however, in people with high blood sugar, this beneficial effect on serum TC levels has not been observed. The natural form (turmeric) and curcumin appear to have more positive effects on patients with metabolic syndrome. Related to the forms of interference, turmeric extract may have a better beneficial effect on TC levels in the blood, compared to concentrations of turmeric in its natural form **(Si et al., 2017).**

Sahebkar,(2013) conducted the effects of curcumin on blood lipid levels and found no significant improvements in the lipid profile in any

aspect**.** Several explanations could be tendered to explain why the results of their study were contrary to those of the present study. Firstly, both parallel and crossover randomized trials were selected, and these may have adversely influenced the ultimate results. The effect of low-dose and moderate-dose curcumin slightly lowers the total cholesterol, In the case of the curcumin effect on LDL cholesterol level, the low-dose has demonstrated the highest decrease (-8.6%), followed by the moderate-dose (3.4%) and therefore the worst effect has been demonstrated within the high-dose, i.e. an increase by 15.4%. However, it was not significantly different when compared to the placebo **(Alwi et al., 2008).**

Secondly, most of the selected studies were conducted with unformulated curcumin, which is considered to have low bioavailability. Curcumin has poor bioavailability owing to its fast metabolism, its bad absorption and rapid elimination from the body. **Mohammadi et al. (2013)** demonstrated the hypothesis that curcuminoids (1 g/day for 30 days) lead to a significant decrease in serum TG concentrations in obese individuals. During a trial among patients with arteriacoronaria disease, although curcumin supplementation decreased serum levels of TC, LDL-C, and TG, there was no obvious difference in comparison to placebo **(Mirzabeigi et al., 2015)** possibly due to the small size of the study. Subsequently, a study by **Soare et al. (2014)** found that 900 mg of curcumin did not influence plasma lipid levels in non-obese relatively healthy individuals.

Babu and Srinivasan. (1997) reported a hypolipidemic effect of curcumin in streptozotocin-induced diabetic rats and fed with 0.5% curcumin for 8 weeks. The cholesterol level decreased significantly in rats fed with a curcumin diet. In order to understand the mechanism of lowering cholesterol in the curcumin diet, a measurement was taken on the activity of hepatic cholesterol-7a-hydroxylase. It was apparent that the hepatic cholesterol-7a-hydroxylase level was significantly higher in diabetic rats fed with curcumin, which demonstrated a higher cholesterol catabolism rate.**Neerati and Gangi (2014)** reported that curcumin could counter Insulin resistance. Through the improvement of metabolic

disturbance and the possible binding of curcumin with peroxisome proliferator-activated receptor-gamma, curcumin could play a protective role in diet-induced insulin resistance **(Jayakumar et al., 2016).**

Sao et al. (2012) confirmed that Insulin was less effective in lowering the glucose level in HFD animals, while curcumin supplementation efficiently blocked this effect of HFD. These data suggest that curcumin improves whole-body glucose disposal by both stimulations of insulin sensitivity and inhibition of hepatic gluconeogenesis. Curcumin improved insulin signaling in fat and hepatocytes. Which suppressed expression of the LDL-C receptor gene, and could thereby reduce plasma LDL-C concentrations **(Kang and Chen 2009)**. Furthermore, curcumin is expected to affect both synthesis and catabolism of triglyceride-rich lipoproteins **(Sahebkar[1] 2014).** Thus, curcumin supplementation may lower plasma triglycerides and cholesterol concentrations by mitigating the expressions of lipogenic genes **(Sahebkar[2] 2014 and Sahebkar et al., 2014).**

Si et al. (2017) found that consumption of turmeric and curcumin was safe and well-tolerated in general. And dosages as high as 8000 mg/day have been shown to be well-tolerated with no apparent toxicity **(Cheng et al., 2001)**. Oral curcumin supplementation was shown to prevent the development of -associated inflammation insulin resistance, as well as diabetes **(Weisberg et al., 2008)**.

Table (3): Effect of turmeric on serum lipid profile and glucose in rats after 6 weeks.

Groups	CH (mg/dl)	TG (mg/dl)	HDL (mg/dl)	LDL (mg/dl)	GlU. (mg/dl)
Co.(-)	76.00 ^{b} ± 15.70	68.20 ^{b} ± 9.78	48.40 ^{b} ± 9.74	32.80 ^{b} ± 8.79	79.20 ^{b} ± 9.36
Co.(+)	132.80 ^{a} ± 26.19	124.00 ^{a} ± 21.71	35.40 ^{a} ± 18.58	81.20 ^{a} ± 4.09	108.20^{d} ± 4.4
G1	73.80 ^{a} ± 8.23	102.20 ^{a} ± 7.26	37.60 ^{a} ± 13.24	52.80 ^{a} ± 7.19	79.60^{b} ± 9.58
G2	82.60 ^{ab} ± 9.29	79.80 ^{a} ± 10.03	43.40 ^{ab} ± 9.07	34.40 ^{a} ± 14.29	72.60 ^{bc} ± 2.30
G3	84.80 ^{ab} ± 8.58	72.20 ^{a} ± 22.81	41.00 ^{a} ± 3.94	32.40 ^{a} ± 8.29	73.00 ^{a} ± 3.39

Co (-), normal diet; Co (+) high-fat diet; G(1), high-fat diet plus turmeric (4g); G (2), high-fat diet plus turmeric (6g);G (3), a high-fat diet plus turmeric (8 g).Values with the same letters by column indicate no significant difference ($p< 0.05$) and vice versa.

4- Effect of turmeric on liver function in rats fed a high-fat diet.

In this study, the effect of turmeric on liver function in rats after 6 weeks illustrated in the table (4). Where groups G1, G2 and G3 gave significant difference in ALT and AST when compared with control negative group, however, I found a significant decrease in ALK in group G1, G2 and G3 when compared with control negative and positive groups.

Boonjaraspinyo et al. (2009) show the activities of serum ALT, ALP, and concentration of direct bilirubin. The serum markers (ALT, ALP) in the turmeric group remained within normal levels. Serum ALT levels increased about five- to sixfold after hamsters were administered nitrosodimethylamine and two- to threefold after infection when compared with values in the uninfected control and in that administered turmeric alone. There was a significant decrease in serum ALT in the group of nitrosodimethylamine+turmiric at 1 month. Decreased inflammatory cells led to decreased serum in ALT and decreased direct bilirubin levels in all groups treated with a turmeric diet. This result agrees with previous reports that the curcumin in turmeric reduces inflammation in many types of diseases **(Yadav et al. 2009)**. Moreover, turmeric decreases liver

detoxification, leading to a reduction of toxic metabolite products **(Choi et al. 2008; Sugiyama et al. 2006; Surh and Chun 2007).**

Table (4): Effect of turmeric on liver function in rats after 6 weeks.

Groups	ALT (µ/ml)	AST (µ/ml)	ALK (µ/ml)
Co.(-)	22.20 ^{b} ± 5.22	7.20 ^{b} ± 1.79	44.00 ^{c} ± 2.12
Co.(+)	40.80 ^{a} ± 19.21	5.60 ^{a} ± 2.19	42.20 ^{b} ± 2.59
G1	43.40 ^{a} ± 8.85	7.20 ^{a} ± 1.79	37.40 ^{b} ± 3.85
G2	48.00 ^{a} ± 8.09	7.20 ^{a} ± 1.79	32.80 ^{a} ± 2.49
G3	31.00 ^{a} ± 7.65	5.80 ^{a} ± 1.79	38.60 ^{b} ± 5.46ease

Co (-), normal diet; Co (+) high-fat diet; G(1), high- fat diet plus turmeric (4g); G (2), high- fat diet plus turmeric (6g);G(3), a high-fat diet plus turmeric (8 g). Values with the same letters by column indicate no significant difference ($p< 0.05$) and vice versa.

5- Effect of turmeric on kidney function in rats fed on a high-fat diet:

Table (5) shows that the Effect of turmeric on kidney function in rats after 6 weeks, total protein and creatinine ratio gave significant increase in G1, G2 and G3 when compared with control negative and positive groups, however uric acid and urea gave significant decrease in groups G2 and G3 when compared with Co. (+)., also found the significant increase in both albumin and bilirubin in G 3 when compared with control negative and positive groups.

Boonjaraspinyo et al. (2009) demonstrated that all of the groups that were administered turmeric. The serum direct bilirubin level (which was lower in groups given a turmeric diet than in the untreated groups) shows that turmeric enhanced bile flow and biliary contraction. Serum direct bilirubin levels in the turmeric, nitrosodimethylamine and nitrosodimethylamine+turmeric groups remained within normal levels. Serum direct bilirubin levels increased about two- to eightfold after infection when compared with the uninfected control groups. The anti-inflammatory property of turmeric was obviously demonstrated by the reduction of inflammatory cells in hepatic tissue compared with the

untreated group at both 30- and 60-day time periods. Decreased inflammatory cells led to decreased direct bilirubin levels in all groups treated with a turmeric diet. This result agrees with previous reports that the curcumin in turmeric reduces inflammation in many types of diseases **(Yadav et al., 2009)**, including liver diseases and toxicity from CCl4 **(Reyes-Gordillo et al., 2008)** by inhibiting cyclooxygenase-2, lipoxygenase, **(Unnikrishnan and Rao 1995; Sreejayan and Rao 1994; Menon and Sudheer 2007; Pae et al., 2008).** Moreover, **Boonjaraspinyo et al. (2009)** show the property of turmeric to enhance bile flow and gall bladder contraction through decreased direct bilirubin level, a result which is supported by **Deters et al. (2000)**.

Table (5): Effect of turmeric on kidney function in rats after 6 weeks.

Groups	T.P (mg/dl)	Creat. (mg/dl)	Urea (mg/dl)	U.A. (mg/dl)	BIL. (mg/dl)	ALB. (mg/dl)
Co.(-)	5.58 ^{c} ± 1.64	0.63 ^{b} ± 0.08	26.00 ^{b} ± 2.24	3.36 ^{c} ± 0.26	0.52 ^{c} ± 0.02	3.84 ^{c} ± 0.38
Co.(+)	5.96 ^{b} ± 0.90	0.48 ^{b} ± 0.06	24.60 ^{b} ± 4.56	3.40 ^{ab} ± 0.64	0.52 ^{b} ± 0.02	3.68 ^{ab} ± 0.75
G1	7.20 ^{b} ± 0.57	0.71 ^{b} ± 0.23	30.00 ^{b} ± 7.04	5.60 ^{a} ± 0.81	0.51 ^{ab} ± 0.01	3.28 ^{ab} ± 1.65
G2	7.10 ^{a} ± 0.44	0.66 ^{ab} ± 0.09	22.40 ^{a} ± 4.51	3.09^{ab} ± 0.91	0.55 ^{a} ± 0.06	4.10 ^{a} ± 0.14
G3	6.10 ^{ab} ± 0.90	0.81 ^{b} ± 0.12	18.40 ^{ab} ± 2.88	3.08 ^{ab} ± 0.51	0.53 ^{ab} ± 0.03	3.92 ^{ab} ± 0.63

Co (-), normal diet; Co (+) high-fat diet; G(1), high- fat diet plus turmeric (4g); G (2), high- fat diet plus turmeric (6g);G(3), a high-fat diet plus turmeric (8 g). Values with the same letters by column indicate no significant difference ($p< 0.05$) and vice versa.

Histopathological effects:

1- Morphologic changes of rat heart stained with hematoxylin and eosin:

Representative heart sections stained with hematoxylin and eosin in each group are shown in Figure (1:5) the heart in the control rat of group Co. (-) (Fig. 1) showed no histopathological alteration and the normal histological structure of the myocardium. Heart of rat in group Co. (+) (Fig.2) revealed intermyocardial oedema deposition of fat in pericardium with inflammatory cells infiltration, while in group 1 (Fig.3) slight

intermuscular edema. On the other hand, the heart of rats in group 2 and group 3 (Fig.4and 5) showed histopathological alteration and the normal histological structure of the myocardium. The morphologic features of the heart in the rats of groups 2 and 3 were close to that of the control rats group Co. (-), which indicated a similar preventive effect of turmeric against hyperlipidemia in this experimental model. Also, agreed with a previous report that turmeric has no toxic effect in hamster models **(Kaewsamut et al. 2007).**

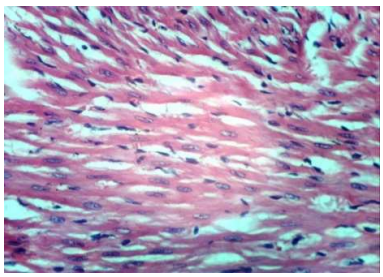


Fig. (1): Heart of rat from group Co.(-) showing no histopathological changes.

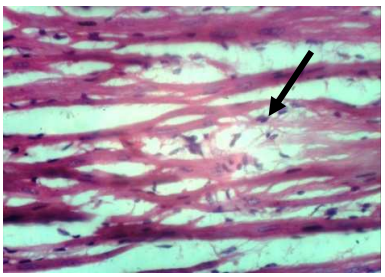


Fig. (2): Heart of rat from group Co. (+) showing intermyocardialoedema

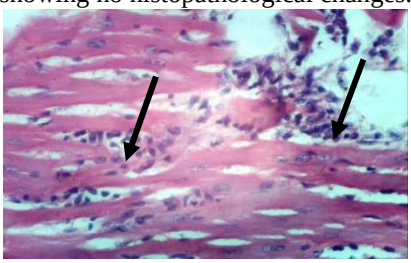


Fig. (3): Heart of rat from group 1 showing focal myocarditis.

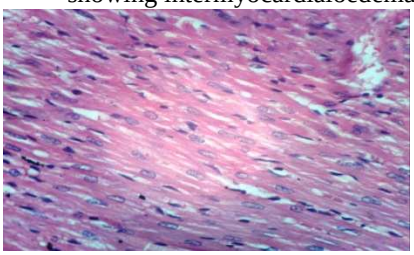


Fig. (4): Heart of rat from group 2 showing no histopathological changes

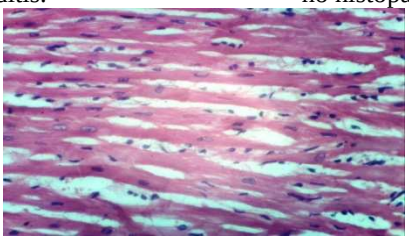


Fig. (5): Heart of rat from group 3 showing no histopathological changes.

Figure (1:5). Morphologic changes of rat heart stained by hematoxylin and eosin using a light microscope(H & E X 400). **Co. (-)** rat fed standard diet (control), **Co. (+)** high-fat diet; **G (1)**, high-fat diet plus turmeric (4g) ; **G (2)**, high-fat diet plus turmeric (6g);**G (3)**, high-fat diet plus turmeric (8g).

2- Morphologic changes of rat liver stained with hematoxylin and eosin:

Representative liver sections stained with hematoxylin and eosin in each group are shown in Figure (6:10). The liver in the control rat of group Co. (-) (Fig. 6) showing the normal histological structure of hepatic lobule. Liver of rat in group Co (+) (Fig.7) showing hyperplasia of the epithelial lining bile duct and thickening in its wall. Result in group 1 (Fig.8) showing slight vacuolization of hepatocytes. On the other hand, the liver of rats in group 2 (Fig.9) Showing Kupffer cells activation and cytoplasmic vacuolization of hepatocytes, group 3 (Fig.10) showed slight activation of Kupffer cells. The morphologic features of the liver in the rats of G 2 and G 3 were closed to that of the control rats group Co. (-), which indicated a similar preventive effect of turmeric in this experimental model. The histopathological results showed that turmeric has no toxic side effects in normal hamsters; this was supported by the liver function test results **(Boonjaraspinyo et al. 2009).**

Shao et al. (2012) examined histological changes in the liver of each group of mice. HFD consumption increased liver lipid content, demonstrated by both H&E staining.In the curcumin group, however, the effect of HFD on the elevation of lipid content was blocked. The effect of HFD on macrophage infiltration was also blocked by curcumin consumption.In this chronic HFD mouse model, although the liver weight was not significantly increased, intra-hepatic lipid content was increased more than 6 fold, consistent with the observation by H&E. Curcumin significantly reduced liver weight and prevented the effect of HFD on rising intra-hepatic lipid content.

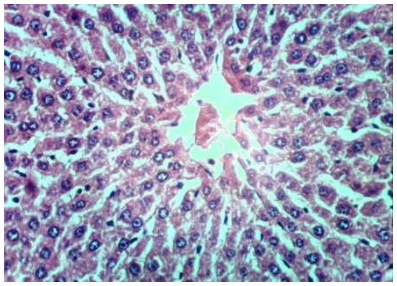


Fig. (6): Liver of rat from group Co. (-) showing the normal histological structure of hepatic

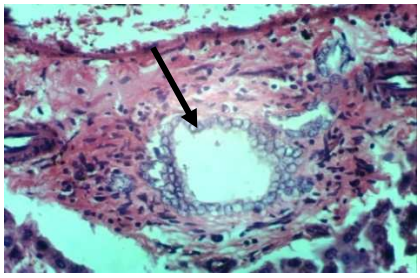


Fig. (7): Liver of rat from group Co. (+) showing hyperplasia of lobule.epithelial lining bile duct and thickening in its wall.

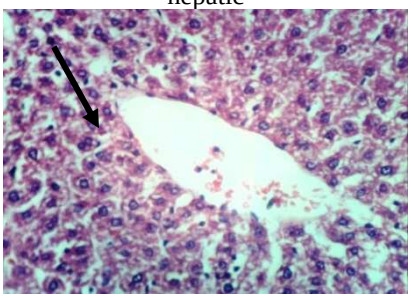


Fig. (8): Liver of rat from group 1 showing activation of Kupffer cells.

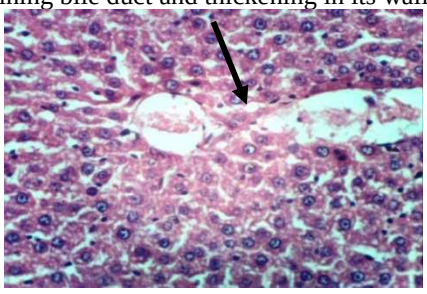


Fig. (9): Liver of rat from group 2 showing slightly slight vacuolization of hepatocytes

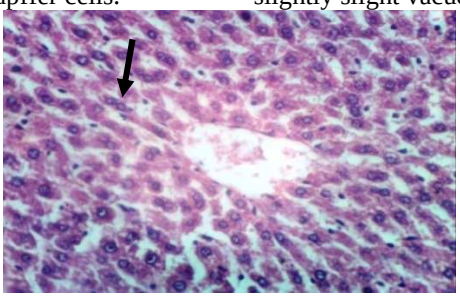


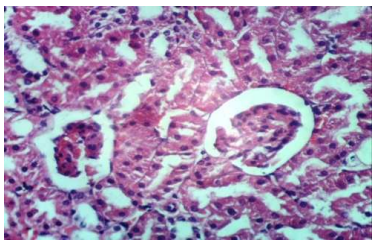
Fig. (10): Liver of rat from group 3 showing slight Activationn of Kupffer cells

Figure (6:10). Morphologic changes of rat heart stained by hematoxylin and eosin using a light microscope (H & E X 400)**.Co. (-)** rat fed standard diet (control), **Co. (+)** high-fat diet; **G (1)**, high-fat diet plus turmeric (4g) ; **G (2)**, high-fat diet plus turmeric (6);**G (3)**, high-fat diet plus turmeric (8g).

3- Morphologic changes of rat kidney stained with hematoxylin and eosin:

Representative kidney sections stained with hematoxylin and eosin in each group are shown in Figure (11:15), kidney of rat in group Co. (+) (Fig.12) showing distension of Bowman's space and focal tubular necrosis

associated with inflammatory cells infiltration, while group 1 (Fig.12) showing congestion of glomerular tufts, the kidney in the control rat of group Co. (-) (Fig. 11) showing the normal histological structure of renal parenchyma, found a similar result in the experimental groups (Fig.14:15) the morphologic features of kidney in the rats of group 2 and 3 were closed to that of the control rats group Co. (-), which indicated a similar preventive effect of turmeric. The histopathology was similar to previous reports **(Thamavit et al. 1987; Boonmars et al. 2007; Boonmars et al. 2008).**



Distension of Fig. (11): Kidney of rat from group Co.(-) showing the normal ahistological structure of renal parenchyma

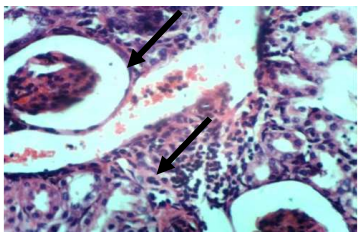


Fig. (12): Kidney of rat from group Co.(+) showing Bowman's space and focal tubular necrosis associated with inflammatory cells infiltration

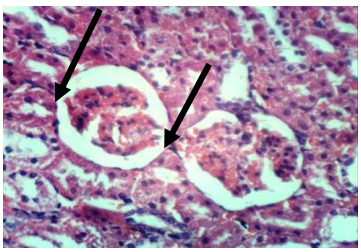


Fig. (13): Kidney of rat from group 1 showing congestion of glomerular tufts.

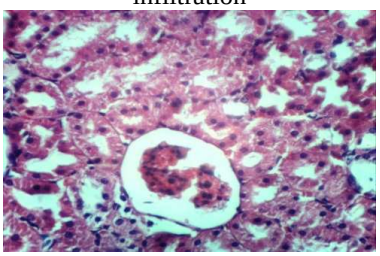


Fig. (14): Kidney of rat from group 2 showing normal renal parenchyma.

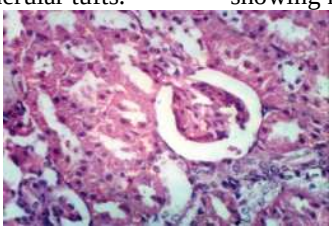


Fig. (15): Kidney of rat from group 3 showing no histopathological changes.

Figure (11:15). Morphologic changes of rat heart stained by hematoxylin and eosin using a light microscope (H & E X 400)**.Co. (-)** rat fed standard diet (control), **Co. (+)** high-fat diet; **G (1)**, high-fat diet plus turmeric (4g) ; **G (2)**, high-fat diet plus turmeric (6g);**G (3)**, high-fat diet plus turmeric (8g).

CONCLUSION

This study shows that curcumin improves insulin level, glucose disposal, and blocks obesity during HFD consumption.our observations confirm that curcumin reduces total cholesterol, triglyceride and LDL cholesterol levels. There is also a tendency that the higher of curcumin dose, the higher its lowering effect on LDL cholesterol level, such as the moderate-dose curcumin. This study demonstrates a tendency of high-dose curcumin to increase the HDL cholesterol level.

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فعالية وسلامة الكركم في خفض مستويات دهون الدم والجلوكوز لدي الفئران المغذاة علي وجبات مرتفعة الدهون

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الملخص العربي

فرط الكركم ينتمي الي المجموعة النباتية curcuma التي تعد جزءًا من عائلة الزنجبيل من الأعشاب ، ويستخدم الكركم في جميع أنحاء العالم كعنصر رئيسي في الكاري ، والتوابل ، و كمصدر للكركمين. يتم استخدامه للأغراض الطبية. تم دراسة تاثير الكركم على مستوى الدهون في الدم والجلوكوز في فئران التجارب مع الإجهاد التأكسدي الخفيف الناجم عن اتباع نظام غذائي عالي الدهون. تم استخدام عدد ٣٠ من فئران التجارب، مقسمة إلى مجموعتين رئيسيتين: الأولى ، المجموعة الضابطةالسالبة (ن = ٦) ، غذيت على الوجبة الغذائيةالاساسية. المجموعة الثانية (ن = ٢٤) تغذت على نظام غذائي غني بالدهون (يحتوي على الوجبةالغذائيةالأساسية + ٥ ٪ دهون البقر + ١ ٪ كوليستيرول + ٠,٠٢ ٪ املاح الصفراء). تم تقسيم هذه المجموعة إلى أربع مجموعات فرعية لكل مجموعة (ن = ٦): المجموعة الضابطة الموجبة غذيت على نظام غذائي غني بالدهون فقط ، المجموعات G (1)، G (2) و G (3) غذيت على نظام غذائي غني بالدهون بالإضافة إلى ٤ و ٦ و ٨ جم كركم / كجم من الوجبةالاساسية على التوالي. بعد ٦ أسابيع تم قياس الكوليسترول الكلي (TC)، و الدهون الثلاثية (TG) ، HDL-C و LDL-C ، بالإضافة إلى مستوى الجلوكوز في الدم و وظائف الكبد والكلى. تم فحص التغيرات الهستوباثولوجية للقلب والكبد والكلى،تم استخدام برنامج SPSS و ANOVA لتحليل النتائج احصائيا. أشارت النتائج إلى أن الكركمين الغذائي منع بشكل كبير من تأثيرالنظام الغذائي عالي الدهونعلى زيادة وزن الجسم ، وكانت أفضل قيمة في G (3)، وكانت أفضل معاملة الكركم (٦ جم و ٨ جم) الذي كان لديه أدنى قيم في الكوليسترول الكلي ، الدهون الثلاثية والكوليسترول الدهني منخفض الكثافة، وأفضل قيم في الكوليسترول الدهني عالي الكثافة وأيضا أفضل تحسن في مستوى الجلوكوز في G (3) مقارنة بالمجموعة الضابطة ، أظهرت النتائج بوضوح أن أفضل معاملة كان الكركم (٨ جم / كجم من الوجبة) الذي أعطىأقل قيم فيوظائف الكبد كما أظهرت النتائج انخفاضا كبيرا فيحمض اليوريك واليوريا لدى المجموعات G2 و G3أعطت الجرعة المعتدلة والأعلى من الكركم بنية نسيجية طبيعية في القلب والكبد والكلى في التغيرات المورفولوجية. في الختام ، أظهرت النتائج أن الكركم كان لديه إمكانات لتخفيف المعاملات المتعلقة بقياسات دهون الدم و وظائف الكبد و الكلى و مستوى سكر الدم في الإجهاد التأكسدي الخفيف الناجم عن اتباع نظام غذائي غني بالدهون للىفئران التجارب.

وتوصي الدراسة بضرورة تناول الكركم لمرضي القلب وتصلب الشراين

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