Biological Study to Evaluate the Protective Effect of Curcumin on Health Problems Associated with High Calorie Diet

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***Abstract*—The aim of the study was to investigate the effects of curcumin on biochemical parameters of male rats. Thirty five rats weighing 82±2 g were divided randomly into five groups. The control negative and positive groups were not being treated with curcumin. The remaining three groups were treated with curcumin by the following doses: 25 mg, 50 mg, and 100 mg /kg b. wt. / day by oral gavage for eight weeks. The results showed that curcumin treatment at dose (100 mg/kg b. wt.) significantly reduced glucose concentration, decrement in total cholesterol (TC), triglycerides (TG) and low-density lipoprotein (LDL) concentration, increment in high-density lipoprotein (HDL) concentration, reduced aspartate aminotransaminase (AST), alanine aminotransaminase (ALT), alkaline phosphatase (ALP) and bilirubin concentration in the serum. The study concluded that Curcumin can be used to overcome some health problems such as diabetes, obesity and cardiovascular diseases.**

***Index Terms*—obesity- curcumin- biological- health problem**

I. Introduction

Obesity rates have been steadily climbing over recent decades, with significant implications for public health. Worldwide obesity has more than doubled since 1980; in 2014, more than 1.9 billion adults were overweight, and of these over 600 million were obese [1]. Obesity is reaching epidemic proportions in the USA, affecting more than one third of the population [2]. Also, "Reference [3]" found that the Middle East and the North Africa region has the highest rates of overweight and obesity populations of the developing world with implications for the global disease burden and local health service capacity.

In addition to its serious health consequences, obesity costs and health-care expenses for obesity related problems of nearly 21% of annual medical spending in the USA are greater than the investment in any other medical condition [4].

Curcumin is a lipophilic agent that is nearly insoluble in water yet quite stable in the acidic pH of the stomach. Furthermore, it has been prized since ancient times for its various pharmacological benefits associated with its antioxidant and anti-inflammatory properties [5].

Curcumin exhibits strong anti-inflammatory, anticancer antioxidant, and activity. Free radicals mediate membrane lipid peroxidation and oxidative damage of DNA and proteins and are believed to be associated with a variety of chronic pathological complications such as cancer, neurodegenerative diseases, aging and atherosclerosis [6].

As a result of life style and food habits of a lot of people to enjoy junk foods, it leads to consume high calories. The excessive calorie consumption has many effects on health problems and in the forefront is overweight and obesity, which automatically results in a number of diseases associated with them such as (diabetes, cancer, high blood pressure, high blood cholesterol, heart disease and hardening of the arteries). So, recent evidence has shown that some dietary components such as spices may play a key role in the protection and treatment of obesity and other related metabolic disorders. Among these spices, turmeric has received considerable research interest because of its active ingredient, curcumin. Curcumin is considered to be safe by The Joint FAO/WHO Expert Committee on Food Additives (JECFA) and the European Food Safety Authority (EFSA) [7]. Hence, the present study aimed to evaluate the protective effects of curcumin on health problems associated with high calorie diet

II. Materials and Methods

Curcumin ($C_{21}H_{20}O_6$) with molecular weight 368.39 and melting point 170-180℃ powder was purchased from EL- Gomhouria Co. for Drugs and Chemicals in Alexandria, Egypt. The doses of curcumin were dissolved in 20 ml polyethylene glycol (PEG) 400 $H(OCH_2CH_2)_n$ OH and 100 ml distilled water. Commercial kits were purchased from Bio-Diagnostic Co. in Cairo, Egypt.

Thirty-five male Wistar strain rats weighing 82±2 g were used in this study. Animals were obtained from the Faculty of Agriculture, Alexandria University, Egypt. The animals were kept under standard healthy laboratory

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conditions (light period of 12 h per day and temperature 27 ±2 ℃). Seven rats were fed on standard diet (Control negative) which consisted of 22% protein, 10% sucrose, 5% soy oil, 2% choline chloride, 1% vitamin mixture, 3.5% salt mixture and 3% fibers and the remainder is corn starch up to 100% and the energy was not less than 3100 Kcal/Kg. Twenty-eight rats were fed on high caloric diet which was prepared as the standard diet and added melted hydrogenated palm oil (Every 1 Kg of standard diet was mixed with 200g of melted hydrogenated palm oil). They were divided randomly into four groups where each group has seven rats as the following: Control positive group was fed on a high calorie diet. The rest of the rats were fed on a high calorie diet and was injected orally by gastric tube with 25, 50 and 75 mg/kg b. wt. curcumin.

Solution concentrations were adjusted weekly based on the animal average weight. Feed and water were available to the animals during the experimental period *ad libitum*.

All experimental protocols were approved by the Animal Experimentation Ethics Committee of the Alexandria University, Egypt for the care and use of laboratory animals (permission number: AU08181231304.

Feed intake and body weight were determined weekly. Feed efficiency ratio will be calculated. At the end of the experimental period (8 weeks), rats were fasted overnight. Then animals were anesthetized with Diethyl ether and sacrificed by decapitation. The blood samples were collected from each rat in serum tubes. Serum was obtained by centrifugation of samples at 5000 rpm for 20 minutes.

Biological evaluation of the different tested diets was carried out by determination of feed intake (FI) and body weight gain% (BWG %) according to [8].

The total feed consumed was calculated by subtracting the remaining food for each animal at the end of each week from that allocated to it at the start of the week. Food wastage was weighted and subtracted. The feed efficiency ratio was calculated according to "Reference [9]".

Serum Total Cholesterol (TC), triglycerides (TG) and high density lipoprotein cholesterol (HDL) were determined according to the method described by "References"[10]-[12]" , respectively. The methods of "Reference [13]" were used to calculate low density lipoproteins cholesterol (LDL) after measuring very low density lipoproteins cholesterol (VLDL) in serum. Serum glucose was measured according to the "Reference [14]". Urea and Creatinine concentrations were measured according to the method of "Reference [15], [16]" respectively. Aspartate aminotransaminase (AST), Alanine aminotransaminase (ALT) and alkaline phosphatase (ALP) activity were assayed by the method of [17, 17 and 18], respectively. Albumin and total bilirubin concentrations in the serum were determined by the method of [19] and [20], respectively. Colorimetric methods of using commercial kits were in accordance with the manufacturer's instructions.

Statistical analysis was carried out using SAS statistical analysis software package [21]. The obtained data were presented as means ± standard Error (SE). Statistical analysis of variance was performed using one-way ANOVA test followed by the least significant difference (LSD) test to locate significance between all treatments. Differences were considered significant at $p<0.05$.

III. Results and Discussion

The changes in final body weight and body weight gain percent (BWG%) in male rats treated with curcumin at different doses (25, 50 and100 mg/kg b. wt.) are presented in Table I. There was a decrease in final body weight in all treated groups with curcumin compared with the control positive group. The results showed that there was a significant change in the final body weight in all treated groups with curcumin, at $P<0.05$ compared with the control positive group.

The reduction in body weight operates by increasing concentration of curcumin. It is clear that the highest reduction was obtained in dose of 100 mg/kg b. wt. curcumin by 23.88% followed by dose of 50 mg/kg b. wt. curcumin by 16.59% then dose of 25 mg/kg b. wt. curcumin by 12.55% when compared with the control positive group. For body weight gain percent, the data showed a significant increase in the positive group compared with negative group. The body weight gain percent in the control negative group, control positive group and the three groups treated with curcumin at doses 25, 50 and 100 mg/kg b. wt. was 145 ± 4.28, 202 ± 9.81, 158 ± 1.74, 152 ± 8.35, 123 ± 3.52, respectively. Administration of curcumin at doses 25, 50 and 100 mg / kg b. wt. significantly decreased the BWG% at $P<0.05$ when compared with the positive group by 21.78%, 24.75%, 39.10%, respectively.

These results are in agreement with those obtained by Hasan [22] who found that the body weight gain in three groups of mice on fed high fat Western style diet containing 21% by weight milk fat, 0.2% cholesterol which were supplemented with curcumin at concentrations 500 mg, 1000 mg and 1500 mg /kg diet for 16 weeks were significantly lower than mice fed on high fat diet only.

A similar result was reported by [23] who found that six-week-old male mice were given a high-fat diet (HFD, 60% calories from fat, 20% calories from protein, 20% calories from carbohydrate). The mice fed with HFD were administered with curcumin (80 and 40 mg/kg/day) for 12 weeks by oral gavage. The results of this study showed that curcumin treatment with dose of (80 mg/ kg) significantly reduced body weight gain by 20.7%.

Curcumin may reduce body weight by inhibiting obesity-driven inflammatory pathways [24]. It has been shown to inhibit activation of the c-Jun N-terminal kinase (JNK) pathway and expression of NFkB p65, thereby downregulating the proinflammatory responses [25]. Also, curcumin may increase the basal metabolic rate, thereby contributing to increased energy expenditure and weight loss [26].

TABLE I. INITIAL BODY WEIGHT (G), FINAL BODY WEIGHT (G) AND BODY WEIGHT GAIN PERCENT (BWG%) IN MALE RATS TREATED WITH CURCUMIN (MEAN ± SE)

Parameters / Experimental groups	Body weight		
	Initial body weight	Final body weight	Body weight gain
Control negative	82.20 ±1.01 [a]	201 ±2.70 [bc]	145 ±4.28 [bc]
Control positive	82.00 ±0.94 [a]	247 ±5.94 [a]	202 ±9.81 [a]
Curcumin (25 mg/kg b. wt.)	83.60 ±0.60 [a]	216 ±2.61 [b]	158 ±1.74 [b]
Curcumin (50 mg/kg b. wt.)	81.80 ±0.96 [a]	206 ±7.35 [bc]	152 ±8.35 [bc]
Curcumin (100 mg/kg b. wt.)	84.40 ±1.02 [a]	188 ±4.67 [c]	123 ±3.52 [c]

Values with different letters within same column are significantly at P<0.05.

TABLE II. FEED INTAKE (FI: G/D) AND FEED EFFICIENCY RATIO (FER) IN MALE RATS TREATED WITH CURCUMIN (MEAN ± SE)

Parameters / Experimental groups	Feed intake	Feed efficiency ratio
Control negative	18.71 ±1.5 [a]	0.014 ±0 .0003 [c]
Control positive	19.97 ±1.7 [a]	0.024 ±0 .0010 [a]
Curcumin (25 mg/kg b. wt.)	15.51 ±1.1 [a]	0.019 ±0 .0003 [b]
Curcumin (50 mg/kg b. wt.)	15.08 ±1.3 [a]	0.018 ±0 .0010 [b]
Curcumin (100 mg/kg b. wt.)	17.13 ±1.2 [a]	0.013 ±0 .0005 [c]

Values with different letters within same column are significantly, at P<0.05

Feed Intake (FI) and feed efficiency ratio (FER) of the different treated male rats are presented in Table II. Data showed that there was no significant change in FI in all treated groups with curcumin, control negative group and control positive group. Data revealed that the feed efficiency ratio in the control negative group, control positive group and the three groups treated with curcumin at doses 25, 50, 100 mg/kg b. wt. was 0.014 ± 0.0003, 0.024 ± 0.0010, 0.019 ± 0.0003, 0.018 ± 0.001, 0.013 ± 0.0005, respectively. The control positive group increased FER than that of the control negative group and its value was the highest one by 45.83%, at P<0.05. Treatment with curcumin at dose of 100 mg/kg b. wt. returned the FER to normal control level, at P<0.05. While treatment with dose 25 mg/kg b. wt. and 50 mg/kg b. wt. curcumin decreased the FER than that of positive control group by 20.83% and 25%, respectively but failed to normalize it, at P<0.05.

These results are in consistence with the results of [27] who revealed that 0.05g/100g curcumin diet for 10 weeks did not affect feed intake and fat pad mass in high-fat–fed hamsters compared with the control group. Also, Shin [28] found that there was no significant change in feed intake in mice which was treated with curcumin at dose 0.02% w.w in a high-cholesterol diet for 18 weeks compared with placebo-treated mice.

These results are in agreement with those obtained by [23] who found that six-week-old male mice were given a high-fat diet (HFD, 60% calories from fat, 20% calories from protein, 20% calories from carbohydrate). The mice fed with HFD were administered with curcumin (80 and 40 mg/ kg/ day) for 12 weeks by oral gavage. The results of this study showed that there was no significant difference in feed intake between all groups treated with curcumin(40 mg/kg and 80 mg/kg) and lovastatin (30 mg/kg) during the experimental period (12 weeks), suggesting that curcumin induced body weight loss was not through the restriction of feed intake.

On the other hand, "Reference [22]" reported that supplementing the high fat diet of mice with curcumin at different concentrations 500 mg, 1000 mg, and 1500 mg/kg diet slightly but significantly increased feed intake relative to high fat diet only.

Table III showed the highest value of TC (147 ±6.65 mg/dl) in male rats which was recorded in the control positive group and the lowest value of TC in male rats was 101 ±5.26 mg/dl and were recorded in the control negative group. The present results revealed that rats treated with all three doses of curcumin showed a significant decrease in TC compared with control positive group, at P<0.05.

The male rats treated with 25 mg/kg b. wt. curcumin recorded the highest level (125 ±3.58 mg/dl) of TG in the control positive group, while the lowest value (86.10 ±4.53 mg/dl) was recorded in the control negative group. There was a significant decrease in TG in 50 mg curcumin group and 100 mg curcumin group, at P<0.05 compared with control positive group [Table III].

The control positive group recorded the lowest value of HDL (29.16 ±1.18 mg/dl), while the rats treated with 100 mg/kg b. wt. curcumin recorded the highest value of HDL (47.83 ±1.62 mg/dl). The 100 mg curcumin group had a significant increase by -64.03%, while the 25 and 50 mg curcumin groups had no significant change, at P<0.05 compared with control positive group in Table III.

Table III showed that the lowest value of LDL (42.87 ±4.69 mg/dl) in 100 mg curcumin group, followed by 47.51 ±4.11 mg/dl in 50 mg curcumin group, then 51.19 ±8.14 mg/dl in 25 mg curcumin group; while the highest value (93.50 ±6.54 mg/dl) was showed in the control positive group. These results reveled that there was a significant decrease in all treated groups, at P<0.05 compared with the control positive group.

The present results in Table III revealed that the control negative group recorded the lowest value of VLDL (18.05 ±1.56 mg/dl), while the control positive group recorded the highest value of VLDL (25.00 ±0.71 mg/dl).

Treatment with curcumin at all three doses 25, 50 and 100 mg/kg b. wt. had no significant decrease, at P<0.05 compared with the control positive group.

TABLE III. SERUM LIPID PROFILE (MG/DL) IN MALE RATS TREATED WITH CURCUMIN (MEAN ± SE)

Parameters / Experimental groups	TC	TG	HDL	LDL	VLDL
Control negative	101 ±5.26^{b}	86.10 ±4.53^{c}	41.16 ±2.32^{ab}	41.81 ±5.20^{b}	18.05 ±1.56^{b}
Control positive	147 ±6.65^{a}	125 ±3.58^{a}	29.16 ±1.18^{b}	93.50 ±6.54^{a}	25.00 ±0.71^{a}
Curcumin (25 mg/kg b. wt.)	115 ±4.11^{b}	111 ±5.00^{ab}	42.79 ±5.65^{ab}	51.19 ±8.14^{b}	21.61 ±1.43^{ab}
Curcumin (50 mg/kg b. wt.)	109 ±1.89^{b}	96.20 ±4.41^{bc}	42.25 ±3.13^{ab}	47.51 ±4.11^{b}	19.90 ±1.44^{ab}
Curcumin (100 mg/kg b. wt.)	110 ±5.10^{b}	99.78 ±4.91^{bc}	47.83 ±1.62^{a}	42.87 ±4.69^{b}	19.21 ±1.87^{ab}

Values with different letters within same column are significantly at P<0.05

"Reference [22]" demonstrated that a significant decrease was found in TC and TG and a significant increase in HDL in the mice group which was supplemented with a high fat diet of mice with curcumin at concentration (1500 mg /kg diet) for 16 weeks compared with the group which was supplemented with high fat diet only, at P<0.05.

These results are in agreement with those obtained by [29] who found that there were significant changes in CH, TC, LDL and HDL between the groups which was treated with 50 mg/kg b. wt. turmeric, 100 mg/kg b. wt. turmeric, 50 mg/kg b. wt. curcumin for 30 days compared with the control negative group.

These results are in consistence with the results of [23] who revealed that Curcumin (40 mg/kg and 80 mg/kg) dramatically reduced serum TC, TG and LDL-C level, but not affect serum HDL-C level compared with the mice of diet induced obesity (DIO) mice after 12 weeks treatment.

Curcumin may inhibit lipid synthesis and storage and stimulate fatty acid degradation. These effects are mediated by regulating the activities of several key enzymes and the expression of transcription factors that regulate lipid metabolism [30]. Curcumin may stimulate fatty acid oxidation by increasing the carnitine palmitoyltransferase-1 mRNA expression [26].

The present results in Table IV showed that curcumin at dose 100 mg/kg b. wt., showed the lowest value (100 ±2.28 mg/dl) of glucose and it is very close to the normal rats (108 ±6.78 mg/dl), followed by dose 50 mg/kg b. wt. curcumin (127 ±3.42 mg/dl), then 25 mg/kg b. wt. curcumin (153 ±10.34 mg/dl). Also, it could be seen that glucose levels decreased by 40.93%, 50.97% and 61.39 % in rats treated with curcumin at doses 25, 50 and 100 mg/kg b. wt., respectively, compared with the glucose level of the control positive group. The groups that received 25, 50 and 100 mg/kg b. wt. curcumin significantly decreased in serum glucose levels, at P<0.05 compared with the control positive group. The glucose levels decreased in a dose-dependent manner. On the other hand, the control positive group significantly increased in glucose levels, at P<0.05 compared with the control negative group.

These results are in consistence with the results of [31] who revealed that blood glucose was significantly decreased in 75% of healthy human volunteers who take 500 mg curcumin capsule twice a day, for 15 days in comparison with the normal value.

These results are in agreement with those obtained by Hasan [22] who found that high fat feeding showed a trend toward increasing blood glucose levels in mice, and supplementing the diet with concentration of curcumin (1500 mg /kg diet) tended to reduce the levels back to those observed in the low fat control group.

The impaired insulin sensitivity seen with obesity is thought to be due to the presence of high concentrations of free fatty acids in plasma and tissues [32]. High levels of pro-inflammatory cytokines in the blood can be seen in insulin resistance associated with obesity and Type 2 diabetes mellitus [33]. The lipid-induced insulin resistance in obesity is mainly due to the free fatty acid-mediated activation of nuclear factor kappa B (NFkB) and other signaling pathways. Activation of the NFkB pathway causes overproduction of tumor necrosis factor alpha (TNF-a) and interleukin (IL)-6 from 3T3-L1 adipocytes. TNF-a and IL-6 can disturb the transcriptional activity of insulin receptors (insulin receptor substrate-1, IRS-1) and protein transporters, such as glucose transporter-4 (GLUT-4). Curcumin may be a good antidiabetic agent because it's role as an NFkB inhibitor is thought to participate in mitigating insulin resistance [25].

Data in Table V showed that urea levels in the control negative group, control positive group and the three groups treated with curcumin at doses 25, 50 and 100 mg/kg b. wt. were 54.01 ±4.43, 50.24 ±3.71, 44.07 ±3.41, 48.74 ±4.63, 44.22 ±4.02 mg/dl, respectively. Data showed that there was no significant change in urea levels in the serum in all groups treated with curcumin, at P<0.05 compared with the control positive group.

Table V showed the highest value of creatinine (0.65 ±0.035 mg/dl) was recorded in the control positive group, while the lowest value (0.55 ±0.020 mg/dl) was recorded in the control negative group. Data revealed that there was no significant decrease in serum creatinine levels in all groups treated with curcumin, at P<0.05 compared with the control positive group.

These results are in consistence with the results of [34] who revealed there was no significant change in urea and creatinine levels in the group which was treated with 100 mg/kg b. wt. curcumin for 8 weeks in male rats compared with the normal control group which received Phosphate buffer saline.

These results are in agreement with those obtained by [29] who found that there were no significant differences in the value of the urea and creatinine levels of the male rats

between the groups which were treated with 50 mg/kg b. wt. turmeric, 100 mg/kg b. wt. turmeric, 50 mg/kg b. wt. curcumin for 30 days compared with the control negative group.

These results are in disagreement with those obtained by [31] who indicated that the levels of creatinine and urea showed a significant decrease in 87% and 68%, respectively in healthy human volunteers who take 500 mg curcumin capsule twice a day, for 15 days comparison with the normal value.

TABLE IV. SERUM GLUCOSE LEVELS (MG/DL) IN MALE RATS TREATED WITH CURCUMIN (MEAN ±SE)

Parameters / Experimental groups	Glucose
Control negative	108±6.78[c]
Control positive	259±9.03[a]
Curcumin (25 mg/kg b. wt.)	153±10.34[b]
Curcumin (50 mg/kg b. wt.)	127±3.42[bc]
Curcumin (100 mg/kg b. wt.)	100±2.28[c]

Values with different letters within same column are significantly at P<0.05

TABLE V. SERUM UREA AND CREATININE LEVELS (MG/DL) IN MALE RATS TREATED WITH CURCUMIN (MEAN ±SE)

Parameters / Experimental groups	Urea	Creatinine
Control negative	54.01±4.43[a]	0.55±0.020[ab]
Control positive	50.24±3.71[a]	0.65±0.035[a]
Curcumin (25 mg/kg b. wt.)	44.07±3.41[a]	0.56±0.020[ab]
Curcumin (50 mg/kg b. wt.)	48.74±4.63[a]	0.57±0.013[ab]
Curcumin (100 mg/kg b. wt.)	44.22±4.02[a]	0.59±0.027[ab]

Values with different letters within same column are significantly at P<0.05.

These results are in disagreement with those obtained by [35] who found that curcumin treatment at dose 200 mg/kg in methotrexate-intoxicated rats significantly decreased in serum creatinine and urea levels compared to methotrexate alone treated rats.

Interleukin-6 has long been highlighted as a pro-inflammatory cytokine associated with renal allograft ejection, while IL-6 levels are low in the serum and urine of healthy individuals [36]. Interleukin-6 is rapidly expressed in a highly transient manner during inflammation [37]. Curcumin may help to reduce the levels of the inflammatory cytokine IL-6 [38].

The obtained results in Table VI demonstrated that the highest value of AST is recorded as 81.60±6.04 U/L in the control positive group, while the lowest levels is recorded as 46.20±2.61 U/L in the group treated with 100 mg/kg b. wt. cucumin. The AST levels decreased in a dose-dependent manner. There was a significant decrease in levels of AST in serum by 28.68%, 39.95%, and 43.38 % in male rats given curcumin at doses 25, 50 and 100 mg/kg b. wt., respectively, compared with the control positive group. There was no significant change in AST between the three groups treated with curcumin. Data showed in Table 6 that the levels of ALT in serum recorded these values of 43.40±1.05, 82.60±2.81, 60.40±1.22, 48.40±0.80, 44.40±1.28 U/L in the control negative group, control positive group and the three groups treated with curcumin at doses 25, 50 and 100 mg/kg b. wt., respectively. The highest decrease was obtained in dose 100 mg/kg b. wt. curcumin by 46.25% followed by dose 50 mg/kg b. wt., curcumin by 41.40%, then dose 25 mg/kg b. wt. curcumin by 26.88% when compared with the control positive group. The result showed that there was a significant change in ALT levels in the serum in all treated groups with curcumin, at P<0.05 compared with the control positive group. There was no significant change in ALT between groups treated with 50 and 100 mg/kg b. wt. curcumin while there was a significant change between group treated with 25 mg/kg b. wt. curcumin and the two other groups treated with curcumin.

Data showed in Table VI that the ALP levels in the serum of the control negative group, control positive group and the three groups treated with curcumin at doses 25, 50 and 100 mg/kg b. wt. were 58.40±0.98, 70.13±1.49, 67.66±1.28, 61.50±1.25, 52.00±1.65 U/L. The control positive group increased in ALP than that of the control negative group and its value was the highest one, at P<0.05. Treatment with curcumin at dose 100 mg returned the ALP less than normal control level, at P<0.05. ALP demonstrated a significant decrease at doses 50 and 100 mg/kg b. wt. compared with the control positive group. ALP had no significant change between the two groups treated with 25 and 50 mg/kg b. wt. curcumin, while had a significant change between groups treated with 100 mg/kg b. wt. curcumin and the two other groups treated with curcumin.

These results are in consistence with the results of Fan [39] who revealed that curcumin decreased serum AST and ALT Levels after intestinal schemia/reperfusion (I/R). Compared with the sham group, AST dramatically increased in I/R group, at P<0.01. Curcumin decreased AST markedly in curcumin treated groups compared with the I/R group, at P<0.01. AST level was decreased by 19% with 1 mg-curcumin group and by 26% with 5 mg-curcumin group compared with the I/R group, respectively.

These results are in agreement with the results of Ahmed [29] who revealed the groups which were treated

with 50 mg/kg b. wt. turmeric, 100 mg/kg b. wt. turmeric, 50 mg/kg b. wt. curcumin for 30 days significantly lowered the AST, ALT and ALP activities in male rats compared with the control positive group.

The protective role of curcumin against liver damage has been predominantly attributed to antioxidant and anti-inflammatory activities [40]. Curcumin is mainly based on the suppression of pro-inflammatory mediators like cyclooxygenase-2 (COX-2), lipooxygenase (LOX), inducible nitric oxide synthase (iNOS or NOS-2), nuclear factor kappa B (NF-κB) [41].

It is clear from the present results in Table VII that the highest value of albumin 4.23±0.21 mg/dl was recorded in 25 mg curcumin group, followed by 4.16±.0.06 mg/dl in negative group, then 4.04±0.20 mg/dl in 100 mg curcumin group; while the 50 mg curcumin group recorded the lowest value of albumin 3.82±0.27mg/dl, followed by 3.96±0.19 mg/dl in the control positive group. Data revealed that treatment with curcumin at all doses did not cause any significant decrease in albumin in the serum, at $P < 0.05$ compared with the control positive group.

Data showed that in Table VII the bilirubin levels in serum of the control negative group, control positive group and the three groups treated with curcumin at doses 25, 50 and 100 mg/kg b. wt. were 0.76±0.05, 1.95±0.13, 1.11±0.04, 0.92±0.04, 0.97±0.02 mg/dl.

It is clear that the highest reduction was obtained in dose 50 mg/kg b. wt. curcumin by 52.82%, followed by dose 100 mg/kg b. wt. curcumin by 50.26%, then dose 25 mg/kg b. wt. curcumin by 43.08% compared with the control positive group. The results showed that there was a significant change in bilirubin levels in the serum of all treated groups with curcumin, at $P < 0.05$ compared with the control positive group.

These results are in agreement with those obtained by Gandhi [31] who indicated that the total bilirubin was also found to be low in 75% of healthy volunteers who were treated with 500 mg/kg curcumin twice daily for 15 days. These results are in consistence with the results of Venkatanarayana [33] who revealed that there was no significant change in albumin level in the group which was treated with 100 mg/kg b. wt. curcumin for 8 weeks in male rats compared with the normal control group which received phosphate buffer saline.

The results revealed that curcumin consumption in small doses had a significant effect on weight reduction and obesity prevention. Curcumin consumption decreased the final body weight, body weight gain%, and feed efficiency ratio. Also, curcumin improved the lipid profile through decreasing total cholesterol, triglycerides, low density lipoprotein and increasing high density lipoprotein in the serum.

The results of this study concluded that curcumin can be used to overcome some health problems such as diabetes, obesity and cardiovascular diseases.

TABLE VI. SERUM AST, ALT AND ALP LEVELS (MG/DL) IN MALE RATS TREATED WITH CURCUMIN (MEAN ±SE)

Parameters / Experimental groups	AST	ALT	ALP
Control negative	45.60±6.12^{b}	43.40±1.05^{c}	58.40±0.98^{c}
Control positive	81.60±6.04^{a}	82.60±2.81^{a}	70.13±1.49^{a}
Curcumin (25 mg/kg b. wt.)	58.20±3.38^{b}	60.40±1.22^{b}	67.66±1.28^{ab}
Curcumin (50 mg/kg b. wt.)	49.00±5.18^{b}	48.40±0.80^{c}	61.50±1.25^{bc}
Curcumin (100 mg/kg b. wt.)	46.20±2.61^{b}	44.40±1.28^{c}	52.00±1.65^{d}

Values with different letters within same column are significantly at P<0.05

TABLE VII. SERUM ALBUMIN AND BILIRUBIN LEVELS (MG/DL) IN MALE RATS TREATED WITH CURCUMIN (MEAN ±SE)

Parameters / Experimental groups	Albumin	Bilirubin
Control negative	4.16±0.06^{a}	0.76±0.05^{c}
Control positive	3.96±0.19^{a}	1.95±0.13^{a}
Curcumin (25 mg/kg b. wt.)	4.23±0.21^{a}	1.11±0.04^{b}
Curcumin (50 mg/kg b. wt.)	3.82±0.27^{a}	0.92±0.04^{bc}
Curcumin (100 mg/kg b. wt.)	4.04±0.20^{a}	0.97±0.02^{bc}

Values with different letters within same column are significantly at P<0.05.

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