Zagazig Veterinary Journal, ©Faculty of Veterinary Medicine,
Zagazig University, 44511, Egypt.
Volume 49, Number 1, p. 114-123, March 2021
DOI: 10.21608/zvjz.2021.50988.1129

RESEARCH ARTICLE

Glutathione Metabolism in Rat Tissue

Medhat M. Fawzy[1], Doaa M. Abdel-Fattah[1], Reham A Ibrahim[2*]

[1]Biochemistry Department, Faculty of Veterinary Medicine, Zagazig University, 44511 Zagazig, Egypt

[2]Environmental Affairs Agency, Ministry of Environment, Zagazig

Article History: Received: 05/03/2021 Received in revised form: 31/03/2021 Accepted: 31/03 /2021

Abstract

The present research was designed to study the positive effect of curcumin and the bad effects of dietary high fat diet (beef tallow) which causes nonalcoholic fatty liver disease, very harmful affecting health, also our study was designed to study the important role of curcumin, against (HFD-induced obesity). Sixty male albino rats weighing(165-170gm), were be obtained from animal house at the Faculty of Veterinary Medicine ,Zagazig University .After acclimatization at 23-25 ^{0}Cand and free availability of water and diet rats were divided into four main groups, each contains 15 rats for 12 weeks.G1(Control),G2(Curcumin),G3(HFD),G4(HFD+cur) .At the end of the experiment, all rats were euthansized and blood collected weekly to biochemical examination during 12 weeks. Our results after statistical analysis revealed that showed that rats Fed on curcumin (3% w/w), had a significant increase in (total glutathione ,GSH, glutathione quotient) and a significant decrease in oxidized glutathione level in hepatic tissue ,a significant increase in the activity of liver glutathione peroxidase and reductase but a significant decrease in the glutathione state in rats fed on beef tallow on G3 (HFD) when compared to the control group .a significant increase in glutathione state in G4(HFD+CUR) when compared to G3(HFD). our results revealed a significant increase in insulin level ,HDL ,and a significant decrease in blood glucose, TAG, total cholesterol ,MDA ,LDL in G2(Curcumin) and (HFD+CUR) but a small significant decrease in total bilirubin in only (HFD+CUR) group when compared to group 3(HFD). A significant decrease in insulin level, HDL-c in G3(HFD)when compared to curcumin group a significant increase in blood glucose, TAG , TC ,LDL-c ,VLDL, MDA, bilirubin in high fat diet .Rats fed on curcumin 3% showed a significant decrease in body weight gain but rats fed on beef tallow revealed a significant increase in body weight.

Key words: Glutathione peroxidase, GR, Curcumin, HFD, NAFLD

Introduction

Glutathione is the master of antioxidants among all tissues because it has an important role in the biological systems such as maintenance of intracellular redox activities, xenobiotic metabolism [1]. Some diseases such as liver damage, cancer, AIDS, leukocyte loss and heart problems result from a decreased level of cellular glutathione [2]. Glutathione oxidized form (GSSG) and the reduced form (GSH) are the two types of glutathione. A glutathione defense mechanism stems from its capacity to react with reactive oxygen species and reactive nitrogen species by acting as a cofactor for various enzymes, including glutathione peroxidases and glutathione S-transferases [3].

Glutathione has a role in prevention the brain from oxidative stress and its regulation synthesis, by limitation thiol amino acids transport in blood brain barrier [4]. Mitochondrial function and survival are dependent on the glutathione system. Due to the presence of a broad array of detoxifying enzymes and antioxidants, mitochondria are the main sites of cellular reactive oxygen species production. In some cells, more than 90% of the total cellular reactive oxygen species in Mitochondria is produced. [5]

Corresponding author e-mail: (rehamalwakeel22@gmail.com), Environmental Affairs Agency, Ministry of Environment, Zagazig

Lipid peroxidation is a biologically significant process that results in unstable intermediate species of oxidized lipids and stable end products serving as mediators of bioactive lipids. Lipid peroxides (LPOs), being more polar than their parent lipids, can disrupt membrane bilayers, affect the structure of the membrane and interfere with intracellular functions. Lipid peroxidation products are mostly self-reactive and either hydroxyl acids or reactive aldehydes [6]. Cells have a vast means of antioxidant and detoxification systems to reduce the level of accumulation lipid peroxide and reactive aldehyde to sub toxic levels. [7].

Nonalcoholic fatty liver disease is accompanied by more fat deposition in hepatocytes, in the absence of significant alcohol intake. It is thought to be the hepatic manifestation of metabolic syndrome and is considered one of the main chronic nutritional consequences. It will progress towards damage to the liver [8]. It is closely related to obesity, blood glucose elevation, hyperlipidemia, insulin resistance and is known to represent a hepatic metabolic syndrome manifestation [9]. Fat accumulation in liver tissue through direct cellular cytotoxicity induced by free fatty acids (FFAs), oxidative stress, lipid peroxidation, liver damage, causing hepatocellular injury. [10-11]**.** In addition, excessive liver fat accumulation destroys mitochondria, which are the key cellular sites for the use of fatty acids [12].

Roots of Curcuma longa represent the main source of turmeric, a yellow spice with a long history of use for dietary and medicinal purposes in Indian and Chinese cultures [13]. Due to the ability of natural plants as curcuma longa to scavenge reactive oxygen species and their safety and less side effects, our study depends on the biological benefit effects. Curcuminoids have strong antioxidant, anti-inflammatory and anti-cancer effects. [14]. The predominant species of curcumin in plasma are represented by its conjugated metabolites (glucuronides and sulfates) and products of reduction reactions represented by (tetrahydro- and hexahydrocurcumin and hexahydrocurcuminol**)** but less effective than the parent compound.These metabolites are believed to be responsible for systemic activity as lowering plasma levels of glucose, cholesterol, triglycerides, anti-obesity effect after curcumin consumption **.** [15]. Curcumin induces the activities of GSH-Px and the level of MDA in mice liver and prevents the liver from oxidative damage. The curcumin treatment revealed a Significant increase of the insulin levels and the decrease of blood glucose, cholesterol, triglycerides, free fatty acids, VLDL, and LDL-c levels in serum of rats by curcumin. The main objective of this experiment was to determine the effects of curcumin supplementation on fat deposition and oxidative stress in the liver of rats with high fat (HF) diet-induced nonalcoholic fatty liver disease.

Material and Methods

Animal management and grouping

A total of sixty healthy adult male albino rats which, weighing at the beginning of the experimental (165-170g) were used in the experimental investigation of this study. These rats were housed in groups of four clean cages with free access to basal diets and water . All animals were acclimatized for minimum period of two weeks prior to the beginning of the study. All procedures were carried out in accordance with the principles of laboratory Animal Care **.**Rats were then randomly and subdivided into 4 groups (each group 15rats) for 12 weeks: ,G1(control),G2(curcumin), fed on curcumin 3%w/w,G3(HFD) ,fed on high fat diet (beef tallow),G4(HFD+ Curcumin) .

The natural plant and its dose

Curcumin was dissolved in corn oil, (almost 10 g curcumin mixed in one liter of corn oil) , then 30 ml of mixture with one kilo of each diet, so, reaching corn oil concentration < 1 percent) and mixed well with the normal diet to reach the final concentration of 3 percent (w/w). This dose showed the most protective effect on (NAFLD). [16].

High Fat Diet composition (beef tallow)

In our experiments, the rats were fed experimental diets for 12 weeks. The experimental diets differed in quality and quantity of fat (table 1), prepared by mixing mineral salts and vitamins to the combinations to ensure that the daily requirements of the animals were achieved according to Longhi *et al*. [17].

Table 1: Chemical composition of the experimental high fat diet (beef tallow) used for 12 weeks.

Ingredient (g/kg)	Experimental diets	
	Control diet	**Beef tallow**
Yellow corn	56	20
Soybean meal, 48%	32.50	32.50
Corn gluten, 60%	5	5
Soybean oil	2	2
Linseed oil	-	-
Hydrogenated oil	-	-
Beef tallow	-	360
Calcium carbonate	2	2
Monocalcium phosphate	1.30	1.30
Common salt	0.30	0.30
Premix[1]	0.30	0.30
Sodium bicarbonate	0.20	0.20
Lysine, HCL, 78%	0.25	0.25
DL-Methionine, 98%	0.15	.15
Calculated composition		
ME, kcal /kg	3047.90	5009.90
Cp, %	23.04	20.27
EE, %	4.56	38.83
CF%	2.33	1.54
Ca, %	1.01	1.00
Available phosphorus, %	0.46	0.43
Lysine, %	1.36	1.27
Methionine, %	0.52	0.46

[1] Muvco premix: Each 2.5kg contain vit . A (10, 000000IU), vit.D3 (2, 000000 IU), vit E (10g), vit. k3(1000mg), vit.B1(1000mg), vit.B2 (5g), vit.B6(1.5g), pantothenic acid (10g), vit.B12(10mg), niacin (30g), folic acid (1000mg), biotin (50g), Fe (30g), Mn (60g), Cu(4g), I(300mg), Co(100mg), Se (100mg) and zn (50gm).

Sampling

Immediately after scarifying, left lobes of liver of albino rats were taken and used for tissue homogenate .1.0g of each sample was homogenized in 9ml of normal saline using electrical homogenizer, centrifuged at 3000

rpmfor 15 minutes, the resulting supernatant was collected and used for estimation of :

Glutathione state, consisted of Total glutathione (Reduced form of glutathione (GSH)- Oxidized form of glutathione (GS.SG)- Glutathione Quotient (GSH:GS.SG), (GPX) peroxidase-(GR) reductase- according to**,** [18-20**]**respectively.

Blood samples

Whole blood was collected from retro-orbital plexus in a test tube, then left to clot un disturbed at room temperature for thirty minutes. Then centrifuging at 2000 rpm for 10 minutes. The separated serum were used to determine the sera TAG, total cholesterol, LDL-cholesterol ,HDL-C,VLDL-C, Serum insulin, blood glucose , Bilirubin, MDA concentration using specific kits specialized for each parameter according to [21-26] respectively.

The rats were individually weighted at the start of experiment and then recorded once each week during experiment for 12 weeks to monitor the changes in weight of each group.

Statistical analysis

For statistical analysis, comparisons between groups were analyzed using one –way analysis of variance (ANOVA).Differences between groups were evaluated by Bonferroni post - test $p<0.05$ was considered statistically significant .The results expressed as means ± SE.The statistic analyzed data were calculated by GraphPad prism8 (GraphPad software Inc., San Diego, 189CA, USA).

Results

The effect of high fat diet and curcumin treatment (3%) for 12 weeks on hepatic glutathione state

Glutathione state corresponding to (hepatic total glutathione, GSH, glutathione quotient, glutathione peroxidase glutathione reductase and shows a significant increase in curcumin group when compared to control group after administration of curcumin 3% w/w for 12 weeks. In the contrast, A significant decrease in hepatic total glutathione, GSH, glutathione quotient, glutathione peroxidase glutathione reductase, in HFD group when compared to control group. These reductions changed by increasing the hepatic total glutathione, GSH, glutathione quotient, glutathione peroxidase glutathione reductase and in (HFD+ Curcumin) group when compared to HFD, (Table 2).

Table 2: Effect of curcumin and high fat diet (beef tallow) on glutathione state in hepatic tissue of rats (µmol/g protein) for 12 weeks

Groups	**Control**	**Curcumin**	**HFD (high fat diet)**	**HFD+ Curcumin**	*P-value*
Total glutathione	61.17 ± 4.11	61.85 ± 5.11	59.92± 4.88	60.22 ± 4.95	3.11
Reduced glutathione (GSH)	47.58 ± 2.36 ^{b}	52.27 ± 3.21 ^{a}	43.12± 3.09 ^{c}	47.51± 2.88 ^{b}	2.99
Oxidized glutathione (GS.SG)	13.59 ± 1.19 ^{b}	9.65 ± 1.32 ^{c}	16.80±2.16 ^{a}	12.71± 2.12 ^{b}	2.11
Glutathione Quotient (GSH/ GS.SG)	3.50 ± 0.87 ^{b}	5.42 ± 0.92 ^{a}	2.57± 1.03 ^{c}	3.74±1.12 ^{b}	1.15

means ±SE in the same row and carrying different superscript are significantly different at $p< 0.05$.

The effect of high fat diet and curcumin treatment (3%) for 12 weeks on blood lipid profile, glucose, insulin levels

The results illustrated in (Table 3) showed that ,feeding curcumin 3% , HFD (beef tallow) resulted in marked decrease TAG, total cholesterol, LDL-C, MDA in curcumin group but an increase of HDL-C, insulin level when compared to control. On the other hand, an increase in serum TAG, total cholesterol,

LDL-C, decrease serum insulin, increase serum glucose, MDA in HFD group when compared to control. A decrease in TAG, total cholesterol, increase serum insulin, decrease serum glucose, bilirubin, MDA.

Table 3: Effect of curcumin 3% w/w and HFD (beef tallow) on biochemical parameters and body weight gain of adult male rats.

Group	control	Curcumin	HFD	HFD+Curcumin	*P- value*
TAG (mg/dL)	99.38 ^{b} ±22.93	93.78^{bc} ±9.53	106.78± 21.18^{a}	89.36 ±7.51 ^{c}	7.12
Total cholesterol (mg/dL)	98.20 ± 6.68^{b}	93.21±7.99 ^{bc}	106.80 ± 7.66^{a}	96.70 ±8.74 ^{bc}	6.15
LDL-C (mg/dL)	40.59 ± 12.04 ^{a}	38.19±11.89 ^{b}	41.05 ± 17.08^{a}	43.27 ± 12.27 ^{a}	4.24
HDL-C (mg/dL)	47.63 ± 2.94	51.33 ± 1.81	49.34 ± 1.82	50.57 ± 3.24	5.12
VLDL-C (mg/dL)	16.23 ± 1.83	16.97 ± 2.65	17.92 ± 2.34	17.70 ± 3.43	2.16
Serum insulin (NIU/mL)	41.0 ± 8.96^{a}	41.67 ± 6.33^{a}	38.33 ± 8.29 ^{b}	42.0 ± 9.17 ^{a}	3.98
Serum glucose (mg/dL)	88.56 ±4.46^{c}	94.25 ± 4.97 ^{bc}	123.69±5.29 ^{a}	103.63 ± 2.05 ^{b}	9.95
Bilirubin (mg/dL)	1.10 ± 0.10^{b}	1.17 ± 0.12 ^{a}	1.20 ± 0.23^{a}	1.17 ± 0.20 ^{a}	.10
Serum MDA (n mol./mL)	103.0 ± 20.60^{b}	99.0 ± 23.44^{bc}	109.0 ± 23.07^{a}	86.67 ± 19.67 ^{c}	5.12
bodyweight gain (g)	266.99 ±19.73 ^{b}	235.96 ± 14.44^{c}	270.94 ±17.52^{a}	266.56 ± 15.29 ^{b}	3.95

Means ±SE in the same row and carrying different superscript are significantly different at $p< 0.05$.

Discussion

In our present work, we study the possible bad effect of nonalcoholic fatty liver disease which results from the dietary fat (high fat diet) beef tallow and the protective effect of curcumin and its role against nonalcoholic fatty liver disease. The oxidative stress in hepatic tissue, biochemical parameters in serum and the gain of body weight were measured in adult male albino rats. Non-alcoholic fatty liver disease involves a broad clinical range of liver defects associated with fat accumulation in the liver in the absence of inherited metabolic disorders or exposure to harmful substances, including alcohol. [27].

Over nutrition of fatty acids caused obesity that promotes the production of reactive oxygen species (ROS), and NAFLD can be encouraged by high hepati ROS levels which suffers a decrease in the activity of the antioxidant enzymes and concentrations of glutathione associated with an increase in the levels of lipid peroxides,(LPO) [28].

Glutathione protects cells from oxidative stress and xenobiotic. For maintaining antioxidant defense, both in detoxifying pathways and in redox signaling, the glutathione quotient (GSH: GSSG ratio) is fundamental. It protect the cells and prevent producing amounts of hydrogen peroxides and lipid hydroperoxide during oxidative stress [29] . GSSG is produced when the glutathione peroxidase-mediated detoxification takes place, and the GSH can be denovo synthesis via glutathione reductase (from GSSG). Enzymatic and nonenzymatic antioxidants work together through their properties as free radical scavengers to prevent ROS-induced oxidative injury to cells [30]

The level of cellular GSH and GSH synthesis induced by the activity of GCL (glutamyl cysteinyl ligase) gene expression, a rate limiting enzyme in GSH synthesis by

curcumin administration[31]. Several previous studies proved that curcumin has the ability to induce glutathione. Our results are comparable to Bulku et al. [32] who reported a potent antioxidant effect for curcumin and the ability of curcumin to induce antioxidant enzymes and GSH formation

On the other hand the high fat diet (beef tallow) leads to increase lipid peroxidation and a reduction in glutathione state. The results of the present study revealed depletion in GSH level of, (beef tallow group) in the liver of rat and administration of curcumin replenishes intracellular GSH. By increasing the content of hepatic glutathione, curcumin reduces oxidative stress, leading to a reduction in the level of lipid hydroperoxide. These findings support our results [33].

HFD-fed rats showed a significant decrease in tissue antioxidant enzymes and an increase serum lipid profiles , hyperglycemia and lipid peroxidation (MDA). Our results agree with who proved that high-fat diets caused non-alcoholic hepatic steatosis (as first stage of NAFLD), which is characterized by an excessive accumulation of triacylglycerol (TAG) within hepatocytes causing hyper-lipidaemia [34,35]. A strong increase in total cholesterol, LDL and VLDL levels was observed in the high fat diet.

Curcumin upregulates LDL receptor expression and increases the uptake activity of LDL receptors, causing an increase of cholesterol clearance from the body, also curcumin can suppress hepatic cholesterol biosynthesis and has an inhibitory effect on HMG-CoA reductase activity [36,37]. Curcumin lowers the fatty acid synthesis oxidation ratio, (through stimulating a fatty acid oxidizing enzyme) and (acyl-CoA oxidase). The hypolipidemic effect of curcumin was previously reported [38, 39]

Previous reports showed that curcumin can increase insulin level after administration dietary curcumin that increases adiponectin expression and adiponectin has been found to enhance insulin sensitivity and decrease insulin resistance by decreasing triglyceride content in muscle and liver in obese mice. Adiponectin increases FA oxidation in liver and improves insulin sensitivity, and decreases glucose production, resulting in decreased circulating FFAs and TAG and glucose levels in blood [40] .our results shows that curcumin increase insulin level but feeding high fat diet (beef tallow) reduces insulin level and increases glucose level.

By inducing, heat-shock protein 70 a reaction protein, and HO-1, which induces an increase in insulin level, curcumin treatment improves the recovery of pancreatic islet cells**.** [41].

Our results show an increase in the bilirubin level in the HFD (beef tallow) after 12 weeks as a comparison with the control group. The observed elevation in the serum total bilirubin in high fat diet group is also in covenant with findings of Okechukwu et al. [42] that mentioned HFD caused hepatic damage, (infiltration).

In our study there is no significant difference in bilirubin level in curcumin group, we also agree with [43] who confirmed that curcumin did not change serum bilirubin. On the other hand, serum bilirubin levels decreased in the (curcumin +HFD) group as a protective effectiveness of curcumin dose. This settles with who indicated that curcumin can do a significant decrease in bilirubin level, A slight reduction in bilirubin level after administration of curcumin [44].

Our results go in hand with those who mentioned that curcumin decreased lipid peroxidation and serum MDA levels [45].Also our results approve with who demonstrated that curcumin plays a role in fatty liver treatment, by suppressing the formation of MDA and maintaining the status of intracellular antioxidants by inducing upregulation of GSH. [46]

The body weight (gain) of rats increased by HFD, but curcumin reduced it .Our results are in the same line to those who observed that Curcumin was also ,associated with a small but significant decrease in body weight gain and fat content, (Foxo1) and (adiponectin)

expression in adipose tissue, increased and higher circulating adiponectin levels cause free fatty acid oxidation by Curcumin . Curcumin feeding suppressed the dyslipidemic mice's body weight gain without altering food intake. [47].

Conclusion

From all the above obtained results, it can be concluded that feeding high fat diet disrupts the normal metabolic state in the body and resulted in marked increase in the body weight, serum glucose, lipid profile, malondialdhyde, total bilirubin and reduction in glutathione state but feeding in the diet containing (curcumin 3%),improves all the previous parameters and protects against obesity.

Conflict of interest

The authors have no conflict of interest to declare.

References

[1] Wu, B.Y.; Wang, C. W.; Chen, P. C.; Chang, H. T. (2017): Glutathione assisted preparation of gold nanoclusters using minimum amount of protiens, Sens. Actuators B Chem. 238: 1258-1265

[2] Zaidi, S.A. and Shin, J.H. (2016): A review on the latest developments in nanostructure-based electrochemical sensors for glutathione, (Minireview) Anal. Methods. 8(8): 1745-1754

[3] Marí, M.; Morales, A.; Colell, A.; García-Ruiz, C.; Fernández-Checa, J.C. (2009): Mitochondrial glutathione, a key survival antioxidant. Antioxid. Redox Signal. 11 (11): 2685–700.

[4] Valdovinos-Flores, C. and Gonsebatt, M.E. (2012): The role of amino acid transporters in GSH synthesis in the blood-brain barrier and central nervous system. Neurochem. Int. 61(3):405-14

[5] Balaban RS, Nemoto S, Finkel T (2005): Mitochondria, oxidants, and aging. Cell 120 (4): 483–95.

[6] Wong-Ekkabut, J.; Xu, Z.; Triampo, W.; Tang, I.M.; Tieleman, D.P.; Monticelli, L. (2007): Effect of lipid peroxidation on the properties of lipid bilayers: a molecular dynamics study. Biophys. J. 93(12): 4225-4236.

[7] Gaschler, M. M. and Stockwell, B. R. (2017): Lipid peroxidation in cell death. Biochem. Biophys. Res. Commun. 482(3): 419-425

[8] Schrader, C.; Schiborr, C.; Frank, J.; Rimbach, G. (2011): Curcumin induces paraoxonase 1 in cultured hepatocytes in vitro but not in mouse liver in vivo. Br. J. Nutr. 105(2): 167–170.

[9] Sanyal, A.J. (2002): AGA technical review on nonalcoholic fatty liver disease. Gastroenterology 123(5): 1705-1725.

[10] Fabbrini, E.; Sullivan, S.; Klein, S. (2010): Obesity and nonalcoholic fatty liver disease: biochemical, metabolic, and clinical implications. Hepatology 51(2): 679-689.

[11] Tilg, H. and Moschen, A.R. (2010): Evolution of inflammation in nonalcoholic fatty liver disease: the multiple parallel hits hypothesis. Hepatology 52(5): 1836-1846

[12] Wang, S.; Kama, T.A.; Pergola, P.; Swamy, A.; Tio, F.; Cusi, K. (2011): Metabolic factors in the development of hepatic steatosis and altered mitochondrial gene expression in vivo. Metabolism 60(8): 1090-1099.

[13] Hatcher, H.; Planalp, R.; Cho, J.; Torti, F.M.; Torti, S.V. (2008): Curcumin: from ancient medicine to current clinical trials. Cell Mol Life Sci 65 (11): 1631–1652.

[14] Shishodia, S.; Sethi, G.; Aggarwal, B.B. (2005): Curcumin: getting back to the roots. Ann NY Acad. Sci., 1056 (1): 206-217.

[15] Basnet, P.; Skalko-Basnet, N. (2011): Curcumin:An anti-inflammatory molecule from a curry spice on the path to cancer treatment. Molecules 16(6): 4567–4598.

[16] Weisberg S.P.; Leibel, R.; Tortoriello D.V. (2008): Dietary curcumin significantly improves obesity-associated inflammation and diabetes in mouse models of diabesity. Endocrinology 149 (7): 3549-3558.

[17] Longhi, R.; Almeida, R.F.; Machado, L.; Duarte, M.M.M.F; Souza, D.G.; Machado, P.; de Assis, A.M.; Quincozes-Santos, A.; Souza, D.O. (2017): Effect of a trans fatty acids enriched diet on biochemical and inflammatory parameters in wistar rats. Eur. J. Nutr. 56(3): 1003-1016

[18] Gross, R.T.; Bracci, R.; Rudolph, N.; Schroeder, E.; Kochen, J.A. (1967): Hydrogen peroxide toxicity and detoxification in the erythrocytes of newborn infants. Blood, 29: 481-493.

[19] Goldberg, D.M. and Spooner, R.J. (1983): In Methods of Enzymatic Analysis, Bergmeyen, H.V.(Ed.),3rd edn verlog chemie, Deerfield beach,FI 3: 258-265.

[20] Halaas, J.L.; Gajiwala, K.S.; Maffei, M.; Cohen, S.L.; Chait, B.T.; Rabinowitz, D.; Lallone, R.L.; Burley, S.K.; Friedman, J.M. (1995): Weight-reducing effects of the plasma protein encoded by the obese gene. Science, 269(5223): 543-546.

[21] Mashek, D.G.; Li, L.O.; Coleman, R.A. (2007): Long-chain acyl-CoA synthetases and fatty acid channeling. Future Lipidol. 2(4): 465-476.

[22] U.K. (2011): Highly Accurate direct Clearance method for LDL cholesterol from Randox.

[23] Matas, C.; Cabre, M.; La Ville, A.; Prats, E.; Joven, J.; Turner, P.R.; Masana, L.; Camps, J. (1994): Limitations of the Friedewald formula for estimating low-density lipoprotein cholesterol in alcoholics with liver disease. Clin. Chem. 40(3): 404-406.

[24] Shimomura, I.; Matsuda, M.; Hammer, R. E.; Bashmakov, Y.; Brown, M. S.; Goldstein, J. L. (2000): Decreased IRS-2 and increased SREBP-1c lead to mixed insulin resistance and sensitivity in livers of lipodystrophic and ob/ob mice. Mol. Cell. 6(1): 77-86.

[25] Pyorala, K. (1979): Relationship of glucose tolerance and plasma insulin to the incidence of coronary heart disease: results from two population studies in Finland. Diabetes Care:2(2):131-141

[26] Draper, H.H.; Hadley, M. (1990): [43] Malondialdehyde determination as index of lipid Peroxidation. Methods Enzymol. 186: 421-431.

[27] Shah, J.; Okubote, T.; Alkhouri, N. (2018): Overview of updated practice guidelines for pediatric nonalcoholic fatty liver disease. Gastroenterol. Hepatol. 14(7): 407.

[28] Fang, Y. L.; Chen, H.; Wang, C. L.; Liang, L. (2018): Pathogenesis of non-alcoholic fatty liver disease in children and adolescence: From "two hit theory" to "multiple hit model". World J. Gastroenterol. 24(27): 2974.

[29] Damiani, E.; Brugè, F.; Cirilli, I.; Marcheggiani, F.; Olivieri, F.; Armeni, T.; Cianfruglia, L.; Giuliani, A.; Orlando, P.; Tiano, L. (2018): Modulation of oxidative status by normoxia and hypoxia on cultures of human dermal fibroblasts: how does it affect cell aging?. Oxid. Med. Cell Longev. Volume 2018, Article ID 5469159, 15 pages0

[30] Abdollahi, M.; Ranjbar, A.; Shadnia, S.; Nikfar, S.; Rezaiee, A. (2004): Pesticides and oxidative stress: a review. Med. Sci. Monit. 10(6): RA141-RA147.

[31] Zheng, S. and Chen, A. (2007): De novo synthesis of glutathione is a prerequisite for curcumin to inhibit hepatic stellate cell (HSC) activation. Free radic. Bio. Med. 43:444-453

[32] Bulku, E., J; Stohs, S.; Cicero, L.; Brooks, T.; Halley, H.D Ray, S. (2012): Curcumin exposure modulates multiple pro-apoptotic and anti-apoptotic signaling pathways to antagonize acetaminophen-induced toxicity. Curr. Neurovasc. Res. 9(1): 58-71.

[33] Kuo, J. J.; Chang, H. H.; Tsai, T. H.; Lee, T. Y. (2012): Positive effect of curcumin on inflammation and mitochondrial dysfunction in obese mice with liver steatosis. Int. J. Mol. Med. 30 (3): 673-679.

[34] Kalaivani, A.; Vadivukkarasi, S.; Uddandrao, V.S.; Saravanan, G. (2020): Attenuation of Obesity-Associated Oxidative Stress by Cucurbita maxima Seed Oil in High Fat Diet-Induced Obese Rats. In Pathophysiology of Obesity-Induced Health Complications (pp. 305-316). Springer, Cham.

[35] Madkhali, H. A. (2020): Morin attenuates high-fat diet induced-obesity related vascular endothelial dysfunction in Wistar albino rats. Saudi Pharm. J. 28(3): 300-307.

[36] Tai, M. H.; Chen, P. K.; Chen, P. Y.; Wu, M. J.; Ho, C. T.; Yen, J. H. (2014): Curcumin enhances cell-surface LDLR level and promotes LDL uptake through downregulation of PCSK9 gene expression in HepG2 cells. Mol. Nutr. food. Res.58(11): 2133-2145.

[37] Shin, S.K.; Ha, T.Y.; McGregor, R.A.; Choi, M.S. (2011): Long-term curcumin administration protects against atherosclerosis via hepatic regulation of lipoprotein cholesterol metabolism. Mol. Nutr. Food Res. 55: 1829–1840.

[38] Shao, W. and Espenshade, P. J. (2012): Expanding roles for SREBP in metabolism. Cell Metab. 16(4): 414-419.

[39] Guo, C.; Ma, J.; Zhong, Q.; Zhao, M.; Hu, T.; Chen, T.; Qiu, L.; Wen, L. (2017): Curcumin improves alcoholic fatty liver by inhibiting fatty acid biosynthesis. Toxicol. Appl. Pharmacol. 328: 1-9.

[40] Yamauchi, T.; Kamon, J.; Waki, H.; Terauchi, Y.; Kubota, N.; Hara, K.; Mori, Y.; Ide, T.; Murakami, K.; Tsuboyama-Kasaoka, N.; Ezaki, O. (2001): The fat-derived hormone adiponectin reverses insulin resistance associated with both lipoatrophy and obesity. Nat. Med. 7(8): 941-946.

[41] Kanitkar, M.; Gokhale, K.; Galande, S.; Bhonde, R.R. (2008): Novel role of curcumin in the prevention of cytokine-induced islet death in vitro and diabetogenesis in vivo. Br. J. Pharmacol. 155(5): 702-713.

[42] Okechukwu, G.N.; Nweke, O.B.; Nwafor, A.J.; Godson, A.G.; Kenneth, E.U.; Ibegbu, A.O. (2019: Beta (β)-carotene-induced effects on the hepato-biochemical parameters in wistar rats fed dietary fats. Jordan J. Biol. Sci, 12: 283-288.

[43] Kim, S.W.; Ha, K.C.; Choi, E.K.; Jung, S.Y.; Kim, M.G.; Kwon, D.Y.; Yang, H.J.; Kim, M.J.; Kang, H.J.; Back, H.I.; Kim, S.Y. (2013): The effectiveness of fermented turmeric powder in subjects with elevated alanine transaminase levels: a randomised controlled study. BMC Complement. Altern. Med. 13(1): 1-8.

[44] Nouri-Vaskeh, M.; Malek Mahdavi, A.; Afshan, H.; Alizadeh, L.; Zarei, M. (2020): Effect of curcumin supplementation on disease severity in patients with liver cirrhosis: A randomized controlled trial. Phytother. Res. 34(6): 1446-1454.

[45] Mrudula, T.; Suryanarayana, P.; Srinivas, P.; Reddy, G. B. (2007): Effect of curcumin on hyperglycemia-induced vascular endothelial growth factor expression in streptozotocin induced diabetic rat retina. Biochem. Biophys. Res. Commun. 361(2): 528-532.

[46] Inzaugarat, M.E.; De Matteo, E.; Baz, P.; Lucero, D.; García, C.C.; Gonzalez Ballerga, E.; Daruich, J., Sorda, J.A.; Wald, M.R.; Cherñavsky, A.C., (2017): New evidence for the therapeutic potential of curcumin to treat nonalcoholic fatty liver disease in humans. PLoS One, 12(3): p.e0172900.

[47] Himesh, S.; Sharan, P. S.; Mishra, K.; Govind, N.; Singhai, A. K. (2011): Qualitative and quantitative profile of curcumin from ethanolic extract of *Curcuma longa*. Int Res J Pharm, 2(4): 180-184.

الملخص العربي

ايض الجلوتاثيون في أنسجة الجرذان

مدحت فوزي، دعاء عبدالفتاح، ريهام ابراهيم

[1]قسم الكيمياء الحيويه-كليه الطب البيطري-جامعه الزقازيق-44511-مصر

[2]جهاز شئون البيئة-وزارة البيئة-الزقازيق

يعتبر الكركومين مهم لأنشطة مضادات الأكسدة ووقاية الكبد. من أهم العوامل التي تعتبر مسؤولة عن كل نشاط الكركمين في قدرته على التخلص من الشوارد الحرة والتفاعل معها مثل الأكسجين التفاعلي والشوارد الحرة للنيتروجين.. كفاءة الكركومين وسلامة استخدامه دوائيا تجعله مركبًا محتملًا للعلاج والوقاية من مجموعة واسعة من الأمراض التي تصيب الإنسان. يمكن أن يؤدي النظام الغذائي عالي الدهون إلى زيادة إنتاج أنواع الأكسجين التفاعلية وتقليل مضادات الأكسدة مما يؤدي إلى تلف الكبد مما يؤدي إلى أكسدة الدهون لتدمير البنية الداخلية وتغيير نفاذية خلايا الكبد. وقد اجريت الدراسة الحالية لدراسة التأثير الوقائي للكركمين والآثار السيئة للنظام الغذائي الغني بالدهون (شحم البقر) الذي يسبب مرض الكبد الدهني غير الكحولي وهو ضار للغاية لانه يؤثر على الصحة ،ولذلك اجريت التجربة علي عدد 60ذكرا من الجرذان وتم تقسيمهم في اربع مجموعات وهم الكنترول ومجموعة الكركومين ومجموعة تتغذي علي نظام غذائي عالي الدهون (الشحم البقري) ومجموعة الدهون العالية +الكركومين يحتوي كل منهم علي عدد 15جرذا تزن حوالي مابين (165-170) جم واستمرت التجربة 12 اسبوعا وأدت تغذية الجرذان علي علائق عالية الدهون الي انخفاض ملحوظ في الجلوتاثيون الكلي الكبدي وانزيمات الجلوتاثيون الاوكسيديز والجلوتاثيون الريدكتيزفي الكبد بينما التغذية علي الكركومين نتجت زيادة ملحوظة في تلك القياسات بالمقارنه بالكنترول . وايضا زيادة ملحوظة في الدهون الكلية والكوليسترول الكلي وارتفاع سكر الدم و البليروبين والمالدونالدهيد في المصل في حالة المجموعة التي تغذت علي الدهون العاليه(الشحم البقري)بينما أدت النتائج الي أنخفاض ملحوظ في تلك القياسات في مجموعات الكوركومين.زيادة وزن الجسم في الجرذان التي تغذت علي الدهون العاليه وفي المقابل انخفاض في وزن الجسم في الجرذان التي تغذت علي الكركومين