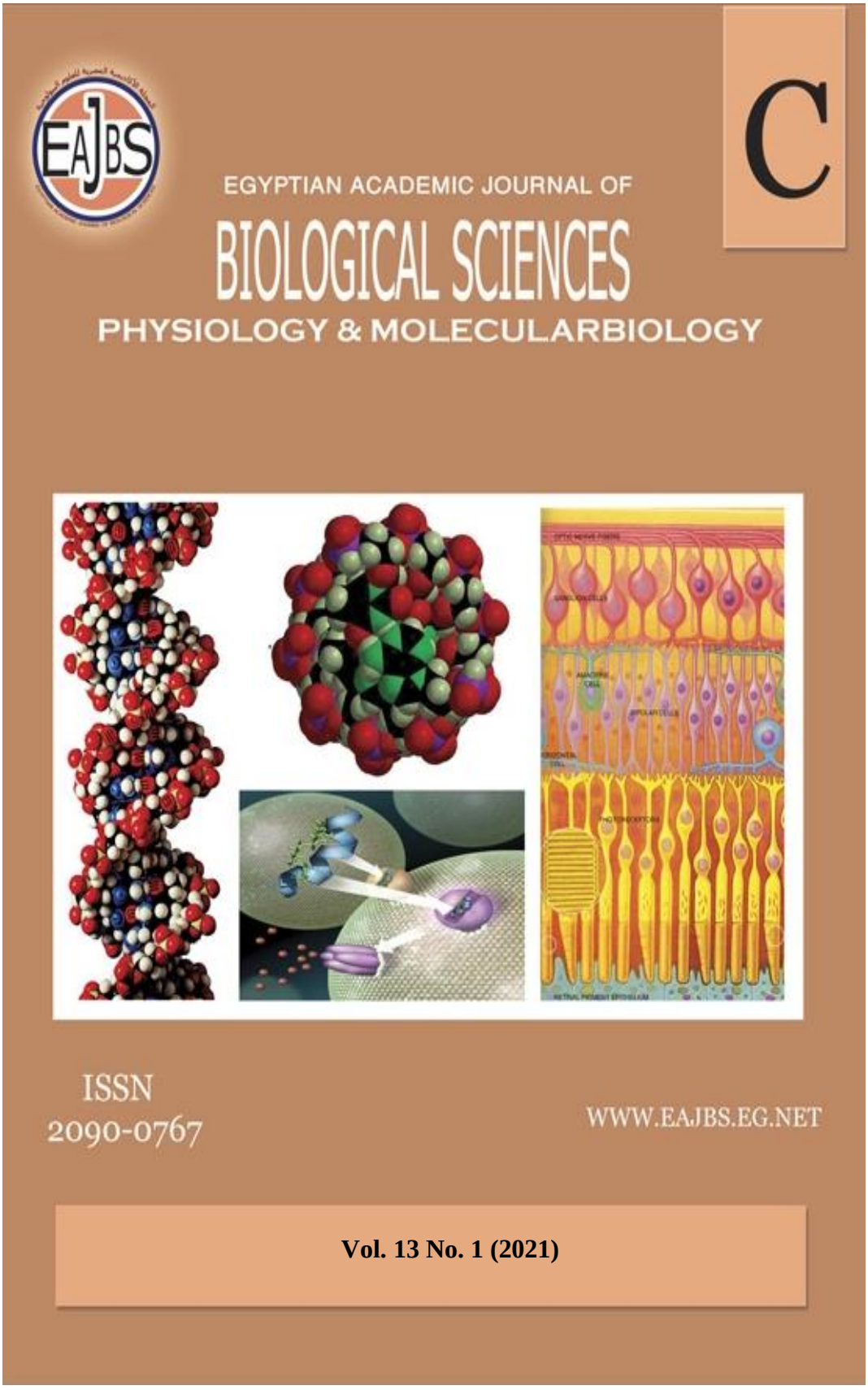

.

Citation: *Egypt.Acad.J.Biolog.Sci. (C.Physiology and Molecular biology) Vol. 13(1) pp183-188 (2021)*
DOI: 10.21608/EAJBSC.2021.184621

Egypt. Acad. J. Biolog. Sci., 13(1):183-188 (2021)

Egyptian Academic Journal of Biological Sciences

C. Physiology & Molecular Biology

ISSN 2090-0767

www.eajbsc.journals.ekb.eg

Protective Effect of Curcumin on Lipid Profile in Rats Intoxicated by Cyclophosphamide

Fatma Khairallah Ali[1], Ahmed Mohamed[2] and Ahmed A. M. Hassan[2]

1- Lecturer at Chemistry Department, Benghazi University, Almarj city, Libya.

2- Biochemistry Department, Faculty of Science, Al-Azhar University, Egypt.

E.mail*: fatma198573@yahoo.com

ARTICLE INFO

Article History

Received:13/4/2021

Accepted:22/6/2021

Keywords:

Cyclophosphamide, curcumin, lipid profile and rats.

ABSTRACT

The present study was carried out to evaluate the protective effects of curcumin on Cyclophosphamide-induced deleterious lipid profile in rats. Experimental rats were randomly divided into four groups of five rats each. Group 1: served as the control rats, Group 2: was administered daily curcumin at a dose (150 mg/kg b.wt). Group 3: a single dose of cyclophosphamide (150 mg/kg, i.p.) intraperitoneal injection, Group 4: was injected with cyclophosphamide + curcumin along the experimental period (30 days). The results refer to a significant elevation of lipid parameters (cholesterol, triglyceride and LDL-C) while a significant decrease in some other parameters (HDL-C). On the 30 days in rats injected intraperitoneal with cyclophosphamide as compared to the control groups. The administration of the curcumin has beneficial and decrease side effects against the deleterious changes of CCl_4. Concluded that supplementation of curcumin reverted these abnormalities in the lipid levels to near normalcy after cyclophosphamide administration.

INTRODUCTION

Disorders have been identified as a common side effect of treatment with chemotherapeutic agents such as cyclophosphamide, 5-fluorouracil, methotrexate, and doxorubicin (Schagen and Wefel 2013).

Cyclophosphamide is an alkylating chemotherapeutic agent, and it has extensive use for adjuvant or neoadjuvant purposes in the treatment of hematological malignancies, neuroblastoma, retinoblastoma, rhabdomyosarcoma, breast, lung, endometrium and ovarian cancers. Despite its frequent use, catastrophic side effects on the genitourinary, reproductive, and gastrointestinal system organs are still not preventable today (Yilmaz *et al.,* 2018).

The use of natural antioxidants in order to minimize the side effects of chemotherapeutic agents such as Cyclophosphamide has increased in recent years. Curcumin is the most prominent of these. Curcumin is derived from "Curcuma longa". Its homeland is East India and is defined as "the queen of spices". It includes natural polyphenol derivatives, gives a yellow color to natural turmeric plants, has antioxidant, anti-inflammatory, and apoptosis-inducing features and naturally inhibits cancer cell proliferation (Kreutz *et al.,* 2018).

Curcumin (diferuloylmethane) [1,7-bis(4-hydroxy-3-methoxyphenyl)-1,6-heptadiene-3,5-dione] is the principal component of the turmeric pigment of Curcuma longa which is commonly used as a spice and food-coloring agent (Ammon and Wahl 1991). in preclinical animal models, curcumin has shown antioxidant (Ak and Gülçin 2008), antidiabetic (Meghana *et al.,* 2007), antineoplastic (Yoysungnoen *et al.,* 2008) and anti-inflammatory (Jacob *et al.,* 2007) properties.

Because of its anti-inflammatory, antioxidant, and other potentially protective properties (Maheshwari *et al.,* 2006), curcumin has been tested in animal models of Alzheimer's disease (AD), with favorable results (Lim *et al.,* 2001). Curcumin decreased total plasma cholesterol in studies of mice, rats, and rabbits (Arafa 2005). In human subjects, oral administration of 0.5 g/day of curcumin for 1 week decreased total serum cholesterol by 12% and increased HDL cholesterol by 29% (Jacob *et al.,* 2007).

MATERIALS AND METHODS

24 male Wister albino rats' averaged weights (210±10 g) were conducted in accordance with the criteria of the investigations and Ethics Committee of the Community Laws governing the use of experimental animals. The rats obtained from the Egyptian Holding Company for Biological Products and Vaccines were used as experimental animals. The rats were placed in regularly designed cages and maintained in conditions of good ventilation, normal temperatures, and humidity range. Five rats were placed into each cage. Food and water were provided *ad-libitum* to the animals.

The rats were classified into main four groups as follow: Group 1: Normal control, Group II: Rats treated orally with curcumin in dose (150 mg/kg) suspended in olive oil daily, Group III Rats injected intraperitoneal with cyclophosphamide (150 mg/kg, i.p.) a single dose (Arafa 2009). Group IV Rats injected with cyclophosphamide and treated orally with curcumin daily. All treatments were given for 30 days. The sign of toxicity was recorded daily during the experimental period. Each group contains 6 rats, rats were anesthetized and sacrificed after the 30 days for biochemical parameters.

Biochemical Parameters:

The levels of cholesterol, triglyceride, low-density lipoprotein-cholesterol (LDL-C) and high-density lipoprotein-cholesterol (HDL-C) in serum were estimated spectrophotometrically using commercial diagnostic kits, Serum cholesterol concentration was determined according to the method of (Allain *et al.,* 1974); Serum triglyceride level was determined according to the method described by (Fossati and Prencipe 1982) and Serum LDL-C level was determined according to the method described by (Wieland and Seidel 1982)and Serum HDL-C level was determined according to the method described by (Burstein *et al.,* 1970) using a commercial kit purchased from Bio-diagnostic Company Egypt.

Statistical Analysis:

The statistical package for social sciences SPSS/PC computer program (version 19) was used for statistical analysis of the results. Data were analyzed using a one-way analysis of variance (ANOVA). The data were expressed as mean ± S.E. Differences were considered statistically significant at ($P < 0.05$).

RESULTS

The groups treated with cyclophosphamide recorded significantly ($p < 0.05$) elevated serum cholesterol, triglyceride and LDL-C levels while a significant decrease in some other parameters (HDL-C) when compared to the control group after 30 days. On the other hand, insignificant differences with recorded in curcumin when compared to control groups. Rats treated with cyclophosphamide + curcumin observed a significant decrease ($p < 0.05$) in serum cholesterol, triglyceride and LDL-C levels

and a significant increase in some other parameters (HDL-C) when compared with cyclophosphamide groups after 30 days. As shown in Tables (1, 2, 3 and 4).

Table 1: Serum cholesterol concentration (mg/dL) in adult male albino rats subjected to Cyclophosphamide and treated with Curcumin for 30 days.

	Cholesterol	
Groups	30 days	
Control	Mean± S.E	94.60±1.7[a]
Curcumin	Mean± S.E	94.40±1.9[a]
	%	-0.21
Cyclophosphamide	Mean± S.E	176.00±3.5[b]
	%	86.05
Cyclophosphamide + Curcumin	Mean± S.E	132.20±1.5[c]
	%	39.7

Each value represented means of 6 records ± S.E.
[a,b,c] means comparison between all groups which the groups have the same letter mean there is no significance difference, and which have different letter mean there is a significance change. %: Percent of changes from control values.

Table 2: Serum Triglyceride concentration (mg/dL) in adult male albino rats subjected to Cyclophosphamide and treated with Curcumin for 30 days.

	Triglyceride	
Groups	30 days	
Control	Mean± S.E	74.60±1.9[a]
Curcumin	Mean± S.E	73.80±0.5a
	%	-1.1
Cyclophosphamide	Mean± S.E	125.40±2.0[b]
	%	68.1
Cyclophosphamide + Curcumin	Mean± S.E	96.80±1.9[c]
	%	29.8

Each value represented means of 6 records ± S.E.
[a,b,c] means comparison between all groups in which the groups have the same letter means
there is no significant difference and which have different letter mean there is a significant change. %: Percent of changes from control values.

Table 3: Serum LDL-Cholesterol concentration (mg/dL) in adult male albino rats subjected to Cyclophosphamide and treated with Curcumin for 30 days.

	LDL-C	
Groups	30 days	
Control	Mean± S.E	19.68±2.2[a]
Curcumin	Mean± S.E	17.64±0.9[a]
	%	-10.4
Cyclophosphamide	Mean± S.E	116.92±4.7[b]
	%	494.1
Cyclophosphamide + Curcumin	Mean± S.E	68.44±2.7[c]
	%	247.8

Each value represented means of 6 records ± S.E.
[a,b,c] means comparison between all groups in which the groups have the same letter means
there is no significant difference, and which have different letter mean there is a significant change. %: Percent of changes from control values.

Table 4: Serum HDL-Cholesterol concentration (mg/dL) in adult male albino rats subjected to Cyclophosphamide and treated with Curcumin for 30 days.

	HDL-C	
Groups	30 days	
Control	Mean± S.E	60.00±1.0[a]
Curcumin	Mean± S.E	62.00±1.2[a]
	%	3.3
Cyclophosphamide	Mean± S.E	34.00±1.8[b]
	%	-43.3
Cyclophosphamide + Curcumin	Mean± S.E	44.40±2.0[c]
	%	-26.0

Each value represented means of 6 records ± S.E.
[a,b,c] means comparison between all groups which the groups have the same letter mean there is no significance difference and which have different letter mean there is a significance change. %: Percent of changes from control values.

DISCUSSION

The present study was conducted to evaluate the effect of the curcumin against Cyclophosphamide induced disorders in the lipid profile of rats.

In this study, we examined the effects of curcumin against redox imbalance and alterations in biomolecules associated with lipid profile in rats treated with cyclophosphamide. The obtained data showed a significant increase in serum cholesterol, triglyceride and LDL-C levels while a significant decrease in some other parameters (HDL-C). in Cyclophosphamide, and Cyclophosphamide + curcumin groups when compared to the corresponding values in the control group because the administration of Cyclophosphamide leads to an increase in biosynthesis and decrease in its utilization. Cyclophosphamide induces free radicals (Lee *et al.,* 1996), which may cause cellular cholesterol accumulation, (a) by increasing cholesterol biosynthesis and its esterification, (b) by decreasing cholesteryl ester hydrolysis and (c) by reducing cholesterol efflux (Gesquière *et al.*, 1999). The conversion of cholesterol to bile acids is quantitatively the most important mechanism for the degradation of cholesterol. However, (McClure and Stupans 1992) previously reported that after 7 days following a single dose of cyclophosphamide (200 mg/kg body weight) there was a decrease in cytochrome P450 activity in male rats, which may, in turn, depress cholesterol 7-hydroxylase activity, the key enzyme in the conversion of cholesterol to bile acids. A decline in the cardiac phospholipid content with a concomitant increase in the serum could be due to the peroxidation of unsaturated membrane lipids by free radicals in biomembranes and tissues causing the leakage of these lipids into circulation (Muralikrishnan *et al.*, 2001)

Cyclophosphamide treatment resulted in elevated serum lipids and lipoprotein fractions. Abnormal activities of lipid metabolizing enzymes contributed to these hyperlipidemic changes induced by cyclophosphamide (Mythili *et al.*, 2006).

Cholesterol and phosholipids are carried in plasma by lipoproteins, which are synthesized and secreted by the intestine and liver. VLDL and HDL are secreted from the liver into the bloodstream.

The obtained data showed a significant decrease in serum cholesterol, triglyceride and LDL-C in Cyclophosphamide + curcumin groups while a significant increase in some other parameters (HDL-C) when compared to the corresponding values in Cyclophosphamide group due to curcumin prevented increases in serum cholesterol concentrations in the animal studies by inhibiting dietary cholesterol absorption (Arafa 2005). Some of the biological

activities exerted by curcumin include antioxidant, anticancer, anti-inflammatory, anti-angiogenic, anti-hyperglycemic, and anti-rheumatic activities ((Maheshwari *et al.*, 2006); (Anand *et al.*, 2008).

These results agree with Arafa 2005 which recorded that Curcumin decreased the total plasma lipid profile in studies of mice, rats, and rabbits.

In human subjects, oral administration of 0.5 g/day of curcumin for 1 week decreased total serum cholesterol by 12% and increased HDL cholesterol by 29%. Therefore, curcumin might serve as a cholesterol-lowering drug. As part of a double-blind, placebo-controlled, randomized trial of curcumin for possible treatment of Alzheimer's disease (Soni and Kutian 1992).

REFERENCES

Ak, T. and I. Gülçin.(2008).Antioxidant and radical scavenging properties of curcumin.*Chemical Biology Interact*,174.(1):27-37.

Allain, C. C., L. S. Poon, C. S. Chan, W. Richmond and P. C. Fu.(1974). Enzymatic determination of total serum cholesterol.*Clinical Chemistry*,20.(4):470-475.

Ammon, H. P. and M. A. Wahl. (1991).Pharmacology of Curcuma longa.Planta Medica.57.(1):1-7.

Anand, P., S. G. Thomas, A. B. Kunnumakkara, C. Sundaram, K. B. Harikumar.(2008).Biological activities of curcumin and its analogues (Congeners) made by man and Mother Nature. *Biochemical Pharmacology*, 76.(11):590-611.

Arafa, H. M.(2005).Curcumin attenuates dietinduced hypercholesterolemia in rats.*Medical Science Monitor*, 11.(7):Br228-234.

Arafa, H. M.(2009).Uroprotective effects of curcumin in cyclophosphamide-induced haemorrhagic cystitis paradigm. *Basic Clinical Pharmacology and Toxicoloyg*,104.(5):393-399.

Burstein, M., H. R. Scholnick and R. Morfin.(1970).Rapid method for the isolation of lipoproteins from human serum by precipitation with polyanions.*Journal of Lipid Researches*,*11*.(6):583-595.

Fossati, P. and L. Prencipe.(1982).Serum triglycerides determined colorimetrically with an enzyme that produces hydrogen peroxide. *Clinical Chemistry*,28.(10):2077-2080.

Gesquière, L., N. Loreau, A. Minnich, J. Davignon and D. Blache. (1999).Oxidative stress leads to cholesterol accumulation in vascular smooth muscle cells. *Free Radical Biology & Medicine*,27.(1-2):134-145.

Jacob, A., R. Wu, M. Zhou and P. Wang.(2007).Mechanism of the Anti-inflammatory Effect of Curcumin:PPAR-gamma Activation.PPAR Resches. (5): 893-69.

Kreutz, D., C. Sinthuvanich, A. Bileck, L. Janker, B. Muqaku. (2018). Curcumin exerts its antitumor effects in a context dependent fashion.*Journal of Proteomics*, 182:65-72.

Lee, C. K., G. S. Harman, R. J. Hohl and R. D. Gingrich.(1996).Fatal cyclophosphamide cardiomyopathy: its clinical course and treatment.*Bone Marrow Transplant*,18.(3):573-577.

Lim, G. P., T. Chu, F. Yang, W. Beech, S. A. Frautschy.(2001).The curry spice curcumin reduces oxidative damage and amyloid pathology in an Alzheimer transgenic mouse.*Journal of Neuroscience*, 21.(21):8370-8377.

Maheshwari, R. K., A. K. Singh, J. Gaddipati and R. C. Srimal.(2006).Multiple biological activities of curcumin: a short

review.*Life Sciences, 78*.(18): 2081-2087.

Maheshwari, R. K., A. K. Singh, J. Gaddipati and R. C. Srimal.(2006).Multiple biological activities of curcumin: a short review.*Life Sciences,*78.(18): 2081- 2087.

McClure, M. T. and I. Stupans.(1992).Investigation of the mechanism by which cyclophosphamide alters cytochrome P450 in male rats.*Biochemical Pharmacology,* 43.(12):2655-2658.

Meghana, K., G. Sanjeev and B. Ramesh.(2007).Curcumin prevents streptozotocin-induced islet damage by scavenging free radicals: a prophylactic and protective role.*European Journal of Pharmacology,*577.(1-3):183-191.

Muralikrishnan, G., V. Amalan Stanley and K. Sadasivan Pillai. (2001).Dual role of vitamin C on lipid profile and combined application of cyclophosphamide, methotrexate and 5-fluorouracil treatment in fibrosarcoma-bearing rats.*Cancer Letters,*169.(2):115-120.

Mythili, Y., P. T. Sudharsan, V. Sudhahar and P. Varalakshmi.(2006). Protective effect of DL-alpha-lipoic acid on cyclophosphamide induced hyperlipidemic cardiomyopathy.*European Journal of Pharmacology,*543.(1-3):92-96.

Schagen, S. B. and J. S. Wefel. (2013). Chemotherapy-related changes in cognitive functioning.*European Journal of Cancer Supplements* ,11.(2):225-232.

Soni, K. and R. Kutian.(1992).Effecf of oral curcumin administranon on serum peroxides and cholesterol levels in human volunteers.*Indian Journal of Physiology and Pharmacology,*36.(4):273-275.

Wieland, H. and D. Seidel. (1982). Improved assessment of plasma lipoprotein patterns. IV. Simple preparation of a lyophilized control serum containing intact human plasma lipoproteins. *Clinical Chemistry*, 28.(6):1335-1337.

Yilmaz, E., R. Melekoglu, O. Ciftci, S. Eraslan, A. Cetin.(2018).The therapeutic effects of curcumin and capsaicin against cyclophosphamide side effects on the uterus in rats. *Acta Cirúrgica Brasileira,*33.(6):499-507.

Yoysungnoen, P., P. Wirachwong, C. Changtam, A. Suksamrarn and S. Patumraj.(2008)."Anti-cancer and anti-angiogenic effects of curcumin and tetrahydrocurcumin on implanted hepatocellular carcinoma in nude mice.*World Journal of Gastroenterology*, 14.(13):2003-2009.