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

Fatma Khairallah Ali¹, Ahmed Mohamed² and Ahmed A. M. Hassan²
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 CCl₄. 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 I: 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 cyclophosphamid 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-diagnostics 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 cyclophosphamid 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 cyclophosphamid + 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.

<table>
<thead>
<tr>
<th>Groups</th>
<th>Cholesterol</th>
<th>30 days</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>Mean± S.E</td>
<td>94.60±1.7a</td>
</tr>
<tr>
<td>Curcumin</td>
<td>Mean± S.E</td>
<td>94.40±1.9a</td>
</tr>
<tr>
<td>Cyclophosphamide</td>
<td>Mean± S.E</td>
<td>176.00±3.5b</td>
</tr>
<tr>
<td>Cyclophosphamide + Curcumin</td>
<td>Mean± S.E</td>
<td>132.20±1.5c</td>
</tr>
</tbody>
</table>

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.

<table>
<thead>
<tr>
<th>Groups</th>
<th>Triglyceride</th>
<th>30 days</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>Mean± S.E</td>
<td>74.60±1.9a</td>
</tr>
<tr>
<td>Curcumin</td>
<td>Mean± S.E</td>
<td>73.80±0.5a</td>
</tr>
<tr>
<td>Cyclophosphamide</td>
<td>Mean± S.E</td>
<td>125.40±2.0b</td>
</tr>
<tr>
<td>Cyclophosphamide + Curcumin</td>
<td>Mean± S.E</td>
<td>96.80±1.9c</td>
</tr>
</tbody>
</table>

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.

<table>
<thead>
<tr>
<th>Groups</th>
<th>LDL-C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>Mean± S.E</td>
</tr>
<tr>
<td>Curcumin</td>
<td>Mean± S.E</td>
</tr>
<tr>
<td>Cyclophosphamide</td>
<td>Mean± S.E</td>
</tr>
<tr>
<td>Cyclophosphamide + Curcumin</td>
<td>Mean± S.E</td>
</tr>
</tbody>
</table>

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.

<table>
<thead>
<tr>
<th>Groups</th>
<th>HDL-C</th>
<th>30 days</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>Mean± S.E</td>
<td>60.00±1.0a</td>
</tr>
<tr>
<td>Curcumin</td>
<td>Mean± S.E</td>
<td>62.00±1.2a</td>
</tr>
<tr>
<td>Cyclophosphamide</td>
<td>Mean± S.E</td>
<td>34.00±1.8b</td>
</tr>
<tr>
<td>Cyclophosphamide + Curcumin</td>
<td>Mean± S.E</td>
<td>44.40±2.0c</td>
</tr>
</tbody>
</table>

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


