HEPATOPROTECTIVE EFFECT OF SILYMARIN IN CYCLOSPORINE-INDUCED OXIDATIVE STRESSED MALE RATS

Mohammad A. A. Alozy[*], Jabbar A. A. Al-Sa'aidi[**], Jassim M. AlKalby[***]

[*]Department of Physiology, College of Dentistry, University of Al-Muthanah, Al-Muthanah, Iraq.

[**]Depaertment of Physiology and Pharmacology, College of Veterinary Medicine, University of Al-Qadisiyah, Al-Qadisiyah Iraq.

[***] Department of Physiology, Pharmacology and Chemistry, College of Veterinary Medicine,University of Basrah, Basrah, Iraq.

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Corresponding Author: jabbaralsadi@qu.edu.iq.

ABSTRACT

The present study aimed to quantify the hepatic ameliorating potency of silymarin in oxidative stressed male rats induce by cyclosporine. One hundred and twenty adult male rats were equally allocated to control and three treated groups. Control (C) were drenched with drinking water, whereas treatment groups were drenched with silymarin silymarin (200 mg/kg bw), cyclosporine (5mg/kg/day) and combined of cyclosporine and silymarine (5mg/kg/day) and silymarin (200 mg/kg bw). Animals treated for 30 days and left without treatment for 15 days. Each group were allocated to three subgroups (10 each), were sacrificed after 15, 30 and 45 of the experiment. After each treatment period, body weight and liver weight were measured. Blood samples were obtained for assessment of serum concentrations of glucose, cholesterol, malondialdehyde, alanine aminotransferase, aspartate aminotransferase and alkaline phosphatase. Liver samples were obtained for histopathological examination. The results revealed a significant increase of blood biochemical parameters in cyclosporine treated group, whereas both of silymarin treated groups showed values close to control group. Liver tissue sections of cyclosporine treated group male rats showed dilation of central vein, disarrangement of hepatic cords, degeneration and necrosis of hepatocytes, expansion of sinusoids and

congestion of central vein, whereas silymarin and combination treatment showed normal hepatic cords, mild degenerative hepatocytes and congestion of central vein. The biochemical and histopathological changes were duration dependent. In conclusion, silymarin treatment in combination with cyclosporine has hepatic an ameliorating effect.

INTRODUCTION

Oxidative stress is the most common result of toxicity, since they may affect many fundamental aspects of body functions such as cellular respiration, lipid metabolism, and immunological responses (1). The increased release of reactive oxygen species during oxidative stress is normally neutralized by different kinds of non-enzymatic antioxidants and enzyme systems such as superoxide dismutase peroxidase, catalase and glutathione reductase to protect the integrity of cells or tissues (2). Cyclosporine, as an effective immunosuppressive agent, is a metabolite isolated from *Cylindrocarpon lucidum* and *Tolypocladium inflatum* (3). Cyclosporine has been broadly used in transplant medicine and it has evidently improved implant survival rates in organ transplantation (4). Although cyclosporine has been successfully used in the treatment of several autoimmune disorders (5,6), its therapeutic application is accompanied by numerous side effects including hepatic, renal, cardiac, neural, alimentary, and reproductive toxicity (7-10). Silymarin is a flavonoid with efficient antioxidant activity has been isolated from the milk thistle *Silybum marianum* seeds. Silymarin has been reported to protect against hepatotoxicity induced by many different agents (11-16). The present study aimed to quantify the ameliorating potency of silymarin in hepatic oxidative stressed male rats induces by cyclosporine.

MATERIALS AND METHODS

Experimental animals: Mature male Sprague-Dawley rats were used in the present experiment. Animals were fed on the standard chow and drinking water *ad libitum* throughout the experimental periods. Room temperature was maintained at 22 ± 2°C, the light-dark cycle was

on a 12:12 h with light on at 06:00 a.m and off at 06:00 p.m throughout the experimental period.

Experimental design: After acclimatization for one week, 120 adult male rats were allocated to four equal groups. Control (C) group male rats were drenched with drinking water. Silymarin treated (Sil) were drenched with silymarin (200 mg/kg bw), suspended in 0.5 ml of drinking water. Cyclosporine treated (Cyc) were drenched with cyclosporine (5mg/kg/day). Combined treatment of cyclosporine and silymarine (Sil+Cyc) were drenched with cyclosporine (5mg/kg/day) and silymarin (200 mg/kg bw). Male rats were treated for 30 days. Each group were allocated to three subgroups (10 each), subgroup 1 were sacrificed after 15 days of treatment, subgroup 2 were sacrificed after 30 days of treatment, and subgroup 3 were treated for 30 days and left without treatment for further 15 days and sacrificed at day 45 of the experiment. After each treatment period, body weight and liver weight were measured. Blood samples were obtained for assessment of serum concentrations of glucose, cholesterol, MDA, ALP, ALT and AST. Liver samples were obtained for histopathological examination.

Blood glucose assessment: Blood glucose was measured using GLUCOSE MRR kit (Cromatest, Spain).

Determination of total serum cholesterol: The procedure was described by Richmond (17).

Assessment of MDA: The procedure was described by Buege and Aust (18).

Assessment of ALP, ALT and AST concentration: Assessment has been performed by using the colorimetric method of Reitman and Frankel (19).

Histological study: According to Luna (20), histological sections have been prepared from pancreas, liver, and kidneys, stained, and examined under light microscope.

Statistical Analysis:

All values were expressed as mean ± SD. Comparisons were performed using one way analysis of variance (ANOVAI) and Newman- Keuls to test all groups' unpaired values. Differences were considered to be significant at the level of $P<0.05$. All statistical analysis was carried out using the GraphPad Prism 5 (SAS Institute, Inc., USA).

RESULTS

Body weight: The results revealed a significant increase ($p<0.05$) of body weight gain in control, silymarin treated (Syl) and combination of silymarin and cyclosporine treated (Syl+Cic) groups started after 15 days and continued after 30 and 45 days periods, whereas cyclosporine treated group (Cic) revealed no significant differences ($p>0.05$) among treatment periods. In comparison between groups for each period, Syl group male rats recorded the highest elevation ($p<0.05$) of body weight gain among experimental groups at all experimental periods, whereas Cic group male rats recorded the lowest elevation ($p<0.05$) among experimental groups at all experimental periods. On the other hand, Syl+Cic group male rats decreased significantly ($p<0.05$) than control male rats at 15 day period of treatment, but it showed a significant increase ($p<0.05$) than control at 30 days treatment period and no significant changes ($p>0.05$) at 45 days treatment period (Table 1).

Liver weight: As illustrated in table (1), Cic and Syl+Cic group male rats, revealed a significant elevation ($p<0.05$) of liver weight among experimental groups, at all treated periods, whereas Syl group male rats showed no significant changes ($p>0.05$) in comparison with control group male rats, at all treated periods. In comparison between periods for each group, Cic group male rats recorded elevated liver weight at 30 days period which showed further increase at 45 days period, whereas Syl+Cic group male rats showed significant decline ($p<0.05$) of their liver weight at 45 gays period. On the other hand, neither control nor Syl group male rats showed any significant changes ($p>0.05$) in comparison between treated periods.

Glucose concentration: In comparison with control, Syl group male rats showed a significant decline ($p<0.05$) of serum glucose concentration at 15 and 30 days periods and no significant changes ($p>0.05$) at 45 days treatment period, whereas Cic group male rats recorded a significant elevation ($p<0.05$) among other experimental groups at all treatment periods, while Syl+Cic group male rats showed a significant) elevation ($p<0.05$) at 15 and 30 days periods but returned to the control level at 45 days period. In comparison between periods, Syl group male rats showed no significant difference ($p>0.05$) between 15 and 30 days periods but significantly elevated ($p<0.05$) at 45 days period. Cic group male rats recorded a significant increase ($p<0.05$) at 30 days period compared with 15 days period, and significantly decreased ($p<0.05$)

at 45 days period, whereas Syl+Cic group male rats showed no significant difference ($p>0.05$) between 15 and 30 days periods and a significant decreased ($p<0.05$) at 45 days period (Table 1).

Cholesterol concentration: As illustrated in table (1), Syl group male rats showed a significant decline of serum cholesterol concentration compared with control male rats at 15 and 30 days periods ($p<0.05$) and no significant changes ($p>0.05$) at 45 days treatment period, whereas Cic group male rats recorded a significant ($p<0.05$) elevation among other experimental groups at all treatment periods, while Syl+Cic group male rats showed no significant changes ($p>0.05$) compared with control at all treatment periods. In comparison between periods, Syl group male rats showed no significant difference ($p>0.05$) between 15 and 30 days periods but significantly elevated ($p<0.05$) at 45 days period. Cic group male rats recorded no significant changes ($p>0.05$) between 15 and 30 days periods but significantly decreased ($p<0.05$) at 45 days period, whereas Syl+Cic group male rats showed no significant difference ($p>0.05$) between at treatment periods.

Malondialdehyde (MDA) concentration: As illustrated in table (1), control, Syl and Syl+Cic groups male rats showed no significant difference ($p>0.05$) of serum MDA concentration when compared with each other at all treatment periods, whereas Cic group male rats recorded significant elevation ($p<0.05$) at 15 and 30 days periods but returned to control level at 45 days period. In comparison between periods for each group, control, Syl and Syl+Cic groups male rats showed no significant difference between ($p>0.05$) treatment periods, whereas Cic group male rats recorded significant elevation ($p<0.05$) at 30 days period compared with 15 days period, but significantly decreased ($p<0.05$) at 45 days period compared with 15 and 30 days period.

Serum ALT concentration: Serum ALT concentration of Syl group male rats revealed no significant ($p>0.05$) difference compared with control male rats at all treatment periods. In contrast, Cic group male rats showed significant elevation ($p<0.05$) among experimental groups at all treatment periods, whereas Syl+Cic group male rats recorded significant elevation ($p<0.05$) than control male rats at 15 and 30 days of treatment period, but showed no significant changes ($p>0.05$) at 45 days period. In comparison between periods for each group, Syl group male rats recorded no significant changes ($p>0.05$) among treatment periods, whereas Cic group male rats showed significant ($p<0.05$) increase at 30 days period but recorded significant decrease ($p<0.05$) at 45 days period in comparison with 15 days period. Syl+Cic group male rats showed

no significant changes ($p>0.05$) in comparison between 15 and 30 days periods but significantly decreased ($p<0.05$) at 45 days period (Table 1).

Serum AST concentration: As compared with control, Syl and Syl+Cic groups male rats showed no significant difference ($p>0.05$)of serum AST concentration at all treatment periods, whereas Cic group male rats recorded significant elevation ($p<0.05$) at all of the treatment periods. In comparison between periods for each group, control, Syl and Syl+Cic groups male rats showed no significant difference ($p>0.05$) between all treatment periods, whereas Cic group male rats recorded significant increase ($p<0.05$) at 30 days period compared with 15 days period, and significantly decreased ($p<0.05$) at 45 days period (Table 1).

Serum ALP concentration: The results illustrated in table (1) recorded no significant differences ($p>0.05$) of serum alkaline phosphatase (ALP) concentration between control, Syl and Syl+Cic groups male rats, whereas Cic group male rats recorded significant elevation ($p<0.05$) at 15 and 30 days treatment periods and no significant difference ($p>0.05$) at 45 days treatment period in comparison with other experimental groups. In comparison between periods for each group, control, Syl and Syl+Cic groups male rats showed no significant difference ($p>0.05$) between all treatment periods, whereas Cic group male rats recorded significant increase ($p<0.05$) at 30 days period compared with 15 days period, and significantly decreased ($p<0.05$) at 45 days period.

Histopathological changes of liver: As observed in liver tissue sections obtained from control group male rats (Figure 1-C), sylimarin treated group male rats (Figure 1-Syl.) revealed normal architecture of hepatic tissue after 15 days of treatment, in terms of the normal size of central vein which surrounded by delineated hepatic cords with progress proliferation of hepatocytes which are permeated by hepatic sinusoids and Kupffer cells. Cyclosporine treated group male rats liver sections (figure 1-Cic) showed dilation of central vein, disarrangement of hepatic cords, degeneration and necrosis of hepatocytes, expansion of sinusoids and congestion of central vein. Combination of sylimarin and cyclosporine treated group male rats sections (Figure 1-Syl+Cic) showed normal hepatic cords, mild degenerative hepatocytes and congestion of central vein.

After 30 days of treatment, sylimarin treated group male rats liver sections (Figure 2-Syl) showed progress proliferation of hepatocytes arranged in well delineated hepatic cords around central vein as compared with liver sections obtained from control group male rats at the same period (figure 2-C). Cyclosporine treated group male rats liver sections (Figure 2-Cic) showed

more sever histopathological changes represented by sever degenerative and necrotic hepatocytes, disarrangement of hepatic cords, expansion of sinusoids, decreased number of Kupffer cells, distributed macrophages and engorgement of central veins. Combination of sylimarin and cyclosporine treated male rat section (Figure 2-Syl+Cic) showed normal hepatic cords, mild degenerative and necrotic hepatocytes, decreased number of Kupffer cells and sever congestion of central veins.

In liver sections obtained from male rats of the studied experimental groups which have been treated for 30 days and left without treatment until 45 days, control (Figure 3-C) and sylimarin treated groups male rats sections (Figure 3-Syl) showed normal architecture of hepatic tissue with progress proliferation of hepatic tissue of sylimarin treated groups male rats. Cyclosporine treated group male rats sections (Figure 3-Cic) still showed disarrangement of hepatic cords, degeneration and necrosis of hepatocytes, expansion of sinusoids and congestion of central vein. Combination of sylimarin and cyclosporine treated group male rats sections (Figure 3-Syl+Cic) showed normal hepatic cords and hepatocytes.

Table 1: Effect of silymarin on body weight gain, liver weight, blood biochemical parameters and liver function test in cyclosporine treated male rats.

Parameters		Periods	Groups			
Body weight gain (g)		15 d	15.8 ± 1.874 Bc	22.8 ± 2.860 Ac	5.4 ± 3.062 Da	9.80 ± 0.632 Cc
		30 d	18.6 ± 1.838 Cb	36.0 ± 3.651 Ab	3.8 ± 1.751 Da	22.8 ± 3.910 Bb
		45 d	29.9 ± 2.331 Ba	46.4 ± 5.038 Aa	7.3 ± 3.466 Ca	31.9 ± 2.807 Ba
Liver weight (g/100g bw)		15 d	4.68 ± 0.168 Ca	4.72 ± 0.118 Ca	6.18 ± 0.099 Ab	5.59 ± 0.054 Ba
		30 d	4.77 ± 0.402 Ca	4,61 ± 0.223 Ca	6.39 ± 0.069 Ab	5.76 ± 0.271 Ba
		45 d	4.38 ± 0.352 Ca	4.59 ± 0.217 Ca	6.77 ± 0.195 Aa	4.98 ± 0.221 Bb
Blood biochemistry	Glucose conc. (mg/dL)	15 d	117.0 ± 14.2 Ca	91.00 ± 11.3 Db	279.0 ± 16.2 Ab	145.0 ± 10.2 Ba
		30 d	116.0 ± 10.3 Ca	93.00 ± 12.3 Db	355.0 ± 14.2 Aa	150.0 ± 12.3 Ba
		45 d	117.0 ± 13.2 Ba	115.0 ± 12.3 Ba	175.0 ± 18.1 Ac	121.0 ± 14.2 Bb
	Cholesterol conc. (mg/dL)	15 d	71.70 ± 7.18 Ba	61.00 ± 5.29 Cb	112.0 ± 10.2 Aa	71.00 ± 7.23 Ba
		30 d	71.30 ± 6.26 Ba	65.00 ± 5.26 Cb	116.0 ± 9.23 Aa	72.00 ± 6.24 Ba
		45 d	72.00 ± 6.17 Ba	73.00± 5.28 Ba	96.00 ± 8.19 Ab	72.00 ± 6.19 Ba
	MDA conc (nmole/L)	15 d	1.650 ± 0.18 Ba	1.620 ± 0.29 Ba	2.410 ± 0.19 Ab	1.730 ± 0.23 Ba
		30 d	1.680 ± 0.26 Ba	1.710 ± 0.26 Ba	2.730 ± 0.23 Aa	1.780 ± 0.24 Ba
		45 d	1.690 ± 0.17 Aa	1.650 ± 0.26 Aa	1.850 ± 0.19 Ac	1.790 ± 0.20 Aa
Liver function test	ALT conc. (IU/L)	15 d	32.30 ± 4.18 Ca	33.20 ± 4.29 Ca	47.90 ± 4.19 Ab	37.80 ± 4.23 Ba
		30 d	34.40 ± 3.26 Ca	35.10 ± 4.26 Ca	52.20 ± 4.23 Aa	38.20 ± 4.24 Ba
		45 d	33.20 ± 4.17 Ba	34.30 ± 3.46 Ba	44.60 ± 3.39 Ac	34.40 ± 3.49 Bb
	AST conc. (IU/L)	15 d	105.2 ± 7.18 Ba	104.8 ± 8.29 Ba	143.5 ± 7.19 Ab	108.5 ± 8.23 Ba
		30 d	110.3 ± 8.26 Ba	105.0 ± 8.26 Ba	162.9 ± 7.23 Aa	111.0 ± 7.24 Ba
		45 d	107.6 ± 7.17 Ba	105.1 ± 9.46 Ba	139.3 ± 8.39 Ac	105.1 ± 8.49 Ba
	ALP conc. (IU/L)	15 d	188.4 ± 15.2 Ba	192.0 ± 14.3 Ba	239.0 ± 17.2 Aa	192.0 ± 16.2 Ba
		30 d	180.9 ± 12.3 Ba	186.0 ± 17.3 Ba	255.0 ± 15.2 Aa	183.0 ± 15.2 Ba
		45 d	182.2 ± 14.2 Aa	184.0 ± 15.8 Aa	193.0 ± 16.4 Ab	188.0 ± 15.5 Aa

All male rats were treated for 15 and 30 days and were left untreated for up to 45 days.

C group: Drenched with drinking water. Syl group: Drenched with silymarin (200 mg/kg bw), suspended in 0.5 ml of drinking water. Cic group: Drenched with cyclosporine (5 mg/kg/day). Syl+Cic group: Drenched with cyclosporine (5 mg/kg/day) and silymarin (200 mg/kg bw).

Data were presented as Mean ±SD of 10 observations (n=10). Different capital letters denote a significant difference ($p<0.05$) between groups for each period. Different small letters denote a significant difference ($p<0.05$) between periods for each group.

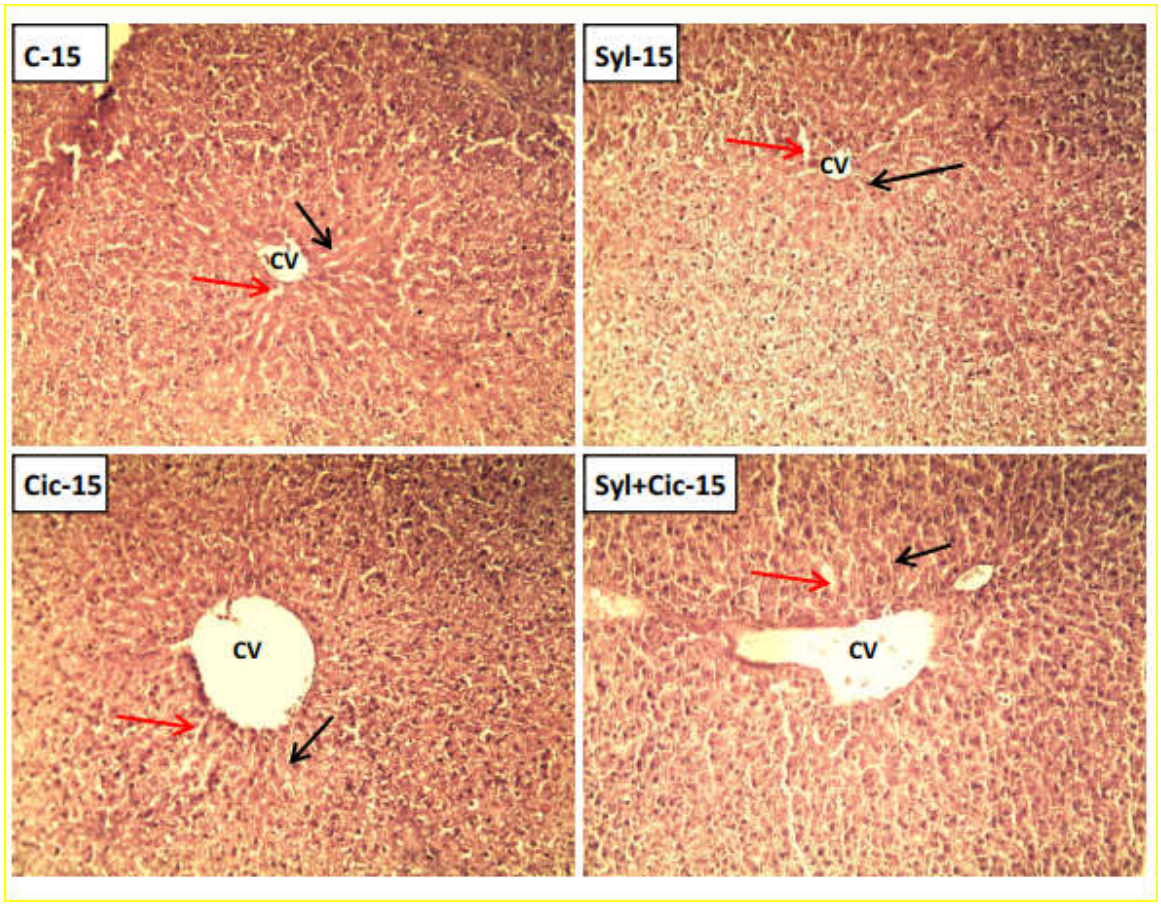

Figure 1: Liver sections obtained from experimental male rat groups after 15 days of treatment. Control male rat section (C) showed normal architecture of hepatic tissue. Sylimarin treated male rat section (Syl.) showed progress proliferation of hepatocytes. Cyclosporine treated male rat section (Cic) showed disarrangement of hepatic cords, degeneration and necrosis of hepatocytes, expansion of sinusoids and congestion of central vein. Combination of sylimarin and cyclosporine treated male rat section (Syl+Cic) showed normal hepatic cords, little degenerative hepatocytes and congestion of central vein. CV: central vein, black arrow: hepatic cord, red arrow: sinusoid. H&E (100x).

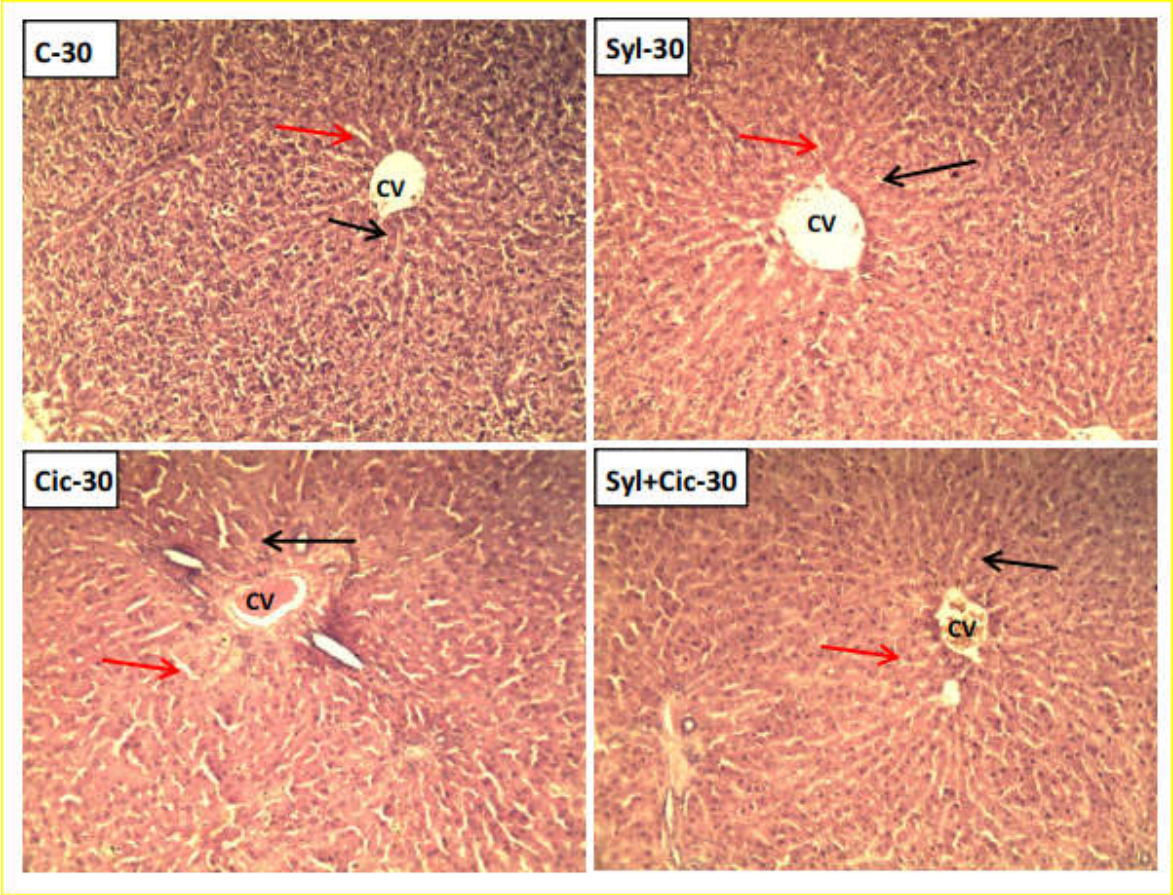

Figure 2: Liver sections obtained from experimental male rat groups after 30 days of treatment. Control male rat section (C) showed normal architecture of hepatic tissue. Sylimarin treated male rat section (Syl.) showed progress proliferation of hepatocytes. Cyclosporine treated male rat section (Cic) showed disarrangement of hepatic cords, degeneration and necrosis of hepatocytes, expansion of sinusoids and congestion of central vein. Combination of sylimarin and cyclosporine treated male rat section (Syl+Cic) showed normal hepatic cords, little degenerative and necrotic hepatocytes and congestion of central vein. CV: central vein, black arrow: hepatic cord, red arrow: sinusoid. H&E (100x).

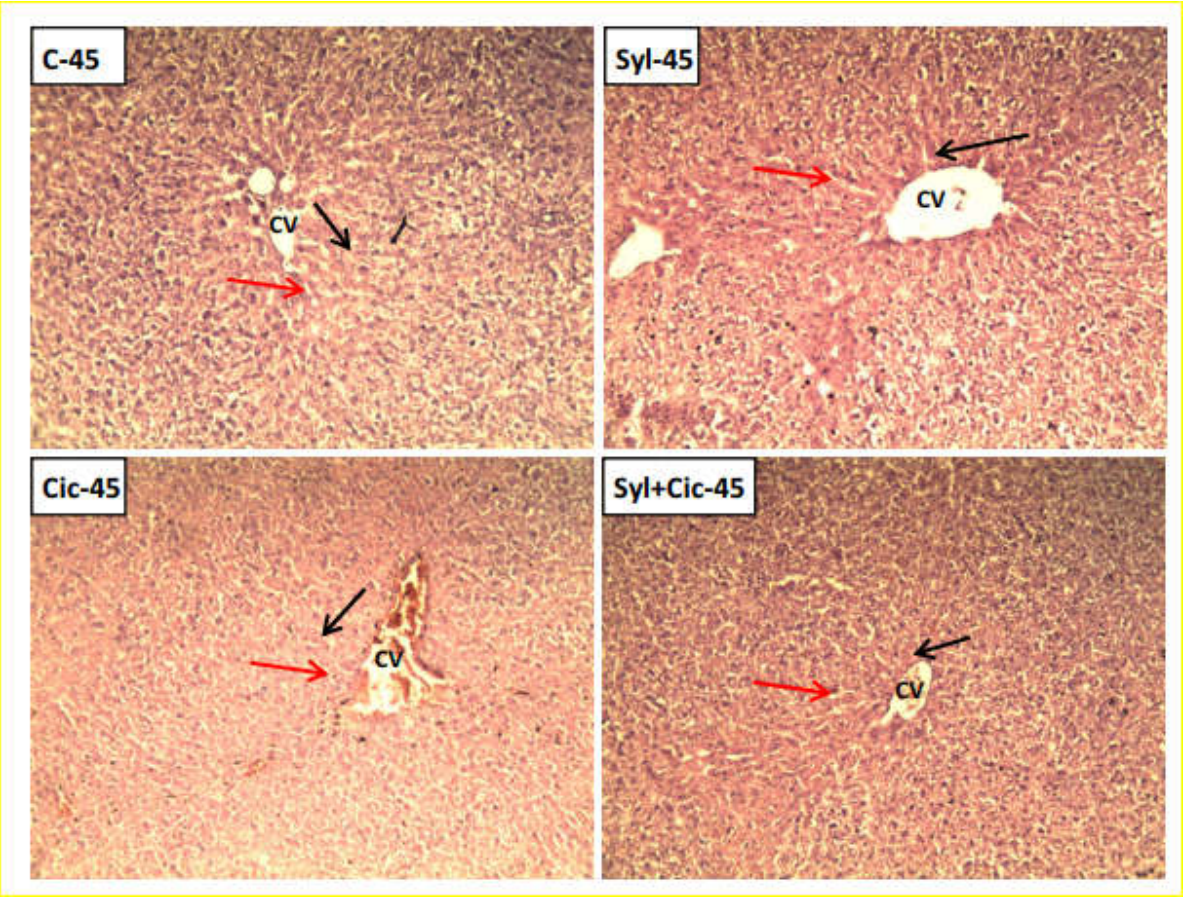

Figure 3: Liver sections obtained from experimental male rat groups treated for 30 days and left without treatment until 45 days. Control male rat section (C) and sylimarin treated male rat section (Syl.) showed normal architecture of hepatic tissue. Cyclosporine treated male rat section (Cic) showed disarrangement of hepatic cords, degeneration and necrosis of hepatocytes, expansion of sinusoids and congestion of central vein. Combination of sylimarin and cyclosporine treated male rat section (Syl+Cic) showed normal hepatic cords and hepatocytes. CV: central vein, black arrow: hepatic cord, red arrow: sinusoid. H&E (100x).

DISCUSSION

The study revealed significant increase of body weight gain in silymarin treated group male rats compared with control. This finding may be attributed to the fact that stimulatory role of silymarin on protein synthesis, where it has been postulated that silymarin can enters into the nucleus and stimulates RNA polymerase I enzymes and thus the transcription of rRNA, resulting in elevation of ribosomal formation and acceleration of protein and DNA biosynthesis, and therefore improves the biosynthetic rate of both structural and functional proteins. On the other hand, this stimulation may provide more transporters and enzymes to the body cells such as hepatocytes. This action has an important role in the regeneration of hepatocytes and increasing the normal functions of liver (21).

Decreased body weight gain in cyclosporine treated male rats may be related to the oxidative effects of cyclosporine as when the cellular antioxidant defense capacity is overloaded, reactive oxygen species start to attack the cellular macromolecules such as DNA, lipids and proteins (22,23) as well as cellular amino acids stores (24). Therefor changes of the oxidative parameters will lead to significant oxidizing of amino acids pool and lipids and proteins will be significantly affected in parallel with cytotoxicity. Conversely the protection of silymarin against the cyclosporine toxicity, however, was achieved in the present study by means of the stable antioxidant activity by both enzymatic and non-enzymatic sets of antioxidants. So silymarin treated male rats (in both Syl and Syl+Cic groups) revealed a significant improvement of body weight gains.

In the current study, cyclosporine-mediated oxidative stress was reported by increasing serum MDA concentrations in male rats, when administered cyclosporine once daily for 15 and 30 days at a dose of 5 mg/kg/day per gavage, exhibited duration-dependent increased MDA levels in the serum. This agrees with the elevated lipid peroxidation measured in the blood of cyclosporine-treated rats (25).

The interesting part of the present study is the aim to determine the role of silymarin to improve the antioxidant status, immunological aspects as well as the reproductive activity in intact and immune suppressed animals, since in various animal models researchers examine the role of silymarin in liver disorders, from which they pointed

out to the observed antioxidant activities of silymarin (26) as it could effectively attributed to the hepatoprotection, therefore they suggested that silymarin has direct effects on cell functions which is responsible for the prevention of liver disorders in these animal models (27).

In general, the ameliorative effects of silymarin that revealed in the present study could attributed to the mechanism of action of silymarin that derives from its ability to counter arrest the action of oxidative stress due to the huge production of free superoxide radicals, which are formed due to cell membrane lipid peroxidation (the damage the cell membranes), competitive inhibition through the hepatocytes external cell membrane modification; stimulation of hepatic cell metabolism, in addition to activating of RNA biosythesis of the ribosomes, stimulating of protein biosynthesis (28).

One of the most important potency of silymarin, as proved by previous researchers (13-14,29) is by increasing the levels of GSH in serum and live subcellular fluid as well as elevation of Gss gene expression level in liver cells, as it has been mentioned that *Gss* gene encoded mitochondrial and cytoplasmic glutathion synthetase biosynthesis in most body cells particularly in hepatocytes, which is responsible for glutathione production (30,31). Therefor it can be postulated that the increment of serum and liver subcellular glutathione content of the rats treated with silymarin could one of the factors that responsible for inhibition of lipid peroxidation induced by cyclosporin.

Liver histopathological changes of Cic group male rats shown in the present study could be attributed to the hepato-cytotoxic effects of cyclosporine due to the increment of hepatic cells lipid peroxidation, where lipid peroxidation of hepatocyte membrane was confirmed as a common cause of cell death by direct destruction of the cell membrane or by changing the fluidity of the membrane (32). Contrary to lipid peroxidation, oxidative alteration of proteins gives the impression of being also important regarding the cyclosporine hepatotoxicity, where cyclosporine decreases the cellular contents of protein sulfhydryl groups and therefor induces loss of protein thiols. In silymarin treated male rats (Syl and Syl+Cic groups), we can suggest that improvement of body weight gain may be attributed to the cytoprotective effect of silymarine by keeping thiol groups of proteins from loss, as it has been described that direct relationship between the protein thiol groups depletion and increased apoptosis was confirmed (33). In this study silymarin proved to be protective against hepato-cytotoxicity. It has been

reported by the present study, cyclosporine treated male rats revealed liver injury, which represented by functional and morphological changes, where functional changes include increased serum levels of liver ALT, AST and ALP, as well as serum cholesterol. This results is in agreement with previous study (34). The observed morphological changes in cyclosporine treated male rats include congestion and widening of hepatic sinus, trabecular structure impairment, congestion and oedema of portal tracts, monocytes infiltration within portal tracts, and hepatocytes degeneration and focal necrosis. These changes were in agreement with that mentiond by other researchers (35). The suggested mechanisms of cyclosporine to induce hepatic injury include the hypermetabolic state development in the liver and inhibition of bilirubin and bile salts transport through the hepatocyte membranes and through bile ducts (36). The use of silymarin, as an antioxidants, in this experiment reduces liver functional and morphological damage, therefor it can be suggested that the mechanisms of cyclosporine in induction of hepatotoxicity is due to its action as an oxidative agent. It has been postulated that cyclosporine highly concentrated in liver tissues after oral administration, and therefor because of the high lipophilicity, cyclosporine might accumulate in liver tissue, so that local cyclosporine is enough to be effective in generating hepatocytes destruction.

التأثير الوقائي للسيليمارين لكبد ذكور الجرذان المستحدث فيها الإجهاد التاكسدي بوساطة السيكلوسبورين

محمد عبد العزيز علي اللوزي* ، جبار عباس احمد الساعدي، جاسم محمد احمد الكلبي *****

*فرع الفسلجه. كلية طب الاسنان ، جامعة المثنى ،المثنى ،العراق.

فرع الفسلجه والادويه ،كلية الطب البيطري، جامعة القادسيه ، القادسيه،العراق.

فرع الفسلجه والادويه ،كلية الطب البيطري، جامعة البصرة ،البصره،العراق.

الخلاصة

هدفت الدراسة الحالية إلى تحديد مدى كفاءة السيليمارين في وقاية كبد ذكور الجرذان المستحدث فيها الإجهاد التاكسدي بوساطة السيكلوسبورين ، استخدمت مائة وعشرون من ذكور الجرذان البالغه وزعت بشكل متساوي إلى مجموعة السيطرة وثلاث مجموعات معاملة. تم تجريع مجموعة السيطرة (C) بمياه الشرب ، في حين جرعت مجموعة المعاملة الاولى بالسيليمارين (200) ملغم / كغم من وزن الجسم) ، والسيكلوسبورين (5) ملغم/كغم من وزن الجسم ، ومجموعة جرعت ب 200ملغم/ كغم

من وزن الجسم +5 ملغم/كغم من وزن الجسم. تمت معاملة الحيوانات لمدة 30 يوما وتركت بعد ذلك دون معاملة لمدة 15 يوما. قسمت كل مجموعة إلى ثلاث مجموعات فرعية (10 لكل مجموعة) ، وتمت التضحية بها بعد 15 و 30 و 45 من التجربة. بعد كل فترة علاج ، تم قياس وزن الجسم ووزن الكبد. تم الحصول على عينات الدم لتقييم تركيز الكلوكوز ،الكوليستيرول ، المالوندالديهايد ، ألانين أمينو ترانسفيريز ، الأسبارتيت امينوترانسفيريز ، والفوسفاتيز القلوية في مصل الدم. اخذت عينات من الكبد للفحص النسجي المرضي. أوضحت النتائج زيادة معنوية في المعايير الكيموحيوية في المجموعة المعاملة بالسيكلوسبورين ، بينما أظهرت كلا المجموعتين المعاملة بالسيليمارين قيم قريبة من مجموعة السيطرة. وأظهرت مقاطع الأنسجة الكبدية لذكور الجرذان المعاملة بالسيكلوسبورين توسع الوريد المركزي ، وعدم انتظام لاشرطة الكبدية ، وتنكس وتنخر الخلايا الكبدية ، وتوسع الجيبانيات الوريدية واحتقان الوريد المركزي ، في حين أظهر العلاج بالسيليمارين ومجموعة الخليط، اشرطة كبدية طبيعية ، وخلايا كبدية متوسطة التنكس واحتقان الوريد المركزي. كانت التغيرات الكيموحيوية والنسجية المنضية تعتمد على المدة. في النهاية ، علاج سيليمارين بالاقتران مع السيكلوسبورين له تأثير محسن

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