Zagazig J. Pharm. Sci., December, 2008 ISSN 1110-5089
Vol. 17, No. 2, pp. 17-24

INVESTIGATION OF THE CURATIVE EFFECTS OF SILYMARIN, CURCUMIN AND TAURINE ON CCl_4-INDUCED LIVER CIRRHOSIS IN RATS

Shimaa M. Elshazly, Mohamed N.M. Zakaria, Ahmed F. Ahamed and Mohamed A. Mohamed
Department of Pharmacology, Faculty of Pharmacy, Zagazig University, Zagazig, Egypt

ABSTRACT

The present study was designed to clarify the effects of silymarin, taurine and curcumin on hepatic toxicity in rats. Hepatic toxicity was induced with carbon tetrachloride (25 µl /100gm) I.P. 3 times /weekly for 6 weeks. Rats were treated with silymarin (100 mg/kg), taurine (1 gm/kg) and curcumin (75 mg/kg) for 30 days after induction of hepatic toxicity. Plasma alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phoshatase (ALP), blood glucose, total protein and albumin activities were determined, in addition to histopathological examination. Plasma ALT, AST, ALP and blood glucose activities were increased in CCl_4 treated rats, in addition to reduction in the level of total protein, albumin and globulin. Histopathological examination showed mono-lobular cirrhosis, represented by fibrous tissue encircling individual hepatic lobules, in addition, the portal triads showed extensive cirrhosis with round cells infiltration. Treatment of cirrhotic rats with taurine, silymarin or curcumin showed a significant reduction in ALT, AST and ALP levels. However the previous mentioned drugs caused a significant increase in the level of total protein, albumin and A/G ratio. Oral treatment of cirrhotic rats with silymarin showed remnants of portal fibrosis. However, liver of curcumin or taurine treated rats were apparently normal. Cirrhotic rats treated with curcumin or taurine showed more pronounced effect on ALT, AST, ALP and proteins than silymarin.

INTRODUCTION

The liver contains the highest concentration of enzymes involved in phase I oxidation-reduction reactions[1]. It is the primary site of biotransformation and detoxification of xenobiotics[2]. This may cause injury liver cells. The liver responds to injury in a limited number of ways. Cells may accumulate fat (steatosis) or biliary material (cholestasis). They may undergo necrosis or apoptosis (forming shrunken, non functioning, eosinophilic bodies)[3].

Carbon tetrachloride (CCl_4) is a hepatotoxic agent causing centrolobular necrosis associated with fatty liver. Carbon tetrachloride is considered one of the most intensively studied hepatotoxicants and provides a relevant model for other halogenated hydrocarbons that are used widely[4].

Silymarin is one of active constituents of the fruits, seeds, and leaves of Milk thistle (*Silybum marianum*) family (*Compositae*)[5]. The active constituents of Milk thistle are flavanolignans including silybin, silydianin, and silychristine, collectively known as silymarin. Silybin is the component with the greatest degree of biological activity, and milk thistle extracts are usually standardized to contain 70-80% silybin. Silybum seeds also contain essential fatty acids, which may contribute to silymarin's anti-inflammatory effect[6].

Curcumin (diferuloryl methane) is a polyphenolic compound present in the rhizomes of Curcuma Longa Linn (turmeric)[7]. It is a yellow coloring spice and is widely used in Indian cooking and used as a folk remedy[7]. Taurine is a non-protein amino acid. It is an end product of L-cysteine metabolism and the principle free intracellular amino acid in many tissues of humans and other animal species. Taurine is present in high amounts in the brain, retina, myocardium, skeletal and smooth muscle, platelets and neutrophils[8].

The aim of the present study is to investigate the possible curative effect of silymarin, curcumin and taurine against CCl_4 induced liver cirrhosis.

MATERIALS AND METHODS

Animals:

Adult male albino rats weighing about 150-200 gm. (obtained from the Faculty of Veterinary Medicine, Zagazig University, Egypt) were used in the present investigation .The animals were housed in cages with wood shaving bedding, 6-8 per cage, and allowed to become acclimatized to laboratory conditions for one week before the experiment.

Induction of liver cirrhosis:

Liver cirrhosis in rats was induced by intraperitoneal injeetion of CCl_4 3 times a week for 6 weeks in a dose of 25 µl/100 g. b.w, diluted 1: 6 with paraffin oil[9].

Experimental design:

Rats were divided into 5 groups (12 rats for each). ***Group (1)*** received CCl_4 three times a week for 6 weeks in a dose of 25µl / 100 g., b.w, i.p. diluted 1:6 with liquid paraffin. ***Group (2)*** received liquid paraffin (0.3 ml/kg, i.p.) for 6 weeks. ***Group (3)*** cirrhotic rats received silymarin (100 mg/kg, orally) as a single daily dose for 30 days. ***Group (4)*** cirrhotic rats received curcumin (75 mg/kg, orally) as a single daily dose for 30 days. ***Group (5)*** cirrhotic rats received taurine (I gm /kg, orally) 3 times a week for 30 days.

The serum was collected and used immediately for the determination AST, ALT, ALP, blood glucose, total protein and albumin levels. In addition, histopathological examination was performed.

Statistical analysis:

All results are expressed as mean ± standard error of the mean (S.E.M.). Student's "t" test for unpaired data at $p < 0.05$ was used to test significance of the differences between control and treated groups[10]. Linear regression was done to determine the r2 value for the standard curve of aminotransferase enzyme concentration versus absorbance at 505 nm. A value of $p<0.05$ was used as the limit for statistical significance[11].

RESULTS

I. Effect on alanine aminotransferase (ALT):

1. Effect of CCl_4 administration (25 µl / 100 gm, I.P., 3 times weekly for 6 weeks) on ALT level in adult male rats.

The results presented in table (1) illustrate that injection of CCl_4 (25µl / 100 gm, I.P.) three times weekly for 6 weeks to normal adult male rats induced a significant increase in the level of ALT (U/L) from 19.21±1.05 to 98.77±7.34 (by 414.15%) compared to normal control group.

2. Effect of oral treatment with silymarin (100 mg /kg/daily), curcumin (75 mg/kg/daily) or taurine (1 g /kg/3 times /week) for 30 days on ALT level in adult male cirrhotic rats

As listed in table (1), oral administration of silymarin, curcumin or taurine in the selected doses for 30 days to adult male cirrhotic rats significantly lowered the level of ALT (U/L) from 98.77±7.34 to 31.18±1.16 (by 68.43%), to 23.98±1.5 (by 75.72%) or to 17.48±1.13 (by 82.3%), respectively, compared to cirrhotic control group.

Table(1): Effect of oral treatment with silymarin (100 mg /kg/daily), curcumin (75 mg/kg/daily) or taurine (1 g /kg/3 times /week) for 30 days on ALT level in adult male cirrhotic rats.

Treatment	ALT (U / L)
Normal control	19.21±1.05
Cirrhotic control	98.77±7.34 #
Silymarin (100 mg / kg)	31.18±1.16 #•
Curcumin (75 mg /kg)	23.98±1.5 #•
Taurine (1 gm /kg)	17.48±1.13 •

Results are presented as the mean ± S.E.M.
#Significantly different from normal control group at $p < 0.05$
•Significantly different from cirrhotic control group at $p < 0.05$

II. Effect on aspartate aminotransferase (AST):

1. Effect of CCl_4 administration (25µl/100 g, I.P., 3 times weekly for 6 weeks) on AST level in adult male rats.

Administration of CCl_4 in the selected dose and period to normal adult male rats resulted in a significant elevation in AST level (U/L) from 63.08±5.37 to 425±29.53 (by 573.74%) compared to the normal control group as shown in table (2).

2. Effect of administration of silymarin (100 mg/kg/daily), curcumin (75 mg/kg/daily) or taurine (1 gm/kg/3 times/week) orally for 30 days on AST level in adult male cirrhotic rats

As shown in table (2), oral administration of silymarin, curcumin or taurine in the selected doses for 30 days to adult male cirrhotic rats induced a significant reduction in AST level (U/L) from 425 ± 29.53 to 148.24 ± 14.01 (by 65.12%), to 21.05±1.9 (by 95.05%) or to 24.56 ± 2.21 (by 94.22%), respectively, compared to cirrhotic rats.

Table (2): Effect of administration of silymarin (100 mg/kg/daily), curcumin (75 mg/kg/daily) or taurine (1 gm/kg/3 times/week) orally for 30 days on AST level in adult male cirrhotic rats.

Treatment	AST (U/L)
Normal control	63.08 ± 5.37
Cirrhotic control	425±29.53 #
Silymarin (100 mg/kg)	148.24 ± 14.01 #•
Curcumin (75 mg/kg)	21.05 ± 1.9 #•
Taurine (1 gm/kg)	24.56 ± 2.21 #•

Results are presented as the mean ± S.E.M.
#Significantly different from normal control group at $p < 0.05$
•Significantly different from cirrhotic control group at $p < 0.05$

III. Effect on serum alkaline phosphate level (ALP):

1. Effect of CCl_4 administration (25 µl/100 g, I.P., 3 times weekly for 6 weeks) on ALP level in adult male rats

As presented in table (3), administration of CCl4 intraperitoneally in the selected dose and period to normal adult male rats induced a significant elevation in ALP level (IU/L) from 80.92 ± 3.13 to 251.10±7.9 (by 210.31%) compared to normal rats.

2. Effect of 30 days treatment with silymarin (100 mg/kg/daily), curcumin (75 mg/kg/daily) or taurine (1 gm/kg/3 times/ week) orally on ALP level in adult male cirrhotic rats

As graphically presented in table (3), oral treatment of adult male cirrhotic rats with silymarin, curcumin, or taurine for 30 days in the selected doses resulted in a significant reduction in ALP level (IU/L) from 251.102 ± 7.9 to 113.45± 10.88 (by 66.11%), to 94.33 ± 3.6 (by 62.43%) or to 85.102 ±5.27 (by 54.82%), respectively, compared to cirrhotic control group.

Table(3): Effect of 30 days treatment with silymarin (100 mg/kg/daily), curcumin (75 mg/kg/daily) or taurine (1 gm/kg/3 times/ week) orally on ALP level in adult male cirrhotic rats

Treatment	ALP (IU/L)
Normal control	80.92 ± 3.13
Cirrhotic control	251.102 ± 7.94 #
Silymarin (100 mg/kg)	113.45± 10.88 #•
Curcumin (75 mg/kg)	94.33 ± 3.6 #•
Taurine (1 gm/kg)	85.102 ±5.27 •

Results are presented as the mean ± S.E.M.
#Significantly different from normal control group at $p < 0.05$
•Significantly different from cirrhotic control group at $p < 0.05$

IV. Effect on serum blood glucose level:

1. Effect of CCl_4 administration (25 µl/100 g, I.P., 3 times weekly for 6 weeks) on serum glucose level in adult male albino rats

The results presented in table (4), illustrate that intraperitoneal injection of CCl4 in the selected dose and period to normal adult male rats significantly increased serum blood glucose level (mg/dl) from 78.67 ± 2.9 to 102.25 ± 5.36 (by 23.1%) compared to normal control group.

Zagazig J. Pharm. Sci., December, 2008
Vol. 17, No. 2, pp. 17-24

ISSN 1110-5089

2.Effect of administration of silymarin (100 mg/kg/daily), curcumin (75 mg/kg/daily) or taurine (1 g/kg/3 times/week) orally for 30 days on serum glucose level in adult male cirrhotic rats:

Oral treatment with silymarin or taurine in the selected doses for 30 days to cirrhotic rats resulted in a significant reduction in serum glucose level (mg/dl) from 102.25 ± 5.36 to 84.09 ± 2.2 (by 17.76%) or to 61.37 ± 2.3 (by 39.98%), respectively, compared to cirrhotic control group. On the other hand, oral administration of curcumin in the used dose for 30 days to cirrhotic rats didn't induce any significant change in serum glucose level as compared to cirrhotic control group (table 4).

Table (4): Effect of administration of silymarin (100 mg/kg/daily), curcumin (75 mg/kg/daily) or taurine (1 g/kg/3 times/week) orally for 30 days on serum glucose level in adult male cirrhotic rats

Treatment	Serum glucose level (mg/dl)
Normal control	78.67 ± 2.9
Cirrhotic control	102.25 ± 5.36 #
Silymarin (100 mg/kg)	84.09 ± 2.2 •
Curcumin (75 mg/kg)	94.14 ± 6.5 #
Taurine (1gm/kg)	61.37 ± 2.3 #•

Results are presented as the mean ± S.E.M.
#Significantly different from normal control group at $p < 0.05$
•Significantly different from cirrhotic control group at $p < 0.05$

V. Effect on serum proteins:

1.Effect of CCl_4 administration (25 µl/100 g, I.P., 3 times weekly for 6 weeks) on serum protein levels in adult male rats:

Intraperitoneal injection of CCl_4 in the previously mentioned dose and period to normal adult male rats produced a significant fall in total protein, albumin and globulin levels (g/dl) from 7.63 ± 0.22 to 6.2 ± 0.08 (by 18.7%) , from 3.83 ± 0.15 to 2.64 ± 0.11 (by 31.07%) and from 4.57 ± 0.1 to 3.02 ± 0.092 (by 33.9%), respectively, compared to normal control group, however, it didn't induce any significant change on albumin/globulin ratio (A/G) as shown in table (5).

2.Effect of oral treatment with silymarin (100 mg/kg/daily), Curcumin (75 mg/kg/daily) or taurine (1 g/kg/3times/week) for 30 days on serum protein levels in adult male cirrhotic rats:

As indicated in table (5), oral administration of silymarin, curcumin or taurine in the used doses for 30 days to adult male cirrhotic rats produced a significant increase in total protein level (g/dl) from 6.2 ± 0.08 to 7.2 ± 0.12 (by 16.13%), to 7.14 ± 0.12 (by 15.16%) or to 7.04 ± 0.09 (by 13.5%), respectively, compared to cirrhotic control group.

Treatment of cirrhotic rats with silymarin, curcumin or taurine in the previously mentioned doses for 30 days significantly increased serum albumin level (g/dl) from 2.64 ± 0.11 to 3.32 ±0.07 (by 25.75%), to 3.77 ± 0.11 (by 42.8%) or to 4.14 ± 0.11 (by 56.8%), respectively, compared to cirrhotic control group.

Treatment of cirrhotic rats with silymarin or curcumin in the used doses for 30 days resulted in a significant elevation in globulin levels from 3.02 ± 0.092 to 4.12 ± 0.05 (by 36.42%) or to 3.67 ± 0.12 (by 21.52%), respectively, compared to cirrhotic control group. While treatment of cirrhotic rats with taurine in the selected dose for 30 days didn't induce any significant change in globulin level.

Treatment of cirrhotic rats with silymarin , curcumin or taurine in the selected doses for 30 days produced a significant increase in A/G ratio from 0.66 ± 0.05 to 0.818 ± 0.02 (by 23.9%), to 1.29 ± 0.09 (by 95.45%) or to 1.43 ± 0.03 (by 116.6%), respectively, compared to cirrhotic control group.

Table (5): Effect of oral treatment with silymarin (100 mg/kg/daily), Curcumin (75 mg/kg/daily) or taurine (1 g/kg/3times/week) for 30 days on serum protein levels in adult male cirrhotic rats

Treatment	Total protein level (gm/dl)	Serum albumin level (gm/dl)	Serum globulin level (gm/dl)	A/G ratio
Normal control	7.63 ± 0.22	3.83 ± 0.15	4 57 ± 0.1	0.61 ± 0.08
Cirrhotic control	6.2 ± 0.08 #	2.64 ± 0.11 #	3.02 ± 0.09 #	0.66 ± 0.05
Silymarin (100 mg/kg)	7.2 ± 0.12 •	3.32 ± 0.07 #•	4.12 ± 0.05 #•	0.81 ± 0.02 #•
Curcumin (75 mg/kg)	7.14 ± 0.12 •	3.77 ± 0.11 •	3.67 ± 0.12 #•	1.29 ± 0.09 #•
Taurine (1 gm/kg)	7.04 ± 0.09 #•	4.14 ± 0.11 •	3.31 ± 0.11 #	1.43 ± 0.03 #•

Results are presented as the mean ± S.E.M
#Significantly different from normal control group at $p < 0.05$
•Significantly different from cirrhotic control group at $p < 0.05$

Histopathological results:

Effect of CCl_4 administration (25 µl/100 gm, I.P., 3 times weekly for 6 weeks) on normal adult male rats:

Liver of normal rats received liquid paraffin (0.3 ml/kg, I.P.) 3 times weekly for 6 weeks was apparently normal. However, in some examined cases, some hepatocytes showed hydropic degeneration (figure 1). Intraperitoneal administration of CCl4 in the previously mentioned dose and period caused mono-lobular cirrhosis, represented by fibrous tissue encircling individual hepatic lobules (figure 2). The portal triads showed extensive cirrhosis with round cells infliteration (lymphocytes, macrophages and plasma cells) together with bile ducts and ductular hyperplasia (figure 3).

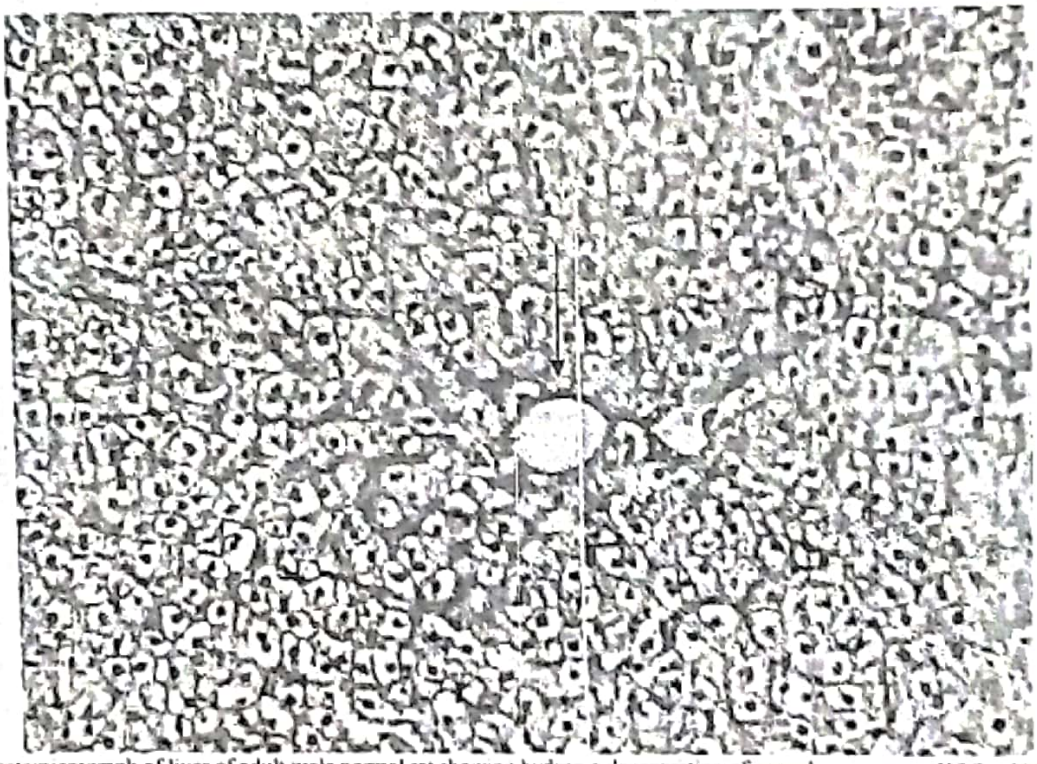

Figure (1): A photomicrograph of liver of adult male normal rat showing hydrop c degeneration of some hepatocytes. (H&E x 300)

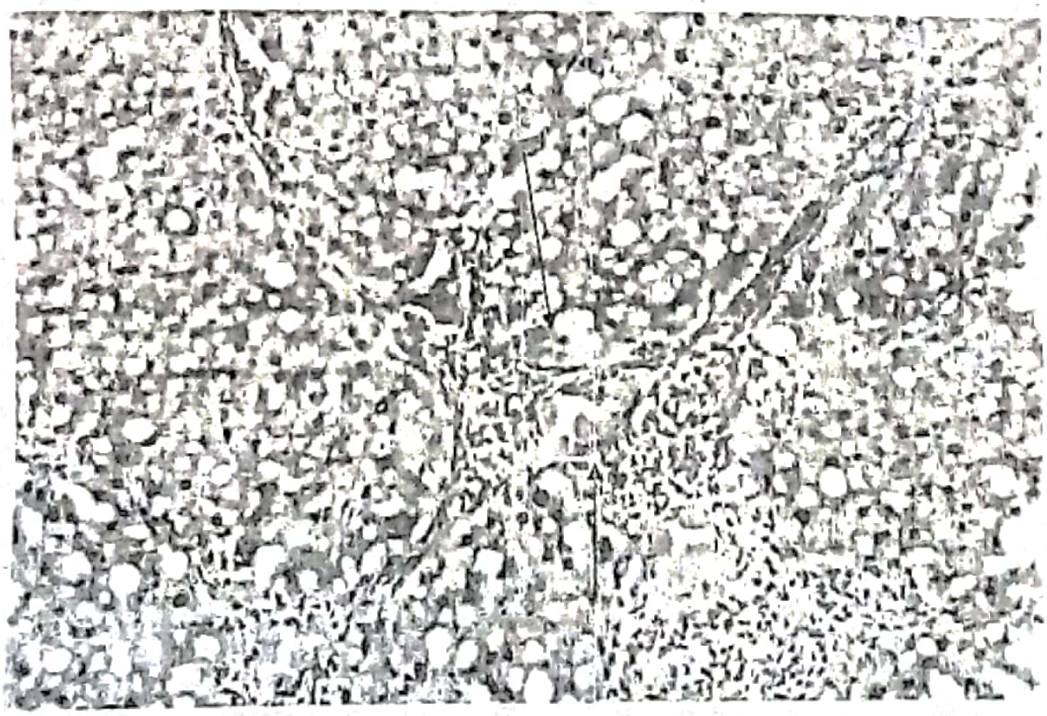

Figure (2): A photomicrograph of liver of adult male cirrhotic rat showing mono-lobular cirrhosis (H&E x 300)

ISSN 1110-5089

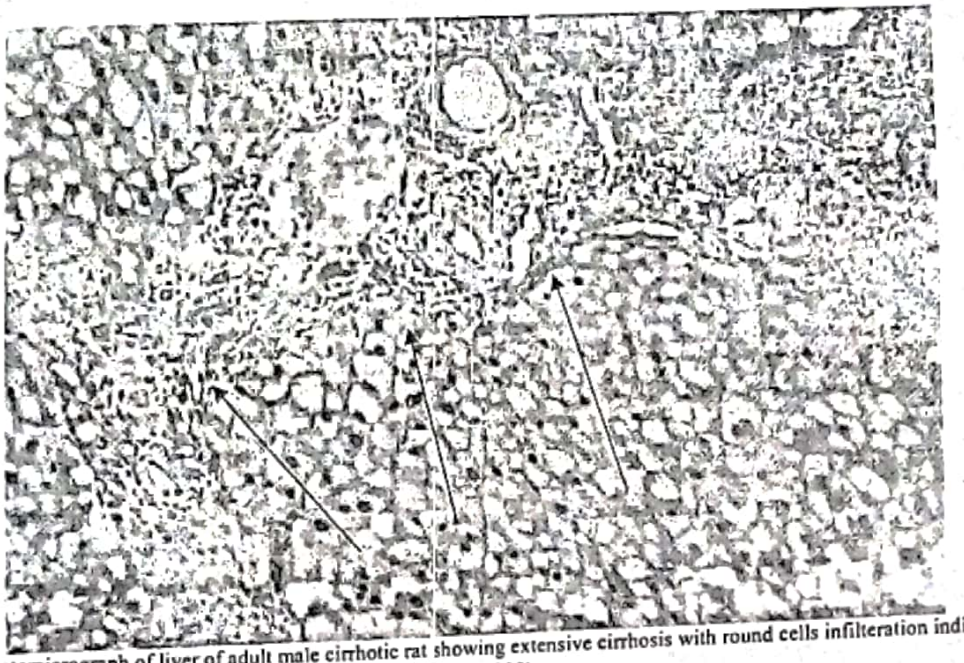

Figure (3): A photomicrograph of liver of adult male cirrhotic rat showing extensive cirrhosis with round cells infilteration indicated by arrows (H&E x 300)

Effect of oral treatment with silymarin (100 mg/kg), curcumin (75 mg/kg) or taurine (1 gm/kg) for 30 days on adult male cirrhotic rats:

1. *Effect of oral treatment with silymarin (100 mg/kg/daily), Curcumin (75 mg/kg/daily) or taurine (1 g/kg/3times/week) for 30 days on* serum protein levels in adult male cirrhotic rats:

Oral treatment of cirrhotic rats with silymarin caused mild enlargement of the liver in most cases. The liver had pale grayish colour and fine granular surface. In addition, most of the examined cases showed remnants of portal fibrosis (figure 4).

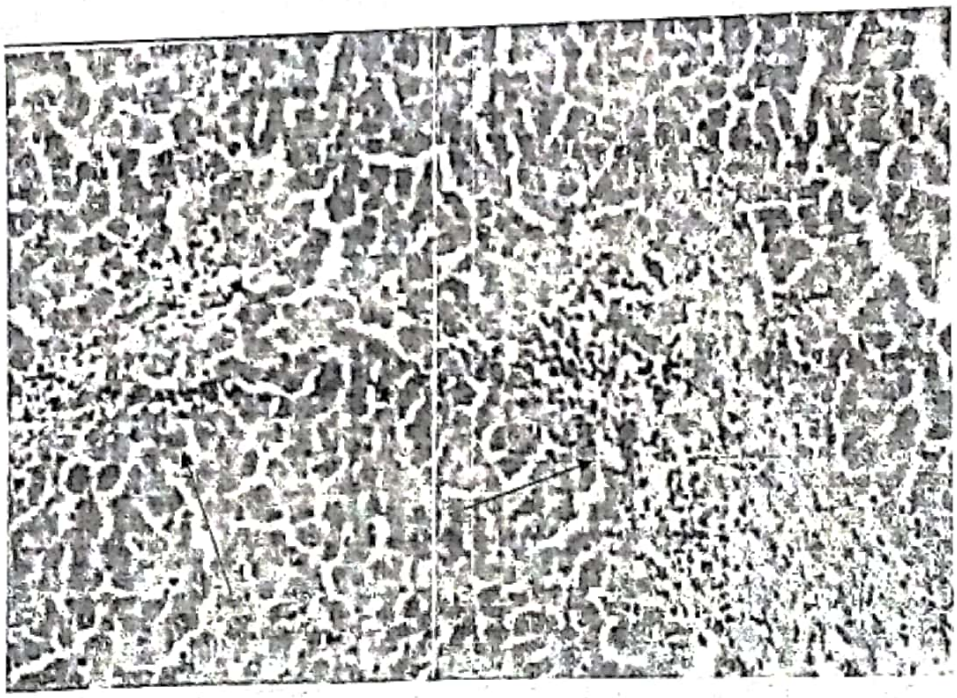

Figure (4): A photomicrograph of liver of silymarin treated cirrhotic rat for 30 days showing remnants of portal fibrosis (H&E x 300)

Effect of oral administration of curcumin (75 mg/kg) for 30 days on adult male cirrhotic rats:

Liver of curcumin treated rats was apparently normal. About 70-90% of the liver parenchyma was normal. While, the remaining parts showed fatty changes and necrosis of the hepatocytes (figure 5).

Figure (5): A photomicrograph of liver of curcumin treated cirrhotic rat for 30 days showing about 10-30% of the liver cells with necrosis (H&E x 300)

Effect of oral administration of taurine (1 gm/kg) for 30 days on adult male cirrhotic rats:

The liver of taurine treated rats was normal. However, in few cases the liver was mildly enlarged, pale in colour and firm in consistency. Regeneration of large number of cells occurred forming new hepatic lobules (figure 6).

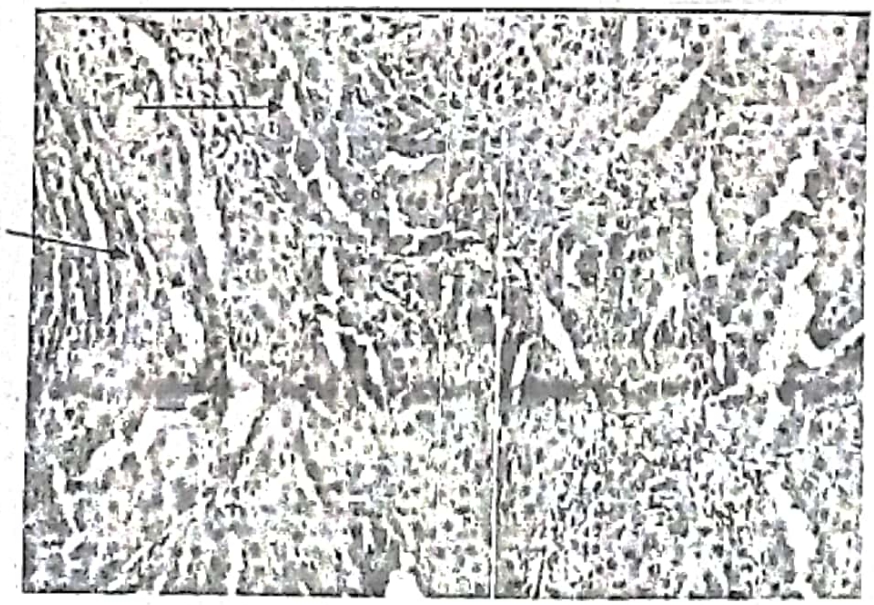

Figure (6): A photomicrograph of liver of taurine treated cirrhotic rat for 30 days showing regeneration of large number cells forming new hepatic lobules (H&E x 300)

DISCUSSION

The results of this work demonstrated that oral treatment rats with silymarin caused a significant reduction in ALT, AST and ALP. In addition, it caused regeneration of large number of hepatocytes with formation of new hepatic lobules as presented in histopathological results.

Silymarin's ability to stabilize cell membrane through its anti-oxidant action that can scavenge free radicals and increase intracellular content of reduced glutathione and superoxide dismutase was mentioned by Lang et al. (1993). This action protects membrane against lipid per-oxidation and damage by free radicals[13,14].

In the present work, oral treatment of cirrhotic rats with curcumin for 30 days caused a significant

ISSN 1110-5089

reduction in ALT, AST and ALP levels. In addition, histopatholgical results showed that large number of liver cells exhibited regeneration changes, sometimes with formation of new hepatic lobules. Curcumin mediated hepatoprotective effect could be attributed to its anti-oxidant and anti-inflammatory properties. Since, it was reported that curcumin is a potent scavenger of a variety of ROS including superoxide anion, the most type of ROS that curcumin able to scavenge it[15], hydroxyl radical, singlet oxygen, nitric oxide and peroxynitrite, which are important to the intiation of lipid per-oxidation[16]. Curcumin has the ability to protect lipids, hemoglobin and DNA against oxidative degradation[15]. Moreover, it was reported that curcumin maintains the activities of anti-oxidant enzymes like superoxide dismutase, catalase and glutathione peroxidase[17]. As a result, it inhibits per-oxidation of membrane lipids and maintain cell membrane integrity and their function, thus it may stabilize the cell membrane[18]. Moreover, curcumin inhibits TNF- α[19] which results in increased expression and secretion of leptin from adipose tissue[20] and this leads to a decrease in the amount of fat storage in the liver[19]. Curcumin was reported to have the capability of enhancement fatty acid catabolism in the liver of rats after treated with CCl_4 and alcohol induced liver disease and this through stimulation of hepatic acyl-CoA oxidase activity, which performs the first catalytic step of fatty acid B oxidation[21].

Treatment of cirrhotic rats with taurine caused a significant reduction in ALT, AST and ALP. Furthermore, it caused regeneration of large number of cells forming new hepatic lobules as shown in our histopathological results. Four mechanisms may contribute to taurine mediated reduction in oxidative stress. First: there is some evidence that taurine might up-regulates the anti-oxidant defenses represented by elevation of superoxide dismutase and glutathione peroxidase activities[23]. Second: N-chlorotaurine suppresses the activity of the neutrophils and thereby reducing their ability to generate free radical Third: taurine may prevent Ca^{2+} overload and thereby minimizing free radical generation. Fourth: is the major cause of taurine mediated cyto-protection against certain xenobiotics is the formation of a taurine conjugate that is incapable of generating free radicals[23].

CONCLUSION

These results suggest that treatment with silymarin, curcumin or taurine could improve liver function after induction of hepatotoxicity.

REFERENCES

1- Guegenrich FP: **Toxicol. Lett.**, 70: 133-138 (1994).
2- Lee KS, Buck M, Houglum K and Chojkier M: **J. Clin. Invest.**, 96: 2461-2468 (1995).
3- Crawford JM: The liver and The Biliary Tract. In: Cotran R.S., Kuar V. and Collins T. (eds.): Robbins pathologic basis of disease, 6th ed. Philadelphia, USA, WB saunders; 845-891 (1999).
4- Recknagel RO, Glende EA and Dolak JA: **Pharmacology and therapeutics**; 43(1): 139-154 (1989).
5- Pepping J: **American Journal of Health-System Pharmacy**; 56: 1195-1197 (1999).
6- Buzzelli G, Moscarella S and Giusti A: A pilot **Int. Clin. Pharmacol. Ther. Toxicol.**; 31: 456-460 (1993).
7- Ammon HPT and Wahel MA: **Planta Medica**; 57: 1-7 (1991).
8- Stipanuk MH: Homocysteine, Cysteine and Taurine. In: Shils M.G., Olson J.A., Shike M and Ross A.C. eds. Modern Nutrition in Health and Disease. 9th (ed.) Baltimore, MD, Williams and Wilkins; 543-558 (1999).
9- Hernandez-Munzo R, Diaz-Munzo M, Lopez V, Yanez L, Vidro S and De-Sanchez VC: **Hepatol.**; 26(5): 1100-1110 (1997).
10- Armitag P and Berry G: Statistical Methods in Medical Research. Blackwell Scientific Publications, Oxford (1994).
11- Nakajima M, Hutchinson HG and Fujinaga M the **National Academy of Sciences of the United States of America**; 92: 10663-10667 (1995).
12- Lang I, Deak G, Muzes G, Pronal L and Feher J: **Biotechnology therapeutics**; 4: 263-270 (1993).
13- Mourelle M, Favari L and Amezcua JL: **Journal of applied toxicology**; 8: 351-354 (1988)
14- Letteron P, Labbe G, Degott C, Berson A, Fromenty B, Delafrge M, Larrey D and Pessayre D: **Biochemical Pharmacology**; 39(12): 2027-2034 (1990).
15- Kunchandy E and Rao MN: **International journal of pharmaceutics**; 38: 239-240 (1990).
16- Schramanian M, Sreejayan-Rao MN, Devasagyam TP and Singh BB: **Mutation Research**; 311: 249-255 (1994)
17- Pulla-Reddy A and Lokesh BP: **Molecular and Cellular Biochemistry**; 111: 117-124 (1992)
18- Pulla-Reddy A and Lokesh BP: **Food and Chemical Toxicology**; 32: 279-283 (1994).
19- Thurman RG: **Am. J. Physiol. Gastrointest. Liver Physiol.**; 275. G605-G611 (1998).
20- Lin SY, Chen WY, Chiu YT, Lee WJ, Wu HS and Sheu WH. **Metabolism**; 54(4): 445-452 (2005).
21- Asai A and Miyazawa T: **J. Nutr.**; 131. 2932-2935 (2001).
22- Vohra BP and Hui X: **Archives of Physiology and Biochemistry**; 109: 90-94 (2001).
23- Roysommuti S, Khongnakha T, Jirakulsomchok D and Wyss JM: **American Journal of Hypertension**; 15: 773-779 (2002).

Received: July 26, 2008
Accepted: Sept. 03, 2008

استقصاء التأثيرات العلاجية لكلا من السليمارين، الكركومين والتورين على التليف الكبدى المحدث فى الجرذان بواسطة رابع كلوريد الكربون

شيماء مصطفى الشاذلى، محمد نجيب محمد زكريا، أحمد فهمى أحمد، محمد عبد العال محمد

قسم الفارماكولوجى- كلية الصيدلة- جامعة الزقازيق – الزقازيق – مصر

أجري هذا البحث لدراسة التأثير العلاجى لعقار السليمارين، الكركومين و التورين. و قد تم ذلك من خلال قياس مستويات كل من أسبارتات أمينو ترانسفيراز، ألانين أمينو ترانسفيراز، الفوسفاتيزالقاعدى ، الجلوكوز، البروتين الكلى و الزلال فى الدم. بالأضافة لأخذ عينات من الكبد لفحصها مجهريا لتوضيح التأثيرات المستحدثة قبل و بعد تجريع العقاقير المستعملة.

أحدثت الأصابة الكبدية فى الجرذان بتكرار الحقن فى التجويف البريتونى لرابع كلوريد الكربون بجرعة ٢٥ميكروليتر/١٠٠ جم ٣ مرات اسبوعيا لمدة ٦ أسابيع. كما أن قد تم علاج الجرذان المصابة بعقار السليمارين بجرعة ١٠٠ مجم/كجم، بالفم، التورين بجرعة ١ جم/كجم و الكركومين بجرعة ٧٥ مجم/كجم لمدة ٣٠ يوم.

و قد تم استنتاج النتائج التالية إن معالجة الجرذان الطبيعية برابع كلوريد الكربون أحدثت تليف فى نسيج الكبد ممثلا فى ارتفاعا حقيقيا فى مستويات كل من أسبارتات أمينو ترانسفيراز، ألانين أمينو ترانسفيراز، الفوسفاتيزالقاعدى و الجلوكوز. بالرغم من ذلك فقد أحدث أنخفاضا فى مستويات كل من البروتين الكلى،الزلال، الجلوبيولين. و كذلك فإن الفحص المجهرى للكبد أوضح وجود تليف أحادى الفص متمثلا فى وجود أنسجة متليفة محيطة بكل فص كبدى. وجود تنكرز بؤرى فى خلايا الكبد مع الأختفاء الكامل للنواة و السيتوبلازم بالخلايا.

كما أن تجريع الجرذان المصابة بالعقاقير المستخدمة أحدثت أنخفاضا حقيقيا فى مستويات كل من أسبارتات أمينو ترانسفيراز، ألانين أمينو ترانسفيراز، الفوسفاتيزالقاعدى.و لقد حدث أرتفاعا حقيقيا فى مستويات كل من البروتين الكلى، الزلال، نسبة الزلال / الجلوبيولين.

و على ضوء النتائج السابقة تبين أن عقارى الكركومين و التورين أكثر فعالية من عقار السليمارين فى علاج الجرذان المصابة بالتليف الكبدى.