Journal

J. Biol. Chem. Environ. Sci., 2009, Vol. 4(1): 381-403
www.acepsag.org

# ANTIOXIDANTS ACTIVITY OF *CORIANDER SATIVUM L.* AND HEPATOPROTECTIVE ROLE AGAINST $CCL_4$-INDUCED OXIDATIVE STRESS IN RATS.

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## ABSTRACT

The present study was examined to investigate the possible hepatoprotective of the natural antioxidants of *Coriander sativum L.* seed powder 10% and Coriander essential oil 290mg/kg diet against $Ccl_4$-induced oxidative stress in Sprague-Dawley albino rats. The rats were divided into two main groups. The first (6 rats) fed on the basal diet as a negative control group. The second group (24 rats) treated with $Ccl_4$ in paraffin oil (50% v/v 2 ml/kg) twice a week intraperitoneal injection and divided into four groups (6 rats each) according to the following scheme for 30 days : (1) positive control (received basal diet), group (2) received basal diet with 25mg/kg silymarin, (3) received basal diet with coriander seed powder 10%, (4) received basal diet with coriander essential oil (290mg/kg)diet. Intraperitoneal injection of $Ccl_4$ resulted in significantly increase in the serum levels of aspartate transaminase (AST) and alanine transaminase (ALT) with the reduction of antioxidant enzymes. Serum total protein and albumin levels were elevated by coriander essential oil and coriander seed powder against $Ccl_4$-treated rats. Kidney and liver functions were improved by a significant increase in antioxidant enzymes like superoxide dismutase (SOD) and glutathione peroxidase (GSH-Px). Histopathological examination showed that liver injury, large local area of hypatocytes necrosis which completely replaced by massive infiltration with leucocytic of $Ccl_4$-treated rats. Coriander essential oil activity has significant reduction of the toxic effect of $Ccl_4$ when compared to control positive group might be correlated with its antioxidant constituents and free radicals scavenger effects.

# INTRODUCTION

Liver is the first organ to metabolise all foreign compounds and the most liver diseases due to exposure to different environmental pollutants e.g., alcohol, carbon tetrachloride, and thioacetamide.

Long- term administration of $Ccl_4$ causes chronic liver injury, and is a widely accepted model to produce hepatic fibrosis (Pierce *et al.*, 1987 and Hernandez *et al.*, 1990). Liver fibrosis is the common end stage of most chronic liver diseases regardless of the etiology (Bataller and Brenner, 2005), and its progression leads to liver cirrhosis and liver cancer.

Oxidative damage is implicated in the pathogenesis of various liver injuries. Reactive oxygen species (ROS) formed in vivo, such as superoxide anion, hydroxyl radical and hydrogen peroxide are highly reactive and potentially damaging transient chemical species. These are continuously produced in the human body, as they are essential for energy supply, detoxification, chemical signalling and immune function. ROS are regulated by endogenous superoxide dismutase, glutathione peroxidase and catalase. There are two main antioxidant defence mechanisms : the first is superoxide dismutase (SOD) which catalyses disputation of superoxide anions to hydrogen peroxide; catalase (CAT) which converts hydrogen peroxide into molecular oxygen and water; the second is with non- enzymatic components, such as polyphenols, ascorbic acid and carotenoids. (Rice-Evans *et al.*, 1997) and (Shahidi *et al.*, 1992) .

The seeds of coriander were found in the ancient Egyptian tomb of Ramses the Second. The Egyptians called this herb "spice of happiness".

Coriander (*Coriander Sativum L*) is used in three parts: young fresh leaves, seeds and oil . Coriander is an important ingredient in making curries and other dishes. It has many vitamins and minerals such as vitamin B, C, calcium, phosphorus, and iron.

The seeds have been used to treat digestive disorders, diabetes, rheumatism, hypercholesterolemia. Coriander oil is used mainly as a flavouring agent in pharmaceutical preparations and for fragrance in cosmetics (Leung, 1980 and Said *et al.*, 1996).

Many antioxidant constituents present in coriander such as d-linalool, borneol, geraniol, geranyl acetate, camphor, carvone, anethole, γ-terpinene, α and β-pinene, d-limonine, P-cymene, β-

phellandrene, camphene, β-sitosterol, cumarins and flavonoids (Higashimoto *et al.*, 1993; Hashim *et al.*, 1994 and Melo *et al.*, 2005). Coriander seeds decreased low density lipoprotein (LDL) + very density lipoprotein (VLDL) cholesterol while high density lipoprotein (HDL) was increased (Dhanapakiam *et al.*, 2008; Lal *et al.*, 2004). Administration of streptozotocin decreased the number of beta cells with insulin secretory activity in comparison with intact rat , but treatment with the coriander seed extract (200mg/kg) increased significantly the activity of the beta cells (Eidi *et al.*, 2008)).Coriander fruit exhibit gut stimulatory ,inhibitory and hypotensive effect mediating possibly through cholinergic, $Ca^{2+}$ antagonist and the combination of these mechanisms respectively, (Jabeen *et al.*, 2009).(Aissaoui *et al.*, 2008), also, reported that coriander plays a protective role against the deleteriony effects in lipid metabolism in experimental colon cancer (Chithra and Leelamma, 2000). Intake of essential oils such as coriander oil affects the host enzymes associated with activation and detoxification of xenobiotic compounds, including chemical carcinogen and mutageny (Baneriee *et al.*, 1994) the present study was designed to examine the antioxidant efficacy of coriander seed, and its essential oil on carbon tetrachloride-induced oxidation stress in rat liver.

## MATERIALS AND METHODS

**Materials:** Coriander (*Coriander Sativum L.*) seeds were purchased from local market then, cleaned , grounded and steam distilled for 2hr. in a Clevenger-type apparatus. Distillation were performed less than 24h after sampling. The essential oil was dried over anhydrous sodium sulphate until the last traces of water were removed and then stored in dark glass bottle at 4 °C. Silymarin was purchased from Sigma Co., carbon tetrachloride ($Ccl_4$) analytical grade from El-Nasr pharmaceutical chemicals. kits used to determined total protein , albumin, urea, uric acid, creatinine,ALT, AST, SOD,GSH-PX, α-amylase, TG, TC, and HDL-C were obtained from Biodiagnostic company.

**Gas Chromatography (GC)**: The gas chromatography Hewllet Packared (series 5890) equipped with Flame Ionization Detector (FID) and carbowax fused silica column (50m long X0.32μmX0.5mm i.d.) was used for analysis of coriander essential oil. The oven temperature

was programmed from 60 to 200 °C at the rate of 3 °C/min .Helium1ml/min was used as a carrier gas ; split ratio 1:100, the injection port detector temperatures were 150 and 200 °C, respectively. Percentage of peak area were calculated with an integrator; Hewllet Packared 3396.

**Animals and Experimental Design:** Thirty male Sprague-Dawley albino rats weighing 242 to 251 gm. were obtained from animal house of Food Technology Research Institute, Agriculture Research Center, Giza, Egypt. All rats were kept in large polypropylene cages (n=6) under hygienic conditions and fed on basal diet for one week (adaptation period) and water ad libitum. The basal diet consisted of protein (casein) 10%, cellulose 5%, salt mixture 4%, vitamin mixture 1%, corn oil 10% and corn starch 70% according to Lane Peter and Pearson, (1971), vitamin mixture was prepared according to (A.O.A.C., 1975) .

**Carbon tetrachloride ($Ccl_4$) hepatotoxicity:** Carbon tetrachloride ($Ccl_4$) is a powerful hepatotoxin which is used extensively to generate experiments to study necrosis and steatosis of the liver in the rat (Pereze- Tamayo, 1983; Wensing *et al.* 1990).

After the adaptation period the rats were divided into two main groups. The first (6 rats) fed on the basal diet as a negative control group. The second group (24 rats) treated with $Ccl_4$ in paraffin oil (50% v/v 2 ml/kg) twice a week intraperitoneal injection according to (Jayasekhar *et al.*, 1997) and divided into four groups (6 rats each) according to the following scheme for 30 days : (1) positive control (received basal diet), group (2) received basal diet with 25mg/ kg diet silymarin, (3) received basal diet with coriander seed powder 10% diet, (4) received basal diet with 290mg/kg diet coriander essential oil.

Blood samples were collected by orbital venous plexuses through heparinized fine capillary glass tube into two kinds of tubes, the first is heparinized tubes for glutathione peroxidase (GSH-Px) and superoxide dismutase (SOD) assay, the second is not heparinized for separation the serum,the blood was left for 15 min. at room temperature, then the tubes were centrifuged at 3000 rpm for 15 min and kept it at -20 °C for analysis. At the end of experimental, the rats were scarified, liver, spleen, pancreas and kidney were dissected,

weighed and kept in formalin solution 10% according to (Yoon *et al.*, 2001).

**Biochemical analysis:** Aspartate amino transferase (AST), alanine amino transferase (ALT) activities were colorimetrically determined according to the method of (Ritman and Frankel, 1957). α- amylase activity was estimated according to (Caraway, 1959).

Blood haemoglobin was measured according to (Dacie and Lewis, 1984), (GSH-Px) and (SOD) were determined according to (Paglia and Valentine, 1967) and (Nishikimi *et al.*, 1972), respectively. Serum total cholesterol (TC), high density lipoprotein (HDL) cholesterol and triglycerides (TG) were determined according to the methods of (Allain *et al.*, 1974);( Lopez- Virella *et al,.* 1977) and (Fassati and Prencipe, 1982), respectively. Serum total protein, albumin, urea and uric acid were measured according to the methods of (Gornal *et al.*, 1949); (Doumas *et al.*, 1971), (Fawcett and Soctt, 1960) and (Barham and Trinder, 1972), respectively.

Statistical analysis: The standard analysis of variance procedure in a completely randomized design was applied for the present data according to (Gomez and Gomez, 1984). Least significant difference (LSD) and Duncans tests were done to compare a pair of group means. The level of statistical significance was set at $P<0.05$.

## RESULTS AND DISCUSSION

The essential oil from coriander is most commonly extracted from the plant seeds by hydrodistillation. The coriander essential oil content extracted from seeds by hydrodistillation was 0.29%, this has been found in the range reported by (Smallfield et al., 2001; Gil et al., 2002) which amounted 0.125% and 1.90% (v/w), respectively. The results in table (1) show that the composition of coriander essential oil. The concentration of the major constituents of coriander oil was linalool, (74.53%) and the mainor constituents were γ-trpinene (5.60%), camphor (4.82%), α-pinene (2.83%), geranyl acetate (2.83%), ρ-cymene (1.52%), geraniol (1.49%) and limonene (1.27%). Our results agree with (Jeliazkova et al., 1997) who reported that the main compound in coriander oil is linalool 70-75% according to the cultivar and seeding date, and ( Burdock and carabin, 2009) who showed that compositional analysis of essential oil was as follows: linalool (60-80%) , geraniol (1.2-4.6%), γ-trpinene (1-8%), limonene

(0.5-4%), α-pinene (0.2-8.5%) , camphene (trace- 1.4%), myrcene (0.2-2%), camphor (0.9- 4.9%) and genranyl acetate (0.1- 4.7%).

**Table (1): Composition of *Coriander Sativum L.* essential oil extracted by hydrodistillation.**

| Groups | Component | RT | RRT | % |
|---|---|---|---|---|
| **Aliphatic hydrocarbons** | B-myrcene | 10.28 | 0.67 | 0.40 |
| **Aromatic hydrocarbons** | P-cymene | 11.41 | 0.74 | 1.52 |
| **Monocyclic terpenes** | Lemonene | 11.76 | 0.76 | 1.27 |
| | γ- terpinene | 13.00 | 0.84 | 5.60 |
| **Bi-cyclic terpenes** | α- pinene | 8.46 | 0.55 | 2.83 |
| | Camphene | 8.82 | 0.57 | 0.47 |
| | β-pinene | 9.77 | 0.63 | 0.31 |
| **Aliphatic alcohols** | Linalool | 15.31 | 1.00 | 74.53 |
| | Geraniol | 21.54 | 1.40 | 1.49 |
| **Cyclic terpene ketones** | Camphor | 16.34 | 1.06 | 4.82 |
| **Terpene esters** | Geranyl acetate | 27.18 | 1.77 | 2.83 |
| **Total known** | - | - | - | 96.07 |
| **Total unknown** | - | - | - | 3.93 |

Hepatoprotective potential effects of silymarin, Coriander seeds powder, and essential oil on body weight in rats administrated with $Ccl_4$-induced hepatotoxicity are presented in table (2).

The results shown in this table (2), indicate that there was a highly significant decrease at $p<0.05$ in body weight gains (BWG) for the $Ccl_4$-treated group compared to (-) control group. On the other hand, all treatments recorded a significant decrease vs. (-) control. The obtained values of BWGs were -14.46±0.382g, 7.32±0.044g, 9.65±0.426g and 18.77±0.289g vs. 35.32± 0.658g for $Ccl_4$-treated group, Coriander seed, Coriander essential oil, silymarin and Normal control, respectively. The BWG were significantly higher than $Ccl_4$-treated rats in the following order: silymarin (25mg/kg) > coriander essential oil (290mg/kg) > coriander seed powder (10g/100g) diet, respectively. BWG for $Ccl_4$-treated group was extremely lower than the (-) control may be due to the disorder and disturbance in

metabolism of diet components, hepatic enzymes secretion, metabolic pathway which reflect the body weight loss.

**Table (2): Effect of *Coriander Sativum L.* seed, coriander essential oil and silymarin on gain in body weight (g) in carbon tetrachloride intoxicated rats.**

| Weight / Groups | Initial | | Final | | Gain | |
|---|---|---|---|---|---|---|
| | Mean | ±SE | Mean | ±SE | Mean | ±SE |
| **Normal control** | 247.60[a] | 1.92 | 283.00[a] | 1.44 | 35.40[a] | 0.658 |
| **$Ccl_4$-treated** | 248.40[a] | 1.80 | 233.70[e] | 1.44 | -14.46[e] | 0.382 |
| **Silymarin (25mg/kg)** | 247.91[a] | 1.44 | 266.88[b] | 1.17 | 18.77[b] | 0.289 |
| **Coriander seed (10g/100g)** | 246.9[a] | 2.06 | 254.60[d] | 2.10 | 7.77[d] | 0.044 |
| **Coriander essential oil (290mg/kg)** | 248.10[a] | 1.61 | 257.56[c] | 1.19 | 9.46[c] | 0.426 |
| **LSD** | 5.601 | - | 2.829 | - | 1.297 | - |

Values are expressed as Mean ±SE
Mean values in each column have different letters are significant($p<0.05$).

Relative organs weight (%) as a results of the previous treatments are tabulated in table (3), this results indicate that organs weight relative to body weight of the $Ccl_4$-induced hepatic injury group were significantly higher than that of the negative control rats for all organs (liver, spleen, pancreas and kidney). The rats treated with coriander essential oil (290mg/kg), silymarin as reference drug (25 mg/kg) and coriander seed powder (10g/100g), respectively inhibited the increase of the organs weight compared to $Ccl_4$-treated group (positive control). This effects may be due to some chemicals such as $Ccl_4$ catabolised radicals induced lipid peroxidation damage the membranes of liver cells and organelles, causes the swelling and necrosis of hepatocytes (Singh *et al.,* 1998 and Xiong *et al.,* 1998). The protective effect of coriander essential oil or seed powder against $Ccl_4$ may be due to altering the level of antioxidant enzymes which may play an important role in antioxidative defence against oxidative

damage and protect the biological function of the cells (Rajesh and

**Table (3): Effect of *Coriander Sativum L.* seed, coriander essential oil and silymarin on relative organ weights (g/100g of bw) in carbon tetrachloride intoxicated rats.**

| Organ / Group | Liver | | Spleen | | Pancreas | | Kidney | |
|---|---|---|---|---|---|---|---|---|
| | Mean | ±SE | Mean | ±SE | Mean | ±SE | Mean | ±SE |
| Normal control | $2.44^{a}$ | 0.003 | $0.172^{a}$ | 0.007 | $0.124^{a}$ | 0.003 | $0.547^{a}$ | 0.009 |
| $Ccl_4$-treated | $4.55^{d}$ | 0.021 | $0.584^{d}$ | 0.005 | $0.471^{c}$ | 0.023 | $0.933^{c}$ | 0.034 |
| Silymarin (25mg/kg) | $2.78^{b}$ | 0.035 | $0.221^{b}$ | 0.005 | $0.159^{a}$ | 0.005 | $0.647^{b}$ | 0.009 |
| Coriander seed (10g/100g ) | $3.23^{c}$ | 0.047 | $0.248^{c}$ | 0.007 | $0.225^{b}$ | 0.005 | $0.680^{b}$ | 0.015 |
| Coriander essential oil (290mg/kg) | $2.86^{b}$ | 0.006 | $0.218^{b}$ | 0.006 | $0.158^{a}$ | 0.004 | $0.640^{b}$ | 0.020 |
| LSD | 0.08913 | - | 0.01942 | - | 0.03437 | - | 0.06196 | - |

Values are expressed as Mean ±SE

Mean values in each column have different letters are significant ($p<0.05$).

Latha, 2004). The results are shown in table (4) indicate that the level of serum total protein, albumin, urea, uric acid and creatinine were improved according to treatments of rats with silymarin (reference drug), coriander essential oil and coriander seed powder respectively, when compared to $Ccl_4$ control group. Total protein and albumin values were significantly decreased (4.07 ±0.129g/dL and 2.19±0.012 dL) at $p<0.05$ by $Ccl_4$ treated rats than (-) control rats (7.34±0.189 dL and 5.24±0.150 dL). From this table, it was observed that total protein and albumin for $Ccl_4$ –treated group were lower than the (-) ones by about 44.55% and 58.21%, respectively. Conversely treatments with silymarin, coriander essential oil and coriander seed powder were about 17.44%, 18.33%; 25.89%, 30.73 % and 30.25 % and 40.27 %, respectively. This effect may be due to the constituents of the coriander essential oil which play an important role as anti-protein oxidant activity and repair organ tissue from free radicals. The present data are in a good agreement with the findings of (Abraham *et al.*, 1999) who found that $Ccl_4$ administrated resulted in oxidative damage of proteins in rats, also within 24h following $Ccl_4$ administration albumin gene transcription decreased by 85 % whereas alfa-

fetoprotein transcription increased from undetectable levels to 50% of that observed for albumin (Panduro *et al.,* 1986). On the other hand, $Ccl_4$- treated group showed that serum urea nitrogen about (36.97±0.928 mg/dl) higher than (-) control which was (21.99±0.284 mg/dl). All treatments had significant decrease serum urea nitrogen level as compared to $Ccl_4$-treated group. The best value (29.34 ± 0.505 mg/dl) for coriander essential oil with comparable that of the reference drug silymarin (26.53±0.611 mg/dl).

**Table (4): Effect of *Coriander Sativum L.* seed, coriander essential oil and silymarin on total protein, albumin, urea and kidney functions in carbon tetrachloride intoxicated rats.**

| Parameter / Group | Total protein (g/dl) | | Albumin (g/dl) | | Urea (mg/dl) | | Uric acid (mg/dl) | | Creatinine (mg/dl) | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Mean | ±SE | Mean | ±SE | Mean | ±SE | Mean | ±SE | Mean | ±SE |
| Normal control | 7.34$^{a}$ | 0.189 | 5.24$^{a}$ | 0.150 | 21.99$^{a}$ | 0.284 | 5.04$^{a}$ | 0.038 | 0.67$^{a}$ | 0.022 |
| $Ccl_4$-treated | 4.07$^{d}$ | 0.129 | 2.19$^{e}$ | 0.012 | 36.97$^{e}$ | 0.928 | 8.03$^{d}$ | 0.145 | 1.89$^{d}$ | 0.022 |
| Silymarin (25mg/kg) | 6.06$^{b}$ | 0.148 | 4.29$^{b}$ | 0.060 | 26.53$^{b}$ | 0.611 | 5.67$^{b}$ | 0.088 | 0.91$^{b}$ | 0.062 |
| Coriander seed (10g/100g) | 5.12$^{c}$ | 0.064 | 3.13$^{d}$ | 0.069 | 31.85$^{d}$ | 0.828 | 6.27$^{c}$ | 0.053 | 1.34$^{c}$ | 0.034 |
| Coriander essential oil (290mg/kg) | 5.44$^{c}$ | 0.130 | 3.63$^{c}$ | 0.057 | 29.34$^{c}$ | 0.505 | 5.99$^{bc}$ | 0.116 | 1.21$^{c}$ | 0.055 |
| LSD | 0.4352 | - | 0.2611 | - | 2.117 | - | 0.3041 | - | 0.1338 | - |

Values are expressed as Mean ±SE
Mean values in each column have different letters are significant (P<0.05).

From the data in the same table, it could be observed that uric acid and creatinine levels were increased significantly at $p< 0.05$ in $Ccl_4$-treated group as a compared to the (-) control which represent (8.03±0.145 mg/dl and 1.89±0.022 mg/dl) vs. (5.04± 0.038mg/dl and 0.67 ±0.022mg/dl), respectively. The rats were treated with 290mg/kg coriander essential oil has significant decrease in both serum uric acid and creatinine levels compared to $Ccl_4$ group this agree with (Simerville *et al.,* 2005) who considered the creatinine is possible indicator of hepatic and / or kidney injuries induced through $Ccl_4$ treatment.

The biochemical enzymes activities in normal, $Ccl_4$ control and treated groups were represented in table (5), the activities of marker enzymes (ALT, AST) levels were highly significant ($p<0.05$) increased in $Ccl_4$-treated control compared to normal control group. The levels of the ALT, AST activities were significantly decreased after treatments of rats with silymarin, coriander essential oil and coriander fruits powder compared to $Ccl_4$ group. The hepatoprotective effect of silymarin, essential oil and coriander powder increased by reducing of ALT and AST, the % of reduction were (72.81% and 73.45%), (65.72% and 69.40%) and (56.02% and 61.80%), respectively compared to $Ccl_4$-treated group. $Ccl_4$ causes liver cell damage by generating reactive free radicals and causing lipid peroxidation.

**Table (5): Effect of *Coriander Sativum L.* seed, coriander essential oil and silymarin on ALT, AST, α-amylase and erythrocyte antioxidant enzymes activity in carbon tetrachloride intoxicated rats.**

| Parameter / Group | ALT(U/ml) | | AST(U/ml) | | SOD(U/g Hb) | | GSH- Px (nmol/min/g Hb) | | α-amylase(U/L) | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Mean | ±SE | Mean | ±SE | Mean | ±SE | Mean | ±SE | Mean | ±SE |
| Normal control | $23.10^a$ | 0.06 | $31.88^a$ | 0.58 | $391.24^a$ | 1.16 | $41.62^a$ | 0.44 | $222.83^a$ | 0.48 |
| $Ccl_4$-treated | $126.59^e$ | 0.42 | $166.16^e$ | 2.39 | $256.30^e$ | 1.79 | $21.03^e$ | 0.89 | $642.33^e$ | 2.02 |
| Silymarin (25mg/kg) | $34.42^b$ | 1.58 | $44.12^b$ | 1.26 | $361.32^b$ | 1.71 | $36.09^b$ | 0.93 | $241.58^b$ | 1.57 |
| Coriander seed (10g/100g) | $55.67^d$ | 0.30 | $63.47^d$ | 1.46 | $318.78^d$ | 1.06 | $28.04^d$ | 0.93 | $315.37^d$ | 2.05 |
| Coriander essential oil (290mg/kg) | $43.39^c$ | 1.24 | $50.84^c$ | 1.13 | $331.36^c$ | 1.83 | $31.27^c$ | 0.76 | $290.78^c$ | 1.83 |
| LSD | 2.926 | - | 4.683 | - | 4.867 | - | 2.527 | - | 5.328 | - |

Values are expressed as Mean ±SE
Mean values in each column have different letters are significant ($p<0.05$)

Usually, the extract of hepatic injury achieved when cytoplasmic enzymes (ALT, AST) levels were increased, thus leads to leakage of large quantities of enzymes into the blood circulation, massive centrilobular necrosis, ballooning degeneration of the liver, (Plaa and

Charbonneau, 1989). In our study, the rats treated with coriander Sativum essential oil or powder enhanced ALT and AST enzymes activities, which may be a consequence of the stabilization of plasma membrane as well as repair of hepatic tissue damage by $Ccl_4$ and regeneration of hepatocytes (Thabrew *et al.*, 1987), this results agree with the histopathological findings. On the other hand, hepatic antioxidant enzymes activities such as superoxide dismutase (SOD) and glutathione peroxidase (GSH-Px) were measured as an index for essential for endogenous antioxidative defence system to scavenge the reactive oxygen species (ROS) and maintain cellular redox balance (Venukumar and Lathal, 2002).

There were a highly significant decreased in $Ccl_4$ treated rats for both SOD and GSH-Px levels in erythrocyte (34.5% and 49.5%) compared to normal control. Conversely, there were significant increase in GSH-Px level in rats treated with silymarin, coriander essential oil by about (71.61% and 48.69%) compared to $Ccl_4$-treated group, this may be due to essential oil component such as linalool and terpenes and their stimulatory action which caused an increase in the activity of antioxidant enzymes or stimulatory action on transcription and gene expression of certain antioxidant enzymes (Rohrdanz *et al.*, 2002).

α-amylase is produced in pancreas where it plays an important role in digestion of complex carbohydrates (starch) to glucose. From the data presented in table (5) it was observed that the mean value of normal control was (222.83±0.48U/L). Conversely there was a highly significant increase of α-amylase level in $Ccl_4$-treated group (642.33±2.02U/L). On the other hand, treatments (silymarin, coriander essential oil and coriander seed powder) had significantly decrease of α-amylase activity by about (62.39%, 54.73% and 50.90% respectively) compared to $Ccl_4$-treated group. This effect may be due to that α- amylase released into the circulation by damage to tissues containing high levels of the enzyme or by escape from the gastro-intestinal tract these results agree with (Maezawa *et al.*, 1973) who reported that serum α-amylase level was higher in $Ccl_4$-intoxication rats may be due to decrease in urinary output .

Effect of $Ccl_4$ hepatotoxicity and treatments (silymarin, coriander essential oil and powder) on lipid profile of rats suffering from liver injury were expressed in table (6). $Ccl_4$-treated group had shown a significant increase $P<0.05$ in the mean value of triglycerides

(146.94±0.72 mg/dl) and total cholesterol (162.73±0.81mg/dl) compared to normal group which was (85.01±0.74 and 72.83± 0.7), respectively.

**Table (6): Effect of *Coriander Sativum L.* seed, coriander essential oil and silymarin on triglycerides, total cholesterol and HDL-cholesterol in carbon tetrachloride intoxicated rats.**

| Parameter / Group | Triglycerides (mg/dl) | | Total cholesterol (mg/dl) | | HDL- cholesterol (mg/dl) | |
|---|---|---|---|---|---|---|
| | Mean | ±SE | Mean | ±SE | Mean | ±SE |
| Normal control | $85.01^{a}$ | 0.74 | $72.83^{a}$ | 0.70 | $30.20^{a}$ | 1.90 |
| $Ccl_4$-treated | $146.94^{d}$ | 0.72 | $162.73^{e}$ | 0.81 | $16.13^{d}$ | 0.60 |
| Silymarin (25mg/kg) | $94.54^{b}$ | 0.40 | $87.96^{b}$ | 0.76 | $24.83^{b}$ | 0.30 |
| Coriander seed (10g/100g ) | $99.23^{c}$ | 0.50 | $105.41^{d}$ | 1.12 | $20.94^{c}$ | 0.21 |
| Coriander essential oil (290mg/kg) | $95.72^{b}$ | 0.58 | $96.68^{c}$ | 0.54 | $23.00^{bc}$ | 0.32 |
| LSD | 1.647 | - | 2.553 | - | 2.890 | - |

Values are expressed as Mean ±SE
Mean values in each column have different letters are significant ( $p<0.05$ ).

On the other hand, the results of rats injected with $Ccl_4$ and treated with silymarin, coriander essential oil or powder showed a significant decrease $p<0.05$ in serum level of both TG and TC. The rats treated with coriander oil has a significant decrease by about (34.85%) and (40.59%) for TG and TC, respectivly compared to (+) control group. The results of HDL-C showed a significant decrease for (+) control that read (16.13±0,06mg/dl) by about (46.60%) compared to (-) control which read (30.20±1.9mg/dl). This results agree with (Chithra and Leelamma, 1997), Who reported that feeding of 10% coriander Sativum fruits powder to rats for 75 days resulted in a significant reduction in serum TC level and significant increase in HDL-C.

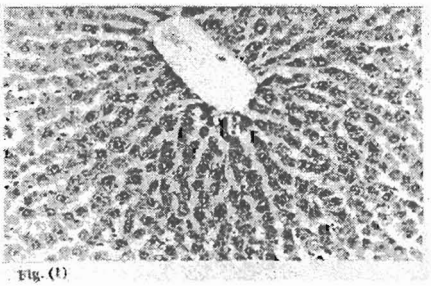
**Histopathological examination:**

**Liver:** microscopical examination of liver normal control rat revealed the normal histology of hepatic lobules from central vein and hypatocytes fig. (l) . Conversely, liver from $Ccl_4$ treated rat showed large local area of hypatocytes necrosis which completely replaced by massive infiltration with leucocytic and fibroblasts figs (2,3), marked kupffer cells activation and portal infiltration with leucocytes fig. (4) were noticed. Meanwhile, apparent normal hypatocytes was noticed in liver of rats fed on silymarin diet fig. (5).The only histopathological finding observed in liver rat from rats fed on coriander seed powder diet was slight activation of kupffer cells fig. (6). However, slight hydropic degeneration of hypatocytes was noticed in fig. (7). The rats treated with $Ccl_4$ and fed on coriander oil or coriander seed powder diets resulted in a high significant improvement in the liver histopathological changes compared to positive control ($Ccl_4$ group).We recommend that coriander oil or coriander seed powder should be incorporated into the treatments of liver hypatotoxicity and it complication due to their hepatoprotective and clinical effects .

**Pancreas:** Examination of pancreas of control (-) ve normal control rat showed no histopathological changes fig. (8). On the other hand , pancreas of positive control ($Ccl_4$ treated) rat revealed congestion of blood vessels, oedema and cystic dilatation of pancreatic dct fig. (9) .conversely, pancreas of rats fed on silymarin, coriander seed powder and coriander oil figs (10,11and12).

**Spleen:** Microscopically, spleen of control (-ve) rat showed normally lymphoid follicls fig. (13). Mean while, spleen sections of control (+ve) rat revealed lymphocytic necrosis and depletion fig. (14). However, no histopathological changes were observed in spleen section of rat from the other group figs (15, 16 and 17) compared to $Ccl_4$-treated group.

**Kidney:** Kidney of control (–) rat showed the normal histology of renal parenchyma fig. (18). on the other hand, kidney of contort (+) rats showed marked distension of renal pelvis with radiating fan shaped crystals surrounded by inflammatory cells and chronic interstitial nephritis figs. (19 and 20). On the other hand, kidney of rat from rat fed on silymarin, coriander seed powder and coriander oil revealed no histopathological changes figs. (21, 22 and 23).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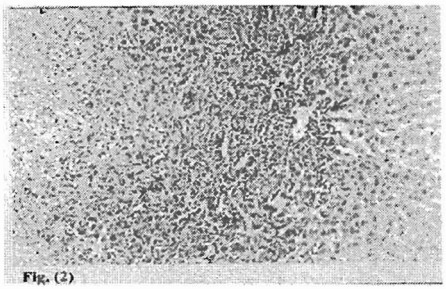
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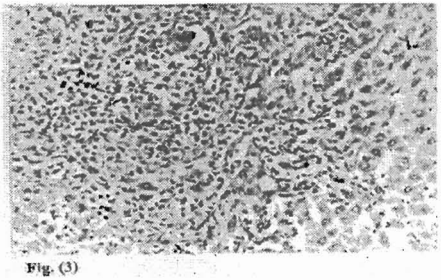
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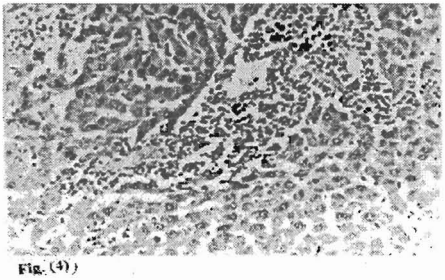
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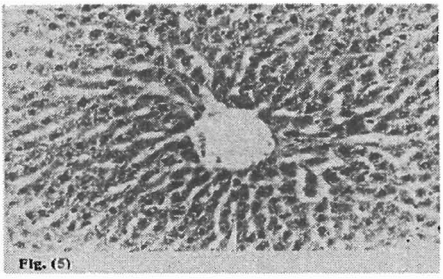
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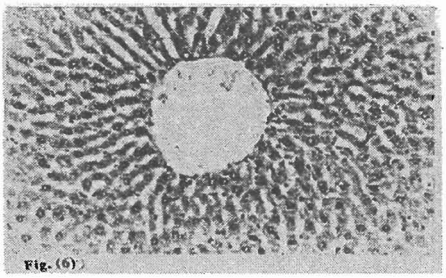
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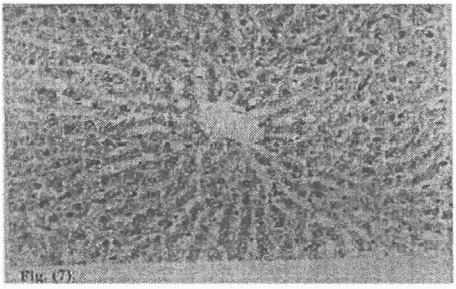


Fig. (7)

**Sections in liver:**

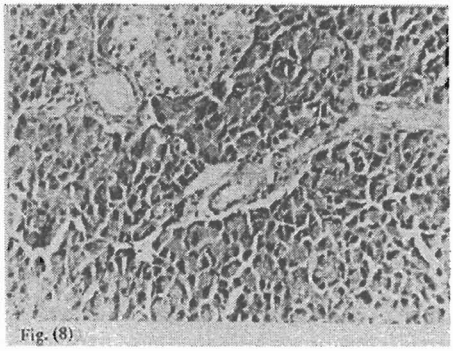
**Fig . (1): Normal group (Negative control).**

**Fig . (2, 3and4): Ccl4 group (Positive control).**

**Fig . (5): Silymarin group.**

**Fig . (6): Coriander seed powder group.**

**Fig . (7): Coriander essential oil group.**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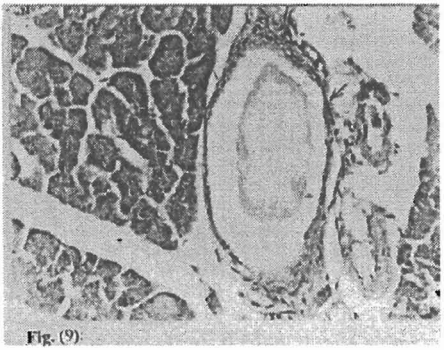
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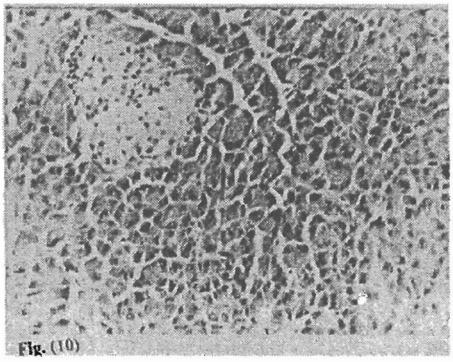
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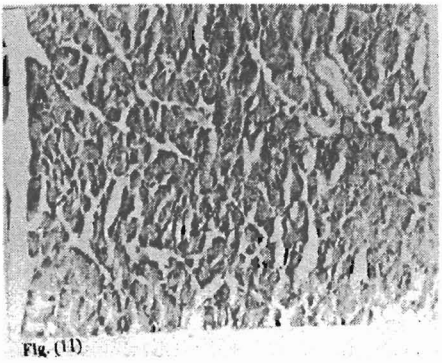
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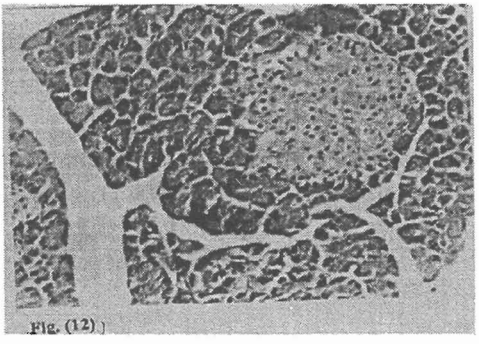
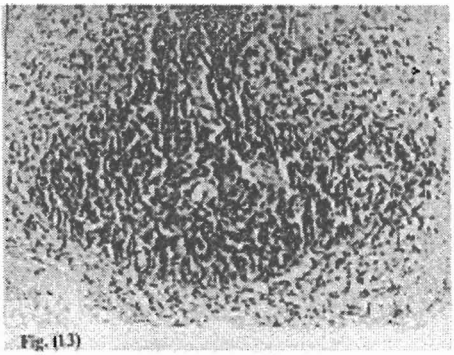


Fig. (12)

**Sections in pancreas:**
**Fig . (8): Normal group (Negative control).**
**Fig . (9): Ccl4 group (Positive control).**
**Fig . (10): Silymarin group.**
**Fig . (11): Coriander seed powder group.**
**Fig . (12): Coriander essential oil group.**



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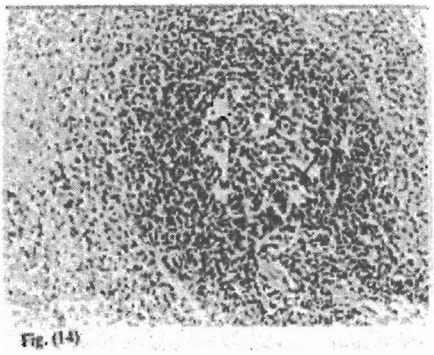

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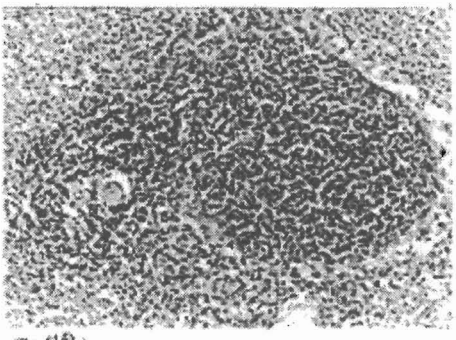

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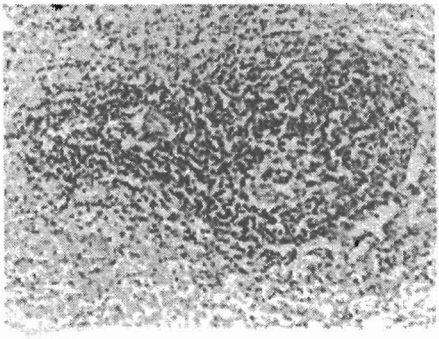

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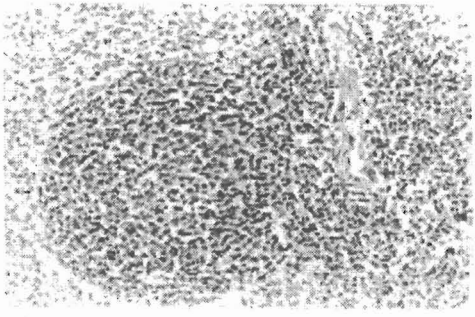
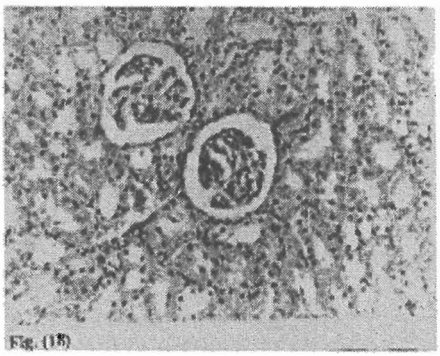


Fig. (17)

**Sections in spleen:**

**Fig . (13): Normal group (Negative control).**
**Fig . (14): Ccl4 group (Positive control).**
**Fig . (15): Silymarin group.**
**Fig . (16): Coriander seed powder group.**
**Fig . (17): Coriander essential oil group.**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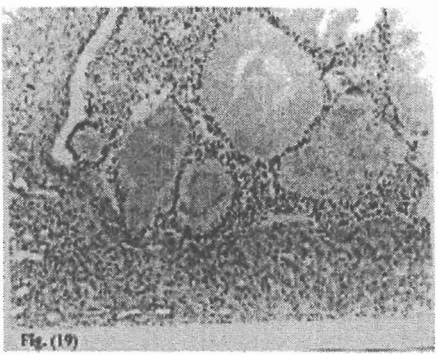
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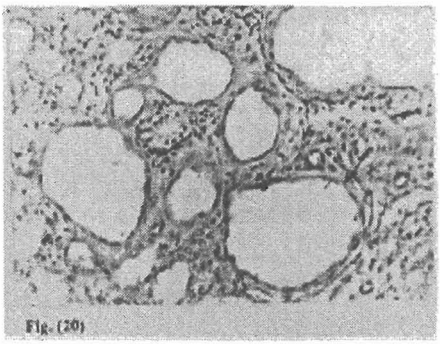
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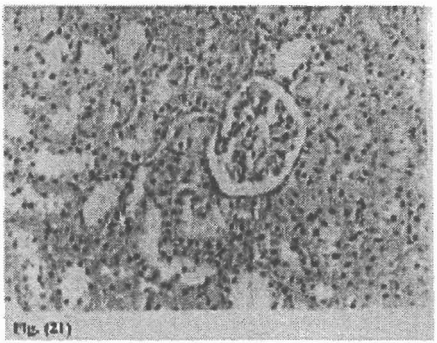
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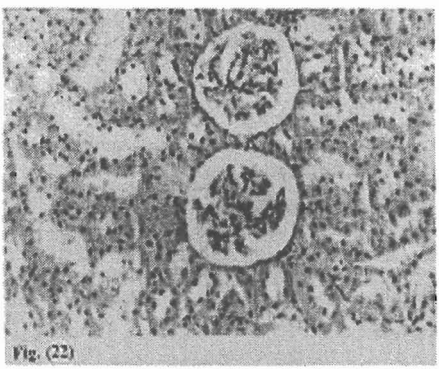
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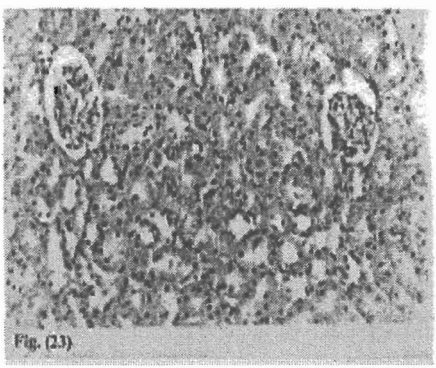
Fig. (23)

**Sections in kidney:**
**Fig. (18): Normal group (Negative control).**
**Fig. (19and20): Ccl4 group (Positive control).**
**Fig. (21): Silymarin group.**
**Fig. (22): Coriander seed powder group.**
**Fig. (23): Coriander essential oil group.**

**Conclusion:**

We recommended that coriander oil and seeds powder should be incorporated into to the treatments of liver hypatotoxicity and it's complications due to their hepatoprotective and clinical effect. So, the people should be consumed spices mixtures or/ and Egyptian public dishes which rich in coriander seed powder such as tamea and cooked Jew' s mallow ground leaves (moloukhia) to protect themselves from cancer hazards.

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## نشاط الكزبرة المضاد للأكسدة و دورها الوقائي ضد رابع كلوريد الكربون المسبب للأكسدة المجهدة في كبد فئران التجارب

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هذه الدراسة صممت لدراسة التأثير الوقائى لمضادات الأكسدة الطبيعية الموجودة فى مسحوق الكزبرة المستخدم بنسبة 10% و الزيت الطيار الخاص بها المستخدم بنسبة 290 مليجرام/كجم عليقة ضد التأثير المؤكسد لرابع كلوريد الكربون فى فئران التجارب الألبينو. حيث تم تقسيم الفئران إلي مجموعتين رئيستين، المجموعة الأولى ( 6 فئران) تم تغذيتها على عليقة أساسية كمجموعة كنترول سالب ، المجموعة الثانية( 24 فأر) تم معاملتها برابع كلوريد الكربون المخفف بزيت البرافين (50% حجم/حجم) بواقع 2 مل/كجم من وزن الفئران مرتين أسبوعيا داخل الغشاء البروتونى ثم قسمت لأربعة مجاميع (6 فئرن لكل منها) و فقا للخطة التالية لمدة 30 يوم : مجموعة (1) كنترول موجب (تناولت عليقة أساسية فقط) ، مجموعة (2) تناولت عليقة قياسية + 25 مليجرام سليمارين /كجم ، مجموعة (3) تناولت عليقة أساسية + مسحوق الكزبرة بنسبة 10% ، المجموعة (4) تناولت عليقة أساسية + زيت الكزبرة الطيار بنسبة 290 مليجرام /كجم عليقة . وو جد ان الحقن داخل الغشاء البروتونى برابع كلوريد الكربون نتج عنه زيادة معنوية فى مستويات الأسبرتيت ترانس أمينيز (AST) و الألانين ترانس أمينيز (ALT) مع قلة فى الانزيمات المضادة للأكسدة. و أن مستويات البروتين الكلى و الألبيومين في السيرم قد زادت بتغذية الفئران المعاملة برابع كلوريد الكربون علي زيت الكزبرة الطيار و مسحوقها. ووجد أيضا ان وظائف الكلى و الكبد قد تحسنت بزيادة معنوية فى الانزيمات المضادة للأكسدة مثل السوبر أوكسيد دسميوتيز (SOD) و الجلوتاثيون بيروكسيديز (GSH.Px) . و اوضح الفحص الهستوباثولوجى حدوث ضرر بالكبد مع وجود مساحات كبيرة من الخلايا الكبدية الميتة الذى حل محلها أ رتشاح كبيرو خلايا ملتهبة و خلايا متليفة فى الفئران المعاملة برابع كلوريد الكربون. ووجد أن الزيت الطيار للكزبرة قلل معنويا التأثير السام لرابع كلوريد الكربون عند مقارنته بالكنترول الموجب وهذا مرتبط بتأثير مكوناته المضادة للأكسدة و الكاسحة للشقوق الحرة.