

The Hepatoprotective Activity of Turmeric Extract against Carbon Tetrachloride Induced Hepatotoxicity in Male Rats

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Abstract

The aim of this study was to evaluate the hepatoprotective effect of turmeric extract of *Curcuma longa* on carbon tetrachloride induced hepatotoxicity in male rats. The hepatoprotective activity was assessed using various biochemical parameters like lipid profile, Liver enzymes, antioxidant enzymes and histological examinations of the liver were also carried out. Forty-five males rats (Wistar strain) weighing approximately 175-205 g were divided into five groups. Each consisted of nine rats as follows: Group A: healthy control rats) subjected to 1ml olive oil administration orally using gastric tube daily for 4 weeks. The rats of Group B, Group C, Group D and Group E were injected with Carbon tetrachloride (0.1 mL/ 100 g body weight) dissolved in olive oil [1:1(v/v)] twice weekly in the first day and fourth day every week for four weeks. Group B: Hepatotoxic control rats (positive control rats). Group C, D and Group E were treated daily with 1 ml of olive oil containing 50,100 and 150 mg of turmeric extract (kg of body weight) for 4 weeks orally using a gastric tube respectively. The hepatotoxic control rats(positive control rats) showed an increase in total triglycerides , total cholesterol, low density lipoprotein, very low density lipoproteins, total Bilirubin, liver enzymes , malondialdehyde concentration (MDA) and decreased in Total protein, Albumin, high density lipoprotein cholesterol, antioxidant enzymes and lipid peroxide compared with the healthy control rats (Group A). Treating the hepatotoxic rats with turmeric extract showed a significant decreased in total triglycerides and total cholesterol, low density lipoprotein, very low density lipoproteins, total Bilirubin, liver enzymes and malondialdehyde concentration (MDA) and increased in Total protein, Albumin, high density lipoprotein cholesterol, antioxidant enzymes and lipid peroxide compared with hepatotoxic control rats(group B). Treating the hepatotoxic rats with turmeric extract showed a significant improvement in all biochemical tests compared with the hepatotoxic control rats (group B). Treating with turmeric extract were improvement in all biochemical and histological analysis in hepatotoxic rats compared with the hepatotoxic control rats(Group B).

Key words Turmeric extract, hepatoprotective effect, lipid profile, Liver enzymes, antioxidant enzymes, histological examinations

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I. Introduction

The liver is a very important vital organ responsible for maintaining most of the vital physiological functions of the human body. It performs multiple regulatory roles in various metabolic, excretory and elimination processes (Eidi *et al.*, 2012). It is also the main organ of the metabolism and detoxification of vital foreign substances, and therefore it is prone to many harmful infections with concurrent impairment in its vital functions which leads to many life-threatening disorders, such as hepatitis, cirrhosis, hepatic failure, and dreadfully hepatocellular carcinoma (Akindele *et al.*, 2010). Liver injuries are mainly caused by many factors, including toxic chemicals, such as CCl₄ and aflatoxin, alcohol, drugs, viruses, as well as dangerous environmental pollutants (Ali *et al.*, 2014). Such hepatic injuries are generally associated with elevated serum liver enzyme levels, hepatocyte necrosis, plasma membrane damage, and increased oxidative stress with significantly glutathione depletion (Navarro and Senior 2006). Around the world, liver disease has undoubtedly become a rapidly increasing health burden with high death rates. Moreover, besides the terrible suffering of the patients, the current treatment methods, including drug therapy and liver transplantation, are modestly effective and are also accompanied by many dangerous complications (Bishayee *et al.*, 2006). Consequently, these concerns have stimulated the search for other safe and effective alternatives to drugs, especially of natural origin. In this context, medicinal plants and their secondary biologically active metabolites have received great attention due to their enormous potential for managing and correcting various forms of hepatopathy (Shen *et al.*, 2015). Diverse plant extracts were assessed for their hepatoprotective effect against different experimentally induced liver toxicities (Rashmi and Shenoy, 2020). Turmeric (*Curcuma longa*) is an evergreen herbaceous plant in the Zingiberaceae (ginger) family. Turmeric is widely used as a flavoring, food preservative and colorant. Turmeric

powder is well-known as one of the main ingredients used in making curry condiment (Rahul Kumar *et al.*, 2018). It also gives a bright yellow mustard color. Aside from its culinary uses, turmeric has been used extensively in traditional medicine all over the world. Curcumin the main bioactive yellow component in turmeric has been shown to have a broad spectrum of biological actions. These include antioxidants, anticancer drugs, antibacterial, anti-inflammatory drugs, anticoagulants, anti-fertility, antidiabetics, antifungal, anti-fibrosis, antiprotozoal, antivirals, antitoxins, anti-ulcers, lowering blood pressure, and hypotension Cholesterol (Nabavi *et al.*, 2014 and Park *et al.*, 2000). For traditional Ayurveda, the turmeric plant was an excellent natural cleanser, antiseptic, anti-inflammatory and analgesic, while the plant is often used simultaneously to aid digestion, improve intestinal flora, and treat skin irritation. Curcumin is a polyphenol extracted from the turmeric (*Curcuma longa*). Turmeric rhizome contains Volatile oil (1-6.5%) mainly composed of α and β termerone, monoterpene, 5% curcuminoids mainly curcumin, demethoxy curcumin and bisdemethoxy curcumin, resin, and abundant zingiberaceous starch grains. The main active constituent of *Curcuma longa* is curcumin (50-60%) which is the yellow substance and is responsible for the therapeutic activities (Anand *et al.*, 2008). The aim of this study was to evaluate the hepatoprotective activity of turmeric extract against carbon tetrachloride induced hepatotoxicity in male rats.

II. Materials and Methods

1- Preparation of turmeric extract

The turmeric rhizomes were cleaned, dried, ground and homogenized in 95% ethanol at a ratio of 1:10 of turmeric powder to ethanol and left to soak for 48 hours at 25°C with occasional shaking and stirring. The mixtures were filtered and the resulting liquid was concentrated under reduced pressure at 45°C in a rotary evaporator to yield a dark gummy-yellow extract (9% w/w). The concentrated extract was then kept in the oven under vacuum at 40°C for 24 hours to evaporate the ethanol residue yielding the crude rhizome extract. Extracts were then dissolved in corn oil before being orally administered to rats in concentrations of 50, 100 and 150 mg/kg body weight

2 – Experimental animals

Forty-five male rats (Wistar strain) weighing approximately 175-205 g were obtained from King Fahd Center for Medical Research, King Abdulaziz University, Jeddah, Saudi Arabia. All animal experiments were performed under protocols approved by the Institutional Animal House of King Abdulaziz University, Jeddah, Saudi Arabia.

Rats were housed in standard laboratory conditions at (25 ± 3 ° C), relative humidity (50-55%) and a 12-hour light / dark cycle (five mice / cage) two weeks prior to the start of the experiment. Cages, bedding, and glass water bottles (equipped with stainless steel tubes) were replaced twice a week. The stainless steel feed containers are changed once a week. All animals are fed standard nutritionally balanced diet, drinking water and libitum.

3 - Experimental design

Forty-five Albino male were randomly divided into five groups. Each consisted of nine rats as follows: Group A: healthy control rats) subjected to 1ml olive oil administration orally using gastric tube daily for 4 weeks.

Induction of hepatotoxicity:

The rats of Group B, Group C, Group D and Group E were injected with mixture of Carbon tetrachloride (0.1 mL/ 100 g body weight) dissolved in olive oil [1:1(v/v)] twice weekly in the first day and fourth day every week for four weeks

Group B: Hepatotoxic control rats) positive control rats.

Group C: Hepatotoxic rats were treated daily with 1 ml of olive oil containing 50 mg of turmeric extract (kg of body weight) for 4 weeks orally using a gastric tube.

Group D: Hepatotoxic rats were treated daily with 1 ml of olive oil containing 100 mg of turmeric extracts (kg of body weight) for 4 weeks orally using a gastric tube.

Group E: Hepatotoxic rats were treated daily with 1 ml of olive oil containing 150 mg of turmeric extract (kg of body weight) for 4 weeks orally using a gastric tube.

All group rats were feed on basal diet and water for 4 weeks.

3 - Methods

At the end of the experimental period, all mice were fasted overnight and then anesthetized with ether and sacrificed. The blood was collected and allowed to clot. Serum was separated by centrifugation at 3000 rpm for 15 min and then the serum was transferred to sterile vials with appropriate markings and stored at -20 ° C until laboratory analysis.

Liver tissue homogenate

A piece of the liver tissue was cut into small pieces and washed with phosphate-buffered saline and then grinded in a homogenization buffer consisting of 0.05 M Tris HCl pH 7.9, 25 % glycerol, 0.1 mM EDTA, and 0.32 M (NH₄)₂SO₄ and containing a protease inhibitor tablet . The lysates mix was homogenized on ice using a homogenizer. The mixture was vocalized in an ice bath to prevent overheating for 15 s followed by 5 min centrifugation at 12,000 rpm and 4°C. The supernatant was split and stored at -70 °C.

Total bilirubin was estimated according to the method by (Fevery *et al.*, 1979), Total protein was determined according to the method (Dumas *et al.*, 1981).Serum albumin was estimated according to the method of (Webster, 1977).

Liver enzymes

Serum alanine aminotransferase (ALT) and serum aspartate transaminase (AST) were determined according to the method of (Henry *et al.*, 1960) and serum alkaline phosphatase (ALP) was estimated according to (King and King, 1954).

Lipid profile evaluation

Serum total cholesterol (TC) was determined according to the method of Richmond , (1973), serum triacylglycerol according to Fossati and Prencipe , (1982) , serum high-density lipoprotein(HDL) by the method of (Steele *et al.* ,1976) while serum low-density lipoprotein (LDL) and very low-density lipoprotein (VLDL) in blood was calculated according to use of the equation of Friedewald *et al.* , (1972) as follows:

$$1\text{-LDL} = \text{TC} - (\text{HDL} + \text{TG}/5).$$

$$2\text{-VLDL} = \text{TC} - (\text{LDL} + \text{HDL}).$$

Malondialdehyde concentration (MDA) was measured as an indication of lipid peroxidation using the colorimetric method described by (Draper and Hadly, 1990).

Antioxidants and lipid peroxide

Antioxidant enzymes (catalase, glutathione-S-transferase), and lipid peroxide were tested in serum and liver tissue homogenate calorimetrically using a bio-diagnostic kit (Saudi Arabia), according to the manufacturer's instructions. Calculations of catalase activity, glutathione-s-transferase activity, and lipid peroxide concentration were estimated by the appropriate formula for the kits.

Histopathological analysis

A portion of the liver was fixed in 10 % formalin, dehydrated in gradual ethanol (50–99 %), cleared in xylene, and embedded in paraffin. Sections were prepared and then stained with hematoxylin and eosin dye for microscopic investigation (Suvarna *et al.*, 2013)

Bioactive components of turmeric extract were determined according to the method of (Sawant and Godghate, 2013, Trease and Evan 1983).

Statistical Analysis

Statistical analysis of the data was carried out by ANOVA using SAS statistical software (SAS, 1998). The significant differences among means were assessed by Duncan's multiple range tests (Duncan, 1955).

III. Results and Discussions

Bioactive components in turmeric extract are presented in Table 1. The results indicated the presence of curcumin, polyphenols, sterols, terpenes, tannins, flavonoids, quinines, reducing compounds and alkaloids.

Table 1: Bioactive components in turmeric extract

Bioactive components	Detection
Flavonoids	+
Alkaloids	+
Tannins	+
Saponins	-
Polyphenols	+
Sterols and Terpenes	+
Quinones	+
Curcumin	+
Reducing compounds	+

Effect of turmeric extract on Total protein, Albumin and Total Bilirubin in in carbon tetrachloride induced hepatotoxicity in male rats are presented in Table. (2). Results of present work indicate that, the hepatotoxic control rats (Group B) were decreased in levels of Total protein, Albumin and significantly ($p < 0.05$) increased in Total Bilirubin mg/dl comparing with healthy control (Group A) by 43.90 %, 49.79 and 215.56 % respectively. Results also indicate that, the hepatotoxic rats treated with turmeric extract with 50 (Group c), 100 (Group D) and 150 mg/kg of body weight (Group E) were increased in Total protein and Albumin by 17.82, 41.67, 70.32 % and 32.48, 66.24. 82.91 Respectively compared with hepatotoxic control rats (Group B). on the other side, the treatment of turmeric extract with hepatotoxic rats at 50, 100 and 150 mg/kg of body weight were

decreased in Total Bilirubin mg/dl by 43.66, 52.11 and 59.86% respectively compared with hepatotoxic control rats (Group B). These results are agreement with Fu et al., 2008. Who found that, carbon tetrachloride induced hepatotoxicity in male rats produced a significant reduction in plasma total protein and albumin level. This may be due to release of these parameter from the cytoplasm into the blood rapidly after cellular damage and a reduction in hepatic protein synthesis. (Khedr and Khedr, 2014) reported that plasma total protein and albumin level was increased by curcumin administration compared to rats exposed to carbon tetrachloride induced hepatotoxicity.

Table 2. Effect of turmeric extract on Total protein, Albumin and Total Bilirubin in carbon tetrachloride induced hepatotoxicity in male rats

Treatments	Total protein	Albumin	Total Bilirubin mg/dl
Healthy control group (Group A)	7.70 ^a	4.66 ^a	0.45 ^e
Hepatotoxic control rats (Group B)	4.32 ^d	2.34 ^d	1.42 ^a
Hepatotoxic rats treated with 50 mg turmeric extract (Group C)	5.09 ^c	3.10 ^c	0.80 ^b
Hepatotoxic rats treated with 100 mg turmeric extract (Group D)	6.12 ^b	3.89 ^b	0.68 ^c
Hepatotoxic rats treated with 150 mg turmeric extract (Group E)	7.38 ^a	4.28 ^a	0.57 ^d

Values with different letters in the same column are significantly different at P<.0.05.

Lipid profile

Effect of turmeric extract on total triglycerides and total cholesterol levels in male rats exposed to carbon tetrachloride induced hepatotoxicity are presented in Fig (1). Results of present work indicate that, hepatotoxic control rats (Group B) were increased in total triglycerides and total cholesterol by 110.23 % and 71.77 % respectively, compared with healthy control rats (Group A). Hepatotoxic rats treated with turmeric extract at 50, 100 and 150 mg/kg of body weight were decreased in serum total cholesterol by 22.31, 32.64 and 38.02 % for (Group C), (Group D) and (Group E) respectively compared with hepatotoxic control rats (Group B). While, hepatotoxic rats treated with turmeric extract at 50 (Group C), 100 (Group D) and 150 mg/kg of body weight (Group E) were reduced of Triglycerides levels by 18.09, 32.16 and 49.78 % respectively when compared to hyperglycemic control rats (Group B). (Arafa, 2005) reported that, the effect of curcumin on cholesterol could be due to an effect on cholesterol absorption, degradation or removal, but not due to an antioxidant mechanism.

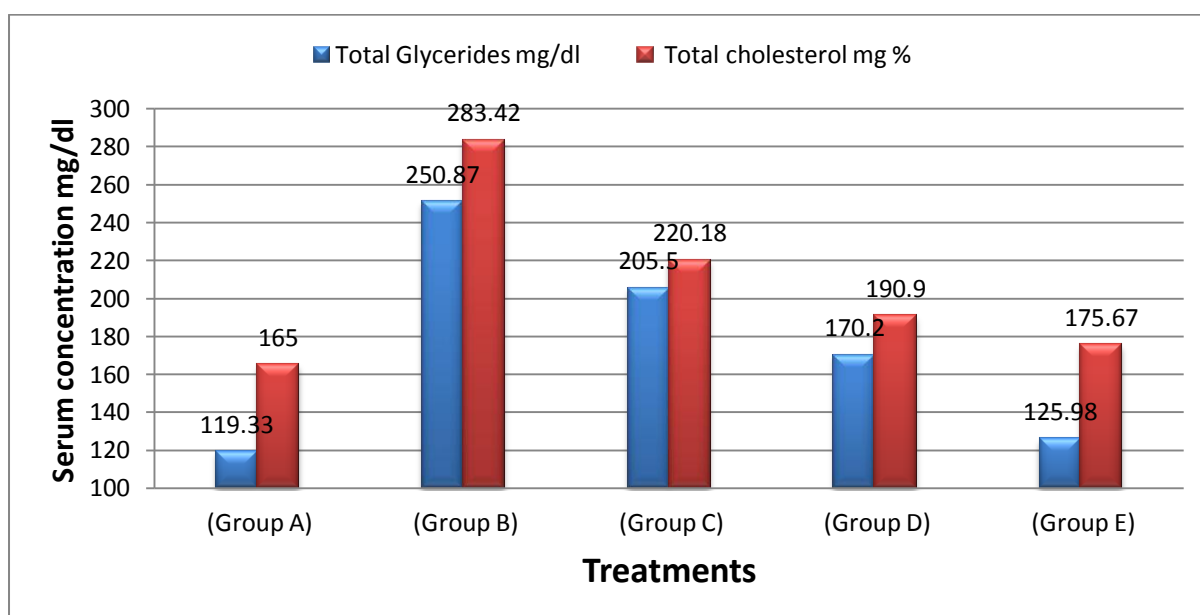


Fig.1.Effect of turmeric extract on total triglycerides and total cholesterol levels in carbon tetrachloride induced hepatotoxicity in male rats

Effect of turmeric extract on high-density lipoprotein cholesterol HDLc, low- density lipoprotein cholesterol LDLc and very low density lipoprotein cholesterol VLDLc in male rats exposed to carbon tetrachloride induced hepatotoxicity are shown in Fig (2). Results of present work indicate that, the hepatotoxic

control rats (Group B) were increased in LDLc and VLDLc compared with the healthy control rats (Group A) by 121.53 and 110.22 % respectively. While, the hepatotoxic control rats (Group B) were decreased in HDLc compared with the healthy control rats (Group A) by 36.65%. Results also indicate that, the hepatotoxic rats treated with turmeric extract (Group c), (Group D) and (Group E) were increased in high density lipoprotein cholesterol HDLc by 18.93, 39.0 and 49.62 % respectively. on the other side, the hepatotoxic rats treated with turmeric extract at 50, 100 and 150 mg/kg of body weight were decreased in LDLc and VLDLc by 29.87, 44.07 and 48.92% for LDLc respectively, while the decrease values of VLDLc were 18.09, 32.14 and 49.80% respectively compared with hepatotoxic control rats (Group B). Curcumin detects a messenger molecule that communicates with genes in liver cells, directing them to increase the production of messenger RNA that directs receptor formation for LDL cholesterol. With more LDL receptors, liver cells are able to remove more harmful cholesterol from the body (Jain *et al.*, 2006).

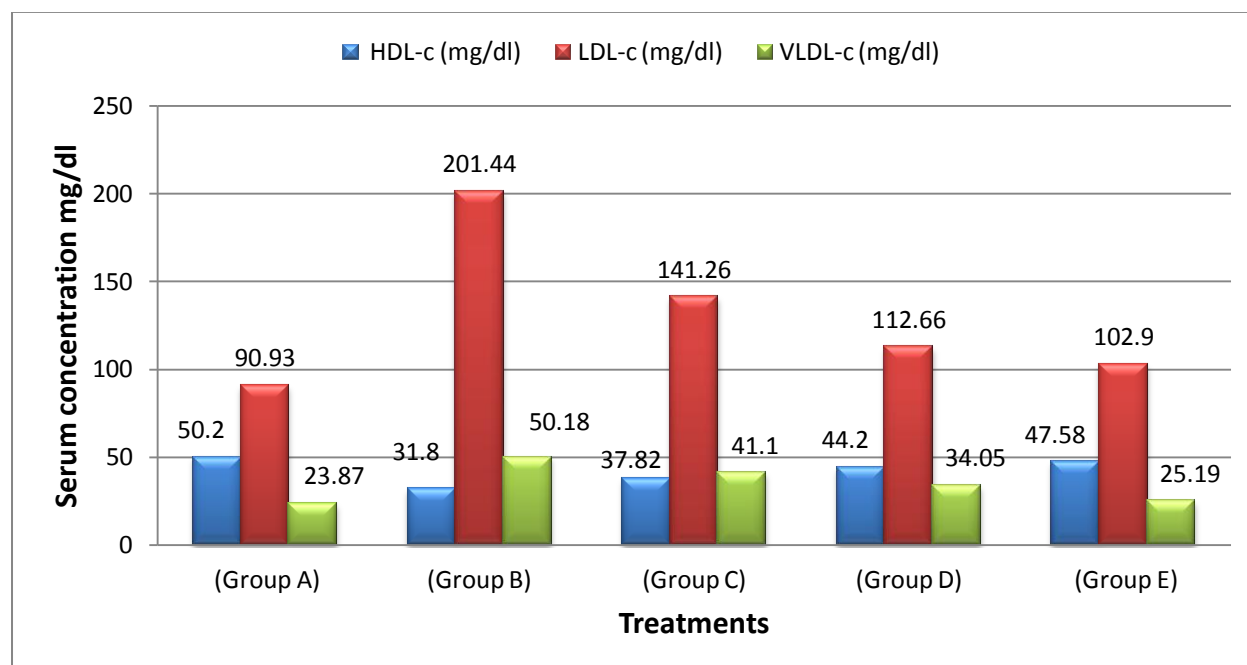


Fig2. Effect of turmeric extract on lipoprotein fraction in carbon tetrachloride induced hepatotoxicity in male rats

Effect of turmeric extract on serum Alanine aminotransferase (ALT), Aspartate aminotransferase (AST) and alkaline phosphatase (ALP) in male rats exposed to carbon tetrachloride induced hepatotoxicity are presented in Table (3). Results of present work indicate that, the hepatotoxic control rats (Group B) were significantly ($p < 0.05$) increased in levels of alanine aminotransferase (ALT), Aspartate aminotransferase (AST) and alkaline phosphatase (ALP) enzymes comparing with healthy control (Group A) by 306.0 % , 193.08 and 93.15 % respectively. These results were confirmed with (Blasco and Puppo 1999), Alanine aminotransferase (ALT), Aspartate aminotransferase (AST) enzymes are known to be increased by liver damaging. Alanine aminotransferase (ALT), Aspartate aminotransferase (AST) enzymes were the most specific marker of liver cell damage in mammals. On the other side, hepatotoxic rats treated with turmeric extract at 50, 100 and 150 mg/kg of body weight were significantly decreased in alanine aminotransferase (ALT), Aspartate aminotransferase (AST) and alkaline phosphatase (ALP) compared with Hepatotoxic control rats (Group B) by 20.10, 37.25 and 53.93 % for alanine aminotransferase (ALT), while the decrease values were 19.74, 34.68 and 54.71 % for Aspartate aminotransferase (AST) and 20.47, 37.49 and 44.05 for alkaline phosphatase (ALP) respectively. These results are agreement with (Xinyan, *et al.*, 2018), who found that, Curcumin treatment has shown distinct protection against acute CCl₄-induced liver injury, which was demonstrated by decreased of serum ALT and AST and improvement in histological lesions. (Fu Y, *et al.*, 2008), showed that treated with Curcumin were protects the liver from injury by decreasing the activities of serum AST, ALT, and ALP, and by improving the histological architecture of the liver.

Table 3. Effect of turmeric extract on serum aspartate aminotransferase (AST) serum alanine aminotransferase (ALT) and serum alkaline phosphatase (ALP) in carbon tetrachloride induced hepatotoxicity in male rats

Treatments	Alanine aminotransferase (ALT) (IU/L)	Aspartate aminotransferase (AST) (IU/L)	alkaline phosphatase (ALP) (IU/L)
Healthy control group (Group A)	24.11 ^e	27.61 ^e	150.22 ^e
Hepatotoxic control rats (Group B)	74.02 ^a	80.92 ^a	290.15 ^a
Hepatotoxic rats treated with 50 mg turmeric extract (Group C)	59.32 ^b	64.95 ^b	230.75 ^b
Hepatotoxic rats treated with 100 mg turmeric extract (Group D)	46.45 ^c	52.86 ^c	180.84 ^c
Hepatotoxic rats treated with 150 mg turmeric extract (Group E)	34.10 ^d	36.65 ^d	162.33 ^d

Values with different letters in the same column are significantly different at P<0.05.

Effect of turmeric extract on serum catalase activity , Superoxide dismutase (SOD) , Glutathione reductase (GSST) U/ml and MDA nmol / ml in male rats exposed to carbon tetrachloride induced hepatotoxicity are presented in Table (4). Results of present work indicate that, the hepatotoxic control rats (Group B) had a significantly (p< 0.05) decreased in catalase activity (CAT) , Superoxide dismutase (SOD), Glutathione reductase (GSST) compared with the healthy control rats (Group A) by 94.64 , 67.07 and 65.7 % respectively. On the other hand, the hepatotoxic control rats (Group B) had a significantly (p< 0.05) increased in MDA compared with the healthy control rats (Group A) by 559.52%. Results also indicate that, the hepatotoxic control rats treated with turmeric extract at 50(Group C), 100 (Group D) and 150 mg/kg of body weight(Group E) were significantly (P<0.05) increased in catalase activity (CAT), Superoxide dismutase (SOD), Glutathione reductase (GSST) compared with hepatotoxic control rats (Group B) by 726.67, 1053.33 and 1526.67 %for catalase activity, while, the increased values of Superoxide dismutase were 69.89, 134.55 , 186.09% and the increased values of Glutathione reductase were 55.84, 103.86 and 171.76 % respectively. On the other side, the hepatotoxic rats treated with turmeric extract at 50, 100 and 150 mg/kg of body weight were significantly (P<0.05) decreasing values of MDA by 32.85, 67.15 and 76.17% for (Group C), (Group D) and (Group E) respectively compared with hepatotoxic control rats (Group B).these results were confirmed with (Meister, 1991), who found that, The decrease in liver catalase (CAT), superoxide dismutase (SOD) and reduced glutathione (GSH)exposed to carbon tetrachloride induced hepatotoxicity compared with control group due to Reduced glutathione is the most abundant thiol in mammalian tissues involved in the protection of the cell against damage from electrophiles free radicals and ROS formed during xenobiotic metabolism .Treatment with curcumin had improved liver function by decreasing superoxide production and by suppressing pro-inflammatory mediators and activating anti-inflammatory signaling pathways (Armendariz-Borunda *et al.*, 1993).

Table 4. Effect of turmeric extract on serum Catalase (CAT), Superoxide dismutase (SOD), Glutathione reductase (GSST) and Malondialdehyde concentration (MDA) in carbon tetrachloride induced hepatotoxicity in male rats

Treatments	Catalase (CAT) U/I	Superoxide dismutase (SOD) U/ml	Glutathione reductase (GSST) U/ml	MDA nmol/ml
Healthy control group (Group A)	2.80 ^a	640.28 ^a	730.76 ^a	0.42 ^e
Hepatotoxic control rats (Group B)	0.15 ^e	210.85 ^e	250.52 ^e	2.77 ^a
Hepatotoxic rats treated with 50 mg turmeric extract (Group C)	1.24 ^d	358.22 ^d	390.42 ^d	1.86 ^b
Hepatotoxic rats treated with 100 mg turmeric extract (Group D)	1.73 ^c	494.54 ^c	510.70 ^c	0.91 ^c
Hepatotoxic rats treated with 150 mg turmeric extract (Group E)	2.44 ^b	603.22 ^b	680.82 ^b	0.66 ^d

Values with different letters in the same column are significantly different at P<.0.05.

Effect of turmeric extract on Liver catalase activity (CAT),Superoxide dismutase, Glutathione reductase (GSST) (unit / g of wet tissue) and MDA nmol / g. Liver tissue in male rats exposed to carbon tetrachloride induced hepatotoxicity are presented in Table (5). Results of present work indicate that, the hepatotoxic control rats (Group B) had a significantly (p< 0.05) decreased in catalase activity (CAT) , Superoxide dismutase (SOD), Glutathione reductase (GSST) compared with the healthy control rats (Group A) by 96.13 , 72.60 and 51.51 % respectively. On the other hand, the hepatotoxic control rats (Group B) had a significantly (p< 0.05) increased in MDA compared with the healthy control rats (Group A) by 506.28.65%. Results also indicate that, the hepatotoxic rats treated with turmeric extract at 50(Group C), 100(Group D) and

150 mg/kg of body weight (Group E) were significantly ($P < 0.05$) increased in catalase activity (CAT), Superoxide dismutase (SOD), Glutathione reductase (GSST) by 938.10, 1600.0 and 2261.62 % for catalase activity, while the increased values of Superoxide dismutase were 113.75, 161.74 143.33% and increased values of Glutathione reductase were 49.15, 77.46 and 105.84% respectively. On the other side, the hepatotoxic rats treated with turmeric extract at 50, 100 and 150 mg/kg of body weight were significantly ($P < 0.05$) decreasing values of malondialdehyde concentration (MDA) by 33.24, 48.87 and 66.60% for (Group C), (Group D) and (Group E) respectively compared with hepatotoxic control rats (Group B). (Barzegar and Moosavi-Movahedi 2011), found that, the antioxidants play an important role in protecting liver against free radical-induced hepatotoxicity by directly scavenging or inhibiting them. Curcumin is a natural antioxidant, which can inhibit reactive oxygen species and induce antioxidative enzymes like glutathione-S-transferase generation, which expedite the elimination of toxic substances from the body.

Table 5. Effect of turmeric extract on Liver catalase activity (CAT) (unit / g of wet tissue), Superoxide dismutase (SOD) (unit / g of wet tissue), Glutathione reductase (GSST) (unit / g of wet tissue) and malondialdehyde concentration (MDA) nmol / g. Liver tissue in male rats exposed to carbon tetrachloride induced hepatotoxicity.

Treatments	Catalase (CAT) U/g. Liver tissue	Superoxide dismutase (SOD) U/g. Liver tissue	Glutathione reductase (GSST) U/g. Liver tissue	MDA nmol / g. Liver tissue
Healthy control group (Group A)	5.42 ^a	840.74 ^a	744.20 ^a	2.87 ^e
Hepatotoxic control rats (Group B)	0.21 ^c	230.35 ^e	360.84 ^e	18.95 ^a
Hepatotoxic rats treated with 50 mg turmeric extract (Group C)	2.18 ^d	492.38 ^d	538.22 ^d	12.65 ^b
Hepatotoxic rats treated with 100 mg turmeric extract (Group D)	3.58 ^c	602.92 ^e	640.36 ^e	9.72 ^c
Hepatotoxic rats treated with 150 mg turmeric extract (Group E)	4.96 ^b	790.86 ^b	742.75 ^b	6.33 ^d

Values with different letters in the same column are significantly different at $P < 0.05$.

Histopathological analysis

Liver of healthy control rats (Group A) revealed the normal histological structure of hepatic Lobule photo 1. Meanwhile, liver of hepatotoxic control rats (Group B) revealed cytoplasmic vacuolation of hepatocytes, dilatation of hepatic sinusoids (photo 2) However, the hepatotoxic rats treated with 50 mg *turmeric extract* (Group C) showing nearly normal hepatocytes. Hepatotoxic rats treated with 100 and 150 mg *turmeric extract* (Group D and Group E) photo 4 and photo 5 showed the normal histological structure of hepatic Lobule. Treating the hepatic rats with 100 (Group D) and 150 mg (Group E) turmeric extract improved the liver tissues and nearly restored them to the normal. Treated rats with curcumin can effectively protect the liver, by its antioxidant effect, toxicity. Protective activity of curcumin may be due to its potent antioxidant activity and ability to eliminate free radicals and oxidative stress as previously reported in literature. In particular (Barzegar and Moosavi-Movahedi 2011).

In conclusion, the data obtained from this study showed that the treatment with turmeric extract protected against CCl₄ induced hepatic injury. This can be attributed to the antioxidant and free-radical scavenging properties of turmeric. Thus, dietary inclusion of Curcumin could exert protective effects against hepatic toxic effects resulting from CCl₄ exposure.

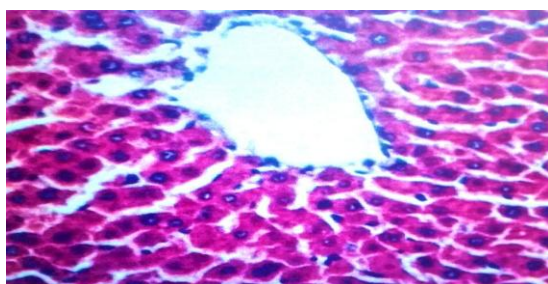


Photo 1. Liver rats from healthy control group (Group A).

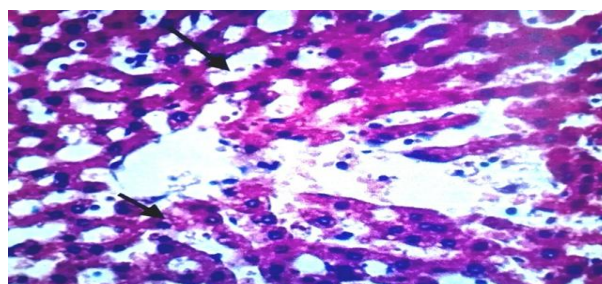


Photo 2. Liver rats from hepatotoxic control group (Group B).

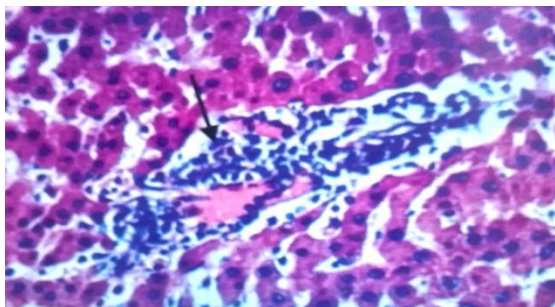


Photo 3. Liver rats from hepatotoxic rats treated with turmeric extract at 50 mg mg/kg of body weight (Group C).

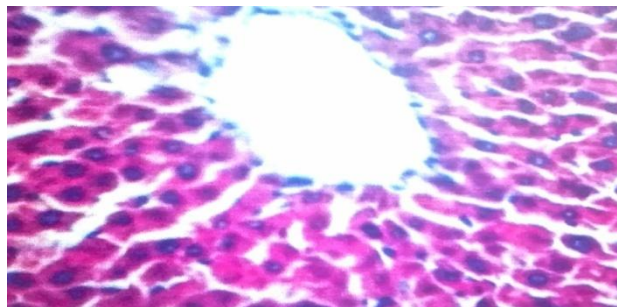


Photo 4. Liver rats from hepatotoxic rats treated with turmeric extract at 100 mg mg/kg of body weight (Group D).

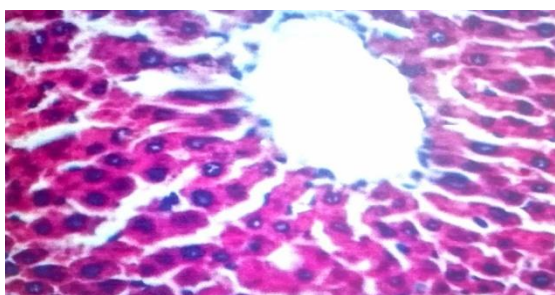


Photo 5. Liver rats from hepatotoxic rats treated with turmeric extract at 150 mg mg/kg of body weight (Group E).

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