The Synergistic Hepatoprotective Effect of Curcumin and Ginger Against Carbon Tetrachloride Induced- Liver Fibrosis in Rats

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Abstract: The present study aimed to assess the hepatocellular protective activity of the co-administration of curcumin fortified by ginger against carbon tetrachloride (CCl4)-induced liver fibrosis in rats. Five groups were included: control, CCl4, CCl4 treated with curcumin, CCl4 treated with ginger and CCl4 treated with curcumin and ginger. Liver fibrosis was evidenced by significant increase in liver hydroxyproline, the inflammatory cytokine tumor necrosis factor-α (TNF-α) and lipid peroxidation, increased activities of serum aspartate transaminase (AST), alanine transaminase (ALT) and alkaline phosphatase (ALP). Liver enzymes, oxidative status and histological examinations revealed that co-administration of curcumin and ginger significantly arrested progression of hepatic fibrosis induced by CCl4. Elevated activities of serum (AST), (ALT) and (ALP) by CCl4 intoxication were synergistically reduced, while the levels of total protein and albumin were normalized. In addition, the altered levels of malondialdehyde (MDA), reduced glutathione (GSH), superoxide dismutase (SOD) and hydroxyproline in liver tissues of CCl4 hepatotoxied rats were normalized by the oral co-administration of curcumin and ginger. Also, tumor necrosis factor-α (TNF-α) level and catalase (CAT) activity elevated by CCl4 intoxication, were significantly reduced (p<0.05) in liver tissues mainly in the combined treated group. Histological examinations showed that the combined administration of curcumin and ginger returned collagen fiber distribution to almost normal pattern. In conclusion, combined oral administration of both curcumin and ginger are potentially effective in the protection of hepatic fibrosis on the experimental level.

Key words: Curcumin, Ginger, CCl4, Liver enzymes, Antioxidant enzymes, Tumor necrosis factor-α, Histological examinations.

INTRODUCTION

Chronic liver disease, which is most widely spread in the developing countries, is considered the seventh leading cause of death, (Heidelbaugh and Sherbondy, 2006). Hepatic fibrosis occurs during most chronic liver diseases and is driven by inflammatory responses to the injured tissue. Human and animal studies suggest that hepatic immunity is altered in fibrosis and that liver inflammation is the hallmark of early-stage liver fibrosis, ultimately resulting in hepatic stellate cells (HSC) activation and extra cellular matrix (ECM) deposition. Various immunoregulatory cytokines such as tumor necrosis factor-α (TNF-α) is a critical mediator in fibrosis, (Michael et al., 2009).

Oxidative stress, resulting from an imbalance in the generation of free radicals and antioxidant defense molecules, affects biological macromolecules causing their structural alterations that lead to cell damage and its death, (Ryter et al., 2007). This phenomenon is considered to be a major factor in the pathogenesis of a variety of liver diseases, (Flora, 2007). In this regard, reduction of oxidative stress may be a good target for prevention and treatment of hepatic fibrosis.

Considering the hazards of treatment failure, drug resistance and heavy costs associated with current hepatic therapy, there is strong interest in the study of natural compounds with free radicals scavenging capacity. Medicinal plants, especially those with traditional use have always been considered as a rich source of antioxidants. The polyphenol curcumin (diferuloylmethane), is the active component of turmeric, found in the rhizomes of the turmeric plant (Curcuma longa L.); a perennial herb belonging to the ginger family (Zingiberaceae family). Turmeric is used in curries and mustard in India, Asia, and the Middle East. Turmeric has also been used for centuries as a traditional Indian medicine, (Aggarwal et al., 2007). Curcumin has been shown to exhibit anti-inflammatory, antioxidant, antiviral, antibacterial, antifungal, anticancer and hepatoprotective activities, (Joanna et al., 2010).

Studies over the past three decades related to absorption, distribution, metabolism and excretion of curcumin have demonstrated poor absorption and rapid metabolism of curcumin that severely curtails its bioavailability, (Ajaikumar et al., 2008). To overcome these limitations, modern techniques, such as structural modifications and various formulations were designed to specifically enhance uptake from the gastrointestinal tract. More clinical trials with curcumin either alone or in combination with existing therapies are needed to...
fully appreciate its potential. Ginger, (*Zingiber officinale* Roscoe, family Zingiberaceae) is one of the most highly consumed dietary spices in the world known in Western societies for its antiemetic and carminative uses, (Janet *et al.*, 2009).

The major pungent principle of ginger is 6-gingerol. It possesses many pharmacological activities; antioxidant, anti-inflammatory, antitumor and cardioprotective activity, (Mahmoud *et al.*, 2008). Regular intake of ginger in diet can protect against oxidative tissue damage, (Nirmala *et al.*, 2007). The present study was performed to examine the hepatocellular protective activity of the co-administration of curcumin fortified by ginger against the hepatotoxicity induced by CCl₄ in rats.

**MATERIALS AND METHODS**

**Animals:**

A total of 50 adult male Swiss albino rats weighing 190-210 g were provided from the breeding unit of the Medical Research Center, (Faculty of Medicine, Al-Azhar University, Cairo, Egypt) and used through this study. The animals were housed in steel mesh cages, (five per cage) and had a free access to a commercial pellet diet and tap water ad libitum for one week before the start of the experiment as an acclimatization period.

**Chemicals:**

Curcumin and Ginger powders (purity > 95%) were provided from Sigma Co. (St. Louis, USA) and Indian botanic gardens, incorporation respectively. Carbon tetrachloride (CCl₄), Dimethyl sulfoxide (DMSO), Phenyl methyl sulfonlfyl fluoride (PMSF), ethylenediamine tetraacetic acid (EDTA), thio-barbituric acid (TBA) were supplied by Sigma Co. (St. Louis, USA). All other chemicals were of analytical grade.

**Study Design:**

The body weight of all animals was recorded at the beginning of the experiment. The animals were randomly distributed into five equally sized groups according to the following scheme: Group I (control), Group II: (CCl₄), Group III: (CCl₄+curcumin), Group IV (CCl₄+ginger), Group V: (CCl₄+curcumin+ginger). Groups II, III, IV and V were i.p. injected with a mixture of CCl₄ and olive oil [1:1] (1ml/kg body weight) every other day for 8 consecutive weeks, (Yumei *et al.*, 2008)[11]. Curcumin and/or ginger (0.5g/kg body weight) were dissolved in 5%DMSO and given once daily by oral gavage. Gr.I was similarly treated with olive oil and DMSO.

**Blood Collection And Tissue Sampling:**

Twenty-four hours after the last treatment, the animals were weighed and dissected under light ether anesthesia. The percentage of increase in the body weight was calculated compared to the initial weight of all animals. Blood was collected from the abdominal aorta, allowed to clot and centrifuged. Serum was separated and used for biochemical analysis.

**Preparation Of Liver Homogenate:**

At autopsy, livers were immediately excised, rinsed from blood in saline, blotted dry and weighed. The liver weight to total body weight ratio was calculated for each animal. Each liver was cut longitudinally into two halves; one half was fixed in 10% phosphate-buffered formalin for histological examination, while the other half was stored at – 70 °C for biochemical analysis. Liver tissues from all animals were accurately weighed, sliced and homogenized in ice cold sucrose-tris buffer (50 mM tris-HCl, 0.25 M sucrose, pH 7.4) to obtain ultimately 10% (w/v) whole liver homogenate, which was used for determination of reduced glutathione(GSH), malondialdehyde (MDA) and hydroxyproline concentration. An aliquot of the whole tissue homogenate was centrifuged at 10,000 rpm for 15 minutes at 4°C and the cytosolic supernatant was used for the determination of superoxide dismutase (SOD) and catalase (CAT) activities, as well as the proinflammatory cytokine TNF-α.

**Biochemical Studies:**

Serum alanine aminotransferase (ALT), aspartate aminotransferase (AST) activities were measured colorimetrically according to the method of Reitman and Frankel (Reitman and Frankel, 1957) using a commercial assay kit (Quimica clinical aplicada, Spain). Serum alkaline phosphatase (ALP) was determined according to the method of Young *et al.*, 1975 using a commercial assay kit (Bio-med company, Germany). Serum total protein and albumin concentrations were measured colorimetrically according to the methods of Gornall *et al.*, 1949 and Doumas *et al.*, 1971 respectively. Reduced glutathione (GSH) was colorimetrically estimated in the whole liver homogenate using the method of Beutler *et al.*, 1963. Superoxide dismutase (SOD) and catalase activities (CAT) were determined in the tissue homogenates by the colorimetric methods of Minami and Yoshikawa, 1979 and Sinha, 1972 respectively. The malondialdehyde (MDA) concentration was assessed in the whole liver homogenate as thiobarbituric acid reactive substances (TBARS) according to the method of
Niehaus and Samuelsson, 1968 and calculated using an extinction coefficient of 1.56 x 10^5 M^(-1)cm^(-1). Hepatic TNF-α and hydroxyproline levels were measured using research rat- specific ELISA kit (Assay pro, USA) and the colorimetric method of Neuman and Logan, 1949 respectively.

**Histological Examination:**
Fixed liver specimens were embedded in paraffin cubes. Sections of 5-6μm in thickness were cut and stained with Hematoxylin & Eosin (H&E) and Masson Trichrome (MT) then subjected to photo microscopic examination.

**Statistical Analysis:**
Data were analyzed using statistical software (SPSS version 15). Differences between means of all parameters were carried out using analysis of variance (ANOVA), followed by Bonferroni’s test for multiple comparisons. Differences were considered statistically significant at p<0.05.

**RESULTS AND DISCUSSIONS**

Table (1) shows the effect of curcumin and/or ginger treatments on the increase in total body weight and relative liver weight. CCl₄ intoxication significantly decreased the percent increase in body weight with slight significant increase in relative liver weight. Curcumin and/or ginger treatments increased the rate of growth and normalized the relative liver weight.

<table>
<thead>
<tr>
<th>Groups</th>
<th>Initial body weight(g)</th>
<th>Final body weight(g)</th>
<th>%increase in body weight</th>
<th>Relative liver weight (x10⁻³)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>195±9.7</td>
<td>312±11.3</td>
<td>60ª</td>
<td>3.9ª</td>
</tr>
<tr>
<td>CCl₄ Mean±SD</td>
<td>206±8.9</td>
<td>310±9.9</td>
<td>50.5ª</td>
<td>4.2ª</td>
</tr>
<tr>
<td>CCl₄+Curcumin Mean±SD</td>
<td>209±10.2</td>
<td>335±12.5</td>
<td>60.3ª</td>
<td>3.9</td>
</tr>
<tr>
<td>CCl₄+ginger Mean±SD</td>
<td>207±9.8</td>
<td>329±10.7</td>
<td>58.9ª</td>
<td>3.95</td>
</tr>
<tr>
<td>CCl₄+curcumin+ginger Mean±SD</td>
<td>204±8.7</td>
<td>325±11.7</td>
<td>59.3ª</td>
<td>3.85</td>
</tr>
</tbody>
</table>

Values are given as Mean ± SD for groups of ten rats. Each value is considered statistically significant at p<0.05. Groups sharing the same superscripts are not significantly different.

Table (2) shows the effect of curcumin and/or ginger treatments on the liver function tests, total protein and albumin in the serum of CCl₄-intoxicated rats. CCl₄ intoxication caused significantly sharp increases in serum levels of ALT, AST and ALP activities, and significant reductions in serum total protein and albumin concentrations, compared to normal controls. Curcumin and ginger treatment significantly reduced liver enzyme activities, while combined treatment of curcumin and ginger synergized this reduction. The serum levels of total protein and albumin returned to normal level with curcumin and/or ginger treatment.

<table>
<thead>
<tr>
<th>Groups</th>
<th>ALT (U/L)</th>
<th>AST (U/L)</th>
<th>ALP (U/L)</th>
<th>Total protein (g/dl)</th>
<th>Albumin (g/dl)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control Mean ± SD</td>
<td>32.2±4.9ª</td>
<td>125.5±17.8ª</td>
<td>104.2±8.5ª</td>
<td>7.05±1.0ª</td>
<td>3.51±0.6ª</td>
</tr>
<tr>
<td>CCl₄ Mean ± SD</td>
<td>463.5±40.6ª</td>
<td>1053.2±133ª</td>
<td>905.8±17.1ª</td>
<td>5.11±0.6ª</td>
<td>2.58±0.8ª</td>
</tr>
<tr>
<td>CCl₄ + curcumin Mean ± SD</td>
<td>153.8±14.2ª</td>
<td>432±10.8ª</td>
<td>328±17.9ª</td>
<td>6.41±0.8ª</td>
<td>3.44±0.5ª</td>
</tr>
<tr>
<td>CCl₄ + ginger Mean ± SD</td>
<td>196±15.4ª</td>
<td>462±12.6ª</td>
<td>419.3±14.4ª</td>
<td>6.28±0.8ª</td>
<td>3.45±0.45ª</td>
</tr>
<tr>
<td>CCl₄ + curcumin + ginger Mean ± SD</td>
<td>74.7±5.7ª</td>
<td>260±8.6ª</td>
<td>228±13.4ª</td>
<td>6.86±0.74ª</td>
<td>3.47±0.5ª</td>
</tr>
</tbody>
</table>

Values are given as Mean ± SD for groups of ten rats. Each value is considered statistically significant at p<0.05. Groups sharing the same superscripts are not significantly different.

Table (3) illustrates the effect of curcumin and/or ginger treatments on lipid peroxidation and antioxidant defense in liver tissue. CCl₄ intoxication gave rise to significant reduction in SOD, CAT and GSH activities and,
in contrast significant increase in MDA level compared to normal controls. Although curcumin treatment significantly reverted their levels more than ginger, combined treatment synergistically reverted their levels returning SOD, GSH, and MDA to normal levels.

Table 3: Levels of antioxidant enzymes, reduced glutathione and malondialdehyde in liver tissue of control and experimental groups.

<table>
<thead>
<tr>
<th>Groups</th>
<th>SOD (U/mg protein)</th>
<th>CAT (U/mg protein)</th>
<th>GSH (µmol/g tissue)</th>
<th>MDA (nmol/g tissue)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>Mean ± SD</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>4.1±0.8a</td>
<td>136.5±9.32a</td>
<td>38.5±2.80a</td>
<td>46.8±2.22a</td>
</tr>
<tr>
<td>CCl4</td>
<td>Mean ± SD</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>2.1±0.5b</td>
<td>54.0±8.48b</td>
<td>13.7±1.21b</td>
<td>100.8±9.3b</td>
</tr>
<tr>
<td>CCl4 + curcumin</td>
<td>Mean ± SD</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>3.85±0.7c</td>
<td>84.6±4.93c</td>
<td>25.6±2.07c</td>
<td>67.2±3.3c</td>
</tr>
<tr>
<td>CCl4 + ginger</td>
<td>Mean ± SD</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>3.52±0.5c</td>
<td>70.0±4.58c</td>
<td>20.33±1.53c</td>
<td>74.1±4.1c</td>
</tr>
<tr>
<td>CCl4 + curcumin + ginger</td>
<td>Mean ± SD</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>4.08±0.6a</td>
<td>103.2±6.57a</td>
<td>34.6±3.2a</td>
<td>51.9±3.7a</td>
</tr>
</tbody>
</table>

Values are given as Mean ± SD for groups of ten rats. Each value is considered statistically significant at p<0.05 Groups sharing the same superscripts are not significantly different.

Table (4) illustrates the effect of curcumin and/or ginger treatments on hydroxyproline and TNF-α level of liver tissue. CCl4 intoxication produced a highly significant increase in hepatic hydroxyproline and TNF-α concentration. Treatment of curcumin and ginger significantly decreased their levels, while the combined treatment produced a significantly sharp reduction returning the hydroxylproline concentration normal.

Table 4: Levels of hydroxyproline and TNF-α in liver tissue of the control and experimental groups.

<table>
<thead>
<tr>
<th>Groups</th>
<th>Hydroxyproline (µmol/g tissue)</th>
<th>TNF-α (pg/g tissue)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>Mean ± SD</td>
<td>3.69±0.4a</td>
</tr>
<tr>
<td>CCl4</td>
<td>Mean ± SD</td>
<td>6.16±0.6b</td>
</tr>
<tr>
<td>CCl4 + curcumin</td>
<td>Mean ± SD</td>
<td>4.66±0.5c</td>
</tr>
<tr>
<td>CCl4 + ginger</td>
<td>Mean ± SD</td>
<td>5.37±0.8d</td>
</tr>
<tr>
<td>CCl4 + curcumin + ginger</td>
<td>Mean ± SD</td>
<td>4.02±0.9a</td>
</tr>
</tbody>
</table>

Values are given as a Mean ± SD for groups of ten rats. Each value is considered statistically significant at p<0.05 Groups sharing the same superscripts are not significantly different.

Light Microscopic Examination:
The histological examination of liver sections basically supported the biochemical results. Liver sections from control rats showed normal lobular architecture and normal hepatic cells with well preserved cytoplasm and well defined nucleus (Figs.1a, 1b). Challenged with CCl4 showed bridging fibrous bands (severe fibrosis) joining adjacent portal tracts with impending nodule formation. (Figs 2a, 2b). Treatment of curcumin showed moderate amount of periportal fibrosis with impending cirrhotic nodule formation made up of regenerating hepatocytes and separated by porto-portal bridging fibrosis (Figs 3a, 3b). While protection with ginger showed proportal and procentral fibrosis, separating the regenerating hepatocytes with loss of normal hepatic architecture (Figs 4a, 4b). The liver sections from combined treatment showed an excellent result, in which the residual treated fibrosis is minimal located mainly around the portal tracts and most of the fibrosis induced by CCl4 was replaced by regenerating hepatocytes with preservation of the hepatic architecture (Figs 5a, 5b).

Discussion:
The present study was conducted to evaluate the protective effect of co-administration of curcumin and ginger for 8 consecutive weeks against experimental liver fibrosis in rats. Hepatic fibrosis induced by CCl4 has been extensively used in rats as hepatic responses were shown to be superficially similar to human cirrhosis, (Pe’rez, 1983). Results obtained from this study demonstrate that CCl4 intoxication caused hepatocellular damage represented by the marked elevation in serum ALT, AST and ALP activities, compared to the control group (Table 2). These enzymes are considered the most sensitive markers of liver injury as they are found in the cytoplasm of liver cells, thus damage of these cells lead to their rapid leakage into the blood circulation,
(Ramaiah, 2007). Parallel findings were reported, (Yumei et al., 2008). The combined treatment with curcumin and ginger caused a more pronounced reduction in the liver enzyme activities than that produced by the individual treatments, which suggests the synergistic protection of combined administration of curcumin and ginger against chemically-induced hepatocellular toxicity (Table 2). These findings are in harmony with previous study, which affirmed on the hepatocellular protective effects of other herbal compounds although they did not normalize the liver enzymes, (Hwang et al., 2009). Our biochemical findings are supported by the histological examination of the liver tissues, which revealed almost normal liver architecture in the combined treatment.

![Fig. 1](image)

**Fig. 1:** A photomicrograph of a liver section of a control rat apparently showing normal hepatic tissue. a- (H& E. X 200), b-(MT X100).

F: fibrosis  →: cirrhotic nodule
PT: portal tract  CV: central vein
In chronic liver diseases, the serum albumin level is reduced due to protein synthesis disruption in the liver, (Mi-Ok and Jeon-Ok, 2010). Treatment of curcumin and/or ginger reverted the serum protein and albumin levels back to normal, which reflects the well functioning of hepatocytes in protein synthesis. Hydroxyproline is an amino acid found almost exclusively in collagens. Determination of hydroxyproline content in liver tissue is regarded as a good marker to quantify fibrosis and to evaluate the effectiveness of new antifibrotic agents, (Miao-Xian et al., 2009). Results indicate that the elevated hepatic hydroxyproline concentration in CCl₄-intoxicated rats was significantly reduced by treatment with curcumin or ginger, whereas normalized by the combined treatment (Table 4). These findings confirm that combined treatment of curcumin and ginger maximize the protection of liver from injury and fibrogenesis due to CCl₄ intoxication.

Inflammation is commonly associated with hepatic fibrogenesis during chronic liver disease, (Marra, 2002). Reducing the burden of cirrhosis include removal of injurious stimulus, limiting hepatic injury and inflammation. The proinflammatory cytokine, TNF-α is a major player in the hepatic inflammation, which stimulates the development of hepatic fibrosis, (Yin et al., 1999). Also many experimental and clinical data reported that the common link between chronic liver damage and hepatic fibrosis may be related to oxidative stress, which is associated with HSC activation. Lipid peroxidation could change the properties of biological membranes, resulting in severe cell damage and thus play a significant role in the pathogenesis of disease. It has been shown that certain lipid peroxidation products induce fibrogenic cytokines and increase the synthesis of collagen by initiating HSC activation, (Mi-Ok and Jeon-Ok, 2010). Thus, agents that inhibit production of TNF-α and reduce the oxidative stress are effective in attenuating liver cirrhosis. Curcumin has a known activity in limiting the activation of nuclear factor kappa B (NFkB), a precursor of TNF-α and to block oxidative injury,
Fig. 3: A photomicrograph of a liver section of a rat challenged with CCl₄ and treated with curcumin showing a moderate amount of perportal fibrosis with impending cirrhotic nodule formation made up of regenerating hepatocytes and separated by porto-portal bridging fibrosis. a- (H&E. X 200), b-(MT X100).

F: fibrosis →: cirrhotic nodule
PT: portal tract CV: central vein

(Anand et al., 2008). As to ginger, may be due to its content of volatile oils that are capable of inhibiting T-lymphocytes dependant immune reactions, (Zhou et al., 2006). Moreover the anti-inflammatory activity of ginger is due to the presence of gingerols which have the ability to inhibit prostaglandins and leukotriene synthesis, (Nurtjahja et al., 2003). In the present study, although the treatment of curcumin or ginger significantly reduced the TNF-α and malondialdhyde levels in the liver of CCl₄ intoxicated rats, yet their combination normalized malondialdhyde level and synergistically reduced the level of TNF-α (Table 3&4).

The oxidative damage in tissue can be limited by the exogenous antioxidants and the antioxidant defense system of the host. Of the most important defenses are enzymatic antioxidants, such as SOD, CAT and non-enzymatic antioxidants as GSH, (Wang et al., 2004). SOD, a manganese-containing enzyme is the first antioxidant enzyme to deal with oxyradicals by accelerating the dismutation of superoxide to hydrogen peroxide, while CAT is a peroxisomal heme protein that catalyses the removal of hydrogen peroxide formed during the reaction catalyzed by SOD, (Weydert et al., 2006). These antioxidant enzymes are effortlessly inactivated by lipid peroxides or free radicals, which results in decreased activities of these enzymes in CCl₄ toxicity, (Szymonik-Lesiuk et al., 2003). The levels of these enzymes activity in the liver tissue were significantly decreased (p<0.01) in CCl₄ intoxicated rats, compared to the control group reflecting impaired antioxidative defense, impaired functions and damage of liver (Table 3). Previous studies on the mechanism of CCl₄ hepatotoxicity have demonstrated that liver necrosis causes substantial depletion of mitochondrial GSH, which is a critical determinant for cell survival and death in oxidative conditions, (Hidaka et al., 2007). Therefore, GSH conjugation is critically essential to decrease the toxic effect of CCl₄. Data presented in table (3) show that the hepatic content of GSH was significantly decreased in CCl₄-intoxicated rats, compared to
controls. This is in agreement with Muhammad and Dawood, 2009, who reported a significant decrease of CAT, SOD and GSH in oxidative stress induced by CCl4. On the contrary, treatment with curcumin or ginger significantly increased the antioxidant enzyme levels back. This increase is due to the ability of curcumin to prevent the formation of free radicals, enhance the endogenous antioxidant activity beyond its free radical scavenging property and the reduction of hepatic lipoperoxide formation, (Rafael et al., 2007). Ginger shares curcumin in prevention pathway through inhibition of the induction of several genes involved in the inflammatory response, (Nemat et al., 2010). These increases were more notable in the combined treatment returning SOD and GSH back to normal levels which provides a further evidence for the value of the combined treatment.

Fig. 4: A photomicrograph of a liver section of a rat challenged with CCl4 and treated with ginger showing proportal and procentral fibrosis, separating the regenerating hepatocytes with loss of normal hepatic architecture. a- (H& E. X 200), b-(MT X100).
F: fibrosis →: cirrhotic nodule
PT: portal tract CV: central vein

Conclusion:
Combination of curcumin and ginger ameliorate the oxidative stress induced-liver injury demonstrated by restoring the liver enzymes activity towards normal, inhibiting lipid peroxidation and enhancing the endogenous antioxidant defense system. The complementary hepatoprotective effect might be due to the fact that both compounds belong to the same family and share most of their active components. The hepatocellular protective effect of curcumin stems from its potent antioxidant effect, while that of ginger is due to its anti-inflammatory activity. The combined effect might be due to enhancement of curcumin uptake by ginger through attaching curcumin to its lipophilic oily portion, thus increasing its bioavailability. Results obtained from this study recommend regular dietary consumption of curcumin and ginger during the course of liver therapy to exacerbate the improvement of liver functions, decrease the need for high doses of drugs and may shorten the duration of treatment.
Fig. 5: A photomicrograph of a liver section of a rat challenged with CCl₄ and treated with curcumin and ginger showing minimal fibrosis located mainly around the portal tracts and most of the fibrosis induced by CCl₄ was replaced by regenerating hepatocytes with preservation of the hepatic architecture. a- (H& E. X 200), b-(MT X100).

F: fibrosis → cirrhotic nodule
PT: portal tract CV: central vein

REFERENCES


