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Hepatoprotective and Antioxidant Activities of Combination of *Cinnamomum zeylanicum* and *Zingiber officinale* in CCl4-intoxicated Rats

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Abstract

Introduction: Liver is the most important organ of drugs and xenobiotics metabolism and any damage to the liver is associated with dysfunction of this organ. This study was carried out to find the possible additive effect of the co-administration of *Cinnamomum zeylanicum* (cinnamon) and *Zingiber officinale* (ginger) extracts on carbon tetrachloride (CCl_4)-induced liver damage in rats.

Methods: Forty-two male Wistar rats were randomly divided into 7 groups (n=6). Group I: Normal control, Group II: Control of the extract (25 mg/kg of cinnamon extract and 125 mg/kg of ginger extract), Group III: CCl_4 control, Group IV: 50 mg/kg of cinnamon extract; Group 5: 250 mg/kg of ginger extract; Group VI: As in group II, a combination of 25 mg/kg cinnamon extract and 125 mg/kg ginger extract, and group VII: 100 mg/kg of silymarin (as the standard drug). These treatments were performed daily for 14 days. On the fourteenth day, all groups received 1ml of CCl_4 along with olive oil (1:1 v/v), except for the groups I and II. The last two groups received only olive oil.

Results: Intraperitoneal injection of CCl_4 into rats significantly increased the levels of liver enzymes, bilirubin, and malondialdehyde (MDA), and decreased total antioxidant and total protein levels compared to the control group ($P<0.001$). Pre-treatment with a combination of cinnamon and ginger extracts significantly improved these factors.

Conclusion: The results of this study showed that co-administration of cinnamon and ginger extracts is more efficient in protecting liver from the damaging effects caused by CCl_4.

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Introduction

Liver is one of the most vital and important organs that plays a role in the production of proteins, regulation of most chemicals, and excretion of bile (1). Drug-induced liver injury is a common and well-known recognized problem caused by the metabolism of many medications and xenobiotics. For example, compounds such as thioacetamide, carbon tetrachloride, ethanol, and acetaminophen are metabolized by

the cytochrome P450 in the endoplasmic reticulum of the liver, and during this process free radicals and reactive oxygen species (ROS) are produced (2). If the generation of these free radicals exceeds the protective effect of antioxidants, it can damage liver cells and may cause several diseases like liver cirrhosis and necrosis (3).

CCl_4 is one of the oldest and most widely used toxic substances for experimental induction of liver damage in laboratory animals. CCl_4 is biotransformed by the liver microsomal cytochrome P450 and produces trichloromethyl and *proxy trichloromethyl* radicals that can bind to biological macromolecules and impair their function and, therefore, damage the cell (4, 5).

In recent years, many efforts have been made to increase use of synthetic drugs for the prevention of liver damage, but due to their side effects and relatively their high cost, no adequate results have been obtained so far (6, 7). Hence, several phytomedicines have become increasingly popular and their use has been widespread. Some previous studies have indicated the effects of medicinal herbs such as *Acanthus ilicifolius* (8), *Tanacetum parthenium* (9), Curcumin (10), cinnamon (11), *Coccinia grandis* (12), and *Agaricus blazei Murill* (13) on liver damages. These findings support and substantiate traditional consumption of medicinal plants as protective agents against lipid peroxidation in the liver (14).

Cinnamomum zeylanicum L. (Cinnamon) is a small evergreen tropical tree and is used as a traditional herb for the treatment of various diseases. It contains flavonoids and antioxidants such as linalool and coumarin (15). Some other studies have shown that bioactive compounds of cinnamon have antidiabetic, antimicrobial, anti-tyrosinase, anticancer and anti-oxidant activities (11, 16).

Ginger, the rhizome of *Zingiber officinale*, belongs to the family Zingiberaceae and possesses various pharmacological and physiological activities including antibacterial, antioxidants, and anti-inflammation activities (17, 18). Ginger also contains a biologically active compound, gingerol, which has been shown to help scavenging of free radicals and thus preventing damage to the liver (19).

The biological characteristics of these plants, and the history of researches about their activities to prevent various diseases raises the question that whether the co-administration of cinnamon and ginger extracts has additive or synergistic effects in the protection of liver damages. The aim of this study was to investigate the antioxidant and hepatoprotective effects of the co-administration of ginger and cinnamon extracts on CCl_4 induced liver damage in rats.

Materials and Methods

Chemicals

The commercial kits of Aspartate Aminotransferase (AST), Alanine Aminotransferase (ALT), Alkaline Phosphatase (ALP), Gamma Glutamyl Transferase (GGT), Total Protein (TP), and Bilirubin (Bil) were purchased from Pars Azmoon Company (Tehran, Iran). Chemical substances including hydrogen peroxide, methanol, thiobarbituric acid, serum albumin, coomassie brilliant blue R-250, CCl_4, iron sulfate, ferric chloride, sodium acetate, diethyl ether, and butanol were purchased from Merck Company (Germany). The compound 2,4,6-tris (2-pyridyl)-1,3,5-triazine (TPTZ) was bought from Fluka Company.

Extract preparation

Dried cinnamon and ginger were purchased from local food outlets in Ardabil, Iran. The identities of the plants were confirmed by the herbarium staff. After crushing to smaller pieces, they were powdered using an electric mill and then soaked in an aqueous methanol solution (70:30) for 4 days at room temperature with daily shaking. After this period, the extracts were filtered and poured into glass plates for 3 days for evaporation of the solvent. Finally, the extracts were placed at 37° C for evaporation of the remaining alcohol, and this process was repeated several times. Finally, the crude extract was stored in an air-tight container. The methanolic extract of cinnamon and ginger were prepared fresh each time using distilled water immediately before the administration.

Animals

In this experimental study, 40 male wistar male rats (200-250 g body weight and 6 weeks of age) were divided into the 7 groups, each group of six. The rats were acclimatized for 7 days without any intervention under standard conditions at room temperature (25±2º C) with 12 hr/12 hr light/dark cycles. The rats were fed with a standard commercial rat chow during the study. This research has been approved by the ethics committee of Payame Noor University (Approval number: IR.PNU.REC.1396.4). The study was conducted in accordance with the Guide for the Care and Use of Laboratory Animals published by the US National Institutes of Health.

Experimental design

In order to induce liver damage, CCl_4 was dissolved in olive oil at a ratio of 1:1, and 1 ml/kg of the obtained mixture was injected intraperitoneally (20).

Animal grouping

Group I: received oral distilled water for 14 days and on the 14th day, they were treated with olive oil (1 ml/kg, i.p.).

Group II: The control extract group that received 25 mg/kg of cinnamon extract and 125 mg/kg of ginger extract once daily for 14 days and on the 14th day, they were treated with olive oil (1 ml/kg, i.p.).

Group III: The CCl_4- induced toxic control group that received distilled oral water for 14 days, and on the 14th day they received CCl_4 (1 ml/kg i.p.) diluted with olive oil (1:1).

Group IV: This group was the pretreatment group with the cinnamon in which the rats received 50 mg/kg cinnamon extract for 14 days and 1 mg/kg of CCl_4 and olive oil mixture on the 14^{th} day.

Group V: This group was the pretreatment group with the ginger in which the rats received 250 mg/kg ginger extract for 14 days and 1 mg/kg of CCl_4 and olive oil mixture on the 14th day.

Group VI: This group was the pretreatment group with the cinnamon + ginger in which the rats received 25 mg/kg of cinnamon extract and 125 mg/kg of ginger extract once a day for 14 days and 1 mg/kg of CCl_4 and olive oil mixture on the 14^{th} day.

Group VII: This group was the positive control group with silymarin in which the rats received 100 mg/kg silymarin for 14 days and 1 mg/kg of CCl_4 and olive oil mixture on the 14^{th} day.

All animals in the corresponding groups received CCl_4 (1 ml/kg i.p.) diluted with olive oil (1:1), 2 hrs. after the administration of the last dose of the extract.

Blood and tissue sampling

Fifty hours after the CCl_4 injection, all animals were anesthetized by using diethyl ether inhalation and blood samples were collected from the heart tissue. Then, the serum was separated by centrifugation (Eppendorf, 5810 R) at 3000 rpm for 10 min. The sera were distributed in 0.5 ml quantities in small sterile tubes, and were frozen and maintained at -20° C. After blood collection, the abdominal cavity was opened and a piece of the liver (right distal lobe) was removed for morphological examination and malondialdehyde (MDA), total antioxidant (TA), and catalase (CAT) analyses. Then, a fragment of the liver was fixed in formalin (10%) for histological analysis.

Serum biochemical factors

Serum transaminases (AST and ALT) activity was measured by IFCC method, ALP activity was performed using DGKC method, and GGT activity was determined using Szasz's method. Total and direct bilirubin measurements were performed calorimetrically and estimation of serum total protein was done according to the method of Biuret. All serum parameters were measured using an Autoanalyzer (Biochemistry Analyzer BT 3000, Italy).

Liver homogenate

Fifty mg of frozen liver tissue was chopped and poured into an ice-cold tube and 1.5 ml of homogenization phosphate buffer 50 mM [(14.35g Na2HPO4.12H2O + 1.37g NaH2PO4.H2O) / 1 liter distilled water] was added to it. Then, it was homogenized using a homogenizer for 2 min at 10000 rpm. The suspension was re-centrifuged at 12,000 rpm for 30 min at 4 ° C, so that the unhomogenized cells deposited. The pure homogeneous solution was used to measure MDA, TA, and CAT.

Tissue protein measurement

Protein levels in the samples were measured according to Bradford method using concentrated Coomassie blue R-250 reagent (21). Bovine serum albumin (BSA) was used as the standard protein in the range of 0 to 1 mg/ml.

Measurement of MDA

MDA measurement was performed according to the method reported by Mihara & Uchiyama (22). Briefly, 500 µl of homogenate was added to the same volume of trichloroacetic acid (TCA) (10%, w/v). After centrifugation, 400 µl of the supernatant was mixed with 2400 µl of phosphoric acid 1%. After vortexing, 1 ml of thiobarbituric acid solution 67% was added to the test tube and after being vortexed once again was placed in a boiling temperature for 60 min. After cooling, 1600 µl n-butanol was added to the samples and they were vortexed vigorously for 1–2 min. Then, they were centrifuged at 3000 rpm for 10 minutes. After separating the supernatant organic phase, light absorption was measured in the wavelength of 532 nm against n-butanol as the blank. MDA concentration of the samples were determined after transferring the data to 1,1,3,3-tetraethoxypropane standard curve.

Assay of Total Antioxidants Capacity (TAC)

Determination of total antioxidant capacity was done by FRAP method (23). This method is based on the ability of homogenate in reducing of Fe^{3+} to Fe^{2+} in the presence of TPTZ. The created blue color was read spectrophotometrically at 593 nm.

Measuring catalase activity

The catalase assay was carried out by spectrophotometric method described by Aebi (24). In this assay, 50 µl of the supernatant of liver homogenate was diluted 500 times with phosphate buffer. Then, 2 ml of this solution was poured into the cuvette. Afterward, 1 ml of hydrogen peroxide 30 mM was added to it. Then, absorbance was monitored in 1 min at 240 nm against the blank (2 ml diluted supernatant + 1 ml phosphate buffer).

Histopathological study

The pieces of liver tissue in formalin 10% was embedded in paraffin and manually sectioned with a microtome to obtain 4-5 µm-thick. The sections were stained by hematoxylin and eosin (H&E) method and examined for histopathological changes using a microscope.

Statistical analyses

All values were reported as mean ± standard deviation (SD). Statistical analysis was carried out using one-way analysis of variance (ANOVA) and through SPSS22. Additional analysis was performed using post hoc test. P-value less than 0.05 was considered as statistically significant.

Results

Liver enzymes

The CCl_4 injection significantly increased ALT, AST, ALP and GGT activities ($p<0.001$). Pretreatment with cinnamon, ginger, and the combination of these two extracts reduced the activity of AST by 24.43%, 35.97% and 41.88%, respectively, and reduced the activity of ALT by 27.40%, 25.40% and 36.05%, respectively. ALP activity was decreased by 31.97%, 32.32% and 33.33% respectively, and GGT activity was decreased 31.52%, 31.52% and 33.16%, respectively, in comparison to CCl_4 control group (Table 1).

Table 1. Comparison of Liver enzymes in the studied groups

Groups	AST (IU/L)	ALT (IU/L)	ALP (IU/L)	GGT (IU/L)
I (Normal control)	1.60±25.93	57.16±9.15	341.66±41.61	2.57±0.18
II (Control Cinnamon 25 mg/kg + Ginger 125 mg/kg)	139.66±16.60	53.80±9.60	313.40±33.76	3.02±0.46
III (CCl4 control)	575.40±27.82**	501.40±22.61**	747.00±58.92**	6.09±0.70**
IV (Cinnamon 50 mg/kg)	434.80±31.38††	364.00±41.80†	508.16±79.23††	4.17±0.40†
V (Ginger 250 mg/kg)	368.40±34.54††	374.00±50.28†	505.50±50.18††	4.17±0.70†
VI (Cinnamon 25 mg/kg + Ginger 125 mg/kg)	334.40±35.22††♠	320.60±59.65††	498.00±56.08††	4.07±0.74†
VII (Silymarin 100 mg/kg)	273.75±54.48††	277.00±68.00††	409.00±83.29††	3.89±0.23†

Results presented in the table were expressed as the mean values ± standard deviation (SD) for 6 rats in each group. **: the significance of difference with the normal control group ($P < 0.001$). † and †† : significance of difference with the damaged control group ($P < 0.05$ and $P < 0.001$ respectively). ♠: the significance of difference with the cinnamon group ($P < 0.05$)

Bilirubin and total protein

Injection of CCl_4 increased the serum levels of total and direct bilirubin levels significantly ($p<0.001$). Pretreatment with cinnamon, ginger, and their combination extract, caused a significant decrease in total bilirubin ($p<0.05$). The statistically significant changes were not observed in serum concentrations of direct bilirubin. Injection of CCl_4 into rats significantly decreased the serum level of total protein ($p<0.05$).

Pretreatment with extracts of cinnamon, ginger and the combination of these two extracts increased the level of this factor ($p<0.05$ only in combined extract group). Increasing protein levels in cinnamon, ginger and combination of cinnamon and ginger extracts were 18.89%, 19.80% and 21.57% respectively (Table 2).

Table 2. Comparison of bilirubin and total protein in the studied groups

Groups	BilT (mg/dl)	BilD (mg/dl)	Total Protein (mg/dl)
I (Normal control)	0.60±0.10	0.030±0.008	6.61±0.29
II (Control Cinnamon 25 mg/kg + Ginger 125 mg/kg)	0.65±0.12	0.036±0.008	7.21±0.45
III (CCl_4 control)	1.20±0.23**	0.078±0.008**	4.98±0.43**
IV (Cinnamon 50 mg/kg)	0.90±0.15†	0.072±0.009	6.14±0.47
V (Ginger 250 mg/kg)	0.86±0.05†	0.078±0.009	6.21±0.47†
VI (Cinnamon 25 mg/kg + Ginger 125 mg/kg)	0.80±0.10†	0.077±0.009	6.35±0.41†
VII (Silymarin 100 mg/kg)	0.72±0.09†	0.045±0.012†	6.52±0.38†

Results presented in the table have been expressed as the mean values ± standard deviation (SD) for 6 rats in each group. **: the significance of difference with the normal control group ($P < 0.001$). †: significance of difference with the damaged control group ($P < 0.05$)

Effect on lipid peroxidation

In our study, the levels of malondialdehyde (MDA) as lipid peroxidation increased significantly in CCl_4-damaged group as compared with healthy control rats ($p<0.001$). Pretreatment with cinnamon, ginger, and combination of these two extracts as well as silymarin significantly reduced this oxidative factor ($p<0.001$) compared with the CCl_4 control group (Figure 1).

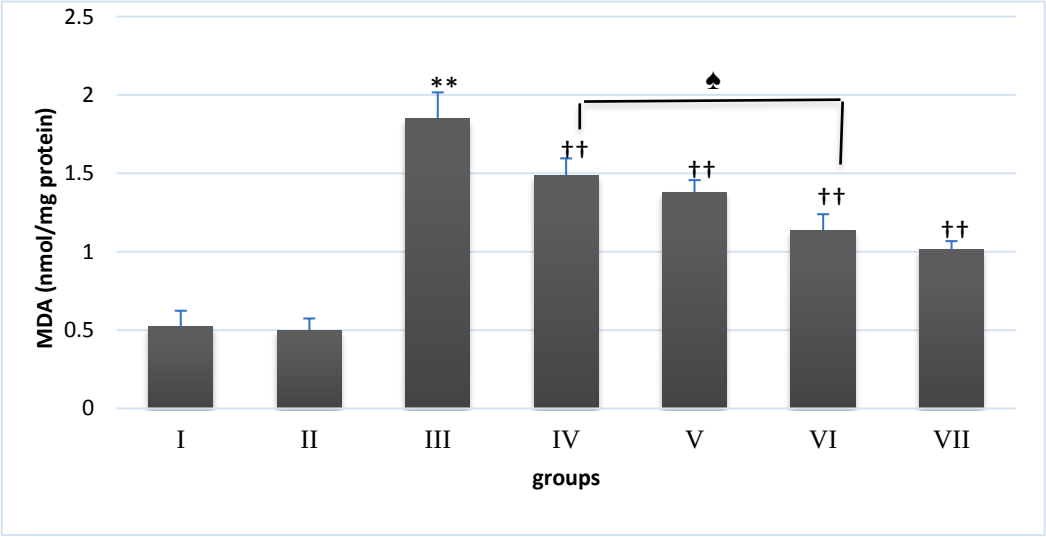

Figure 1. The effect of cinnamon and ginger extract and the combination of them on MDA level in CCl4-damaged rats

The bar signs on top of the columns indicate mean ± standard deviation (n = 6). **: the significance of difference with the normal control group ($P < 0.001$), ††: significance of difference with the damaged control group ($P < 0.001$), ♠: the significance of difference with the cinnamon group ($P < 0.05$), I:Normal control, II: Control Cinnamon 25 mg/kg + Ginger 125 mg/kg, III: CCl_4 control, IV: Cinnamon 50 mg/kg, V: Ginger 250 mg/kg, VI: Cinnamon 25 mg/kg + Ginger 125 mg/kg, VII: Silymarin 100 mg/kg

Effects on total antioxidant capacity

Injection of CCl_4 caused a significant decrease of liver total antioxidant capacity (69.95%) compared to the control normal group ($p<0.001$). Pretreatment with extracts of cinnamon, ginger, combination of these two extracts, and silymarin increased this factor significantly ($p<0.05$) by 52.65%, 53.48%, 54.2%, and 55.35%, respectively compared with the CCl_4 control group (Figure 2).

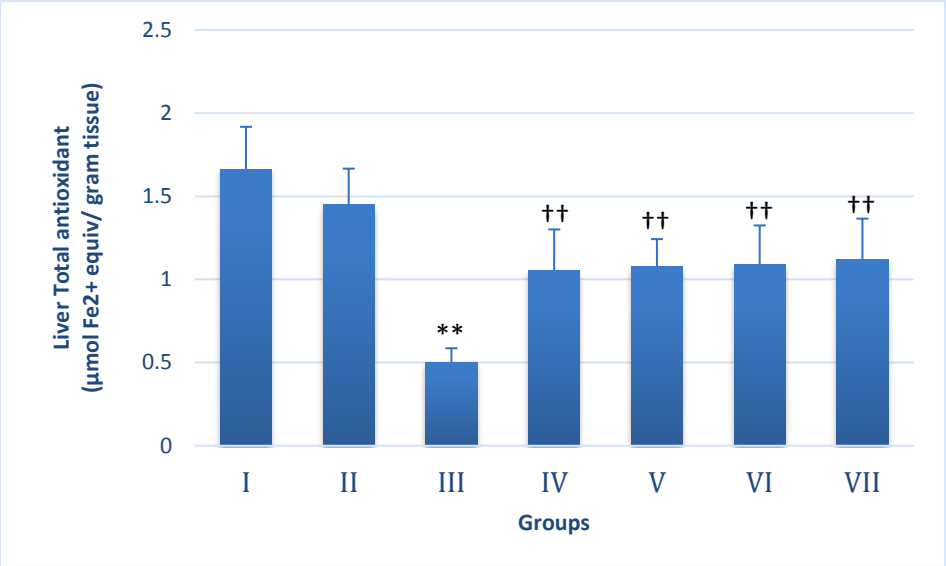

Figure 2. The effect of cinnamon and ginger extract and the combination of them on total antioxidant level in CCl4-damaged rats

The bar signs on top of the columns indicate mean ± standard deviation (n = 6). **: the significance of differences with the normal control group ($P < 0.001$), ††: significance of differences with the damaged control group ($P < 0.001$), I: Normal control, II: Control Cinnamon 25 mg/kg + Ginger 125 mg/kg, III: CCl_4 control, IV: Cinnamon 50 mg/kg, V: Ginger 250 mg/kg, VI: Cinnamon 25 mg/kg + Ginger 125 mg/kg, VII: Silymarin 100 mg/kg

Effects on catalase activity

The activity of catalase in the CCl_4-damaged rats showed a significant decrease ($p<0.001$) compared with the normal control group. Pretreatment with cinnamon, ginger, combination of these two extracts, and silymarin increased this amount by 29.44%, 24.88%, 39.33% and 35.88%, respectively which The changes in the pretreatment groups with the combination of extracts and silymarin were more significant ($p<0.01$, Figure 3).

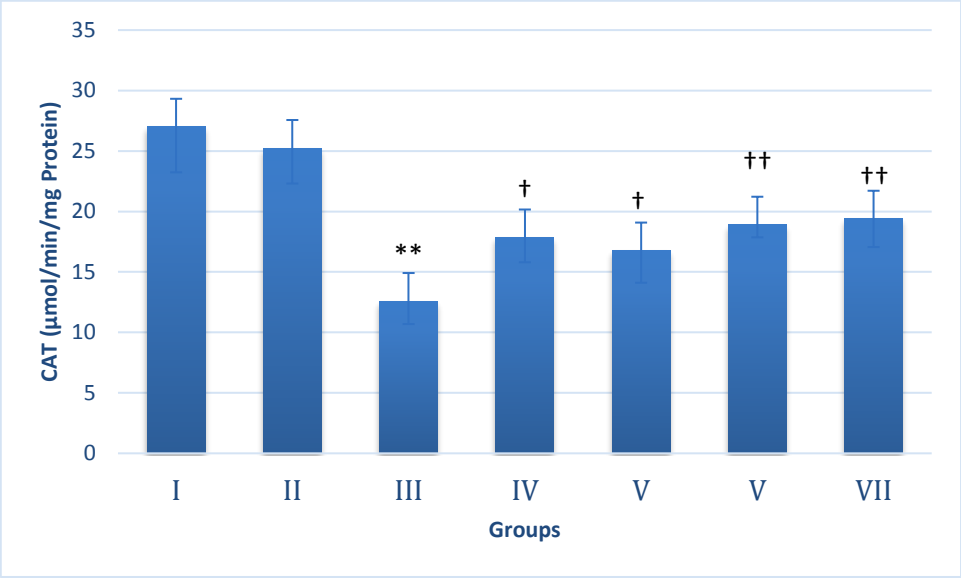

Figure 3. The effect of cinnamon and ginger extract and the combination of them on catalase activity in CCl4-damaged rats

The bar signs on top of the columns indicate mean ± standard deviation (n = 6). **: the significance of difference with the normal control group ($P < 0.001$), † and ††: significance of difference with the damaged control group ($P < 0.05$ and $P < 0.01$ respectively), I: Normal control, II: Control Cinnamon 25 mg/kg + Ginger 125 mg/kg, III: CCl_4 control, IV: Cinnamon 50 mg/kg, V: Ginger 250 mg/kg, VI: Cinnamon 25 mg/kg + Ginger 125 mg/kg, VII: Silymarin 100 mg/kg

Effects on liver morphology and histopathology

The morphological studies of liver showed injuries such as increased necrosis, visible pale and irregular surface suggesting the severe liver damage in CCl_4-treated group as compared to healthy control rats. The effect of hepatic protection of extracts on liver damage induced by CCl_4 was further confirmed by histopathological studies. Some abnormalities such as vacuolization of cells, necrosis of hepatocytes, infiltration of inflammatory cells, and bile duct degeneration were shown in the CCl_4 damaged control group. However, in the groups administered with extracts, less extensive areas of necrosis were seen in the pretreatment groups (Figures 4 and 5).

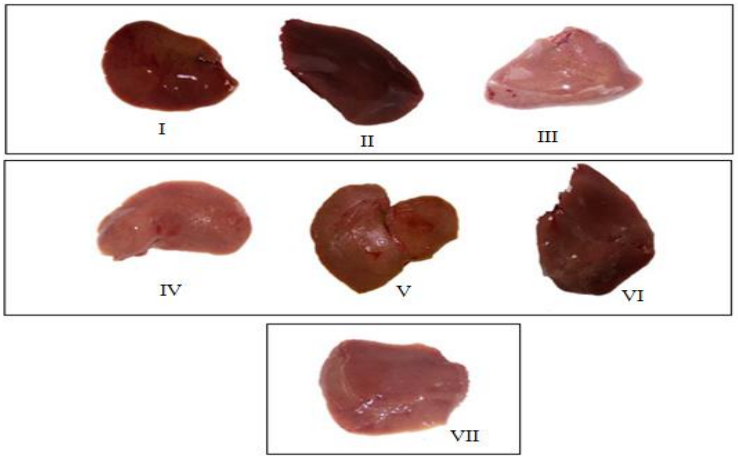

Figure 4. Macroscopic images of liver tissue in the study groups

I: Normal control, II: Control Cinnamon 25 mg/kg + Ginger 125 mg/kg, III: CCl_4 control, IV: Cinnamon 50 mg/kg, V: Ginger 250 mg/kg, VI: Cinnamon 25 mg/kg + Ginger 125 mg/kg, VII: Silymarin 100 mg/kg

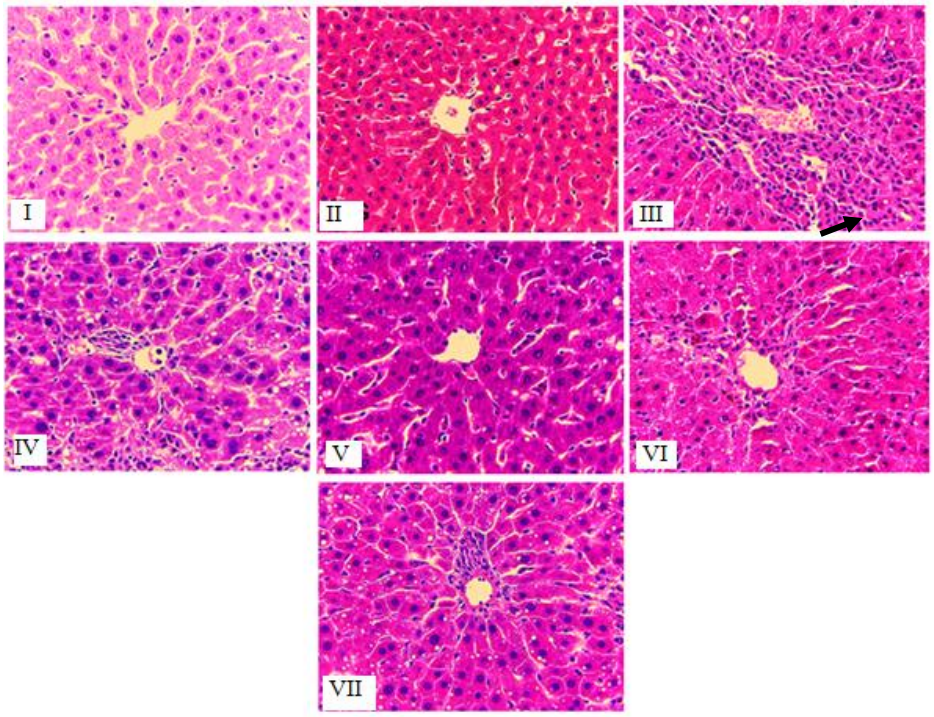

Figure 5. H & E stained microscopic images of liver tissue in the study groups

I: Normal control, II: Control Cinnamon 25 mg/kg + Ginger 125 mg/kg, III: CCl_4 control, IV: Cinnamon 50 mg/kg, V: Ginger 250 mg/kg, VI: Cinnamon 25 mg/kg + Ginger 125 mg/kg, VII: Silymarin 100 mg/kg

Discussion

Liver is a very important organ as it is responsible for the metabolism of harmful and toxic substances derived from human metabolites and some foreign chemicals. It has also been widely recognized that reactive oxygen species (ROS) and free radicals produced during the metabolism of drugs and toxic substances may cause pathological changes in the liver (4, 25).

Among the liver injury biomarkers, elevation of AST and ALT are probably the most commonly used in both clinical diagnosis and research relating hepatocyte damage. Increased serum activity of AST and ALT indicate enzyme leakage from cells and increased membrane permeability. ALP is responsible for the hydrolysis of phosphate esters and is a biomarker for liver function. Increased serum ALP also indicates biliary system damage (26). GGT is an enzyme involved in the breakdown of extracellular glutathione antioxidants, and it seems to be an oxidative and subclinical inflammatory marker (27). Since, the GGT is present in the plasma membrane of hepatocytes and in the canalicular region, so elevation of this enzyme in the serum may indicate hepatocyte damage (28). In this study, intraperitoneal injection of CCl_4 increased the serum levels of ALT, AST, ALP, and GGT enzymes, similar to other researchers (29, 30). In our study, pre-treatment with cinnamon and ginger extract, as well as the combination of these two extracts, could significantly reduce liver enzymes levels compared to the CCl_4 control group. Bioactive compounds such as gingerol and shogaol in ginger can protect membranes from oxidation against free radicals and possesses strong radical scavenging activity (31, 32). It is also true for cinnamon,

due to the presence of antioxidant bioactive compounds such as eugenol and linalool, which can protect the plasma membrane of hepatocytes against CCl_4-induced free radicles and prevent liver enzymes from leaking into the bloodstream (33, 34). The combination of cinnamon and ginger extract, due to possing different bioactive compounds with various antioxidant capacities, can have a synergistic effect on protection of liver against toxic substances or drugs.

The results of MDA in this study indicated that pretreatment with combination of two extracts of cinnamon and ginger, reduced the lipid peroxidation effectively. Furthermore, the observations suggest that some compounds such as cinnamon and gingerol can prevent lipid peroxidation and hepatotoxicity upon exposure to the free radical-generating agent, carbon tetrachloride (35, 36). It seems that the cause of the decrease in lipid peroxidation in the groups treated with these two extracts may be due to their free radical scavenging activities.

In the liver damage caused by CCl_4, the balance between the production of ROS and the antioxidant defense system of the organism is distorted. Active oxygen species are normally *regulated* by the antioxidant system, which contains enzymatic and non-enzymatic antioxidants. CAT is one of the enzymatic antioxidants that, along with SOD and GP_X, has an effective defense mechanism against free radicals. SOD is a special antioxidant for the conversion of anion superoxide to hydrogen peroxide, which is dehydrated by CAT and glutathione peroxidase (GSH-px) (37). Maintenance of normal status of total antioxidants and catalase in treated groups with the combination of extracts after CCl_4 damage suggest the ability of stimulatiing antioxidant mechanisms defense (11).

Bilirubin is produced in the liver mainly as conjugate bilirubin and is excreted as bile (38). Serum total bilirubin (direct and indirect) can indicate the metabolic status of the liver. Injection of CCl_4 resulted in a significant increase in the direct and total bilirubin, which is similar to Oshaghi et.al findings who examined the effect of *Anethum graveolens* on liver damage induced by CCl_4 (39). Direct bilirubin elevations are more related to structural or functional disorders in the biliary system. Thus, it can be said that CCl_4 prevents the excretion of bilirubin into the bile by biliary obstruction, which causes increase of direct bilirubin level in the bloodstream. Pretreatment with ginger extract and also the combination of cinnamon and ginger extracts significantly reduced the indirect bilirubin content. It can be concluded that pretreatment with the extracts significantly inhibits hepatocellular damage.

Serum total protein levels indicate liver function, and their measurements can be used to diagnose liver disorders (40). CCl_4 injection significantly reduced total protein in damaged rats, and this is consistent with findings of other researches on total protein and albumin (41, 42). Free radicals produced by CCl_4 can interfere with protein synthesis through binding to ribosomes and mRNAs, thereby disrupting the synthesis of proteins. Pretreatment with cinnamon, ginger and their combination could significantly increase total protein levels. The possible mechanism for this action might be due to the protective effects of cinnamon and ginger bioactive compounds against harmful effects of CCl_4.

Protection effects of the combination of cinnamon and ginger extract on liver damage induced by CCl_4 is further confirmed by examining the morphology and histology of the liver tissue. The liver tissues of animals that received only CCl_4 showed damages such as edema and cell vacuolization, more

areas of necrosis, degeneration of nucleus and destruction of the biliary tract (9). However, in the groups treated with combination of cinnamon and ginger extract, less sponge-like state was observed and tissue restoration was seen after necrosis and destruction of the biliary in the liver. It seems that the combination of cinnamon and ginger extract can prevent liver injury or can reconstruct the injured liver.

Conclusion

The results of this study indicated a better protective effect of the combination of ginger and cinnamon on liver parameters (ALT, AST, ALP, GGT), bilirubin and total serum protein, and antioxidant indices. This study showed that the co-administration of cinnamon and ginger extracts is more efficacious than use of the single extract.

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Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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