The effect of some phytochemical combinations on liver disorders induced by carbon tetrachloride in rats

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Tأثير بعض توليفات الكيماويات النباتية على اعتلالات الكبد المستحث برابع كلوريد الكربون الفئران

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باحثة دكتوراه بقسم الاقتصاد المنزلي - كلية التربية النوعية - جامعة بورسعيد

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In the present study, some phytochemical combinations were investigated for their effect on liver disorders induced by carbon tetrachloride in rats. The study was conducted on forty-eight rats divided into six groups:
- Group I: Control group, fed with a standard diet.
- Group II: Control group fed with the experimental diet.
- Group III: Fed with the experimental diet and treated with carbon tetrachloride.
- Group IV: Fed with the experimental diet and treated with the experimental diet plus phytochemical combination.
- Group V: Fed with the experimental diet and treated with carbon tetrachloride and phytochemical combination.
- Group VI: Fed with the experimental diet and treated with carbon tetrachloride and phytochemical combination.

The results showed that the phytochemical combination had a significant effect in reducing the liver enzymes AST, ALT, and ALP, as well as improving the body weight gain (BWG) and food intake (FI) in the rats treated with carbon tetrachloride. In addition, the group treated with the phytochemical combination showed a significant decrease in the levels of bilirubin and cholesterol in the blood. The study concluded that the phytochemical combination has a promising effect in the treatment of liver disorders induced by carbon tetrachloride.
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The study evaluates the effects of some phytochemical combinations on liver disorders induced by carbon tetrachloride (CCl4) in rats. The phytochemicals tested were

- Turmeric (Curcuma longa) extract
- Green tea (Camellia sinensis) extract
- Red onion (Allium cepa) extract

The study found that these phytochemicals were effective in improving liver function, reducing levels of blood lipids and glucose, and mitigating oxidative damage.

Keywords: Phytochemicals, Liver function, Blood lipids, Glucose, Oxidative damage
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Abstract:

The modern pharmacological therapy is costly and associated with multiple side effects resulting in patient non-compliance. Thus, there is a need to explore alternative therapies particularly from nutritional/plant sources as these are cost effective and possess minimal side effects. The present study aimed to determine the effect of phytochemical combinations on liver disorders induced by carbon tetrachloride in rats. The normal rats feeding with basal diet were recorded 19.00, 41.18 and 0.092 for FI, BWG and FER respectively. The injected rats with CCl4 (control positive) showed significantly (P ≤ 0.05) decreased in FI, BWG and FER compared to normal rats by the ratio of -25.51, -38.98 and -21.11%, respectively. On the other side there were significantly (P ≤ 0.05) increased in FI, BWG and FER by the all tested formulae. Treatment of rats with CCl4 caused a significantly (P ≤ 0.05) increased in AST, ALT and ALP by the percent of change 71.45, 22.77 and 155.77%, respectively compared to normal control. On the other side there were significantly (P ≤ 0.05) increased in AST, ALT and ALP by the all tested formulae. The increasing rate was raised with the increasing of the tested formulae feeding levels. Also, Formulae II induced significant higher improvements in AST, ALT and ALP than formula I. Furthermore, feeding of the tested formulae exhibited significant (P ≤ 0.05) improvements in total bilirubin, serum lipid profile, lipoprotein cholesterol fractions and serum glucose of rats induced by CCl4. In conclusion, the present study has demonstrated the potency of the selected formulae to partially ameliorate liver disorders in rats induced by CCl4. The complications include improved the liver functions, blood lipid profile and serum glucose and serum oxidant/antioxidant status.

Keywords:

plant parts, liver functions, serum lipid profile, glutathione, malonaldehyde.
Introduction

Liver plays a critical role in all vertebrates (from human to fish). Reasons for this include the following: 1) this organ plays numerous important metabolic functions, such as the regulation of carbohydrate metabolism, the production of plasma proteins, and the synthesis of bile, 2) nutrients derived from intestinal absorption are stored in hepatocytes and released for further catabolism by other tissues, 3) the yolk protein, vitellogenin, destined for incorporation into the oocyte, is synthesized entirely within the liver, 4) it is the major site of the cytochrome P450-mediated, mixed-function oxidase system, and, while this system inactivates or detoxifies some xenobiotics, it activates others to their toxic forms, and 5) bile synthesized by hepatocytes aids in the digestion of fatty acids and carries conjugated metabolites of toxicants into the intestine for excretion or intrahepatic recirculation Voet and Voet, 1990 and Maton et al., 1993. It that means, the liver is responsible for many critical functions within the body and should it become diseased or injured, the loss of those functions can cause significant damage to the body.

Cancer begins when cells in a part of the body start to grow out of control. There are many kinds of cancer, but they all start because of out-of-control growth of abnormal cells. Cancer cell growth is different from normal cell growth. Instead of dying, cancer cells continue to grow and form new, abnormal cells. Cancer cells can also invade (grow into) other tissues, something that normal cells cannot do. Growing out of control and invading other tissues are what makes a cell a cancer cell. In most cases the cancer cells form a tumor like liver cancer (Howlader et al., 2012). Hepatocellular cancer (HCC) can have different growth patterns like: Some begin as a single tumor that grows larger. Only late in the disease does it spread to other parts of the liver. The second type seems to start as many small cancer nodules throughout the liver, not just a single tumor. This is seen most often in people with cirrhosis (chronic liver damage) (American Cancer Society, 2013). Hepatocellular carcinoma (HCC) is one of the most common malignant tumors in the world, representing the third leading cause of death from cancer (Bosch et al., 1999); El-Serag and Rudolph, 2007) and the fifth most prevalent malignancy worldwide (Farazi and Depinho, 2006). Owing to advances in diagnostics and therapeutics, HCC can be creatively treated when detected at an early stage by applying therapies including radiofrequency ablation (RFA), transcatheter arterial chemoembolization (TACE) and surgical resection. However, curative treatments are often hampered by frequent recurrence of HCC (Okuda, 2007) because the remaining liver retains the potential for de novo carcinogenesis (Kumada et al., 1997). Although systemic chemotherapy has also been challenged to patients with advanced stages of HCC, it is mostly ineffective (Thomas, 2008).
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The modern pharmacological therapy is costly and associated with multiple side effects resulting in patient non-compliance. Thus, there is a need to explore alternative therapies particularly from nutritional/plant sources as these are cost effective and possess minimal side effects. Plants produce an amazing amount of complex chemicals we can use as medicines to “curb and cure” disease. Many of authorities and academic centers of research pay more attention towards the area of cancer chemoprevention compounds (El-Serag and Rudolph, 2007). One of the most impressive findings in the field of chemoprevention is the very large number of compounds that have been demonstrated to prevent the occurrence of cancer. Many of these classes are lies in an enlarged group of compounds called phytochemicals (phyto is Greek for plant). It is differ from vitamins and minerals in that they have known nutritional value. Some are antioxidants, protecting against harmful cell damage from oxidation (Ohkawa et al., 1991). Others perform different functions that help prevent cancer (Mori et al., 1986; and Tanaka et al., 1993 a,b). Also, many studies found that some phytochemical compounds have pharmacologically active as antioxidant, antimutagenic, and anticarcinogenic agents (Stich, 1991; Newmark et al., 1992; Huang et al., 1992; and Stavric et al., 1992). Phytochemical compounds which naturally occurring in food materials can be classified into several families include allyle sulfides, indoles, phenolic compounds, saponins and terpens. Amongst of different families of phytochemicals, phenolic compounds have been occupied the central position. The term of phenolic compound embraces a wide range of compound plant substances, which possess in common an aromatic ring bearing one or more hydroxyl substituents. They most frequently occur combined with sugar glycoside and usually located in the cell vacuole (Harborne, 1973). Phenolic acids are a group of phenolic compound, which may be identified as hydroxycarboxylic acids with phenolic hydroxyl groups (Misaghi, 1982). Phenolic acids and their derivatives are widely distributed in all plant derived food systems and in most diets. The levels vary dramatically, especially as influenced by factors such as the species, germination, ripening, and storage and processing. For example, potato tubers were shown to have several kinds of phenolic acids and most of these phenolics are concentrated in the outer part (Kumar et al., 1991; Dao and Friedman, 1992; and Rodriguez et al., 1994 a-b). Many of phenolic acids exhibits their antioxidative, (Majid et al., 1991; and Laranjinha et al., 1994), anticarcinogenic (Gali et al., 1991; and Harttig et al., 1996) and antibacterial effects (Nakane et al., 1990; and Nowosielska et al., 1991). Recently, many laboratories are still deciphering the many ways phytochemical in food may offer frontline defense against cancer although they still not fully understood (Thomas, 2008). Therefore, the present study aimed to determine the
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Materials and Methods

**Plant parts:** Plant parts used in food combinations will obtained purchased from the herbs merchandize, local markets, Egypt. Plant parts include: Marjoram "*Origanum majorana*", Molokheya "*Corchorus capsularis* Linn", Sweet fennel "*Foeniculum vulgare*", Ginseng "*Panax ginseng*", Black seeds "*Nigella sativa* L.", Eucalyptus "*Eucalyptus globules*", Cinnamon "*Cinnamomum verum*", Spearmint leaves "*Menta spicata*", Lemon peels "*Citrus limon*", Potato peels "*Solanum tuberosum*", Orange peels "*Citrus sinensis*", Onion skin "*Allium Cepa* L", Apricot kernels "*Prunus Armeniaca*" and Gum arabic "*Sengalia Senegal*".

**Wily mill:** A wily mill (Tecator, Boulder, Co, USA) fitted with a 60 mesh screen sieve was used for grounding and sieving the all tested dried plant parts.

**Chemicals and reagents**

**Basal diet:** Basal diet constituents will obtain from El- Gomhorya Company for Trading Drug, Chemical and Medical Instruments, Cairo, Egypt.

**Carbon tetrachloride (CCl₄):** was obtained from El-Gomhoryia Company for Chemical Industries, Cairo, Egypt as 10% liquid solution. It was dispensed in white plastic bottles each containing one liter as a toxic chemical material for liver poisoning according to Passmore and Eastwood (1986). In the same time, it was mixed with olive oil which obtained from the pharmacy for dilution during the induction.

**Kits:** For determination of liver and kidney functions, serum glucose, oxidative stress markers malondialdehyde (MDA), antioxidant activity enzymes (glutathione-peroxidase, GPx and catalase, CAT) which were obtained from Biodiagnostic Co. Dokki, Giza, Egypt.

**Chemicals, solvents and buffers:** All chemicals, reagents and solvents were of analytical grade and purchased from Al-Gomhoryia Company for Trading Drugs, Chemicals and Medical Instruments, Cairo, Egypt.

**Methods**

**Tested Formulae preparation**

Each formula was prepared by mixing its herbs content by the listed ratio in blend mixture (Toshiba ElAraby Company, Benha, Egypt) for 5 min. The resulted mixtures were packed in tied polyethylene bags and kept in refrigerator at 4°C until analysis.
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Preparation of tested formulae extracts

Extracts of the tested formulae were prepared according to the method of Amin et al., (2004) with some modifications. In brief, the homogenized tested formulae were dissolved in aqueous solvent (deionized water) as the following: In aqueous extract: (20 g from dried plant +180 ml deionized water). The homogenized sample was weighed and transferred to a beaker and stirred at 200 rpm in an orbital shaker (Unimix 1010, Heidolph Instruments GmbH & Co. KG, and Germany) for 1 h at room temperature. The extract was then separated from the residue by filtration through What man No. 1 filter paper. The remaining residue was re-extracted twice, and then the two extracts were combined. The residual solvent of aqueous extract was removed under reduced pressure at 40°C using a rotary evaporator (Laborata 4000; Heidolph Instruments GmbH & Co. KG, Germany).

Table (1): Plant parts include of formula I

| Plant parts         | Percentage (%) |
|---------------------|----------------|
| Black seeds         | 8.70           |
| Ginseng             | 8.70           |
| Cinnamon            | 15.22          |
| Eucalyptus (Cavour) | 10.87          |
| Marjoram            | 17.39          |
| Molokhia            | 26.09          |
| Sweet fennel        | 13.04          |
| Total               | 100.00         |

Table (2): Plant parts include of formula II

| Plant parts          | Percentage (%) |
|----------------------|----------------|
| Black seeds          | 15.22          |
| Spearmint leaves     | 8.70           |
| Marjoram leaves      | 13.04          |
| Sweet fennel         | 8.70           |
| Lemon peels          | 6.52           |
| Potato peels         | 6.52           |
| Orange peels         | 6.52           |
| Onion skin           | 6.52           |
| Apricot kernels      | 6.52           |
| Gum arabic           | 21.74          |
| Total                | 100.00         |
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Biological experiments

Rats

Mature male albino rats of Sprague - Dawley strain rats weighing (190±15) g were used in this work. Animals were obtained from Research Institute of Ophthalmology, Medical Analysis Department, Giza, Egypt. The animals were allocated in plastic cages with metallic stainless covers and kept under strict hygienic measures. Rats were fed on basal diet for 7 days before the beginning of the experiment for adaptation. Diets were presented to rats in special non-scattering feeding cups to avoid loss of food and contamination. Water and food was provided ad libitum via a narrow mouth bottle with a metallic tube tightly fixed at its mouth by a piece of rubber tube.

Basal diet

The basal diet was prepared according to NRC, (1996). It was consisted of 20% protein (casein), 10% sucrose, 4.7% corn oil, 0.2% choline chloride, 0.3 % methionin 1% vitamin mixture, 3.5% salt mixture and 5% fiber (cellulose). The remainder was corn starch as it was recorded in the Table (3), salt mixture and vitamins mixture were prepared according to Hegested et al., (1941) and Campbell, (1963), as shown in Table (4-5).

Preparation of liver impaired rats

Liver impaired was induced in normal healthy male albino rats by subcutaneous injection of carbon tetrachloride, CCl₄ (0.1 mg/kg body weight) for two weeks according to Jayasekhar et al., (1997). The liver functions for the infected rats will check periodically to make sure the induction of liver disorders.

Experimental design

Rats (n=40 rats) will house individually in wire cages in a room maintained at 25 ± 2 °C and kept under normal healthy conditions. All rats (50 rats) will feed on basal diet for one-week before starting the experiment for acclimatization. After one week period, the rats were divided into three main groups, the first group (Group 1, 5 rats) still fed on basal diet and the second main group (45 rats) will inject by CCl₄ to induce liver impaired rats then classified to 7 subgroups as follow:

- Group (2): fed on standard diet only as a positive control
- Group (3): Fed on standard diet containing 1% formula I.
- Group (4): Fed on standard diet containing 2% formula I.
- Group (5): Fed on standard diet containing 3% formula I.
- Group (6): Fed on standard diet containing 1% formula II.
- Group (7): Fed on standard diet containing 2% formula II.
- Group (8): Fed on standard diet containing 3% formula II.
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Blood sampling
At the end of the experiment animals were fasted overnight, then exposed to ether anesthesia and blood samples were withdrawn from eye plexus of veins into heparinized capillary tubes. They were left to clot by standing at room temperature for 20 minutes, and then centrifuged at 3000 rpm (round per minute) for 10 minutes. Serum was carefully aspirated and transferred into clean quite fit Plastic tubes and Kept Frozen at - 20°C until used for biochemical assays. Rats were there after opened, liver, spleen, heart, lungs and kidneys removed and washed in saline solution, then dried and weighted. Relative weights of mentioned organs were calculated using the following formula

Relative organ weight = \( \frac{\text{Organ weight}}{\text{body weight}} \times 100 \)

Hemolysate preparation
After collecting blood samples in EDTA containing tubes, they were centrifuged at 3000 rpm for 15 min, the plasma were removed and the packed cells of the bottom were washed thrice with saline solution (0.9% NaCl). A known amount of erythrocytes was lysated.

Biological evaluation
During the period of the experiment, all rats were weighed once a week and the consumed diets were recorded everyday (daily feed intake). At the end of the experiment, biological evaluation of the experimental diets was carried out by determination of body weight gain (BWG) and feed efficiency ratio (FER). According to Chapman et al., (1959), using the following equations:

\[
\text{BWG} \% = \frac{\text{Final weight} - \text{Initial weight}}{\text{Initial weight}} \\
\text{FER} = \frac{\text{Body weight gain (g)}}{\text{Feed Intake (g)}}
\]

Hematological analysis
Liver functions
Serum glutamic pyruvic transaminase (SGPT/ALT) and serum glutamic oxaloacetic transaminase (SGOT/AST), and alkaline Phosphatase (ALP) activities were measured in serum using by the method of Tietz et al., (1976) and Vassault et al., (1999), respectively.
Serum glucose
Enzymatic determination of serum glucose was carried out colorimetrically according to Yound, (1975).
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Glutathione (GSH)

GSH was determined by HPLC according to the method of McFarris and Reed (1987). In brief, 100 µl of aliquot were placed in 2 ml of 10% perchloric acid containing 1 mM bathophenanthroline disulfonic acid and homogenized. The homogenate was cold centrifuged at 10000 rpm for 5 min and the internal standard (γ-glutamyl glutamate) was added to the supernatant. A 250 µl aliquot of acidic extract was mixed with 100 µl of 100 mM iodoacetic acid in 0.2 mM cresol purple solution. The acid solution was brought to pH 8.9 by the addition of 0.4 ml of KOH (2 M) – KHCO₃ (2.4 M) and allowed to incubate in the dark at room temperature for 1 hr to obtain S-carboxymethyl derivatives. The N-nitrophenol derivatization of the samples were taken overnight at 4 °C in the presence of 0.2 ml of 1% 1-fluoro-2, 4-dinitrobenzene and injected onto the HPLC system.

Malondialdehyde content (MDA)

Lipid peroxide levels measured as malondialdehyde in serum and liver were determined by as thiobarbituric acid reactive substances (TBARS) as described by Buege and Aust, (1978). Half milliliter of plasma were added to 1.0 ml of thiobarbituric acid reagent, consisting of 15% TCA, 0.375% thiobarbituric acid (TBA) and 0.01% butylated hydroxytoluene in 0.25 N HCl. Twenty-five microliters of 0.1 M FeSO₄.7H₂O was added and the mixture was heated for 20 min in boiling water. The samples were centrifuged at 1000 rpm for 10 min and the absorbance was read at 535 nm using Labo-med. Inc., spectrophotometer against a reagent blank. The absorbance of the samples was compared to a standard curve of known concentrations of malonaldehyde.

Statistical Analysis

All measurements were done in triplicate and recorded as mean±SD. Statistical analysis was performed with the Student t-test and MINITAB-12 computer program (Minitab Inc., State College, PA).

Results and Discussion

Effect of feeding of tested formulae on FI (Feed intake), BWG (body weight gain) and FER (Feed efficiency ratio) of rats treated with CCl₄

Effect of feeding of tested formulae on FI (Feed intake), BWG (body weight gain) and FER (Feed efficiency ratio) of rats treated with CCl₄ were shown in Table (3). From such data it could be noticed that the normal rats feeding with basal diet were recorded 19.00, 41.18 and 0.092 for FI, BWG and FER respectively. The injected rats with CCl₄ (control positive) showed significantly (P ≤ 0.05) decreased in FI, BWG and FER compared to normal rats by the ratio of -25.51, -38.98 and -
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21.11%, respectively. On the other side there were significantly (P ≤ 0.05) increased in FI, BWG and FER by the all tested formulae. The increasing rate was raised with the increasing of the tested formulae feeding levels. Also, Formulae II induced significant higher improvements in FI, BWG and PER than formula I.

These result were agreement with Dickerson and Lee, (1988) who reported that many patients with acute or chronic liver disease are ill, and commonly lose weight. On other side these results seemed to agree with Bhavanishankar et al., (1986) who indicated that values of BWG % of animals given different plant parts were not different from values in control. Also, Kamal (2014) indicated that different plant parts were induced significantly improvements in FI, BWG and PER of rats treated with CCl4. Also, they showed that feeding some plant parts i.e. artichoke, milk thistle, turmeric, gum arabic powders and their formula showed significantly (P ≤0.05) increased in heart, liver, kidneys, lungs and spleen compared to normal rats by the ratio of 27.58, 27.04, 4.54, 24.13 and 58.82% respectively.

Table (3): Effect of feeding of tested formulae on FI (Feed intake), BWG (body weight gain) and FER (Feed efficiency ratio) of rats treated with CCl4

| Groups              | FI (g/d) Mean ±SD | % of change | BWG (g/28d) Mean ±SD | % of change | FER Mean ±SD | % of change |
|---------------------|-------------------|-------------|-----------------------|-------------|--------------|-------------|
| Group 1: Control Ve-  | 19.00 a           | -----       | 41.18 a               | -----       | 0.092 a      | -----       |
| Group 2: Control     | 14.15 c           | -25.51      | 2.513 c               | -38.98      | 0.072 c      | -21.11      |
| Group 3: Formula I (1%) | 16.53 ab          | -13.02      | 29.18 b               | -29.14      | 0.076 bc     | -16.55      |
| Group 4: Formula I (2%) | 16.74 ab         | -11.89      | 31.62 b               | -23.20      | 0.079 b      | -13.89      |
| Group 5: Formula I (3%) | 17.56 a          | -7.57       | 33.80 b               | -17.91      | 0.080 b      | -13.07      |
| Group 6: Formula II (1%)  | 16.64 ab         | -12.42      | 30.99 b               | -24.75      | 0.079 b      | -14.02      |
| Group 7: Formula II (2%)  | 17.96 a          | -5.46       | 38.32 a               | -6.94       | 0.086 a      | -6.05       |
| Group 8: Formula II (3%)  | 18.26 a          | -3.89       | 39.44 a               | -4.23       | 0.088 a      | -3.94       |

Each value represents mean ± SD. Means with different letters in the same column are significantly different (P ≤0.05) while those with similar letters are non-significantly different.
Effect of feeding of tested formula on serum liver enzymes activity of rats treated with CCl₄

Effect of feeding of tested formulae on serum liver enzymes activity (U/L) of rats treated with CCl₄ were shown in Table (4). From such data it could be noticed that treatment of rats with CCl₄ caused a significantly (P ≤ 0.05) increased in aspartate amino transferase (AST), alanine amino transferase (ALT) and alkaline phosphates (ALP) by the percent of change 71.45, 22.77 and 155.77%, respectively compared to normal control. On the other side there were significantly (P ≤ 0.05) increased in AST, ALT and ALP by the all tested formulae. The increasing rate was raised with the increasing of the tested formulae feeding levels. Also, Formulae II induced significant higher improvements in AST, ALT and ALP than formula I.

These results are in accordance with those of Murayama et al., (2008) and Abdalla et al., (2013). It is clear from the increased enzymatic levels that ALP was the most affected enzyme meanwhile AST was the least one. Lin et al. (1997) demonstrated that ALT is more sensitive test for hepatocellular damage than AST. CCl₄ impair the integrity, structure and function of the hepatocytes via its ROS, leading to defective secretion of the bile due to the damaged bile ducts consequently elevation of ALP level in the blood (Sreelatha et al., 2009).

Toxic effects of CCl₄ on liver have been extensively studied (Amin and Mahmoud, 2009 and Kim et al., 2010a). Serum AST, ALT are the most sensitive biomarkers used in the diagnosis of liver diseases (Pari and Kumar, 2002). During hepatocellular damage, varieties of enzymes normally located in the cytosol are released into the blood flow. Their quantification in plasma is useful biomarkers of the extent and type of hepatocellular damage (Pari and Murugan, 2004). Serum ALT catalyses the conversion of alanine to pyruvate and glutamate, and is released in a similar manner. Therefore, serum ALT is more specific to the liver, and is thus a better parameter for detecting liver injury (Williamson et al., 2006). In conjunction with the reports of (Hegde and Joshi, 2009; Kim et al., 2010b), data from the present study showed that CCl₄ caused hepatic damage with a significant increase in serum levels of AST and ALT. Serum ALP level is also related to the status and function of hepatic cells. CCl₄ administration in the present study also caused significant increase in the serum ALP which may be due to increased synthesis in presence of increasing biliary pressure (Moss and Butterworth, 1974).

Our emerged data revealed that our tested data significantly ameliorated the increase of hepatic enzymes AST, ALT and ALP which in accordance with the
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Results of Mehmetick et al. (2008) ; Kucukgerin et al. (2010) and Elhassaneen et al. (2016). Also, Swamy et al., (2012) and Al-Kenanny et al., (2012) studied that received of GA orally to mice at concentration 10gm/kg for eight days, have ability as antioxidant because have a significantly ameliorating hepatotoxicity by increase the level of GSH and reduction MDA in addition to enzymatic level ALT and AST in serum of mice although it haven't reach to normal value. Furthermore, Nishiumi et al., (2011) mentioned that dioxins enter the body mainly through diet and cause the various toxicological effects by binding to the cytosolic aryl hydrocarbon receptor (AhR) followed by its transformation. It has been shown that certain natural compounds suppress AhR transformation in vitro. It was demonstrated that ethanolic extract from molokhia, known as Egyptian spinach, showed the strongest suppressive effect on AhR transformation induced by 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) in cell-free system using rat hepatic cytosol among 41 kinds of extracts from vegetables and fruits. The molokhia extract also suppressed TCDD-induced AhR transformation in mouse hepatoma Hepa-1c1c7 cells and in intestinal permeability system constructed with human colon adenocarcinoma Caco-2 cells and human hepatoma HepG2 cells. Fennel is a widely distributed plant in most tropical and subtropical countries and have long been used in folk medicines to treat obstruction of the liver, spleen and gall bladder and for digestive complaints such as colic, indigestion, nausea and flatulence. GA administration dramatically reduced acetaminophen-induced hepatotoxicity as evidenced by reduced serum alanine (ALT) and aspartate aminotransferase (AST) activities. Acetaminophen-induced hepatic lipid peroxidation was reduced significantly by GA pretreatment. The protection offered by arabic gum does not appear to be caused by a decrease in the formation of toxic acetaminophen metabolites, which consumes glutathione (GSH), because arabic gum did not alter acetaminophen-induced hepatic GSH depletion.
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Table (4): Effect of feeding of tested formula on serum liver enzymes activity (U/L) of rats treated with CCl₄

| Groups                | AST     | ALT     | ALP     |
|-----------------------|---------|---------|---------|
|                       | Mean ± SD | % of change | Mean ± SD | % of change | Mean ± SD | % of change |
| Group 1: Control Ve-  | 71.45 b  | -------- | 22.77 d  | -------- | 155.77 d | -------- |
| Group 2: Control (Ve+) | 109.09 a | 52.67 a  | 41.33 a  | 81.50 a  | 207.54 a | 33.23 a   |
| Group 3: Formula I (1%) | 100.23 b | 40.28 a  | 38.95 a  | 71.05 a  | 190.66 a | 22.40 a   |
| Group 4: Formula I (2%) | 87.32 b  | 22.20 a  | 34.73 b  | 52.53 b  | 183.09 b | 17.54 b   |
| Group 5: Formula I (3%) | 85.81 b  | 20.10 b  | 32.76 b  | 43.85 b  | 175.05 b | 12.37 b   |
| Group 6: Formula II (1%) | 93.59 b  | 30.98 b  | 36.69 b  | 61.11 b  | 188.49 b | 21.00 b   |
| Group 7: Formula II (2%) | 81.62 d  | 14.23 d  | 25.38 d  | 11.46 d  | 172.35 b | 10.64 b   |
| Group 8: Formula II (3%) | 79.01 d  | 10.58 d  | 24.32 d  | 6.81 d   | 168.93 b | 8.45 b    |

Each value represents mean ± SD. Means with different letters in the same column are significantly different (P ≤0.05) while those with similar letters are non-significantly different.

Effect of feeding of tested formula on serum total billirubin of rats treated with CCl₄

Effect of feeding of tested formula on serum total billirubin of rats treated with CCl₄ was shown in Table (5). From such data it could be noticed that the normal rats feeding with basal diet was recorded 0.27 mg/dl for billirubin respectively. The injected rats with CCl₄ (control positive) showed significantly (P ≤ 0.05) decreased in bilirubin compared to normal rats by the ratio of 64.37%. On the other side there were significantly (P ≤ 0.05) increased in billirubin by the all tested formulae. The increasing rate was raised with the increasing of the tested formulae feeding levels. Also, Formulae II induced significant higher improvements in billirubin than formula I. These results are in agreement with Ghanem et al., (2009) who attributed this reduction in serum bilirubin to plant parts phytochemicals which stimulates the clearance of bile from the liver, preventing congestion in the liver and diminishing the liver damage.

CCl₄ is one of the most commonly used hepatotoxins in the experimental study of liver diseases. The hepatotoxic effects of CCl₄ are largely due to its active metabolite, trichloromethyl radical (Johnson and Kroening, 1998). These activated radicals bind covalently to the macromolecules and induce peroxidative degradation of membrane lipids of endoplasmic reticulum rich in polyunsaturated fatty acids. This leads to the formation of lipid peroxides. This lipid peroxidative degradation of
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Biomembranes is one of the principle causes of hepatotoxicity of CCl4 (Kaplowitz et al., 1986). This is evidenced by an elevation in the serum marker liver enzymes namely, total bilirubin and decrease in protein. In the assessment of liver damage by CCl4 the determination of liver enzymes levels is largely used. Necrosis or membrane damage releases the enzyme into circulation and hence it can be measured in the serum.

Table (5): Effect of feeding of tested formula on serum total bilirubin (mg/dl ) of rats treated with CCl4

| Groups                  | Mean±SD | % of change |
|-------------------------|---------|-------------|
| Group 1: Control Ve-    | 0.27 ad | ------      |
| Group 2: Control (Ve+)  | 0.44 a  | 64.37       |
| Group 3: Formula I (1%) | 0.41 ab | 54.47       |
| Group 4: Formula I (2%) | 0.37 ab | 37.51       |
| Group 5: Formula I (3%) | 0.33 c  | 24.84       |
| Group 6: Formula II (1%)| 0.39 ab | 46.08       |
| Group 7: Formula II (2%)| 0.30 c  | 12.16       |
| Group 8: Formula II (3%)| 0.29 cd | 7.51        |

Each value represents mean ± SD. Means with different letters in the same column are significantly different (P ≤0.05) while those with similar letters are non significantly different.

High levels of AST indicates liver damage, such as that caused by viral hepatitis as well as cardiac infarction and muscle injury, AST catalyses the conversion of alanine to pyruvate and glutamate and is released in a similar manner. Therefore ALT is more specific to the liver, and is thus a better parameter for detecting liver injury. Elevated levels of serum enzymes are indicative of cellular leakage and loss of functional integrity of cell membrane in liver (Drotman, 1978). Serum ALP, bilirubin and total protein levels on other hand are related to the function of hepatic cell. Increase in serum level of ALP is due to increased synthesis, in presence of increasing biliary pressure (Muriel et al., 1992). Also, Kamal, (2014) reported that some plant parts ameliorates the liver functions of CCl4 treated rats due to their phytochemicals content.

Effect of feeding of tested formulae on serum lipid profile of rats treated with CCl4

Effect of feeding of tested formulae on lipid profile of rats treated with CCl4 was shown in Table (6). From such data it could be noticed that treatment of rats with
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CCl₄ caused a significantly (P ≤ 0.05) increased in total cholesterol (TC) and triglycerides (TG) by the percent of 35.82 and 50.49%, respectively compared to normal control. On the other side there were significantly (P ≤ 0.05) increased in TC and TG by the all tested formulae . The increasing rate was raised with the increasing of the tested formulae feeding levels. Also, Formulae II induced significant higher improvements in TC and TG than formula I. These result accordance with Kucukgergin et al. (2010) who found that plant leaf extracts decreased serum lipids, as well as hepatic and cardiac oxidative stress in rats fed on high cholesterol diet. Also phytochemicals decreased cholesterol synthesis in rat liver homogenates (Skottova and Krecman, 1998). On the other hand Asai and Miyazawa., (2001) indicated that dietary phytochemicals lowered liver cholesterol and TG, plasma TG. Also Chuengsamarn et al., (2014) found that phytochemical slowers the atherogenic risks by reducing the insulin resistance, TG, visceral fat and total body fat. Various mechanisms have been proposed to explain the hypocholesterolemic effect of GA. Some studies have suggested that the viscosity of fermentable dietary fibers contribute substantially to the lipid lowering effects in animals and humans. The mechanism most clearly implicated is related to increased fecal bile acid and neutral sterol excretion or a modification of lipid digestion and absorption (Moundras et al., 1994; Annison et al., 1995 and Tiss et al., 2001). Also, a high cholesterol diet caused a decrease in CAT and GPx activity, while apricot kernel oil caused a significant activity increase of these enzymes (P < 0.05).

Table (6): Effect of feeding of tested formulae on serum lipid profile including total cholesterol and triglycerides (mg/dl) of rats treated with CCl₄

| Groups                  | Total cholesterol (TC) | Triglycerides (TG) |
|-------------------------|------------------------|--------------------|
|                         | Mean ± SD               | % of change        | Mean ± SD               | % of change        |
| Group 1: Control Ve-    | 105.84 ᵃ               | ------             | 51.13 ᵃ                | ------             |
| Group 2: Control (Ve+)  | 143.75 ᵃ              | 35.82              | 76.95 ᵃ                | 50.49              |
| Group 3: Formula I (1%) | 137.61 ᵃ              | 30.02              | 70.60 ᵃ                | 38.08              |
| Group 4: Formula I (2%) | 125.27 ᵆ              | 18.36              | 61.50 ᵆ                | 20.27              |
| Group 5: Formula I (3%) | 123.20 ᵐ              | 16.40              | 59.58 ᵇ                | 16.52              |
| Group 6: Formula II (1%)| 129.70 ᵘ              | 22.55              | 66.76 ᵈ                | 30.57              |
| Group 7: Formula II (2%)| 114.48 ᵇ              | 8.17               | 56.85 ᵇ                | 11.19              |
| Group 8: Formula II (3%)| 111.88 ᵇ              | 5.71               | 55.44 ᵇ                | 8.42               |

Each value represents mean ± SD. Means with different letters in the same column are significantly different (P ≤0.05) while those with similar letters are non significantly different.
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The group fed with apricot kernel oil supplementation showed higher enzyme activities than sunflower oil groups irrespective of cholesterol (P < 0.05). Results indicated that apricot kernel oil causes improvement in liver antioxidant status of rats in comparison to sunflower oil which is a commonly consumed vegetable oil (Erdogan-orhan and Kartal, 2010).

Effect of feeding of tested formulae on lipoprotein cholesterol fractions of rats treated with CCl₄

Effect of feeding of tested formulae on lipoprotein cholesterol fractions including HDL-c, LDL-c and VLDL-c of rats treated with CCl₄ were shown in Table (7). From such data it could be noticed that treatment of rats with CCl₄ caused a significantly (P ≤ 0.05) increased in HDL-c, LDL-c and VLDL-c by the percent of -22.87, 52.15 and 10.23%, respectively compared to normal control. On the other side there were significantly (P ≤ 0.05) increased in HDL-c, LDL-c and VLDL-c by the all tested formulae. The increasing rate was raised with the increasing of the tested formulae feeding levels. Also, Formulae II induced significant higher improvements in HDL-c, LDL-c and VLDL-c than formula I.

These result agreement with those Magielse et al. (2014) found that plant parts extracts protect low-density lipoprotein (LDL) from oxidation in vitro and rats were fed a high cholesterol diet then given silymarin (found in artichoke) had improved hepatic LDL clearance. Also plant parts extracts decreased cholesterol synthesis in rat liver homogenates (Skottova and Krecman, 1998). Plant parts extracts prevents the oxidation of LDL inhibits platelet aggregation, and reduces the incidence of myocardial infarction (Swamy et al., 2012). Also, Asai and Miyazawa., (2001) indicated that dietary plant parts extracts lowered liver TC and TG, plasma triacylglycerol and VLDL-c. Plant parts extracts decreased TC, TG and LDL (schmandke., 2007). Furthermore, Sharma, (2001) reported that reductions of total serum cholesterol by 6% and 10.4%, respectively when subjects received 25 g/day and 30 g/day of GA for periods of 21 and 30 days.
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Table (7): Effect of feeding of tested formulae on lipoprotein cholesterol fractions including HDL-c, LDL-c and VLDL-c (mg/dl) of rats treated with CCI4

| Groups                  | HDL-c Mean ± SD | % of change | LDL-c Mean ± SD | % of change | VLDL-c Mean ± SD | % of change |
|-------------------------|-----------------|-------------|----------------|-------------|-----------------|-------------|
| Group 1: Control Ve-     | 43.46 ± 6       | ------      | 52.15 ± 6      | ------      | 10.23 ± 6      | ------      |
| Group 2: Control (Ve+)   | 33.52 ± 6       | -22.87      | 81.85 ± 6      | 66.12       | 15.39 ± 6      | 50.49       |
| Group 3: Formula I (1%)  | 36.86 ± 6       | -15.19      | 86.63 ± 6      | 14.12       | 38.08 ± 6      | 30.57       |
| Group 4: Formula I (2%)  | 38.93 ± 6       | -10.43      | 41.97 ± 6      | 12.30       | 20.27 ± 6      | 15.62       |
| Group 5: Formula I (3%)  | 39.31 ± 6       | -9.56       | 38.01 ± 6      | 11.92       | 16.52 ± 6      | 11.19       |
| Group 6: Formula II (1%) | 37.71 ± 6       | -13.22      | 78.63 ± 6      | 13.35       | 30.57 ± 6      | 8.42        |
| Group 7: Formula II (2%) | 39.98 ± 6       | -8.01       | 63.13 ± 6      | 21.05       | 11.37 ± 6      | 11.19       |
| Group 8: Formula II (3%) | 41.19 ± 6       | -5.22       | 59.61 ± 6      | 14.29       | 11.09 ± 6      | 8.42        |

Each value represents mean ± SD. Means with different letters in the same column are significantly different (P ≤ 0.05) while those with similar letters are non-significantly different.

The decrease was confined to LDL and VLDL cholesterol only, with no effect on HDL and TG. Finally, Khan et al., (2012) reported that some plant parts ameliorates the serum lipid profile treated of CCl4 rats due to their phytochemicals content.

Effect of feeding of tested formula on serum glucose of rats treated with CCl4

Effect of feeding of tested formula on serum glucose of rats treated with CCl4 was shown in Table (8). From such data it could be noticed that the normal rats feeding with basal diet was recorded 98.18mg/dl for serum glucose respectively. The injected rats with CCl4 (control positive) showed significantly (P ≤ 0.05) decreased in serum glucose compared to normal rats by the ratio of 40.36%. On the other side there were significantly (P ≤ 0.05) increased in serum glucose by the all tested formulae. The increasing rate was raised with the increasing of the tested formulae feeding levels. Also, formulae II induced significant higher improvements in serum glucose than formula I. These results agree with El-Moselhy et al. (2011) showed that oral administration of plant parts extracts was an antihyperglycemic effect and improved insulin sensitivity, which was attributed by its anti-inflammatory properties as evident by attenuating TNF-α levels. Also Chuangsamarn et al., (2014) found that plant parts extracts helps to improve relevant metabolic profiles in type 2 diabetic population. Treated with plant parts extract had significant decreases in fasting glycemia, mean daily blood glucose, glycosuria, and insulin needs over six months (Velussi et al., 1997). Also Phillips et al. (2008) GA has a low glycaemic index and
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reduces plasma glucose concentrations in healthy individuals because it is a non-digestible polysaccharide that has been shown to retard glucose absorption. Furthermore, Khan et al., (2012) reported that some plant parts ameliorates the serum glucose treated of CCl4 rats due to their phytochemicals content.

Table (8): Effect of feeding of tested formula on serum glucose (mg/dl ) of rats treated with CCl4

| Groups               | Glucose Mean±SD | % of change |
|----------------------|-----------------|-------------|
| Group 1: Control Ve- | 98.18g          | -----       |
| Group 2: Control (Ve+) | 137.81^a     | 40.36       |
| Group 3: Formula I (1%) | 130.77^b     | 33.19       |
| Group 4: Formula I (2%) | 124.06^c     | 26.35       |
| Group 5: Formula I (3%) | 118.44^d     | 20.63       |
| Group 6: Formula II (1%) | 128.29^b     | 30.67       |
| Group 7: Formula II (2%) | 113.13^e     | 15.23       |
| Group 8: Formula II (3%) | 107.51^f     | 9.50        |

Each value represents mean ± SD. Means with different letters in the same column are significantly different (P ≤0.05) while those with similar letters are non-significantly different.

Effect of feeding of tested formula on RBC's enzymes antioxidant of rats treated with CCl4

Effect of feeding of tested formulae on RBC,s enzymes antioxidant of rats treated with CCl4 were shown in Table (9). From such data it could be noticed that treatment of rats with CCl4 caused a significantly (P ≤ 0.05) increased in RBC,s glutathione peroxidase (GSH-Px), glutathione reductase (GSH-Rd) and catalase (CAT) by the percent of change -48.31, -34.00 and -33.62%, respectively compared to normal control. On the other side there were significantly (P ≤ 0.05) increased in GSH-Px, GSH-Rd and CAT by the all tested formulae . The increasing rate was raised with the increasing of the tested formulae feeding levels. Also, Formulae II induced significant higher improvements in GSH-Px, GSH-Rd and CAT than formula I.

Erythrocytes are permanently in contact with potentially damaging levels of oxygen, but their metabolic activity is capable of reversing this injury under normal conditions (Avci et al., 2008). Erythrocytes are equipped by many defence systems representing their antioxidant capacity (Kurata et al., 1993). This protective system includes superoxide dismutase (SOD), catalase (CAT),
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Reduced glutathione (GSH), glutathione peroxidase (GSH-Px), glutathione S-transferase (GST), and glutathione reductase (GSH-Rd). However, the cellular antioxidant action is reinforced by the presence of dietary antioxidants (Kenan and Bulbuloglu, 2005 and Avci et al., 2008). It was known that CCl₄ induced changes in erythrocytes membrane composition and membrane bound Na⁺/K⁺ and Ca²⁺ dependant ATPase activities (Adaramoye and Akinloye, 2000). In accordance with our result, Escobar et al., (1996) and Sanzgiri et al. (1997) have reported that the enhanced free radical concentration resulting from the oxidative stress conditions can cause loss of enzymatic activity. Moreover, Szymonik-Lesiuk et al., (2003) reported that CCl₄ intoxication would lead to damage of antioxidant enzymes or reactive intermediates formed in the course of bioactivation of CCl₄ may bind to these enzymes that are responsible for their inactivation. Catalase (CAT) is one of the important enzymes in the supportive team of defense against reactive oxygen species (ROS).

Table (9): Effect of feeding of tested formula on RBC's enzymes antioxidant (U/mg Hb) of rats treated with CCl₄

| Groups                  | GSH-Px | GSH-Rd | CAT        |
|-------------------------|--------|--------|------------|
|                         | Mean ± SD | % of change | Mean ± SD | % of change | Mean ± SD | % of change |
| Group 1: Control Ve-    | 22.15 a | ------ | 13.56 a | ------ | 183.78 a | ------ |
| Group 2: Control (Ve+)  | 11.45 b | -48.31 | 8.95 c  | -34.00 | 122.000 b | -33.62 |
| Group 3: Formula I (1%) | 15.02 c | -32.21 | 9.45 b  | -30.32 | 134.870 b | -26.61 |
| Group 4: Formula I (2%) | 17.29 a | -21.96 | 10.35 ab | -23.69 | 155.090 c | -15.61 |
| Group 5: Formula I (3%) | 18.19 a | -17.86 | 11.16 a | -17.69 | 156.780 c | -14.69 |
| Group 6: Formula II (1%) | 16.19 ab | -26.92 | 10.14 b | -25.23 | 146.540 c | -20.26 |
| Group 7 : Formula II (2%) | 18.90 a | -14.65 | 12.54 a | -7.53 | 165.780 b | -9.79 |
| Group 8: Formula II (3%) | 19.76 a | -10.78 | 12.90 a | -4.84 | 171.780 b | -6.53 |

Each value represents mean ± SD. Means with different letters in the same column are significantly different (P ≤0.05) while those with similar letters are non-significantly different.

Catalase is a haemoprotein containing four haeme groups, that catalyses the decomposition of H₂O₂ to water and O₂ and thus, protects the cell from oxidative damage by H₂O₂ and OH (Gupta et al., 2004). Viewed in conjunction with the report of Szymonik-Lesiuk et al., (2003), the inhibition of CAT activity following CCl₄ intoxication in the present study may be due to the enhancement of
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The peroxidation end product MDA, which is known to inhibit protein synthesis and the activities of certain enzymes. Also, these results are in the line with the findings of Chidambara et al., (2002) who found that rats treated with CCl4 decreased the level of CAT activity. Accordance these result the protective actions are due to the plant parts phytochemicals ability to modify antioxidant enzymes such as SOD, CAT, and GSH-Px (Nabavi et al., 2012b). Also the indirect antioxidant capacity of plant parts extract is defined by its ability to induce the expression of cytoprotective proteins such SOD, CAT, GSH-Rd, GSH-Px , glutathione-S-transferase (GST) (Panchal et al., 2008; Ye et al., 2010 and Yarru et al., 2009).

It was chosen the experimental prooxidant system: Fe2SO4 and ascorbic acid to induce lipid peroxidation in rat RBCs and human RBC membranes. Potato peel extract (PPE) was found to inhibit lipid peroxidation with similar effectiveness in both the systems (about 80-85% inhibition by PPE at 2.5 mg/ml). While PPE did not cause any morphological alteration in the erythrocytes, under the experimental conditions, PPE significantly inhibited the H2O2-induced morphological alterations in rat RBCs as revealed by scanning electron microscopy. Further, PPE was found to offer significant protection to human erythrocyte membrane proteins from oxidative damage induced by ferrous–ascorbate. In conclusion, results indicated that PPE is capable of protecting erythrocytes against oxidative damage probably by acting as a strong antioxidant (Singh et al., 2004). Also, GA have been shown to inhibit lipid peroxidation, decreases cytochrome P450 content but increases glutathione (GSH) content and the of glutathione-dependent antioxidant enzymes (Sharma et al., 2001). Several bacterial infections are associated with the risk of certain cancer, cinnamon had potent antimicrobial activities against the organisms (De et al., 1999). Extracts of cinnamon have also been shown to have antioxidant effects in part through activating antioxidant enzymes in various tissues that prevent free radical formation, remove radicals before damage can occur, repair oxidative damage, eliminate damaged molecules, or prevent mutations are important mechanisms in cancer prevention (Dhuley, 1999 and Anilakumar et al., 2001). Finally, kamal, (2014) reported that some plant parts ameliorates the RBC's antioxidants enzymes including SOD, CAT, GSH-Px and GST treated of CCl4 rats due to their phytochemicals content. GA leads to statistical significant increase of antioxidants parameters such as ACT, GSH-Px, SOD and GSH in consistency with the studies of Al-kenanny et al., (2012), and Gado and Aldahmash (2013) who confirmed antioxidants properties of GA.
Effect of feeding of tested formula on serum lipid peroxidation (MDA) of rats treated with CCl4

Effect of feeding of tested formula on serum MDA of rats treated with CCl4 was shown in Table (10). From such data it could be noticed that the normal rats feeding with basal diet was recorded 230.29 nmol/mg Hb for serum MDA, respectively. The injected rats with CCl4 (control positive) showed significantly (P ≤ 0.05) increased in MDA compared to normal rats by the ratio of 29.66%. On the other side there were significantly (P ≤ 0.05) increased in serum MDA by the all tested formulae. The increasing rate of MDA was raised with the increasing of the tested formulae feeding levels. Also, formulae II induced significant higher improvements in serum MDA than formula I.

Since the erythrocyte oxidative stress increased in human patients with severe hepatic disease (Solov’eva, 2009). So, the current investigation studied the erythrocytes oxidative stress as a consequence of hepatic injury induced by CCl4. Oxidative stress in the erythrocytes in the present investigation can be assessed by induction in MDA and reduction in GSH levels as well as inhibition of the GST and CAT activities. In conjunction with the earlier studies of Hatherill et al. (1991), and Eritsland (2000), erythrocytes may be prone to oxidative stress because they exposed to high oxygen tension, have polyunsaturated fatty acids in the membrane and hemoglobin bound iron. Jayaraman et al. (2008) reported that the decrease in the enzymatic antioxidant activities in erythrocytes following ethanol intoxication in rats could be attributed to either inhibition of enzymes synthesis or damage to the enzyme protein. Antioxidant and anti-inflammatory agents play a critical role against CCl4 intoxication by scavenging active oxygen and free radicals and neutralizing lipid peroxides (Gutierrez and Navarro, 2010).

The result agreement with those Mehmetcik et al., (2008) who recorded that there was a significant decrease in hepatic MDA in CCL4 group pretreated with plant parts extract. Gebhardt, (1997). In human mesangial cell cultures that had been incubated with glucose, plant parts extracts worked as an antioxidant, inhibiting the formation of malondialdehyde, a product of lipid peroxidation (Wenzel et al., 1996). Several reports have documented the potent antioxidant capacity of plant parts extracts where by mitigation of lipid peroxidation and oxidative stress in several tissues were demonstrated (Nabavi et al., 2012). Also, Khan et al., (2012) reported that some plant parts ameliorates the serum fat peroxidation (MDA) treated of CCL4 rats due to their phytochemicals content. Furthermore, Al-Kenanny et al., (2012) studied that received of GA orally to mice at concentration 10gm /kg/for eight days, have ability as antioxidant because have a significantly ameliorating hepatotoxicity by increase the level of GSH and reduction MDA.
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Table (10): Effect of feeding of tested formula on serum MDA (nmol/mg Hb) of rats treated with CCl4

| Groups                      | MDA     | % of change |
|-----------------------------|---------|-------------|
| Group 1: Control Ve-        | 230.29<sup>e</sup> | -----       |
| Group 2: Control (Ve+)      | 298.59<sup>a</sup> | 29.66       |
| Group 3: Formula I (1%)     | 277.64<sup>b</sup> | 20.56       |
| Group 4: Formula I (2%)     | 267.02<sup>c</sup> | 15.95       |
| Group 5: Formula I (3%)     | 265.28<sup>c</sup> | 15.19       |
| Group 6: Formula II (1%)    | 273.47<sup>bc</sup> | 18.75       |
| Group 7: Formula II (2%)    | 253.56<sup>d</sup> | 10.10       |
| Group 8: Formula II (3%)    | 247.10<sup>d</sup> | 7.30        |

Each value represents mean ± SD. Means with different letters in the same column are significantly different (P ≤0.05) while those with similar letters are non-significantly different.

Apricot kernel oil is a rich source of MUFA and PUFA, including mainly oleic (about 70%) and linoleic acids, respectively. In addition, apricot kernel oil could be considered as a good source of bioactive compounds such as tocopherols and phytosterols consisting mainly of the α-isomer and β-sitosterol, respectively. Due to its high content of oleic acid, apricot kernel oil is considered as a healthy supplement in diet. It was investigated the effects of apricot kernel oil supplementation on cholesterol and malondialdehyde (MDA) levels and glutathione peroxidase (GPx) and catalase (CAT) activity in hypercholesteremic rats. Hypercholesteremia was produced by feeding rats with a semisynthetic diet that contained high cholesterol and cholic acid (Erdogan-orhan and Kartal, 2010). The antioxidant potency of freeze-dried aqueous extract of potato peel was investigated employing various established in vitro systems, such as lipid peroxidation in rat liver homogenate 1,1-diphenyl-2-picrylhydrazyl (DPPH)/superoxide/hydroxyl radical scavenging, reducing power, and iron ion chelation. Freeze-dried aqueous extract of potato peel powder (PPE) showed strong inhibitory activity toward lipid peroxidation of rat liver homogenate induced by the FeCl2-H2O2 system. Furthermore, PPE exhibited a strong concentration-dependent inhibition of deoxyribose oxidation (Singh et al., 2004). Due to cinnamon antioxidant activity and its common use to season lamb in Indian cuisine, it has been studied as an additive to radiation-processed lamb meat, and was found effective in delaying oxidation of fats and reducing formation of harmful substances, which can be detected using thiobarbituric acid as a reagent (Blamey and Wilson, 1989). Researchers have also studied American ginseng for its potential in enhancing overall health and in the
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Treatment of specific conditions. Some of these include: Prevention of free radical damage and support of cardiovascular health. (Huang, 1989) and (Li et al., 1999). Enhanced immunity (Wang and Ng, 2000). Also, Trommer and Neubert (2005) studied lipid peroxidation antioxidant and reducing effects in vitro of various polysaccharides in GA. They found that GA reduces lipid peroxidation of skin in a dose-dependent. Furthermore, Badreldin et al., (2009) who indicated that GA is a strong antioxidant so it has a protective effect against lipid peroxidation and Said et al., (2014) showed that statistical significant decrease of oxidants parameters such as MDA and nitric oxide is as a result of administration of GA with indomethacin because it has free radical scavenging.

In conclusion, the present study has demonstrated the potency of the selected formulae to partially ameliorate liver disorders in rats induced by CCl₄. The complications include improved the liver functions, blood lipid profile and serum glucose and serum oxidant/antioxidant status.
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