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Potential hepatoprotection exerted by ginseng against chlorpyrifos-induced hepatotoxicity in albino rats

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Abstract

Insecticides gained public reputation and widespread application to control the spread of different insects in various habitats. However, the deleterious effects of these chemicals could not be ignored and should be dealt seriously. The present work was conducted to test the efficacy of the natural plant ginseng in alleviating toxicity of chlorpyrifos. The organophosphorus insecticide chlorpyrifos induced hepatotoxicity and changes in some serum biochemical parameters. The liver of rats administered chlorpyrifos manifested cytoplasmic vacuolization, leucocytic infiltration, hemorrhage and remarkable dilatation of veins. The nuclear chromatin was condensed. There was a significant increase in alanin aminotransferase (ALT) while there was a significant decrease in albumin, catalase (CAT) and superoxide dismutase (SOD) in the serum of treated rats. Treating animals with ginseng was found in this study to alleviate hepatotoxicity and restore the levels of the tested serum parameters to nearly normal values.

Key words: chlorpyrifos, rats, liver, Histology, ginseng, ALT, albumin, antioxidants.

1. Introduction

Insecticides are used specifically to kill or control insects' growth by disruption of vital processes via chemical actions. Insecticides use has resulted in several problems such as environmental contamination, risk of poisoning harmless insects and threatening of wildlife and humans. A sprayed insecticide may drift from the areas to which it is applied into wildlife areas, especially when it is sprayed aerially (Palmer et al., 2007). Organophosphorus insecticides (OPs) are widely used for a variety of agricultural and public health applications (Goel et al., 2007). The toxicity of OP involving many organs such as liver and kidney (Cemek et al., 2010) was recorded. Many studies attributed the mechanism of organophosphates toxicity to neurotoxicity (Karanth et al., 2004), immunotoxicity (Fukuyama et al., 2009) and generation of reactive oxygen species (ROS) inducing damage to various cellular membranous components coupled with consumption of endogenous antioxidants store (Sivapiriya et al., 2006). Aaron (2001) and Clark (2002) indicated that organophosphorus insecticides inhibit acetylcholinesterase enzyme, resulted in accumulation of acetylcholine in preganglionic and postganglionic parasympathetic receptors (muscarinic action), sympathetic preganglionic synapses including adrenal medulla and neuromuscular junctions (nicotinic action).

Organophosphate insecticides are the most acutely toxic of all insecticides to vertebrate animals. Organophosphate insecticides are nerve poisons that kill the target pest and are toxic to mammals because of essentially irreversible combination with acetylcholinesterase, and ester-hydrolyzing enzyme involved in the normal transmission of nerve impulses through nerve tissue. Acetylcholinesterase hydrolyses acetylcholine, the major chemical mediator of nerve impulses across the synaptic junction or to be associated with the production of the potential necessary for nerve action (Gunther and Jeppson, 1960).

There are many evidences that organophosphate compounds cause damage many body systems such as urinary system (Wedin, 1992), immune system (Newcombe, 1992; Rodgers et al., 1992; Handy et al.,

2002), the cardiovascular system (Baskin and Whitmer, 1992 and Pimental and Dacosta, 1992), hematological (De-Blaquiere et al., 2000), cytotoxic effects (Li and Zhang, 2002) and direct skeletal muscle fibre necrosis possibly via calcium influx (Bright et al., 1991).

From the histopathological point of view, it was found that chlorpyrifos increased cytoplasmic vacuolization, necrosis and dilatation of sinusoids. Mice treated with 16 mg/kg dimethoate exhibited rupture in some hepatocytes, dark stained hepatocytic nuclei indicating cell pycnosis and some hepatocytes had shrinked nuclei (Khogali et al., 2005).

In addition, Kerem et al. (2007) observed blood vessels congestion of liver of Wistar rats exposed to 25 or 50 mg/ kg fenthion and hepatocytes swelling and vacuolization by 75 or 100 mg/ kg of the same insecticide.

Moreover, Khogali et al. (2005) indicated that administration of dimethoate to pregnant rats induced enzymatic changes associated with mild pathomorphological changes in liver and brain. However, Galloway and Handy (2003) explained the immunotoxicity on the basis of inhibition of immune system is through the oxidative damage to immune organs.

Mense et al. (2006) found that the organophosphate insecticides chlorpyrifos and cyfluthrin altered the expression of a subset of genes with diverse functions in primary human astrocytes.

Chlorpyrifos is a broad-spectrum insecticide kills insects upon contact by affecting the normal function of the nervous system. Chlorpyrifos affects the nervous system by inhibiting the breakdown of the neurotransmitter acetylcholine (Smegal, 2000). Upon insect exposure, chlorpyrifos binds to the active site of the cholinesterase, which prevents breakdown of acetylcholine in the synaptic cleft. The resulting accumulation of acetylcholine in the synaptic cleft causes overstimulation of the neuronal cells, leading to neurotoxicity and eventually death (Karanth and Pope, 2000).

Chlorpyrifos caused hepatic atrophy (Miyazaki and Hodgson, 1972) and profile of liver marker enzymes and essential trace elements adversely affected in rats subjected to chlorpyrifos (Goel et al., 2000, Goal and Dhawan, 2001). Regarding action of chlorpyrifos, it was found that it inhibits acetylcholinesterase and kills insect pests by disrupting their nervous system. It is highly toxic to birds, fish, aquatic invertebrates, and honeybees (Kidd and James, 1991).

The use of plants or plant extracts to treat diseases is a therapeutic modality. Ginseng, garlic and ginger are examples of botanical sources gaining popularity among modern physicians (Gilani and Rahman, 2005). The active ingredients of ginseng are ginsenosides that are called ginseng saponins. Ginseng was used as a tonic to invigorate week bodies and help restoration of homeostasis. However, current *in vivo* and *in vitro* studies had shown that ginseng exerted beneficial effects in cardiovascular diseases (Wood et al., 1964), immune deficiency (Zhu, 1998), cancer (Yun, 2001) and hepatotoxicity (Lee et al., 2005a, b). Some ginseng active ingredients exert beneficial actions on aging and central nervous system disorders (Van Kampen et al., 2003).

Shin et al. (2000) provided evidence for the antioxidant activity of Asian ginseng and there is evidence that medicinal effect of ginseng was attributed to its protective properties against free radicals attack (Maffei Facino et al., 1999). Ginseng has the ability to scavenge free radicals and to neutralize ferryl ion-induced peroxidation (Bastianetto et al., 2000).

Moreover, ginseng has been indicated to have anticancer effects (Park et al., 2004; Xie et al., 2005; Zhang et al., 2008).

In this concern, it was found that oral administration of Korean red ginseng inhibited liver cancer induced by diethylnitrosamine in Wistar rats (Wu and Zhu, 1990) as well as significantly inhibiting lung adenoma induced by urethane (Yun, 1991). Jeong et al. (1997) observed that administration of red ginseng saponins may potentially recover hepatotoxicity induced by carbon tetrachloride in male Sprague Dawley rats. Ginseng administration was found to improve immune functions, reduce stress-induced ulceration, provide antioxidant effects, inhibit tumor formation and improve oxygen utilization Zhu (1998), prevent myocardial ischemia / reperfusion damage and impairment of endothelial functionally induced by reactive oxygen species arising from hyperbaric oxygen exposure , through an antioxidant intervention (Maffei Facino et al., 1999). A study carried out by Suh et al. (2002) demonstrated reduction of relapse of gastric cancer by ginseng. On the other hand, ginseng berry extract was found to reduce hyperglycemia in mice (Attele et al., 2002) and some ginseng's active ingredients have beneficial actions on aging, CNS disorders and neurogenerative diseases (Radad et al., 2004). The present work studied the effect of ginseng on chlorpyrifos-induced hepatotoxicity in albino rats.

2. Materials and Methods

Healthy adult male albino rats (*Rattus norvegicus*) about three months old and weight (120± 5 g) were used. Animals were kept in special rodent cage for at least one week before starting experimentation. Animals were kept on standard rodent diet and water *ad libitium.*

Chlorpyrifos was commercially obtained from El-Helb Pesticide and Chemical Company, Free Zone, New Damietta, Egypt. The required concentration was prepared freshly by dilution with corn oil. Ginseng obtained from Pharco Pharmaceuticals, Alexandria, Egypt was prepared in a dose 8.1 mg/kg and given to rats (Human therapeutic dose; Paget and Barnes, 1964).

Animals were divided into control group that fed on normal diet, Ginseng administered group that was orally administered ginseng daily (8.1 mg/kg) for total 4 weeks. Chlorpyrifos treated group that was given chlorpyrifos orally (1/10 LD_{50} ; 13.5 mg/kg) daily for 4 weeks. Chlorpyrifos-ginseng treated group that was given ginseng and chlorpyrifos in the same doses as previous daily for 4 weeks. Animals from all treatment groups were sacrificed

after 3 and 4 weeks and few animals left for one week post-treatment for recovery test. For histological preparations small pieces of liver were fixed, dehydrated, cleared and mounted. Sections of 5 µm were stained according to Lillie Fulmer (1976). Sera were collected for measurement of serum alanine aminotransferase (ALT), serum albumin, superoxide dismutase (SOD) and catalase activity (CAT).
Results were expressed as mean ± standard error and analyzed using Microsoft Excel and Student's "t" test using Origin 41 program at levels of significance P≤ 0.05 and ≤ 0.01 (Snedecor and Cochran, 1980).

3. Results

Histological results
Examination of liver sections obtained from normal rats and rats given ginseng showed no pathological abnormalities (Fig. 1). Inspections of liver sections obtained from rats administered with chlorpyrifos for three weeks manifested enlargement in the central vein, widening in the sinusoids and enlargement of some nuclei added to the enlargement of bile ductile, inflammatory leucocytic infiltration and Kuppfer cells activation (Fig. 2a & b). After 4 weeks had lapsed on rats subjected to chlorpyrifos administration, the cord-like arrangement of the normal liver cells was lost. In addition, interahepatic blood vessels (portal) were congested. Enlargement of bile ductile, widening of the sinusoidal spaces and activation of Kupper cells were observed (Fig. 2c). Still, hepatocytes exhibited cytoplasmic vacuolization, ill-defined cell boundaries and presence of pyknotic nuclei, lecucocytic infiltration and fatty infiltration (Figs. 2d & e). However, in the recovery period, slight improvement in the hepatic architecture was noticed but the sinusoidal spaces were still widened and activated Kuppfer cells were still evident (Fig. 2f). Inspection of liver sections obtained from rats subjected to the dual treatment (i.e. chlorpyrifos and ginseng) for 3 weeks showed nearly normal central veins and improvement in hepatic architecture in comparison to chlorpyrifos treated group (Fig. 3 a & b). Examination of liver sections obtained from rats treated for 4 weeks exhibited little pathological alterations compared to that of chlorpyrifos treated animals. The condition of hepatocytes was improved and the spaces between sinusoids became better, despite of the appearance of some binucleated cells and slight leucocytic infiltration (Fig. 3 c & d). Sections of the liver of rats one week-post ginseng and chlorpyrifos treatment showing marked improvement of the hepatic structure. Hepatic cells appeared to be arranged in strands radiating from the central vein with no cytoplasmic vacuolization, neither hemorrhage nor leucocytic infiltration was encountered and the sinusoidal spaces became better (Fig. 3e).

Biochemical results

1. Changes in serum alanine aminotransferase (ALT)
It was found that administration of ginseng alone had no effect of ALT levels. A significant increase (P≤ 0.01) in serum ALT after 3 and 4 weeks of chlorpyrifos or chlorpyrifos plus ginseng administration in comparison to controls (Fig. 4). In the recovery period, there was an improvement in serum ALT levels in chlorpyrifos or chlorpyrifos plus ginseng groups. However, significant change between chlorpyrifos and chlorpyrifos plus ginseng groups was recorded where there was an evidence for the ameliorative effect induced by ginseng.

2. Changes in serum albumin
Regarding serum albumin, a significant decrease was induced both in chlorpyrifos and chlorpyrifos and ginseng-administered groups (P≤ 0.01) after 3 and 4 weeks. There was an improvement in serum albumin level in all treatment groups in the recovery period (Fig. 5). Figure 5 indicated significant changes between chlorpyrifos and ginseng plus chlorpyrifos- treated rats giving rise to evidence that ginseng exerted an ameliorative action against chlorpyrifos- induced toxicity.

3. Catalase activity (CAT)
Administration of ginseng alone caused insignificant increase in catalase level , but chlorpyrifos induced significant decrease (P≤ 0.01) in the enzyme level after 3 and 4 weeks. However, rats administered with ginseng together with chlorpyrifos exhibited significant decrease (P≤ 0.01) in the enzyme only after 3 weeks in comparison to control. During the recovery period there was an improvement in the catalase enzyme level in chlorpyrifos and ginseng with chlorpyrifos (Fig. 6).

4. Superoxide dismutase activity (SOD)

The level of SOD was significantly decreased (P≤ 0.01) in all treatment groups in comparison to control rats. However, in the recovery period there was an improvement in the enzyme activity in all groups (Fig. 7). However, the level of the enzyme indicated significant changes between ginseng and ginseng plus chlorpyrifos pointing out to the extent of protection given by ginseng.

4. Discussion

Although insecticides are used to kill insects, they can carry harmful effects to animals and humans. Organophosphates are of very high toxicity to mammals (Pimentel and Lehman, 1993). In this work alteration in liver histology was induced by chlorpyrifos in the form of loss of normal architecture, cytoplasmic vacuolization, blood vessel congestion, fatty changes, leucocytic infiltration, condensed nuclei and activation of Kuppfer cells. Similar results were obtained by El-Dursi et al. (2006) who found cell hypertrophy with stenosis of the sinusoids, congestion of blood vessels, necrosis and hemorrhagic spots on the subcapsular spaces.
In the present study, a remarkable cytoplasmic vacuolation of the hepatocytes and dilatation of sinusoids were observed by chlorpyrifos treatment. Coincides with these that was recorded by Goel et al. (2005) who found that chlorpyrifos intoxication caused cytoplasmic vacuolation, necrosis and ballooning of the hepatocytes and dilatation of

Fig. 1: Section in the liver of a control rat showing the basic structure: central vein (CV), hepatocytes (H), blood sinusoids (S) and Kupffer cells (arrowhead). X200

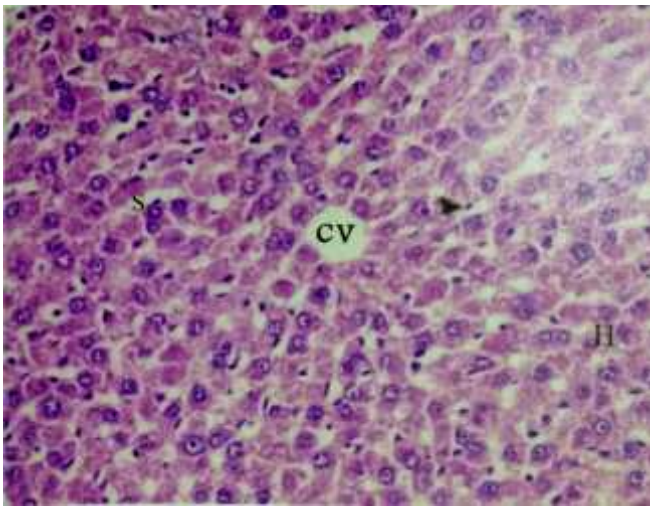


Fig. 2a: Section in the liver of a rat treated with chlorpyrifos for 3 weeks showing enlarged central vein (CV), giant nucleus (Gn) and widened sinusoids (S). X400

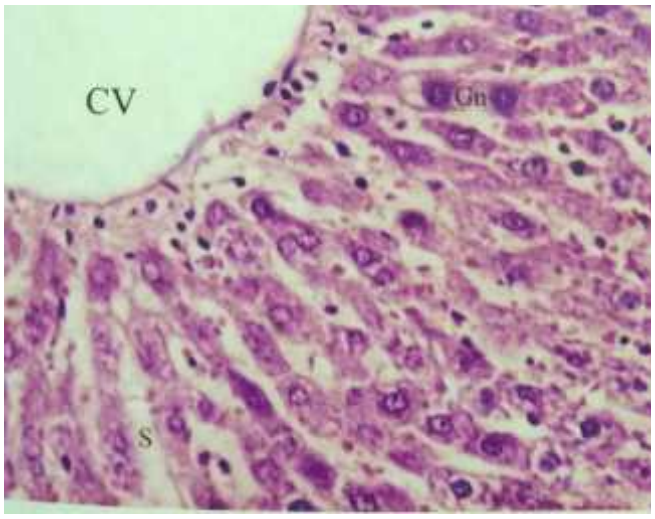


Fig. 2b: Section in the liver of another rat treated with chlorpyrifos for the same pervious mentioned period showing enlarged and proliferated bile s (BD), leucocytic infiltration (Li), slight vacuolization and activated Kupffer cells (arrowhead). PV: Portal vein. X400

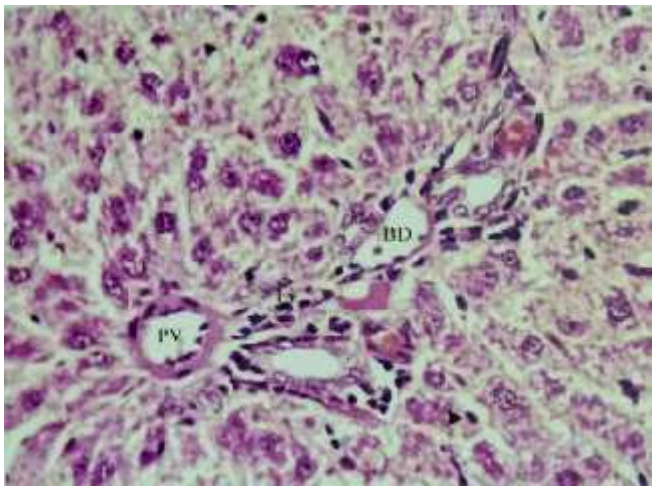


Fig. 2c: Section in the liver of a rat treated with chlorpyrifos for 4 weeks showing disruption of the normal hepatic strands pattern, congested portal vein (PV), enlarged bile ductule (BD), widened sinusoids (S) and activated Kupffer cells (arrowhead). X400

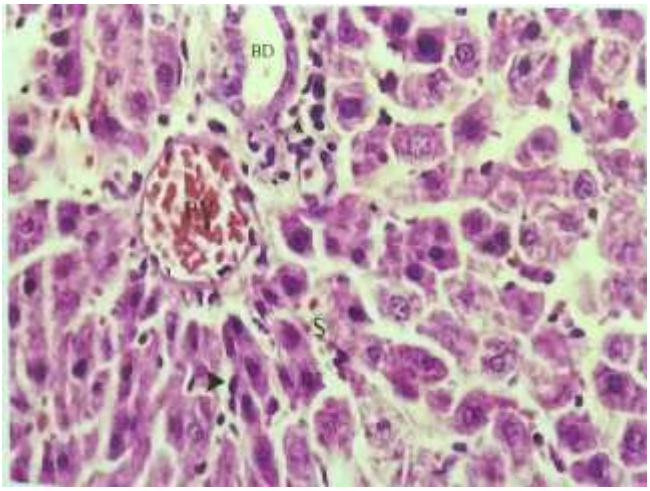


Fig. 2d: Section in the liver of a rat treated with chlorpyrifos for 4 weeks showing loss of the characteristic hepatic architecture added to the cytoplasmic vaculation (C) and the presence of pyknotic nuclei (P). X400

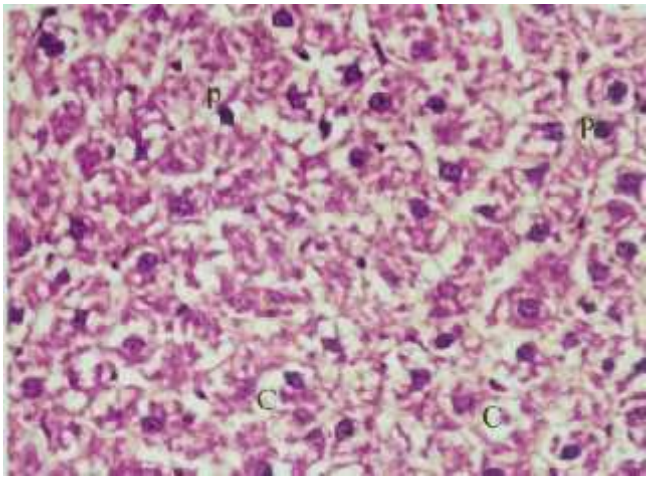


Fig. 2e: Section in the liver of a third rat treated with chlorpyrifos for 4 weeks showing fatty infiltration (F), vacuolization of most cells, enlarged portal vein (PV), widened sinusoids (S) and leucocytic infiltration (Li). X400

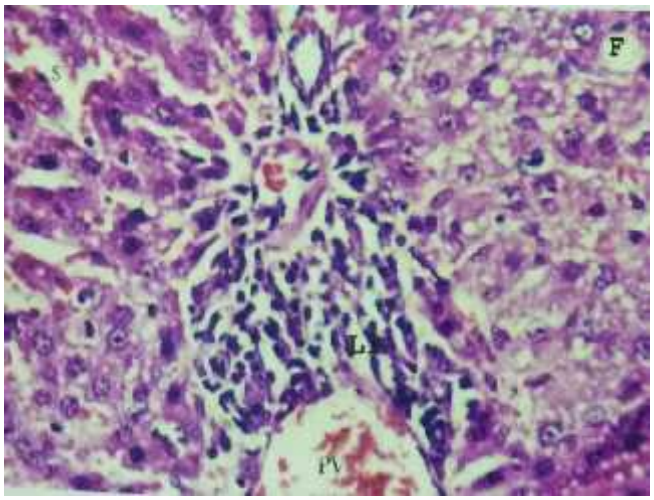


Fig. 2f: Section in the liver of a rat one week post-stopping chlorpyrifos showing slight improvement in the hepatic architecture but still enlarged central vein (CV), widened sinusoids (S) observed and activated Kupffer cells (arrowhead). X400

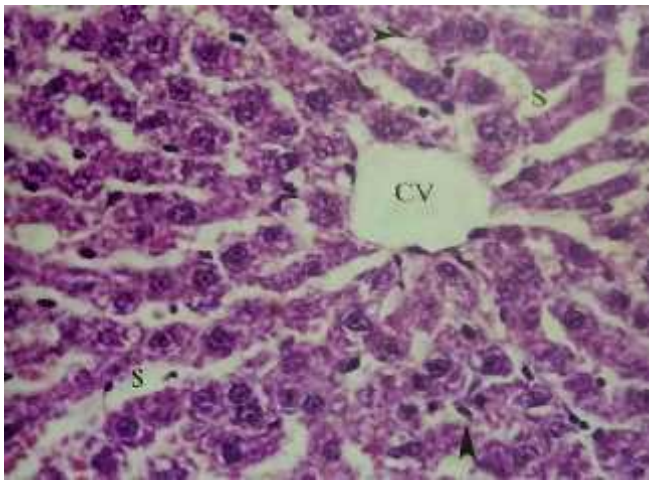


Fig. 3a: Section in the liver of a rat treated with ginseng and chlorpyrifos for 3 weeks showing a slight alteration in liver histology, somewhat normal organization of the hepatic tissue, nearly normal central vein (CV), but still widened sinusoids (S) and activated Kupffer cells (arrowhead). X400

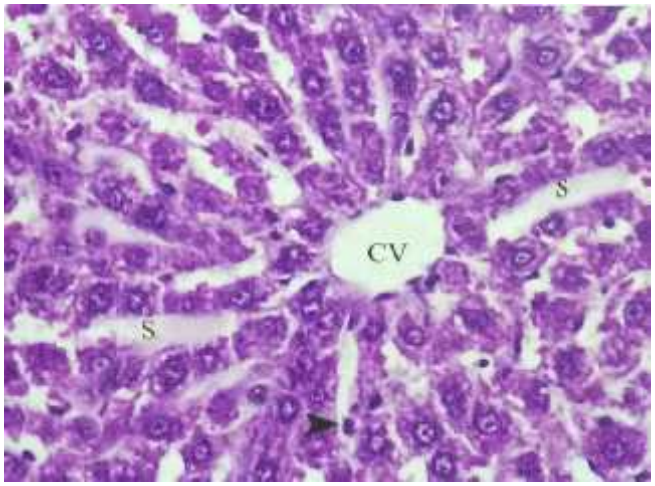


Fig. 3b: Section in the liver of another rat treated with ginseng and chlorpyrifos for 3 weeks showing improvement in the histoarchitecture in comparison to that of rats treated with chlorpyrifos alone although some histological alterations were still present. X400

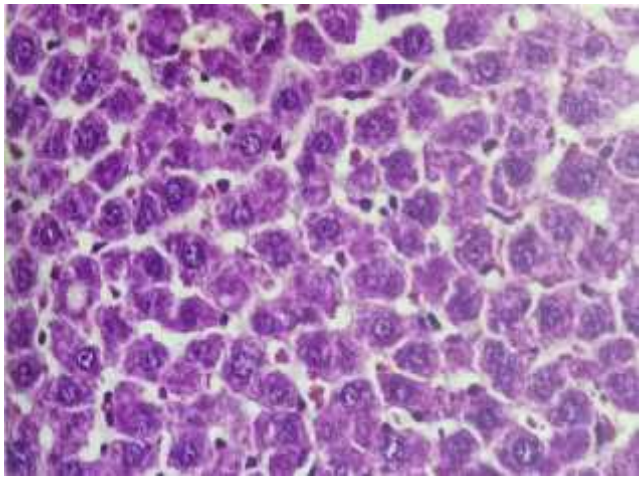


Fig. 3c: Section in the liver of a rat treated with ginseng and chlorpyrifos for 4 weeks showing improvement in hepatopcytes (H), better sinusoid spacing (S), binucleated cells (arrow) is observed. X400

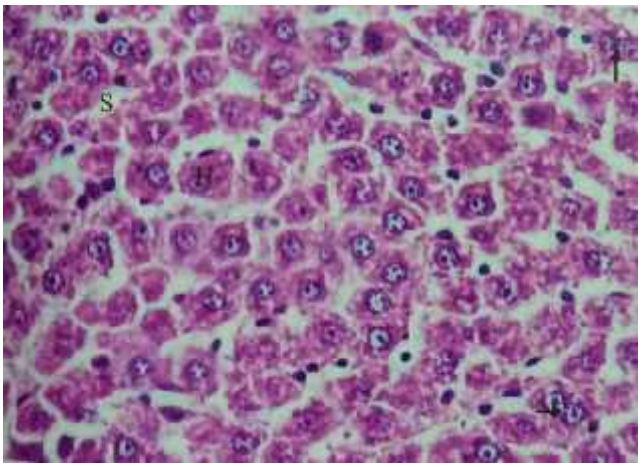


Fig. 3d: Section in the liver of another rat treated with ginseng and chlorpyrifos for 4 weeks showing the presence of slight leucocytic infiltration (Li), moderately enlarged central vein (CV), better sinusoid (S) spacing as well as noticeable improvement in hepatic architecture. X200

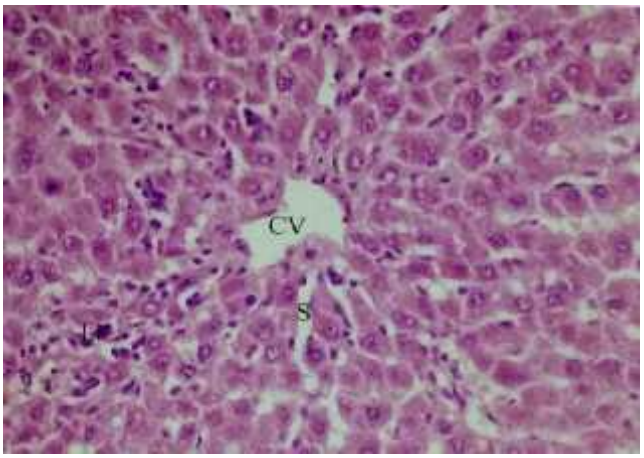
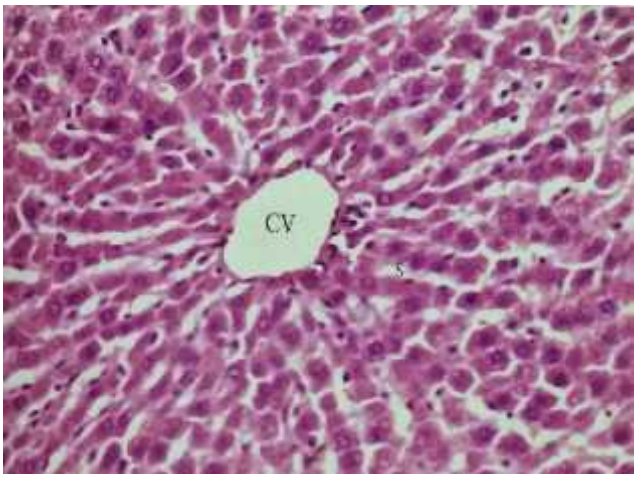


Fig. 3e: Section in the liver of a rat one week post-stopping of ginseng and chlorpyrifos showing improvement in the hepatic structure, where hepatic cells appeared to be arranged in strands radiating from the central vein (C) and better sinusoids (S) spacing. X200



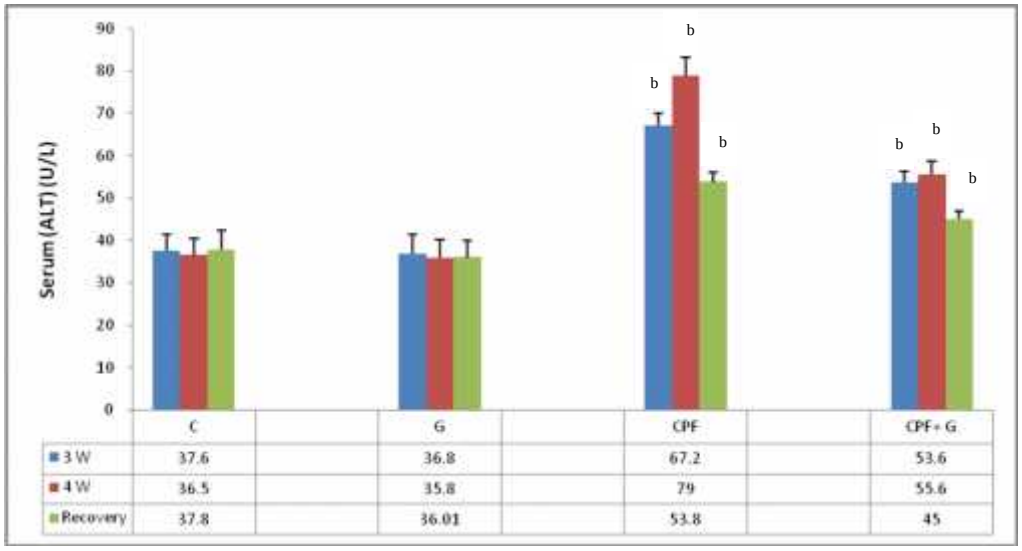


Fig. 4: Effect of chlorpyrifos or chlorpyrifos + ginseng on serum ALT

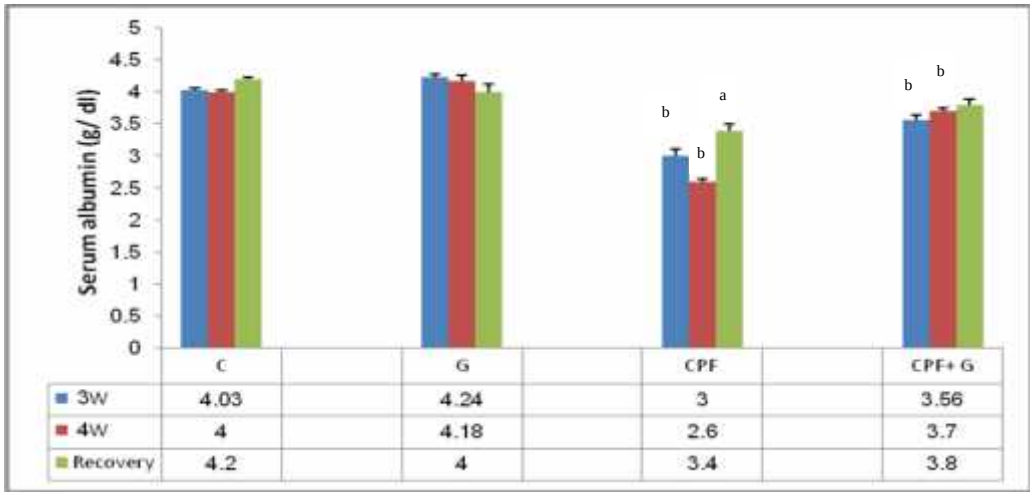


Fig. 5: Effect of chlorpyrifos or chlorpyrifos + ginseng on serum albumin

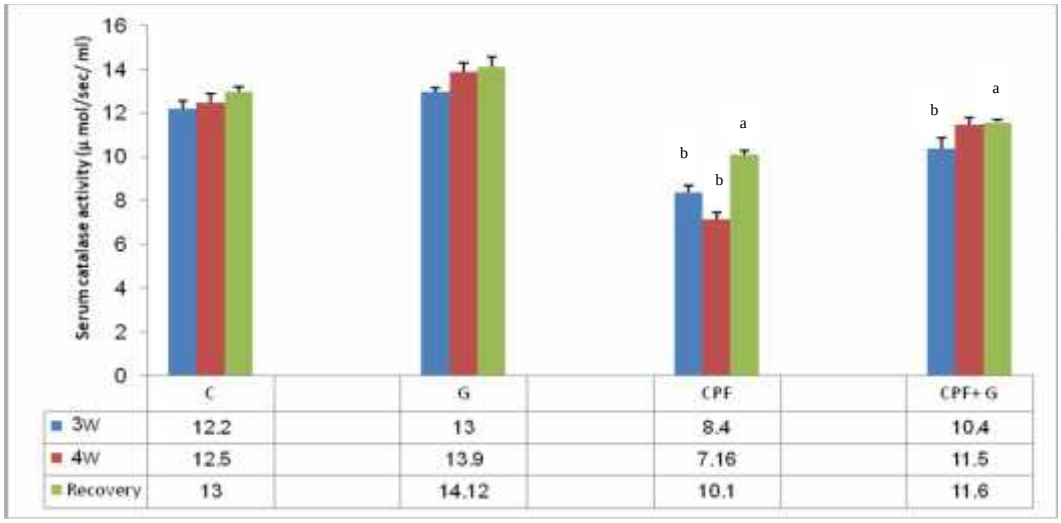


Fig. 6: Effect of chlorpyrifos, ginseng or both on serum CAT activity (µ mol/sec/ ml)

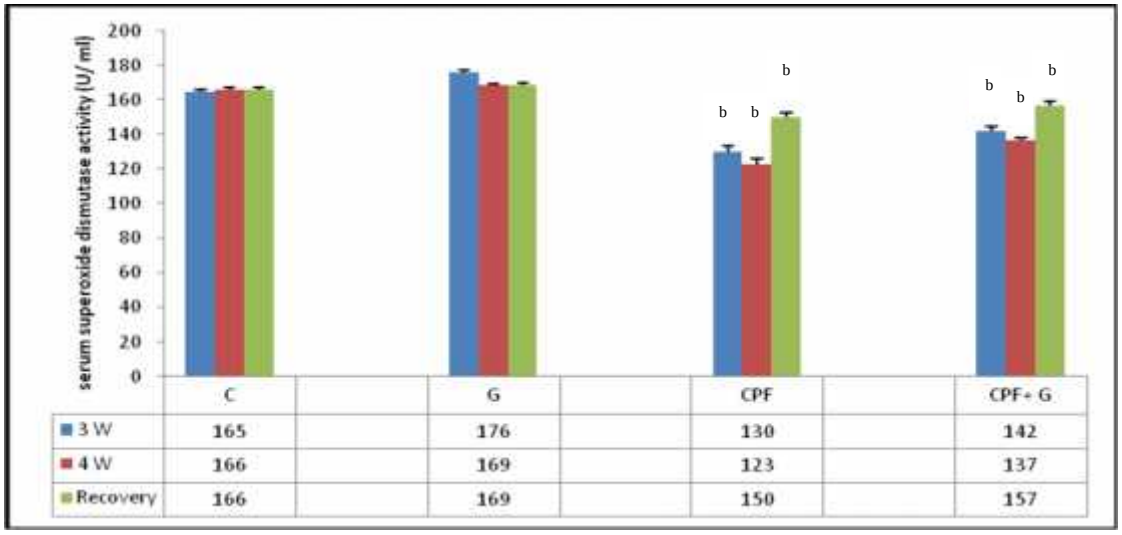


Fig. 7: Effect of chlorpyrifos or chlorpyrifos + ginseng on serum SOD

sinusoids as well as an increase in number of binucleated cells in rats. Srivastava et al. (2006) indicated hypertrophy of nuclei in liver of freshwater catfish *heteropneustes fossilis* treated with clorpyriphos for 48 hours. While, treatment for 72 hours caused vacuolar degeneration and 96 h treatment induced rupture of cell walls and vacuolization. In addition, Sayim (2007) indicated that dimethoate caused liver congestion, enlargement of the veins and sinusoids, hepatocellular damage, necrotic changes and increased number of Kupffer cells, cytoplasmic vacuolization and degeneration of liver cells' nuclei in rats. Moreover, Tripathi and Srivastav (2009) announced that 10 mg/kg chlorpyrifos induced dilation of sinusoids, hepatocytes vacuolation and degeneration and hyperchromatic and hypertrophied nuclei. A recent study conducted by Ezzi et al. (2015) confirmed the histotoxicity of chlorpyrifos on liver tissue. The authors found that chlorpyrifos induced histopathological alterations in liver parenchyma where lymphoid infiltration observed in liver sections.

The protective effect offered by ginseng in the present study was studied by other investigators against various xenobiotics. In this concern, Shim et al. (2009) found that ginsan, a polysaccharide extracted from *Panax ginseng* prevents liver injury caused by carbon tetrachloride. Another study carried out by Li et al. in (2010) demonstrated the effectiveness of saponins from *Panax japonicas* in the treatment of alcohol-induced hepatic injury in mice. In the present work, administration of ginseng only to normal healthy rats did not cause any histopathological alterations in the liver tissue. These results are in complete accordance with the findings of Kitts and Hu (2000) who decided the safety of ginseng administration. Also, saponins isolated from the root *of Panax notoginseng* showed protective effects against CCl_4- induced hepatotoxicity in mice and inhibit the progress of hepatic fibrosis in rats (Peng et al., 2009). Treatment of rats with ginseng and chlorpyriphos exhibited a moderate degree of improvement in liver histology compared with chlorpyrifos only. There were marked decreases in the inflammatory leucocytic infiltration, cytoplasmic vacuolization, congestion and marked improvement in the structure of the hepatocytes. In this concern, Jeong et al. (1997) indicated recovery of liver vacuolization induced by carbon tetrachloride by red ginseng saponins administration. Kemabonta and Akinhanmi (2013) indicated that brain, liver, lung and kidney showed edema, inflammations, congestions, nephritis and necrosis by exposure to chlorpyrifos and dichlorvos in addition to insignificant increase in aspartate aminotransferase, alkaline phosphatase, creatinine and urea levels ($P<0.05$) except the alanine phosphatase which showed a significant increase ($P<0.05$).

Regarding the effect of chlorpyrifos on ALT, there was elevation in the enzyme level. Results obtained in this work were strengthened by the work of many investigators. In this concern, Kossmann et al. (1997) found elevation in ALT in workers engaged in the production of chlorphenvinfos. Also, results in the present study showed that chlorpyrifos intoxication significantly increased activity of serum ALT while ginseng treatment improved normal activities of the enzyme. These results are in consistence with those obtained by Goel et al. (2000) who reported significant increase in the activity of ALT, AST and alkaline phosphatase by chlorpyrifos in rats. Begum et al. (2015) recorded significant increase in serum alkaline phosphatase, aspartate aminotransferase, alanine aminotransferase and uric acid and significant decrease in cholinesterase values in chlorpyrifos- treated indigenous chicken. Protective actions of other materials comparable to that provided by ginseng were demonstrated by many investigators. In this concern, Ncibi et al. (2008) indicated the efficacy of *Opuntia ficus indica* (cactus) extract in alleviating clorpyrifos-induced liver damage in male Swiss mice reflected by recovery of ALT, AST alkaline phosphatase, lactate dehydrogenase, cholesterol and albumin in the serum.

In the present study, chlorpyrifos administration caused reduction in albumin level. This result agreed with the report of Peeples et al. (2005). This reduction could be attributed to changes in the protein and free amino acid metabolism and their synthesis in the liver (Ncibi et al., 2008). Similarly, El-Banna et al. (2009) recorded significant decrease in albumin by chlorpyrifos treatment. In addition, they observed that garlic reversed these parameters to control values. In this study, ginseng had similar action to garlic since administration of ginseng reversed the parameters to nearly normal values. In the present work, there was significant decrease in serum albumin levels and elevation in ALT induced by chlorpyrifos. Similar results were reported by Kalender et al. (2010) who found that malathion caused significantly lower serum albumin levels and significantly higher serum ALT and AST. In addition, Mohamed et al. (2010) recorded significant elevation in serum total bilirubin and ALT and marked decrease in albumin level by repeated doses (17.8 mg/ kg bw) daily for 15 days of organophosphate profenofos.

Raina et al. (2015) indicated significant ($P < 0.05$) increase in aspartate and alanine aminotransferases, alkaline phosphatase, and lactate dehydrogenase with single or combined exposure of chlorpyrifos (1 mg/kg, b.w.) ten times of such doses orally. Significant increased oxidative damage of hepatocytes as indicated by increased malondialdehyde levels with decrease in tissue ascorbate and catalase, superoxide dismutase, and glutathione peroxidase in groups treated with chlorpyrifos. Supplementation of ascorbic acid restored the hepatic specific marker enzymes in blood following exposure to chlorpyrifos. Uzun and Kalender (2013) recorded changes in serum total protein, albumin, aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase, lactate dehydrogenase, trigliceride, total cholesterol levels, hematological changes, superoxide dismutase, catalase, glutathione peroxidase, glutathione-S-transferase activities and malondialdehyde content in rat's liver tissues by chlorpyrifos with some protective effects offered by catechin and quercetin.

The results of measuring the antioxidant enzymes in this work revealed that there was a significant decrease in the level of serum antioxidant enzymes, i.e. superoxide dismutase (SOD) and catalase (CAT) especially in chlorpyrifos-treated group. This result was similar to that of Gultekin et al. (2006) who found that chlorpyrifos caused a significant decrease in superoxide dismutase (SOD), catalase (CAT) and glutathione peroxidase. Also, Verma et al. (2007) showed that exposure to chlorpyrifos decreased the levels of serum SOD and catalase CAT. In addition, there was significant increase in the level of antioxidant enzymes, SOD and CAT activities in ginseng plus chlorpyrifos treated rats in comparison to chlorpyrifos treated rats only. These results are similar to those obtained by Kim and Park (2003) on human, that administration of *Panax ginseng* extracts increased the levels of serum antioxidant enzymes, superoxide dismutase (SOD) and catalase (CAT) activities. Kim et. (2005) showed that administration of ginseng increase the levels of serum SOD and CAT. In 2008, Yu et al., found that oral administration of chlorpyrifos (63 mg/kg) to mice caused decrease in SOD and CAT while cell apoptosis, lipid peroxidation and DNA damage were increased. A study carried out by Basha and Poojary (2011) indicated a marked decrease in SOD and CAT activities after chlorpyrifos exposure.

Biochemically, ginseng administration plus chlorpyrifos significantly decreased the elevated levels of serum ALT activity in comparison to chlorpyrifos-treated rats. Similarly, albumin level increased by shared administration of both ginseng and chlorpyrifos. Ginseng plus chlorpyrifos resulted in increase in the SOD and CAT activities when compared to that received chlorpyrifos alone. According to results obtained in this work, ginseng seemed to have no effect on serum ALT and albumin in comparison to control. These results are in agreement with those of Song et al. (2004) who found that ginsan, a polysaccharide isolated from *Panax ginseng* did not change serum ALT, AST, alkaline phosphatase activities, total bilirubin or albumin. Lee et al. (2005b) studied the hepatoprotective effect of red ginseng on *tert*-butyl hydroperoxide (*t*-BHP)- induced hepatotoxicity of HepG2 cells in mice. Intraperitoneal and oral administration of ginseng significantly inhibited the increase of ALT and AST activities. Similarly, Gum et al. (2007) indicated that pretreatment of rats with panax ginseng protected the liver from benzo[alpha] pyrene (BP)-induced hepatotoxicity as reflected by decrease of ALT levels. Li et al. (2014) indicated that in alcohol- and CCl4-treated rats, ginsenoside Rg1 administration dose-dependently suppressed the marked increases of serum ALT, AST, LDH and ALP levels, inhibited liver inflammation and reduced liver fibrosis scores. Rg1 significantly increased the activities of antioxidant enzymes (SOD, GSH-Px and CAT) and reduced MDA levels in liver tissues. Recently, Ding et al. (2015) indicated that acute alcohol gavage dramatically significantly increased serum activities of ALT and AST and hepatic triglyceride level. These elevations were significantly diminished by pretreatment with *Panax notoginseng* saponins at dose of 100 mg/kg or 300 mg/kg. Additionally, saponins suppressed the elevation of reactive oxygen species production and malondialdehyde content, reduced TNF-α and IL-6 levels, restored glutathione level, enhanced the superoxide dismutase activity in liver, and abrogated cytochrome P450 2E1 (CYP2E1) induction. These data demonstrated that pretreatment with *Panax notoginseng* saponins protected against acute ethanol-induced liver injury, possibly through ameliorating hepatic lipid accumulation and reducing CYP2E1-mediated oxidative stress.

In conclusion, chlorpyrifos exerted deleterious effects on liver tissue and increased serum ALT and decreased albumin, superoxide dismutase and catalase. Co-treatment with ginseng protected liver from most of these changes and restored liver histology and biochemical parameters to nearly normal values.

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