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RESEARCH ARTICLE

Ameliorative effect of Korean red ginseng (Panax ginseng) on selenium induced hepatic toxicity in broilers

***Shimaa A Elgaml**

Clinical Pathology Department, Faculty of Veterinary Medicine, Zagazig University, Zagazig, Sharkyia, Egypt.

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Corresponding Author

Shimaa A Elgaml

Abstract

Poultry liver is sensitive to dietary selenium (Se) content. It was well known that selenium induced hepatic toxicity in animal models. However, little is known about the negative effects of selenium toxicity in the liver of birds. The aim of this study was to investigate possible beneficial protective effects of Ginsenoside Rb1from panax ginseng (PG) root on selenium induced hepatic toxicity in broiler chickens. To investigate this effect, one-day-old chicks received Se (as 0.48 mg Na_2SeO_3/kg b.w.) in the diet for 4 weeks, PG+Se (received 100 mg Ginsenoside Rb_1/kg b.w. in the diet for 1o days before administration of 0.48 mg Na_2SeO_3/kg b.w. in the diet for 20 days and PG alone (as 100 mg Ginsenoside Rb_1/ kg b.w.) in the diet for 4 weeks. hepatic marker enzymes (aspartate aminotransferase-AST, alanine aminotransferase-ALT, gama glutamil transferase-GGT), some biochemical parameters (total protein, albumin, globulin cholesterol, triglycerides and glucose), beside hepatic antioxidants (catalase-CAT, superoxide dismutase-SOD and glutathione peroxidase-GPx) and malondialdehyde-MDA were estimated. Selenium intoxication elevated serum hepatic enzymes, some biochemical parameters and MDA. These effects were prevented by the pretreatment of chickens with PG. It could be concluded that PG extract has significant hepatic and antioxidative effects against the liver damage of chicken intoxicated with selenium and so it can be used as a valuable neutraceutical application in poultry farms.

Introduction

Selenium is a natural element in both animals and human diets. It is essential for some enzyme functions, protects against certain cancers, blocks the action of free radicals and helps stimulate the immune system (Nuttall, 2006). Selenium at high concentration is toxic and known to trigger oxidative stress in a wide variety of tissues mainly the liver (Manikandan et al., 2010). It is widely used in many commercial applications, thus constituting a common source of human exposure as it present in steel and copper alloying, glass and paint manufacturing, and nutritional supplements (Aldosary et al., 2012). Selenium toxicity can affect the oxidative stability of the broiler chickens and unfortunately, there is little information available on its effects in broiler chicks (Ryu et al., 2005).

Panax ginseng (Korean ginseng), is one of the most important renowned herbal plants worldwide, has a long history of medicinal use in the oriental regions as a tonic to promote health in last year's (Han et al., 2006). It contains ginsenosides which are phenolic acids, flavonoids and popular phytotherapeutic triterpenoid saponins. These properties of the ginseng are thought to provide many beneficial effects against organs damage (Kitts and Hu, 2000). It has many physiological and/or pharmacological effects on systemic immune, cardiovascular, central nervous systems, endocrine glands and glucose metabolism (Choi, 2008). It has various antiapoptotic effects that

including in the liver (Karakus et al., 2011). Thus, we evaluate the possible beneficial effect of ginseng on selenium toxicity through estimation of the hepatic functions. Also, we clarify the ability of ginseng to adjustment the hepatic antioxidant status in chickens.

2. MATERIAL AND METHODS

2.1. Material:

2.1.1. Chickens Forty, one-day-old, commercial boiler chickens (Hubbard strain) were purchased from Al-Kahira Poultry Company. Chickens were maintained in the Laboratoty Animal Center. College of Veterinary Medicine, Zagazig University kept in clean well ventilated hygienic cages under standard managerial, environmental and hygienic conditions. Chickens were divided into 4 main groups, acclimatized for 14 days prior the experiment and maintained on a commercial well balanced ration and drinking water were allowed *ad.libitium* throughout the experimental period.

2.1.2. Sodium selenite (Na_2SeO_3) was purchased from Sigma Chemicals Company for Pharmaceutical Industries. It was used as 1/20 from LD_{50} of Na_2SeO_3 of broiler chickens, at a dose of 0.48 mg /kg b.w., in the diet according to (Kumar et al., 2013).

2.1.3. Panax ginseng root extract (Ginsenoside Rb_1=saponin of panax ginseng**)** was obtained from Sigma Chemicals Company for Pharmaceutical Industries. It was used at a dose of 100 mg /kg b.w., in the diet according to (Karakus et al., 2011).

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2.2. Methods:

2.2.1. Experimental design

All procedures used in this experiment were approved by the Institutional Animal Care and Use Committee of Fac. of Vet. Med. Zagazig University. Chickens were divided into four groups (n=10 per group). Group I (control) were fed a basal diet; Group II (Se-intoxicated) were fed with the basal diet supplemented with 0.48 mg /kg b.w. Na_2SeO_3 for 30 days; Group III (PG+Se) were fed with the basal diet supplemented with 100 mg/kg b.w. for 1o days before administration of 0.48 mg Na_2SeO_3/kg b.w. in the diet for 20 days; Group IV (PG treated group) were fed with the basal diet supplemented with 100 mg/kg b.w PG for 30 days.

2.2.2. Blood sampling

The blood samples were collected on the 31th day from the wing vein. 5 ml of blood collected without anticoagulant into a clean dry centrifuge tube and allowed to clot for 30 min at room temperature. Blood samples were centrifuged at 3000 rpm for 5 min. The collected clear sera were separated for biochemical analysis.

2.2.3. Estimation of biochemical parameters

All parameters were colorimetric measured using commercial kits provided by Biomerieux, Egypt. All analysis was done using spectrophotometer 5010 v5^{+}, Berlin, Germany for biochemical serum analysis.

Serum enzymes, measuring the activity of serum aspartate aminotransferase (AST), alanine aminotransferase (ALT) activity (Reitman and Frankel, 1957) & gamma glutamyl transferase (GGT) activity (Fuke et al., 1976). ***Serum proteins***, serum total protein according to (Krohn, 2002) and serum albumin according to (Fernandez et al., 1966). Serum globulin level was determined by subtracting the albumin from the total proteins. ***Metabolic profile,*** serum cholesterol according to (Taylor et al., 1978), triglyceride according to (Fossati and Prencipe, 1982) and glucose according to (Carroll et al., 1971).

2.2.4. Antioxidants and (MDA) lipid peroxidation Assay

The liver from all groups was collected at days 31th. One gram of each liver sample added to 9 ml of normal saline 0.9% and homogenized using electrical tissue homogenizer, centrifuged at 3000 rpm/15 minutes. The supernatant was collected, and used for estimation of antioxidants (CAT, SOD, and GPx) and MDA, the marker of lipid peroxidation (Sidhu et al., 2005). The catalase activity (CAT) was performed according to (Aebi, 1984), superoxide dismutase (SOD) was determined according to (Weydert and Cullen, 2010), Glutathione proxidase (GPx) was performed according to (Weydert and Cullen, 2010) and malondialdehyde (MDA) according to (Valenzuela, 1991).

2.2.5. Statistical analysis

Statistical Analysis System software package were used to analyze the data by one-way analysis of variance ANOVA (Bewick et al., 2004) and the significant differences between means were determined at a level of ($P < 0.05$). Further analysis was carried out. All data showed a normal distribution and passed equal variance testing. Differences between means were assessed using Tukey′s honestly significant difference test for post hoc multiple comparisons. Data are expressed as the mean±S.E.

3. RESULTS

3.1. Biochemical results

The activities of AST, ALT and GGT were estimated in serum samples as the liver marker enzymes. These results are given in Figure 1. The Se intoxication markedly affected the liver specific enzymes. It was found that a significant ($p < 0.05$) increase in serum AST, ALT and GGT activities of chickens given Se (group II) compared with the control. This result suggests that liver markers are elevated in the serum due to release of the enzymes from damaged liver. However a significant ($p < 0.05$) decrease was observed in above serum activities of chickens given PG + Se and PG compared with the Se intoxicated group (group II).

The serum total protein and albumin (Figure 2) were significantly ($p < 0.05$) decreased in the Se group compared with the control. However a significant ($p < 0.05$) increase was observed in serum total protein and albumin in chickens given PG + Se and PG compared with the Se intoxicated group. The serum globulin level showed a non significant change in all groups, Figure 2.

The level of some serum biochemical parameters of chickens in all groups are presented in Figure 3. Cholesterol, triglycerides and glucose levels were significantly ($p < 0.05$) increased in the Se group compared with the control. There were a significant ($p < 0.05$) decrease in cholesterol, triglyceride and glucose levels in the PG + Se and PG groups compared with the Se intoxicated group.

3.2. Antioxidant and MDA profile

Selenium enhances the intracellular formation of reactive oxygen species causing hepatic damage. In the present study we analyze the hepatic levels of several antioxidants (CAT, SOD and GPX) and MDA, Figure 4. A significant ($p < 0.05$) decrease in serum hepatic CAT, SOD and GPX levels. Meanwhile a significant ($p < 0.05$) increase in MDA was observed in chickens given Se alone (group II). On the contrary, a significant ($p < 0.05$) increase was observed in the activity of CAT, SOD and GPX with a significant ($p < 0.05$) decrease in MDA in chickens given PG + Se and PG alone compared with the Se intoxicated group.

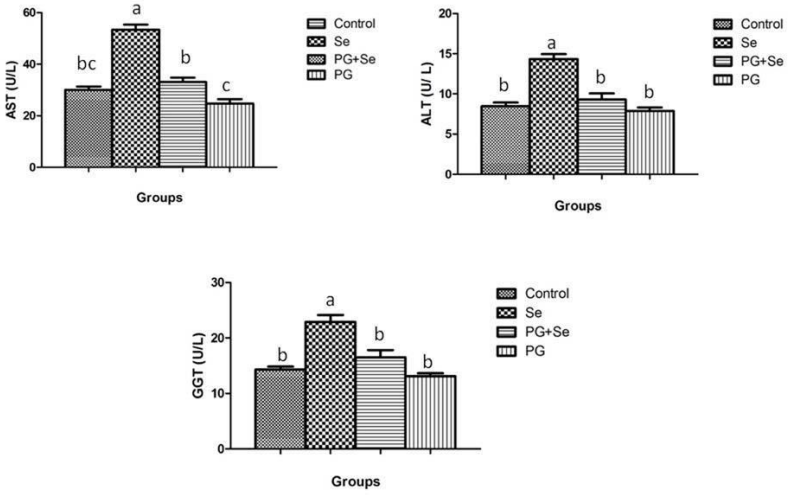

Fig.1. Effect of selenium and panax ginseng on the activity of hepatic serum enzymes in chickens. Each value is the mean±S.E. of 5 chickens Bars showing the same letter (a, b, c) are not significantly different ($p < 0.05$).

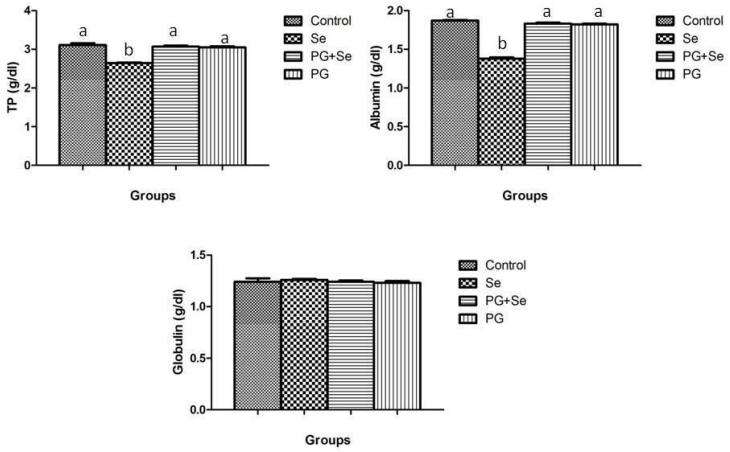

Fig.2. Effect of selenium and panax ginseng on the total protein, albumin and globulin in chickens. Each value is the mean±S.E. of 5 chickens Bars showing the same letter (a, b) are not significantly different (p < 0.05).

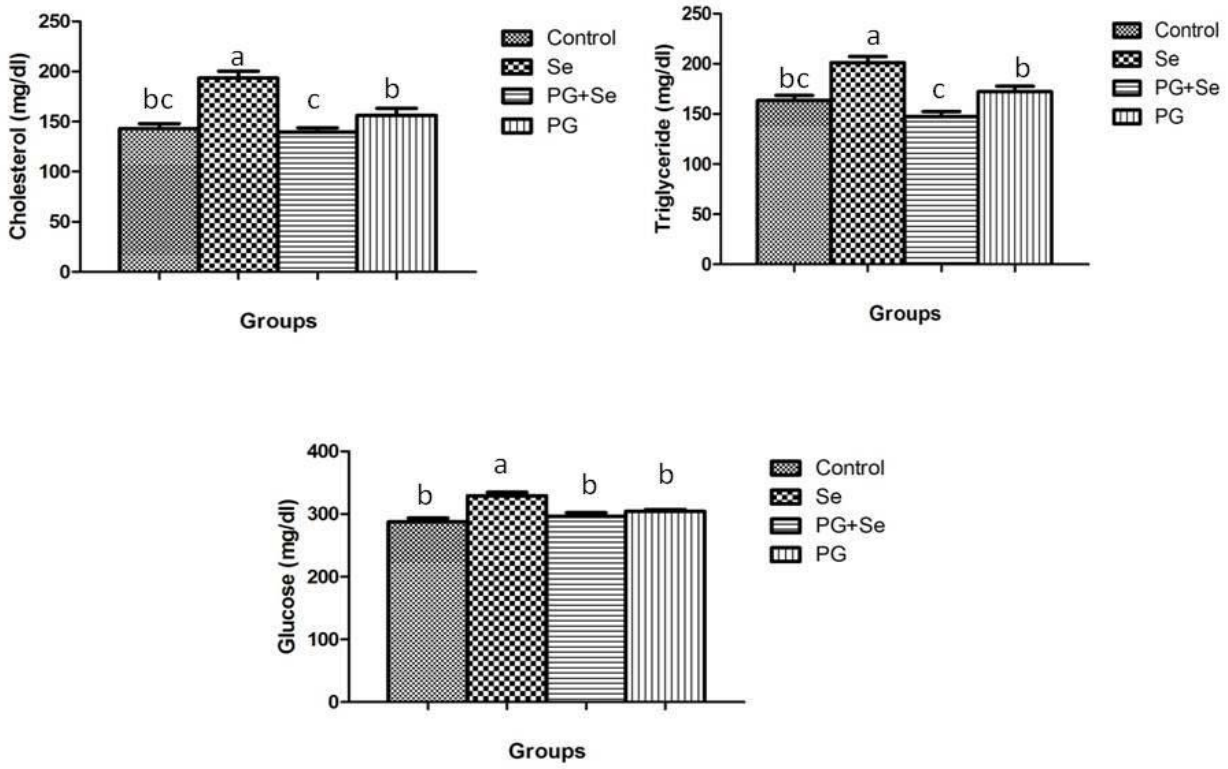

Fig.3. Effect of selenium and panax ginseng on the some biochemical parameters in chickens. Each value is the mean±S.E. of 5 chickens Bars showing the same letter (a, b, c) are not significantly different (p < 0.05).

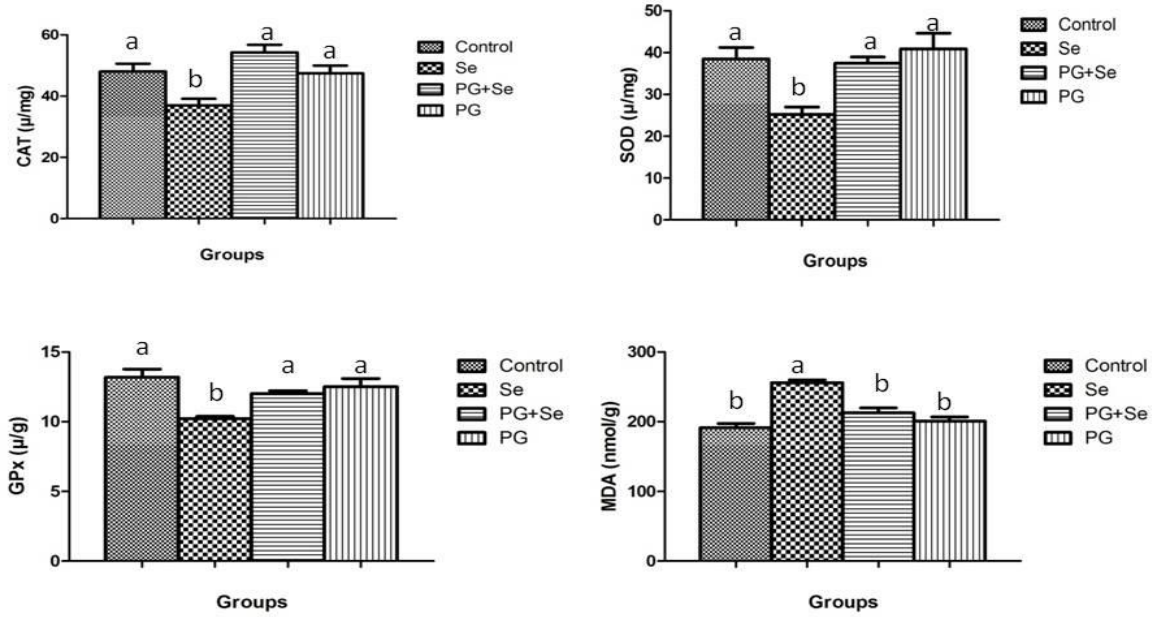

Fig.4. Effect of selenium and panax ginseng on the hepatic antioxidants and MDA level in chickens. Each value is the mean±S.E. of 5 chickens Bars showing the same letter (a, b) are not significantly different ($p < 0.05$).

4. Discussion

Selenium toxicity can be found in poultry production causing tissue lesions and even a large number of deaths (Peng et al., 2012). Excess Se can leading to growth depression, anemia, impaired immune function and reduced egg production (Zwolak and Zaporowska, 2012). The predominant pathological changes were characterized by local necrosis in the liver (Xu et al., 2014). Selenium at high concentrations is one of the most commonly used hepatic toxins in the experimental liver studies. Liver is the largest organ in the metabolism and detoxification, known as the "Se storehouse." Selenium has a great biological significance in the liver. Poultry liver is sensitive to dietary Se content (Sun et al., 2011). In the present study, it showed a significant increase in the serum level of hepatic markers such as AST, ALT and GGT activities as compared to respective control indicating hepatic dysfunction. The present study showed that serum total protein and albumin levels were significantly decreased but a significant increase in serum cholesterol, triglyceride and glucose were observed in chickens with Se intoxication in comparison with control group. The increased serum levels of hepatic markers have been attributed to the liver injury, because these enzymes are place in cytoplasmic area of the cell and are released into circulation in case of cellular damage with changing the permeability of hepatocyte membranes (Eliot and Jamali, 1999). Selenium toxicity induced the increase of serum AST, ALT and GGT levels which source from cell membrane and mitochondrial damages in liver cells as these enzymes activities were significantly elevated after Se intoxication (Hasegawa et al., 1996). The first reports about of hepatotoxic effects by Se, are lipid peroxidation origin, and are largely due to its active metabolite. This metabolite can abstract hydrogen from fatty acids, initiating the lipid peroxidation, lead to cell injury, and finally liver damage (Hoffman, 2002). On the other hand, pretreatment with ginseng was found to significant suppressed the increase in serum AST, ALT and GGT activities induced by Se intoxication. This finding implies that ginseng administration has hepato-protective effect as it protects the liver tissue from Se intoxication. Current studies have provided a considerable support for evidencing the protective

effects of ginseng on liver damage by scavenge and destroy lipid peroxyl radicals and reactive oxygen species (Karadeniz et al., 2009; Kitts and Hu, 2000). Also, these studies declared that the antioxidant properties of ginsenosides those phenolic acids, flavonoids and saponins contribute to protection against Se induced hepatotoxicity in chickens. These compounds may be responsible for its hepatoprotective action by scavenge and destroy lipid peroxyl radicals and reactive oxygen species such as like the superoxide anion (O_2 −), the hydrogen peroxide (H_2O_2) and the hydroxyl radical (OH) (Jahn et al., 1985).

Se intoxication was associated with a decrease in the total protein and albumin concentration, which may have resulted from decreased food intake, increased loss of the nutrient through the intestine, immunosuppressive effect of the selenium, disturbed metabolism of the liver, hyperfiltration induced toxicity nephropathy and increased protein catabolism (Manikandan et al., 2010). Panax ginseng ameliorated this decrease in serum protein concentration, an effect that was previously reported (Khalil et al., 2008). Selenium intoxication causing the increase in triglyceride and cholesterol levels as it responsible for triglyceride catabolism (Dicks-Bushnell et al., 1968).This situation could be also attributed to the reduction of lipase activity, which could lead to decrease in triglyceride hydrolysis (Dicks-Bushnell et al., 1968). On the other hand, it can be assumed that hypercholesterolemia in Se intoxicated chickens has resulted in damage of hepatic parenchymal cells that lead to disturbance of lipid metabolism in liver (Dicks-Bushnell et al., 1968). The lipid lowering mechanisms of ginseng are mainly unknown, but recent researches informed that ginseng saponins has a strong inhibitory activity on microsomal acyl coenzyme A: cholesterol acyltransferease in vitro, which is responsible for acylation reactions in liver (Kwon et al., 1999). However, there are recent researches reported that ginseng may have a supportive effect like that antiatherosclerotic agent by diminishing high level of serum cholesterol (Li et al., 2011; Liu et al., 2010). Also, (Hwang et al., 2008) informed that the administration of ginseng saponins decreased the serum cholesterol level in rabbits which feeding high cholesterol diet. This result indicates that ginseng or saponins can be affecting the pathway of cholesterol biosynthesis. As shown in our results, Se intoxicated group have much higher blood glucose levels than control. By ginseng administration to Se intoxicated chickens, however, blood glucose levels were declined to a certain degree. The main mechanism of hypoglycemic activity for PG is not clearly, but three possibilities mechanisms can be suggested that modulation of glucose transport (Khalil et al., 2008), insulin secretion and glucose disposal (Yokozawa et al., 1984).on the other hand, some components such as phenolics and flavonoids are known to be responsible for hypoglycemic activity (Yokozawa et al., 1984).

It's known to trigger oxidative stress in a wide variety of tissues (Kamble et al., 2009; Padmaja and Raju, 2005). We have recently shown the role of selenium in triggering liver diseases, primarily by means of free radical generation with the severity of lipid peroxidation and the depletion of antioxidant status which causing by damage in the cell membrane and the organelles of the hepatocyte (Manikandan et al., 2010). This free radical mediated was inhibited by pretreatment with PG. Its, a traditional herb, has been used to important roles in maintaining oxidative status, by possessing either direct or indirect antioxidant functions, and has been a component of effective formulations for treatment of liver diseases (Kalkan et al., 2012; Karakus et al., 2011). Selenium intoxication seemed to point to a direct and major role for oxidative stress as an inducer of hepatic toxicity. Selenium is known to disturb the oxidative balance of the organism and the free radical processes have been recognized to be involved in the mechanisms of health effects of intoxication with these substances. It induces oxidative damage by increasing the production of ROS (Maraldi et al., 2011) and decreasing the biological activities of some antioxidants, such as CAT, SOD and GPx (Zikic et al., 1998) which play an important role in antioxidant defense and in the elimination of free radicals. In the current study, the results of the present work are in agreement with previous studies, which clearly demonstrated that Se intoxication increases LPO and suppresses the anti-oxidant defense mechanisms in liver tissue with significant morphological changes (Agarwal and Behari, 2007; Atencio et al., 2009). Panax ginseng treatment partly counteracts the toxic effect of Se on the bird liver. This element is a well-established antioxidant and can prevent or decrease the harmful effects of oxidants and ROS in various tissues (Li et al., 2013). This upregulation of GPx production induced by PG may explain why the GPx activity levels in the liver tissues of the PG+Se group were higher than in the Se group in the present work. PG also decreased the MDA concentration in the PG+Se group. These results can be explained by the important role of PG in preventing LPO and in protecting the integrity and functioning of liver tissues. However, some have reported that PG exerts its protective effect by significantly decreasing Se accumulation in organs or by inducing are distribution of Se (Hassan et al., 2014; Ramesh et al., 2012).

In conclusion, we found that PG enhanced the biochemical parameters and demonstrated a protective effect against Se-induced liver damage. We suggest that PG may be used to protect against Se intoxication and other

chemical agents in poultry farms. The results of this study indicate that the panax ginseng extract (PGE) effectively improve serum hepatic biochemical changes and oxidant metabolism in chickens and corroborates the use of this medicinal plant extract in traditional medicine for treatment of Se intoxication. The use of PGE contribute to the prevention of hepatic damage with any toxic material, however, additional studies on the biochemical and functional characterizations of the active components of PG, which influence serum hepatic function and oxidant metabolism, are needed for better understanding of this plant extract and its benefits.

Conflict of interest: The author declares that there are no conflicts of interest.

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