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Original article

Potential Protective Effect of *Panax ginseng* (roots) against Minerals and Lipid Profile Changes in Adult Male Rabbits administered with Stannous Chloride

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ABSTRACT

Background and aims. *The present study was undertaken to evaluate the potential protective effects of Panax ginseng (P. ginseng). Changes in levels of some minerals and lipid profiles induced by stannous chloride ($SnCl_2$) in male rabbits were studied.* ***Methods***. *Sixteen rabbits were randomly divided into four equal groups (each four rabbits). The first group was used as a control and received an equivalent volume of corn oil alone. The second group was used to study the effect of P. ginseng (100 mg/kg body weight) and the third group was used to study the effect of $SnCl_2$ (20 mg/kg body weight). The fourth group was used to study the effect of P. ginseng plus $SnCl_2$. Animals were treated orally daily for 10 weeks.* ***Results***. *P. ginseng alone caused a non-significant increase in levels of low-density lipoprotein (LDL), sodium (Na^+), Magnesium (Mg^{+2}), and Zinc (Zn^{+2}). Treatment with P. ginseng alone caused a non-significant decrease in levels of cholesterol, phosphorus (Po_4^-), and calcium (Ca^{+2}). P. ginseng alone causes a significant decrease in levels of triglycerides (TG) and high-density lipoprotein (HDL). Overall means indicated that treatment with $SnCl_2$ caused a non-significant increase in levels of LDL, Ca^{+2}, and Mg^{+2}. The same treatment caused a significant increase in the level of (Zn^{+2}). Meanwhile, treatment with $SnCl_2$ caused a non-significant decrease in levels of cholesterol, Po_4^- and Na^+. This treatment caused a decrease in levels of TG and HDL. The combination of P. ginseng and $SnCl_2$ minimized the effect of $SnCl_2$ in all previous parameters to be close to control values.* ***Conclusion***. *The results of the present study convincingly demonstrated that $SnCl_2$ exposure resulted in varying degrees of effect in values of some minerals and lipid profiles. Thus P. ginseng may be helpful to combat $SnCl_2$-associated sufferings in human as well as animals.*

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INTRODUCTION

Tin (Sn) is a natural element within the crust of the earth. Tin compounds have been used extensively in a variety of human activities. Tin can combine with chemicals such as chlorine, sulfur, and oxygen to form inorganic tin compounds such as stannous chloride, stannous sulfide, and stannic oxide. These inorganic tin compounds are used in a diversity of industrial processes, including glass toughening, a base for color, catalysts, perfume, soap stabilizers, and dental cryogenic agents [1]. Sn also combines with carbon to form organotin compounds such as (dibutyltin, tributyltin, and triphenyltin), which are used in the manufacture of food packages, plastic pipes, plastics, paints, and pest repellents [2]. Humans are exposed to stannous chloride ($SnCl_2$) in packaged foods, soft drinks, biocides, and dentifrices. Since $SnCl_2$ is widely used in the production of food cans and beverage packaging, many studies have focused on its toxic effects [3,4]. $SnCl_2$ induces changes in many biochemical parameters in experimental animals [5].

A previous study showed that the administration of $SnCl_2$ to male rats caused a significant increase in calcium levels

[6]. In addition, various studies have mainly shown that excessive dietary tin reduces essential serum minerals such as iron, copper, zinc, calcium, and selenium, and reduces antioxidant activity, mainly in the liver [7,8]. Additionally, previous studies mentioned that administration with $SnCl_2$ caused an increase in the levels of plasma total lipid (TL), cholesterol, triglyceride (TG), low-density lipoprotein (LDL), very low-density lipoprotein (VLDL), glucose, urea, and total bilirubin, while the levels of plasma high-density lipoprotein (HDL), total protein (TP), albumin (A) and globulin (G) were decreased [5].

Medicinal plants generally contain compounds that are useful in the treatment or administration of diseases in animals and humans [9]. Ginseng has been used as a panacea for over 2,000 years and was believed to promote longevity [10]. *Panax ginseng* is one of the most widely used herbal medicines and is reported to have a wide range of therapeutic and pharmacological applications [11]. The main bioactive components of ginseng are triterpenoid saponin glycosides, also called ginsenosides [12,13]. Ginsenosides are the main pharmacologically active components of *P. ginseng*, and appear to be involved in most of the activities of *P. ginseng*, including vasorelaxation, antioxidant, anti-inflammatory, and anti-cancer [14]. These properties of ginseng are thought to provide many beneficial effects against organ damage [13].

P. ginseng may play a protective role by enhancing liver enzymatic activity and restoring biochemical parameters against carbon tetrachloride-induced liver injury in rats [15]. Treatment with *P. ginseng* resulted in a decrease in serum concentrations of triglyceride, total cholesterol, high-density lipoprotein-cholesterol, and low-density lipoprotein-cholesterol in rats [16]. Therefore, the present study was conducted to determine the ability of *P. ginseng* to minimize the detrimental effects of stannous chloride on lipid profile concentrations and mineral levels in male rabbits.

METHODS

Tested compounds

$SnCl_2$ was brought from the chemistry department, faculty of science, Omar Al-Mukhtar University (20 mg/ml body weight every other day). *P. ginseng* (Root powder) was purchased from a local pharmacy, with a dose of 100 mg/ml body weight every other day for 12 weeks. Sixteen male New Zealand white rabbits (6 months old) were individually housed in cages and weighed weekly throughout 10 weeks' experimental period.

Study design

Sixteen mature male rabbits were randomly divided into four equal groups (n=4 for each group) as follows:

Group I: Rabbits were used as control and received an equivalent of 1 ml of the vehicle (corn oil) alone by oral gavage twice per week for 10 successive weeks.

Group II: In this group rabbits were given oral administration of *P. ginseng* with a dose of 100 mg/kg/day [17].

Group III: These rabbits received orally with $SnCl_2$ 20 mg/kg/day [5].

Group IV: These rabbits were administered orally with a combination of $SnCl_2$ and *P. ginseng*.

Rabbits were orally administered their respective doses for 3 months. Blood samples were collected from the ear vein of all animals every week throughout the experimental period and at the end of the experiment. Each blood sample was placed in a dry clean centrifuge tube and then centrifuged for 10 min at 3000 revolutions per minute (rpm) to separate the serum for determining the lipids profile concentration, minerals, and electrolytes level.

Assay of a lipid profile

Total cholesterol was determined according to the method of [18], and triglycerides (TG) by the method [19]. High-density lipoprotein (HDL) and low-density lipoprotein (LDL) were assayed by using the methods of [20].

Assay of electrolytes

The levels of Sodium (Na^+), Potassium (K^+), and Magnesium (Mg^{+2}) were measured using an automatic electrolyte analyzer (EasyLyte from MediaCorp, USA). Serum phosphorus was determined by phosphomolybdate UV endpoint [21], using an Ammonium Molybdate Diagnostic kit, and the level of calcium (Ca^{+2}) was measured using the method of [22]. Also, serum was assayed to determine the concentration of Zn^{+2} according to the method of [23].

Statistical Analysis

The data obtained were expressed as mean ±SEM. The significant differences were assessed by one-way ANOVA and Tukey test. After the detection of the normal distribution of the data and appropriate P-values, less than 0.05 is considered significant.

RESULTS

The mean values of Cholesterol, Triglycerides (TG), Low-density lipoprotein (LDL), High-density Lipoprotein (HDL) throughout 10 weeks of the experimental period were shown in (Table 1). Treatment with *P. ginseng* /$SnCl_2$ alone caused a significant decrease in levels of (TG and HDL) and a non-significant decrease in levels of cholesterol compared to the control group (Table 1). On the other hand, treatment with *P. ginseng*/ $SnCl_2$ alone caused a non-significant increase in levels of LDL compared to the control group (Table 1). Treatment with the combination of *P. ginseng* and $SnCl_2$ retained levels of cholesterol, TG, LDH, HDL, and LDL close to the values of the control group (Table 1). All these changes started from the second week of the experiment as shown in (1-4 Figures).

Table 1. Illustrate the levels of plasma lipid and lipoprotein profiles of male rabbits treated with P. ginseng, $SnCl_2$, and their combination at end of the experiment.

Lipids (mg/dl)	Experimental groups			
	Group I	**Group II**	**Group III**	**Group IV**
Cholesterol	78.2±10.47[a]	59.00±5.75[a]	52.11±7.44[a]	62.22±7.43[a]
P. values	**Groups**= 0.132		**Weeks**= 0.161	
TG	63.22±3.71[a]	41.44±1.66[c]	46.11±3.63b[c]	57.33±4.26[ab]
P. values	**Groups**= 0.000		**Weeks**= 0.738	
LDL	63.33±3.95[a]	72.22±5.23[a]	72.11±4.96[a]	60.22 ±7.31[a]
P. values	**Groups**= 0.310		**Weeks**= 0.106	
HDL	48.39±5.76[a]	38.56±1.77[ab]	35.44±1.18[b]	37.22±0.99[ab]
P. values	**Groups=** 0.027		**Weeks**= 0.014	

Values are expressed as means ± SEM; n = 4 for each treatment group. Mean values within a row not sharing common superscript letters (a, b, c) were significantly different, p<0.05

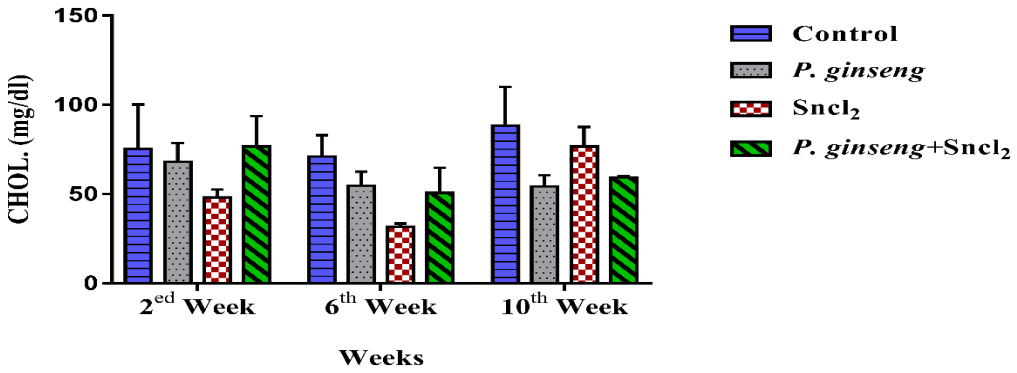

Figure 1. ***Biweekly values of Cholesterol (Mean± SEM) in male rabbits treated with P. ginseng, $SnCl_2$ and their combination.***

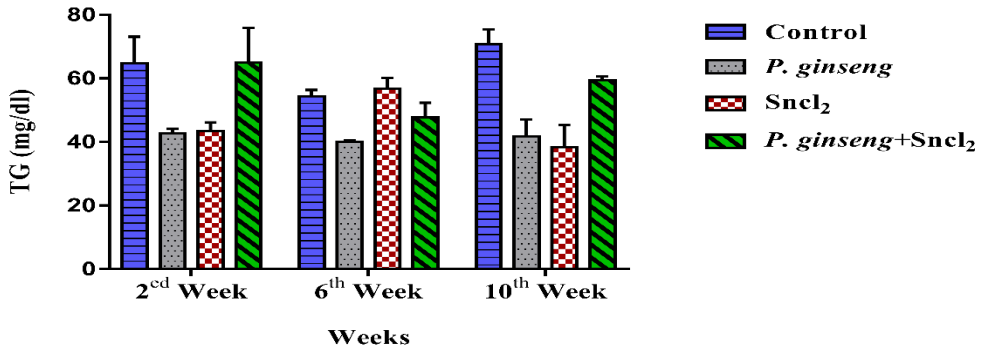

Figure 2. ***Biweekly values of Triglycerides (TG) (Mean± SEM) in male rabbits treated with P. ginseng, $SnCl_2$ and their combination***

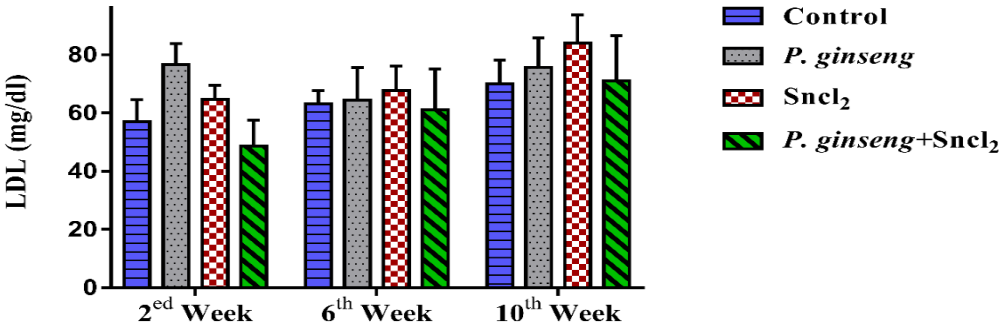

Figure 3. ***Biweekly values of LDL (Mean± SEM) in male rabbits treated with P. ginseng, $SnCl_2$ and their combination***

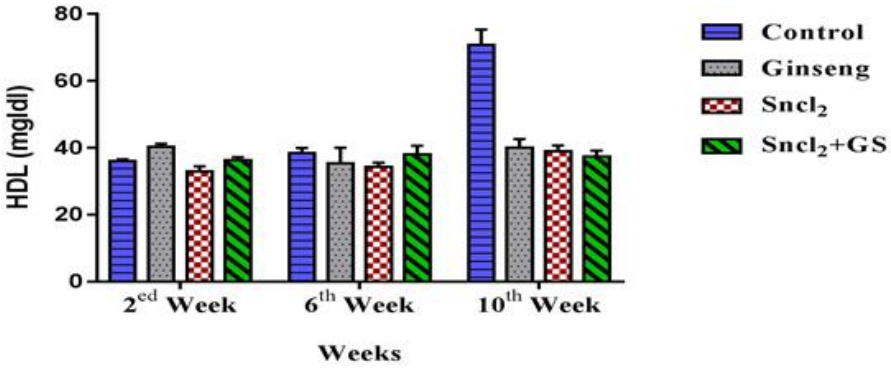

Figure 4. ***Biweekly values of HDL (Mean± SEM) in male rabbits treated with P. ginseng, $SnCl_2$, and their combination***

Treatment with $SnCl_2$ resulted in a significant increase in the level of Zn^{+2} and a non-significant increase in Ca^{+2} and Mg^{+2} compared to the control group (Table 2). The values of Po_4^- and Na^{+2} were decreased in $SnCl_2$ alone treated group (Table 2). On the other hand, the present study indicated that treatment with *P. ginseng* alone had a non-significant decrease level of Po_4^- and Ca^{+2}, while the levels of Na^{+2} and Mg^{+2} increased without significant difference and a significant increase in the level of Zn^{+2} in male rabbits (Table 2). *P. ginseng* minimized the effect of $SnCl_2$ to be close to control values. All these changes started in the second week of the experiment as shown in (5-9 Figures).

Table 2. Illustrate the levels of minerals in male rabbits treated with P. ginseng, $SnCl_2$, and their combination at end of the experiment

Parameter	Experimental groups			
	Group I	**Group II**	**Group III**	**Group IV**
PO_4^-(mg/dl)	6.378±0.35[a]	5.767±0.50[a]	5.711±0.30[a]	6.178±0.41[a]
P. values	**Groups=** 0.579		**Weeks=** 0.006	
Na^+ (mEq/l)	149.67±5.16[a]	150.33±7.05[a]	145.33±2.82[a]	147.33±5.72[a]
P. values	**Groups=** 0.910		**Weeks=** 0.020	
Ca^{+2} (mg/dl)	10.022±0.24[a]	9.667±0.24[a]	10.322±0.24[a]	9.978±0.19[a]
P. values	**Groups=** 0.267		**Weeks=** 0.482	
Mg^{+2}(mg/dl)	2.322±0.17[a]	2.544±0.18[a]	2.900±0.12[a]	2.767±0.13[a]
P. values	**Groups=** 0.054		**Weeks=** 0.196	
Zn^{+2} (mg/dl)	155.7±19.43[b]	184.1±11.17[ab]	234.44±9.53[a]	178.7±28.7[ab]
P. values	**Groups=** 0.040		**Weeks=** 0.000	

Values are expressed as means ± SEM; n = 4 for each treatment group. Mean values within a row not sharing common superscript letters (a, b, c) were significantly different, $p<0.05$

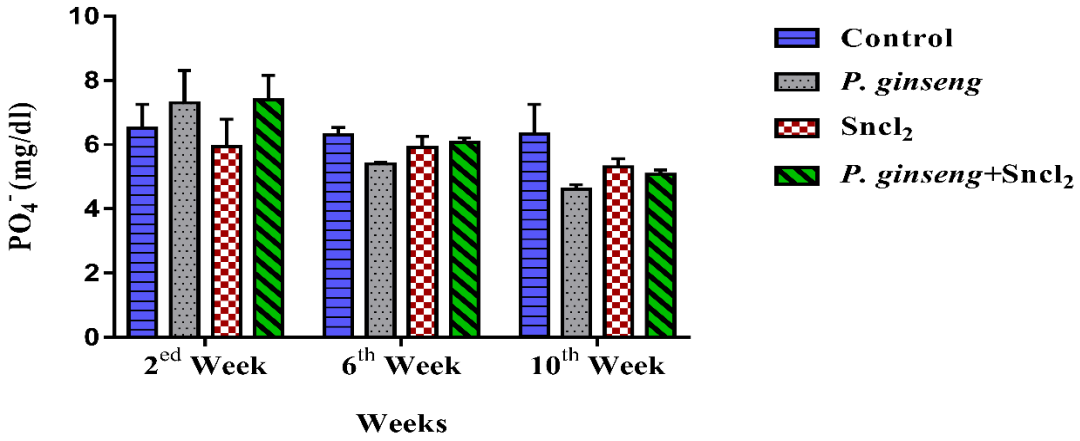

Figure 5. Biweekly values of Po_4^- (Mean± SEM) in male rabbits treated with P. ginseng, $SnCl_2$ and their combination

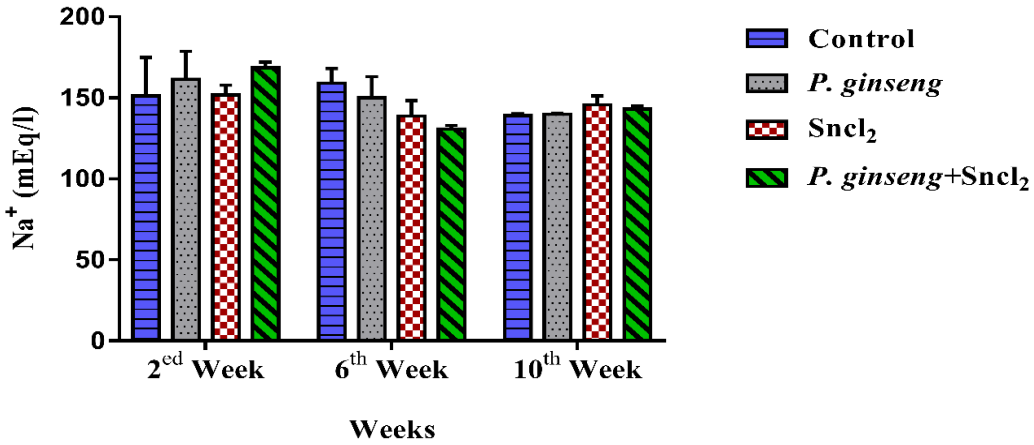

Figure 6. *Biweekly values of Na^+ (Mean± SEM) in male rabbits treated with P. ginseng, $SnCl_2$ and their combination*

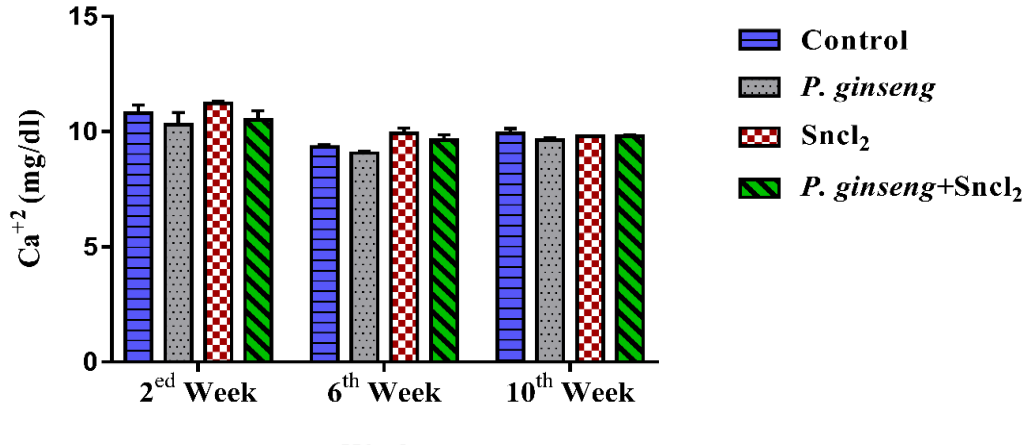

Figure 7. *Biweekly values of Ca^{+2} (Mean± SEM) in male rabbits treated with P. ginseng, $SnCl_2$ and their combination*

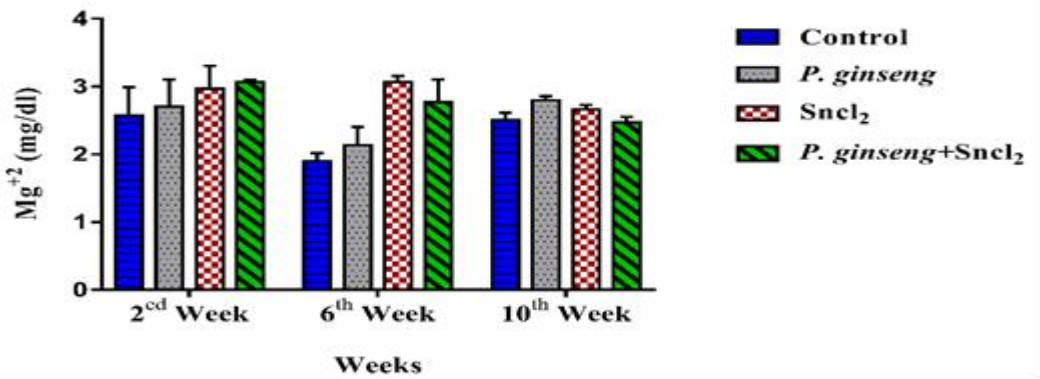

Figure 8. Biweekly values of Mg^{+2} (Mean± SEM) in male rabbits treated with P. ginseng, $SnCl_2$ and their combination

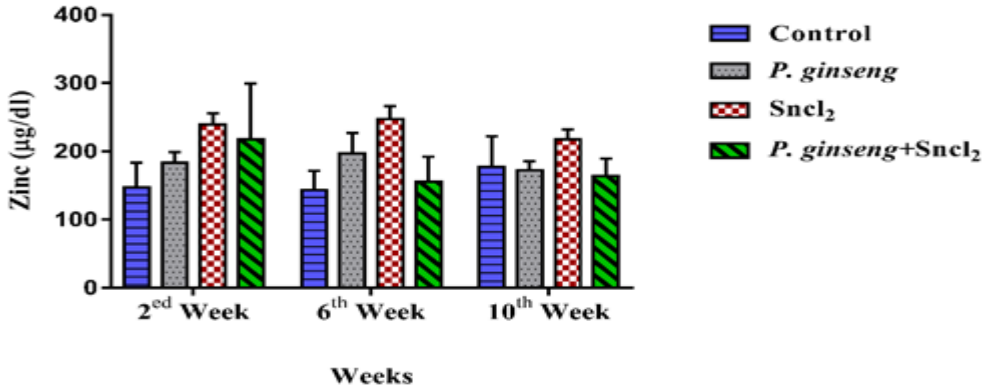

Figure 9. Biweekly values of Zn^{+2} (Mean± SEM) in male rabbits treated with P. ginseng, $SnCl_2$ and their combination.

DISCUSSION

Humans are exposed to $SnCl_2$ by the consumption of food, especially packaged food, and soft drinks, which are considered the main source of inorganic forms of tin [24]. Therefore, several laboratory studies have focused on the toxic effects of $SnCl_2$ [3, 4]. The present study was undertaken to evaluate the potential protective effects of *P. ginseng*, and their combination after 10 weeks against lipid profile concentration and levels of some minerals (Na^+, Ca^{+2}, Mg^{+2}, Po_4^- and Zn^{+2}) of male rabbits induced by $SnCl_2$.

Changes in serum cholesterol and TG levels indicate disturbances in lipid metabolism. The current study found that treatment with *P. ginseng* or $SnCl_2$ alone led to lower TG, HDL, and cholesterol levels compared to the control group. On the other hand, the administration with *P. ginseng* or $SnCl_2$ alone increased the levels of LDL compared to the control group. A previous study showed that the level of lipids such as TG, total cholesterol, HDL and LDL were decreased in the serum of rats as a result of treatment with *P. ginseng* [16, 25]. These observations were not in agreement with a previous study that found $SnCl_2$ increased the levels of plasma total lipid (TL), cholesterol, TG, LDL and very low-density lipoprotein (VLDL), While, the level of plasma HDL was decreased [5]. These alterations, in lipid profile, can be due to oxidative stress resulting from an imbalance of the prooxidant/antioxidant ratio, thus inducing tissue damage. Increased oxidation potential within the cell milleau promotes cholesterol synthesis, absorption, and distribution, and reduces the conversion of cholesterol to bile acids [26]. This leads to an increase or decrease in serum lipid levels in the body. As an alternative explanation, increases in plasma lipids with $SnCl_2$ administration indicate a loss of membrane integrity [27].

P. ginseng also lowered serum TG and cholesterol levels, according to several researchers [25,28,29]. Ginseng saponins can partially restore LDL biosynthesis in fowl fed a high-cholesterol diet [30]. The solubilizing activity of saponin may aid in the elimination of fat from circulation. Results from the current study showed that treatment with *P. ginseng* alone resulted in a decreased level of Po_4^- and Ca^{+2}. While the levels of Na^{+2}, Zn^{+2} and Mg^{+2} were increased in the serum of male rabbits. On the other hand, $SnCl_2$ administration increased the levels of Zn^{+2}, Ca^{+2} and Mg^{+2}, and decreased the values of Po_4^- and Na^{+2} compared to the control group. These observations are not in agreement with the previous study

that indicated Fe, Cu, and Zn^{+2} status was influenced by dietary Sn concentrations lower than 50 mg/kg causing decreased plasma and tissue concentrations of Fe, Cu, and Zn^{+2} by up to 15%. In addition, Sn is added to the diet as $SnCl_2$, concentrations up to about 200 mg Sn/kg can affect Fe, Cu and Zn^{+2} state in rats, but the effects are inconclusive [31]. Zinc act as a fundamental cofactor for the activity of up to 300 zinc-containing enzymes, including alcohol dehydrogenase, carbonic anhydrase, and superoxide dismutase [32,33].

They suggested that the extract of *P. ginseng* induces the mRNA expression of zinc transport such as ZIP4, which has been shown to promote zinc uptake into cells [34]. If food-derived factors that promote zinc absorption by targeting the intestinal zinc absorption mechanism, specifically by targeting zinc transport (ZIP4 and ZNT1), are identified, these factors may be effective in preventing zinc deficiency through the daily diet. This may indicate that *P. ginseng* affects zinc metabolism, which indirectly affects immunoglobulin production. Similarly, *p. ginseng* may be a factor involved in certain enzymatic activities, most commonly zinc [35]. Zinc acts as an antioxidant stress agent by inhibiting the oxidation of macromolecules such as DNA and proteins [36].

This observation was in agreement with a previous study that found the calcium content in the femur of rats was significantly decreased by the oral administration of $SnCl_2$ (3.0 mg /100 g body weight, 6 times at 12-h intervals) [37]. A previous study also reported that the administration of $SnCl_2$ for 3 days significantly reduced serum calcium and femoral calcium levels in rats orally given $SnCl_2$ (3.0mg Sn/100g body weight, every 12 hours) [6]. And this disagreement may refer to a difference in the amount of calcium between serum and femur or the dose of $SnCl_2$ that was used in these studies. The effect of $SnCl_2$ on urinary calcium concentration was studied in rats intraperitoneally administered with $SnCl_2$. The concentration of calcium in urine was significantly decreased by the administration of $SnCl_2$ (3.0 mg/100 g). The reduction of urinary calcium concentration, induced by $SnCl_2$, was not restored by the injection of calcium in rats treated with $SnCl_2$. A study was carried out by [38] referred that $SnCl_2$ lead to inhibit the excretion of calcium in the urine of rats. $SnCl_2$ has been shown to facilitate the transmitter release by promoting Ca^{+2} influx at the nerve terminals, but not by blocking the potassium channels and the mechanism of action of $SnCl_2$ in mice is identical to that in the frog [39]. It was demonstrated that tin, such as $SnCl_2$, can facilitate neuromuscular transmission by accelerating the transmitter release from the nerve terminals in the mouse. When this salt is injected into laboratory animals, it can produce stimulation or depression of the central nervous system [40].

CONCLUSION

The results obtained from the present study convincingly demonstrated that $SnCl_2$ exposure resulted in varying degrees of biochemical parameters in rabbits. *P. ginseng* has promise as a nutritional supplement to help prevent disorders involving $SnCl_2$-induced toxic effects on these parameters *P. ginseng* is a potent antioxidant due to its ability to attenuate the reactivity of ROS and to enhance the activities of detoxifying enzymes. Thus *P. ginseng* may be helpful to combat $SnCl_2$-associated sufferings in humans as well as animals.

Disclaimer

The article has not been previously presented or published, and is not part of a thesis project.

Conflict of Interest

There are no financial, personal, or professional conflicts of interest to declare.

REFERENCES

1. Assis M, De Mattos J, Caceres M, Dantas F, Asad L, Asad N, Asad, NR, Bezerra, RJAC, Caldeira-de-Araujo, A, Bernardo-Filho, M. Adaptive response to H2O2 protects against SnCl2 damage: the OxyR system involvement. Biochimie. 2002;84(4):291-4.
2. Harper C. Toxicological profile for tin and tin compounds: Agency for Toxic Substances and Disease Registry; 2005.
3. Sun L, Zhang N, Zhai Q, Gao X, Li C, Zheng Q, et al. Effects of dietary tin on growth performance, hematology, serum biochemistry, antioxidant status, and tin retention in broilers. Biological trace element research. 2014;162(1-3):302-8.
4. Hiles RA. Absorption, distribution and excretion of inorganic tin in rats. Toxicology and applied pharmacology. 1974;27(2):366-79.
5. Yousef M, Awad T, Elhag F, Khaled F. Study of the protective effect of ascorbic acid against the toxicity of stannous chloride on oxidative damage, antioxidant enzymes and biochemical parameters in rabbits. Toxicology. 2007;235(3):194-202.
6. Yamaguchi M, Kitade M, Okada S. The oral administration of stannous chloride to rats. . Toxicology letters. 1980;5:275-8.
7. Reicks M, Rader J. Effects of dietary tin and copper on rat hepatocellular antioxidant protection. Proceedings of the Society for Experimental Biology and Medicine. 1990;195(1):123-8.

8. Johnson M, Greger J. Effects of dietary tin on tin and calcium metabolism of adult males. The American journal of clinical nutrition. 1982;35(4):655-60.
9. Okolie N, Abu O. Effects of Aqueous Extract of Annona muricata Leaves on Cyanide–induced Toxicity in New Zealand Rabbits. NISEB Journal. 2019;16(4).
10. Lee FC. Facts about ginseng: the elixir of life: Hollym International Corporation; 1992.
11. Buettner C, Yeh G, Phillips R, Mittleman M, Kaptchuk T. Systematic review of the effects of ginseng on cardiovascular risk factors. Annals of Pharmacotherapy. 2006;40(1):83-95.
12. Fuzzati N. Analysis methods of ginsenosides. Journal of Chromatography B. 2004;812(1-2):119-33.
13. Kitts DD, Wijewickreme AN, Hu C. Antioxidant properties of a North American ginseng extract. Molecular and cellular biochemistry. 2000;203(1):1-10.
14. Hofseth LJ, Wargovich MJ. Inflammation, cancer, and targets of ginseng. The Journal of nutrition. 2007;137(1):183S-5S.
15. Karakus E, Karadeniz A, Simsek N, Can I, Kara A, Yildirim S, et al. Protective effect of Panax ginseng against serum biochemical changes and apoptosis in liver of rats treated with carbon tetrachloride (CCl4). Journal of hazardous materials. 2011;195:208-13.
16. Park H, Lee J, Song Y, Park K. Effects of dietary supplementation of lipophilic fraction from Panax ginseng on cGMP and cAMP in rat platelets and on blood coagulation. Biological and Pharmaceutical Bulletin. 1996;19(11):1434-9.
17. Inoue M, Wu C, Dou D, Chen Y, Ogihara Y. Lipoprotein lipase activation by red ginseng saponins in hyperlipidemia model animals. Phytomedicine. 1999;6(4):257-65.
18. Allain C, Poon L, Chan C, Richmond W, Fu P. Enzymatic determination of total serum cholesterol. Clinical chemistry. 1974;20(4):470-5.
19. Bucolo G, David H. Quantitative determination of serum triglycerides by the use of enzymes. Clinical chemistry. 1973;19(5):476-82.
20. Burstein M, Scholnick H, Morfin R. Rapid method for the isolation of lipoproteins from human serum by precipitation with polyanions. Journal of lipid research. 1970;11(6):583-95.
21. Tietz N, Rinker AD, Morrison S. When is a serum iron really a serum iron? The status of serum iron measurements. Clinical chemistry. 1994;40(4):546-51.
22. Glick M, Ryder K, Jackson S. Graphical comparisons of interferences in clinical chemistry instrumentation. Clinical Chemistry. 1986;32(3):470-5.
23. Parker M, Humoller L, Mahler D. Determination of copper and zinc in biological material. Clinical chemistry. 1967;13(1):40-8.
24. Nordberg G, Fowler B, Nordberg M. Handbook on the Toxicology of Metals: Academic press; 2014.
25. Elnaggar A, Ghonem M, Abdelkhalek E. Impact Of Ginseng (Panax Ginseng) On Growth Performance, Blood Biochemical Parameters And Antioxidative Status Of Japanese Quail. Egyptian Poultry Science Journal. 2022;42(2):137-56.
26. Amin I, Hussain I, Rehman M, Mir B, Ganaie S, Ahmad S, et al. Zingerone prevents lead‐induced toxicity in liver and kidney tissues by regulating the oxidative damage in Wistar rats. Journal of food biochemistry. 2021;45(3):e13241.
27. Yousef MI. Aluminium-induced changes in hemato-biochemical parameters, lipid peroxidation and enzyme activities of male rabbits: protective role of ascorbic acid. Toxicology. 2004;199(1):47-57.
28. Yan L, Meng Q, Lee J, Wang J, Kim I. Effects of dietary wild-ginseng adventitious root meal on growth performance, blood profiles, relative organ weight and meat quality in broiler chickens. Asian-Australasian Journal of Animal Sciences. 2010;24(2):258-63.
29. Jang H, Kim H, Cho J, Chen Y, Yoo J, Min B, et al. Effects of dietary supplementation of fermented wild-ginseng culture by-products on egg productivity, egg quality, blood characteristics and ginsenoside concentration of yolk in laying hens. Korean Journal of Poultry Science. 2007;34(4):271-8.
30. Kim JW, Lee H, Joo CN. Biochemical studies on ginseng saponin (XXV) ginseng saponin–protein interaction. Korean Journal of Biochemistry. 1985;18:453-8.
31. Pekelharing H, Lemmens A, Beynen A. Iron, copper and zinc status in rats fed on diets containing various concentrations of tin. British journal of nutrition. 1994;71(1):103-9.
32. McCall K, Huang C, Fierke C. Function and mechanism of zinc metalloenzymes. The Journal of nutrition. 2000;130(5):1437S-46S.
33. Vallee B, Falchuk K. The biochemical basis of zinc physiology. Physiological reviews. 1993;73(1):79-118.
34. Ikeda Y, Munekane M, Yamada Y, Kawakami M, Amano I, Sano K, et al. Enhancing effect of Panax ginseng on Zip4-mediated zinc influx into the cytosol. Journal of ginseng research. 2022;46(2):248-54.
35. Hashimoto A, Kambe T. Overview of the zinc absorption mechanism for improving zinc nutrition. Metallomics Research. 2022;2(1):rev-20-rev-8.
36. Prasad A, Bao B. Molecular mechanisms of zinc as a pro-antioxidant mediator: clinical therapeutic implications. Antioxidants. 2019;8(6):164.
37. Masayoshi Y, Mituko K, Shoji O. Decrease in calcium content in the femur of rats orally administered stannous chloride. Toxicology Letters. 1979;3(1):7-10.

38. Yamaguchi M, Naganawa M, Yamamoto T. Decreased gastric secretion in rats treated with stannous chloride. Toxicology and applied pharmacology. 1976;36(1):199-200.
39. Hattori T, Maehashi H. Augmentation of calcium influx by stannous chloride at mouse motor nerve terminals. Research communications in chemical pathology and pharmacology. 1994;84(2):253-6.
40. Silva C, Oliveira M, Melo S, Dantas F, De Mattos J, Bezerra R, et al. Biological effects of stannous chloride, a substance that can produce stimulation or depression of the central nervous system. Brain research bulletin. 2002;59(3):213-6.