Biol Trace Elem Res (2016) 169:129–133
DOI 10.1007/s12011-015-0403-7

Effect of Selenium on the Levels of Cytokines and Trace Elements in Toxin-Mediated Oxidative Stress in Male Rats

S. Ansar [1]

Received: 18 May 2015 / Accepted: 8 June 2015 / Published online: 20 June 2015

Abstract Selenium is an essential cofactor in the key enzymes involved in cellular antioxidant defense. This study was designed to investigate the protective effects of selenium on mercury chloride (HgCl2)-induced toxicity. Male Wistar rats were randomly divided into four groups of six animals each. The first group was control; the second group was treated with mercuric chloride (HgCl2: 50 mg/kg/bw). The third group was treated with sodium selenite (Se 0.2 mg/kg/bw), and the fourth group received Se (0.2 mg/kg/bw) plus HgCl2 (50 mg/kg for 24 h). The influence of Se on mercury induced levels of malondialdehyde (MDA) and the activity of superoxide dismutase (SOD) and zinc, copper, and iron in serum of rats were observed. The serum MDA, SOD, zinc, and iron concentrations were found to be statistically different among the control and toxin-treated group. The serum levels of IL-6, IL-10, and TNF-α were also measured. There was a significant decrease in the levels of TNF-α, IL-6, and IL-10 in toxin-treated group II compared with that of the control group ($p < 0.05$). A significant increase in the serum levels of inflammatory cytokines IL-6, TNF-α, and IL-10 after administration of Se seemed to counteract some of the damage, as indicated by differences in the serum concentrations of major elements.

Keywords Selinium · Serum · Toxicity · Trace elements · Inflammation · Cytokines

✉ S. Ansar
sansar@ksu.edu.sa

[1] Department of Clinical Laboratory Sciences, College of Applied Medical Science, King Saud University, Riyadh, Saudi Arabia

Introduction

Mercury is a widespread environmental and industrial pollutant [1]. It is known that mercury may cause accidental and occupational exposures and poisoning can result from inhalation, ingestion, and absorption through the skin [2–4]. People can be exposed to mercury through contaminated water and food [5]. The kidney, liver, gastrointestinal system, and central nervous system are the main target sites of mercury toxicity [6]. Past studies have already documented the deleterious effects of heavy metal toxins in humans which may induce lipid peroxidation and may promote oxidative stress in tissues [7–10]. Lead and mercury exposure, air pollution, and organic compounds all have the potential to damage brain functioning yet remain understudied [6].

Thiol-containing enzymes have been recognized as the targets of inorganic Hg. Moreover, binding of mercuric ions to thiol groups may cause decreased glutathione (GSH) levels, leading to increases in levels of reactive oxygen species (ROS), such as superoxide anion radicals, hydrogen peroxide, and hydroxyl radicals, which provoke lipid, protein, deoxyribonucleic acid (DNA), and ribonucleic acid (RNA) oxidation [1, 11, 12]. Considering that oxidative stress and endogenous thiol depletion are involved in inorganic Hg toxicity, it has been suggested that antioxidants could contribute to the treatment of Hg poisoning [13, 14]. Antioxidants like melatonin, curcumin, and vitamin E have been found to play a protective effect against mercuric chloride (HgCl2)-induced acute renal toxicity [15–17]. Similarly, a number of plant extracts with antioxidant properties have been shown to inhibit HgCl2-induced toxicity [16, 18, 19].

Another important trace element in the metabolism is selenium (Se). Se has the ability to counteract free radicals and protects the structure and function of proteins, DNA, and chromosomes against the injury of oxidation [20]. Several

studies reported that selenium protects against the toxicity of heavy metals [4, 21–29]. Se can effectively counteract oxidative damage toxic agents caused by scavenging reactive oxygen radicals and protect membrane integrity. Se is considered as an essential trace mineral for living organisms, it is a structural component of several enzymes like glutathione peroxidases and thioredoxin reductase, and its role against mercury intoxication [6, 24, 30, 31]. Selenium has been found to have detoxification effects on various heavy metals [32].

It is also known that Se alters the Hg distribution in the organism, and due to this effect, Hg toxicity can be reduced [33, 34]. Moreover, Se can reduce the Hg toxicity through the prevention of oxidative damage [24, 35]. Therefore, the evaluation of toxic potentials of metals is important for the risk assessment of human beings ordinarily exposed to these substances.

Materials and Method

Maintenance of Animals

Male Wistar rats weighing approximately 180–200 g were procured. The animals were acclimatized for 7 days prior to experiments. The institutional ethics committee approved the experimental protocols. All the animals used in this study were placed in cages in an air-conditioned room maintained at a temperature of 25 ± 30 °C and 12-h light/dark schedule.

Experimental Protocol

Animal Treatments Different groups of animals were used to study the effects of Se on mercuric-induced oxidative stress. In total, 24 animals were divided into four groups of six rats each. Group I received saline injection intraperitoneally (0.85 % NaCl) at a dose of 10 ml/kg bodyweight. Group II received a single intraperitoneal injection of mercuric chloride at a dose of 50 mg/kg bodyweight. Groups III and IV received pretreatment with Se i.p. once a day for 7 days at a dose of 0.2 mg/kg bodyweight. After the last treatment with Se, the rats of group IV received a single intraperitoneal injection of HgCl2 at a dose level of 50 mg/kg body weight. After 24 h of the last administration, the animals were euthanized under mild ether anesthesia.

The blood samples were collected in test tubes without anticoagulant. The samples were centrifuged at 3000 rpm for 15 min and the clear serum was carefully separated from all samples and stored at stored at −80 °C. The concentrations of IL-6, TNF-a, and IL-10 in the serum were measured using commercially available enzyme amplified sensitivity immunoassay kits (BioSource). All assays were conducted according to the manufacturer's instructions. The samples, which have shown higher concentrations, were diluted and measured in duplicate.

For estimation of trace elements, the serum was separated and diluted with double-distilled water. The samples were then analyzed following established procedures for trace elements by means of a Unicam 929 atomic absorption spectrophotometer.

Malondialdehyde and Superoxide Dismutase Measurements

The oxidant–antioxidant status of the rat was assessed by determining the level of malondialdehyde (MDA) and the activity of superoxide dismutase (SOD). Lipid peroxidation was determined by measuring the level of MDA, which is considered to be a standard marker for oxidative lipid damage. Serum MDA levels were measured by the method of Draper and Hadley [36]. The results were expressed as micromoles per liter. Serum SOD activity was measured by the method of Sun et al. [37]. The results were expressed as units per liter.

Statistical Analysis

Results were expressed as the mean ± standard error of the mean (SEM). Data for multiple variable comparisons were analyzed by one-way analysis of variance (ANOVA). For the comparison of significance between groups, Duncan's test was used as a post hoc test according to the Statistical Package for the Social Sciences (SPSS version 17.0). All p values are two-tailed and $p < 0.05$ was considered significant for all statistical analysis in this study.

Results

Mercury is known to cause disturbance in immune response. In this study, its effect on the inflammatory markers TNF-α, IL-6, and IL-10 in the serum was studied (Table 1). Intraperitoneal injection of HgCl2 to rats resulted in a significant decrease in these biomarkers (compared group II with group I). However, pretreatment of HgCl2-injected rats with 0.2 mg/kg body weight selenium per day for 7 days resulted in the significant prevention of this decrease in the biomarkers (compared group IV with group II). Selenium by itself in group III did not affect the levels of these inflammatory markers when compared to group I rats. These results suggest that mercury-induced decrease in the inflammatory markers is significantly prevented with the pretreatment of selenium in these rats ($p < 0.05$).

Next, the effect of mercury on the levels of trace elements in the serum of these rats was studied. Again, exposure of these rats to mercury resulted in a decrease of Cu, Zn, and

Table 1 Levels of serum TNF-α, IL-6, and IL-10 in rats

Experimental groups				
Parameters	Control (I)	Hg (II)	DAS (III)	DAS + HgCl2 (IV)
TNF-α (pg/ml)	10.13 ± 0.41	4.89 ± 0.28*	10.12 ± 1.42	8.52 ± 1.40**
IL-6 (pg/ml)	39.41 ± 12.14	10.45 ± 4.21*	40.32 ± 6.17	32.35 ± 7.15**
IL-10 (pg/ml)	22.21 ± 3.18	11.34 ± 2.76*	23.31 ± 7.41	18.28 ± 6.36**

TNF- α tumor necrosis factor-α, *IL-6* interleukin-6, *IL-10* interleukin-10

*$P < 0.05$ compared with control group **$P < 0.05$ compared with Hg-exposed group

Fe. The decrease in Cu was not statistically significant when compared to control rats in group I (Table 2). However, Zn and Fe were reduced significantly by mercury injection and this decrease was prevented by the treatment with selenium in group IV ($p < 0.05$).

Mercury is known to increase oxidative stress and, therefore, levels of MDA and SOD in these rats were also measured. Administration of mercury chloride to rats resulted in a significant increase in the levels of MDA when compared to saline injected control rats (Fig. 1). Administration of selenium alone in group III resulted in an insignificant decrease of MDA compared to control group. Pretreatment of mercury chloride-injected rats in group IV with selenium significantly prevented the increase in MDA levels that was seen in group II rats.

Also exposure of rats to mercury resulted in a significant decrease in the levels of SOD in serum and this decrease was reversed by the treatment with selenium (Fig. 2). However, there were no significant differences between the same parameters in group II (Se-alone treated) and group 1 (control). These data suggest that administration of mercury caused oxidative stress in rats which was significantly blocked by the treatment with selenium ($p < 0.05$).

Discussion

Several reports have suggested that all three forms of mercury (vapor, inorganic, and methyl mercury) are associated with human health hazards. However, in general, for nonclinical studies, efficacy and safety pharmacological studies are performed keeping in mind target organ toxicities, dose selection, and known lethal dose. Mercury is most toxic of all the heavy metals [22, 38–43] and is known to induce toxicity in the cardio respiratory system, reproduction system, kidneys, liver, brain, and lungs [3, 44–46]. Humans are exposed to these metals from numerous sources, including contaminated air, water, soil, and food. Selenium has been shown to alter heavy metal toxicity specially mercury which cause adverse effects on the various tissue parameters [15, 24, 31, 47–54].

Therefore, the aim of the present study is to study possible mitigating effect of Se against acute HgCl2 toxicity based on oxidative stress and inflammation induction in rats. Results show significant changes in serum Cu, Fe, and Ca levels found in the rats after mercury treatment when compared with controls. Conditioned deficiencies of trace elements may develop in states of decreased absorption or excessive excretion or utilization [55].

The present study was also designed to evaluate the protective effect of sodium selenite treatment on IL-6, TNF-α, and IL-10 in serum of mercuric chloride intoxicated rats. IL-6, IL-10, and TNF-α are effective cytokines of inflammation and endothelial functions. In this study, mercury caused decrease in the levels of IL-6 released from mononuclear phagocytes and TNF-α and IL-10 released from monocytes. The levels of these cytokines, which have different synthesis locations and functions, were decreased together as observed. Therefore, it can be said that intraperitoneal administration of mercury had an effect on the inflammatory process as mercury reduces the levels of IL-6, TNF-α, and IL-10 that are inflammatory cytokines.

Also in this study, supplementation of Se to the mercuric chloride-treated groups ameliorated malondialdehyde and SOD activities. Earlier, it has been reported that major role of sodium selenite is in inhibiting lipid peroxidation and in protecting the wholeness and functioning of tissues and cells [56]. It was observed that serum MDA levels increased while

Table 2 Serum trace elements concentrations in rats

Experimental groups				
Parameters	Control (I)	Hg (II)	DAS (III)	DAS + HgCl2(IV)
Cu (μg/dl)	8.21 ± 1.23	6.89 ± 1.49	9.93 ± 1.41	7.89 ± 1.34
Zn (μg/dl)	20.231 ± 8.52	13.45 ± 4.34*	19.37 ± 6.23	18.34 ± 5.56**
Fe (μg/dl)	99.12 ± 13.1	76.34 ± 12.13*	98.31 ± 11.23	96.28 ± 12.67**

*$P < 0.05$ compared with control group; **$P < 0.05$ compared with Hg-exposed group

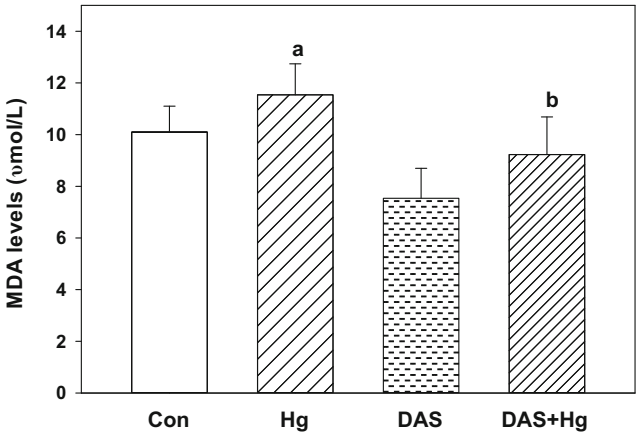

Fig. 1 Serum malondialdehyde (MDA) levels in all groups. *a* and *b* indicate statistically significant differences with those of control groups ($p < 0.05$)

serum SOD levels decreased in the serum of the rats after HgCl2 treatment. The rise in MDA and decrease in SOD could be due to the increased generation of reactive oxygen species due to the excessive oxidative damage generated in rats. Oxidative stress refers to excessive generation of reactive oxygen species [57]. MDA content manifests the level of lipid peroxidation and indirectly represents the level of damage of the cell and tissue [30]. Results of the present study showed that the amount of MDA was very high in mercuric chloride-treated rats which were supported by the previous studies [2, 58]. The elevated level of MDA might be due to enhanced formation of free radicals.

In conclusion, the present study showed that mercuric chloride intoxication caused reactive oxygen species generation which in turn induced biochemical alterations in rats. Administration of sodium selenite proved to be beneficial in attenuating the mercuric chloride-induced oxidative toxicity.

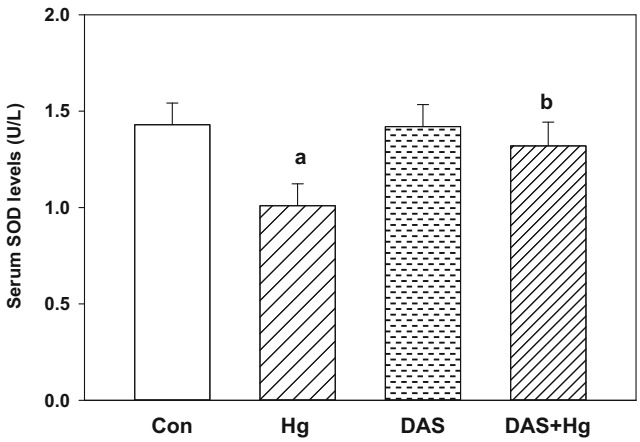

Fig. 2 Serum superoxide dismutase (SOD) levels in all groups. *a* and *b* indicate statistically significant differences with those of control groups ($p < 0.05$)

Acknowledgments This research project was supported by the "Research Center of the Center for Female Scientific and Medical Colleges," Deanship of Scientific Research, King
, Saud University, Riyadh, Saudi Arabia.

References

1. Clarkson TW, Magos L (2006) The toxicology of mercury and its chemical compounds. Crit Rev Toxicol 36:609–662
2. Rao MV, Chhunchha B (2010) Protective role of melatonin against the mercury induced oxidative stress in the rat thyroid. Food Chem Toxicol 48:7–10
3. Agarwal R, Raisuddin S, Tewari S, Goel SK, Raizada RB, Behari JR (2010a) Evaluation of comparative effect of pre- and posttreatment of selenium on mercury-induced oxidative stress, histological alterations, and metallothionein mRNA expression in rats. J Biochem Mol Toxicol 24:123–135
4. El-Shenawy SM, Hassan NS (2008) Comparative evaluation of the protective effect of selenium and garlic against liver and kidney damage induced by mercury chloride in the rats. Pharmacol Rep 60:199–208
5. Magos L, Clarkson TW (2006) Overview of the clinical toxicity of mercury. Ann Clin Biochem 43:257–268
6. Agarwal R, Kumar R, Behari JR (2007) Mercury and lead content in fish species from the river Gomti, Lucknow, India, as biomarkers of contamination. Bull Environ Contam Toxicol 78:118–122
7. Lucena GM, Franco JL, Ribas CM, Azevedo MS, Meotti FC, Gadotti VM, et al. (2007) Cipura paludosa extract prevents methyl mercury-induced neurotoxicity in mice. Basic Clin Pharmacol Toxicol 101:127–131
8. Taber KH, Hurley RA (2008) Mercury exposure: effects across the lifespan. J Neuropsychiatry Clin Neurosci 20:iv–389
9. Liu WW, Jiang CQ, Hu ZB, Zhang C, Xu QR, Zhou G (2006) Mercury concentration in cerebrospinal fluid in patients with chronic mercury poisoning. Zhonghua Lao Dong Wei Sheng Zhi Ye Bing Za ZhiZhonghua Laodong Weisheng Zhiyebing Zazhi Chin J Ind Hyg Occup Dis 24:403–405
10. Farina M, Franco JL, Ribas CM, Meotti FC, Missau FC, Pizzolatti MG, et al. (2005) Protective effects of Polygala paniculata extract against methylmercury-induced neurotoxicity in mice. J Pharm Pharmacol 57:1503–1508
11. Clarkson TW (1997) The toxicology of mercury. Crit Rev Clin Lab Sci 34:369–403
12. Li Z, Wu J, Deleo CJ (2006) RNA damage and surveillance under oxidative stress. IUBMB Life 58:581–588
13. Patrick L (2002) Mercury toxicity and antioxidants: part 1: role of glutathione and alpha-lipoic acid in the treatment of mercury toxicity. Altern Med Rev 7:456–471
14. Pillai A, Gupta S (2005) Antioxidant enzyme activity and lipid peroxidation in liver of female rats co-exposed to lead and cadmium: effects of vitamin E and Mn2+. Free Radic Res 39:707–712
15. Agarwal R, Goel SK, Chandra R, Behari JR (2010b) Role of vitamin E in preventing acute mercury toxicity in rat. Environ Toxicol Pharmacol 29:70–78
16. Ahn CB, Song CH, Kim WH, Kim YK (2002) Effects of Juglans sinensis Dode extract and antioxidant on mercury chloride-induced acute renal failure in rabbits. J Ethnopharmacol 82:45–49
17. Nava M, Romero F, Quiroz Y, Parra G, Bonet L, Rodriguez-Iturbe B (2000) Melatonin attenuates acute renal failure and oxidative stress induced by mercuric chloride in rats. Am J Physiol Ren Physiol 279:F910–F918

18. Gado AM, Aldahmash BA (2013) Antioxidant effect of Arabic gum against mercuric chloride-induced nephrotoxicity. Drug Des Devel Ther 7:1245–1252
19. Kumar D, Singh S, Singh AK, Rizvi SI (2013) Pomegranate (Punica granatum) peel extract provides protection against mercuric chloride-induced oxidative stress in Wistar strain rats. Pharm Biol 51:441–446
20. Tanguy S, Boucher F, Besse S, Toufektsian MC, Ducros V, Favier A, et al. (1999) Oral selenium supplementation in rats does not protect isolated rings of aorta against exogenous hydrogen peroxide. J Trace Elem Med Biol 13:238–241
21. Kouba A, Velisek J, Stara A, Masojidek J, Kozak P (2014) Supplementation with sodium selenite and selenium-enriched microalgae biomass show varying effects on blood enzymes activities, antioxidant response, and accumulation in common barbel (Barbus barbus). Biomed Res Int 2014:408270
22. Song E, Su C, Fu J, Xia X, Yang S, Xiao C, et al. (2014) Selenium supplementation shows protective effects against patulin-induced brain damage in mice via increases in GSH-related enzyme activity and expression. Life Sci 109:37–43
23. Ghadi FE, Ghara AR, Bhattacharyya S, Dhawan DK (2009) Selenium as a chemopreventive agent in experimentally induced colon carcinogenesis. World J Gastrointest Oncol 1:74–81
24. Agarwal R, Behari JR (2007a) Role of selenium in mercury intoxication in mice. Ind Health 45:388–395
25. Erkekoglu P, Rachidi W, De Rosa V, Giray B, Favier A, Hincal F (2010) Protective effect of selenium supplementation on the genotoxicity of di(2-ethylhexyl)phthalate and mono(2-ethylhexyl)phthalate treatment in LNCaP cells. Free Radic Biol Med 49:559–566
26. Bosse AC, Pallauf J, Hommel B, Sturm M, Fischer S, Wolf NM, et al. (2010) Impact of selenite and selenate on differentially expressed genes in rat liver examined by microarray analysis. Biosci Rep 30:293–306
27. Yu X, Xu X, Su J (2008) Protective effects of nanometer selenium on acute gastric mucosal lesion in rats. Wei Sheng Yan Jiu 37:594–596
28. Micke O, Schomburg L, Buentzel J, Kisters K, Muecke R (2009) Selenium in oncology: from chemistry to clinics. Molecules 14: 3975–3988
29. Dziaman T, Huzarski T, Gackowski D, Rozalski R, Siomek A, Szpila A, et al. (2009) Selenium supplementation reduced oxidative DNA damage in adnexectomized BRCA1 mutations carriers. Cancer Epidemiol Biomark Prev 18:2923–2928
30. Su L, Wang M, Yin ST, Wang HL, Chen L, Sun LG, et al. (2008) The interaction of selenium and mercury in the accumulations and oxidative stress of rat tissues. Ecotoxicol Environ Saf 70:483–489
31. Agarwal R, Behari JR (2007b) Effect of selenium pretreatment in chronic mercury intoxication in rats. Bull Environ Contam Toxicol 79:306–310
32. Diplock AT, Watkins WJ, Hewison M (1986) Selenium and heavy metals. Ann Clin Res 18:55–60
33. Goyer RA (1995) Nutrition and metal toxicity. Am J Clin Nutr 61: 646S–650S
34. Goyer RA, Cherian MG, Jones MM, Reigart JR (1995) Role of chelating agents for prevention, intervention, and treatment of exposures to toxic metals. Environ Health Perspect 103:1048–1052
35. El-Demerdash FM (2004) Antioxidant effect of vitamin E and selenium on lipid peroxidation, enzyme activities and biochemical parameters in rats exposed to aluminium. J Trace Elem Med Biol 18:113–121
36. Draper HH, Hadley M (1990) Malondialdehyde determination as index of lipid peroxidation. Methods Enzymol 186:421–431
37. Sun Y, Oberley LW, Li Y (1988) A simple method for clinical assay of superoxide dismutase. Clin Chem 34:497–500
38. Uzunhisarcikli M, Aslanturk A, Kalender S, Apaydin FG, Bas H (2015) Mercuric chloride induced hepatotoxic and hematologic changes in rats: the protective effects of sodium selenite and vitamin E. Toxicol Ind Health
39. Kalender S, Uzun FG, Demir F, Uzunhisarcikli M, Aslanturk A (2013) Mercuric chloride-induced testicular toxicity in rats and the protective role of sodium selenite and vitamin E. Food Chem Toxicol 55:456–462
40. Frouin H, Loseto LL, Stern GA, Haulena M, Ross PS (2012) Mercury toxicity in beluga whale lymphocytes: limited effects of selenium protection. Aquat Toxicol 109:185–193
41. Blanusa M, Orct T, Vihnanek Lazarus M, Sekovanic A, Piasek M (2012) Mercury disposition in suckling rats: comparative assessment following parenteral exposure to thiomersal and mercuric chloride. J Biomed Biotechnol 2012:256965
42. Yu D, Zhang ZW, Yao HD, Li S, Xu SW (2014) Antioxidative role of selenoprotein W in oxidant-induced chicken splenic lymphocyte death. Biometals 27:277–291
43. Joshi D, Mittal DK, Shukla S, Srivastav AK, Srivastav SK (2014) N-acetyl cysteine and selenium protects mercuric chloride-induced oxidative stress and antioxidant defense system in liver and kidney of rats: a histopathological approach. J Trace Elem Med Biol 28:218–226
44. Azevedo BF, Futuro Neto Hde A, Stefanon I, Vassallo DV (2011) Acute cardiorespiratory effects of intracisternal injections of mercuric chloride. Neurotoxicology 32:350–354
45. Pal M, Ghosh M (2012) Studies on comparative efficacy of alpha-linolenic acid and alpha-eleostearic acid on prevention of organic mercury-induced oxidative stress in kidney and liver of rat. Food Chem Toxicol 50:1066–1072
46. Houston MC (2011) Role of mercury toxicity in hypertension, cardiovascular disease, and stroke. J Clin Hypertens (Greenwich) 13:621–627
47. Zhu X, Guo K, Lu Y (2011) Selenium effectively inhibits 1,2-dihydroxynaphthalene-induced apoptosis in human lens epithelial cells through activation of PI3-K/Akt pathway. Mol Vis 17:2019–2027
48. Taskin E, Dursun N (2012) The protection of selenium on adriamycin-induced mitochondrial damage in rat. Biol Trace Elem Res 147:165–171
49. Liu Y, Li BH, Sun XM, Lin AH, Wang DB (2012) Effect of selenium on the interaction between daunorubicin and cardiac myosin. Biol Trace Elem Res 147:240–245
50. Dong JZ, Wang Y, Wang SH, Yin LP, Xu GJ, Zheng C, et al. (2013) Selenium increases chlorogenic acid, chlorophyll and carotenoids of Lycium chinense leaves. J Sci Food Agric 93:310–315
51. Yilmaz DM, Haciyakupoglu E, Haciyakupoglu S, Polat S, Ozgur H, Sencar L, et al. (2011) Effects of sodium selenite and amiloride on calvarial calcification in closing small cranial defects. J Neurosurg 114:478–484
52. Shi D, Guo S, Liao S, Su R, Guo M, Liu N, et al. (2012) Protection of selenium on hepatic mitochondrial respiratory control ratio and respiratory chain complex activities in ducklings intoxicated with aflatoxin B(1). Biol Trace Elem Res 145:312–317
53. Dong JZ, Lei C, Ai XR, Wang Y (2012) Selenium enrichment on Cordyceps militaris link and analysis on its main active components. Appl Biochem Biotechnol 166:1215–1224
54. Chen YC, Prabhu KS, Das A, Mastro AM (2013) Dietary selenium supplementation modifies breast tumor growth and metastasis. Int J Cancer 133:2054–2064
55. Schwartz LH, Urban T, Hercberg S (1994) Antioxidant minerals and vitamins. Role in cancer prevention. Presse Med 23:1826–1830
56. Ognjanovic BI, Markovic SD, Pavlovic SZ, Zikic RV, Stajn AS, Saicic ZS (2008) Effect of chronic cadmium exposure on antioxidant defense system in some tissues of rats: protective effect of selenium. Physiol Res 57:403–411
57. Yang H, Xu Z, Liu W, Deng Y, Xu B (2011) The protective role of procyanidins and lycopene against mercuric chloride renal damage in rats. Biomed Environ Sci 24:550–559
58. Leal ML, de Camargo EV, Ross DH, Molento MB, Lopes ST, da Rocha JB (2010) Effect of selenium and vitamin E on oxidative stress in lambs experimentally infected with Haemonchus contortus. Vet Res Commun 34:549–555