Punjab Univ. J. Zool., Vol. 30 (2), pp. 045-050, 2015

ISSN 1016-1597 (Print)
ISSN 2313-8556 (online)

Original Article

Effects of the selenium nanoparticles on the biomarkers of oxidative status in the Wistar rats spleen following the experimental cadmium toxicity

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(**Article history:** Received: November 13, 2015; Revised: December 03, 2015)

Abstract

Exposures to heavy metals in environment produce several harmful health effects. The generation of oxidative stress creates by the common mechanism their carcinogenicity and toxicity. The present study was planned to determine whether an oral administration of nano-selenium (nano-Se) influencing on biomarkers of oxidative status in the rats spleen exposed to the cadmium (Cd) metal. For this purpose, thirty male rats equally divided into six groups, group I received nano-Se (0.1mg/kg) alone as dose, group II selenite sodium (0.1mg Se/kg) alone, group III Cd chloride (300mg/250cc), group IV Cd along with nano-Se, group V Cd along with selenite sodium and group VI (control) given (1 ml) saline. All doses was orally (gavage) given to rates.Protein carbonyls (PC) andthiobarbituric acid reactive substances (TBARS),superoxide dismutase (SOD) glutathione peroxidase (GPx) and catalase (CAT) values in spleen were measured. An increase in TBARS and PC levels was obtained in rats' spleen of the Cd-group than controls and nano-Se decreased this effect close to the control. The CAT values of all groups did not differ significantly. The values of SOD and GPx were reduced in splenic tissue of Cd-intoxicated rats, but the nano-Se was able improve these undesirable effects. However, these findings imply that the nano-Se could be an efficient material in cases of Cd-intoxication.

Key words: Cd, oxidative stress, rat, intoxication, nano-Se

To cite this article: DEHORDI, S.K., MOHEBBI, A. AND SHAHANINPOUR, K., 2015. Effects of the selenium nanoparticles on the biomarkers of oxidative status in the Wistar rats spleen following the experimental cadmium toxicity. *Punjab Univ. J. Zool.,* **30**(2): 45-50.

INTRODUCTION

Heavy metals stimulate environmental pollution by sources like of the industrial effluents, leaded petrol and filter of metal ions. Of these, lead, cadmium and mercury are the most common pollution because of their prevalent usage in the industry (McIntyre, 2003**;** Jomova and Valko, 2011). Improper distribution between homeostasis of metal ions may because oxidative stress, a situation that increases the production of reactive oxygen species (ROS) defeating body antioxidant defense and, afterwards makes lipid peroxidation, DNA injury, protein change *etc* (Flora *et al.*, 2008). For redox inert metals, the toxicity mechanism included decline of glutathione and attachment to sulphydryl groups of proteins (Valko *et al.*, 2005). Cd is an immunotoxicant that has been stated to affect both cell mediated immunity and humoral immune response (Descotes, 1991; Dan *et al.*, 2000). The apoptotic potential of Cd causes suppression of B and T cell immune, as has been displayed by (Feng *et al.*, 2001). Cd always starts oxidation stages, therefore its major mechanism is the disturbance of electron exchange chain and the causing of mitochondrial ROS (Wang *et al.*, 2004). Researchers have presumed that efficient treatment for cadmium poisoning is antioxidants (Shaikh *et al.*, 1999**;** Casalino *et al.*, 2002). Spleen can recover the 0.55% of the administered cadmium dose within 5–10 min after a single intraperitoneal injection, while a subcutaneous injection caused in a maximal level of 0.08% after 40 min (Johnson and Miller, 1970). Selenium (Se) as a biocatalyst and functional component of numerous enzymes

27-PUJZ-51023111/15/0045-0050

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have a important function in thioredoxin reductase (Xia *et al.*, 2003), glutathione peroxidase (Rotruck *et al.*, 1973), and other enzymes as well as possesses anticarcinogenic effects (El-Bayoumy, 2001). Nano-Se has same effectiveness in increasing the activities of GPx in plasma and liver of mice compared with selenomethionine group (Wang *et al.*, 2007). The present study reports the effect of nano-Se on exposure with Cd in rats.

MATERIALS AND METHODS

Animals, experimental procedure and Chemical

Thirty male Wistar rats (*Rattus norvegicus albinus*) 2 month old and weighting 265±15 g, were used in the study after the approval of University Research Committee. They were kept in appropriate cages with 12 h-day/night at 22±1ºC.Animals were permitted *ad libitum* access to water and rodent's laboratory pellets, and underwent a 1-wek adaptation period. The animals were orally (gavage) given nano red selenium (group I, 0.1mg/kg BW), sodium selenite (group II, 0.1mg Se/kg BW), Cadmium chloride (group III, 300 mg/250 cc distilled water), cadmium along with nano red selenium (group IV) and cadmium along with sodium selenite (group V). The control group was given saline (group VI) for 30 consecutive days.The samples of spleen were collected by using dissection of abdominal cavity and its remove.

Assay

The malondialdehyde concentrations (MDA), thiobarbituric acid reactive substances (TBARS), were determined calorimetrically (Buege and Aust, 1978). The protein kit (Bio-Red) were used for total protein estimation. The concentration of protein carbonyl (PC) was determined based on the reaction of protein carbonyl with 2, 4-dinitrophenylhydrazine (Reznick and Packer, 1994). Total tissue superoxide dismutase (SOD) activity was measured following Sun *et al.* (1988). The inhibition of nitroblue tetrazolium (NBT) reduction was performed by xanthine–xanthine oxidase system as a superoxide generator. The enzyme activity included as one unit of SOD due to 50% inhibition in the NBT reduction rate. Tissue glutathione peroxidase (GPX) activity was calculated by Paglia and Valentine (1967) method (Paglia and Valentine, 1967). The serum CAT activity was assayed according to the method of Goth (1991).

Statistical analysis

One-way analysis of variance (ANOVA) followed by LSD post hoc test were used for analysis of data ($p<0.05$).

RESULTS

Effects of Cd on splenic TBARS, PC, FRAP, CAT, SOD and GPx in rats (*Rattus norvegicus albinus*) are given in Figures 1 to 6.
Tissue TBARS levels showed a significant increase in rats that received Cd (containing 300 mg/250 ml) compared with rats which received nano-Se, selenite sodium and Cd along with nano-Se and those in control group ($P<0.05$). However, there were no significant differences in TBARS value between other group neither with the controls nor with each other.

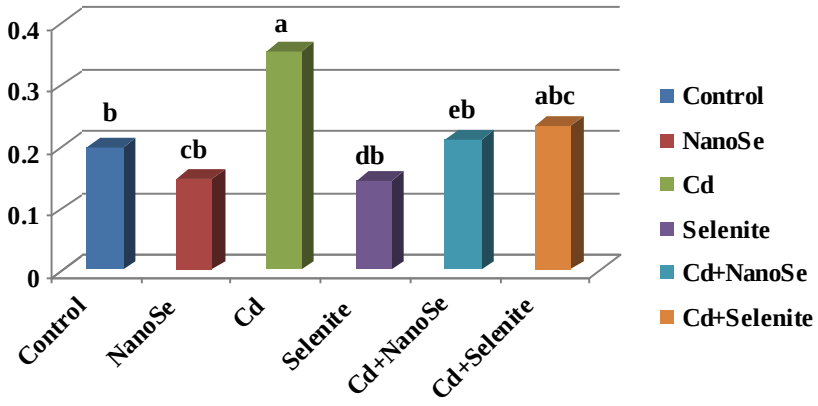

Figure 1: Thiobarbituric acid reactive substances (TBARS) levels in spleen rats. Group (bar) sharing a letter did not different significantly P>0.05.

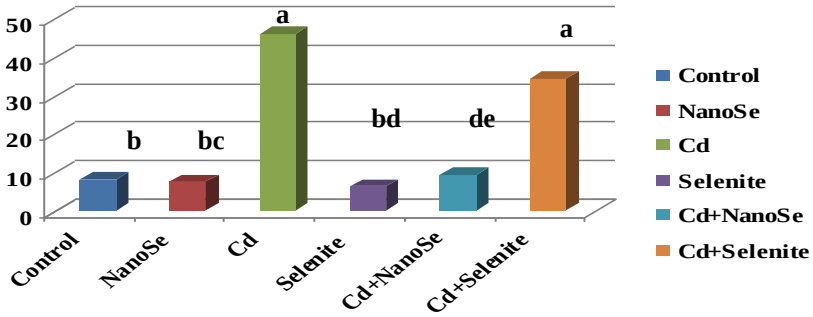

Figure 2: Protein carbonyl (PC) levels in rats that received Cd and nano-Se. Group (bar) sharing a letter did not different significantly P>0.05.

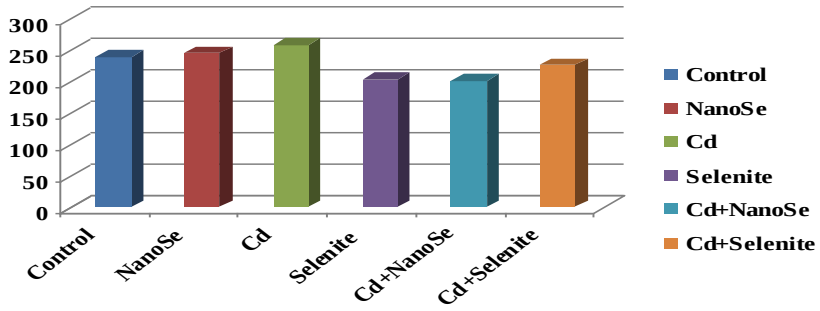

Figure 3: Catalase (CAT) levels in rats that received Cd and nano-Se.

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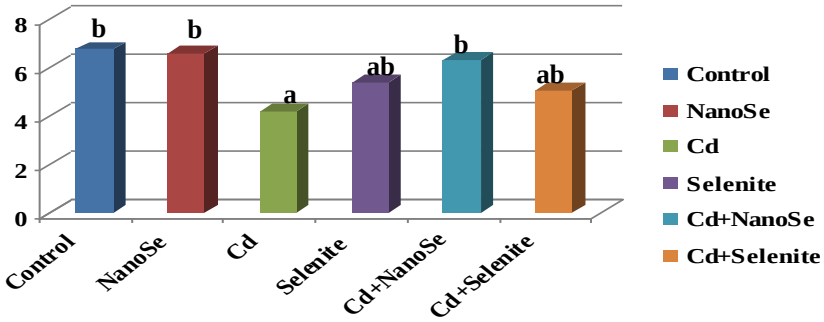

Figure 4: Superoxide dismutase (SOD) levels in rats that received Cd and nano-Se. Group (bar) sharing a letter did not different significantly P>0.05.

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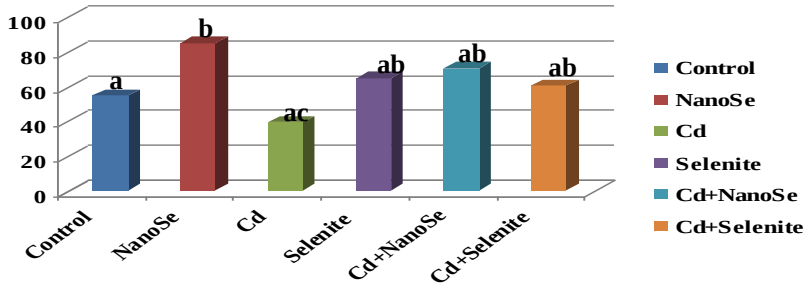

Figure 5: Glutathione peroxidase (GPx) levels in rats that received Cd and nano-Se. Group (bar) sharing a letter did not different significantly P>0.05.

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We observed a significant increase in the concentrations of carbonyl groups on plasma proteins (PC) in Cd-treated rats when compared with nano-Se and selenite sodium and those of controls, also there was a significant increase between cadmium along with selenite group with nano-Se, selenite sodium and controls groups ($P<0.05$). Cd along with nano-Se group displayed a significant decrease than Cd and nano-Se groups ($P<0.05$).

The CAT values of all groups significant different on the 30^{th} day but a significant decrease had occurred in SOD value in Cd group compared with the nano-Se, selenite sodium and cadmium along with nano-Se on the 30th day ($P<0.05$).In this study, the GPx value in group Cd was reduced after the 30^{th} day, but was increased in group nanoselenium ($P<0.05$

DISCUSSION

In often parts of word, receiving oral of environmental Cd is the fundamental source of exposure with this element. Mining activities and usage of Cd on farm land may conduct to the pollution of nutrients (Järup and Åkesson, 2009). Reports show that apoptosis process can begins in low Cd concentrations, which cell death occurs in some tissues due to generation of oxidative stress (Wätjen and Beyersmann, 2004). Obviously, understanding action process of Cd in experimental animals will prepare insight into its different effects in humans. Recognizing environmental symptoms of Cd, which can contribute to disturbances in enzymatic activities of the serum antioxidant, is a first step to prevention (Gonçalves *et al.*, 2010). In present investigation the animals orally poisoned with Cd and/or treated with nano-Se in order to assess its probable effects in spleen tissue. This study displayed that treatment with nanoselenium improve toxicity in rats spleen after exposure to Cd.

Spleen of rats exposed to Cd showed an increase in TBARS and CP levels, but when nanoselenium was co-administered Cd effects decreased. Similar to our finding, several studies show that Cd causes oxidative stress into tissue via increasing lipid peroxidation (TBARS)and using changing the antioxidant status (Manca *et al.*, 1991; Sarkar *et al.*, 1997).Harvest of the lipid oxidation is aldehydes and hydroperoxides such as malondialdehyde, which may be measured by reactions with thiobarbituric acid (TBARS) and comprising a functional index of lipid peroxidation (Ohkawa *et al.*, 1979).

One of the most important indexes of oxygen radical-mediated protein damage is protein carbonyl content that generates under different pathophysiological conditions (Gong *et al.*, 2008). Proteins that are oxidized in the reaction with transition metal ions can be generate additional radicals. Although oxidized proteins that product are functionally inactive and are eliminated, but progressively accumulate and cause damage (Kehrer, 2000).

Our finding obviously demonstrate that spleen tissue endured damages due to oxygen mediated protein as is apparent from increased protein carbonyl of the spleen tissue. This data also reveal that oxidized proteins are generated after exposure of experimental rats to Cd. The nano-Se seems that is very effective in scavenging the toxic free radicals; therefore protect the critical cellular proteins from oxidization. In this study, Cd exposure decreased significantly SOD and GPx levels without change in CAT values compared with controls ($P<0.05$). It seems that oxidative stress being one of the causes for spleen damages induced by Cd in this experimental model. Some previous reports have shown the principle role of oxidative stress in cell damages induced by Cd and other toxicants.

Cd can decrease the activities of antioxidative enzymes, including the glutathione and SOD and in this way it can induce the prooxidative state (Stohs *et al.*, 1999**;** Jurczuk *et al.*, 2004; Nemmiche *et al.*, 2007). The formation of reactive oxygen species (ROS) is stimulated by Cd that can causes lipid peroxidation into cellular membranes conducting to their loss of membrane functions and its destruction (Murugavel and Pari, 2007**;** Cuypers *et al.*, 2010). The decreasing activity of SOD and GPx in spleen reveals that the Cd-induced oxidative stress can be combined with a disruption of the enzymatic antioxidants (Valko *et al.*, 2006). A role of protective was noted at nano-Se function in present study, which not only causing reduction in TBARS and PC levels of Cd+nano-Se group, but also causing increases in SOD and GPx values of Cd+nano-Se group than Cd group and close to basal level (control). Control of oxidative stress and redox status of the cell can is performed by Se, due to its partnership as selenocysteine to GSH-Px (Segalés *et al.*, 2005) and thioredoxin reductase (Yu *et al.*, 2005).

It is worth noting that Se have a defensive effect against Cd by decreasing Cd content in the some tissues (Chen *et al.*, 1975). Zhang et al. (2005) is clearly demonstrated that nano-Se possess an interference effect on antioxidative balance in Se-deficient mice (Zhang et al., 2005).

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