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Effect of Boron on the Potassium Dichromate Induced Oxidative Damage in Brain Tissue of Sprague Dawley Rats

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ABSTRACT

In this study the effect of the trace mineral, boron (B) was determined on the potassium dichromate induced oxidative damage in the brain tissue of Sprague Dawley rats. Malondialdehyde (MDA) levels and activities of superoxide dismutase (SOD), catalase (CAT) and glutathione peroxidase (GSH-Px) enzymes were estimated in the brain tissues of the Sprague Dawley rats. Compared to the control groups, a significant increase in the brain tissue MDA level of the group which received only 10 mg/kg $K_2Cr_2O_7$ was observed, whereas no statistically significant change was detected in SOD, CAT and GSH-Px enzyme activities. It was further observed that after administration of Boron at 5 and 10 mg/kg the lipid peroxidation in brain tissue of $K_2Cr_2O_7$-treated rats decreased significantly, but no significant changes were observed in the levels of antioxidant enzyme. It can be concluded that administration of 5 and 10 mg/kg B may have beneficial effects against lipid peroxidation caused by $K_2Cr_2O_7$ in the brain tissue of rats.

INTRODUCTION

Two important forms of chromium, Cr(III) and Cr(VI) are biologically quite active chromium ions and Cr(VI) has a high toxicity for oxidative stress. Chromium (VI) which passes fast through anionic channels to spread in the cell is produced with industrial processes. In case of exposure, it reacts with the oxygen in the body causing serious damages such as allergic dermatitis, acute and chronic toxicity, neurotoxicity, dermatoxicity, genotoxicity, carcinogenicity and immunotoxicity (Akinwumi *et al*., 2016; Deraz *et al*., 2016; Dashti *et al*., 2016). Chromate ions [$(CrO4)^{-2}$] are neutral aqueous solutions of Cr(VI) and aggressive compound that can pass cell membrane through nonionic anionic channels (Bagchi *et al*., 1997). There are many studies that explain the effects of chromium forms on tissue damage (Stohs and Bagchi, 1995; Soudani *et al*., 2012; Bashandy *et al*., 2016; Wang *et al*., 2016). Zhang and Li (1987) reported in their epidemiological study conducted in Liaoning region of China that total cancer cases, stomach cancer and lung cancer cases increased as a result of contamination of water sources by a Cr mine in the region. Linos *et al*. (2011) reported that there was increase in liver, lung and kidney cancers as a result of contamination of water sources with Cr (VI) for at least 20 years in the Oinofita region of Greece. Especially Cr (VI) compounds such as potassium dichromate ($K_2Cr_2O_7$), sodium chromate and chromic acid are widely used in the leather industry, electro-coating industry, welding workshops, chrome coating industry and paint and coating industry. Chromium effects can be seen in the tests conducted with the blood, urine and some tissues of the people working in these industries. Lung and sinus cancer can develop when the person is exposed through inhalation and accidental or intentional high dose Cr exposure can cause potentially fatal respiratory, cardiovascular, gastrointestinal, hepatic, renal and neurological consequences. Additionally, it can have negative effects on reproduction and fetal development (Garcia-Nino *et al*., 2015).

Boron (B) is an essential element for humans and animals and it is considered to play an active role in various metabolisms in the body, have important functions in the brain together with the endocrine system, have effects of physical performance and have potential effect on bone tissue diseases such as osteoporosis, osteoarthritis (Nielsen, 1997). The daily B requirement of humans can be 0.5 mg/day (Nielsen *et al*.,1988). Boron is taken into the body with food and drinks, and through inhalation and skin (Becking *et al*., 1998). However, it is used for

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therapeutic purposes for skin diseases such as eczema and psoriasis (Demirtaş, 2010).

Penland (1994) concluded that daily intake of 3.25 mg B in post menopausal women led to an improvement in motor activities, reaction times, short and long term memory and memory skills. When taken in lower doses people were found to show lower levels of psychomotor and cognitive performance. Recent studies found that B has an important role in many mechanisms such as mineral metabolism, regulation of endocrine functions, vitamin D metabolism, bone metabolism and lipid metabolism in humans and animals and a positive effect on carbohydrate and protein structures (Hegsted *et al*.,1991; Rainey, 1999; Eren, 2004; Eren *et al*., 2006; 2012; Kurtoğlu *et al*., 2005; Çiftçi *et al*., 2013; Yıldız *et al*., 2013; Nielsen, 2014).

This study aims to determine the effect of the trace mineral B, on the oxidative stress caused by $K_2Cr_2O_7$ in Sprague Dawley rats.

MATERIALS AND METHODS

Animal material

The ethics approval for the study was obtained from the Animal Experiment Ethics Committee of Erciyes University in Turkey (ERÜ HADYEK) (decision no: 12/56 dated 11.04.2012). In this study, 60 Sprague-Dawley female rats (average weight 250-300g) obtained from the Experimental Research Center of Erciyes University Turkey were used. Rats were kept in the accommodation conditions for experimental animals at a controlled temperature (21±2 ˚C), humidity (50 ±5%), lighting (12 hours of light, 12 hours of darkness) and *ad libitum* feeding.

Study groups

Sixty female Sprague Dawley rats weighing 200-250 g, were divided into six groups of 10 in each group. The rats in the first group were given 2 ml distilled water and this group was assigned as the control group; 2nd group received 5 mg/kg (live weight)/day B; 3rd group received 10 mg/kg (live weight)/day B; 4th group received 10 mg/kg $K_2Cr_2O_7$; 5th group received 10 mg/kg $K_2Cr_2O_7$ + 5 mg/kg (live weight)/day B; 6th group $K_2Cr_2O_7$ + 10 mg/kg (live weight)/day B. Distilled water, $K_2Cr_2O_7$ and B (in boric acid form) were given to the animals via gavage for two weeks. $K_2Cr_2O_7$ dose used in the study was based on the results of the study of Mohammed and Saber (2011) while B doses used in this study were based on the results of the study of Price *et al*. (1997). Investigators determined that B supplement up to 10 mg/kg (live weight) would not have any adverse effect. Negative effects could be seen in doses exceeding 10 mg. No observed adverse effect level (NOAEL) was 10 mg B/kg live weight/day and the lowest observed adverse effect level (LOAEL) was 13 mg B/kg live weight/day at which toxicity signs might develop based on blood B levels.

Analysis methods

At the end of the experiment, animals were sacrificed under ketamine/xylazine anesthesia and their brain tissues were removed, washed with cold distilled water, homogenized in phosphate buffer pH 7.4 (Heidolph, Silent Crusher M), centrifuged at 15,000 rpm, at +4°C for 45 min and supernatant was transferred to eppendorf tubes. All samples were stored at -80°C until analysis.

Malondialdehyde levels and superoxide dismutase (SOD), catalase (CAT) and glutation peroxidase (GSH-Px) enzyme activities were measured in the brain tissue samples. Tissue MDA analyses were done with the method developed by Yoshioka *et al*. (1979) CAT analyses with the spectrophotometric method developed by Luck (1965), SOD activity analyses were done with the method reported by Sun *et al*. (1988), GSH-Px activity measurements were done with the spectrophotometric method developed by Paglie and Valentine (1967).

Statistical analyses of data were done with the SPSS 20.0 program for Microsoft. Differences between groups were determined with one way variance analysis (ANOVA). When F value was significant, Duncan's Multiple Range Test was conducted to identify the group the difference came from. Data are provided as the mean and standard error of mean.

RESULTS

Compared to the control groups, a significant increase ($P<0.001$) in the brain tissue MDA level of the group which received only $K_2Cr_2O_7$ was observed. These MDA levels which increased in the brain tissues of rats administered $K_2Cr_2O_7$ decreased significantly ($P<0.001$) with 5 and 10 mg/kg B administration. On the other hand the brain tissue SOD, CAT and GSH-Px enzyme activities of the group of rats that were administered only $K_2Cr_2O_7$ decreased though not statistically significant compared to the control groups. However, administration of 5 and 10 mg/kg B to the $K_2Cr_2O_7$ groups, although not statistically significant, increased these antioxidant enzyme activities to a level close to the values of the control group ($P>0.05$; Table I).

DISCUSSION

In recent years, studies which use herbal (Mohammed and Saber, 2011; Soyer-Sarıca and Liman, 2016),

Table I.- Effect of boron on $K_2Cr_2O_7$ induced oxidative stress parameters in brain tissue of Sprague Dawley rats.

Oxidative stress parameters	N	Control	Boron		$K_2Cr_2O_7$	$K_2Cr_2O_7$ + 5 mg/kg B	$K_2Cr_2O_7$ + 10 mg/kg B	F	P
			5 mg/kg	10 mg/kg					
MDA(nmol/mg-protein)	6	13.09±1.85[b]	13.48±1.64[b]	17.07±1.42[b]	24.74±1.88[a]	15.97±3.39[b]	11.84±1.47[b]	5.195	0.000***
SOD(U/mg-protein	6	4.97±0.88	3.91±0.52	4.04±0.36	3.83±0.33	4.40±0.62	5.21±0.81	0.871	0.512
CAT(katal/g-protein)	6	5.46±0.61	5.58±1.04	5.04±0.76	3.18±0.63	5.65±0.62	4.12±0.26	2.048	0.100
GSH-Px(U/g-protein)	6	26.59±10.64	36.05±4.92	35.78±4.02	23.27±3.13	32.10±5.38	31.99±5.99	0.683	0.640

[a,b], Values within each row with different superscripts differ significantly; ***, P<0.001
MDA, Malondialdeyde; SOD, Superoxide dismutase; CAT, Catalase; GSH-Px, Glutathione peroxidase.

xenobiotic (Kanbur *et al*., 2016) and mineral substances (Çolak *et al*., 2011; Eren and Şentürk, 2016) have been common as protective agents against environmental toxicity. Hexavalent Cr compounds are highly toxic and can penetrate into cells and cause cancerogenous, cytotoxicity, DNA destruction and lipid peroxidation (Rasool *et al*., 2014). Limited number of studies about the potential harmful effects of Cr(VI) on brain tissue was found (Travacio *et al*., 2001; Garcia-Nino *et al*., 2015; Dashti *et al*., 2016; Salama *et al*., 2016; Hao *et al*., 2017).

In the cerebellar granule neuron cell culture study (Dashti *et al*., 2016), mature and immature cerebellar cells were exposed to Cr and the investigators reported that mature cells were more affected by Cr exposure and their lipid peroxidation and GSH-Px activities increased.

Hao *et al*. (2016) orally administered $K_2Cr_2O_7$ (6% LD50) for 42 days and reported that it caused a histologically degenerative effect in brain cell structures. Additionally compared to the control group, there was a statistically significant increase in the MDA levels of the group that was administered $K_2Cr_2O_7$. These investigators concluded that long term exposure to Cr (VI) can cause histological changes and oxidative stress in the chicken brain and this can occur with the accumulation of Cr (VI) in the brain tissue. It is claimed that Hexavalent Cr compounds increase the production of nitric oxide and reactive oxygen species (ROS) which lead to an increase in MDA levels (Bagchi *et al*., 2001; Hao *et al*., 2016; Stohs and Bagchi, 1995).

Travacio *et al*. (2001) found a significant increase in brain tissue MDA levels when they gave 25 mg/kg $K_2Cr_2O_7$ with drinking water for 3 days. Rasool *et al*. (2014) found an increase in serum MDA levels, and a decrease in SOD, CAT and GSH-Px activities when male rats were orally administered 5 mg/kg $K_2Cr_2O_7$ for 30 and 60 days. Histopathologically, these investigators demonstrated that $K_2Cr_2O_7$ increased reactive oxygen species in rats' testicles causing a significant increase in lipid peroxidation.

Salama *et al*. (2016) intranasally administered three different doses of $K_2Cr_2O_7$ (0.5, 1 and 2 mg/kg, live weight) and reported that the highest brain MDA level was in 2 mg/kg group and no change was observed in other doses. In another study conducted in rats i.p administration of a single 15 mg/kg dose of $K_2Cr_2O_7$ triggered oxidative stress in liver (MDA, GSH, SOD, CAT levels) but did not cause oxidative stress and histopathological change in organs such as brain, heart, lung, kidney, spleen. In this study it was claimed that the fact that $K_2Cr_2O_7$ did not show any toxic effect in the above mentioned tissues could be associated with the administration method of the element, absorption through portal circulation, low dose or single dose administration, and how long it was administered (Garcia-Nino *et al*., 2015).

Boron trace element is considered to reduce oxidative stress when nicotinamide adenine dinucleotide phosphate (NADP) increases reduced glutathione (GSH) amount in cells (Uçkun, 2013). Hoang *et al*. (2017) reported that they provided protection from oxidative stress using a synthetic boric acid derivative mask they developed, by restricting angiogenesis stimulation which is effective in amyotrophic lateral sclerosis (ALS), a neurodegenerative disease.

Şahin *et al*. (2012) gave rats a normal diet, a high fat diet and a diet supplemented with B for 12 weeks and recorded that rats that consumed high fat diet had elevated levels of brain tissue MDA; and that these values in rats fed with the diet supplemented with B decreased similar to the control group. Çolak *et al*. (2011) administered 3.25, 36 and 58.5 mg/kg boric acid (4.375, 6.3 and 10.23 mg/kg, B) against the damage that aluminium chloride could cause in the brain. They reported that the lowest dose of boric acid had a protective effect on neurons in the brain tissue and in other doses it caused damage in the brain tissue. In another study, rats were administered different doses of B (5, 10 and 20 mg/kg/day) i.p against lipid peroxidation caused by cyclophosphamide and administration of B had a positive effect on the increased

MDA values and reduced antioxidant enzymes in the brain tissue after the cyclophosphamide administration (İnce *et al*., 2014). Çoban *et al*. (2015) demonstrated that oxidative stress in the tissues caused by 100 mg/kg/day malathion in rats could be prevented with different doses of B (5, 10 and 20 mg/kg/day).

Küçükkurt *et al*. (2015) administered 100 mg/kg B against adverse effects of arsenic given to male and female Wistar albino rats in drinking water for 28 days and reported a significant decrease in brain tissue MDA levels of the rats which were exposed to arsenic and B. These investigators determined that a decrease occurred in brain tissue SOD and CAT enzyme activities in male rats with arsenic administration and that administration of B did not have any effect on this decrease. Furthermore, they found that neither arsenic group not arsenic plus B group did not cause any change in these antioxidant enzymes in female rats. In another study, male Wistar albino rats which had diabetes induced with streptozotocin (STZ), 5 and 10 mg/kg (live weight) B (in boric acid form) significantly reduced serum MDA levels that were increased with diabetes but its effect on total antioxidant capacity was not statistically significant and just brought the total antioxidant capacity levels close to the the values in the control group and this could be due to the B's reducing effect on lipid peroxidation (Çakır *et al*., 2018). In this study, it was observed that brain tissue SOD, CAT and GSH-Px activities were not affected.

CONCLUSION

In conclusion, comparable to the findings of some studies (Travacio *et al*., 2001; Dashti *et al*., 2016; Salama *et al*., 2016; Hao *et al*., 2016), 10 mg/kg $K_2Cr_2O_7$ orally administered for two weeks in rats increased the production of reactive oxygen types and thus increased brain tissue MDA levels. On the other hand, increased brain tissue MDA levels caused by $K_2Cr_2O_7$ decreased after administering 5 and 10 mg/kg B due to the protective effect of this element against lipid peroxidation (İnce *et al*., 2014; Çoban *et al*., 2015; Küçükkurt *et al*., 2015; Çakır *et al*., 2018). The reason why $K_2Cr_2O_7$ did not have an adverse effect on antioxidant enzymes in the brain tissue, as also reported by Garcia-Nino *et al*. (2015) could be the administration method of this agent, its absorption through portal circulation, applied doses and for how long it was given. In conclusion B can have a protective effect against various agents that could cause oxidative stress.

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Statement of conflict of interest

Authors have declares that there is no conflict.

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