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# Effect of Sodium Tetraborate on Oxidative Damages in Heart Tissue in Chromium Intoxication

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**The cardioprotective effects of sodium tetraborate in chromium intoxication, correction of lipid profile and oxidative stress have been investigated. The experiment has been performed on 36 Wistar male rats, divided into 6 groups. I - control; II, III, and IV groups received potassium bichromate ($K_2Cr_2O_7$) 700 mg/l with drinking water; rats of the III and IV groups received additionally orally a solution of sodium tetraborate ($Na_2B_7O_7$) in doses of 22.5 mg/kg and 225 mg/kg per day, respectively. Animals of the V and VI groups received orally only $Na_2B_7O_7$ solution at the rate respectively 22.5 and 225 mg/kg weight per day. The study duration was 21 days. The introduction of $K_2Cr_2O_7$ increases content of malondialdehyde and carbonial protein in cardiac tissue, activates the antioxidant system of the heart, expands the levels of biomarkers of cardiotoxicity and increases the atherogenic index. The introduction of $Na_2B_7O_7$ (22.5 mg/kg) reduces the toxic effect of $K_2Cr_2O_7$ (cardioprotective effect). The use of $Na_2B_4O_7$ (225 mg/kg) does not give a positive effect. In the group receiving only $Na_2B_4O_7$ (22.5 mg/kg), inhibition of lipid oxidation and protein is observed, decrease of toxicity of biomarkers and low density lipoprotein-cholesterol (LDL-C), i.e. antioxidant effect. On the contrary $Na_2B_4O_7$ (225 mg/kg) shows the prooxidant property.**

**Keywords:** Potassium bichromate, Sodium tetraborate, Heart, rats, Oxidative stress, lipid profile, protective effect.

Every year thousands of people die from heart diseases worldwide. The causes of the disease are associated with the internal and external environment. In recent years, an increase of cardiovascular diseases associated with environmental pollution by heavy metals has been

observed[1]. In this aspect, hexavalent chromium presents a particular threat due to its high toxicity[2].

Chromium exists in the environment in three stable states - Cr (0), $Cr^{+3}$ and $Cr^{+6}$, which have different toxicity and transport characteristics[3]. $Cr^{+3}$ is an essential trace element for cells, potentiating the action of insulin[4] and is used in many nutritional supplements[5]. $Cr^{+6}$ is a major environmental toxin and a pollutant emitted by cigarette smoke, car emissions and hazardous waste[6]. Due to widespread industrial use and inappropriate waste disposal, the $Cr^{+6}$content in water, soil, and air leads to environmental pollution[7,8]. It is reported that $Cr^{+6}$ is the most toxic form, since it has a high oxidation potential, high solubility and mobility through membranes of living systems and in the environment[9], easily passes through cell membranes using non-specific anion transporters[10].

The toxic effects of chromium are widely believed to be associated with the stimulation of free radical processes, as well as the formation of intermediates in the reduction of $Cr^{+6}$, which have high reactivity[11]. Inside cells $Cr^{+6}$ are restored to reactive intermediates $Cr^{+5}$, $Cr^{+4}$ and $Cr^{+3}$ by cellular enzymatic or non-enzymatic reducing agents[12]. These reactive intermediates of chromium are able to generate reactive oxygen species (ROS)[13], which cause oxidation of macromolecules of proteins and lipids with damage to organs and systems[14-21], manifesting neuro, hepato, nephro, cardio -, geno - and immunotoxicity, carcinogenicity[21-25]. Recently, $Cr^{+6}$ began to attract particular attention as one of the potential cardiotoxic heavy metals[21,26,27].

The main role in the implementation of the damaging effect of oxidative stress is played by the hydroxyl radical. The damaging role of reactive oxygen species (ROS) is associated with the initiation of a cascade of processes leading to cell damage[28,29]. One consequence of oxidative stress is the irreversible modification of the protein with the formation of markers of oxidative damage to the protein - carbonyl protein (CP) and protein oxidation product (POP). According to[27,30,31], chromium induces protein oxidation in the organs of animals, including the heart of rats, mediating its cardiotoxic effects. Therefore, the use of antioxidants can be considered as an alternative method for the correction of induced oxidative damage.

As it is known, boron (B) is a widely recognized important component of the diet with numerous beneficial effects on health. Rapidly absorbed from the gastrointestinal tract into the blood and in physiological amounts affects a wide range of metabolic processes[32,33,34]. Boron, by inducing an antioxidant system[35], can destroy various oxygen radicals (ROS)[36,37,38]. Boron limits oxidative damage by increasing the body's antioxidant reserves (glutathione and its derivatives), or by inducing other neutralizing agents that react with reactive oxygen[39]. Pawa, Ali[40] suggests that his actions are aimed at maintaining the balance of prooxidant/antioxidant in the affected tissue. Boron compounds have anti-inflammatory, lipid-lowering, and anti-tumor actions[41,42], are not genotoxic[43], do not cause pathological changes in the myocardium[44], and do not affect the degree of myocardial damage after edema[45].

According to a number of scientists[46-49], boron compounds have protective effects on aluminum hepatotoxicity, titanium and aluminum genotoxicity, thioacetamide liver failure, and cyclophosphamide-induced lipid peroxidation and genotoxicity.

As far as we know, the protective effects of boron compounds with chromium-induced cardiotoxicity have not been studied, remain open.

## MATERIALS AND METHODS

The work was performed on 36 Wistar male rats weighing 170-190 g. The animals were kept in the vivarium of the Central Research Laboratory of the West Kazakhstan Marat Ospanov State Medical University (Aktobe, the Republic of Kazakhstan) in standard conditions with free access to food and water. The experiments were carried out in accordance with the European Convention for the Protection of Vertebrate Animals used for experimental and other purposes (Strasbourg, 1986). The program of the experiment was discussed and approved by the regional ethics committee of the university.

In 10 days after acclimatization animals were randomly divided into 6 groups (6 rats in each group). Group I - control, animals of groups II, III and IV received potassium bichromate with drinking water ($K_2Cr_2O_7$ - Chemistry and Technology Ltd, Kazakhstan) (700 mg/l). The

rats of the III and IV groups received additionally sodium tetraborate ($Na_2B_7O_7$ — Joint-Stock Company *Farmak*, Ukraine), respectively, in doses of 22.5 mg/kg and 225 mg/kg per day. Animals of the V and VI groups received a solution of $Na_2B_7O_7$ at the rate of 22.5 mg/kg and 225 mg/kg per day, respectively. The duration of the experiment is 21 days.

The choice of the type of compounds of boron and chromium, doses and methods of administration, the duration is justified according to the literature[21,27,44]. Euthanasia of animals in all groups was carried out at the end of the experimental period by the method of cervical instantaneous decapitation under light ether anesthesia to avoid stress. Blood was collected in tubes and centrifuged at 2200g for 10 minutes. Serum samples were collected and stored at - 80° C until analysis. The heart was obtained by dissecting the chest, placed in cold phosphate buffered saline to remove excess blood, and ground, homogenized in Tris-HCL buffer (pH = 7.4), and centrifuged. The resulting supernatants were kept at 80° C and used for biochemical analyses.

**Biochemical studies**

The activity of marker enzymes alanine aminotransferase (ALAT), aspartate aminotransferase (ASAT), lactatdegidrogenezy (LDH), creatine kinase activity (IC) and lipid profile, total cholesterol (TC), triglyceride (TG), cholesterol LDL density (LDL-C), high-density cholesterol lipoproteins (HDL-C) on the biochemical analyzer *Architect c4000* (Abbott, USA) were determined by using a standard set of reagents in the serum. Relations were also calculated: Atheroegenix Index (Al) = TC – HDL-C/HDL-C; TC/HDL-C and LDL-C/HDL-C.

The content of malon dialdehyde (MDA) in the heart tissues was determined spectrophotometrically by the method of Draper and Hadley[50]. The essence of the method: at high temperature in an acidic medium, MDA reacts with 2-thiobarbaturic acid, forming a colored complex with an absorption maximum at 532 nm. The molar extinction coefficient is $1.56*10^{-5}cmM^{-1}$. MDA level expressed in nmol/mg protein (nmol/mg Pt.)

The content of carbonyl proteins (CP) of the heart was measured by a method based on the reaction of carbonyls with dinitrophenylhydrazine (DNPH), which forms the last yellow compound recorded spectrophotometrically at 370 nm[51]. The carbonyl content was calculated based on the molar extinction coefficient of DNPH ($E=2.2*10^4cm^{-1}M^{-1}$) and expressed nmol/mg protein (nmol/mg protein).

**Antioxidant status of the heart**

Catalase activity (CAT) was measured according to the method[52]. The reaction was started by adding 2.0 ml of hydrogen peroxide to 10 ìl of the supernatant and after 10 minutes it was stopped by adding 1.0 ml of 4% ammonium molybdate. Sample absorption was measured at 410 nm. Activity was expressed in ìmol $Í_2Î_2$ degraded/min/mg/protein (ìmol/min/mgPt - ìmoles $Í_2Î_2$ degraded/min/mg protein).

The activity of superoxide dismutase (SOD) was evaluated by the method of Beauchamp and Fridovich[53]. The method is based on registrations of the change in the rate of reduction of nitro blue tetrazole (NBT) in the presence of reduced nicotinamide adenine dinucleotide and phenazine metasulfate. Optical density was measured at 560 nm. Per unit of SOD activity, this amount of enzyme was taken to be necessary for inhibiting the reduction of NBT by 50% and the activity was expressed in mg of protein (U/Pt).

Glutathione peroxidase (GPx) activity was measured by the Flohe and Gunzler method[54]. Enzyme activity is expressed as nmoles of the oxidized amount of reduced glutathione (GSH) - nmoles of GSN/min/mg/protein.

The level of glutathione in the heart was determined by the method of Ellman [55] in a modification of Jollow et al.[56], based on the formation of yellow staining, when DTNB (5,5-dithiobis 2-nitrobenzoic acid) is added to the sample containing SH-groups. The extinction was measured at 412 nm. The number is expressed in µg/mg protein. The content of non-protein thiol (NPSH) was determined by the Ellman method[55], and the amount was expressed as nmol/mg protein.

The protein content was determined according to the method of Lowry et al.[57] using bovine serum albumin as a standard.

**Statistical analysis**

Statistical data processing was performed using the Statistica 10 software package from StatSoft, Inc USA. The null hypothesis about the absence of differences between the observed distributions was tested using the W-test Shapiro-

Wilk. Evaluation of the differences between the samples was carried out: with a normal distribution of paired variables using Student's t-test, and ANOVA in the case of multiple independent ones. The average arithmetic values of the quantitative indicators presented in the text were calculated as M±m, where **M** is the arithmetic values, **m** is the average error. In all procedures of statistical analysis, the level of significance was taken as pd"0.05.

## RESULTS

Assessment of MDA and CP levels. Under the influence of potassium bichromate, there was an increase in the content of MDA (+50%) and CP (+107.5%) in the heart of rats compared with the data of the control group (Table 1). Co-administration of the tetraborate in the studied (22.5 mg/kg and 225 mg/kg) doses led to a noticeable decrease in the level of MDA (by 23 and 12.4%, respectively) in comparison with rats subjected to $K_2Cr_2O_7$, and the level of PCO decreased, respectively, by 21.5 and 9%.

**Non-enzymatic antioxidant status (AOS)**

In animals exposed to $K_2Cr_2O_7$, the amount of GSH (in the heart) remained at the level of the control data, and NPSH increased by 40.8% (Table 2). With the combined effects of $K_2Cr_2O_7$ and $Na_2B_4O_7$ (at a low dose), the content of GSH and NPSH increased by 34.6% and 13%, respectively, compared to the control, while at a high dose, $Na_2B_4O_7$ decreased by 23 and 6%.

**Enzyme link of antioxidant status**

Exposure to $K_2Cr_2O_7$ resulted in a significant increase in SOD, CAT, GPx activity (+20.5, +129.7, and +36.4%, respectively) in the heart tissue of animals compared to control data (Table 2). When administered together, boron in a low dose caused a decrease in SOD, CAT, GPx activity (by 9, 37.7, and 20%, respectively) in comparison with the data of animals treated with $K_2Cr_2O_7$. Whereas, at a high dose of boron, SOD and GPx activity increased (by 4.5 and 11%, respectively), while CAT activity decreased by 21.5% in comparison with data from rats subjected to $K_2Cr_2O_7$, but increased compared to data from rats treated Cr and B in a low dose of 26%.

**Biomarkers of cardiotoxicity**

Plasma ALAT, ASAT, LDH, and CK activity increased in the group receiving $K_2Cr_2O_7$ by 30, 76, 43, and 119.6% compared with the control (Table 3). In the second group, the ALAT, ASAT, LDH and CK activity decreased by 35, 51,

**Table 1.** Effect of $Na_2B_4O_7$ on the content of malonic dialdehyde and carbonyl protein in cardiac tissue with chromium-induced cardiotoxicity

| Indicators | Animal groups | | | | | |
|---|---|---|---|---|---|---|
| | Control | II | III | IV | V | VI |
| MDA, nmol/mg/protein | 1,4±0,05 | 2.1±0.12* | 1.62±0.06*$_0$ | 1.86±0.14* | 1.17±0.04* | 1.6±0.07* |
| CP, nmol/mg/protein | 0.80±0.033 | 1.66±0.061* | 1.32±0.05*$_0$ | 1.51±0.06* | 0.77±0.03 | 0.94±0.04 |

Units: * - p <0.05 compared with the control group, $^0$ – p<0.05 compared to $K_2Cr_2O_7$ data

**Table 2.** Effect of $Na_2B_4O_7$ on the antioxidant system of the heart during chromium-induced cardiotoxicity

| Indicators | Control | II | III | IV | V | VI |
|---|---|---|---|---|---|---|
| COD[a] | 55.6±1.6 | 67±1.9* | 61±1.8*$_0$ | 70±3.3* | 70±2.1* | 80±3.0* |
| KAT[b] | 56.6±3.6 | 130±5.2* | 81±4.0*$_0$ | 102±5.0*$_0$ | 70±2.4* | 89±3.0* |
| GPx[c] | 22±1.26 | 30±1.5* | 24±1.31$_0$ | 33±1.5* | 20±1.1 | 26±2.0 |
| GSH[d] | 5.2±0.11 | 5.0±0.15 | 7.0±0.16*$_0$ | 4.0±0.1* | 6.3±0.13* | 5.7±0.12* |
| NPSH[e] | 21.3±1.12 | 30±2.1* | 24±1.6$_0$ | 20±1.1$_0$ | 27±1.8* | 24±1.3 |

Units: * - p <0.05 compared with the control group, $^0$ – p<0.05 compared to $K_2Cr_2O_7$ data
a – U/mg protein; b – ìmoles $H_2O_2$ degraded/min/mg protein; c – nmoles of GSH/min/mg protein; d – ìg/mg protein; e – nmoles/mg/ protein.

55 and 36.6%, respectively, compared to the third group, and with the control data, the activity of ALAT, ASAT and LDH decreased by 15, 14, 36%, respectively. The use of sodium tetraborate in a high dose of the activity of the studied enzymes decreased significantly (by 30, 35.5 and 51%, respectively) compared with rats subjected to $K_2Cr_2O_7$. However, in comparison with the data of the control group, the activity of ALAT, ASAT and CK were significantly increased (by 25, 22.7 and 9%, respectively).

**Effect of $K_2Cr_2O_7$ on the lipid profile**

In rats affected with $K_2Cr_2O_7$, significant increases in total cholesterol levels were observed - TS (+21%), TG triglyceride (112%), LDL-C (100%). The coefficients TC/HLC-C, LDL-C and AI increased (by 37.3, 125 and 66.7%, respectively) compared to the control (Table 4). The combined use of $Na_2B_4O_7$ in the doses studied led to a significant decrease in all indicators compared with rats receiving $K_2Cr_2O_7$ almost to control values, except for the level of TG, LDL-C and LDL-C / HDL-C. The last indicators, both with low and high doses of borax, remained higher than the control ones by 53.6 and 31.8%; 57 and 71% and 60 and 75%, respectively.

Analysis of the data obtained shows that the effect of borax in the conditions of their isolated application on the studied biochemical parameters has a difference (Tables 1–4). Thus, low-dose sodium tetraborate causes a significant decrease in MDA (by 16.4%) against the background of an increase in SOD activity, CAT (26 and 23.7%), GSH and NPSH levels (by 21 and 26.8%), then a high dose, an increase in MDA (14.3%) occurs against the background of a significant (even greater) activation of the AOC enzyme link (COD, CAT, GPx +43.9; +57 and + 18.2%, respectively) and several (restraining) inhibition of non-enzymatic - an increase in the level of GSH and NPSH only by 9.6 and 12.7%, respectively.

Biomarkers of cardiotoxicity. ALAT, ASAT and CK activity under the influence of boron at a low dose significantly reduced by 20, 25 and 9.4%, while at a high dose, ALAT and ASAT activity increased by 20 and 27% compared to the control. A high dose of boron inhibits LDH activity by 41.3%, and a low one does not affect.

**Table 3.** Effect of $Na_2B_7O_7$ on biomarkers of cardiotoxicity of rats exposed to $K_2Cr_2O_7$

| | ALAT (U/L) | ASAT (U/L) | LDH (U/L) | CK (U/L) |
|---|---|---|---|---|
| Control | 40±1.2 | 66±1.2 | 150±21 | 138±1.0 |
| II | 52±1.4* | 116±6.3* | 214±23* | 303±2.1* |
| III | 34±2.0*$_0$ | 57±1.6*$_0$ | 96±7.0*$_0$ | 192±3.0*$_0$ |
| IV | 50±2.3* | 81±6.6*$_0$ | 138±8.0$_0$ | 150±1.6*$_0$ |
| V | 30±1.0* | 50±0.8* | 127±6.0 | 125±1.2* |
| VI | 48±1.4* | 84±7.2* | 79±8.0* | 140±2.2 |

Units: * - p <0.05 compared with the control group, $^0$ – p<0.05 compared to $K_2Cr_2O_7$ data

**Table 4.** The effect of $Na_2B_7O_7$ on the lipid profile of the plasma of rats with chromium-induced cardiotoxicity

| Indicators | Control | II | III | IV | V | VI |
|---|---|---|---|---|---|---|
| Total Cholesterol | 1.14±0.075 | 1.38±0.081* | 1.15±0.08$_0$ | 1.1±0.08$_0$ | 1.0±0.06 | 0.97±0.063 |
| Triglycerides | 1.1±0.06 | 2.33±0.08* | 1.69±0.07*$_0$ | 1.45±0.07*$_0$ | 0.97±0.08 | 0.93±0.057* |
| HDL-Ñ | 0.52±0.041 | 0.45±0.04 | 0.52±0.05 | 0.5±0.06 | 0.46±0.04 | 0.5±0.06 |
| LDL-Ñ | 0.21±0.013 | 0.42±0.04* | 0.33±0.03*$_0$ | 0.36±0.033* | 0.16±0.011* | 0.26±0.015* |
| Atherogenix Index | 1.26±0.1 | 2.1±0.016* | 1.25±0.1$_0$ | 1.2±0.08$_0$ | 1.17±0.09 | 0.96±0.083* |
| TC/HDL-C | 2.2±0.16 | 3.02±0.21* | 2.28±0.18$_0$ | 2.2±0.15 | 2.17±0.11 | 1.94±0.12 |
| LDL-C/HDL-C | 0.4±0.03 | 0.9±0.04* | 0.64±0.043*$_0$ | 0.7±0.06*$_0$ | 0.38±0.03 | 0.52±0.036* |

Units: * - p <0.05 compared with the control group, $^0$ – p<0.05 compared to $K_2Cr_2O_7$ data

Lipid profile change - low dose of boron reduces LDL-C by 24%, high - increases LDC-C by 24%. However, with a high dose, the ratio (LDL-C)/(HDL-C) increases by 30%; AI decreases by 24%.

## DISCUSSION

$Cr^{+6}$ is characterized by a wide range of toxicological disorders and physiological and biochemical dysfunctions, which are accompanied by a number of clinical complications, including cardiotoxic effects[21,26,27]. Chromium ions, being a transition metal, can stimulate the processes of free radicals in living systems[58,59]. $Cr^{+6}$ and its compounds do not directly generate free radicals, however, when $Cr^{+6}$ is reduced in $Cr^{+3}$, as well as by Haber-Weiss and Fenton[11,60] mechanisms, various radicals such as superoxide anion, peroxynitrite, nitrous oxide and hydroxyl, which cause damage characteristic of stress[11,61], activate POL, oxidation of the protein and lead to destabilization and disintegration of cell membranes, including myocardial membranes[26], i.e. causes the expression of ROS in the heart and myocardial cells, which leads to a decrease in the function of the cardiovascular system.

In the present study, the effect of $Cr^{+6}$ on rats through drinking water led to a significant increase in lipid and protein oxidation in the heart tissue, which is characterized by a significant increase in the levels of MDA and CP, and are consistent with previously obtained results[20,21,27]. However, under conditions of combined exposure to $Cr^{+6}$ and borax (in low and high doses) there was a decrease in the levels of these parameters. It was interesting that co-processing of the brown leaf visibly protected the rats from chromium-induced POL, indicating its radical cleansing activity and the mechanism of chain disruption. In previous studies[62], we found that low-dose sodium tetraborate inhibited chromium-induced lipid peroxidation in the brain, and high in contrast, stimulates FRO lipids, i.e. borax at a low dose showed an antioxidant effect. It should be noted that the effect of weakening protein oxidation with tetraborate (decreasing the CP) was first shown in this study.

Early studies have shown that chromium exposure induces protein oxidation in several organs of experimental animals, in tissues like the uterus and ovaries of female rats[63], mice[31] and rat lungs[30]. Due to the increase in POL, the biological membranes of the internal organs (liver, kidneys, heart, and others) are affected, which leads to a loss of their fluidity and an increase in their permeability. The activity of transaminases, lactate dehydrogenases and creatine kinases, which are reliable markers of damage to the heart muscles increases. According to[21,64,65], an increase in plasma ASAT, LDT and CK levels can be attributed to a generalized increase in membrane permeability. The results of our study showed that ASAT, ALAT, LDH and CK activities in the blood plasma of rats treated with potassium bichromate were significantly increased. Sodium tetraborate in both low and high doses prevented the leakage of the enzymes studied, with the exception of ALAT, to a greater degree in the low; while ALAT activity in high-dose borax conditions was high against potassium dichromate.

It should be noted that sodium tetraborate with isolated use in a low dose significantly reduced the level of ALAT, ASAT, LDH and CK compared with the control, and high - the activity of these enzymes, with the exception of CK, significantly increased. It is well known that an elevated level of ASAT and ALAT enzymes indicates a myocardial injury. Significant increases in ASAT activity are associated with damage to the liver and myocardium. The higher the ASAT, the larger the size of myocardial injury. These results show that if $Cr^{+6}$ is taken for a long time, it can cause damage to the liver, as well as the heart. Damage to cardiac tissue may be associated with increased oxidative stress and depletion of antioxidants. Our results show that sodium tetraborate, especially at a low dose, plays a key role in reducing the damage to the tissues of internal organs, by reducing and preventing oxidative damage caused by potassium bichromate, due to its powerful antioxidant potential, which provides membrane stabilization[62].

In the current experiment, a change in the non-enzymatic level of AOC was established, especially the content of NPSH increased significantly; GSH level remained at the control level. Thiol-based AOCs form the second line of cellular defense against free radicals. These changes in the enzymatic and non-enzymatic level of AOS against the background of an increase in MDA, apparently, are adaptive in nature. Glutathione

(GSH), the most common low molecular weight thiol, acts as a protective physiological antioxidant in biosystems[67] and functions as a direct reactive acceptor of free radicals. In rats receiving only sodium tetraborate with drinking water, an increase in GSH and NPSH was observed in the subjects (22.5 and 225 mg/kg) in comparison with the control data; under low-dose boron administration, the level of MDA decreased, while the levels of MDA and POC at the background of activation of the AOC enzymatic level increased at high doses.

In the present study, in rats treated with a combination of chromium and tetraborate, sodium, the level of GSH increased only under conditions of co-administration of borax in a low dose compared with control data, and with data of animals exposed to chromium alone. While a high dose of boron under combination conditions caused a decrease in GSH in comparison with the control. The level of NPSH remained within the control, and significantly decreased in rats with chromium-induced cardiotoxicity (to a greater extent under conditions of using a high dose of borax). The increase in GSH and NPSH levels in rats treated with a combination of $Cr^{+6}$ and boron can be explained by the antioxidant activity of boron compounds[62,68]. Preventing a decrease and increase in GSH and NPSH levels can be part of the cardioprotective mechanism of boron compounds.

The lipid profile in rats treated with potassium bichromate showed significant changes. Fluctuation in the lipid profile is very important for monitoring cases of cardiovascular diseases. The concentration of total cholesterol (TC), triglycerides (TG), LDL-C and HDL-C are independent, but are significant predictors of CVD risk[69].

Studies[70] have shown that increasing the concentration of LDL–C means oxidative stress. It is believed that lipids are among the most sensitive biomolecules in terms of susceptibility to ROC. Increased cholesterol levels in rats exposed to $Cr^{+6}$ may be associated with impaired lipid metabolism. Low-density cholesterol lipoprotein (LDL-C) increases, and high-density lipoprotein cholesterol (HDL-C) decreases, indicating that the change in lipase enzyme activity appears to be one of the main factors contributing to increased cholesterol levels. Our data showed that in animals that received potassium dichromate with drinking water, besides AI (atherogenic index), the ratios (LDL-C)/(HDL-C) and TC/HDL, considered[71], as corresponding indicators of cardiovascular vascular risk (atherosclerotic index). According to[21], an increase in cholesterol and triglycerides in the blood plasma of animals that received chromate with drinking water is explained by the development of oxidative stress.

In vitro and in vivo studies have shown that boron compounds (boric acid and borax) show significant antioxidant, hypolipid and antitumor effects[35,41,42]. Under conditions of isolated injection of borax, only the level of lipoprotein - low density cholesterol (LDL-H) decreased significantly, compared to the control group, while conditions of high - significantly increased this indicator (LDL-H) and the ratio LDL-Ñ/ÍDL-C. Obviously, borax with co-administration with potassium biochromate can successfully influence changes in the lipid profile due to $Cr^{+6}$ and reduce the levels of cholesterol, triglyceride, and others, especially at low doses, and exhibit atherogenic effects. Probably, boron acts as an antioxidant and inhibits the oxidative processes of lipids and lipoproteins in cell membranes.

## CONCLUSIONS

Oxidative stress induced by $Cr^{+6}$ in rat cardiac tissue may be responsible for changes in antioxidant status, oxidation of lipids, proteins, and lipid profile disorders. Sodium tetraborate (borax), depending on the dose (at a low level of 22.5 mg/kg body weight), can protect the heart from chromium-induced damage. However, when co-administered with a high dose of sodium tetraborate with chromium, there is no weakening of the cardiotoxic effect. Sodium tetraborate in a low dose with an isolated application shows an antioxidant effect, in a high - prooxidant.

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