Investigation Of Antioxidant System Activity In Rats Liver Exposed To Ammonium Metavanadate And/ Or Nickel Sulfate

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ABSTRACT

The present study was designed to investigate the in vivo effects of ammonium metavanadate (0.15 and 0.30 mg V/ml) and/or nickel sulfate (0.18 and 0.36 mg Ni/ml) in liver of male albino rats. The antioxidative indices including oxidative lipid peroxidation (LPO) and antioxidative enzymes such as superoxide dismutase (SOD), glutathione (GSH) and glutathione-s-transferase (GST) in the liver were investigated, as well as alanine aminotransferase (ALT) and aspartate aminotransferase (AST) in the serum were also measured after 28-day period. The administration of vanadium or nickel alone caused a significant (p<0.01) decrease in fluid intake, body weight gain, SOD and GST activities compared to the controls. Concomitantly significant (p<0.001) increase in the LPO level and the activities of ALT and AST were obtained. GSH content decreased (p<0.001) in rats treated with vanadium and increased (p<0.001) in rats treated with nickel. When the metals were administered in combination, the induction on the lipid peroxidation did not potentiate at the low concentration and decreased at the high concentration (p<0.001) whereas the decrease in the SOD activity was augmented (p<0.001) at both concentrations. The depressions of the GSH level observed by vanadium and GST activity observed by vanadium and nickel were significantly ameliorated by the combined treatment. Signs of toxicity were observed in vanadium alone-treated animals as evidenced by some death and decreased weight gain. The data obtained indicated that vanadium and nickel alone both induced oxidative stress in hepatic tissue, but the oxidative capacity is more profound by vanadium. Combined effect of vanadium-nickel is slightly less toxic than vanadium or nickel alone, suggesting antagonism between these toxicants.

Key words: vanadium, nickel, lipid peroxidation, antioxidative enzymes, alanine aminotransferase, aspartate aminotransferase, rats

Introduction

In recent years, studies on impact of trace heavy metals have continued to assume increasing relevance as beside the beneficial action of these metals they are stable and persistent environmental contaminants. The heavy metals, vanadium and nickel are widely found in our environment due to their environmental pervasiveness. Vanadium is a naturally occurring ubiquitous transition metal usually found in high concentrations in the earth’s crust, oceans, soil and fossil fuels [1]. Despite the fact that some studies showed its beneficial pharmaceutical effects, vanadium therapeutic exposure and the exposure associated with taking vanadium supplements, especially those which can provide more than 10mgV/day [1,2], should be taken into consideration. Long-term intake of even small doses of vanadium could be toxic; no recommended dietary allowance has been clearly established [3] as prolonged consumption of dietary supplements (not recommended) containing vanadium at milligram levels has been reported to lead to mild side effects such as nausea, vomiting and diarrhea and also cause serious kidney and liver toxicity [4].

There has also been a growing interest in nickel (Ni); nickel is a metallic element that is naturally present in the earth’s crust. Due to unique physical and chemical properties, metallic nickel and its compounds are widely used in modern industry. The high consumption of nickel-containing products inevitably leads to environmental pollution by nickel and its by-products at all stages of production, recycling and disposal. The salts of nickel as particles of nickel can be allergens and carcinogens in man while forming the oxygenated radicals.
Materials And Methods

Reagents:

The kits for glutathione (GSH), superoxide dismutase (SOD), glutathione-S-transferase (GST) were obtained from Cayman chemical, E. Ellsworth Road, Ann Arbor, USA. Alanine aminotransferase (ALT) and aspartate aminotransferase (AST) kits were obtained from Vital Diagnostics SPb, Prospect Engelsa 27 St., Saint-Petersburg, Russian. 2-thiobarbituric acid (TBA), Trichloroacetic acid (TCA) and Ethylene diaminetetraacetic acid (EDTA) were obtained from Sigma Chemicals, St. Louis, USA. Ammonium metavanadate (NH₄VO₃), nickel sulfate (NiSO₄.7H₂O) and other chemicals used were purchased from high commercial company from Almaty, Kazakhstan.

Experimental design:

Outbred 6-month-old male albino rats with a body weight of 223-235 g were housed according to the ethical rules in compliance with institutional guidelines. Rats were kept in plastic cages and placed in a well-ventilated rat house (humidity was around 70 %, temperature was 21 ± 2 °C and 12 h light/dark cycle) and fed with commercial pellets (protein 21%, fat 6.78%, fiber 3.26%, salts and vitamins) and water ad libitum. The acclimated animals were segregated into seven different groups of six animals each. Group I (C) served as control, Group II (V₁) and III (V₂) animals were treated with ammonium metavanadate (AMV) at concentrations of 0.15 and 30 mg V/ml. Group IV (N₁) and V (N₂) animals were treated with nickel sulfate (NiSO₄.H₂O at concentrations of 0.18 and 0.36 mg Ni/ml respectively. Group VI (V₁ + N₁) and VII (V₂ + N₂) animals were given combined treatment of vanadium and nickel at both concentrations respectively. The treatments were given orally to the experimental animals for 28 day. The control animals were provided with deionized water. pH of AMV solution administered to rats in drinking water was about (6.97 ± 0.02). During the whole experiment food, fluids and water intake were monitored daily and body weight gain was checked weekly. Vanadium and nickel concentration in drinking water was chosen on the basis of previous studies of other authors [9,10] and [11,12], respectively.

Blood samples were taken by puncturing the retroorbital plexus of anaesthetized rats into plastic tubes with heparin as an anticoagulant. The collected blood samples were kept at room temperature for 30 min and then were centrifuged at 2000 rpm for 10–15 min to separate the serum. Serum was used for the estimation of the liver marker enzymes aspartate aminotransferase (AST) and alanine aminotransferase (ALT). Then the animals were sacrificed by exsanguination under light anesthesia. Livers were removed immediately and processed for the estimations enzymes activities.

Biochemical analysis:

Lipid peroxidation was determined as malondialdehyde (MDA) concentration in liver by the method of Burlakova et al.[13]. Briefly, portions of liver (250 mg) was homogenized in 2 ml of 0.1 M ice-cold potassium phosphate buffer (pH 7.4), then centrifuged at 6000 rpm for 40 min at 4 °C. To 2 ml of the obtained supernatant 0.5 ml of 0.1 M potassium phosphate buffer was added. Then the tube vigorously shakes immediately after adding 1 ml TCA. All samples were centrifuged (15 min, 4000 rpm, 4 °C) then the supernatant was separated and 1 ml TBA (0.75-0.80 %) was added to 2 ml of it and placed for 10 - 12 min in a boiling water bath. The content of MDA (nmol/g wet tissue) measured as the increase in absorbance at 532 nm.
Superoxide dismutase (SOD) activity was assayed in the liver by the method of Marklund [14]. In the assay system, portions of liver (200 mg) was homogenized in 2 ml of 20 mM cold HEPS buffer (pH 7.2) containing 1 mM EGTA, 210 mM mannitol and 70 mM sucrose and then centrifuged at 1,500×g for 5 min at 4 °C, and the obtained supernatant was added to 200 µl tetrazolium salt solution the reaction initiated by adding 20 µl xanthine oxidase, the plate was shake for few seconds and incubated at room temperature for 20 min, the optical density was measured at 450 nm and its activity was measured as (Units SOD/ml).

Glutathione (GSH) concentration was assayed in the liver by the method of Baker et al., [15]. In the assay system, portions of liver (200 mg) was homogenized in 2 ml of 50 mM cold phosphate buffer (pH 6.5) containing 1 mM EDTA then centrifuged at 10,000×g for 15 min at 4 °C, the obtained supernatant was deproteinized by 5% sulfoalicylic acid and used for assay by adding 150 µl from cocktail that freshly prepared by mixing the following reagent in 20 ml vial (11.25ml of MES buffer, 0.45 ml of reconstituted cofactor mixture, 2.3 ml water and 0.45 ml reconstituted DTNB) to 50 µl of the obtained supernatant, then the plate was shake for few seconds and the optical density was measured at 405 nm once every 5 min to obtain for at least 5 time points. Its content was expressed as (µM).

Total glutathione-S-transferase (GST) activity was assayed in the liver by the method of Habig et al., [16]. In the assay system, portions of liver (200 mg) was homogenized in 2 ml of 100 mM cold potassium phosphate buffer (pH 7.0) containing 2 mM EDTA then centrifuged at 10,000×g for 15 min at 4 °C, 20 µl of the obtained supernatant was added to 150 µl assay buffer (100 mM potassium phosphate (pH 6.5) containing 0.1% triton X-100) after adding 20 µl reduced glutathione, the reaction was initiated by adding 10 µl CDNB, and then the plate was shake for few seconds and the optical density was measured at 340 nm once every min to obtain at least 5 time points and its activity was measured as (nmol/min/ml).

Statistical analysis:

All data expressed as mean ± SE and statistical analysis was made using the Statistical Package for Social Sciences (SPSS 18.0 software and Microsoft Excel 2010). For tests, analysis of differences between groups consisted on a one-way analysis of variance (ANOVA) with repeated measures, followed by post-hoc comparisons (LSD test). All data are expressed throughout as an arithmetic mean ± standard error (SE). Differences were considered statistically significant at p<0.05 [17].

Results:

Body weight, fluid and food intake and serum biochemical indices:

Data on the body weight, fluid and food intake are presented in Table 1. Animals on multiple dosing with AMV suffered from signs of intoxication in the form of conjunctivitis, congested facial vessels, dehydration, loss of appetite, weight loss, kyphosis, distress and emaciation, owing to this the chances for the survival of these animals were reduced while in animals on multiple dosing with nickel sulfate alone or in combination with AMV. There were no treatment-related clinical observations because the rats remained in relatively good health throughout the period of experiment. During the exposure period, the percentage of body weight gain in untreated control animals (group C) was 7.9%, while in animals of groups V1, N1, V2 and V2 + N2, the body weight gain was decreased by 26.2, 3.9, 29.1 and 15.2% respectively and increased in animals of groups N1 + V1 and N2 by 9.5 and 10.1% respectively.

The serum activities of ALT and AST were dose-dependently significantly (P<0.001) increased in animals on multiple dosing with AMV by (101.79 and 101.75%) and (164.29 and 45.61%) respectively. Animals on multiple dosing with nickel sulfate showed significant (P<0.001) increase in ALT and AST activities by (248.2 and 56.14%) and (167.86 and 29.82%) at the low and high doses respectively, the increase was higher at the low dose. When the metals were administrated in combination, ALT and AST activities significantly (P<0.001) increased by (126.79 and 71.93%) and (46.43 and 36.84%) at the low and high doses respectively. The increase was higher at the low dose. When the metals were administrated in combination, ALT and AST activities significantly (P<0.001) increased by (126.79 and 71.93%) and (46.43 and 36.84%) at the low and high doses respectively. Combined metals treatments did not potentiate the increase in ALT and AST activities (Table 2).

| Table 1: fluid, food intake and body weight gain in rats subjected to ammonium metavanadate and/or nickel sulfate |
|---------------|--------|---|--------|---------------|--------|---|--------|---------------|--------|---|--------|---------------|--------|---|--------|
|               | Control | AMV 0.15 mg V/ml | NS 0.18 mg Ni/ml | AMV 0.15 mg V/ml | NS 0.18 mg Ni/ml | AMV 0.15 mg V/ml | NS 0.18 mg Ni/ml | F ratio | p value |
| Initial weight (g) | 230.8 ± 1.56 | 229.5 ± 1.73 | 233.0 ± 1.63 | 223.0 ± 1.69 | 231.00 ± 1.98 | 4.165, p<0.003 |
| Final weight (g) | 249.0 ± 2.31 | 229.0 ± 2.31 | 223.8 ± 2.48 | 158.0 ± 3.47 | 254.3 ± 3.57 | 193.053, p<0.000 |
| Fluid intake (mL/kg b.w./24 h) | 110.0 ± 2.31 | 69.0 ± 3.76 | 94.8 ± 4.35 | 43.5 ± 4.24 | 124.5 ± 3.22 | 61.601, p<0.000 |
| Food intake (g/kg b.w./24 h) | 94.0 ± 2.84 | 40.0 ± 3.62 | 86.0 ± 3.77 | 34.5 ± 4.53 | 96.5 ± 3.97 | 56.685, p<0.000 |
| AMV + NS 0.15 mg V + 0.18 mg Ni/ml | 232.0 ± 1.84 | 234.5 ± 2.17 | 4.165, p<0.003 |
Final weight (g)  | 254.0 ±2.24 | 198.8 ± 3.11‡ | 193.053, p<0.000
Fluid intake (mL/kg b.w./24 h) | 96.8 ± 3.50*  | 65.8 ± 3.33‡ | 61.601, p<0.000
Food intake (g/kg b.w./24 h) | 92.5 ± 2.58  | 67.3 ± 2.64‡ | 56.685, p<0.000

Values are significant in comparison with control mean ± S.E. of 6 rats; AMV = ammonium metavanadate, NS= nickel sulfate, Significant, *p < 0.05; †p < 0.01; ‡p < 0.001; Figures in parentheses indicate percent (%) values.

Table 2: Serum aspartate aminotransferase (AST) and alanine aminotransferase (ALT) activities in rats subjected to ammonium metavanadate and/or nickel sulfate

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Control</th>
<th>AMV 0.15 mg V/ml</th>
<th>NS 0.18 mg Ni/ml</th>
<th>AMV 0.30 mg V/ml</th>
<th>NS 0.36 mg Ni/ml</th>
<th>F ratio</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ALT (mMol/L)</td>
<td>0.56±0.030</td>
<td>1.13±0.021‡</td>
<td>1.95±0.029‡</td>
<td>1.48±0.030‡</td>
<td>1.50±0.026‡</td>
<td>327.453, p&lt;0.000</td>
<td></td>
</tr>
<tr>
<td>AST (mMol/L)</td>
<td>0.57±0.020</td>
<td>1.15±0.017‡</td>
<td>0.89±0.012‡</td>
<td>0.83±0.018‡</td>
<td>0.74±0.019‡</td>
<td>107.588, p&lt;0.000</td>
<td></td>
</tr>
<tr>
<td>AST/ALT ratio</td>
<td>1.02</td>
<td>1.02</td>
<td>0.46</td>
<td>0.56</td>
<td>0.49</td>
<td></td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Parameters</th>
<th>AMV + NS 0.15 mg V + 0.18 mg Ni/ml</th>
<th>AMV + NS 0.30 mg V + 0.36 mg Ni/ml</th>
</tr>
</thead>
<tbody>
<tr>
<td>ALT (mMol/L)</td>
<td>1.27±0.020‡</td>
<td>0.82±0.020‡</td>
</tr>
<tr>
<td>AST (mMol/L)</td>
<td>0.98±0.023‡</td>
<td>0.78±0.013‡</td>
</tr>
<tr>
<td>AST/ALT ratio</td>
<td>0.77</td>
<td>0.95</td>
</tr>
</tbody>
</table>

Values are significant in comparison with control mean ± S.E. of 6 rats; AMV = ammonium metavanadate, NS= nickel sulfate, Significant,‡p < 0.001; Figures in parentheses indicate percent (%) values.

Antioxidant Defense System Enzymes And Lipid Peroxidation:

Lipid Peroxidation: dose dependent significant (p<0.001) increase was observed in lipid peroxidation measured as malondialdehyde (MDA) content in AMV treated rats by (18.57 and 50 %). In nickel sulfate treated rats, MDA content was also significantly (p<0.001) increased at both concentrations by (30%). When the metals were administrated in combination, MDA content significantly increased by (30 and 27.14%) at the low and high doses respectively. Lipid peroxidation induction at simultaneous exposure to both metals was not intensified (p<0.001) (Fig. 1).

Superoxide dismutase (SOD): the activity of SOD had significant (p< 0.001, 0.01) decrease following AMV or nickel sulfate treatment. The decrease in SOD activity in rats of groups V1, V2, N1 and N2 was by (28.90, 10.53, 28.90, 22.37, 40.80 and 46.05%) respectively. The depletion was more pronounced (p<0.001) at the low concentration and was much more pronounced by the combined metals treatments (Fig. 2).

Glutathione (GSH): the level of GSH decreased (p<0.001) dose dependently in AMV treatment by (53.50 and 60.06%) and was insignificantly (p>0.05) increased at the low concentration of nickel sulfate by (6.12%) while at the high concentration, the GSH content significantly (p<0.001) increased by (18.36%). Combined treatment of AMV and nickel sulfate at their low and high concentrations, led to significant (p<0.001, 0.01) increase in the GSH content by (16.64 and 11.1%) respectively (Fig. 3).

Glutathione-S-transferase (GST): The activity of GST had a significant (p<0.001) decrease following AMV or nickel sulfate treatment. The decrease in GST activity in rats of groups V1, V2, N1 and N2 was by (33.08, 42.00, 19.70 and 6.09%) respectively. Combined metals treatment at their low concentrations significantly (p<0.001) decreased the GST activity by (18.73%) while combined metals treatment at their high concentrations significantly (p<0.001) increased the GST activity by (16.87%) (Fig. 4).

Discussion:

Body weight is a significant marker of toxicity, the reduction in body weight gain is simple and sensitive indices of toxicity after exposure to toxic substances. In the present study animals treated with vanadium at both concentrations, nickel at the low concentration and combined salts treatment at their high concentrations presented a severe body weight loss. This reduction in weights might be due to low food consumption and reduction in protein levels. As the nickel ions have a higher affinity for proteins and amino acids and have shown to produce oxidation of proteins in cells [18]. Other mechanism of body weight following vanadium and nickel is the increase in the level of free radical species in various tissues. The generated reactive intermediates can interact and disrupt the cell membranes of the affected tissues thereby causing the tissue enzymes and other metabolites to leak out and increase the plasma.
concentrations as observed in this study. This may be an indication that the animals could not convert the feed consumed into useful nutrients required by the body, thus accounting for the reduced final body weight and percentage weight increase when compared to the control (Table 1). The body weight loss was decreased by an increase in the nickel concentration and combined vanadium and nickel treatment at their low concentrations; this indicates an adaptive mechanism to the increased concentration of nickel was developed. Nickel ingested (0.18 mg Ni/ml) at co-exposure to vanadium decreased the deleterious effect of vanadium and therefore the body weight loss in this group animals was reduced. A consistent reduction in body weight by vanadium has also been reported by Thompson and McNeill [19].

The decreased body weight in our study is concomitant with that of [11,20,21] who have also reported decreased body weight in nickel treated rats.

Fig. 1 the content of hepatic malondialdehyde (MDA) in rats subjected to vanadium and/or nickel for 28-day. Values are significant in comparison with control mean ± S.E. of 6 rats, Significant, *p < 0.001

Fig. 2 the activity of hepatic superoxide dismutase (SOD) in rats subjected to ammonium metavanadate and/or nickel sulfate for 28-day. Values are significant in comparison with control mean ± S.E. of 6 rats, Significant, *p < 0.05; ‡p < 0.001
Administration of vanadium and/or nickel caused significant decrease in fluid intake. Decreased consumption of drinking water containing vanadium has been reported and discussed by Scibior and Zaporowska[22]. Due to the reduced fluids intake, it is possible that the rats exposed to vanadium and/or nickel were affected by some degree of dehydration, which might to some extent contribute in the cause of animals death in this study and thus has to be taken into account under interpretation of the results.

AST and ALT are considered to be two of the most important tests to detect liver injury, although ALT is more specific than AST. In vanadium and/or nickel treated rats, the activities of serum ALT and AST were significantly increased, compared to normal control. Therefore the increase in the activities of these enzymes is mainly due to the leakage out of these enzymes from the liver cytosol into the blood stream which gives an indication on the hepatotoxic effect of these metals [23]. In other words it has been found that liver was necrotized in heavy metals exposition [24]. Sometimes AST is compared directly to ALT and an AST/ALT ratio is calculated. This ratio is also an important index for the measurement of toxicity. The decrease in the ratios in the animals exposed to vanadium or/and nickel showed that the liver is likely to be most affected tissue.

Numerous studies have reported toxic and carcinogenic effects induced when animals and humans are exposed to certain metals. Detailed studies in the past two decades have shown that metals like iron, copper, cadmium, chromium, mercury, nickel and vanadium possess the ability to
produce reactive free radicals resulting in DNA damage, lipid peroxidation, depletion of protein, sulphydryl and other effects [25]. Vanadium and nickel are two metals involved in such effects. Due to their extensive use in industry there is also a need to investigate their combined toxicity in organ system. Hence the present study was undertaken in male rat as an animal model. Liver with its metabolic detoxifying function is extremely vulnerable to harmful substances. The in vivo and in vitro toxicity of vanadium and nickel have been demonstrated by [26-28] who primarily highlight the general oxidative stress effects of the metals as their mechanism of toxicity. Oxidative stress is a pathophysiological process in which intracellular balance between endogenous as well as exogenous pro-oxidants and antioxidants is shifted towards pro-oxidants, leaving cells unprotected from free radical attack. The most important consequences of free radical production are lipid peroxidation increase and change in permeability of cell membrane [29]. Lipid peroxidation is often discussed as a cause of metal induced toxicity [30]. In the present study there was a significant increase in the LPO levels after the treatments, enhanced peroxidation of lipids in the present study may result in the damage to the cells, tissues and organs. Corroborating with present data Russianov et al. [9] who have reported high level of lipid peroxidation in liver of vanadium treated rats. Nickel is also found to affect LPO at both concentrations thus leading to cell injury. Corroborate with our findings Misra et al. [31] noted high level of lipid peroxidation in the liver with an increased concentration of H2O2 followed by a reduction in the activity of enzyme catalase which is an H2O2 scavenging enzyme by nickel. These two effects could augment the potential of oxidative cell damage in this study.

Several physiological mechanisms (antioxidative defense mechanisms) dispose of free radicals/ROS by directly scavenging them or by interrupting the already occurring lipid peroxidation chain reaction to limit their tissue damage. Superoxide dismutase is considered as the first line of defense against deleterious effects of oxy radicals in the cell by catalyzing the dismutation of superoxide radicals to hydrogen peroxide and molecular oxygen [32], superoxide that is one of the main reactive oxygen species in the cell. Absence of SOD or decrease in its activity may induce noxious metabolic outcomes as it plays an important role in free radical activity detoxification. So inhibition of the SOD activity of each exposure group in the present study indicated that plenty of superoxide anions (O2−) had been produced through the redox metabolism by vanadium or/and nickel in liver of rats and the antioxidant defense system could not produce strong enough SOD activity to remove these O2−. A decrease in SOD activity in liver of rats would diminish the ability of these organs to scavenge free radicals resulted from vanadium and/or nickel treatments. Our results are uniform with that of Scibior and Zaporowska[22] who reported reduced activity of SOD by vanadium treatment in the erythrocyte. Decreased SOD activity by nickel has also been reported by Sidhu et al.[11].

Glutathione ((L-glutamyl-L-cisteinyl-glycine), a submajor constituent of all cells and almost always the major nonprotein thiol compound present in cells, performs a pivotal role in maintaining the metabolic and transport functions of cells. Its conjugation helps in detoxification by binding electrophiles that could otherwise bind to proteins or nucleic acids, resulting in cellular damage and genetic mutation [33]. Vanadium treatment in the present study decreased the glutathione content. The decreased glutathione content could be due to its involvement in the mechanisms of detoxification of various xenobiotics [34], inhibition of lipid peroxidation by scavenging free radicals [35]. Both the detoxification of contaminants, through the action of GST, and the detoxification of ROS, through the action of some antioxidant enzymatic defences, may lead to depletion of GSH. A decrease in GSH content by vanadium has also reported by Scibior and Zaporowska [22] in support of our data. The observed increase in GSH content in liver of rats treated by nickel alone and rats co-treated by nickel and vanadium may be an improved attempt by liver to mop up MDA produced and may be an adaptive feature. Nickel at both concentrations ingested (0.18 and 0.36 mg Ni/ml) at co-exposure to vanadium decreased the deleterious effect of vanadium, that may be explained by the increased GSH content following combined metals administration. Tissue GSH was shown to participate directly in vanadate inactivation [36]. The increased GSH content reduces damage and promotes better survival under the conditions of oxidative stress.

The GST, a family of multi-functional enzymes involved in Phase II of biotransformation processes, has an important role in the detoxification processes of livers and is known to be linked to their antioxidant defence system. Besides having an active role in the conjugation of electrophilic xenobiotics with GSH, it has been reported that GST enzymes also present a distinct GSH peroxidase activity [37]. The present study showed significantly reduced GST activity in the liver of rats treated with vanadium or nickel and combined vanadium and nickel at their low concentration. This result may be due to the fact that toxic intermediates produced in the liver during contaminants metabolism may inactivate the enzyme, resulting in reduced GST activity in this organ. In the other hand, the elevated levels of GST activity at combined metals treatment at their high concentrations indicate adaptive mechanism to the increased toxicity was developed and potentiate the enhancement of detoxifying capacity to a greater
degree that render the liver more resistant to their toxic effects.

Conclusion:

On the basis of the results obtained we conclude that vanadium-nickel interactions are involved in the induction of oxidative stress under co-exposure to these substances. The disturbances in the oxidative status may be a result of an independent effect of vanadium and/or nickel and also of their interaction. Since the rats treated with vanadium and/or nickel had reduced drinking fluids intake that might result in dehydration, the effect of the both salts on the oxidative status of the body may be not solely due to vanadium and/or nickel treatment, but also the modifying influence of accompanying alterations such as reduced water intake and dehydration. A very important finding of this study is that despite the ability of vanadium and nickel to induce the oxidative stress the effect in the liver is not intensified at simultaneous exposure to both substances. The disturbances in the oxidative status observed in our experimental model indicate a risk of liver damage during exposure to vanadium and/or nickel via the free radical mechanisms.

References