CHAPTER V

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To study the effects of nickel and/or chromium salts in the form of nickel chloride (NiCl₂) and potassium dichromate (K₂Cr₂O₇) on liver, kidney and blood, adult female albino mice (*Mus musculus*) were orally administered at dosage of 5 mg and 10 mg/kg of chromate (K₂Cr₂O₇) and/or 8 mg and 16 mg/kg nickel salt (NiCl₂) respectively for 30 days. Possible ameliorative effects of vitamin A (0.2 mg/kg) and vitamin E (2 mg/kg) alone on combined nickel-chromium induced toxicity was also studied in this rodent model.

Gravimetric parameters, biochemical tests, toxicological and histological studies of liver and kidney in treated, control and vitamin supplemented groups followed by electron microscopic (EM) studies were carried out. The results revealed no significant alteration in body weights of NiCl₂ treated groups whereas reduction was noted in K₂Cr₂O₇ (high dose) treated groups. The combined treatment of nickel and chromium brought about a significant decline in body weights at both dosage levels. The liver and kidney weights also showed a significant reduction by nickel and/or chromium treatment at high dose levels and in combination. The decline in body and organ weights could be attributed to low intake of food due to heavy metal exposure.

Chromium and/or nickel treatments also caused a significant decrease in the protein levels of liver, kidney and serum. This could be due to inhibition and/or reduction in the synthesis of proteins due to their binding with –SH groups of proteins. The activities of alkaline and acid phosphatases in liver and kidney were also reduced in the
treated animals which implies that the heavy metal ions bind to the proteins including enzymes and hence caused an alteration in the membrane permeability and metabolic integrity of these organs. Similarly, succinate dehydrogenase activity was significantly declined in liver by nickel and/or chromium treatments indicating alterations in the oxidative metabolism. This confirms the fact that nickel or chromium are known to inhibit many enzymes of citric acid cycle and are possibly related to the structural alteration in the liver mitochondria after the treatments which is confirmed by the ultrastructural observation.

The results further revealed increased glycogen accumulation followed by a decline in the phosphorylase activity of the liver. This indicates inhibition of glycolysis and hence alteration in carbohydrate metabolism by chromium or nickel and their combined treatments. The declined cholesterol levels in the liver and its increase in the serum respectively by nickel and/or chromium treatments could probably be attributed to alteration in its transport and metabolism.

Creatinine concentration in kidney is an important measure of renal function and the results of the present study revealed a significant fall in its level by these treatments to mice. This suggests impaired glomerular functions and renal damage which is further evidenced by histopathological and ultrastructural changes in the kidney.

Nickel and/or chromium treatments also caused formation of free radicals in the liver. As a result, lipid peroxidation levels were increased in contrast to glutathione and total -SH groups which are declined in the liver. Reduction in total and reduced ascorbic acid levels followed by an increase in dehydroascorbic acid of liver reflected on stress imposed by these heavy metal exposure. Activities of superoxide dismutase and catalase.
were also reduced in the liver. All these changes cumulatively rendered the tissue susceptible to oxidative damage.

The blood parameters included were blood cell counts (RBC and WBC) and haemoglobin in all the experimental groups. Gradual reduction in erythrocyte and leucocyte counts were observed by heavy metal feeding indicating their probable effect on haematopoietic tissue. Further alteration in RBC counts was also related with a significant reduction in haemoglobin levels revealing anemia toxic nature of salts. The elevated SGPT and SGOT levels by chromium and/or nickel treatments indicated damage to liver followed by variation in serum cholesterol and proteins levels. All these toxic symptoms observed in these tissues (liver and kidney) were supported by histopathological as well as ultrastructural changes observed in our study. However, most of these toxic effects observed in these tissues were not evident by simultaneous feeding of vitamin A and vitamin E along with the combined (high dose) treatment of nickel and chromium. Thus nickel and chromium salts induced toxic effects due to their probable accumulation which were mitigated by vitamins due to their antioxidant properties mentioned earlier. This kind of study is important to individuals occupationally exposed to heavy metals.

CONCLUSIONS

Nickel and/or chromium are toxic to vital organs of the mice as these metals affect their structure and function due to induction of oxidative stress. This oxidative stress is due to their probable accumulation and inhibition of antioxidant system in these vital organs.
Vitamin A and vitamin E alone brought about amelioration of nickel and/or chromium induced toxicity by virtue of their antioxidant and detoxifying properties. Thus chromium and nickel together seemed to cause synergistic effects and this induced toxicity is cured by supplementation of antioxidants like vitamins. This study hence reveals that these vitamins could ameliorate the toxic effects of nickel and/or chromium and might be helpful for therapeutic use in occupationally exposed population if standardized.

FUTURE LINES OF WORK

1. Effect of chromium and/or nickel toxicity in other organs requires to be done.
2. Tissue burden of chromium and nickel needs to be investigated.
3. Studies on chromium and nickel affected endemic populations need to be carried out to evaluate their toxic effects.
4. Role of other antioxidants needs to be explored in counteracting the effects of nickel and chromium alone and in combination.
5. Role of combination of antioxidants is to be studied rather than alone.