CHAPTER V

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The present study was carried out to evaluate the effects of oral administration of paraben on vital organs like liver and kidney in female mice. Furthermore, the possible amelioration of paraben-induced effects on treatment with ginger extract was also evaluated.

Paraben treatment for 30 days caused dullness and lethargy with signs of staggering. No treatment related clinical signs were observed in controls and paraben plus ginger extract treated animals.

Body weight

Oral administration of paraben caused dose-dependent significant reduction in body weight of mice as compared to controls. Administration of ginger extract along with paraben caused significant amelioration in paraben-induced reduction in body weight.

Liver

Paraben treatment for 30 days caused, as compared with controls, significant and dose-dependent increase in absolute and relative liver weights in mice. Administration of paraben along with ginger extract significantly ameliorates paraben-induced changes. Amelioration was more in high dose paraben-plus ginger extract-treated mice than that of low dose.
Paraben administration for 30 days caused reduction in reducing, non reducing and total sugar contents, however cholesterol and lipid content was significantly higher as compared to controls in liver of mice. Treatment with ginger extract along with paraben significantly mitigates paraben-induced changes in the liver of mice.

Oral administration of paraben alone caused significant reduction in DNA, RNA as well as acidic, basic, neutral and total protein contents. Paraben-induced changes were significantly ameliorated on paraben plus ginger extract treatment in the liver of mice. Amelioration was almost complete in all parameters in low dose group than in high dose group.

Paraben treatment caused dose-dependent, significant rise in the level of lipid peroxidation by reducing the non-enzymatic antioxidant such as glutathione and total ascorbic acid as well as enzymatic antioxidants such as superoxide dismutase, glutathione peroxidase and catalase as compared to vehicle control in the liver of mice. Paraben-induced changes were significantly mitigated on ginger extract treatment.

Oral administration of paraben caused dose-dependent, significant reductions in the activities of succinic dehydrogenase and adenosine triphosphatase in liver of mice. Treatment with ginger extract along with paraben caused significant amelioration in all parameters as compared to paraben alone treated groups.

The present study clearly indicates alterations in histopathology of liver which revealed necrosis, nuclear pyknosis, cytoplasmic vacuolization along with fatty infiltration in paraben-treated mice. Decrease in hepatocellular compactness was also observed. Administration of aqueous ginger extract ameliorated paraben-induced
histopathological changes in liver of mice. Effect was more in high dose group. No such significant changes were observed in all groups of controls as well as ginger extract plus paraben-treated group of animals.

**Kidney**

Paraben treatment for 30 days caused significant, dose-dependent increase in absolute and relative kidney weights of mice. Oral administration of ginger extract along with paraben caused significant amelioration in absolute and relative kidney weights in mice.

There was no significant change in reducing, non reducing and total sugar as well as cholesterol and lipid content of different control groups. Oral administration of paraben for 30 days caused significant reduction in reducing, non reducing and total sugar contents. However, cholesterol and lipid contents were increased. Oral administration of ginger extract along with paraben caused significant amelioration in all above parameters.

Oral administration of paraben alone treatment caused significant reduction in DNA, RNA and acidic, basic, neutral and total protein contents. Paraben-induced changes were significantly ameliorated on paraben plus ginger extract treatment in mice.

Paraben treatment caused formation of free radicals in kidney. Lipid peroxidation was significantly higher in the kidney of mice treated with paraben which could be due to lower levels of non-enzymatic antioxidant like glutathione and ascorbic acid as well as the enzymatic antioxidants like catalase, superoxide dismutase and glutathione peroxidase.
activities. All treatment related changes were significantly ameliorated on paraben plus ginger extract treatment.

No significant changes were observed in contents in activities of succinic dehydrogenase, adenosine triphosphatase among all control groups. Oral administration of paraben for 30 days caused significant reduction in activities of succinic dehydrogenase and adenosine triphosphatase as compared to controls. Oral administration of ginger extract along with paraben caused significant amelioration in succinic dehydrogenase and adenosine triphosphatase activities as compared to paraben alone treated groups.

No apparent histopathological changes were observed in the kidney of all groups of controls as well as ginger extract plus paraben-treated animals. Normal Bowman’s capsule with glomerulus and proximal and distal convoluted tubules were observed. Paraben treatment for 30 days caused distortion of the tubules, increased vacuolization, disorganization of glomerulus and increased space between glomerulus and capsule wall. All paraben induced changes were significantly ameliorated on treatment with ginger extract along with paraben.

Serum

No significant changes in protein content as well as activities of SGPT and SGOT were noted in serum of different control groups of mice. Paraben treatment caused significant increase in activities of SGOT and SGPT in the serum of mice, as compared to controls. However, protein content significantly decreased in the serum of paraben-
treated mice as compared to controls. Ginger extract treatment along with paraben significantly mitigated paraben-induced changes in serum of mice.

In vitro

In vitro studies on liver and kidney homogenates revealed that H$_2$O$_2$-induced lipid peroxidation increased on addition of paraben. As concentration of paraben in liver and kidney homogenates were increased, lipid peroxidation also increased and it remained more than control consistently. However, addition of paraben along with ginger aqueous extract significantly retards paraben-induced lipid peroxidation.

Incubation of RBC suspension with different concentrations of paraben caused pronounced swelling and hemolysis. Addition of aqueous ginger extract alone to RBC suspensions did not cause any significant effect on hemolysis. However, concurrent addition of aqueous ginger extract along with paraben in incubation medium significantly retarded hemolysis.

Phytochemical analysis of aqueous ginger extract indicated the presence of flavonoids, alkaloids, saponins and terpeniod, while tannins and phlobatannin were absent. The presence of (6)-gingerol in the aqueous ginger extract was confirmed by HPLC chromatography which was performed by running the sample along with the standard.

The present study clearly indicates that administration of paraben caused adverse effects in vital organs like liver and kidney in mice.
The tolerance limit of paraben approved by FDA is 10 mg/kg body weight, in human beings. However, regular occurrence of paraben in food, cosmetics and pharmaceuticals is more. The increased paraben exposure may lead to adverse health-related events.

Biological risk of exposure to paraben is much higher in technologically developed countries than in developing ones. Also, reduced exposure to paraben is technically feasible through the controlled use of preservatives in food, cosmetics and pharmaceuticals.

Apart from this, nutritious diet possessing antioxidants can be adopted for detoxifying such chemicals. Oral administration of aqueous ginger extract along with paraben significantly ameliorates most of paraben-induced effects in mice.

Although the experiments reported in this study could reveal many interesting facts, more challenging work could still be carried out but for the sophisticated analytical facilities. Similarly, selection of animal model, methods for analysis etc. have been chosen taking into consideration availability of funds and facilities.

Extensive survey should be carried on human beings regarding utilization of parabens. Exposure of parabens in human beings could be measured. Also epidemiological studies should be done on paraben related problems in human being. A correlation between consumption of ginger and paraben-induced changes can also be established.
FUTURE PLAN OF WORK

1. In the present study we have reported toxicity of Paraben in liver and kidney of mice. Its toxicity on other organs as well as toxicity in other rodents and primates should be studied.

2. All foods, cosmetics and pharmaceuticals should be analysed for paraben and its concentration should be kept within the permissible limit.

3. Epidemiological studies should be done to establish the correlation between paraben concentration and its toxicity in human beings.

4. Elucidation of the mechanism of toxicity induced by paraben at macro and molecular level in various tissues can be performed.

5. Deep focus can be devoted to study the cancer inducing properties of paraben, its mechanism of action and possible amelioration by ginger extract.