Naphthalene–Induced Hepatotoxicity in Rats

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INTRODUCTION

Naphthalene is a pervasive environmental contaminant its toxicity is highly species, tissue and cell selective (Williams et al., 2001). Reactive oxygen species (ROS) production and resulting oxidative damage is proposed to be an important mechanism of toxicity of naphthalene exposure (Bagchi et al., 2002). Several recent studies suggest that in vivo grape seeds proanthocyanidines exposure may protect multiple organs from a variety of toxic assaults (Bagchi et al., 2000).

AIM OF THE WORK

The objective of the present investigation was to evaluate the in vivo effects of 15-days administration of naphthalene, as an environmental xenobiotic toxicant, on rat liver, in an attempt to ascertain the involvement of lipid peroxidation and glutathione depletion in naphthalene-induced hepatotoxicity. In addition, disturbances in liver biomarkers enzymes were also estimated to assess whether protection could be afforded by concomitant administration of grape seeds proanthocyanidines as natural antioxidants.

MATERIALS & METHODS

Experiments were performed on five groups (n=10 rats). The normal control group was orally administered oil (0.5 ml) for 15 days. The second group received daily doses of naphthalene (1 gm Kg−1, p.o.) for 15 days. The 3rd, 4th, and 5th groups were administered naphthalenes in a similar fashion as group two, in addition to either GSP (10 or 50 mg Kg−1, p.o.) or silymarin (100 mg Kg−1, p.o.) for 15 days and 2hrs before naphthalene administration. The latter drug is usually used as a reference drug for hepatoprotection. At the end of the experiments all animals were killed by decapitation, blood samples were obtained and serum quickly separated and used for enzyme assays. Livers were quickly removed, washed with chilled saline and kept until assayed at -80 °C.

The following methods were utilized for biochemical determinations, using commercial kits (Spinreact, Spain):

1. Serum alanine aminotransferase (ALT) and asparatic acid aminotransferase (AST) activities (Ritman and Frankel, 1957)
2. Serum alkaline phosphatase (AP) activity (Bowers and McComb, 1966)
3. Serum total bilirubin (T Bili) concentration (Martinek 1966)
4. Liver homogonate lipid peroxidation, expressed as MDA equivalents (Ohkawa et al., 1979)
5. Liver homogenate reduced glutathione (GSH) contents (Sedlak and Lindsay 1968).

Statistical analysis

Statistical analysis comparing differences between treatments were performed using one way analysis of variance (ANOVA) and Tukey-Kramer post tests. The results were expressed as mean ± SE of 10 values in each group, with p<0.05 considered significant.

RESULTS

Figures 1-3 illustrate the effect of 15 days concomitant oral administration of grape seeds proanthocyanidines (10 or 50 mg Kg−1) or silymarin (100 mg Kg−1) on (A) serum alanine aminotransferase activity (ALT, U L−1) and (B) serum aspartic aminotransferase activities (AST, U L−1), in male albino given naphthalene (1 gm Kg−1). Each column represents the mean±SE of 10 rats. #p ≤ 0.05, ##p ≤ 0.01. At #, values are significantly different from naphthalene-treated group (# p< 0.05, ## p< 0.01). Note the effectiveness of GSP in protecting rats against naphthaline-evoked elevation in liver enzymes.

Figures 4-6 illustrate the effect of 15 days concomitant oral administration of grape seeds proanthocyanidines (10 or 50 mg Kg−1) or silymarin (100 mg Kg−1) on (A) serum alkaline phosphatase activity (AP, U L−1) and (B) serum total bilirubin (T Bili, mg dl−1) concentration in male albino rats given naphthalene (1 gm Kg−1). Each column represents the mean±SE of 10 rats. #p ≤ 0.05, ##p ≤ 0.01. At #, values are significantly different from naphthalene-treated group (# p< 0.05). Note the effectiveness of GSP in protecting rats against naphthaline-evoked elevation in cholestasis.

Figures 7-9 illustrate the effect of 15 days concomitant oral administration of grape seeds proanthocyanidines (10 or 50 mg Kg−1) or silymarin (100 mg Kg−1) on (A) hepatic reduced glutathione contents (µmol g−1) and (B) hepatic lipid peroxidation estimated as MDA contents (nmol g−1), in male albino rats given naphthalene (1 gm Kg−1). Each column represents the mean±SE of 10 rats. #p ≤ 0.05, ##p ≤ 0.01. Note the effectiveness of GSP in protecting rats against enhanced levels of markers of oxidative stress and lipid peroxidation.

CONCLUSION

Naphthalene intoxication triggered production of ROS and impaired oxidant/antioxidant balance, leading to a state of oxidative stress and the resulting hepatotoxicity. GSP exhibited a beneficial effect as a natural hepatoprotective herbal product. It seemed to abate the oxidative insult in liver tissue, by restoring the altered naphthalene sensitive hepatic biochemical variables to a normal state of oxidative stress and the resulting hepatotoxicity.

REFERENCES

3- Bagchi D, Bagchi M, Stohs SJ, Das DK, Ray SD, Kussuzmeli CA, Joshi SS and Pruess HG. Toxicol. 2000, 146; 157-197.

ACKNOWLEDGEMENT

Special thanks to King Abdulaziz for Science and Technology for their generous grant.