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Toxicity Effect of Zinc Supplementation on the Liver Tissue

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Abstract: The ability of zinc to retard oxidants and to be antioxidant has been recognized for many years. In the present study, it is aimed to determine histological toxic effects of zinc supplementation on hepatic tissue. It was also planned to determine effect of zinc on TAL. In this study, 24 male Wistar albino rats were used. All animals were divided 4 groups; 1 control, 3 experimental group. Three milliliter (227 mg L^{-1} day^{-1}) zinc-sulphate was treated in experimental groups during 15, 30 and 45 days, respectively. TAL, AST and ALT levels from collected cardiac blood samples (3 mL) were measured. For histological investigation, liver tissue was removed and stained with Haematoxilen-eosin. It was determined that, TAL reduced in group I which was given zinc during 15 days and TAL increased in group II and Group III which was given zinc 30 and 45 days, respectively compared to that of group control. Results of the histological investigation showed that no toxicity in even experimental groups.

Key words: Zinc supplementation, wistar albino rats, liver, toxicity

INTRODUCTION

Environmental factors such as harmful gases, smoke form cell destruction by causal of oxidant forming. These oxidants cause to increase permeability by effecting membrane structure (Akkuş, 1999). For this reason, cell blabbing, vacuolization and calcium accumulation occur in effecting cells. Cell death occurs in late stages of cell destruction (Tappel, 1973). Therefore, anti-oxidant defense mechanism has been significant against oxidant attacks (Roberta *et al*., 1996).

Zinc that is involved in most of the vegetables is an essential nutrient and a co-factor of many enzymes (Dhawan and Goel, 1995; Dashti *et al*., 1997; Prasad, 1995; Okada *et al*., 1995). It plays an important role in nucleic acid metabolism, synthesis of protein, growth of fetus, stabilization of biological membrane, growth of leucocytes and formed of antibody, regulation of lymphocyte functions and stimulation of cell immunity, progression of children' mental and motor activities (Barceloux, 1999).

There have been many studies which reported that zinc plays a major role in the preventing cell against oxidants (Marchesini *et al*., 1996; Zago and Oteiza, 2001; Oteiza *et al*., 1996). Chronic zinc deprivation results in increased oxidation of lipid, protein and DNA with oxidative stress and effected alteration of enzyme and agent levels in oxidant defense system (Harris, 1992).

To prevent macromolecules against to oxidation are caused by iron and copper, although the evidence for the anti-oxidant properties of zinc is compelling, the mechanisms are still unclear (Zago *et al*., 2000).

In this study, it is focused on the effect of zinc supplementation in liver tissue and total anti-oxidant levels by biochemical and histological methods.

MATERIALS AND METHODS

Twenty four male Wistar- Albino rats weighing about 240±30 g were employed in this study. Six animals were in each group. Experimental animals were placed in animal rooms with 12 h dark/12 h light period before starting study. All animals in each group were fed a standard laboratory diet and tap water *ad libitum*. Animals were divided into four groups; three experimental and one control group (Table 1).

For determining biochemical parameters, 3 mL blood was drawn in sample tubes with heparin from cardiac under ether anesthesia. By separating plasma, was stored in -70°C until time of analyses. Samples collected from all groups were completed after 45 days (Table 1).

Total anti-oxidant levels were carried out using total anti-oxidant kit from Randox Ltd. and Hitachi 902 instrument. Alanine aminotransferase (ALT) and aspartate aminotranaferase (AST) levels were analyzed with Dade Behring Company kit. From all animals, liver tissue was removed and kept in %10 formaldehyde. After that, suitable pieces of liver tissues were processed for paraffin sectioning and sections of about 4 μm thickness were taken. The sections were stained with hematoxylin and eosin staining.

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Table 1: Administration of $ZnSO_4$ in each group

Groups	$ZnSO_4$ Administration 3 mL (227 mg L^{-1}) daily dose
A	15 days
B	30 days
C	45 days
Control	SF

Table 2: TAL (total anti-oxidant level), ALT and AST values in each group

Groups	TAL (n mol L^{-1})	ALT (μL^{-1})	AST (μL^{-1})
A	0.58±0.18	47.0±11	66.0±17
B	0.90±0.09	50.4±07	116.0±32
C	1.05±0.10	48.3±23	126.0±36
Control	0.92±0.11	53.8±15	132.0±28

RESULTS

As a obtained results, TAL (n mol L^{-1}), ALT (μL^{-1}) and AST (μL^{-1}) levels of group A were 0.58±0.18, 47.0±11 and 66.0±17, respectively. That of group B were 0.90±0.09, 50.4±07, 116±32 and that of group C were 1.05±0.10, 48.3±23, 126±36, respectively (Table 2). Total anti-oxidant level of group A showed a decrease as compared with that of the group control (p: 0.019). However the ratio between total anti-oxidant level of group B and group C was found unimportant (p: 0.11). It was found that as the ratio among all groups for ALT isn't significant, for AST levels the ratio between group control and group A is significant and the ratio between group control and each group isn't significant.

As a result of histopathological investigation, it was determined to present hyperemia in all experiment groups and not to present hyperemia in control group (Fig. 1-4).

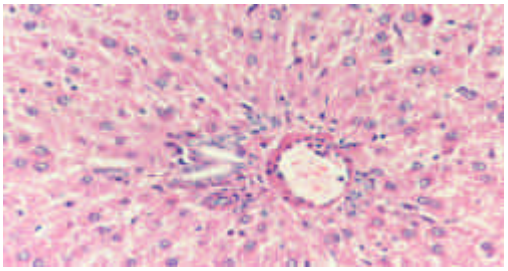

Fig. 1a: Control group: HE X400 normal architecture in portae

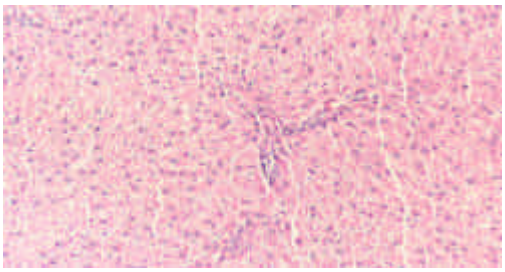

Fig. 1b: Control group: HE X200 normal architecture in portae

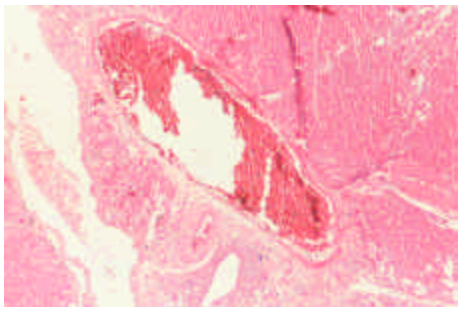

Fig. 2a: Group of $ZnSO_4$ administration during 15 days: HE X400 hypermia

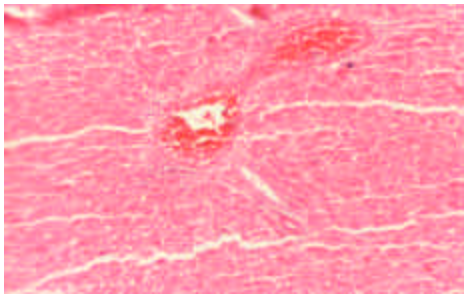

Fig. 2b: A: group of $ZnSO_4$ administration during 15 days: HE X200 hypermia

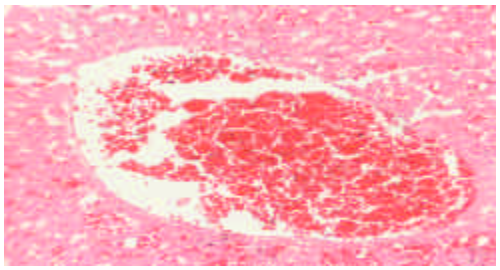

Fig. 3a: Group of $ZnSO_4$ administration during 30 days: HE X400 hypermia

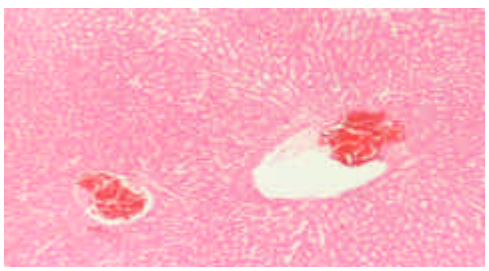

Fig. 3b: Group of $ZnSO_4$ administration during 30 days: HE X200 hypermia

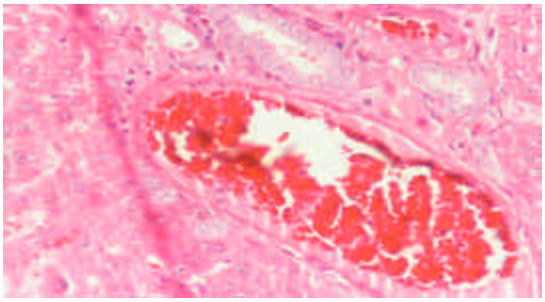

Fig. 4b: A: group of $ZnSO_4$ administration during 45 days: HE X200 hypermia

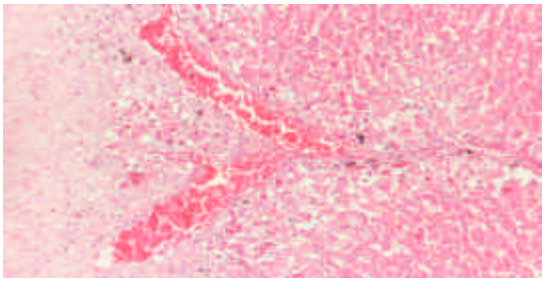

Fig. 4b: C: group of $ZnSO_4$ administration during 45 days: HE X200 hypermia

DISCUSSION

It was reported that acute administration of zinc inhibited hepatic Cyt-P_{450} concerned with protection against liver toxicity in studies of earlier investigators (Powel, 2000). The result may be a sign of a decrease in the level of free radicals that was suggested. In addition, zinc stimulated synthesis of metallothionein in liver and metallothionein is a good free radical scavenger that was also demonstrated (Marchesini *et al*., 1996). There have been lots of investigation about zinc interactivities with membrane and its effects on membrane ecology, zinc prevented interaction of membrane with copper and zinc has a potential role for protection of membrane against oxidation as a member of anti-oxidant mechanism (Zago and Oteiza, 2001; Zago *et al*., 2000; Bettger and O'Dell, 1993). On the other hand, there have been also studies about no observation any significant preventive effect of zinc on the lipid per oxidation in the presence of chemical and physical triggers (Zago and Oteiza, 2001). It was claimed that zinc doesn't have scavenging capability of oxidant species (Zago and Oteiza, 2001). However, in the agreement with the earlier studies have shown that zinc has got pro-oxidant features, zinc decreased activation of glutathione reductase and glutathione S-transferase that was suggested.

In this study, administration of zinc increased total anti-oxidant levels was determined and this increasing wasn't significant as statistically. On the other hand, determination of decreased total anti-oxidant levels 15 days after treatment suggested that zinc may be a pro-oxidant.

Ozaslan *et al*. reported that TAL reduced in Rats induced CCl4 and TAL increased again by zinc supplementation (2005).

In this study, it was seen that TAL increased in 30 days after zinc supplementation. Furthermore, pathological studies have shown that zinc didn't appear to effect on the anti-oxidant defense system as a pro-oxidant. However, more extensive studies are required to understand the exact molecular mechanism of zinc action on the anti-oxidant mechanism.

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