

Amelioration of aluminium-induced liver damage by vitamin E

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ABSTRACT

Objective: To investigate the effects of aluminium sulphate on the microscopic morphology of the liver and on vitamin E amelioration of aluminium-induced liver damage.

Methods: Rats were injected intraperitoneally with aluminium sulphate alone or aluminium sulphate together with vitamin E, with saline injected rats used as the control group. The study took place in Pamukkale University Faculty of Medicine in 2005.

Results: The rats exposed to aluminium showed morphological changes in addition to previously reported biochemical changes in the liver. The anti-oxidant vitamin E significantly diminished the liver damage seen due to aluminium.

Conclusion: There is an apparent protective effect of vitamin E on parenteral aluminium exposure.

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Aluminium, the third most abundant element of the Earth's crust, is a non-essential and toxic metal to humans.¹⁻⁴ Aluminium and its salts are commonly used in daily life, a widespread use that was enhanced by the belief that it is non-toxic and is quickly excreted from the body in the urine. However, this element has a negative impact on human health.⁵ Due to its abundance, every organism contains small quantities of aluminium,^{4,6,7}

and it can be found in practically all of the tissues of mammals, including the brain, liver, kidney, heart, blood, and bones.^{1-3,8} Aluminium accumulation in the liver leads to cholestasis.⁵ There has been considerable debate as to whether chronic exposure to aluminium is involved in neuro-degenerative disorders, such as Alzheimer's disease,⁹⁻¹² dialysis, Parkinson's dementia,^{13,14} and hepatotoxicity.^{15,16} The toxic effects of aluminium appear to be mediated, at least in part, by free-radical generation.^{17,18} The treatment commonly used in aluminium disorders is desferrioxamine.¹⁹ However, desferrioxamine therapy is associated with undesirable side effects, it is very expensive, and it is only efficient when applied intravenously or subcutaneously.²⁰ The goal of this study was to investigate the effects of aluminium exposure on liver tissue. The potential protective effects of the anti-oxidant vitamin E on these aluminium effects on the liver were also analyzed.

Methods. Adult male albino Wistar rats weighing 180-200 g were housed in the Experimental Research Unit of the University of Pamukkale, Denizli, Turkey in 2005. They were reared under the supervision of a veterinarian, kept in a well-ventilated, noiseless environment, and allowed free access to food and water. The male animals were selected at random and divided into 4 groups; each group included 7 rats. The first, control group of rats was injected with saline (2 ml/200 g body weight), and the second group was injected with aluminium sulphate (one mg/200 g body weight) dissolved in saline. The third group of rats were injected with both aluminium sulphate (one mg/200 g body weight) dissolved in saline and vitamin E (100 mg/200 g body weight), while the fourth group of rats were injected with vitamin E only (100 mg/200 g body weight). The injections were performed intraperitoneally for a period of 2 weeks (3 times per week, namely, on Mondays, Wednesdays and Fridays), and at the end of the second week, they were sacrificed under anesthesia. The liver tissues of each rat were collected and processed for routine histology; they were sectioned, stained with hematoxylin and eosin, and analyzed and photographed

under light microscopy. The study was approved by the Pamukkale University Ethical Committee for Experimental Animals.

Results. In contrast to the liver samples from the control group (Figure 1), dilatation and bleeding areas were seen in the liver sinusoids in the rats in the aluminium group (group 2). There were spaces between the hepatocytes and some impairment in the radial arrangement around them. Significant cytoplasmic loss was seen with most of the group 2 hepatocytes; some of these also showed cell membrane defects and spacing around their nuclei. Some also showed nuclei that were greatly enlarged and with some indentations, while in others, the nuclei were small and ellipsoid in shape (Figure 2). In the group 3 rats, which had been co-exposed to aluminium and vitamin E, the liver tissues appeared almost normal. There was no sinusoidal dilatation or bleeding foci. Although there were some relatively small cytoplasmic spacing around the nuclei

in some of these group 3 hepatocytes, they appeared to be much less damaged than those of the group 2 rats (Figure 3). The liver tissues in the rats given only vitamin E (group 4) had the same appearance as those of the control group (compare Figure 4 and Figure 1).

Discussion. Previous studies on aluminium toxicity have been based on biochemical analysis.^{19,21-26} Thus, it has been seen that aluminium accumulation within the liver is associated with a number of biochemical changes, which include the release of enzyme markers of liver injury, and alterations in the oxidant status.^{17,26} Our light microscopy findings following aluminium exposure of rat liver tissue show structural changes in the sinusoids that are accompanied by hepatocyte column and cytoplasmic, nuclear, and cell membrane alterations in these hepatocytes, all of which support the previously reported biochemical alterations that have been reported to be due to aluminium damage to the liver. Our findings therefore add to our current

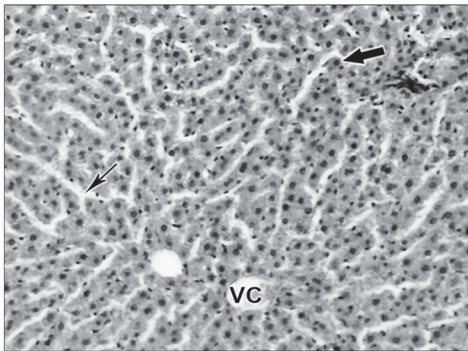


Figure 1 - Liver samples from group I rats (controls). Vena centralis (VC), sinusoid (thin arrow), hepatocyte (thick arrow). Stained with hematoxylin and eosin. Original magnification: 10x.

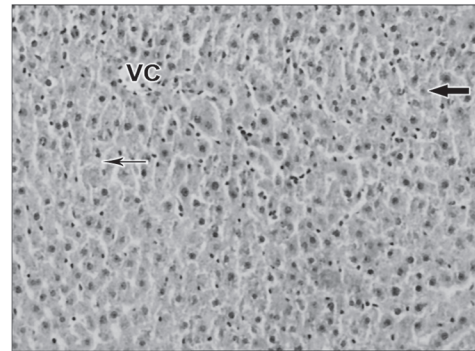


Figure 3 - Liver samples from group III rats (aluminium + vitamin E). Vena centralis (VC), sinusoid (thin arrow), hepatocyte (thick arrow). Stained with hematoxylin and eosin. Original magnification: 10x.

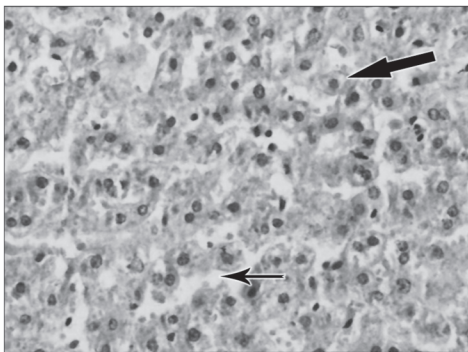


Figure 2 - Liver samples from group II rats (aluminium treated). Sinusoid (thin arrow), hepatocyte (thick arrow). Stained with hematoxylin and eosin. Original magnification: 40x.

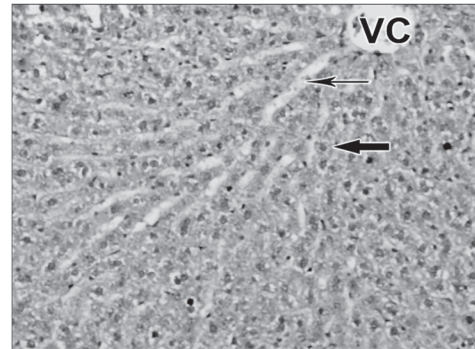


Figure 4 - Liver samples from group IV rats (vitamin E alone). Vena centralis (VC), sinusoid (thin arrow), hepatocyte (thick arrow). Stained with hematoxylin and eosin. Original magnification: 20x.

knowledge of liver pathology in terms of aluminium damage, and they are relevant to those cases where liver biopsies have been obtained from people who have been exposed to environmental or work-place aluminium for certain lengths of time.

The treatment commonly used in aluminium disorders is desferrioxamine, which is a chelator that has a large capacity to decrease the aluminium body burden by increasing its excretion in the urine.¹⁹ However, as indicated above, it is only efficient when it is applied intravenously or subcutaneously and it has been shown that desferrioxamine therapy has side effects that are often not well tolerated.²⁰ Thus, its application limits the success of this therapy, while it has also been seen to be an expensive treatment.²⁰ Aluminium treatment has been associated with significantly reduced vitamin E concentrations in the plasma, which might be due to increased processing of this antioxidant due to the increased levels of oxidant stress.²² Previous studies have also shown that as an antioxidant, vitamin E may improve the pro-oxidant effects of aluminium. Kenneth et al,²⁷ reported that antioxidants can protect mouse hepatocytes from aluminium toxicity, while Chinoy and Memon,²⁸ reported partial protection from aluminium-induced hepatotoxicity in the rat with vitamins E and C. Perhaps more surprisingly, dietary vitamin E supplementation has been associated with a significant reduction in the plasma and hepatic concentrations of aluminium.²²

In the present study, vitamin E was demonstrated to serve as an antioxidant, and to prevent the degenerative effects of aluminium on the microscopic morphology of rat liver tissue. The dilatations in the sinusoids were significantly reduced, and the hepatocyte columns maintained a normal structure in the aluminium plus vitamin E co-exposed group. In addition to this, the cytoplasmic spacing around the nuclei was no longer seen, and the hepatocyte nuclei had a normal appearance. The results of this study thus clearly demonstrate that vitamin E co-treatment under aluminium exposure ameliorates the histological alterations in the liver tissue that is caused by aluminium exposure by itself. On the other hand, the livers of the rats treated only with vitamin E were histologically comparable to those in the control group, suggesting that vitamin E itself has no observable side effects. In addition, vitamin E is much more cost efficient in comparison to desferrioxamine. Thus, this study indicates that vitamin E can be used clinically as a protective treatment against the adverse effects of aluminium. It will also be important to evaluate the effects of such aluminium exposure in liver tissue, and its amelioration by vitamin E, at the electron microscopy level in order to strengthen these findings.

In conclusion, our findings in the present study are in agreement with those of Abubakar et al.²² Thus,

aluminium administration appears to increase the oxidant stress in the liver, and this is an effect that can be offset by concomitant dietary vitamin E, which could be acting via aluminium absorption or excretion.

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