



RESEARCH ARTICLE

CYTOLOGY

HISTOPATHOLOGICAL RESPONSES IN LIVER, KIDNEY, INTESTINE AND TESTIS OF ALBINO MICE AFTER EXPOSURE TO ALUMINUM



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ABSTRACT

We have examined the effect of aluminum (Al) acetate on albino mice. Different doses of aluminum acetate (3.5 mg/kg body weight (b.w), intraperitoneal injection., single dose:3.5mg/kg b.w, double dose:3.5 mg/kg b.w, with 72 h interval on 1st and 4th day and multiple doses: 3.5 mg/kg b.w, with 72 h interval on 1st, 4th, 7th and 10th day) resulted alterations in tissue histology of liver, kidney, intestine and testis. Our findings indicate that the pronounced pathological changes in multiple doses compared to double and single dose administered mice. We found that dose dependent exposure of aluminum acetate causes deleterious effects and make them less fit for better survival.



KEYWORDS

Aluminum acetate, Different tissues, Albino mice, Histological analysis.

INTRODUCTION

Aluminum (Al) is the third most abundant element and most common metal in the earth's crust. Exposure to Al is almost inevitable, since it is present everywhere as an active substance or an additive. This element enters the human body via food, air, water and drugs¹, and is present in many manufactured foods such as processed cheese, baking powders, cake mixes, frozen dough, pancake mixes^{2,3} and pharmaceutical products, especially antacids^{4,5,6}. In recent years, various epidemiological studies have suggested that Al plays a pathogenic role in AD^{7,8}. It has been shown that Al accumulates in kidney, brain and especially in liver experimentally^{5,9,10}. Aluminum has been implicated in age-related changes¹¹ and neurodegenerative diseases such as Alzheimer's disease, amyotrophic lateral sclerosis etc¹². Besides the brain, Al in high doses was also shown to damage the kidneys, bones, heart and lungs^{13,14,15,16}. In drug metabolism, the central role of liver and kidney predisposes them to toxic injury¹⁷. Hepatic metabolism is first, and foremost, mechanisms that converts drugs and other compounds into products that are more easily excreted and that usually have a lower pharmacologic activity than the potent compound¹⁸. Aluminum is toxic for the brain, bone and haematological system but unfortunately very little data exists for other organs. Hence, the present study was carried out to assess morphological changes in liver, kidney, intestine and testis of albino mice after exposure to aluminum.

MATERIALS AND METHODS

Healthy adult albino mice (wistar) of same age group 60 ± 2 days and weight 25 ± 5 g were taken from veterinary college, Bangalore, India. The animals were housed at constant temperature ($28 \pm 2^\circ\text{C}$) and relative humidity ($60 \pm 10\%$) with a 12-h light : 12- h dark cycle. The LD₅₀ of aluminum acetate was estimated¹⁹ and was found to be 35 mg/ kg body weight²⁰. Ten fold lower concentration of LD₅₀ (3.5 mg/kg b.w.) was selected as sublethal dose. The animals were divided into 4 groups. Each group consisted of six animals. The first group of animals were considered as controls, received only distilled water without aluminum. To the animals of second group, single dose i.e 3.5 mg/kg body weight of aluminum acetate was given. Double doses (3.5 mg/kg b.w.) were given with 72h interval to the third group of animals on 1st and 4th days. To the fourth group of animals multiple doses (3.5 mg/kg b. w.) were given with 72h interval i.e on 1st, 4th 7th & 10th days. After 72h both control and experimental animals were sacrificed and the liver, kidney, intestine and testis were isolated in ice cold conditions.

Histopathological Examination:

The different tissues like liver, kidney, intestine and testis were fixed in 10% formalin for 24 h and dehydrated in gradual ethanol (50-100%), cleared in xylene and embedded in paraffin. Sections (4-5 μm thick) were prepared and then stained with hematoxylin and eosin (H-E) dye for photo microscopic observation.



RESULTS

In the present investigation, histological analysis of the tissues reveal the pathological condition subjected to various doses of aluminum acetate administration. Liver exhibited marked pathological changes in double and multiple dose animals (Figs.1-3). These changes include mild degenerative changes in hepatocytes of double dose aluminum administered mice and severe cytoplasmic, nuclear changes besides vacuolation in multiple dose animals. The kidney tissue of mice also showed some pathological changes in experimental animals when compared to control (Figs.4-6). In double dose, the kidney has shown reduced lumen of the proximal tubules. These changes were more

intensified in multiple dose animals besides atrophy of glomeruli (Fig.6).

The intestine did not show any pathological symptoms in single dose but marked pathological changes were observed in double and multiple dose aluminum acetate administered mice. The changes include necrosis in the tips of villi and submucosa and fragmentation of microvilli. Severe changes were observed in multiple dose animals (Figs.7-9). When double dose was given, moderate degenerative changes in the seminiferous tubules were evident (Figs.10,11). Pronounced pathological changes such as severe degenerative changes in spermatozoa and epithelial layer of seminiferous tubules besides severe necrotic changes in the interstitial cells in multiple dose animals were observed (Fig.12).

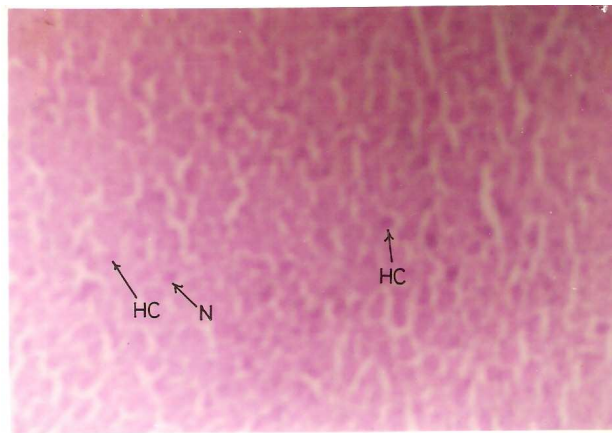


Fig. 1

Mice control liver showing hepatocytes with centrally placed nucleus

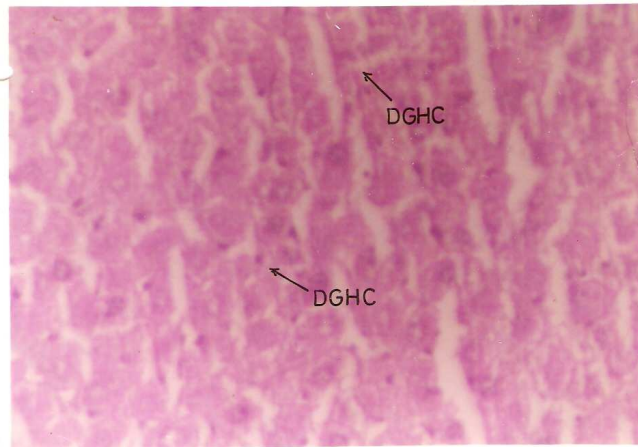


Fig. 2

Mice liver under double dose of aluninum acetate- showing mild degeneration in hepatocytes

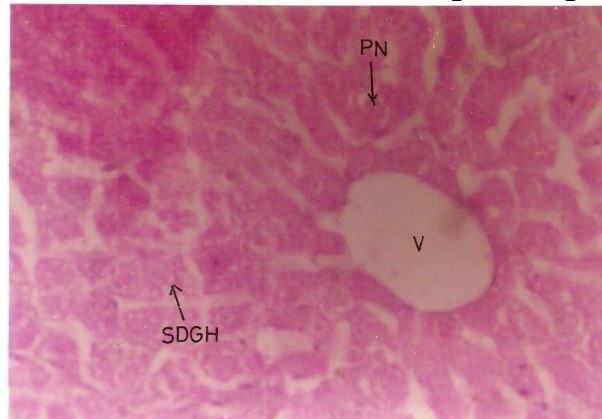


Fig. 3

Mice liver under multiple dose of aluninum acetate showing severe degenerative changes in hepatocytes, pycnotic nuclei and vacuoles

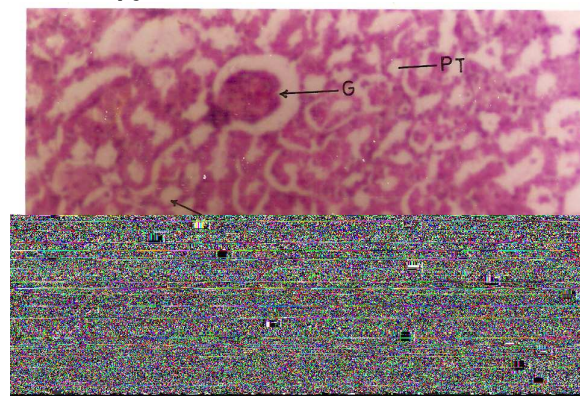


Fig. 4

Control mice kidney with proximal tubules and glomeruli

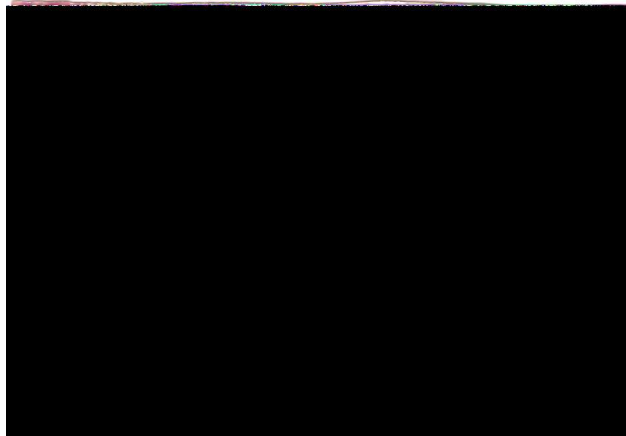


Fig. 5

Mice kidney under double dose of aluninum acetate showing degeneration in proximal tubules, reduction in the lumen of the proximal tubules and atrophied glomeruli

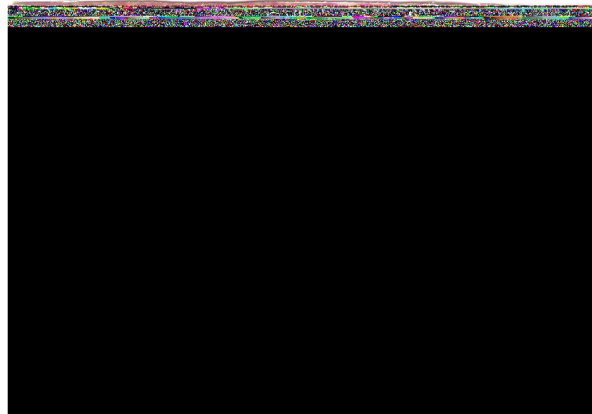


Fig. 6

Mice kidney under multiple dose of aluninum acetate showing severe necrotic changes in proximal tubules and atrophy of glomeruli.



Fig.7

Control mice intestine with circular layer, submucosal layer, lamina propria and microvilli

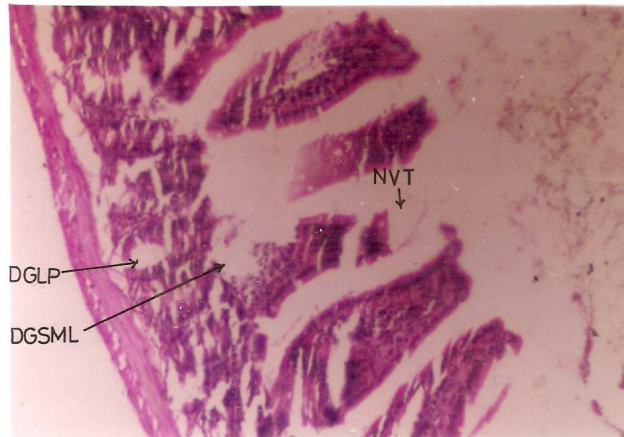


Fig.8

Mice intestine under double dose aluminum acetate- showing degenerative changes in lamina propria, degenerative changes in submucosal layer and necrosis in tips of villi

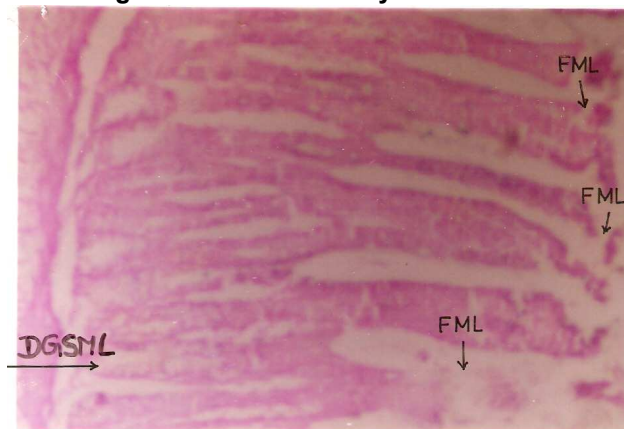


Fig. 9

Mice intestine under multiple dose aluminum acetate –showing severe degenerative changes in submucosal layer and fragmentation of microvilli

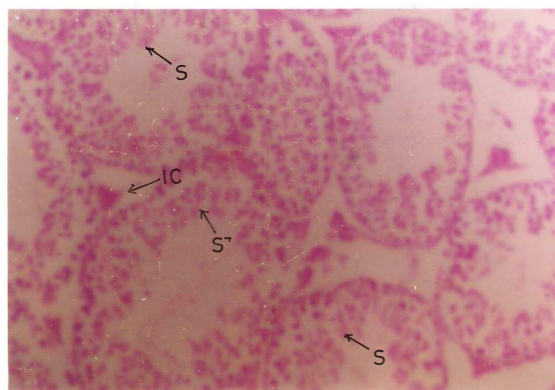


Fig.10

Control mice testis showing seminiferous tubules with matured spermatozoa and interstitial cells

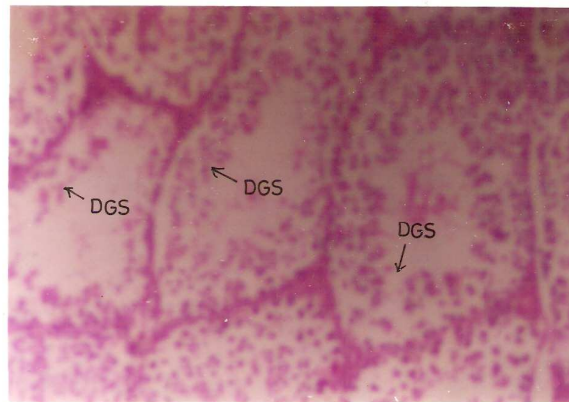


Fig. 11

Mice testis under double dose of aluminum acetate showing moderate degenerative changes in spermatozoa in seminiferous tubules



Fig. 12

Mice testis under multiple dose of aluminum acetate showing severe degeneration in spermatozoa, necrotic changes in epithelial layer and degenerative changes in interstitial cells.

DISCUSSION

Exposure to aluminum acetate has resulted clear architectural changes in liver, kidney, intestine and testis of albino mice. Accumulation of aluminum in different tissues has been reported²¹. Aluminum accumulation has been identified in the histopathological features of alzheimer's disease²². Cell membrane damage in cells exposed to aluminum was confirmed by increased LDH

release²³. Aluminum accumulated in the liver, kidney and intestine²⁴.

Since gut is considered to be the main route for absorption of xenobiotics, the intestine also exhibited moderate degenerative changes in submucosal layer, lamina propria and severe pathological changes in microvillar regions. Such changes will definitely lead to



lowering of absorption capacity in aluminum exposed mice. Aluminum accumulation in liver can be toxic to the hepatic tissue at high concentrations²⁵. The liver in the present investigation also showed cytoplasmic and nuclear degeneration and prominent vacuolation. Aluminum overloaded in liver may lead to cholestasis disturbance of hepatic microsomal functions²⁶. Aluminum accumulation and increased biliary transferring excretion have been observed in liver of rats²⁷. Aluminum accumulated in the liver of experimental rats²⁸. Aluminum acetate administered mice kidney also showed some discrete pathological changes in double and multiple dose animals. Degeneration in

proximal tubules, reduction in proximal tubule lumen, atrophy of glomeruli and necrotic changes in epithelial layer of proximal tubules may be due to accumulation of aluminum in double and multiple dose experimental mice. It was reported that aluminum accumulates in kidney of different animal models²¹. In the Al-treated group, the germinal epithelium of the seminiferous tubules was thinner in places and spermatids were almost absent; sperm numbers were low and there were no sperm in the lumen²⁹. In the $AlCl_3$ treated rats, histopathologic examinations revealed marked lesions in seminiferous tubules of testis³⁰. Thus exposure to aluminum cause histopathological alterations in different tissues of albino mice.

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