

PROPHYLACTIC ACTION OF LIV-52 AGAINST LANTHANUM CHLORIDE INDUCED LIVER INJURY IN MALE MICE

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ABSTRACT

Industrialization and urbanization indicate prosperity and progress. With the advancement of industrialization, the use of chemicals has considerably increased. Many hazardous chemicals like cadmium, mercury, cobalt, beryllium, lanthanum, and cerium are reported to produce a large number of necrotic changes in different organs. In the present study, an attempt has been made to ameliorate the protective actions of an ayurvedic drug Liv-52 against lanthanum chloride induced liver injury. Lanthanum chloride induced numerous histopathological alterations in the liver at the dose of 0.5 m mole/kg body weight. Dose was administered intra peritoneally at once only. A liver cell illustrates hypertrophy, perinuclear vacuolization and disturbed chord arrangements. With the conjoint treatment of Liv-52, liver histoarchitecture was almost maintained after 28 days of exposure.

KEYWORDS : Hazardous chemicals, lanthanum chloride, Liv-52, liver injury

A large number of chemicals are used in industries. These chemicals are used in different ways and ultimately they reach the target and non target tissues of animals and human beings. The rate of intake, dose and duration determine the intensity of harmful toxicants. These harmful chemicals make the environment polluted. The human population is usually exposed to various hazardous chemicals especially adjacent to industrialized area. Metals of group III possess the highest inherent toxicity among the metals but this toxicity is attenuated by the behavior of soluble salts of these metals at physiological pH. They are commonly called Rare Earth Elements (REEs). Lanthanum is the most toxic lanthanides. It is used in modern industries. It was reported that over 900 kg each of cerium, lanthanum and neodymium were released into the environment annually by the coal fired electric power plants in Europe (Goetz et al., 1982). The REEs compounds frequently have magnetic, catalytic and optic properties and therefore they are widely used in industry (Dobrynina et al., 1997). Lanthanides salts cause soft tissue calcification at the site of injection. These metal exert marked anticoagulant effect and induce hepatic lesions (Snyder et. al., 1960), Lanthanum chloride (LaCl₃) and cerium chloride (CeCl₃) are deposited mainly in liver and oocytes (Robinson and Wasnidge 1981). Lanthanum carbonate has been proposed as a calcium and aluminium free-phosphate binder for the treatment of hyperphosphatemia of chronic renal failure (D'haese et. al., 2003).

MATERIALS AND METHODS

Adult male mice weighing 30±5 gm were selected and maintained under uniform husbandry conditions. They were divided into control and experimental groups. 0.05 mM/kg b. wt. dose of lanthanum chloride was administered intraperitoneally to different groups of mice at once only. Autopsy was performed on 7th, 14th, 21st, 28th and 60th days of exposure. Fresh tissue of liver from control as well as experimental groups were collected (excised) and bloated free from adhering tissue, weighed and fixed immediately in alcoholic Bouin's fluid for 7 hours. Paraffin sections were obtained at 4-5 μ, stained with haematoxylineosin and examined for histological changes. Liv-52 syrup was given orally to experimental animals upto 28 days.

RESULTS AND DISCUSSION

Treatment of lanthanum chloride

Intraperitoneal administration of lanthanum chloride at a dose of 0.5 mM/kg b.wt. caused numerous pathological alterations at different days of treatment. Figure 1 shows liver structure of control mice. On 7th day of treatment with lanthanum chloride sinusoids were increased (Figure 2). Chord arrangement of the hepatocytes was not maintained on 14th and 21th day. Liver cells showed hypertrophy and darkly stained hypertrophised nuclei (Figure 3). Degeneration in the portal triads was characterized by vacuolation and infiltration of basophilic cells. Liver showing disturbed chord arrangement (Figure

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Figure 1 : Liver structure of control mice



Figure 2 : Structure of liver on 7th days of treatment with lanthanum chloride

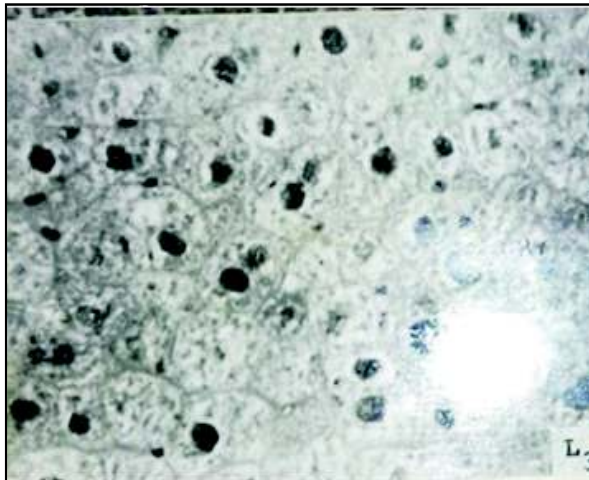


Figure 3 : Liver cells showing hypertrophy and darkly stained hypertrophied nuclei on 14th day with lanthanum chloride

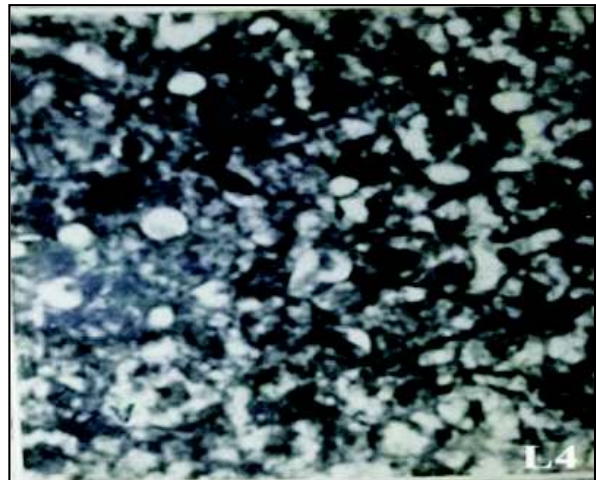


Figure 4 : Liver showing disturbed chord arrangement on 21th day with lanthanum chloride

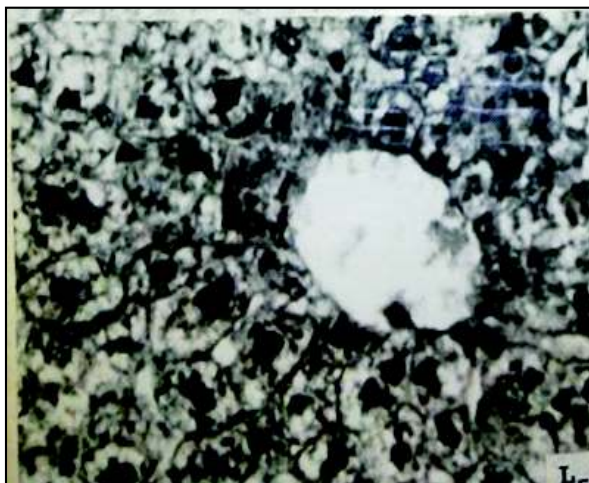


Figure 5 : Structure of liver on 28th day of exposure with lanthanum chloride

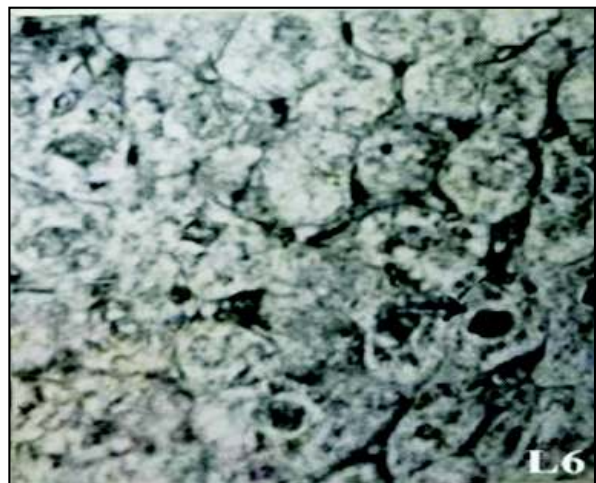


Figure 6 : Structure of liver on 60th day of exposure with lanthanum chloride

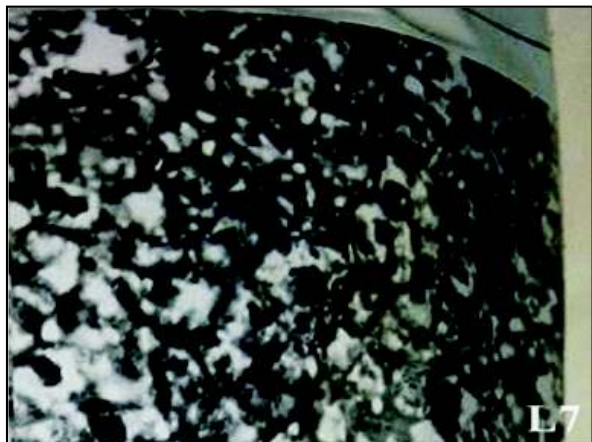


Figure 7 : Structure of liver on 7th day of exposure with conjoint treatment of Liv-52 and lanthanum chloride

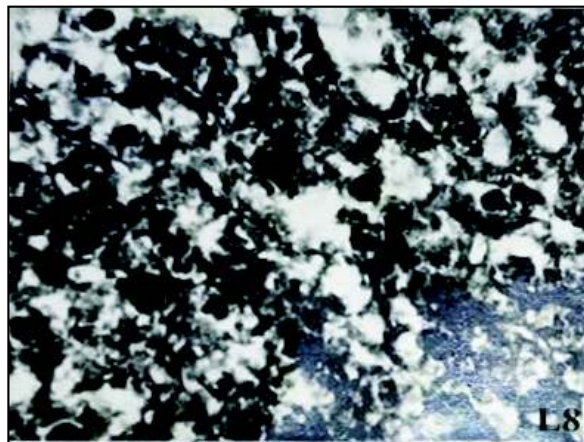


Figure 8 : Liver showing necrosis and focal degeneration on conjoint treatment of Liv-52 and lanthanum chloride



Figure 9 : Structure of liver on 28th day of exposure with conjoint treatment of Liv-52 and lanthanum chloride

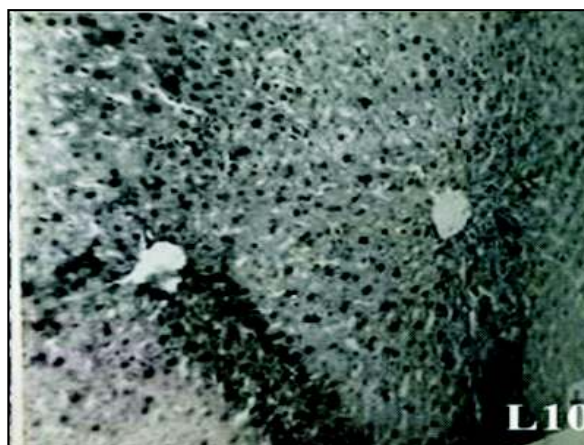


Figure 10 : Structure of liver on 60th day of exposure with conjoint treatment of Liv-52 and lanthanum chloride

4). On 28th day of exposure, a number of anucleated hepatic cells were observed. Endothelial lining of the central canal was damaged and the lumen contained debris. Hypertrophy, vacuolation and granulation were observed (figure 5). On 60th day of treatment, kupffer cells population was increased. Leucocytic infiltration was observed among the hypertrophied hepatocytes. Darkly stained nuclei were also observed (figure 6)

Conjoint treatment of Liv-52 and lanthanum chloride

With the conjoint treatment of Liv-52 and lanthanum chloride, on 7th and 14th day of treatment, sporadic congestion was observed in the central canal, chord arrangement was not maintained. Granular cytoplasm, hypertrophied hepatic cells, granulation and vacuolation were clearly visible (figure 7). In some region necrosis and focal degeneration was observed (figure 8).

After 28 days of treatment irregular hepatocytes with dark nuclei were observed. At some places karyolysis was observed in some vacuolated hepatic cells. After 28 days of exposure, liver histoarchitecture showed less damage as compared to lanthanum chloride per se treated mice. Some hepatic cells were cuboidal and chord arrangement was maintained around the hepatic sinuses. (figure 9). In some cells karyolysis was observed. In hepatic parenchyma regenerative changes were observed in the cytoplasm and nuclei. At 60th days the liver picture was more or less normal with slight damage. Portal triads and sinuses showed normal structure. However, leukocytic infiltration was observed in the peripheral region. Shape and size of hepatic cells were maintained. (figure 10).

The histopathological changes occurring in experimental conditions provide definite information about

the toxicity of the chemical. Mild to moderate fatty changes, observed in hepatocytes and portal triads, showed chronic inflammation in the portal connective tissue. Keenson et al., 1984 examined the liver biopsies of owl and monkeys for histopathological alterations and they observed the mononuclear cellular infiltration into the portal triads and surrounding parenchymal degeneration and necrosis of hepatocytes and hypertrophy of kupffer cells. The heavy lanthanons, including yttrium, induced focal necrosis of the liver, in both female and male rats (Magnusson, 1963). The uptake in liver or skeleton depends on the size of the lanthanon studied. The light lanthanons (La-Sm) deposits primarily in liver and skeleton with 50 and 25% of the administration dose, respectively, whereas the skeletal deposition of heavy lanthanons (Tb-Lu) is as high as 65% (Durbin et al., 1956). Kadas Jobst, 1973 with i.v. administration of lanthanum chloride reported disorganization of the normal architecture of the liver as well as swelling of liver cell nuclei and coarse granulation of their chromatin. The authors also found precipitation of the chromatin material on the nuclear membrane. Lanthanum treatment seems to mobilize glycogen from the lobular zone, parallel with the development of specific necrobiosis, probably along with the loss of activity of phosphorylase and oxidative enzymes (Kadas et al., 1974). In the present study, lanthanum chloride caused granulation, vacuolation of the cytoplasm and degeneration of hepatic cells and nuclei. Irregular spaces were also seen, filled with fluid and debris, indicating atrophy of hepatocytes and development of fibrosis. In Liv-52 treated mice, liver showed disturbed chord arrangement on 7th and 14th days of exposure. Elongated kupffer cells were also observed. On 28th and 60thh days hepatic cells were almost normal and chord pattern was maintained.

CONCLUSION

The present study evaluates the effect of lanthanum chloride on liver of male mice and the effect of herbal preparations Liv-52 in the recovery of injury caused by lanthanum chloride.

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