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Histopathological Changes in the Liver of Swiss Albino Mice After Lead Chromate Intoxication

KEYWORDS: Lead chromate, Histopathology, Liver,Swiss albino mice.

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ABSTRACT *Histopathological changes were observed in the Liver of Swiss albino mice after Lead chromate exposure (75 mg/kg/bw/day and 150 mg/kg/bw/day). Histopathological effects of Lead chromate were cytoplasmic vacuolization of the hepatocytes, accumulation of electron dense granules, fused organelles. These changes were dose dependent.*

Introduction
Lead chromate (PB.CR-04;Mol. Wt.323.19) is a powder , yellow to orange in colour. It is water-insoluble. It is a suspected human carcinogen of the lung, and can cause chronic lead poisoning (Moore and Meredith,1979; Kazantzis, 1989; Goyer,1992). Lead chromate potentially could pose a double hazard and cause signs and symptoms of chronic lead Intoxication- severe gastro-intestinal disturbances, anaemia (Christenson, 1977, Johansson-Sjobech and Larsson, 1979, Hoffman et al., 1985, Graziano et al., 1991), neuromuscular dysfunction, nephritis (Cramer et al., 1974, Weeden et al., 1979, Goyer et al., 1989, Cardenas et al., 1993) and encephalopathy and chromium VI toxicity- sensitization dermatitis, primary irritant dermatitis, ulcerated nasal mucosa and skin and nephropathy. Lead chromate and derived pigments have been tested in rats by sub-cutaneous and intra muscular injection, producing malignant tumors at the site of injection and in one study renal carcinomas (Choie and Richter, 1972). Lead has been found to cross the placenta and cause miscarriage, stillbirths and birth defects. Exposure before birth can cause mental retardation, behavioural disorders and infant death. Lead can also cause reduce sex drive, impotence, sterility and damage the sperm (Cullen et al.,1984, Lerda, 1992), increasing the potential for birth defects. Periods in women can also be affected.

While reviewing literature, it was found that the information concerning the oral exposure of experimental animal to Lead chromate is very limited, specifically at microscopic levels.

The present work was undertaken to study whether or not chronic oral exposure of mice to lead chromate could develop toxic changes in the liver cells and its possible mechanism of action.

Materials and Methods
Male albino mice were used for the experiment. They were divided into control and treated groups. Treated animals were orally given Lead chromate in pellet form at a dose of 75 mg/kg/bw/day and 150 mg/kg/bw/day for 15 days. After the experimental period was over, the animals were kept out from the cages with a minimum disturbance, care being taken to prevent the animals from struggling. They were anaesthetized followed by immediate sacrifice. Liver was taken out. It was washed properly in normal saline and then cut into small pieces with a fine surgical blade. After sectioning, tissues were fixed in 2.5% glutaraldehyde in 0.1% phosphate buffer. Post fixation, cutting and staining were carried out at the Electron Microscopic Division of the Sophisticated Analytical Instrumentation Facility, AIIMS, New Delhi. Sections were photographed with Phillips Morgagni Electron Microscope for ultrastructural analysis.

Results
Transmission Electron Microscopic observation of a normal liver revealed hepatocytes with well organized nucleus and nucleolus when present was prominent.

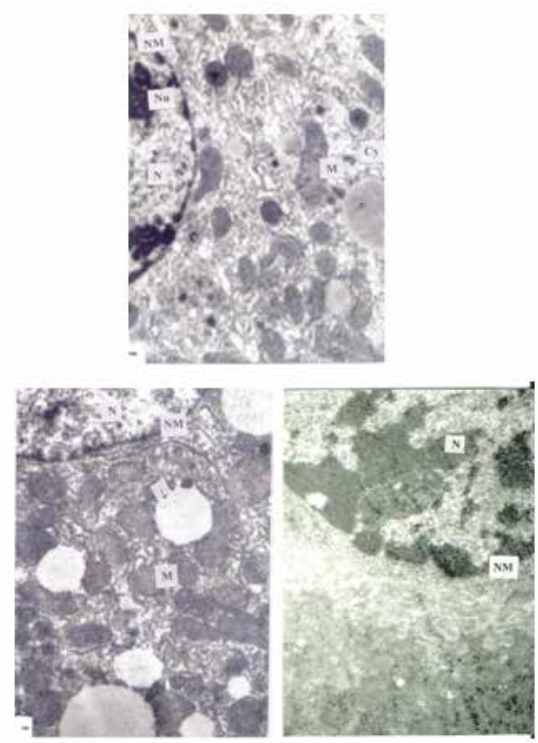

Figure 1(a)
Transmission Electron Microphotograph of liver cell of :-
(a) Control mice: Normal architecture of cell ,
(b) Lead Chromate-treated (75 mg/kg bw /day for 15 days) mice: nucleus(N) normal; increased mitochondria activity; lipid vacuoles prominent
© Lead Chromate-treated (150 mg/kg bw /day for 15 days) mice: damaged liver, heterochromatization , necrotic patches around the nucleus.

75 mg/kg/bw/day Lead chromate treated liver In treated liver, nucleus was normal in shape. At some places, hetrochromatization of the chromatin materials was visible. Nuclear membrane dissolved at some places. There was an increased mitochondrial activity revealing high energy requirement of the cell. Mitochondria became pyknotic. Lipid vacuoles were prominent, some with protuberances. Electron dense gran-

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ules could be seen in the vacuoles which was a sign of toxicity. At some places cytoplasmic organelles were found fused together indicating pathogenic condition of the hepatocytes. [Figure 1(b)].

150 mg/kg/bw/day Lead chromate liver

There was great damage to the liver cells as compared to control. The progressive loss leads to disruption of the normal lobular architecture. Nucleus became disorganized. There was an extensive hetrochromatization of the chromatin materials. Necrotic patches appeared around the nucleus.

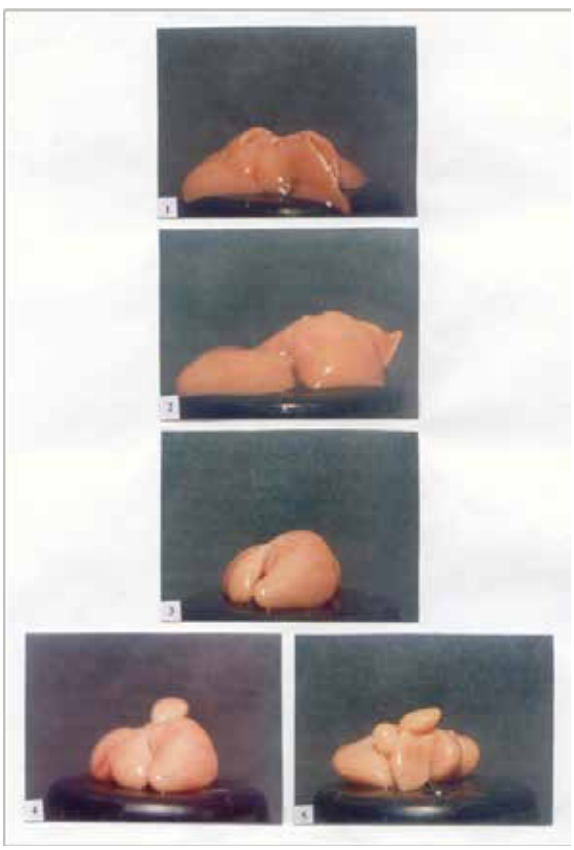

Figure 1©
FIGURE 1=Normal Liver
FIGURE 2-5= Changes in the Morphology of Liver as a result of treatment

Discussion and Conclusion
Ample of literatures are available giving authenticity to the present findings. Exploring through them wealth of informations regarding toxicity induced due to applied chemicals have come up.

In the present investigation, it was observed that hepatic cells become extensively vacuolated after Lead chromate treatment. This condition is known as steatosis/hepatic lipidosis/ fatty liver.It is the accumulation of triglyceride in the liver.It begins with the development of minute membrane-bound lipid inclusions developed near and possibly from endoplasmic reticulum.The condition arises due to the disruption of the normal operation of the triglyceride cycle which takes place in the liver.The cycle consists of four basic components : release,uptake,transformation and export.In short, free fatty acids are constantly released from adipose tissue triglyceride depots and transported as albumin-bound FFA to the liver, where they are either oxidized or resynthesized to triglyceride. The transport is mediated by a local lipase which inturn is modulated by intracellular levels of cyclic AMP. These triglycerides, together with other lipid materials are then combined with a carrier apoprotein and secreted into the blood as very low density lipoproteins. Apoprotein here is regarded as the limiting factor. It's production may be blocked by inhibitors of protein synthesis. If blocked, triglycerides remain in the liver giving rise to steatosis.

Mathur (1965), Bhattacharya and Mukherjee (1975) and Dutta et al (1993) observed vacuolization in hepatic cells.

Magnusson (1963) reported that increased level of neutral fats from extra hepatic sources and dilated cisternae of endoplasmic reticulum to be converted into lipid droplets after cerous chloride injection.

Kumar and Singh (2000) reported that the liver dysfunctioning causes disturbances in lipid metabolism . Similar findings were also enumerated by Gupta and Saxena (2000).

Liver is a central organ of lipid metabolism (Nikitin et al, 1985). Rise in liver total lipid content may be attributed to decrease in lipase activity of liver (Gupta et al, 1986).

Another lesion was the fragmentation or the segregation of the nucleous.

Another important finding was the alteration in the activity of the hepatocellular organelles. Such alterations are designated as Hepatocellular Adaptive Responses. Some chemicals result in the structural and functional adaptive responses in the liver. Although a number of adaptive responses of the hepatocyte are of a metabolic nature, morphologic changes frequently may be noted microscopically and on some occasions, grossly.

Increased number of mitochondria has been observed in the present investigation. This indicates increased energy requirement of the cell in an effort to overcome toxicity. Similar finding was obtained by El- Elaimy et al (1993).

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