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## **CHRONIC TOXICITY OF MICROCYSTIN-LR IN MICE**

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This study is to characterize the microscopical and ultrastructural changes in chronic exposure of Microcystin-LR (MCLR), a cyclic heptapeptide hepatotoxin, comparing to those in acute lethal toxicity. Female ICR mice were injected intraperitoneally with 10, 20, 30 $\mu$ g/kg of MCLR every 3 day for 27 days. Grossly, MCLR-treated livers were slightly enlarged. Microscopically, slight centrilobular dissociation and rounding of hepatocyte were seen in the pericentral lesion after 18 day. Mild centrilobular degeneration with lymphocyte infiltration was also observed. Liver changes developed from the central regions and then extended to the portal regions of liver. After 27 day, strong vacuolar degeneration and marked dissociation of hepatocyte were noted. Changes such as rounding of hepatocyte, lymphocyte infiltration and individual cell death were more severe and progressed. No lesions were found in other organ. Ultrastructurally, hepatic lesions were consisted of widening of sinusoid, loss of microvilli along the sinusoidal surface and mild widening of cell-to-cell contact after 18 day. After 27 day, the space of Disse and sinusoid were markedly widened. Complete hepatocyte separation was seen and bile canaliculi were dilated with loss of microvilli but hepatocellular organelles were almost intact. Conclusively, morphological changes during prolonged sublethal exposure of MCLR progresses in dosage and time dependent manner, and the process of morphological changes are basically similar to those reported in acute lethal exposure.

Keyword : mice, Microcystin-LR, liver, chronic, ultrastructure