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Effects of Orally Administered Cadmium on Alkaline Phosphatase Isoenzymes in Rat Tissues

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Several pathological lesions have been observed experimental rats exposed to cadmium (Cd). Infammation of the submucosa layer of small intestine and testicular necrosis have been found in the early stages of Cd administration. Bone lesions including osteoporosis and osteomalacia have been observed in experimental rats exposed to Cd. Subchronic Cd intoxication inhibits formation of metaphysial trabeculae of femur and produces osteoporosis and these lesions appear before pathological changes in kidney. Osteomalacic changes are found in bone of rat fed 50 ppm of Cd without calcium ; thse bone lesions have been attributed to an affect of Cd upon the kidney. On the other hand, a high Cd accumulation in kidney ($<$300 μg/g wet weight) causes renal tubular dysfunction and results in amino aciduria, enzymeuria, and glucouria. Moreover, renal tubular damage by a high accumulation of Cd results in excretion of β_2-microglobulin and Cd-metallothionein. Hepatic necrosis has been reported in rats exposed to 3.9 mg/kg after 10 h.

Alkaline phosphatase isoenzyme is found in plasma membrane of the mucosa brush border of small intestine, renal tubular brush border, bone or liver which are traget organs for Cd intoxication. Moreover, three isoenzymes in liver, small intestine and bone, are found in serum. Alkaline phosphatase in bone is well known to play an important role in bone formation. Therefore, it seems that assay of alkaline phosphatase activity in traget organs is a valuable method to check for pathological lesions in chronic Cd poisoning.

In this study, we determined the activity of alkaline phosphatase in liver, small intestine, kidney or bone and investigated the relationship between the changes of isoenzymes in target organ and the pathological lesions in Cd poisoning.

Changes of alkaline phosphatase in small intestine, liver, kidney, bone and serum of rats administered 100 ppm (890 nM) of Cd^{2+} in the drinking water were observed during a 12 months period.

After 2 weeks of cadmium administration, decreases in bone and small intestine alkaline phosphatase in serum of Cd-exposed rats were observed by a polyacrylamide gradient gel electrophoresis and the alterations continued through the 9th month of administration. At one month, the activities of the alkaline phosphatase fractions,

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p-1 and p-2, obtained from Sephadex G-200 column gel filtration of bone extracts from Cd-exposed rats were 32% and 43% of those in the controls, respectively, whereas Cd accumulation in the bone was very low (9 nmol/g wet weight). After 3 months, osteoporotic changes of bone and erosion of submucosa layer of the small intestine were observed by light microscopy. Alkaline phosphatase in small intestine of the Cd-exposed rats was 60% of that in the controls after 3 months.

At 12 months, the decreased activity of bone alkaline phosphatase in Cd-exposed rats recovered to the same level as activity in the non-exposed rats. Moreover, the activity in kidney of the Cd-exposed rats was 80% of that in the controls. However, histological conversion from esteoporotic to osteomalacic changes in bone and kidney lesions by Cd administration were not observed by light microscopy. Liver alkaline phosphatase activity of the Cd-exposed rats did not change even at 12 months, whereas 1.2 μmol of Cd per g wet weight accumulated in this organ.

In the present study, there is a relationship between the pathological lesion and the decrease of alkalline phosphatase which were observed in small intestine and in bone of rats at the early stage of Cd administration (100 ppm). Moreover, it is strongly suggested that Cd in bone of Cd-exposed rats is present in an ion form and the Cd ion acts primarily and directly on bone tissues and bone isoenzyme.