

Induction of hepatic zinc-thionein in rat by endotoxin

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Induction and depletion pathways of hepatic zinc-thionein by injection of endotoxin were correlated with time-dependent changes of metal concentrations in serum, liver and kidney supernatant fluids. Low serum zinc level (28 per cent of the control value) induced between 6 and 24 hr after injection of endotoxin was accompanied by a concomitant increase of zinc level in liver supernatant fluid (highest level at 12 hr after injection). The increased zinc in the liver supernatant fluid was attributed to zinc-thionein on an SW column [1], as shown in Fig. 1, metallothionein-II being a predominant isometallothionein during the experiment without any appreciable changes of zinc peaks other than metallothionein peaks. Although copper concentrations in serum and liver supernatant fluid did not change significantly, that in kidney supernatant fluid gradually decreased (45 per cent of the control value during 1-2 days after injection) and then recovered to the control level, as was also observed for zinc injection [2]. Zinc in kidney metallothionein fraction decreased with the decrease of copper in the kidney supernatant fluids, regard-

less of at least higher levels of zinc than the control value during the experiment. Induction and depletion pathways of hepatic zinc-thionein initiated either by excess (zinc injection) [2] or by normal zinc levels (endotoxin injection) were similar except for the faster pathway of the latter case.

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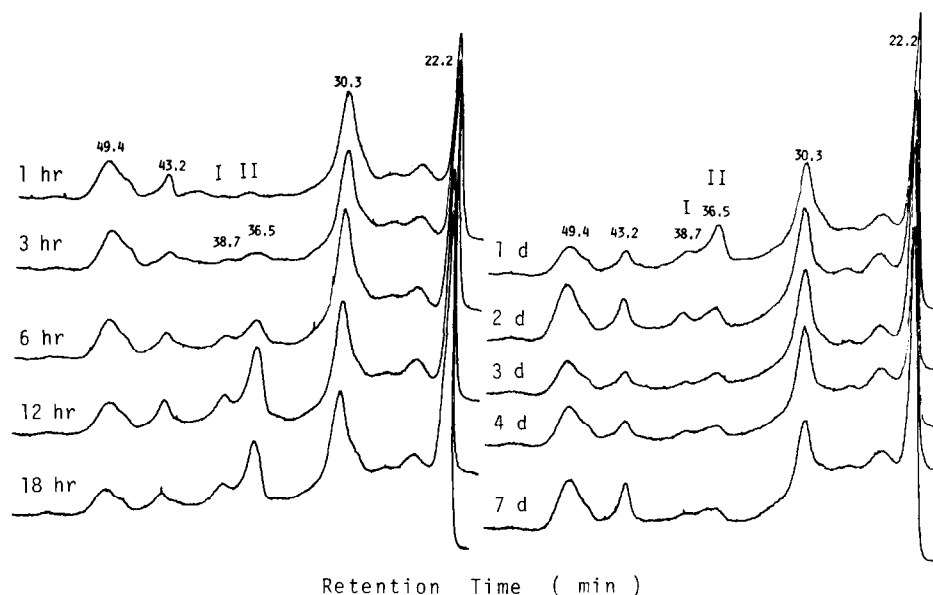


Fig. 1. Gel permeation-zinc atomic absorption chromatograms of liver supernatant fluids after injection of endotoxin. Female rats of the Wistar strain (mean body wt \pm S.D., 264 ± 14 g) were injected intraperitoneally with endotoxin (lipopolysaccharide *E. coli* 055:B5, Difco Lab.) at a dose of 1.2 mg/kg body wt once and the animals (six rats per group) were exsanguinated 1, 3, 6, 12, 18 hr, 1, 2, 3, 4 and 7 days after injection. Livers and kidneys were homogenized in 3 vol. of 0.1 M Tris-HCl buffer (pH 7.4, 0.25 M glucose) and the homogenates were centrifuged at 170,000 g for 60 min. Concentrations of zinc, copper and iron in serum, liver and kidney supernatant fluids were determined by atomic absorption spectrophotometry. Distribution profiles of zinc in the liver supernatant fluids were investigated on an SW 3000 column [TSK GEL, Toyo Soda, Tokyo, 21.5×600 mm with a precolumn (21.5×100 mm)] connected to a high speed liquid chromatograph with a flame atomic absorption spectrophotometer as a detector of metals. A 1-ml portion of the supernatant fluids were applied to the column which was eluted with 50 mM Tris-HCl buffer (pH 8.6) at a flow rate of 3.7 ml/min. I and II indicate metallothionein-I and -II, respectively.