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Suppressive Effect of Zinc on the Toxicity of Mercury

Male rats were given subcutaneous injection of mercuric chloride (0.018 mmole/kg/day) and oral administration of zinc acetate (3.0 mmoles/kg/day). Mercury and zinc were administered at the same time, once every 24 hr for 5 days. Only 1 of 10 rats given mercury alone survived for 3 days, and this one rat died on the 4th day. In the animals given mercury and zinc at the same time, all the 10 animals were alive on the 5th day, indicating the marked effect of zinc in suppressing the toxicity of mercury.

Based on such a marked effect of zinc, examinations were made to see whether biosynthesis of metallothionein would occur by the presence of zinc or mercury from the incorporation of ^{14}C-cysteine into the metallothionein fraction. High rate of incorporation of radioactivity into the metallothionein in the rat liver was observed by the administration of zinc but the incorporation was not so marked by the administration of mercury. This fact seems to suggest that the biosynthesis of metallothionein by zinc is responsible for the suppressive effect of zinc on the toxicity of mercury.

It is known that administration of zinc suppresses the toxicity of cadmium in rats,[1,2] and participation of metallothionein has been suggested as a mechanism for such an antagonism between zinc and cadmium.[3] Presence of a metallothionein fraction with zinc has been found in the bovine duodenum and liver after administration of zinc by Evans and others,[4] in the female rat liver by Webb,[5] and in the rabbit liver and kidneys by Kimura and others.[6] These facts strongly suggest the biosynthesis of metallothionein by zinc and such an increase of metallothionein by zinc indicated a possibility of suppression of the ingested mercury by zinc. Therefore, suppressive effect of zinc on mercury poisoning was examined in the rat.

Male rats of the Wistar strain, weighing 140—160 g, were given subcutaneous injection of mercuric chloride, 0.018 mmole/kg/day, and oral administration of zinc acetate, 3.0 mmoles/kg/day. Mercuric chloride and zinc acetate were each dissolved in 0.9% sodium chloride solution and administered once every 24 hr for 5 days. Mercury and zinc solutions were administered at the same time, once every 24 hr for 5 days. Control rats received 0.9% sodium chloride solution.

Table I. Suppressive Effect of Successive Injections of Zinc Acetate on Survival of Rats Injected with Mercuric Chloride

Treatment	No. of rats	No. of surviving rats on day				
		1	2	3	4	5
Control (0.9% NaCl)	5	5	5	5	5	5
$HgCl_2$	10	10	6	1	0	0
$HgCl_2+Zn(AcO)_2$	10	10	10	10	10	10
$Zn(AcO)_2$	5	5	5	5	5	5

As shown in Table I, only 1 of 10 rats given mercury alone survived for 3 days, and this one rat died on the 4th day. In the animals given mercury and zinc at the same time, all the 10 animals were ailve on the 5th day, indicating the marked effect of zinc in suppressing the toxicity of mercury.

1) J. Parizek, *J. Endocr.*, **15**, 56 (1957).
2) S.A. Gunn, T.C. Gould, and W.A.D. Anderson, *Arch. Path.*, **71**, 274 (1961).
3) M. Webb, *Biochem. Pharmacol.*, **21**, 2767 (1972).
4) G.W. Evans, P.E. Majors, and W.E. Cornatzer, *Biochem. Biophys. Res. Commun.*, **40**, 1142 (1970).
5) M. Webb, *Biochem. Pharmacol.*, **21**, 2751 (1972).
6) M. Kimura and N. Otaki, *Jap. J. Hyg.*, **28**, 104 (1973).

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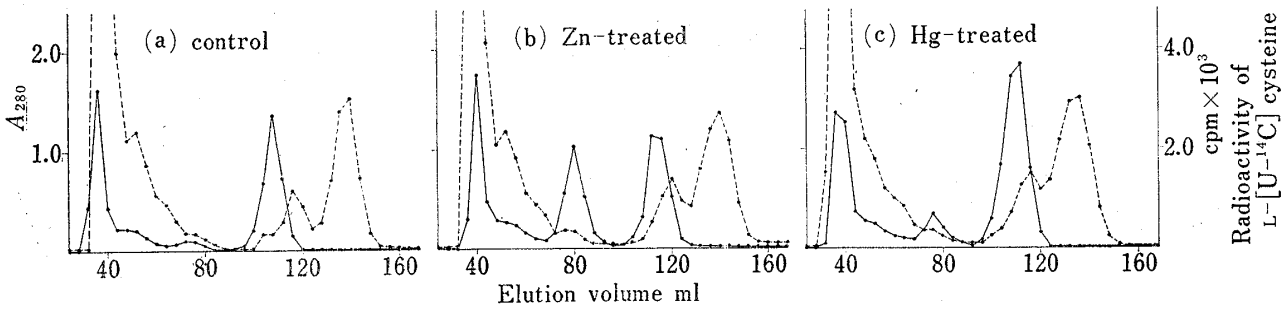

Fig. 1. Chromatogram of Liver Homogenates of Rats treated with L-[U-^{14}C]cysteine

These homogenates were centrifuged at 105000 *g* for 60 min and the supernatant was fractionated by gel filtration on the column (2.5 × 36cm) of Sephadex G-75 which was eluted with 0.01M tris-HCl buffer, pH 7.4 at 4°. Eluates (4 ml fractions) were analysed for L-[U-^{14}C] cysteine (•——•) and protein (A_{280}) (•·····•).

treatment: male rats of the Wistar strain (300 ± 10 g body wt), (a): control, (b): Zn $(AcO)_2$ 0.75 mmole/kg/day 24 hr previously (*s.c.*), (c): $HgCl_2$ 0.01 mmole/kg/day once every 24 hr for 2 days (*s.c.*), (a) (b) (c): 5μCi L-[U-^{14}C] cysteine/rat 24 hr previously (*i.p.*)

As shown in Fig. 1, high rate of incorporation of the radioactivity into the metallothionein in the rat liver was observed by the administration of zinc but the incorporation was not so marked by the administration of mercury. This fact seems to suggest that the biosynthesis of metallothionein by zinc is responsible for the suppressive effect of zinc on the toxicity of mercury.

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