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The influence of selenium on binding of inorganic mercury by metallothionein in the kidney and liver of the rat*

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Inorganic mercury, administered to rats in a single dose [1–5] or by repeated injections [6, 7] is bound in the kidneys, partly also in the liver, by metallothionein-like proteins. The latter are assumed to play a protective role in intoxication by inorganic mercury. On the other hand, recent reports point to a pronounced protective effect of selenium [8–11]. This element does not stimulate the synthesis of metallothionein [12]; its mechanism of action seems therefore entirely different.

Chen *et al.* [10] applying a single dose of $^{203}HgCl_2$ found that in the Se-pretreated rats, mercury did not accumulate efficiently in the kidneys. Changes in relative distribution of ^{203}Hg among subcellular fractions as well as among proteins of the soluble fraction suggested a diminished role of metallothionein in binding mercury in the presence of selenium.

Binding of mercury by metallothionein is especially effective in case of repeated administration of Hg [6, 7]. The aim of this report was therefore to check whether the observations of Chen *et al.* [10] would be reproducible under conditions of repeated exposure. Techniques of the experiments continues our earlier line [6, 7].

The experiment was performed on female rats of the Wistar strain, body wt 170–200 g, fed standard LSM diet. The animals were administered (to the tail-vein) mercuric chloride, labelled ^{203}Hg, in doses of 0.5 mg Hg/kg body wt, every other day over two weeks. Activity of ^{203}Hg was 40 μCi per dose. Selenium was supplied *per os* in a daily dose of 0.5 mg Se/kg, as sodium selenite. A control group was administered solely with mercury. The animals were sacrificed under ether narcosis, kidneys and liver were removed for analysis. The organs were homogenized in 0.25 M sucrose, the homogenate was centrifuged at 3500 rpm, for 10 min and the supernatant was further analysed by chromatography.

Determination of ^{203}Hg was performed by routine gamma counting in a scintillation counter USB-2. The protein content was determined by the method of Lowry *et al.* [13]. The supernatant was analyzed by column chromatography on Sephadex G-75 gel. Columns were calibrated with Dextran Blue and Cytochrome *c*; 0.1 M formate buffer, pH 8–0 was used as eluent.

Figure 1 shows that selenium administered simultaneously with mercury caused an essential redistribution of mercury in the organs. Whereas mercury administered alone was deposited mainly in the kidneys (42 per cent) and only about 7 per cent was found in the liver, simultaneous administration of selenium resulted in reversed proportions: 33 per cent of the dose in the liver, with only 8 per cent in kidneys.

The supernatant of the kidneys contained on average 80 per cent and, that of the liver 63 per cent of mercury present in the homogenate. In animals treated simultaneously with selenium, these figures were reduced to 62 and 39 per cent, respectively.

When administered alone, mercury was bound mainly to the kidneys, and in the liver to an essential degree, with metallothionein-like proteins (Fig. 2a, c) as already reported [7]. In the presence of selenium (Fig. 2b, d) the latter fraction could not be detected and the entire amount of mercury was bound with high mol. wt. proteins.

In general, our observations confirm those of Chen *et al.* obtained for single exposure to mercury. From both of these reports it follows that selenium does not cooperate with the previously-described protective system of metallothionein-like proteins. Moreover, in case of inorganic mercury the role of metallothionein in binding of this metal is almost eliminated by selenium. The mechanism of the above phenomenon may involve formation of a high mol. wt Se-protein with exceptionally strong binding affinity for mercury, as suggested previously [14]. The mechanism of the above phenomenon remains to be explained.

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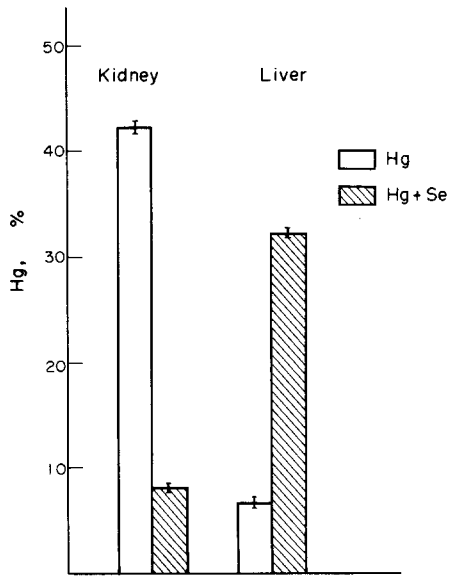

Fig. 1. The levels of mercury, (per cent of the cumulative dose) in the kidneys and liver of rats in the course of prolonged exposure to mercury alone and to mercury and selenite administered simultaneously. Six female rats weighing about 200 g were used in two series and measurements in each series were made jointly; values for both series are marked on the diagram.

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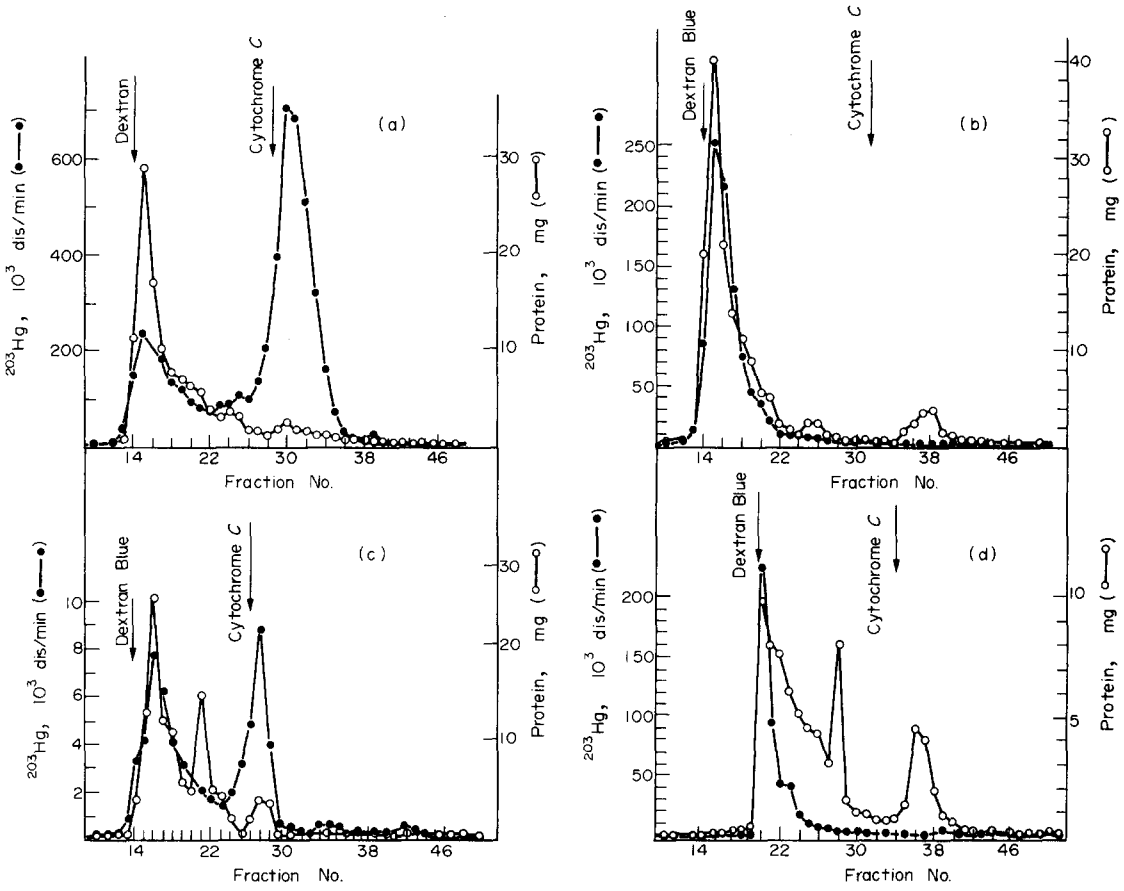

Fig. 2. The chromatography of the tissue supernatants: (a) upper level, kidneys of rats exposed to $HgCl_2$; (b) $HgCl_2$ and Na_2SeO_3; (c) lower level, liver of rats exposed to $HgCl_2$; (d) $HgCl_2$ and Na_2SeO_3. Conditions: Sephadex G-75, column 1.9 × 63 cm, ammonium formate buffer, pH 8.1, ionic strength 0.1 M, flow rate about 1 ml/min.; fractions 5 ml each were collected.

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