Influence of Silver, Mercury, Lead, Cadmium, and Selenium on Glutathione Peroxidase and Transferase Activities in Rats

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Received March 20, 1979; Accepted March 28, 1979

ABSTRACT

At the levels used in the experiments, mercury and silver significantly depressed the activity of glutathione peroxidase (assayed with either H_2O_2 or cumene-OOH) in rat tissues, whereas cadmium or lead had no effect on this activity. The most pronounced effects of mercury and silver on glutathione peroxidase were found in the liver and kidneys, with much less effect in the testes and erythrocytes. Similar trends for the effects of these metals were noted for tissue selenium levels. Silver and mercury significantly depressed the selenium concentrations, but cadmium and lead had no effect upon the selenium levels. Mercury and silver had no effect upon the activity of glutathione transferase in liver and testes, but mercury caused a significant initial increase of its activity in the kidneys. At no time did silver have any significant effect on its activity in this organ.

Key Words: Glutathione peroxidase, effects of Ag, Hg, Pb, Cd, and Se on; glutathione transferase, effects of Ag, Hg, Pb, Cd, and Se on; Se; Ag; Hg; Pb; Cd; rats, effects of trace metals on glutathione peroxidase and transferase activities in.

INTRODUCTION

Shaver and Mason (1) first reported that silver would significantly increase the development of liver necrosis in selenium and vitamin E deficient rats. This has been confirmed by other investigators as indicated in a number of subsequent reports (2–6). This effect of silver in the production of liver necrosis is not shared by other heavy metals such as lead, mercury, cadmium,
or thallium (5, 6). Dietary silver has been shown to decrease the activity of the selenoenzyme, glutathione peroxidase, and this effect of silver is prevented by selenium (7). Therefore, the present investigation was undertaken to determine whether the unique effects of silver in the promotion of liver necrosis resulted from its depression of the activity of glutathione peroxidase.

MATERIALS AND METHODS

Three experiments were conducted with weanling rats. Rats in all three experiments were fed a basal diet as previously reported (8), which was composed of torula yeast, 30%; sucrose, 51.5%; corn oil, 4.0%; solka floc, 7.5%; mineral mix, 5.0%; vitamin mix, 1.0%; and vitamins A (10 mg/kg), D (100 μg/kg) and E (60 mg/kg). This basal diet was shown by analysis to contain 20 ppb selenium.

In the first study, 75 male rats (average weight, 110 g) were used. Three rats were killed initially, and the activity of glutathione peroxidase determined. The remaining 72 rats were divided into 6 groups and fed either the basal diet or this diet containing 0.1 ppm additional selenium with no metal additions or with 500 ppm lead as lead acetate, 100 ppm cadmium as cadmium chloride, 400 ppm mercury as mercuric chloride, or 800 ppm silver as silver acetate. Four rats on each diet were killed at 3, 6, and terminally at 12 weeks after placement on these diets. Their tissues were assayed for glutathione peroxidase using hydrogen peroxide as the substrate and were analyzed for selenium content.

In the second study, a pair-fed experiment was conducted since the levels of mercury and silver used in the first experiment depressed the appetite of the rats. Twelve male rats were divided into 3 groups and fed the basal diet plus 0.1 ppm selenium, or this same diet containing either 800 ppm silver or 400 ppm mercury. The rats assigned to the basal diet with selenium were fed the same amount of food as was consumed by those assigned to the silver and mercury diets. After 11 weeks of feeding these diets, the rats were killed and their tissues assayed for glutathione peroxidase using hydrogen peroxide as the substrate and were analyzed for selenium content.

In the third experiment, 40 rats (av. wt., 50 g) were used. Four rats were killed initially and their tissues assayed for glutathione peroxidase (with either hydrogen peroxide or with cumene hydroperoxide as substrates) and glutathione transferase to obtain initial values. The remaining 36 rats were divided into 3 groups and fed the same diets as indicated in the second study. Four rats on each diet were killed after 2, 4, and 6 weeks of feeding these diets. Their tissues were assayed for glutathione peroxidase (H₂O₂ or cumene-OOH as substrates) and glutathione transferase.

Sprague-Dawley rats, obtained from Simonsen Laboratory in Gilroy, California, were used in all experiments. Glutathione peroxidase (with H₂O₂) was assayed in the tissue soluble fractions by a coupled enzyme procedure (9)