Pretreatment with Aluminum and Gallium Relieved the Acute Lethal Toxicity of Carbon Tetrachloride in Mice

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Introduction

We reported previously the protective effect of trivalent chromium pretreatment by the administration of chromium chloride on acute hepatotoxicity induced by carbon tetrachloride (CCl_4) both in rats and mice.^{1,2)} In this study, we found that aluminium chloride (AlCl_3) and gallium nitrate ($\text{Ga}(\text{NO}_3)_3$) had a similar protective effect as chromium chloride among several metals tested.

To clarify the mechanism of depression of CCl_4 -induced hepatotoxicity by Al and Ga pretreatment, we examined the change of biochemical parameters in mice after CCl_4 exposure with/without pretreatment of Al and Ga, focusing on the effect of this pretreatment on the CCl_4 -metabolic enzymes, cytochromes P-450 and NADPH-cytochrome P-450 reductase, and on substances having radical scavenger activity.

Methods

AlCl_3 or $\text{Ga}(\text{NO}_3)_3$ was injected intraperitoneally to male ddY mice (25–30 g body weight) at a dose of 30 mg Al/kg body weight or 50 mg Ga/kg body weight, and then the animals were fasted for 24 h. Then, a mixture of CCl_4 and olive oil (1:1, v/v) was administered to the animals at a lethal dose of 3 ml CCl_4 /kg. The number of animals surviving was recorded after 2 weeks of the CCl_4 administration. To determine the biochemical parameters, the blood in mice

administered CCl_4 was collected for a given time and the liver was obtained after perfusion.

Results

The increase of glutamic-oxaloacetic transaminase (GOT) and glutamic-pyruvic transaminase (GPT) activities in the plasma after CCl_4 administration was depressed by Al and Ga pretreatment compared to the control. The contents of cytochromes P-450 and the activity of NADPH-cytochrome P-450 reductase in the liver were decreased significantly 24 h after AlCl_3 and $\text{Ga}(\text{NO}_3)_3$ treatment. However, the activities of glutathione peroxidase, superoxide dismutase and glutathione reductase were not influenced by Al and Ga pretreatment. The level of glutathiones in both reduced-form and oxidized-form was not different between the pretreatment groups and the control group in the early period after CCl_4 administration.

Discussion

These results suggest that the initial process of metabolic activation of CCl_4 to form trichloromethyl radical in mouse liver might be suppressed by AlCl_3 and $\text{Ga}(\text{NO}_3)_3$ pretreatment.

References

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- 2) M. Tezuka, S. Ishii and S. Okada, *J. Inorg. Biochem.*, **44**, 261 (1991).