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ACTIVITY OF GLUTATHIONE-RELATED ENZYMES IN RAT TISSUES AFTER FORMALDEHYDE EXPOSURE

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INTRODUCTION

Formaldehyde is known as one of the abundant air pollutants (Balmat & Meadows, 1985). Human exposure to formaldehyde is extensive, in both the indoor and outdoor environment (Godish & Rouch, 1986). Industrial and automobile emissions, some polymeric materials and tobacco smoke are the main sources of this compound (Castell, Vernon & Bailey, 1987; Schaller, Triebig & Beyer, 1989; Flyvholm & Andersen, 1993). According to the present-time theories the toxic effects of formaldehyde can be attributed to disturbances in interactions of membrane proteins followed by membrane disruption (Nagornii, 1978; Stepuro & Kashko, 1989). Increased concentrations of free radicals may also play an important role in the pathogenesis of formaldehyde toxicity. Since glutathione-related enzymes and catalase play a significant role in both the cell antioxidative defence and formaldehyde detoxification, it is very important to determine their activities in the tissues of rat exposed to formaldehyde.

MATERIALS AND METHODS

Animals

Female albino rats (140–160 g body weight) were kept on standard laboratory diet. The animals were divided into two groups, six rats in each. Animals of the first group were placed into the special chamber in which air was flushed, this group was taken as so-called "chamber control". Animals of the second group were also placed into the chamber in which air and formaldehyde at the concentration of 10 mg/m^3 were flushed. The duration of this inhalation procedure was 7 hours per day. The total time of exposure was 35 hours. The animals were killed by decapitation 16 hours after the last inhalation procedure. Blood (prevented from clotting by EDTA) was used immediately for analysis. Fragments of liver were stored in liquid nitrogen before use.

Analytical procedures

The levels of reduced glutathione (GSH) were measured with the Ellman's reagent (Sedlak & Lindsey, 1968), thiobarbituric acid-reactive substances (TBARs) were determined according to Stoks & Dormandy (1971), activities of glutathione peroxidase (GPOx) were assayed by following the GSH consumption (Kruglikova & Shtutman, 1976), glutathione reductase (GR) by measurement the NADPH oxidation (Khotimchenko, Alekseeva, Gvozdeva & Smirnova, 1987), and the activity of catalase was measured according to the method described by Koroluk (1988) in the blood and liver of rats.

Statistical methods

All values are expressed as means for 6 animals ± standard error (SEM). Statistical significance was evaluated using the Student's "t" test, a level of significance of $P \leq 0.05$ was accepted as significant.

RESULTS

Formaldehyde intoxication resulted in an increase of TBARS concentration by 31% in erythrocytes (Fig. 1) and by 39% in the liver homogenates (Fig. 2). The catalase activities were also significantly higher in the blood serum and in the liver of exposed rats in comparison with the control groups

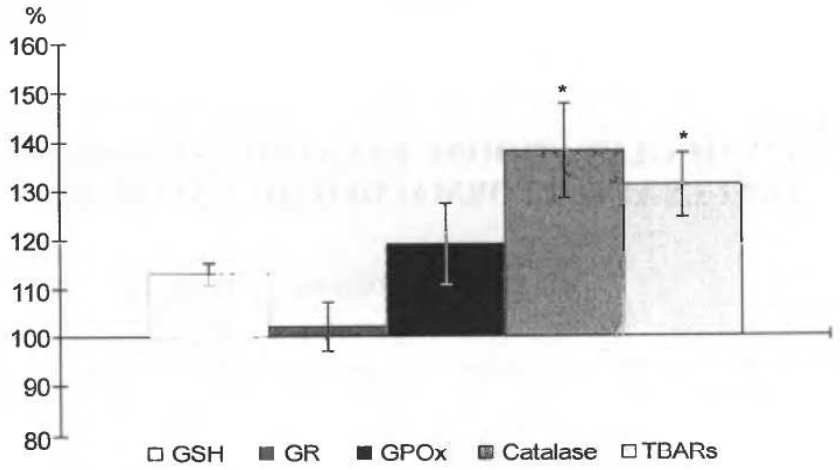

Fig. 1. Changes in the levels of reduced glutathione, TBARS, activities of glutathione reductase, glutathione peroxidase and catalase in the blood of formaldehyde-treated rats. All values are expressed in percentage of the corresponding values in the blood of control rats. Statistically significant differences ($P \leq 0.05$) are marked by *

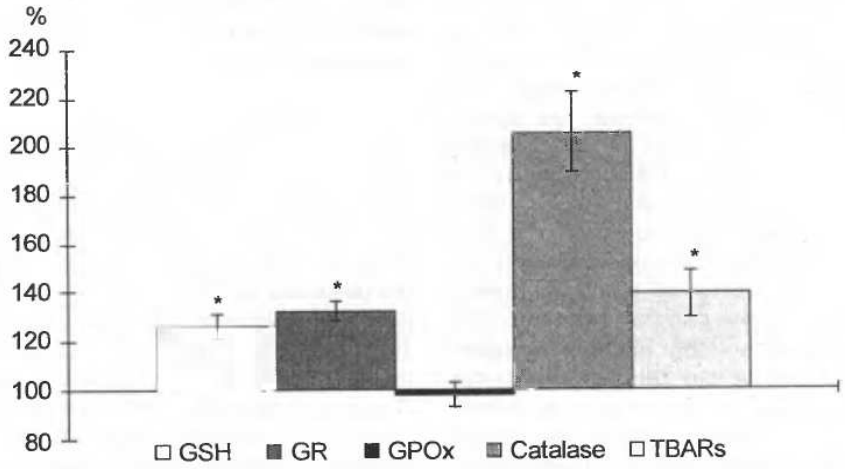

Fig. 2. Changes in the levels of reduced glutathione, TBARS, activities of glutathione reductase, glutathione peroxidase and catalase in the liver of formaldehyde-treated rats. All values are expressed in percentage of the corresponding values in the blood of control rats. Statistically significant differences ($P \leq 0.05$) are marked by *

(by 38% and 106% respectively). No significant changes of GSH level and activities of GR and GPOx in blood were found. The concentrations of GSH and activities of GR were significantly higher in the liver of exposed rats in comparison with the control groups.

DISCUSSION

On the basis of the presented results, it can be concluded that exposure to formaldehyde leads to activation of lipid peroxidation (LPO) processes in erythrocytes and liver of animals. Similar changes were detected by others authors, which found that cigarette smoke can induce LPO in the liver (Helen & Vijayammal, 1997). Howard, Ota, Briggs, Hampton and Pritsos (1998) observed an increase of catalase activity in human blood after tobacco smoke exposure. According to our data, the influence of formaldehyde leads to elevation of catalase activity in blood serum and liver of experimental animals. We consider the increase of catalase activity in the liver as positive. Firstly, catalase removes H_2O_2 which is extensively generated under oxidative stress conditions. Secondly, the

enzyme can oxidize formate (which is a product of formaldehyde metabolism) into CO_2 (Tiunov, 1981). The elevation of catalase activity in blood plasma seems to be due to disturbance in membrane permeability.

Despite its reactivity with many biological molecules formaldehyde is a naturally occurring chemical found virtually in all cells (Winters & Cederbaum, 1990). Formaldehyde can be metabolized primarily by two different pathways, one involving oxidation by the aldehyde dehydrogenase, and the other involving a specific glutathione-dependent formaldehyde dehydrogenase (Kifmerle, Feucht & Kaulfers, 1996; Barber & Donohue, 1998). So, the rate of formaldehyde detoxification depends on the level of GSH. According to our data these processes were not limited in the blood and liver. It can also be proposed that under these conditions in erythrocytes utilization of GSH in a detoxification reactions prevailed, because activities of GR and GPOx were not changed.

In the liver GSH was extensively regenerated from its oxidized form. GSSG formed possibly non-enzymatically. We consider that in the liver glutathione redox-system is involved in the activity of both antioxidant and detoxifying defence mechanisms.

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