# CHANGES IN CONCENTRATION OF SOME VITAMINS IN ORGANS AND URINE OF ALBINO RATS DURING CHRONIC EXPOSURE TO 3,4-BENZPYRENE AND SULFUR DIOXIDE

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In albino rats exposure for long periods to 3,4-benzpyrene alone or in conjuction with sulfur dioxide leads to a decrease in the concentrations of thiamine and riboflavin in the liver and brain and to an increase in the excretion of vitamins, $B_1$, $B_2$, PP, and C in the urine.

The supply of vitamins to the body is reduced in the presence of malignant neoplasms and during exposure to chemicals [1, 4-6, 7, 9, 11]. The substance 3,4-benzpyrene (BP), which is known to possess a carcinogenic action, is present in the atmosphere of modern cities along with various chemical substances, most commonly with sulfur dioxide. The biological action of a combination of these substances has not been studied.

The object of the present investigation was to study the concentrations of thiamine, pyruvic acid, riboflavin, and the pyridine coenzymes (NAD + NADP) in the organs and the excretion of thiamine, pyruvic acid, riboflavin, N'-methylnicotinamide (N'-MNA), and ascorbic acid in the urine of rats exposed for long periods to the action of 3,4-benzpyrene and sulfur dioxide. This last substance is a widespread pollutant which is most commonly found together with BP in the city atmosphere. The role of $SO_2$ in combination with a carcinogenic agent in the induction of tumors has not hitherto been studied.

Experiments were carried out on 300 noninbred albino rats (males and females) in five groups. The animals of group 1 were exposed to the combined effects of BP and $SO_2$, group 2 to $SO_2$, group 3 to BP, group 4 was an absolute control, and the animals of group 5 received polyvinylpyrrolidone by intratracheal injection. BP was administered to the rats in three monthly doses: 1) 2 mg monthly for 12 months, total 24 mg; 2) 2 mg monthly for 6 months and 5 mg monthly for 6 months, total 42 mg; 3) 5 mg monthly for 6 months, total 30 mg. As a preliminary measure, the animals of these groups were exposed to poisoning by $SO_2$ for 6 months. BP was injected intratracheally as a suspension in a solution of polyvinylpyrrolidone, a colloidal plasma expander, with the addition of ink to mark the places of deposition of the carcinogen [12] The animals inhaled $SO_2$ throughout the day and night for 6 months in a concentration of 10 mg/m$^3$.

The concentration of vitamins in organs and urine of the rats was investigated in two stages: their concentration in the liver and brain of the rats was determined at the 6th-7th month of the experiment, when they had received 12-14 mg BP, and excretion of the vitamins in the urine was determined in the rats 4 months after the end of poisoning with BP for 12 months and 10 months after exposure to $SO_2$, when the animals had reached the age of 24 months and had received 24, 30, or 42 mg of the carcinogenic hydrocarbon.

Without delay after decapitation of the animals, homogenates were prepared from the organs and the concentrations of thiamine, pyruvic acid, riboflavin, and the pyridine coenzymes were determined; ascorbic acid, riboflavin, thiamine, pyruvic acid, and N'-MNA were estimated in the urine by modern methods [2, 3, 8, 10, 13]. For the estimation of thiamine, riboflavin, NAD + NADP, and N'-MNA, the ÉF-ZM fluorometer was used. The numerical results were subjected to statistical analysis.

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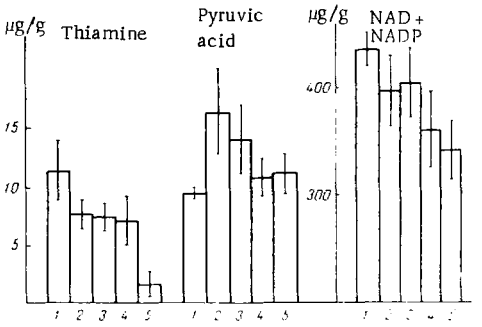


Fig. 1. Concentrations of thiamine, pyruvic acid, and NAD + NADP in rat liver: 1) control; 2) $SO_2$; 3) $SO_2$ + BP; 4) solvent; 5) BP.

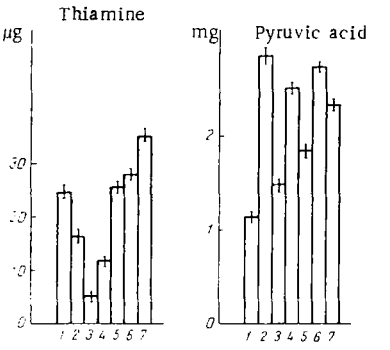


Fig. 2. Excretion of thiamine and pyruvic acid with urine of rats: 1) control; 2) 24 mg BP + $SO_2$; 3) 42 mg BP + $SO_2$; 4) $SO_2$; 5) $SO_2$ + 30 mg BP; 6) 42 mg BP; 7) solvent.

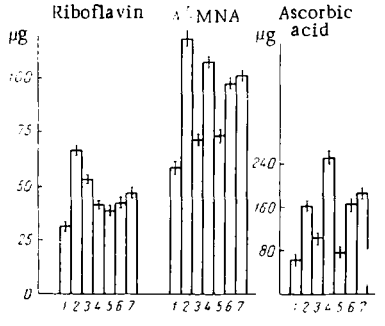


Fig. 3. Excretion of riboflavin, N'-MNA, and ascorbic acid in urine of rats: 1, 2, 3, 6, 7) as in Fig. 2; 4) $SO_2$ + 30 mg BP; 5) $SO_2$.

A decrease in the concentration of thiamine in the liver of the experimental male rats can be seen in Fig. 1 and was most marked in rats exposed to BP alone ($P < 0.01$). A decrease in the thiamine concentration was also found in the brain of the experimental rats, but this was not significant. These findings can apparently be explained on the grounds that different organs lose thiamine at different rates: the thiamine concentration falls most rapidly in the liver, while the brain can retain thiamine longer.

The decrease in the thiamine concentration in the organs was accompanied by an increase in the concentration of pyruvic acids, and this was significant in the brain of rats exposed to BP only ($P < 0.05$). A significant decrease in the concentration of NAD + NADP (Fig. 1) and of total riboflavin was found in the liver of rats exposed to BP alone.

Investigations of homogenates of the liver and brain tissues of the rats thus showed that prolonged exposure to BP in a dose of 12-14 mg, to $SO_2$ in a concentration of 10 mg/m$^3$, and to a combination of substances produces changes in the concentrations of thiamine, pyruvic acid, riboflavin, and NAD + NADP in the organs. The most marked changes were observed under the influence of benzpyrene.

Significant changes also were detected in the excretion of vitamins by the rats in their urine. In the case of male rats of all experimental groups, for example, compared with the controls the excretion of thiamine was reduced, and this decrease was considerable in rats exposed to the combined action of $SO_2$ + BP and also of $SO_2$ alone. The smallest excretion of thiamine was found in the urine of rats exposed to the combined effect of 42 mg BP and $SO_2$. In rats receiving polyvinylpyrrolidone, the excretion of thiamine with the urine was increased (Fig. 2).

The excretion of riboflavin, ascorbic acid, N'-MNA, and pyruvic acid in the urine of all the experimental male rats exceeded the excretion of these vitamins by the control rats (Fig. 3). The smallest quantities of the vitamins were excreted in the urine of rats receiving $SO_2$ alone, and the largest quantities were excreted in the urine of rats receiving a combination of $SO_2$ + BP, or BP alone. Morphological investigations showed that the largest number of malignant neoplasms was formed in animals receiving BP in conjunction with $SO_2$.

The changes thus discovered in the concentrations of vitamins in the organs and in their elimination with the urine of albino rats under the influence of separate and combined exposure to 3,4-benzpyrene and sulfur dioxide thus indicate severe disturbances of metabolism accompained by loss of vitamins. The disturbances are more pronounced as a result of the combined action of 3,4-benzpyrene and sulfur dioxide, so that the latter apparently potentiates the action of the carcinogenic agent.

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