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The influence of simultaneously administered mexamine on the distribution of cystamine-^{35}S

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Summary. The ^{35}S-distribution after simultaneous administration of a mixture of cystamine-^{35}S and mexamine (20 mg/kg + 10 mg/kg) has changed as compared with the groups treated with cystamine-^{35}S only.

The increased and prolonged radioprotective effect of a mixture of aminodisulfides or aminothiols with indolalkylamines has been demonstrated by many authors[1-4]. Some investigators suppose that aminodisulfides or aminothiols protect the gastrointestinal tract against ionizing radiation, whereas indolalkylamines protect bone marrow[1,2]. The distribution of cystamine in the organism of rats and mice was studied several times while ^{35}S-labelled cystamine was used. The irregular distribution of cystamine has been confirmed, the highest level being found in the radiosensitive tissues and kidney[5-7]. Only a few reports have been published concerning the influence of mexamine (5-MOT) on the distribution of cystamine under the simultaneous administration of these 2 agents in mice. Titov and Mordukhovitch[8] found an increased ^{35}S-activity in the small intestine, lungs, liver and brain and a fall in the activity in the kidney and muscles of mice treated with a mixture of cystamine-^{35}S and 5-MOT (comparing with the group treated with cystamine-^{35}S only). In rats, the concentrations of nonprotein SH-groups were followed after the administration of cystamine and 5-MOT, but ^{35}S-distribution has not been studied under these conditions[9]. The aim of our work was to ascertain, if mexamine influenced the ^{35}S-distribution in rats treated with an optimal protective mixture of cystamine-^{35}S and 5-MOT during the period of maximal radioprotective effect (1st h after administration of radioprotective agents).

Material and methods. Adult Wistar rats (males, weight 200 g) were used for the experiments. They were fed standard Larsen diet and water ad libitum. 1 group of rats was treated with ^{35}S-labelled cystamine × 2 HCl (20 mg/kg of b.wt referred to the base content) by an i.p. injection. The 2nd group was treated with a mixture of cystamine-^{35}S × 2 HCl and 5-methoxytryptamine × HCl (20 mg/kg + 10 mg/kg referred to the base content). These amounts were dissolved in an isotonic NaCl solution in such a dilution as to give 0.2 ml of the solution per 20 g b.wt. The total radioactivity administered per rat was 70 μCi. Cystamine-^{35}S × 2 HCl was synthesized by Dr. Kozák from the Biophysical Institute in Prague. 5-Methoxytryptamine (mexamine) was obtained from Koch-Light, Ltd. The number of rats in the experimental groups varied between 6 and 9. The rats were sacrificed by decapitation 10, 20, 30 and 60 min after the administration of radioprotective agents. The determinations were carried out in 10% homogenates of the liver, spleen, kidney, small intestine, bone marrow and in the blood. The blood was collected into the tubes with heparine. The bone marrow was obtained from the femur and tibia. A 10 cm section next to the pylorus was dissected from the small intestine. For experiments, 0.5 ml of the homogenates or 0.1 ml of the blood were used. The samples were solubilized in 1 ml of hyamine (Koch-Light, Ltd) and decoloured with H_2O_2, if necessary. After being solubilized, the samples were neutralized with HCl and 10 ml of Bray's

The concentrations of labelled sulfur in various tissues of rats after the administration of cystamine-^{35}S or a mixture of cystamine-^{35}S with 5-methoxytryptamine (5-MOT) expressed in percent of activity administered

Tissue	10 min		20 min		30 min		60 min	
	Cystamine	Cystamine + 5-MOT	Cystamine	Cystamine + 5-MOT	Cystamine	Cystamine + 5-MOT	Cystamine	Cystamine + 5-MOT
Liver	12.60 ± 1.30	12.20 ± 1.41	10.54 ± 0.81	12.33* ± 0.74	10.76 ± 0.88	12.71* ± 1.42	10.29 ± 1.25	9.67 ± 1.61
Spleen	0.99 ± 0.23	1.10 ± 0.29	0.62 ± 0.04	0.77 ± 0.19	0.72 ± 0.05	0.75 ± 0.13	0.53 ± 0.06	0.48 ± 0.07
Kidney	3.08 ± 0.50	1.89* ± 0.38	2.54 ± 0.27	2.08* ± 0.44	2.16 ± 0.25	2.40 ± 0.22	1.61 ± 0.30	2.04 ± 0.42
Small intestine	3.73 ± 0.71	3.75 ± 0.39	2.19 ± 0.26	3.57* ± 0.63	3.30 ± 0.39	3.32 ± 0.46	3.05 ± 0.41	3.48 ± 0.69
Bone marrow	0.42 ± 0.09	0.12* ± 0.03	0.58 ± 0.06	0.37* ± 0.06	0.56 ± 0.04	0.58 ± 0.07	0.47 ± 0.05	0.55* ± 0.05
Blood	0.28 ± 0.05	0.30 ± 0.02	0.28 ± 0.04	0.39* ± 0.04	0.27 ± 0.05	0.37* ± 0.03	0.23 ± 0.06	0.31 ± 0.08

* Significant difference ($p < 0.05$).

scintillating solution (Spolana) were added. The total activity was measured by a liquid scintillation counter MARK I (Nuclear Chicago). An external standard was used. The radioactivity obtained was expressed in percent of activity administered – in the case of the bone marrow in percent of 1 g, in the case of the blood in percent of 1 ml, and in the other cases in percent of the total wet tissue weight. The data obtained were evaluated statistically and the mean values and the SD were computed. The statistical significance of the differences was checked by means of the Student's t-test.

Results. The distribution of ^{35}S-activity and the influence of simultaneously administered mexamine are shown in the table. A highly significant decrease in activity occurred in the kidney and bone marrow 10 min after the treatment with the mixture of cystamine-^{35}S and 5-MOT. The activity in all other tissues investigated did not differ too much as compared with the group treated with cystamine-^{35}S only. The most pronounced changes were seen at an interval of 20 min after the administration of the radioprotective mixture. The level of activity was increased markedly in the liver, small intestine and blood, whereas in the kidney and bone marrow a decrease was established. The activity in the spleen revealed a slight increase. 30 min after the treatment with the mixture, a high level of activity was found in the liver and blood. The values of activity obtained in all other tissues remained practically unchanged when compared with the animals treated with cystamine-^{35}S only. An increase of activity occurred in the bone marrow, small intestine and kidney (the difference being significant in the bone marrow) 60 min after administration of the radioprotective mixture.

Discussion. The ^{35}S-distribution in rats treated with a mixture of cystamine-^{35}S and 5-MOT has not yet been studied. However, the increased concentration of nonprotein SH-groups was described in the spleen, small intestine, muscles and the blood, whereas the decrease was noticed in the kidney 30 min after the simultaneously administered cystamine and 5-MOT[9]. In our laboratory, characteristic changes were found in the content of SH-groups in various tissues of rats under similar conditions also[10]. These findings indicated the possibility of a changed distribution of cystamine-^{35}S. Our experiments confirmed this assumption. Mexamine caused a significant increase in the ^{35}S-activity in the liver, small intestine and blood, mainly 20 min after the administration of radioprotective agents and a decrease in activity in the bone marrow and kidney at the 1st intervals followed. Our results are in good agreement with the findings of Titov and Mordukhovitch[8] who investigated the influence of 5-MOT on the distribution of cystamine-^{35}S in mice 15 and 30 min after the treatment with a mixture of both radioprotective agents. The changed ^{35}S-distribution caused by simultaneously administered mexamine was found when using other radioprotective agents than cystamine. Ayrapetyan et al.[11] described protracted penetration of cystaphos-^{35}S into various tissues of mice in the 1st 30 min. At the following intervals, an increase in ^{35}S-activity occurred. The fate of labelled sulfur of cystamine-^{35}S in the bone marrow has not yet been studied. Our findings of a decreased activity at the 1st 2 intervals could be explained by the vasoconstrictive effect of mexamine which lowered the penetration of cystamine[12]. However, this effect may not play a decisive role in the other radiosensitive tissues (spleen, small intestine). The prolonged persistence of labelled sulfur in rats treated with mexamine could be understood as a result of the increased concentration of cystamine in the kidney, which leads to a lowered elimination into the urine. This corresponds with the increased activity of labelled sulfur in the blood. The results presented indicate that at the interval during which the experimental animals are usually X-rayed (30 min after the treatment with radioprotective agents at the latest), the ^{35}S-activity of cystamine-^{35}S simultaneously administered with mexamine was increased in radiosensitive tissues (small intestine, spleen); but it was decreased in bone marrow comparing with the group treated with cystamine-^{35}S only. We could not confirm unequivocally the hypothesis of a prior role of SH-groups in the mechanism of radioprotection[13]. Our findings support the assumption of the combined effect of various biochemical mechanisms including the substantial role of hypoxic effect[14].

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Methylmercury sexual dimorphism in the mouse[1]

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Summary. 5–8 days after a single nontoxic dose of radioactive methylmercury chloride adult male mouse kidneys contain twice as much radioactive mercury per unit wet wt as do kidneys of similarly dosed adult females.

In the course of studies designed to evaluate biological variables of significance for estimating hazards of exposure of mammals, including man, to mercury compounds, we have observed that after a single, nontoxic dose of methylmercury, much more mercury is found per unit wet wt of kidney in male than in female adult mice.

Three 8-week-old C129F$_1$ hybrid (BALB/c female × 129 male) female mice were each given a single, nontoxic, i.p.