

CHROMATOGRAPHIC INVESTIGATION OF THE EFFECT OF WHOLE-BODY X-RAY IRRADIATION ON SYNTHESIS OF BILE ACIDS IN FEMALE ALBINO RATS

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All the main stages of synthesis of bile acids in the liver are inhibited in female rats with acute radiation sickness. The formation of the primary bile acids from cholesterol and conversion of desoxycholic acid into cholic are disturbed. The conjugation of free cholic acid with taurine and glyocol is also interfered with, especially in the late stages of the disease. At this time the cholic acid concentration rises while the taurocholic acid concentration falls and glycocholic acid disappears completely from the bile.

Experiments have shown that ionizing radiation influences the intensity of bile formation [1-3, 5, 8-10, 12-17]. Nevertheless, changes in the chemical composition of the bile taking place under these circumstances have been inadequately studied, and this is particularly true of the content of bile acids in the bile.

It was accordingly decided to study changes in the content of bile acids in the bile and the principal disturbances of their synthesis in irradiated animals.

EXPERIMENTAL METHOD

Experiments were carried out on 38 female albino rats weighing 130-160 g using a method described previously [4, 11]. Indices of the intensity of bile formation (rate of bile secretion in mg/min/100 g body weight, total volume of bile secreted during each hour of observation and during the 7 h of the experiment, in mg/100 g) and indices of the content of cholates in the bile (total concentration and concentration of each acid separately, in mg %, and their total content in hourly portions and during the whole 7 h of the experiment) were analyzed. The concentration of bile acids was determined and the acids were separated by ascending paper chromatography as described by Karbach [6, 7].

In the experiments of series I (control) the initial background of intensity of bile secretion and concentration of bile acids in the bile before irradiation was established, while in the experiments of series II-IV changes occurring 1, 2, and 4 weeks after irradiation were determined. Whole-body irradiation of the animals in a single dose was given from a type RUM-11 apparatus under the following conditions: voltage 180 kV, current 10 mA, 0.5 mm copper filter, no tube, skin-focus distance 40 cm, dose rate 34.5 R/min; total dose 600 R.

When irradiated under these conditions the albino rats developed acute radiation sickness. Their leukocyte count per mm³ blood fell from $12,420 \pm 250$ to 5820 ± 130 (after 1 week) to 4320 ± 140 (after 2 weeks), and to 3800 ± 90 (4 weeks after irradiation), and the erythrocyte count fell from 7.9 ± 0.235 million to 7.02 ± 0.18 , 6.32 ± 0.21 , and 6.22 ± 0.25 million respectively. The animals lost their appetite, lost weight, and died in large numbers, especially toward the end of the observation.

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EXPERIMENTAL RESULTS

In the female rats 1 week after irradiation the rate of bile secretion in most cases increased from 3.8 ± 0.4 – 3.5 ± 0.4 to 4.4 ± 0.3 – 4.1 ± 0.2 mg/min/100 g ($P < 0.05$). After 2 weeks it was still raised, but after 4 weeks it had fallen to 2.8 ± 0.2 mg/min/100 g ($P < 0.05$). As a result of this, the total volume of bile obtained in 7 h in the first 2 cases was increased on the average by 11.7 and 10.6% respectively, while in the 3rd case it was reduced by 14.3%.

The concentration of cholates in the bile showed even greater changes. For example, 1 week after irradiation the total concentration of bile acids had fallen on the average from 1214–669 to 967–528 mg %, after 2 weeks to 933–655 mg %, and after 4 weeks to 966–650 mg %. As a result, the index of the total quantity of cholates excreted with the bile during the experiment fell, especially after 1 and 4 weeks, by 10.9 and 23.6%, respectively.

Chromatography of the bile showed that the decrease in concentration of cholates in it took place at the expense of taurocholic acid (by 16.6, 8.2, and 30% at the 3 periods after irradiation), while the concentration of the other acids increased. In particular, the concentration of glycocholic acid was increased during the first 2 periods by 28.4 and 160.7% (in the 3rd period it had completely disappeared from the bile), while that of desoxycholic acid had increased by 116, 85, and 88% at these 3 periods. The concentration of cholic acid also showed a slight increase. These changes led to a sharp disturbance of the ratio between conjugated and free acids: on the average from 13.6–5.3 after 1 week to 7.0 after 2 weeks and to 4.9 after 4 weeks.

The decrease in the indices of the total quantity of cholates excreted with the bile indicates inhibition of bile acid synthesis in the liver of the irradiated animals.

The primary bile acids in rats are desoxycholic and cholic acids [18–20]. Much of the desoxycholic acid becomes converted into cholic, and the cholic into taurocholic and glycocholic acids. For this reason, analysis of the results of the chromatographic investigations shows that in irradiated rats all the principal stages of cholate formation are disturbed. Conversion of cholesterol into primary bile acids, of desoxycholic acid into cholic, and conjugation of cholic acid, especially with taurine, are interfered with. This is shown by a decrease in the total concentration of cholates, an increase in the concentration of primary acids, a decrease in the concentration of taurocholic acid, and a decrease in the ratio between conjugated and free acids.

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