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EFFECTS OF THIOCIN ON 7A-HYDROXYLASE ACTIVITY IN THE COURSE OF EXPERIMENTAL ATHEROSCLEROSIS DEVELOPMENT

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In the liver, cholesterol is converted into bile acids through the catalytic activity of cholesterol 7α-hydroxylase (CYP7A1), the rate-limiting enzyme in the classical bile acid synthesis pathway. The resulting bile acids are secreted into the biliary system and released into the gastrointestinal tract as components of bile, where they play an essential role in the emulsification and intestinal absorption of dietary lipids [4,2]. Cholesterol 7α-hydroxylase regulates the formation of 7α-hydroxycholesterol, the primary precursor of bile acids, thereby maintaining cholesterol homeostasis [5]. Consequently, CYP7A1 is considered one of the key enzymes controlling cholesterol catabolism and elimination from the body. Alterations in its activity may impair bile acid synthesis, promote cholesterol accumulation, and contribute to the development of dyslipidemia and atherosclerosis. Therefore, understanding the regulation of CYP7A1 is of considerable importance for elucidating the mechanisms underlying cholesterol metabolism and for developing novel therapeutic approaches to hypercholesterolemia, atherosclerosis, and other cardiovascular diseases [3].

Aim of the study. To investigate the activity of cholesterol 7α-hydroxylase (CYP7A1) during the progression of experimental atherosclerosis and to evaluate the corrective effects of thiocin.

Materials and Methods. Experimental atherosclerosis was induced in rabbits by daily intragastric administration of cholesterol at a dose of 0.2 g/kg body weight for 3 months according to the method of Anichkov and Khalatov (1913) [1]. Following the induction period, the animals were randomly assigned to six groups: Group 1, intact control; Group 2, untreated

experimental atherosclerosis; Group 3, Levazo-treated (0.057 mg/kg body weight); Groups 4 and 5, thiocin-treated at doses of 35 and 70 mg/kg body weight, respectively; and Group 6, combination therapy. Animals in the treatment groups received the respective drugs for 30 consecutive days. Throughout the treatment period, all animals except those in the intact control group continued to receive cholesterol. Serum cholesterol 7α-hydroxylase (CYP7A1) activity was assessed during the development of experimental hypercholesterolemia and after pharmacological correction using an enzyme-linked immunosorbent assay (ELISA) performed on a Mindray MR-96A immunoassay analyzer.

Results and Discussion. A significant decrease in serum cholesterol 7α-hydroxylase (CYP7A1) levels was observed beginning on day 20 of experimental atherosclerosis, with a reduction of 10.4% compared with the intact group. Progressive suppression of CYP7A1 levels was subsequently detected on days 40, 60, 80, and 90 of the experiment. The most pronounced decline occurred on day 90, when CYP7A1 levels were 50.65% lower than those of the intact animals.

Treatment with Levazo significantly increased serum CYP7A1 levels. On days 20 and 30 of therapy, CYP7A1 levels increased by 34.21% and 57.9%, respectively, compared with the untreated atherosclerotic control group.

On day 10 of treatment, a significant increase in CYP7A1 levels was observed only in the group receiving thiocin at a dose of 70 mg/kg body weight (0.46 ± 0.02 ng/mL, $P < 0.05$). By days 20 and particularly 30 of treatment, thiocin produced a marked dose-dependent elevation in CYP7A1 levels. Compared with the control group, CYP7A1 levels increased by 42.1% and 50.0% on day 20 and by 63.16% and 71.05% on day 30 in the 35 and 70 mg/kg thiocin groups, respectively.

Combination therapy with thiocin and Levazo produced a greater increase in CYP7A1 levels at all observation time points than either treatment administered alone. The maximal effect was observed on day 30 of treatment, when serum CYP7A1 reached 0.72 ± 0.03 ng/mL compared with 0.38 ± 0.02 ng/mL in the untreated control group ($P < 0.05$).

These findings demonstrate that serum CYP7A1 levels progressively decline during the development of experimental atherosclerosis, with the greatest

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reduction occurring on day 90 of the experiment. Thiocin exerted a more pronounced corrective effect on CYP7A1 than Levazo and exhibited a clear dose-dependent response, with the 70 mg/kg dose providing the greatest therapeutic benefit. Furthermore, combination therapy with thiocin and Levazo produced the most substantial restoration of serum CYP7A1 levels, suggesting a synergistic effect on cholesterol metabolism.

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