NEW BIOMEDICAL TECHNOLOGIES

Skin Lipids in Rats Administered with Melatonin

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Effects of the pineal hormone melatonin on skin lipids in Wistar rats were studied by thin-layer chromatography. The reaction was shown to be delayed. Contents of total lipids and the majority of fractions increased over 24 h after administration of melatonin. Concentrations of triglycerides and phospholipids decreased, while the contents of cholesterol, cholesterol esters, and free fatty acids increased by the end of the second day. Our findings indicate that the blood and subcutaneous fat, as well as changed metabolic interrelations of skin lipids are involved in the skin response to increased melatonin concentration.

Key Words: *rats; skin; lipids; melatonin*

Melatonin displays considerable immunoregulatory properties and is involved in the maintenance of circadian rhythms of organism and inhibition of some functions of the pituitary [1,2]. The epiphyseal acid extract was shown to affect metabolic processes, *e.g.*, carbohydrate and lipid metabolism in the blood and liver [6,7]. However, the involvement of melatonin in the regulation of physiological state and some biochemical indexes of the skin received little attention.

Here we studied the effects of exogenous melatonin on rat skin lipids.

MATERIALS AND METHODS

Experiments were performed on 42 male Wistar rats weighing 224.7±20.6 g. The animals were kept in cages (four rats per cage) under natural light-dark cycle (7.05-20.10 light phase) at 20-22°C and *ad libitum* food and water supply. Experiments were conducted during the light day phase (10.00-16.00). Skin samples were taken from intact animals immediately after decapitation. Control rats received intraperitoneally 1 ml of sterile physiological saline. Experimental animals were intraperitoneally injected with 1 mg/kg melatonin in 1 ml physiological saline. The rats were decapitated 6, 24, and 48 h postinjection, and skin samples (80-270 mg) were taken from the interscapular region. Lipids were extracted by the method of Folch and separated by thin-layer chromatography on silica gel [4]. The contents of total lipids (TL) and individual fractions were measured as described previously [4].

The concentration of TL and the absolute and relative contents of main lipid fractions: phospholipids, diglycerides, nonesterified cholesterol, free fatty acids (FFA), triglycerides, and cholesterol esters (CE) were estimated. The data were analyzed using Student's *t* test [5].

RESULTS

Physiological saline had no considerable effects on skin lipids (Table 1). Changes in the absolute contents of individual lipid fractions were statistically insignificant. The relative contents of all fractions remained constant for 2 days.

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TABLE 1. Absolute Content of Skin Lipids in Rats Injected with Melatonin (mg/100 g wet weight, *M±m*)

Group	Time, h	TL	Phospho-lipids	Diglycerides	Cholesterol	FFA	Triglycerides	CE
Intact rats	0	1805±82.3	373.4±12.1	128.7±20.9	136.9±13.8	175.3±16.9	694.9±26.0	296.1±32.2
Control (physio-logical saline)	6	1735.4±82.3	351.2±44.9	111.0±14.7	136.3±10.9	180.2±53.2	686.2±14.1	270.5±19.2
	24	1674.2±102.9	317.9±47.3	113.2±31.0	120.6±24.8	196.4±71.6	649.8±45.9	276.2±41.9
	48	1795.6±121.5	372.9±33.2	127.8±14.6	136.5±9.4	176.5±20.1	688.3±23.0	293.7±38.7
Melatonin	6	1558.6±178.9	305.0±44.4	99.1±19.1	104.3±17.6	175.7±15.2	620.8±67.4	253.7±35.8
	24	2277.1±136.2*+	407.7±28.1	138.1±33.6	159.1±12.2+	270.2±35.0+	966.4±28.3*+	335.5±26.5
	48	2107.4±88.1*	317.9±23.4+	138.8±29.3	192.9±17.5*	274.3±26.9*	708.7±29.6+	474.9±27.6*+

Note. Here and in Table 2: $p<0.05$: *compared with the control, +compared with previous period.

Triglycerides, phospholipids, and CE were the prevalent fractions in the skin. The content of diglycerides, cholesterol, and FFA did not exceed 5.4-10.3%. The ratio between the absolute contents of these lipids was similar.

Exogenous melatonin considerably changed the contents of TL and individual lipid fractions. Skin response developed late postinjection: significant changes were observed by the end of day 1.

The content of TL slightly decreased 6 h after injection of melatonin in comparison with the control value. The absolute contents of individual lipid fractions differed insignificantly from the control values (Table 1). Relative contents of all fractions were similar to those in the control group (Table 2).

Twenty-four hours after administration of melatonin, the content of TL increased by 46.1% compared with the initial level. The absolute contents of the majority of lipid fractions increased by 30.5-55.3%. The contents of triglycerides, FFA, and cholesterol increased most significantly (by 55.8%, 54.3%, and 52.9%, respectively). However, we revealed no significant differences in the relative contents of these fractions (Table 2).

Changes in the content of skin lipids observed 24 h after administration of melatonin are probably associated with the passage of triglycerides, FFA, and cholesterol from the blood and subcutaneous fat into the skin. This agrees with the data showing that melatonin increased the blood content of triglycerides [5].

The content of TL slightly decreased by the end of day 2, but remained above the control level. The contents of cholesterol and CE continued to increase. The levels of diglycerides and FFA remained as high as 24 h postinjection. The contents of phospholipids and triglycerides decreased to the initial level (by 21.9%) and control values (by 26.8%), respectively.

At the later stages, the relative contents of triglycerides and phospholipids were considerably lower, and the relative content of FFA was higher than in the control. Absolute and relative contents of cholesterol and CE surpassed the control values.

Thus, some lipid indexes tended to be restored 48 h after administration of melatonin. Various skin processes during this period are obviously associated with degradation of triglycerides and phospholipids and with changes in metabolic interrelations of lipids [3]. Phospholipids, triglycerides, and FFA formed during

TABLE 2. Relative Content of Skin Lipids in Rats Injected with Melatonin (% of TL, *M±m*)

Group	Time, h	Phospho-lipids	Diglycerides	Cholesterol	FFA	Triglycerides	CE
Intact rats	0	22.2±0.7	6.0±1.0	6.7±0.7	8.5±0.8	39.6±1.4	16.9±1.8
Control (physio-logical saline)	6	21.8±2.8	5.4±0.7	6.9±0.6	9.1±2.7	40.8±0.8	16.1±1.1
	24	20.4±3.1	5.7±1.6	6.3±1.3	10.3±3.8	40.2±2.8	17.0±2.6
	48	22.3±2.0	6.0±0.7	6.7±0.5	8.6±1.0	39.5±1.3	16.9±2.2
Melatonin	6	21.0±3.0	5.4±1.0	5.9±1.0	9.9±10.5	41.0±4.5	16.8±2.4
	24	19.3±1.8	5.1±1.3	6.1±0.5	10.4±1.7	43.9±1.3	15.2±1.2
	48	16.2±1.5*	5.6±1.2	8.0±0.7+	12.3±1.1*	34.7±1.5*+	23.2±1.4*+

hydrolysis are probably involved in the synthesis of cholesterol and CE. These changes can be illustrated by the following scheme:

Triglycerides↓
↓
CE↑←Cholesterol↑←FFA↑←Phospholipids↓,

where ↑ and ↓ are the increase and decrease in lipid fractions, respectively.

Our findings indicate that the decrease in the content of TL observed in the skin by the end of day 2 occurs due to their efflux into the blood or subcutaneous fat or due to lipid excretion by sebaceous glands. The latter suggestion is confirmed by studies of hair lipids. The involvement of lipids in the metabolism of other compounds cannot be excluded.

These results indicate that melatonin considerably affects skin lipids in rats. Changes in skin lipids are a complex and delayed process. Reactions of skin lipids to increased content of melatonin involve lipid metabolism in the skin and subcutaneous fat and changes in metabolic interrelations in the skin and other organs.

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