Effects of Hormones on Phospholipase A_2 Activity in Rat Skin

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Translated from *Byulleten' Eksperimental'noi Biologii i Meditsiny,* Vol. 129, No. 1, pp. 70-72, January, 2000
Original article submitted April 29, 1999

We studied the effects of hydrocortisone, progesterone, estradiol, and testosterone on phospholipase A_2 activity in plasma and lysosomal membranes of rat dermis and epidermis. The dermal enzyme was more sensitive to estradiol, while epidermal to testosterone. The effects of progesterone and hydrocortisone were mediated by lipocortin-like protein, while estradiol and testosterone directly by modulated phospholipase A_2 activity

Key Words: *skin; dermis; epidermis; estradiol; hydrocortisone; progesterone; testosterone; phospholipase A_2*

Phospholipase A_2 (PLA_2) catalyzing the release of fatty acids (primarily arachidonic acid) from phospholipids is localized in different cell membranes [3,4] and participates in the intracellular transduction of hormonal signals. PLA_2 activity is modulated by bioactive substances and radiation. Hydrocortisone has been reported to inhibit this enzyme [3], the effects of other steroid hormones have practically never been studied.

This study investigated the effects of steroid hormones on PLA_2 activity in plasma and lysosomal membranes (PM and LM) from rat skin.

MATERIALS AND METHODS

Experiments were carried out on mature and immature rats (males and females in the diestrus phase verified as described elsewhere [1]). Hydrocortisone, progesterone, estradiol, and testosterone were administered subcutaneously (0.5 ml) in a dose of 10 mg/kg. The animals were sacrificed under light ether anesthesia 5 and 30 min, 1, 24, and 48 h postinjection. Skin homogenates were prepared [5]. PLA_2 activity was measured by the content of water-soluble radioactive products of phospholipid hydrolysis [8]. 1-Acyl-2,1,-^{14}C-arachnoidyl-glycero-3-phosphocholine (2.33 nCi/μg phospholipid) was used as the substrate. Protein content was measured according to Lowry [7]. The data were processed statistically using Student's *t* test.

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RESULTS

At the first stage we determined PLA_2 activity in dermal and epidermal PM and LM from intact rat skin. Since skin properties depend on age [2] and the course of many skin diseases depends on patient's gender, the age and sex of experimental animals were taken into account.

In young mature rats, PLA_2 activity in dermal and epidermal PM showed no sex or tissue specificity (Table 1). The tissues of older rats (6 months) were characterized by lower PLA_2 activities in both PM and LM compared to young mature (1.5-2 months) animals. In the dermis and epidermis of immature 2-3-week-old rats, PLA_2 activity was found only in PM, being significantly (by 16-22%) higher than in young mature animals. Thus, in immature and old animals skin lysosomes are less functionally active and hence the skin is poorly protected from microbial and other injuries.

In the second experimental series, PLA_2 activity was measured at different times (5, 30, 60 min; 24 and 48 h) after subcutaneous administration of hormones in a dose of 10 mg/kg.

The effects of hydrocortisone and progesterone (significant changes in PLA_2 activity) were observed

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TABLE 1. PLA_2 Activity in Rat Skin ($M \pm m$)

Group	Males		Females	
	dermis	epidermis	dermis	epidermis
Plasma membrane				
Immature males (6) and females (7)	9.8±0.53*	10.0±0.33*	10.4±0.24*	9.6±0.2*
Young mature males (8) and females (10)	8.4±0.27	8.2±0.2	8.7±0.37	8.0±0.25
Old males and females (5 each)	7±1±0.31*	6.8±0.16*	7.6±0.26*	6.8±0.5*
Lysosomal membrane				
Immature rats	0	0	0	0
Young mature males and females (5 each)	2.0±0.1	2.3±0.23	3.1±0.15	2.8±0.1
Old males and females (5 each)	1.8±0.14	1.65±0.13	2.5±0.23	2.3±0.2

Note. *$p<0.05$ in comparison with young mature animals.

TABLE 2. Activity of Plasma Membrane PLA_2 under the Influence of Steroid Hormones (nmol/min/g protein, $M \pm m$)

Hormone	Time, min	Males		Females	
		epidermis	dermis	epidermis	dermis
Control		8.2±0.2	8.4±0.3	8.0±0.25	8.7±0.4
Hydrocortisone	30	8.0±0.3	8.4±0.3	7.8±0.45	8.5±0.4
	60	6.2±0.4*	6.1±0.35*	6.3±0.2*	6.5±0.4*
Progesterone	30	8.0±0.3	8.2±0.2	8.3±0.3	8.4±0.3
	60	6.3±0.45*	6.6±0.3*	5.9±0.2*	6.0±0.45*
Estradiol	30	8.4±0.6	9.8±0.7*	8.1±0.2	9.5±0.24
	60	8.7±0.9	9.5±0.17*	8.9±0.15*	9.9±0.1*
Testosterone	30	9.5±0.36*	9.3±0.4*	8.3±0.7	8.7±0.8
	60	9.7±0.35*	9.8±0.5*	9.2±0.2	9.2±0.1*

Note. *$p<0.05$ in comparison with the control.

60 min and the effects of estradiol and testosterone 30 min poistinjection. The effects of steroid hormones were sex- and tissue-specific.

For instance, hydrocortisone inhibited PLA_2 in both PM and LM. This effect was most pronounced in male dermis and least pronounced in female epidermis (Table 2). Progesterone also inhibited PLA_2, but in contrast to hydrocortisone, its effect was most pronounced in females and observed only in PM. PLA_2 activity after hydrocortisone and progesterone administration remained below the initial level for 24 h and returned to normal only after 48 h. Similar to other tissues [3,6], the effect of these hormones on skin PLA_2 is probably mediated by synthesis of protein inhibitor (lipocortin). Sex-specific differences in their effects in different skin layers can be explained by the fact that progesterone and hydrocortisone belong to different groups of steroids.

In contrast to hydrocortisone and progesterone, estradiol and testosterone, stimulated PLA_2 (Table 2). In males, estradiol enhanced PLA_2 activity in dermal, while testosterone in both dermal and epidermal PM. Sixty minutes postinjection the stimulating effect of estradiol was observed in both dermal and epidermal PM and LM from females and in dermal membranes from male skin. Testosterone stimulated PLA_2 activity in both skin layers of males and females (in female dermis this effect was statistically insignificant); PAL_2 activity returned to normal after 24 h. After estradiol administration, the activity remained elevated for 24 h and returned to the baseline only after 48 h. Unlike cortisone and progesterone these hormone directly modulate PLA_2 activity. The long-term effect of estradiol can be due to its interaction with different enzyme cascades.

Thus PLA_2 activity was found in both plasma and lysosomal membranes from the skin. The effect of steroid hormones on this activity depended on experimental conditions and other factors such as hormone type, time after administration, skin layer, intracellular localization of the enzyme, gender, *etc.* Dermal PLA_2 was more sensitive to estradiol, while epidermal to testosterone.

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