The Effect of Progesterone on the Lipid Composition of Blood Plasma and of Plasma Membranes of Rat Uterine Cells

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The first stage in the mechanism of transformation of a hormonal signal into a biological response of a cell is binding of the hormone with receptors on the plasma membranes of the target cell. There are specific binding sites on *X. laevis* oocytes and human sperm cells for progesterone (PG) immobilized on an inert carrier [6,7]. The parameters of specific binding of PG with plasma membranes of uterine cells have been studied in rats [8].

Lipids and phospholipids play an important role in the molecular organization and function of biological membranes. The hormone-dependent growth of tumor cells is accompanied by changes of the lipid composition of cell membranes [15]. Many human tumors exhibit a decrease of the phosphatidylcholine and an increase of the cholesterol contents [1,10], which correspond to a change of the lipid spectrum of the blood plasma in neoplasias [14]. The content of sex hormones in the blood correlates with the degree of development of the tumor process in the uterus [3,11].

We showed that estradiol and hydrocortisone change the spectrum of lipids and phospholipids of plasma membranes of uterine and hepatic cells in rats [4,5]. The effect of PG on the lipid composition of membranes of target cells has not been studied.

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MATERIALS AND METHODS

Experiments were carried out on 80 female rats weighing 110-140 g. Oil solution of PG in doses of 5, 10, and 15 mg/100 g weight was injected i.p. on the 4th day after ovariectomy, performed using the Kirshenblat method [2]. Control animals were injected with 0.2 ml solvent per 100 g weight. Animals were decapitated under ether anesthesia 24 and 48 h after injection. The uteri were freed of adipose and connective tissue and the plasma membranes were isolated using the Lintner method [12]. Extraction of membrane and plasma lipids was performed after Folch [9]. For determination of the composition of the lipids, thin-layer chromatography was performed on Silufol 254 UF plates in the following systems: n- hexane:diethyl ether:glacial acetic acid (80:20:2) and chloroform:methanol:water (65:25:4). Chromatograms were analyzed using an EGR-65 densitometer (Germany). Protein was determined after Lowry [13]. The results were processed statistically using the Student *t* test.

RESULTS

The experimental data are listed in Tables 1 and 2. An increase of the free cholesterol level in the plasma membranes is noted 24 h after PG injec-

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TABLE 1. Lipid Composition of Plasma Membranes of Uterus and of Pasma (Lipids are Expressed in μg/mg of Plasma Membrane Protein or in 100 μl of plasma) in Ovariectomized Rats 24 h after i.p. Injection of PG ($M \pm m$)

PG dose, mg/100 g weight	n	Plasma membranes					Blood plasma							
		Total lipids		Phospholipids			Total lipids				Phospholipids			
		PL	Ch	PC	PE	SM	PL	Ch	FFA	TG	PC	PE	SM	PhS
5	11	480±87	406±59*	424±84	496±63	106±13	385±39	319±68	263±59	490±57	318±48*	194±36	25±8	19±4
10	12	470±53	422±71*	610±80*	570±58*	70±24	468±66*	487±62*	215±33	470±35	281±22	292±31*	38±6	15±8
15	8	526±67	295±32	599±74*	571±63*	89±10	673±78*	330±28	180±26	395±46	288±34	245±41	47±8	16±3
Control	15	417±38	190±23	370±39	361±68	50±8	209±38	207±31	157±28	380±41	187±23	133±52	31±5	22±6

Note. Here and in Table 2: n signifies the number of animals; PL: sum of phospholipids; Ch: cholesterol; PC: phosphatidylcholine; PE: phosphatidylethanolamine; SM: sphingomyelin; FFA: free fatty acids; TG: triglycerides; PhS: phosphatidylserine. An asterisk means $p<0.05$ as compared to the control.

TABLE 2. Lipid Composition of Plasma Membranes of Uterus and of Plasma (Lipids are Expressed in μg/mg of Plasma Membrane Protein or in 100 μl of plasma) in Ovariectomized Rats 48 h after i.p. Injection of PG ($M \pm m$).

PG dose, mg/100 g weight	n	Plasma membranes					Blood plasma							
		Total lipids		Phospholipids			Total lipids				Phospholipids			
		PL	Ch	PC	PE	SM	PL	Ch	FFA	TG	PC	PE	SM	PhS
5	13	308±76	266±43	424±59	475±50	84±13	242±25	283±34	150±39	292±47	203±36	128±29	32±9	20±6
10	11	378±56	256±13	449±84	441±56	95±28	304±65	287±42	141±27	276±44	204±48	158±20	41±7	23±5
15	10	315±36	252±60	475±97	435±68	69±12	249±58	277±23	105±20	241±12	225±39	142±62	31±19	17±7
Control	15	417±38	190±23	370±39	361±68	50±8	209±38	207±31	157±28	380±41	187±23	133±52	31±5	22±6

tion in doses of 5 and 10 mg/100 g (twofold increase) and in a dose of 15 mg/100 g (by 50%). There was only a tendency for the cholesterol level to rise in the plasma membranes of rat uterine cells 48 h after administration of PG, whatever dose was used (Table 2).

A rise of the level of cholesterol in the membrane is accompanied by changes of its characteristics, namely by an increase of the viscosity of the biomembrane and a concomitant decrease of the molecular mobility of the protein components; the permeability for ions and molecules was lowered in parallel.

Progesterone lowered the phospholipids/cholesterol ratio by 40% (in a dose of 5 mg/100 g) and by 60% (in doses of 10 and 15 mg/100 g weight), which also attests to an increase in the viscosity of the membrane bilayer due to the effect of the hormone (Table 1).

Progesterone in a dose of 5 mg/100 g weight does not cause significant changes in the spectrum of phospholipids. The content of the main structural phospholipids of cell membranes, namely phosphatidylcholine and phosphatidylethanolamine, rises 65 and 50%, respectively (Table 1), 24 h after administration of hormone in doses of 10 and 15 mg/100 g. There are no changes as compared to the control in the phospholipid spectrum of plasma membranes of uterine cells 48 h after injection.

The lipid spectrum of the plasma also changes 24 h after PG injection. But a significant increase of the levels of cholesterol and phosphatidylethanolamine (2-fold) is noted only when a dose of 10 mg/100 g is used, which correlates with the changes of the lipid composition of the plasma membranes.

The described effect of PG derives, first, from its stimulation of lipogenesis in the liver and adipose tissue, enhancement of lipoproteinlipase activity, and inhibition of lipolysis [16]; furthermore, it may have to do with the increase of insulin secretion noted for administration of PG [17].

It may be assumed that PG modifies the receptor-transport systems of plasma membranes by altering their lipid composition in the target cell.

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