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INVOLVEMENT OF ADENOSINE IN THE ACUTE ACTION OF PROGESTERONE ON GLUCOSE METABOLISM IN RAT ADIPOCYTES.

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Progesterone and synthetic steroids (RU-5020, progestomimetic ; RU-38486, anti-progesterone and anti-glucocorticoid) inhibit glucose metabolism in female rat adipocytes. The inhibitory effect, which is dose-related, occurred after 20-min of incubation and is sustained during 2-hours of incubation. This effect of progesterone is similar to that observed during pregnancy and after treatment of ovariectomized rats with progesterone (5 mg/rat/day-15 days).

It seems likely that the mechanism of action of progesterone on glucose metabolism is different from the classical concept of steroid hormones. The fact that progesterone increases cAMP levels in a dose-dependent manner strongly support the hypothesis that this steroid utilizes cAMP as second messenger. Since adenosine, which has the potential inhibit adenylyl cyclase, is spontaneously released by isolated fat cells, the involvement of this nucleoside in the acute action of progesterone was investigated.

Adipocytes incubated in the presence of progesterone (10^{-10} to 10^{-4} M) produced a biphasic response, which corresponds to an increase of $[1-^{14}C]$ glucose oxidation at the lowest concentrations and a decrease at the higher concentrations of progesterone. In presence of adenosine deaminase (200 mU/ml), progesterone decreased glucose oxidation at all concentrations of progesterone. Hence, at the lowest progesterone levels, adenosine appeared to antagonize the inhibitory effect of the steroid (FIG. 1).

Furthermore, caffeine (a non-selective adenosine antagonist), theophylline (an $A_1 < A_2$ receptor antagonist) and dipyridamole (an

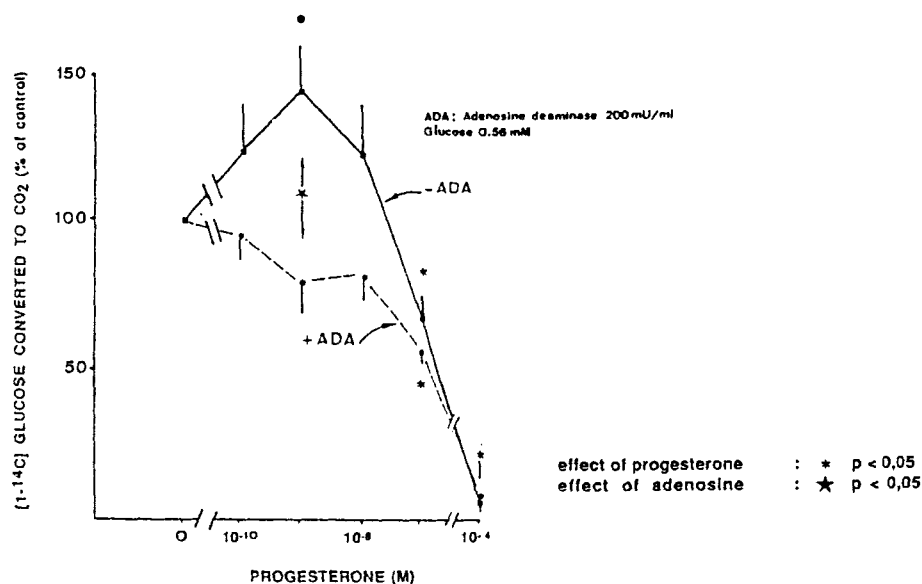


FIG. 1

TABLE 1

IC ₅₀ values				
PDE inhibitor		PDE inhibitor + Progesterone		
		mM		P
Theophylline	(8)	0.182 ± 0.025	0.565 ± 0.169	< 0.05
Caffeine	(8)	0.231 ± 0.022	0.857 ± 0.163	< 0.01
Papaverine	(10)	0.059 ± 0.013	0.043 ± 0.007	n.s.
Dipyridamole	(14)	0.016 ± 0.003	0.077 ± 0.011	< 0.001
Imipramine	(9)	0.087 ± 0.011	0.136 ± 0.028	n.s.

IC₅₀ values (± SEM) are the concentrations of drugs that inhibited [1-¹⁴C]glucose oxydation by 50%. Statistical differences between IC₅₀ values in the absence and the presence of progesterone : $p <$; n.s. = not significant.

adenosine uptake inhibitor) decreased glucose oxidation with the following order of potency : dipyridamole > theophylline > caffeine. These potencies were decreased by the steroid, whereas that of inhibitors of phosphodiesterase activity (papaverine, imipramine) remained unchanged (TABLE 1)

This result seems to indicate that adenosine modulates the influence of progesterone on glucose metabolism in female rat adipocytes.