CHARREAU[8] found that a single injection of testosterone propionate caused growth promotion effect and stimulated RNA synthesis in salivary glands. Also, testosterone increased the growth of salivary glands and could be inhibited by antimetabolites[9]. Experiments performed by LEVI-MONTALCINI and ANGELETTI[10] show that the mouse salivary glands contain a nerve growth factor that increases in female mice upon testosterone administration. The results of the presnt work extend the above findings on the effect of androgens on the salivary glands of mice. The early effect on glycogen synthesis after testosterone on salivary glands is in agreement with the same effect on rat prostate and seminal vesicles reported by SINGHAL et al.[11]. This testosterone stimulatory effect on protein synthesis in salivary glands can be modified by antimetabolites[12].

Effect of testosterone on the glycogen metabolism and 5-FU inhibition

Treatment	Glycogen μg/100 mg gland[a] Parotid	Submaxillary
Control	15 ±1.7	24±2.8
Testosterone (5 mg/100 g b.w.)	21 ±2.2	27±2.1
Testosterone (10 mg/100 g b.w.)	48 ±1.6	37±1.4
Testosterone + 5-FU	18 ±2.1	26±1.0
Testosterone + 5-FU	14.9±1.1	23±1.7

Castrated mice were injected with testosterone, or testosterone plus 5-FU, and killed 24 h later. [a] Each result is the mean from 10 animals ± S.E.

In summary, a single dose of testosterone exerts a very specific effect on target tissues but also exerts effects in organs other than its prime target. The inhibitory action of 5-FU on testosterone-stimulated glycogen synthesis in salivary glands suggest the probability that glycogenesis depends on prior stimulation of RNA and protein synthesis.

Resumen. En el presente trabajo se estudia la accion de testosterona sobre el metabolismo del glucogeno. Se observa que despues de la inyeccion de la hormona aumenta el glucogeno y que y este es inhibido por 5-FU. Se sugiere que la sintesis de glucogeno necesite una estimulacion previa de nucleotidos de RNA y de proteinas.

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Effects of Estrogens and Progesterone upon the Biosynthesis of Melatonin by the Pineal Gland

There is considerable evidence that the pineal gland and the melatonin have an inhibitory influence upon ovarian function in mammals[1]. On the other hand the hydroxyindole-*O*-methyl transferase (HIOMT) activity in the pineal gland varies during the estrous cycle in rats, being higher in metestrus and diestrus and lower in proestrus and estrus[2]. As a single injection of 10 μg of estradiol benzoate lowered the HIOMT activity in the pineal gland measured the day after the injection, it was postulated that the lower rate of melatonin biosynthesis in estrus was due to an inhibitory estrogenic effect[2]. Surprisingly enough, the removal of the ovary did not alter the pineal gland HIOMT activity[2].

The experiments presented in this paper were performed with the object of comparing the effects of estrogens and progesterone upon the HIOMT activity in the pineal gland. Adult female rats from our animal colony were employed. Castrations were performed in all the animals the day before the respective experiment. The animals were daily injected with the drugs dissolved in 0.1 ml of the vehicle for 25 days, control rats received only the vehicle. All animals were kept in controlled lighting conditions (lights from 07.00 to 19.00 h) during the 25 days the experiment lasted. The HIOMT activity in the pineal gland was measured using the method of AXELROD, WURTMAN and SNYDER[3].

In the first experiment (Table I) the following groups of castrated rats were injected: 1. with the vehicle (ethyl oleate); 2. with estradiol benzoate (20 μg/day); 3. with progesterone (200 μg/day); 4. with estradiol benzoate (20 μg/day) and progesterone (200 μg/day).

It is shown that estrogen administration produced a significant decrease in pineal weight and a significant increase in pineal HIOMT activity. Progesterone administration did not affect the pineal weight but produced a significant decrease in pineal HIOMT activity.

In the second experiment (Table II) progesterone was injected to castrated female rats in dosis of 20 μg/day and 200 μg/day in olive oil for 25 days. It is confirmed that while progesterone administration did not change the pineal weight, it produced a significant decrease in pineal HIOMT activity.

The marked inhibitory effect upon the biosynthesis of melatonin, as obtained in these experiments with pharmacological dosis of progesterone, would not appear to be the cause of the changes in pineal gland HIOMT activity

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Table I. Effects of estrogens and progesterone upon HIOMT activity in the pineal glands of castrated female rats

	Controls	Estradiol benzoate	Estradiol benzoate + progesterone	Progesterone
Estradiol benzoate	a)	b)	c)	d)
(μg/day)	0	20	20	0
Progesterone (μg/day)	0	0	200	200
Animals Number	4	4	4	4
Weight (g)	167±9.2	174.8±8.3	175.8±2.8	183.8±12.4
Pineal gland Weight (μg)	1287± 55	1012± 50	950± 87	1300± 104
HIOMT (activity)	43.6±3.0	55.8±4.9	28.8±3.0	2.0± 0.3

Probabilities (employing Student's *t*-test)

	a) vs b)	a) vs c)	a) vs d)	b) vs d)	c) vs d)
Animal wt.	n.s.	n.s.	n.s.	n.s.	n.s.
Pineal wt.	<0.01	<0.02	n.s.	n.s.	<0.05
HIOMT activity (μμmol/mg)	<0.05	<0.02	<0.001	<0.01	<0.001

Table II. Effects of progesterone upon HIOMT activity in the pineal glands of castrated female rats

Dose	a)	b)	c)
(μg/day)	0	20	200
Animals			
Number	4	7	8
Weight (g)	239± 5	232± 9	234± 8
Pineal			
Weight (μg)	1612±183	1378±85	1487±121
HIOMT activity (μμmol/mg)	42.0± 3.7	33.1±4.0	16.6± 4.7

Probabilities (employing Student's *t*-test)

	a) vs b)	a) vs c)	b) vs c)
Animal wt.	n.s.	n.s.	n.s.
Pineal wt.	n.s.	n.s.	n.s.
HIOMT activity	n.s.	<0.01	<0.02

during the estrous cycle of the rat, which might be mediated by gonadotrophins or by nervous pathways. On the other hand, it is of considerable physiological interest to have found a steroid hormone able to alter markedly the pineal gland functions in the rat.

Zusammenfassung. Da die Aktivität der Pinealdrüse bei weiblichen Ratten mit dem Cyklus wechselt, wurde die Wirkung von Oestradiol und Progesteron auf ihre Aktivität bei kastrierten weiblichen Ratten untersucht. Oestradiol bewirkte Gewichtsabnahme und Funktionssteigerung, während Progesteron die Pinealis-Aktivität herabsetzte.

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R_M Values and Biological Action of Testosterone Esters

In a recent communication to this journal, Biagi, Barbaro and Guerra[1] demonstrated a linear correlation between the R_M values of some testoster oneesters, determined by a Boyce-Milborrow technique[2], and the times of maximum biological effect in fowl. Times of maximum effect (BR) were expressed on a molar basis relative to testosterone. Observations in these laboratories[3] reveal that time of maximum effect in rat is not affected significantly when the dose of testoserone ester is increased threefold, indicating that conversion on a molar basis was

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