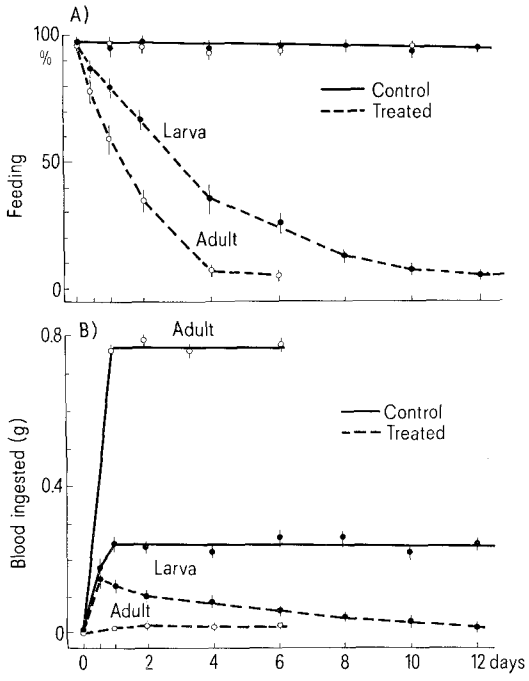
first blood meal. The inhibition of feeding in the treated larvae suggests that, rather than the amount of nutrients ingested by the bug, the level of hormonally initiated biochemical activities which are usually associated with post-diapause development and apolysis regulate the feeding activity in *R. prolixus*. In nature, of course, the rate of production of hormone and the initiation of development processes are synchronized with the ingestion of sufficient amount of blood meal and stretching of abdominal receptors.



Effect of ecdysterone (2 μg/insect) on the feeding activity of the 3-week-old diapausing 5th instar larvae (circles) and male adults (square) of *R. prolixus*, at various times after the treatment. A) Percent inhibition of feeding (± SE) in the treated individuals. B) The amount of blood ingested (in g ± SE) by those individuals which showed feeding activity.

The precise role of ecdysterone in causing mortality and inhibition of feeding activity cannot be explained satisfactorily by the present data. The apparent lethargy and exhaustion in the treated larvae indicated the inability of the diapausing individuals with limited nutrient reserves to sustain various endergonic biosynthetic activities which are usually initiated by ecdysone. For instance, ecdysone stimulates RNA and protein synthesis in the fat body and epidermal cells, leading to moulting in the bugs[2]. Indeed, the 19-week-old larvae, which were in a state of starvation and contained only minute reserves of glycogen, lipids and protein[1,2] succumbed to hormonal treatment much earlier than the 3-week larvae. The mortality in the larvae may thus be attributed to the probable physiological derangement created by the hormone.

The adult mortality was probably due to the opposing actions of exogenous ecdysone and endogenous juvenile hormone; simultaneous administration of the two hormones was fatal to *Tenebrio molitor*[7]. Juvenile hormone regulates ovarian development in the female *R. prolixus*[8]; presumably the males also contain the hormone.

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On the Mineralocorticoid and Hypertensogenic Properties of 16β-Hydroxy-Dehydroepiandrosterone[1]

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Summary. Dosages of either 1 or 2 mg daily of 16β-hydroxy-dehydroepiandrosterone, given to mononephrectomized, salt-loaded female rats, had no detectable effect upon saline consumption, blood pressure, kallikrein excretion or heart and kidney weight. Its alleged mineralocorticoid properties, as judged by these criteria, were not demonstrable.

A recent article synopsizing evidence that low renin essential hypertension is caused by a mineralocorticoid (mc) hormone, reported and identified a possible culprit[2]. The C_{19} steroid, 16β-hydroxy-dehydroepiandrosterone (16β-OH-DHEA), provided the preponderant biologic mc activity in urine of patients with the disorder, in marked contrast to the urine of normotensives, or normal renin essential hypertensives, where the biologic mc potency was due to the aggregate activities of aldosterone, DOC, cortisol and corticosterone. 16β-OH-DHEA was found to have 1/40th the sodium-retaining potency of aldosterone in adrenalectomized rats. With an mc activity of that order, the quantities of 16β-OH-DHEA present in urine might well account for hypertensive disease.

All of the C_{21} mc's capable of causing hypertension in man do so in mononephrectomized, salt-loaded rats – including aldosterone[3,4], deoxycorticosterone[5,6], 18-hydro-

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xycorticosterone[7] and corticosterone[8]. Other studies have shown that urinary kallikrein excretion in both rat[9,10] and man[11,12] is greatly increased by mc's, including aldosterone[12], deoxycorticosterone[10] and fludrocortisone[11], suggesting that 'kallikrein excretion appears to be directly related to the effective level of circulating sodium-retaining steroid'[11]. Excessive mc's also depress plasma renin activity (PRA)[13,14]. The present study was undertaken to determine how blood pressure, kallikrein excretion and PRA of rats were affected by 16β-OH-DHEA treatment.

Table I. Growth, fluid consumption, blood pressure and organ weights in steroid-treated and control rats

		Controls	16β-OH-DHEA	
			1 mg/day	2 mg/day
N		10	10	10
Body wt.	Initial	84 ± 2[a]	86 ± 2	84 ± 2
	Final	161 ± 4	173 ± 2[b]	169 ± 4
Fluid volume (ml)				
Week 1		48 ± 2	57 ± 2[b]	52 ± 2
2		47 ± 2	63 ± 4[b]	52 ± 3
3		57 ± 2	65 ± 3[b]	66 ± 4
Blood pressure (mm Hg)				
Week 0		94 ± 4	98 ± 4	90 ± 3
1		121 ± 3	128 ± 7	128 ± 4
2		123 ± 3	130 ± 6	130 ± 5
3		147 ± 7	149 ± 5	162 ± 10
N. Hypertensive		5	6	6
Organ wt. (mg/100 g body wt.)				
Pituitary		4.4 ± 0.2	3.8 ± 0.2[b]	3.5 ± 0.2[b]
Adrenals		29.7 ± 1.3	24.9 ± 0.9[b]	25.1 ± 1.0[b]
Preputials		41.6 ± 3.4	48.5 ± 4.0	45.1 ± 0.5
Thymus		173 ± 28	163 ± 8	175 ± 9
Heart		324 ± 4	323 ± 7	329 ± 8
Kidneys		710 ± 16	685 ± 19	677 ± 12

[a] Mean ± SEM. [b] Significantly different from control value ($p < 0.05$).

Table II. Effect of 16β-OH-DHEA treatment on urinary volume and composition and on plasma renin activity

		Controls	16β-OH-DHEA	
			1 mg/day	2 mg/day
			Urine values	
Week 3	Vol. (ml)	7.0 ± 1.0[a]	9.1 ± 1.1	15.9 ± 3.1[b]
	Kallikrein (E.U./24 h)	139 ± 15	166 ± 20	141 ± 36
Week 4	Vol. (ml)	12.2 ± 2.8	12.9 ± 0.9	16.9 ± 3.0
	Kallikrein (E.U./24 h)	414 ± 58	447 ± 51	491 ± 87
	mOsm/L	970 ± 76	845 ± 39	784 ± 73
	Protein (g/100 ml)	3.8 ± 0.5	2.7 ± 0.2	2.4 ± 0.5
Plasma renin activity (ng/ml/h)		0.05 ± 0.0	0.16 ± 0.1	0.18 ± 0.1

[a] Mean ± SEM. [b] Significantly different from control values ($p < 0.05$).

16β-OH-DHEA was synthesized according to the method of AOKI et al.[15]. The steroid, obtained as the diacetate, proved by multiple system single layer chromatography to have physical properties identical to an authentic sample obtained from steraloids, and to yield on hydrolysis a compound indistinguishable from a sample of 16β-OH-DHEA provided by Dr. KIRK from the Steroid Reference Collection (London).

Either 1 or 2 mg/day (in sesame oil) of 16β-OH-DHEA diacetate was injected s.c. into young mononephrectomized female SPD rats. Controls received the same volume of oil. A 1% NaCl solution was given to drink. Daily fluid intake of each rat was measured on 3 consecutive days each week, the average being taken as representative for the week. Systolic blood pressure of unanesthetized animals was measured periodically and indirectly (tail) with a Physiograph (Narco Biosystems, Houston, Texas). Values above 150 mm Hg were regarded as hypertensive. 24-hour urine samples were collected in the 2nd and 3rd weeks under toluol, and kept in stoppered vials at 4 °C until kallikrein content was measured by a modification[11] of BEAVAN's[16] method, using a Bayer standard testing 1060 kallikrein esterase units per mg. On the second occasion protein concentration (Protein meter: American Optical Co.) and osmolality (Model 5100 Vapour Pressure Osmometer: Wescor, Inc.) were measured. The animals were killed by decapitation on the 21st day, and trunk blood was collected within 5 sec into chilled, heparinized flasks, transferred to stoppered vials, and frozen at –20 °C until PRA was measured[17]. Organs were placed in neutral 10% formalin for subsequent weight.

Table I shows that a dose-related effect of steroid treatment was not obtained on body weight or fluid consumption. Only animals on the lower dose grew slightly better and drank slightly more than controls, but the difference was slight. Salt hypertension developed at a comparable rate and intensity in all groups (Table I). There were no differences between weights of the hearts or kidneys, prominently enlarged during steroid-induced hypertension. Steroid treatment caused a slight hypotrophy of the pituitary and adrenal glands (Table I).

Although steroid treatment caused a dose-related increase in urine volume and a decrease in protein concentration and osmolality, such differences were usually not significant statistically (Table II).

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Kallikrein excretion (Table II) was higher in all groups in the 3rd week than it had been in the 2nd, but in both instances the quantities voided did not differ among the groups.

PRA was greatly depressed in all 3 groups, doubtless because of the salt excess to which they were exposed. All of the control values fell below 0.1 ng/ml/h (Table II), but both steroid-treated groups averaged slightly higher because several individual values ranged 0.1–1.2 ng/ml/h (Table II).

If 16β-OH-DHEA has 1/40th and DOCA 1/25th (the generally accepted figure) the potency of aldosterone, then 2 mg of 16β-OH-DHEA should be equivalent to 1.25 mg of DOCA, which is 6^7 to 10^{17} times the quantity needed to cause hypertension in the rat. The failure of that dosage of 16β-OH-DHEA to have an effect on saline intake, prominently enhanced by DOCA under similar circumstances[18], blood pressure, heart and kidney weight, or kallikrein excretion, casts serious doubt upon its mineralocorticoid status.

In that context FUNDER et al.[19] find that neither renal mc (aldosterone) receptors, nor those responsive to estrogen – a secondary renal sodium-retrieval system – display significant binding affinity for 16β-OH-DHEA. Such binding is considered to be an obligatory prerequisite for mc action, correlating exceedingly well with mc hormone activity. Furthermore, neither EDELMAN et al. (personal communication) using concentrations as high as 5×10^{-6} *M*, nor HIGGINS (personal communication) with concentrations up to 7×10^{-5} *M*, have detected any effect of 16β-OH-DHEA on sodium transport of isolated toad bladders, a generally accepted mc bioassay in which aldosterone exerts maximal stimulation at 4×10^{-8} *M*.

Finally, one of our laboratories (at Dallas) has been unable to demonstrate an effect of 16β-OH-DHEA on the urinary Na/K ratio of adrenalectomized rats at dosages as high as 30 μg, whereas 10 ng of aldosterone, and proportionately larger quantities of the weaker mc's are readily detected in parallel experiments.

These findings do not support the candidacy of 16β-OH-DHEA either as a mc or as a steroid capable of causing hypertension. The significance of its abundance in urine of patients with low renin essential hypertension is thus obscure, and of doubtful etiologic importance. It could be a metabolite of a more active steroid causative of hypertension, or, alternatively, other as yet unidentified steroids may be responsible.

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Effect of Progesterone on the in vivo Binding of Estrogens by Uterine Cells[1]

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Summary. Progesterone selectively inhibits estradiol uptake by the nuclei of the luminal epithelial cells but not by other uterine cells. This inhibition in estrogen binding parallels the inhibition by progesterone of some estrogenic responses in the luminal epithelial cells only.

Two important estrogen receptor systems have been found to exist in the rat and human uterus: the cytosol-nuclear and the eosinophil receptor systems[2–6]. Each receptor system seems to be involved independently in the mechanisms of estrogen action[2,7,8]. Therefore, it is possible to produce or selectively block the effects mediated by one of the receptor systems without interfering with the estrogenic response mediated by the other receptor system[9,10].

The cytosol-nuclear receptor system exists in the luminal epithelial, glandular epithelial, stromal and muscular cells of the uterus[3]. It does not necessarily follow that the binding of estrogens to the cytosol-nuclear receptor system must behave in the same manner in all uterine cell types under different physiological conditions. If each cell-type plays a different role in uterine physiology, and if it is possible selectively to block (or stimulate) estrogen binding in one cell type, then it would be possible to modify selected parameters of estrogen stimulation. The present report demonstrates that progesterone selectively blocks estrogen binding in luminal epithelial cells, and correlates this finding with a selective blockage of some parameters of estrogen stimulation in this cell type.

Material and methods. Female rats in proestrus, estrus and in the 1st and 2nd days of diestrus were used, as well as rats in the 2nd day of diestrus pretreated i.p. with either 5 mg of progesterone, 0.3 μg of estradiol, or both together 24 h before the injection of the isotope. Tritiated estradiol (500 μCi, corresponding to 1.4 μg) was injected into the jugular vein, and the animals were sacrificed 10 min or 1 h after receiving the injection of ^{3}H-estradiol. The uteri were excised and processed by a dry radioautographic technique for soluble compounds[11], modified

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