

Enhancement of Myotrophic and Androgenic Responses by Aqueous Suspension of Steroids.* (18258)

CHARLES D. KOCHAKIAN[†] AND EVANGELINE ROBERTSON.

From the Department of Physiology and Vital Economics, School of Medicine and Dentistry, University of Rochester, N. Y.

Estrogens(1-4), progesterone(2), desoxycorticosterone(5) and androgens(6) have been reported to be more effective when administered as aqueous suspensions than in oil solution. In this study a comparison of the effect of oil solution with aqueous suspension of certain androgens on the temporal muscle and accessory sex organs of the guinea pig(7) has been made.

Procedure. The guinea pigs were of the Hartley strain (Tumblebrook Farms) and were obtained at 325-375 g body weight(8). They were kept in individual cages and fed Rockland guinea pig diet containing vitamin C, *ad libitum*. Once per week each animal was given 12.5 mg vitamin C in a tablet by mouth. When the guinea pigs reached 395-405 g body weight they were castrated.

Thirty to 35 days later the androgens[‡] were injected subcutaneously at approximately 5 p.m. on each day for 14 days. The guinea pigs were weighed 3 times per week beginning at arrival and also at autopsy. Any animal that did not show a good growth response was discarded. On the morning of the 15th day the animals were killed and the accessory sex organs and the temporal muscles were removed and weighed on a Roller-Smith torsion balance.

Results. Body Weight. All of the androgens except testosterone in oil solution at 0.25 mg/day produced a greater increase in body weight than was shown by the control animals.

Myotrophic and Androgenic Effects. At both dose levels the aqueous suspension of testosterone produced a much greater increase in the weight of temporal muscles and seminal vesicles and prostates than the oil solution did (Table I); the aqueous suspension enhanced the myotrophic effect roughly 3 times and the androgenic 9-16 times depending on the dose. Furthermore, the aqueous suspension of testosterone was only slightly less effective than testosterone propionate in oil solution.

An aqueous suspension of androstanediol-3 α , 17 α had a slightly smaller androgenic effect but a greater myotrophic effect than the aqueous suspension of testosterone.

Discussion. The increase in body weight produced by the androgens is in agreement with previous observations after implantation of pellets of androgens(7).

The greater efficacy of the aqueous suspension of the androgens on the temporal muscle of the guinea pig suggests this method of administration as suitable for stimulation of protein anabolic processes.

The greater efficacy of the aqueous suspension of androstanediol-3 α , 17 α as compared to testosterone on the temporal muscle

* This investigation was supported by a grant from Ayerst, McKenna and Harrison Ltd.

[†] Present address: Oklahoma Medical Research Institute, Oklahoma Medical Center, Oklahoma City, Oklahoma.

1. Richards, R. K., Spruth, H. C., and Russell, M. K., *Proc. Soc. Exp. Biol. and Med.*, 1941, v48, 100.

2. Miescher, K., Gasche, P., and Frye, H., *Helv. Physiol. et Pharm. Acta*, 1944, v2, 515.

3. Simond, A., Lindquist, K. M., Tendick, F. H., and Rowe, L. W., *J. Am. Pharm. Assn.*, 1950, v39, 52.

4. Bates, R. W., and Lowry, C., *Proc. Soc. Exp. Biol. and Med.*, 1950, v73, 576.

5. Meier, R., Gasche, P., and Frey, H., *Schweiz. Med. Woch.*, 1946, v76, 107.

6. Meier, R., personal communication.

7. Kochakian, C. D., Humm, J. H., and Bartlett, M. N., *Am. J. Physiol.*, 1948, v155, 242.

8. Kochakian, C. D., and Robertson, E., *Proc. Soc. Exp. Biol. and Med.*, 1950, v73, 388.

[‡] The testosterone propionate (Perandren) testosterone, and the androstanediol-3 α , 17 α ("micro-crystalline" aqueous suspension) were provided by Ciba Pharmaceutical Products, Inc. and the testosterone ("micro-crystalline" aqueous suspension) by Ayerst, McKenna, Harrison and Co.

TABLE I. Enhancement of Myotrophic and Androgenic Responses by Aqueous Suspension of Steroids.

Treatment		Guinea pigs No.	Dose, mg/day	Body wt		Increase		M/A†
Steroid	Vehicle			Initial, g	Increase, g	Temporal muscles (M) mg*	Sem. ves. + pros. (A) mg*	
Control		14		539	54	(690)	(550)	
Testosterone	Oil	4	.25	535	56	83	129	
	Susp.	4	.25	564	86	184	1072	.17
Androstenediol-3 α , 17 α	"	5	.25	551	79	256	960	.27
Testosterone	Oil	4	.50	539	85	131	114	1.15
	Susp.	4	.50	584	79	426	1756	.24
Test. propionate	Oil	4	.50	574	77	456	2230	.21
Androstenediol-3 α , 17 α	Susp.	4	.50	573	85	452	1560	.29

* The values are the increases above the control values which are in parentheses.

† M/A = The growth of the temporal muscles divided by the growth of the seminal vesicles and prostates.

plus its smaller effect on the accessory sex organs in agreement with pellet studies(7) now makes it possible to carry out clinical studies with this interesting steroid. The extremely low solubility of androstenediol-3 α , 17 α in oil(9) has previously made such studies difficult.

Summary. An aqueous microcrystalline suspension of testosterone was 3 times more effective in stimulating the growth of the

temporal muscles and 9-16 times more effective on the accessory sex organs than an olive oil solution of testosterone and as effective as a sesame oil solution of testosterone propionate. An aqueous microcrystalline suspension of androstenediol-3 α , 17 α was slightly more effective on the temporal muscle and less effective on the accessory sex organs than a similar suspension of testosterone.

9. Kochakian, C. D., *Am. J. Physiol.*, 1950, v160, 53.

Received August 11, 1950. P.S.E.B.M., 1950, v75.

Protein Anabolic Activity of Pregnant Mares' Urine.* (18259)

CHARLES D. KOCHAKIAN.**

From the Department of Physiology and Vital Economics, School of Medicine and Dentistry; University of Rochester.

The presence of a protein anabolic factor(s) in androgenic male urine extracts was reported(1) 15 years ago. A similar factor(s) now has been found in pregnant mares' urine.

* This investigation was supported by a grant from Ayerst, McKenna and Harrison Ltd

** Present address: Oklahoma Medical Research Institute, Oklahoma Medical Center, Oklahoma City, Oklahoma.

1. Kochakian, C. D., and Murlin, J. R., *J. Nutrition*, 1935, v10, 437.

Procedure. Pregnant mares' urine was extracted† by the method used for human male urine(1) with minor modifications. The neutral extracts were fractionated‡ by separation into ketonic and non-ketonic portions by means of Girard's T reagent and were then further fractionated by chromatography with magnesium silicate as adsorbent(2). The

† The neutral extracts were prepared by the Ayerst, McKenna and Harrison Ltd.

‡ The following phase of the program was carried out at Rochester with the assistance of Betty Beall.