Myotrophic and Androgenic Activities of Androstanazole. A New Heterocyclic Steroid. (25528)

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Recent reports(1,2) indicated that 17β-hydroxy-17α-methylandrostano [3,2-c] pyrazole (hereafter referred to as androstanazole) is a powerful, orally active, anabolic agent. Multiple dose level assessment(3) of nitrogen retaining activity using nitrogen equilibrated castrated male rats(4), showed that androstanazole was 30 times more active than methyltestosterone when both compounds were administered orally, but when administered subcutaneously, androstanazole was only 1/20 as active as testosterone propionate. For all practical purposes, androstanazole was as active orally as subcutaneously. In recent years, use of nitrogen-balance studies with laboratory animals to assess anabolic properties of steroids has been generally abandoned in favor of simple and less tedious myotrophic assay(5,6). This report presents our observations on myotrophic and androgenic activities of androstanazole following subcutaneous and oral routes of administration. Testosterone propionate and methyltestosterone were tested concurrently with androstanazole for comparative purposes.

Materials and methods. Test materials were administered as solutions or suspensions in 10% v/v ethanol cottonseed oil, the physical state depending upon concentration and solubility. Steroids were triturated in mortar and pestle with gradual addition of the vehicle so that suspensions were finely dispersed. Myotrophic and androgenic activities were determined by modification of method reported by Hershberger, Shipley and Meyer(5). Male rats of Sprague-Dawley strain, 22 days of age (41-45 g) were castrated and maintained on lab. chow and tap water *ad lib.* in air conditioned quarters. Androstanazole and testosterone propionate were administered subcutaneously daily except Sunday, from 7th to 16th days after castration. Daily dose of each drug was contained in 0.2 ml of vehicle. Animals were autopsied on the 17th post-castration day, 24 hours after last medication. Levator ani muscle and ventral prostate were removed, blotted and weighed.

Oral studies were conducted in the same manner except that total daily dose of androstanazole or methyltestosterone was divided into 2 equal portions administered by stomach tube at 9:00 a.m. and at 4:00 p.m. each day of medication.

Results. Androstanazole was 1/7 as myotrophic and 1/33 as androgenic as testosterone propionate when both compounds were administered subcutaneously (Table I). Androstanazole was twice as myotrophic and 1/3 as androgenic as methyltestosterone when both compounds were administered orally (Table I).

Discussion. The experimental data clearly indicate that androstanazole is relatively more anabolic than androgenic. Nitrogen retention(3) and myotrophic assays indicate that androstanazole administered orally is 30 times more active in promoting nitrogen retention, 2 times more myotrophic than methyltestosterone, and is 1/3 as androgenic. Compared with testosterone propionate, subcutaneously, androstanazole is 1/20 as active in promoting nitrogen retention, is 1/7 as myotrophic and is 1/33 to 1/40 as androgenic. The interesting feature of androstanazole is the high oral anabolic activity coupled with low order androgenicity.

Androstanazole is 30 times more anabolic orally than methyltestosterone based on multiple dose level assessment of nitrogen retention in rats(3). This relative potency figure is considerably higher than the 2:1 ratio obtained from the above described results of the myotrophic assays. This difference is apparent by the larger dose of androstanazole required orally (10-40 mg/kg) to produce substantial increase in weight of levator ani

TABLE I. Relative Myotrophic and Androgenic Activities of Androstanazole, Testosterone Propionate and Methyltestosterone.

Compound	No. of animals	Dose, mg/kg/day × 9	Myotrophic response, levator ani wt, mg ± S.E.	Androgenic response, ventral prostate wt, mg ± S.E.
None	66		31.6 ± .4	6.1 ± .3
Androstanazole (s.c.)	12	1.4	35.3 ± 1.5	7.3 ± .4
	12	2.8	43.7 ± 2.5	13.0 ± .7
	12	5.6	47.9 ± 2.2	14.5 ± 1.0
	12	11.2	72.9 ± 4.0	39.6 ± 2.8
Testosterone propionate (s.c.)	12	.175	34.9 ± 1.5	19.8 ± 1.8
	12	.35	40.8 ± 2.6	33.6 ± 3.3
	12	.70	49.5 ± 1.9	57.5 ± 2.1
	12	1.40	66.8 ± 3.0	78.4 ± 6.1
Relative activity of androstanazole to testosterone propionate*			1/7	1/33
None	52		29.5 ± .9	5.1 ± .2
Androstanazole (i.g.)	6	5.25	28.6 ± 3.1	4.3 ± .7
	6	10.50	39.3 ± 4.1	8.6 ± .9
	18	21.	51.3 ± 2.4	13.4 ± .9
	12	42.	67.1 ± 3.3	24.2 ± 2.4
Methyltestosterone (i.g.)	12	5.25	31.6 ± 1.7	10.6 ± .8
	12	10.50	33.0 ± 1.5	21.9 ± 1.2
	12	21	41.9 ± 1.0	32.6 ± 1.7
	12	42	48.5 ± 2.5	45.3 ± 3.2
	6	84	63.8 ± 2.2	57.7 ± 3.9
Relative activity of androstanazole to methyltestosterone*			2	1/3

* Calculated according to method of Gaddum(7).

muscle than needed (0.5 to 5.0 mg/kg) to achieve marked improvement in nitrogen retention(3). On the other hand, the dose of methyltestosterone required for significant myotrophic and nitrogen retention (3,8) responses is identical for all practical purposes (20-80 mg/kg in each case). Early clinical observations(9) corroborate results of nitrogen retention studies in rats and imply that levator ani response does not fully reflect the anabolic potential of this new heterocyclic steroid.

Summary. Myotrophic and androgenic activities of androstanazole have been evaluated using immature castrated male rats. The data indicate that androstanazole is 1/7 as myotrophic and 1/33 as androgenic as testosterone propionate when both agents are administered subcutaneously, whereas it is 2 times more myotrophic than, and ⅓ as androgenic as, methyltestosterone when the 2 agents are given orally. The data show that androstanazole is relatively more anabolic than androgenic regardless of route of administration. The results are discussed in light of nitrogen retention data previously reported for this compound.

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