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Uptake and Distribution of ^{3}H Testosterone in Tissues of Male Praomys (Mastomys) Natalensis

An in vivo and in vitro Study on the Prostate

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Summary. Following the administration of labelled testosterone into 4-6 month old intact, or 24 h orchiectomized Praomys (Mastomys) Natalensis, the uptake of radioactivity by the prostate and other tissues was measured at different intervals. Two hours after the injection of the hormone, the concentration of radioactivity in the prostate was significantly higher than in most of the other organs, but less than that of the liver and kidney. Most of the radioactivity taken up by the liver and kidney disappeared 8-16 h after the administration of the hormone. Orchiectomy enhanced the uptake of the radioactivity by the prostate. Administration of unlabelled testosterone prior to the injection of labelled hormone or the addition of unlabelled testosterone in the incubation media significantly reduced the uptake of radioactivity by the prostate. These changes did not occur in the non target tissues. In an in vitro system prostatic tissue took up significantly more radioactivity than the diaphragm. These findings have been compared with the results of the similar experiments reported on the prostate of the male rat and the female Mastomys.

Key words: Mastomys, Prostate, Testosterone, Uptake, in vitro incubation, in vivo studies.

It has been demonstrated that the accessory sex glands of male animals are androgen dependent and one of the primary steps by which androgens interact with these glands involves the uptake of the steroid by the gland. The selective uptake and retention of androgens by the prostate have been demonstrated in several species (2). Recently, interest has been shown in the rodent Praomys (Mastomys) Natalensis, as an experimental animal. The female of this rodent possesses a well developed prostate (1) which selectively takes up and retains androgen (5). The present study was designed to investigate the similarity between the prostate of the male and female Mastomys in regard to the uptake and retention of androgens.

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MATERIALS AND METHODS

Animals

Four to six month old male Praomys (Mastomys) Natalensis were bred in our colony and used throughout the experiments. Bilateral orchiectomy was carried out under Fluothane anaesthesia 24 h prior to experiments.

Radioactivity

1 α , 2 α -^{3}H testosterone (specific activity 47 Ci/mmol purity greater than 97 %) for in vitro experiments, and 1, 2, 6, 7-^{3}H testosterone (specific activity 94 Ci/mmol. purity 99 %) for in vivo studies, were obtained from the Radiochemical Centre, Amersham. A solution of ^{3}H testosterone (in 20 % ethanol : saline) was prepared for in vivo experiments.

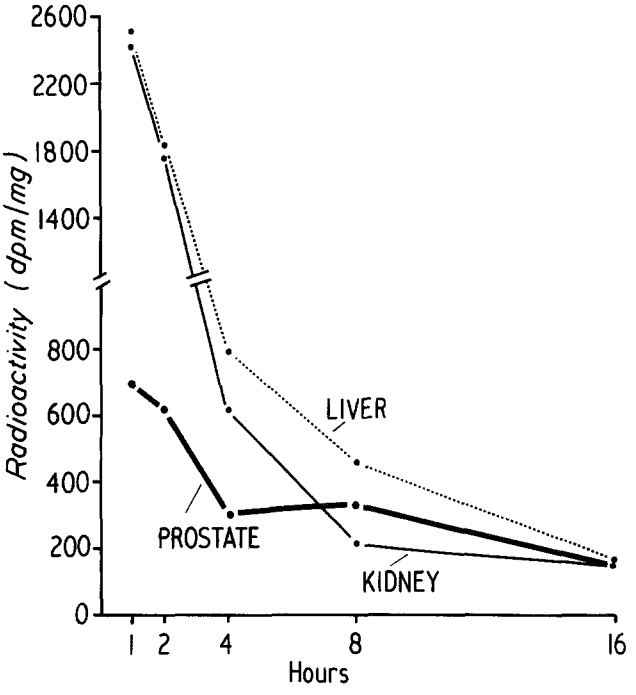

Fig. 1. Comparison of in vivo uptake of radioactivity by the prostate with liver and kidney, 1, 2, 4, 8 and 16 h following administration of ^{3}H testosterone into 24 hour castrated rat

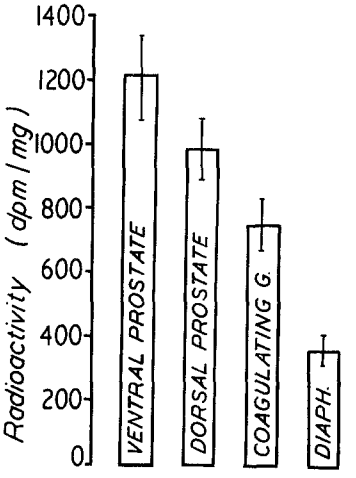

Fig. 2. In vitro uptake of radioactivity by ventral prostate, dorsal prostate, coagulating glands and diaphragm of intact rat. Each incubation media contained 0.25 μ Ci of 1, 2 -^{3}H testosterone in 2 ml Tc199. Each Bar represents the mean ± S.E.M. of 7 experiments

Table 1. Distribution of radioactivity in the tissues of male Mastomys, 1, 2, 4, 8 and 16 h following administration of ^{3}H testosterone. Animals were castrated 24 h prior to injection. Values are mean ± S.E.M. of 4-5 experiments expressed as d.p.m./mg tissue

Tissue	Concentration of radioactivity after				
	1 h	2 h	4 h	8 h	16 h
Prostate (ventral+dorsal)	696 ± 41.0	615 ± 33.6	304 ± 37.1	330 ± 35.0	132 ± 12.8
Coagulating glands	568 ± 64.4	437 ± 51.6	181 ± 35.9	258 ± 4.3	106 ± 19.5
Seminal vesicle	794 ± 141.9	734 ± 128.1	378 ± 52.9	282 ± 63.8	120 ± 14.5
Ampullary glands	516 ± 51.0	581 ± 86.7	158 ± 11.9	226 ± 48.7	118 ± 17.9
Pituitary	387 ± 38.3	261 ± 63.6	157 ± 36.8	335 ± 178.5	72 ± 17.9
Adrenal	1001 ± 312.4	427 ± 30.9	225 ± 93.1	115 ± 18.6	108 ± 10.7
Liver	2504 ± 451.3	1825 ± 334.4	783 ± 208.5	456 ± 37.2	167 ± 16.1
Kidney	2428 ± 354.8	1749 ± 148.5	613 ± 163.2	214 ± 30.8	134 ± 16.3
Lung	873 ± 121.3	362 ± 28.2	164 ± 23.5	128 ± 28.3	87 ± 5.7
Spleen	326 ± 12.2	192 ± 11.7	129 ± 33.5	105 ± 32.7	87 ± 9.4
Abdominal muscle	281 ± 36.2	188 ± 9.5	126 ± 13.8	129 ± 28.2	96 ± 6.8
Diaphragm	312 ± 42.0	238 ± 23.9	138 ± 19.9	111 ± 18.5	74 ± 8.4

Table 2. Comparison of the in vivo uptake of ^{3}H testosterone in prostate with some other non target tissues in castrated and intact male Mastomys. Values are mean ± S.E.M. of 4-5 experiments expressed as d.p.m./mg tissue. (NS: not significant)

Tissue	Uptake of radioactivity					
	after 1 h			after 2 h		
	Castrated	Intact	Significance (value for P)	Castrated	Intact	Significance (value for P)
Prostate (ventral + dorsal)	696 ± 41.0	349 ± 43.9	<.001	615 ± 33.6	331 ± 60.2	<.001
Liver	2504 ± 451.3	2437 ± 1167	NS	1835 ± 334.4	1413 ± 308.0	NS
Lung	873 ± 121.3	815 ± 292.3	NS	362 ± 28.2	277 ± 75.5	NS
Diaphragm	312 ± 42.0	321 ± 97.4	NS	238 ± 23.9	175 ± 30.2	NS
Kidney	2428 ± 354.8	2226 ± 209.4	NS	1749 ± 148.5	992 ± 392.9	NS
Spleen	326 ± 12.25	259 ± 107.8	NS	192 ± 11.7	151 ± 66.7	NS
Abdominal muscle	281 ± 36.2	360 ± 93.3	NS	188 ± 9.5	238 ± 77.5	NS

Table 3. Effect of unlabelled testosterone on the in vivo uptake of ^{3}H testosterone by prostate and other tissues of male Mastomys. Each animal has received 100 µg of unlabelled testosterone prior to administration of labelled testosterone and sacrificed 2 hours later. Values are mean ± S.E.M. of 4-5 experiments expressed as d.p.m./mg tissue

Tissue	Uptake of ^{3}H testosterone	Uptake of ^{3}H testosterone in presence of unlabelled testosterone	Significance value for P
Prostate (ventral + dorsal)	615 ± 33.6	213 ± 19.7	<0.001
Liver	1835 ± 234.4	2127 ± 138.3	<0.1
Kidney	1749 ± 148.5	1208 ± 152.1	<0.1
Spleen	192 ± 11.7	185 ± 12.4	<0.1
Lung	362 ± 28.2	379 ± 46.2	<0.1
Adrenal	427 ± 30.9	422 ± 63.0	<0.1
Diaphragm	238 ± 23.9	198 ± 13.0	<0.1

In vitro Experiments

The measurement of labelled steroid in vitro was carried out using the method previously described (3) with the exception that Krebs-Ringer bicarbonate glucose albumin was substituted by culture media (Tc 199) and Hyamine Hydroxide was replaced by Soluene 350 (Packard).

In vivo Experiments

Either intact or 24 h castrated male Mastomys were given deep intramuscular injections of ^{3}H testosterone (100 Ci/100 g body weight). In order to study the effect of unlabelled testosterone on the uptake of labelled hormone, a solution of 100 g of testosterone in 20% ethanol saline was administered before injection of radioactive hormone. Animals were sacrificed 1, 2, 4, 8 or 16 h after injection, the prostate and other tissues were dissected out, weighed on a torsion balance and placed in scintillation vials. Soluene 350 (0.5 ml) was added to each vial and the tissue was dissolved overnight at room temperature. 10 ml scintillation fluid (0.4 g P.P.O. in 1000 ml toluene) was added to each vial and the radioactivity was counted in a scintillation spectrometer to give a standard of error of less than 1%. Quenching was corrected by the internal standard method using ^{3}H testosterone. The results were expressed as dpm/mg tissue.

RESULTS

In vivo Uptake of ^{3}H Testosterone by Tissues of Orchiectomized and Intact Mastomys

Following the administration of labelled testosterone, substantial amounts of radioactivity were found in most of the tissues of intact and castrated Mastomys. One hour after injection a decrease in the concentration of the radioactivity with time was observed (Table 1). Two hours after the injection of labelled hormone, the uptake or radioactivity by ventral and dorsal prostate as well as by coagulating glands, seminal vesicles and ampullary glands was significantly higher than by abdominal muscle or diaphragm, but less than that by liver and kidney. Most of the radioactivity taken up by liver and kidney disappeared 8-16 h after receiving labelled testosterone. Sixteen hours after the administration of labelled hormone the level of radioactivity reached the same order as the prostate (Fig. 1).

The distribution of radioactivity in intact animals 1-2 h after injection was also investigated. A comparison between the level of radioactivity in intact and orchiectomized animals during this period is shown in Table 2. The results also showed an increase in the uptake of radioactivity by the prostate of the orchiectomized animal.

Effect of Unlabelled Testosterone on the Uptake of Radioactivity

Administration of unlabelled testosterone prior to injection of labelled testosterone substantially reduced the uptake of radioactivity by the prostate. This decrease was as high as 65.4% in the prostate following the administration of 100 µg of unlabelled testosterone to each animal. However, no significant changes occurred in other tissues such as liver, kidney, diaphragm, spleen, lung or adrenal (Table 3). Similarly, in the in vitro studies addition of 10 µg of unlabelled testosterone in 2 ml incubation media reduced the level of radioactivity to 67.8% in the prostate, the values being 1215 ± 137.9 and 379 ± 49.6 for the uptake of radioactivity without and with the presence of unlabelled testosterone respectively ($p < 0.001$).

In vitro Studies

The ability of the prostatic tissue to take up ^{3}H testosterone was compared with the diaphragm. The results are shown in Figure 2. Under the experimental conditions described, the uptake of radioactivity by the ventral prostate was 3 to 4 times higher than by the diaphragm. Similarly, the dorsal prostate and coagulating glands took up significantly more radioactivity than the diaphragm. The uptake of radioactivity by the ventral prostate was significantly higher than by the dorsal or coagulating glands.

DISCUSSION

The present study demonstrated that the prostate of male Mastomys is able to accumulate and retain radioactivity following the injection of ^{3}H testosterone into the animal or in vitro incubation of prostatic tissue in a medium containing labelled testosterone. The nature of the compounds with which the radioactivity is associated in the prostate has not been investigated in this study. Although a high level of radioactivity appears to occur in the liver and kidney following the administration of labelled hormone, these organs are not able to retain radioactivity for a long period of time. Similar findings have been reported in the rat (6).

The significant decrease in the uptake of radioactivity by the prostate, due to the ad-

ministration of unlabelled testosterone or presence of unlabelled testosterone in the incubation media, suggests that the prostate in this rodent may contain specific receptors for androgens which have a limited capacity for finding androgens. This view is in accordance with the increased uptake of radioactivity in 24 h orchiectomized Mastomys. Similar findings have been reported for the rat prostate (6). The in vitro uptake of radioactivity by the Mastomys prostate also suggests that the ability of the ventral prostate to take up radioactivity is higher than that of the dorsal prostate or coagulating glands. This finding also is similar to the ability of the different lobes of the rat prostate to take up androgens.

The in vivo and in vitro experiments reported in this paper suggest a fundamental similarity in regard to the uptake and retention of androgens by this rodent with those previously reported for the rat (4, 6). The results also demonstrate that the uptake of radioactivity by the prostate of the male Mastomys is similar to that by the prostate of the females in this rodent (5).

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