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SPECIFIC BINDING OF OESTRADIOL TO GUINEA-PIG PROSTATE CYTOSOL AND NUCLEAR FRACTIONS

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Summary—A high affinity ($K_d \sim 0.15$ nM), saturable oestradiol binding site, which is specific for natural and synthetic oestrogens has been identified in guinea-pig prostate cytosol fractions. The binding site is protein in nature (heat- and protease-sensitive) and has a sedimentation coefficient of approx. 8S on glycerol gradients. A high affinity ($K_d \sim 0.16$ nM), saturable oestradiol binding site was also identified in salt-extracted (0.5 M KCl) nuclear fractions. The optimum incubation conditions for measuring the cytosolic and nuclear oestradiol binding sites were determined to be 20 h at 4°C. Saturation analysis studies revealed that following oestrogen treatment of intact animals, approx. 80% of the specific oestradiol binding sites in prostatic cytosol fractions were transferred into the nucleus. The presence of a specific oestradiol binding protein with characteristics of an oestrogen receptor in the guinea-pig prostate, is consistent with oestrogen having biological activity in this tissue. In view of the abundance of stroma in the prostate of this species, and the consistent finding that the stroma of male accessory sex tissues is oestrogen sensitive, the guinea-pig may be an appropriate experimental animal for further investigating the role of oestrogen in the growth and development of the prostate.

INTRODUCTION

Benign prostatic hyperplasia (BPH) is an almost universal phenomenon in ageing men [1, 2] and, in approx. 10% of males, results in sufficient obstruction to urinary outflow to necessitate surgery [2]. The observation that a functional testis is a prerequisite for the development of prostatic hyperplasia [3] is generally considered to indicate that this growth process is androgen dependent. However, attempts to overcome outflow obstruction using either anti-androgen therapy or other hormonal manipulations, have been unsuccessful [2, 4]. It is possible therefore, that testicular androgens are not solely responsible for the hyperplastic growth of the prostate gland.

The presence of specific receptors for oestradiol and dihydroteststerone in human BPH tissue cytosol fractions [5, 6, 7] suggests that both hormones may be important in the aetiology of hyperplastic growth of the prostate. In men, the plasma free oestrogen to androgen ratio increases with age [8]. Activation of smooth muscle cells and stromal overgrowth appear to be early events in the development of prostatic hyperplasia in man [9] and the plasma and urinary levels of oestradiol are reportedly positively correlated with the amount of prostatic stroma in human BPH tissues [10]. A consistent action of oestrogen in adult male accessory sex organs is stimulation of the fibromuscular stromal tissue [8]. Furthermore, many features of canine prostatic hyperplasia are induced in sexually mature castrate dogs by combined treatment with androgen and oestrogen [11].

In spite of the considerable body of circumstantial evidence suggesting that oestrogen may be important in the aetiology of hyperplastic growth of the prostate, it is not known whether oestrogen is important in the regulation of normal prostatic growth. A fundamental requirement for oestrogen to have such an effect, would be the existence of a functional oestrogen receptor mechanism in the prostate.

The present study examined whether the binding of oestradiol to prostatic cytosol fractions is characteristic of binding to a specific receptor, and whether the receptor mechanism is functional—at least to the level of nuclear translocation of the receptor–steroid complex. The guinea-pig was chosen as the experimental animal because its prostate has a substantial fibromuscular component, and the fact that a number of studies [9, 10, 12] have suggested recently that the stroma may be important in the development of prostatic hyperplasia.

EXPERIMENTAL

Chemicals

[2,4,6,7-^{3}H]Oestradiol-17β (sp. act. > 85 Ci/mmol) was purchased from the Radiochemical Centre, Amersham (U.K.). Radioinert steroids, protease (Type XIV), bovine serum albumin and dithiothreitol were obtained from Sigma Chemical Co. (U.S.A.). Activated charcoal was purchased from Ajax Chemicals (Aust.), Dextran-T70 from Pharmacia (South Seas), sodium molybdate from BDH Chemicals (Aust.) and

PCS scintillation fluid from Amersham–Searle (Aust.).

Animals and tissues

Sexually mature male guinea-pigs (IMVS coloured; outbred strain), with body weight between 550 and 750 g, were used in this study. In contrast to the rat, the guinea-pig prostate does not contain a large ventral lobe, but is comprised of dorsal and lateral lobes and the coagulating gland [13]. Each lobe of the guinea-pig prostate, as illustrated by the lateral lobe shown in Fig. 1, is characterized by an extensive interacinar fibromuscular stromal component.

Animals were killed by an intraperitoneal (i.p.) injection of sodium pentobarbitone (80 mg/kg). The prostate gland was excised rapidly, dissected clear of connective tissue, weighed and placed in chilled homogenization buffer.

For histological examination, tissues were fixed in phosphate-buffered formalin (pH 7.4) and embedded in paraffin wax. The fixed tissues were sectioned and stained with haematoxylin and eosin.

Administration of steroids

Guinea-pigs received an i.p. injection of either 0.2 ml carrier (10% ethanol; 45% propylene glycol; 45% sterile water) or oestradiol (0.1 mg/kg body wt) in 0.2 ml carrier.

Preparation of cytosol and nuclear fractions

Cytosol fractions were prepared in buffer consisting of 10 mM Tris, 1.5 mM EDTA and 10% glycerol adjusted to pH 7.4 at 4°C. Prior to tissue homogenization, dithiothreitol was added to produce a final concentration of 1 mM (TEDG buffer). Nuclear receptors were extracted from crude nuclear pellets using TEDG buffer containing 0.5 M KCl (pH 8.0 at 4°C).

The excised prostate glands were teased into 2–4 mm fragments using forceps, resuspended in TEDG buffer and disrupted using 4 × 15 s bursts of an Ultra Turrax homogenizer. A crude nuclear pellet was obtained by centrifugation of the homogenate at 900 *g* for 20 min. The nuclear pellet was washed twice in TEDG buffer prior to extracting the nuclear receptors. The final cytosol and nuclear fractions were obtained by centrifugation at 105,000 *g* for 60 min at 4°C.

Oestrogen receptor assay

Oestrogen receptor levels were measured using a saturation analysis method. Five incubating concentrations of [^{3}H]oestradiol ranging from 0.05 to 1.2 nM were used to determine total binding to the cytosolic and nuclear fractions. A parallel series of incubations, containing the radioligand in the presence of a 100-fold excess of diethylstilboestrol (DES), was used to estimate the level of nonspecific binding. Incubations were conducted in duplicate in microtiter plates, with a final incubation volume of 0.1 ml.

Bound and free hormone were separated by addition of an equal volume of a chilled dextran-coated charcoal (DCC) suspension consisting of 0.5% activated charcoal and 0.05% Dextran-T70 in TEDG buffer adjusted to pH 7.4 at 4°C. The DCC incubations were maintained at 0–2°C for 20 min prior to centrifugation at 800 *g* for 15 min.

A 0.1 ml aliquot of the resultant supernatant was removed and counted for 2 min in 5.0 ml of PCS scintillation fluid (Amersham–Searle), using a Searle Mk III 6880 liquid scintillation system with a counting efficiency of 48% for tritium. The binding data was analysed according to the method of Scatchard[14]. Protein determinations were performed according to the method of Lowry *et al.*[15] using bovine serum albumin as a standard.

Association–time experiments

To determine the optimum incubation conditions for measuring the level of [^{3}H]oestradiol specifically bound to prostatic cytosol and nuclear fractions, and to check for possible degradation of binding sites during the incubation procedure, aliquots (0.05 ml) of cytosol and nuclear fractions were incubated in triplicate with 2 nM [^{3}H]oestradiol for varying times at 0, 15 and 30°C in the presence and absence of competitor hormone. The incubations were terminated by the addition of an equal volume of a chilled DCC suspension.

To evaluate the extent of exchange between added radioligand and receptor bound steroid, the association–time experiments were modified in the following ways. Cytosolic fractions prepared from guinea-pig prostates were preincubated with 2 nM radioinert oestradiol for 2 h at 4°C. Both the control and oestradiol-exposed cytosol fractions were treated with dextran-charcoal (20 min, 0°C) prior to conducting the association–time experiments. Alternatively, guinea-pigs were injected with either carrier only or oestradiol (0.1 mg/kg body wt) 60 min prior to removing the prostate glands. Salt-extractable nuclear fractions were prepared and the association–time experiments repeated.

Specificity of oestradiol binding sites

To determine the specificity of oestradiol binding to prostatic cytosol fractions, aliquots of cytosol were incubated with [^{3}H]oestradiol and increasing concentrations of various competitor hormones. Tritiated oestradiol was used at a final concentration of 1 nM and incubations were conducted in triplicate for 20 h at 4°C. Receptor bound and free ligand were separated by charcoal adsorption. The binding of [^{3}H]oestradiol in the presence of competitor was expressed as a percentage of control binding (i.e. in the absence of competitor) and plotted against the log of the competitor concentration.

Glycerol density gradient ultracentrifugation

Prostatic cytosol fractions were prepared in TEDG

buffer containing 20 mM sodium molybdate (TEDGM buffer), adjusted to a protein concentration of 5–8 mg/ml and incubated in duplicate with 5 nM [^{3}H]oestradiol, both alone and in the presence of a 100-fold excess of radioinert DES, for 16 h at 4°C. Following treatment with DCC, a 0.3 ml aliquot of each supernatant was layered on linear 10–30% glycerol density gradients which were prepared in buffer containing 10 mM Tris, 1.5 mM EDTA and 20 mM sodium molybdate, pH 7.4. The gradients were centrifuged at 192,000 *g* for 16 h at 4°C using a Beckman SW50.1 swinging bucket rotor and subsequently fractionated using a top harvesting method into 24 × 0.24 ml fractions. The fractions were counted in 4.5 ml of a toluene based scintillation fluid (0.4% PPO and 0.005% POPOP) to determine the peak of bound radioactivity. The sedimentation coefficients of the [^{3}H]oestradiol binding molecules were estimated by comparison with the rate of sedimentation of bovine serum albumin and human gamma-globulin protein standards in parallel gradient tubes. Following fractionation, the positions of the marker proteins were determined by u.v. adsorption at 280 nm using a Gilford 250 spectrophotometer.

RESULTS

Storage of prostatic tissues

Preliminary studies (Table 1), indicated that storage of guinea-pig prostatic tissues at −76°C resulted in a reduction in the measurable level of specific oestradiol binding sites. Less than 70% of the original binding activity was detected in cytosol fractions derived from tissues stored for 1 day. After 2, 6 and 10 days storage, specific binding of [^{3}H]oestradiol was either undetectable or considerably reduced, the median values being 37, 39 and 12%, respectively, of the original levels determined in the fresh tissues. In all subsequent experiments, therefore, fresh tissues were routinely used.

Characterization of oestradiol binding to guinea pig prostate cytosol fractions

Sedimentation profile. The presence of a specific oestradiol binding molecule in guinea-pig prostatic cytosol fractions was demonstrated using glycerol density gradient ultracentrifugation. The sedimentation profile shown in Fig. 2 indicates that there is a single peak of bound [^{3}H]oestradiol corresponding to a molecule with a sedimentation coefficient of approx. 8S. The ability to completely eliminate this 8S peak of bound radioactivity with a 100-fold excess of radioinert DES, demonstrates that the molecule has a limited capacity to bind steroid which is characteristic of steroid receptor proteins.

Table 1. Recovery of specific oestradiol binding sites following storage of prostatic tissue

Storage (days)	Number of tissues	Specific [^{3}H]oestradiol binding* (% of control)
1	4	59 (49–70)
2	10	37 (0–71)
6	4	39 (0–75)
10	4	12 (0–60)

*Median values, range in parentheses; all tissues were assayed fresh (i.e. control) and at various times after snap freezing in liquid nitrogen and storage at −76°C.

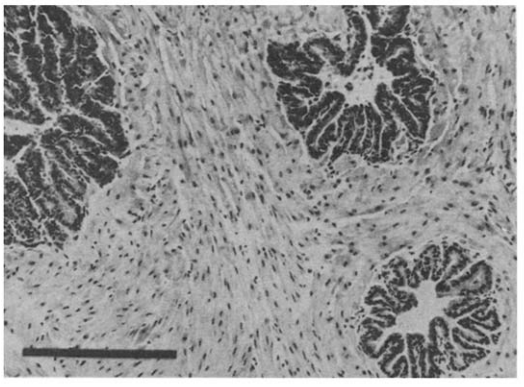

Fig. 1. Lateral lobe of adult guinea-pig prostate. The acinar epithelial structures are surrounded by an extensive fibromuscular stroma. Stained with haematoxylin and eosin. The bar represents 100 μm.

Specificity. The competition of various unlabelled hormones for [^{3}H]oestradiol binding to prostatic cytosol fractions is shown in Fig. 3. Oestrogens, but not other classes of steroid hormones, competitively inhibited the cytosolic binding of [^{3}H]oestradiol. The order of competitor effectiveness was DES > oestradiol > oestrone > oestriol > tamoxifen > dihydrotestosterone. Testosterone, progesterone

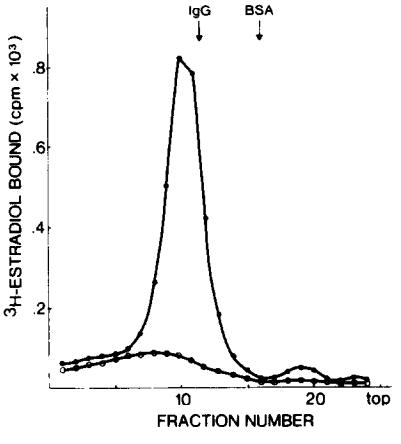

Fig. 2. Glycerol density gradient sedimentation profiles of [^{3}H]oestradiol labelled guinea-pig prostate cytosol. Cytosol fractions were incubated with 5 nM [^{3}H]oestradiol, both alone (●——●) and in the presence of a 100-fold excess of radioinert DES (○——○), for 16 h at 4°C. Free steroid was removed by dextran–charcoal adsorption, and 0.3 ml of the resultant supernatant layered onto linear 10–30% glycerol gradients. The gradients were centrifuged at 192,000 *g* for 16 h at 4°C using a Beckman SW50.1 rotor. Bovine serum albumin and human gamma globulin were used as molecular weight markers.

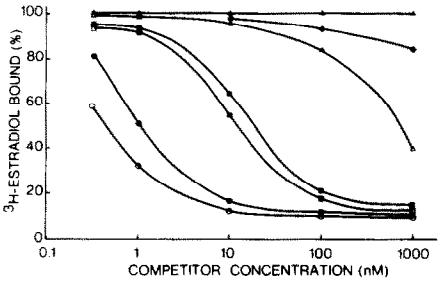

Fig. 3. Competition of various hormones for the binding of [^{3}H]oestradiol (1 nM) to prostatic cytosol fractions; key: oestradiol ●——●, DES ○——○, oestrone □——□, oestriol ■——■, tamoxifen △——△, dihydrotestosterone ◆——◆, progesterone, cortisol and testosterone ▲——▲. Aliquots of cytosol were incubated with [^{3}H]oestradiol for 20 h at 4°C with increasing concentrations of competitor hormone (0.5–1000 nM), prior to dextran–charcoal treatment. Values are mean of triplicate determinates for a typical experiment.

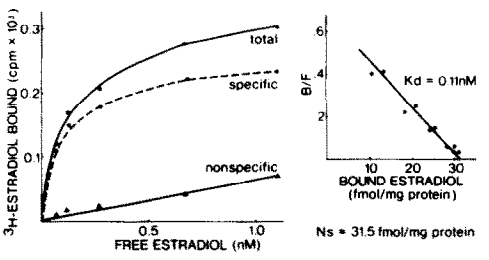

Fig. 5. (a) Saturation analysis of the binding of [^{3}H]oestradiol (0.05–1.2 nM) to guinea-pig prostate cytosol fractions. Specific binding was determined by subtracting nonspecific from total binding. Incubations were conducted in duplicate for 20 h at 4°C; nonspecific binding of [^{3}H]oestradiol was measured in the presence of a 100-fold excess of DES. (b) Scatchard plot transformation of the saturation analysis binding data. The dissociation constant (K_d) and number of specific binding sites (Ns), for an example experiment are indicated.

and cortisol were ineffective competitors for [^{3}H]oestradiol binding sites, irrespective of their concentration.

Optimum incubation conditions. Typical association time curves generated by incubating aliquots of prostatic cytosol with 2 nM [^{3}H]oestradiol for varying times at 4, 15 and 30°C are shown in Fig. 4. It is evident from these curves that the maximum specific binding of [^{3}H]oestradiol occurred after approx. a 2–3 h incubation at 30°C. However, the level of specific binding achieved at this temperature was variable and declined when the incubation was continued beyond 3 h. At the 15 and 20 h timepoints, no specific binding could be detected using a 30°C incubation. In comparison, the binding at 4°C reached a maximum after 15–20 h incubation and was considerably more stable. When a 15°C incubation temperature was used, maximum specific binding of [^{3}H]oestradiol was attained after 6–10 h incubation, the level attained being stable and similar to that achieved at 4°C. Figure 4 also indicates that no specific binding of [^{3}H]oestradiol to the cytosol fractions preincubated for 2 h with 2 nM radioinert oestradiol was detected following a short-term incubation at 4°C. After 20 h incubation at 4°C, however, a level of specific [^{3}H]oestradiol binding similar to that measured in control cytosol fractions was attained. Additional experiments indicated that incubation of prostatic cytosol fractions for 30 min at 60°C completely abolished the specific binding of [^{3}H]oestradiol. A similar effect on binding activity was achieved by incubation with protease (0.1 mg/ml) for 30 min at 37°C.

Finite binding capacity. The total, nonspecific and specific binding of [^{3}H]oestradiol (0.05–1.2 nM) to guinea-pig prostate cytosol fractions following a 20 h incubation at 4°C is shown in Fig. 5a. Although the plot of total binding never reached a plateau phase, subtraction of the linear nonspecific binding component from the total binding indicated that saturation of the specific oestradiol binding sites was achieved within the range of ligand concentrations employed.

Affinity and concentration of binding sites. Scatchard plot analysis (Fig. 5b) demonstrated that the

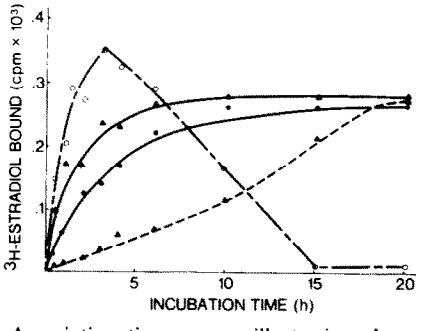

Fig. 4. Association–time curves illustrating the specific binding of [^{3}H]oestradiol (2 nM) to prostate cytosol fractions at various times during incubations conducted at 4°C (●——●), 15°C (▲——▲) and 30°C (○--○). Cytosol fractions were also exposed to 2 nM radioinert oestradiol (▲--▲) for 2 h prior to conducting the 4°C incubations.

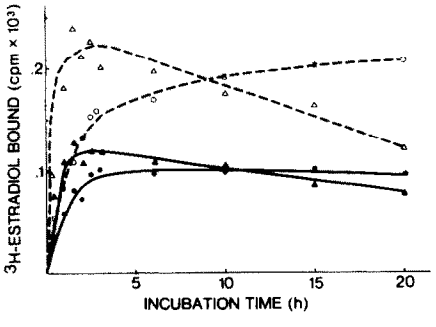

Fig. 6. Association–time curves for the specific binding of [^{3}H]oestradiol (2 nM) to 0.5 M KCl nuclear extracts of prostates from control and oestradiol treated (0.1 mg/kg; 1 h) adult guinea-pigs. Key: control 4°C ●——●, 30°C ▲——▲; oestradiol treated 4°C ○—○, 30°C △—△. Incubations were conducted in triplicate for various times at 4 and 30°C prior to dextran-charcoal adsorption of unbound ligand.

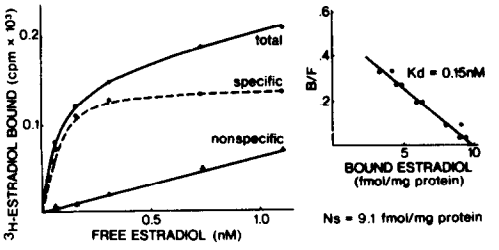

Fig. 7. (a) Saturation analysis of the binding of [^{3}H]oestradiol (0.05–1.2 nM) to guinea-pig prostate nuclear fractions extracted with 0.5 M KCl. Specific binding was determined by subtracting non-specific from total binding. Incubations were conducted in duplicate for 20 h at 4°C; nonspecific binding of [^{3}H]oestradiol was measured in the presence of a 100-fold excess of DES. (b) Example Scatchard plot of the saturation analysis binding data for the interaction of [^{3}H]oestradiol with nuclear binding sites. The dissociation constant (K_d) and number of specific binding sites (Ns) were calculated from the Scatchard plot.

cytosolic binding of [^{3}H]oestradiol was to a single class of high affinity binding sites, the equilibrium dissociation constant being 0.14(±0.05 M) nM (mean ± SD for 33 determinations). The binding site concentration (mean ± SD), calculated from the Scatchard plot analyses was 28.6(±8.7) fmol/mg protein. Expressed as total estradiol specifically bound, the mean value was 0.77(±0.15) pmol/prostate.

Binding of [^{3}H]oestradiol to guinea-pig prostate nuclear fractions

Optimum nuclear incubation conditions. Figure 6 illustrates the association–time curves for the specific binding of [^{3}H]oestradiol to nuclear extracts derived from prostates of both control and oestradiol treated (0.1 mg/kg; 1 h) guinea-pigs. Although maximum specific binding of [^{3}H]oestradiol was attained earlier at 30 than at 4°C for both control and oestrogen primed animals, the maximum levels of specific binding achieved within each treatment group were similar irrespective of the incubation temperature. The binding at 4°C, however, was more stable. At 30°C the level of specific binding progressively declined when the incubation time was extended beyond 3–4 h. At either incubation temperature, the effect of priming guinea pigs with oestradiol was to increase the maximum level of [^{3}H]oestradiol specifically bound to prostatic nuclear fractions approx. 2-fold.

Finite binding capacity. The binding curves shown in Fig. 7a indicate that the total binding of [^{3}H]oestradiol (0.05–1.2 nM) to guinea-pig prostate nuclear fractions never attained a plateau phase. Correction for nonspecific binding, however, resulted in a typical saturation curve.

Affinity and concentration of binding sites. Scatchard plot analysis (Fig. 7b) of the binding of [^{3}H]oestradiol to 33 prostatic nuclear fractions, indicated a mean (±SD) dissociation constant of 0.16(±0.07) nM. The mean (±SD) number of specific binding sites was 8.0(±3.2) fmol/mg protein.

Effect of oestradiol priming in vivo

Saturation analysis studies revealed that administration of oestradiol (0.1 mg/kg) to sexually mature guinea-pigs, reduced the level of specific oestradiol binding sites in prostatic cytosol fractions by approx. 80% (Fig. 8). The cytosolic value (median; range) 1 h after oestrogen treatment (0.17; 0.06–0.39 pmol/prostate) was significantly lower ($P < 0.005$; Wilcoxon's Sum of Ranks Test) than that measured in control animals (0.79; 0.61–1.11 pmol/prostate). This initial, rapid depletion of cytosolic binding sites was accompanied by a significant ($P < 0.005$) increase in the level of specific [^{3}H]oestradiol binding sites in the nuclear fraction, from 0.06(0.02–0.14) to 0.44(0.27–0.51) pmol/prostate. The cytosolic binding of [^{3}H]oestradiol was still reduced 12 h after priming with oestradiol, but after 24 h, the binding had returned to control levels. The elevated nuclear binding of [^{3}H]oestradiol observed 1 h after administration of oestradiol progressively declined to control levels at 24 h.

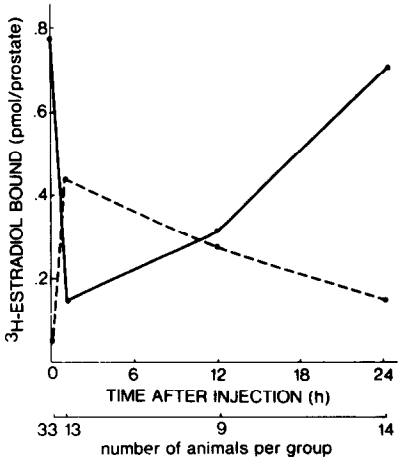

Fig. 8. Effect of oestradiol administration on the distribution of specific oestradiol binding sites in adult guinea-pig prostate cytosol (●——●) and nuclear (●—●) fractions. Prostates were excised at 0 (control), 1, 12 and 24 h after administration of oestradiol (0.1 mg/kg; i.p.). The median specific binding value was plotted for each group of animals.

DISCUSSION

The interaction of steroid hormones with cytosolic receptors in the target cell, nuclear translocation of the receptor–steroid complex, and nuclear binding are generally believed to be integral steps in the mechanism of steroid hormone action [16]. To establish that oestrogen acts in a similar manner in the prostate would suggest that oestrogen may be capable of influencing normal prostatic growth.

The present study has identified saturable, high affinity ($K_d \sim 0.15$ nM), and specific oestradiol binding sites in guinea-pig prostate cytosol fractions. The proteinaceous nature of the binding sites was evident

from the loss of specific [^{3}H]oestradiol binding activity following proteolytic digestion and heat denaturation of prostatic cytosol fractions.

The preceding observations are consistent with the existence of an oestrogen receptor in the guinea-pig prostate, which was originally proposed by Blume and Mawhinney[17] to explain the capacity of the gland to accumulate and retain [^{3}H]oestradiol *in vivo*. In some earlier studies, however, the inability to demonstrate an 8S form of the prostatic oestradiol binding molecule using density gradient ultracentrifugation, was taken to indicate that the prostatic molecule differs from the classical oestrogen receptor [18]. The findings of this study do not support such a conclusion. Ultracentrifugation of [^{3}H]oestradiol labelled prostatic cytosol on low-salt glycerol density gradients, revealed a specific binding component with a sedimentation coefficient of approx. 8S. Similarly, an 8S oestradiol binding molecule has been demonstrated in rat ventral prostate cytosol fractions [19, 20]. Thus, the ability to detect an 8S form of the oestrogen receptor may depend on the particular experimental conditions (e.g. the use of glycerol gradients containing molybdate) employed in different studies.

Saturable, high affinity ($K_d \sim 0.16$ nM) oestradiol binding sites were also identified in salt-extracted guinea pig prostate nuclear fractions. The temporal change in distribution of cytosolic and salt-extractable nuclear oestradiol binding sites following oestrogen administration to sexually mature animals was consistent with translocation of cytosolic oestradiol–receptor complexes into the nucleus. Similar patterns of cytosolic and nuclear binding have been reported for classical oestrogen target tissues in various species following treatment with oestradiol [21, 22]. It is noteworthy, however, that these experimental observations do not prove that translocation occurs *in vivo*. Recently, it has been proposed that steroid receptors are located in the nucleus, with free receptor being found in the cytosol fraction only as a result of tissue disruption [23, 24]. According to this hypothesis, administration of oestradiol to guinea-pigs would result in an apparent nuclear translocation of the prostatic oestrogen receptor, because more oestradiol–receptor complexes would be tightly bound within the nucleus and not released during cell disruption. In any event, increased nuclear binding would be consistent with oestradiol having biological activity in the prostate.

Despite this demonstration of apparent nuclear translocation, the increase in salt-extractable nuclear binding sites accounted for only 61% of the observed reduction in cytosolic binding sites following oestrogen treatment. It is unlikely that this discrepancy in binding site numbers is due to an increase in salt-resistant binding sites in prostatic nuclei of oestrogen treated animals, because inclusion of dithiothreitol in KCl-buffers appears to facilitate extraction of normally salt-resistant steroid-binding sites [25]. A possible, but again unlikely explanation, is that the numbers of cytosolic and nuclear oestradiol binding sites were underestimated in the treated animals due to occupation to these binding sites by exogenous ligand.

Due to the instability of the prostatic oestradiol binding sites at elevated temperatures, it was inappropriate to use conventional oestrogen-receptor exchange assay procedures [22] in the present study. However, the ability to detect similar numbers of oestradiol binding sites in both control and oestrogen presaturated prostatic cytosol fractions using a 20 h incubation at 4°C, suggests that bound oestradiol completely exchanged with added [^{3}H]oestradiol under these incubation conditions. It would appear, therefore, that a real difference exists between the loss of cytosolic oestradiol binding sites and the increase in nuclear binding sites following oestrogen treatment. A similar situation has been demonstrated using both MCF-7 and T47D human breast cancer cells [26, 27]. In those studies, it was found that processing of nuclear bound oestrogen receptor and progesterone receptor occurs within minutes of exposure of the cells to oestradiol and progesterone, respectively. Whether similar, rapid processing of oestrogen receptors also occurs in prostatic nuclei has not been established.

The present study has demonstrated that the guinea-pig prostate contains a specific oestradiol binding protein with characteristics of an oestrogen receptor. In view of the abundance of the prostatic stroma in this species, and the consistent finding that the stroma in male accessory sex tissues is oestrogen sensitive [8], the guinea-pig may be an appropriate experimental animal for further investigating the role of oestrogen in the growth and development of the prostate. This in turn may lead to a better understanding of prostatic disease, and may provide an insight into how abnormal prostatic growth processes may be modified by hormonal means.

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