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INTERACTION BETWEEN LABELED ESTROGENS AND RECEPTORS IN HUMAN UTERINE CYTOSOL

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The composition of the estrogen-binding system in the mammalian uterus remains a matter for debate. There is evidence that uterine cells contain estrogen-binding components of several types [8, 11, 12]. At the same time it has been shown [2-4] that rat uterine cytosol contains a single macromolecular form of estrogen receptor. The results of investigations undertaken in the authors' laboratory [1, 7] demonstrated the homogeneity of the estrogen receptor population in uterine cytosol of guinea pigs, rats, and monkeys.

The aim of this investigation was to assess the composition of the estrogen-receptor system of the human uterus by analysis of data relating to interaction between various labeled estrogens and this system.

EXPERIMENTAL METHODS

Uterine cytosol from postmenopausal women was used as the test object because of the low endogenous estradiol content [9]. The cytosol was obtained as described previously [5]. The ratio of weight of tissue to volume of buffer was 1:4. The following reagents were used. Tritium-labeled estrone, estradiol, ethinylestradiol, and estriol, with specific activity of 88,

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100, 46, and 75 Ci/mmole respectively, were obtained from Amersham International, England and their unlabeled analogs and testosterone from Calbiochem (USA), 10 mM Tris-buffer, pH 7.4 (at 20°C) with 1.5 mM EDTA, and 0.5 and 5% suspensions of Norit A carbon (from Sigma, USA) in buffer with the addition of gelatin. The experimental techniques were published previously [1, 7].

EXPERIMENTAL RESULTS

Analysis of dissociation of complexes of the four labeled estrogens with estrogen-binding sites of human uterine cytosol showed that this process is a first-order reaction. The velocity constant of dissociation of complexes with estrone, estradiol, ethinylestradiol, and estriol were $(0.71 \pm 0.01) \times 10^{-4}$ sec^{-1}, $(0.13 \pm 0.01) \times 10^{-3}$ sec^{-1}, $(0.10 \pm 0.01) \times 10^{-3}$ sec^{-1}, and $(0.12 \pm 0.03) \times 10^{-3}$ sec^{-1}, respectively. Dissociation curves for the test complexes, plotted between semilogarithmic coordinates, were linear ($r = 0.99$, $p < 0.05$). The linearity of the dissociation curves is evidence of homogeneity of the estrogen-binding sites involved in each of the four dissociation reactions.

Determination of concentrations of estrogen receptors for each of the four labeled compounds was carried out simultaneously by the ligand exchange method [10]. It was found that the concentration of receptors in the cytosol for these estrogens did not differ significantly ($p < 0.05$) and its mean value was 1.2 ± 0.2 nM.

It was shown previously that natural and synthetic estrogens compete in human uterine cytosol with estradiol for binding with estrogen receptors, and that the estrogens can be arranged in the following order of decreasing affinity: ethinylestradiol > estradiol > estriol > estrone [6, 9].

The linearity of the dissociation curves, the equal binding capacity of the estrogen-receptor system for the four ligands used, and the ability of estrogens to compete for binding sites on the receptor all suggest that the estrogen receptor population in human uterine cytosol is composed of binding sites of only one type.

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