

The Effects of Flutamide and Diethylstilbestrol Exposure on the Reproductive Organs and Thyroid of Male Rats by the Rodent 20-day Thyroid/Pubertal Assay

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To establish a test protocol for the rodent 20-day thyroid/pubertal assay, flutamide and diethylstilbestrol (DES) were administered to intact male Sprague-Dawley rats from postnatal day 33 for 20 days. Flutamide (1, 5, and 25 mg/kg/day) or DES (10, 20, and 40 ug/kg/day) was given once daily by oral gavage to immature male rats. Prepuce separation was significantly delayed in flutamide group and in DES group. One day after the last dose, the rats were killed and pituitary, thyroid, and reproductive organs were removed and weighed. Flutamide treatment resulted in a significant reduction in the weights of epididymides, ventral prostate, seminal vesicles plus coagulating glands and fluid (SVCGF), levator ani bulbocavernosus muscles (LABC), Cowper's glands, and glans penis. The weight of adrenal glands decreased at 25 mg/kg/day, while testes and any other organ weights were unaffected. No microscopic changes were observed in the thyroid glands. Serum levels of testosterone were significantly increased in the flutamide-treated groups and serum levels of estradiol were also increased. A significant reduction in the weights of testes, epididymides, ventral prostate, SVCGF, LABC, Cowpers glands, and glans penis of DES treated group. Serum testosterone and LH decreased significantly in DES group. Decrease of estradiol was observed, but not significant. These results indicate that flutamide and DES delay puberty in the male rat and its mode of action appears to be via altered secretion of steroids, which subsequently affect the development of the reproductive tract. (Supported by the grant from NITR/Korea FDA for Endocrine Disruptor Research.)