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THE EFFECT OF FLUTAMIDE ON PUBERTY IN MALE RATS: AN EVALUATION OF THE PROTOCOL FOR THE ASSESSMENT OF PUBERTAL DEVELOPMENT AND THYROID FUNCTION

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To establish a test protocol for the rodent 20-day thyroid/pubertal assay, we dosed flutamide(fl), a non-steroidal androgen antagonist to intact male SD rats from postnatal day 33 for 20 days, and examined several reproductive endpoints for assessing the sensitivity of a list of parameters for detecting endocrine-related effects of endocrine-disrupting chemicals. Immature male rats were divided into four groups and administered fl once daily by oral gavages at doses of 0(control), 1, 5, and 25 mg/kg/day. Prepuce separation(PPS) was significantly delayed in fl treated rats(5, 25 mg/kg/day). One day after the last dosing the rats were killed. fl treatment resulted in a significant reduction in the weights of epididymes, ventral prostate, seminal vesicles, levator ani bulbocarvenus muscles, Cowper's glands, and glans penis. Testes and any other organ weights were unaffected. Serum testosterone increased significantly in fl group(5, 25 mg/kg/day) and estradiol in fl(25 mg/kg/day). No differences were observed in thyroxin level between the treatment groups and control. These results indicate that fl delays puberty in the male rat and its mode of action appears to be altering the secretion of steroids and having subsequent effects on the development of the reproductive tract. Thus, this assay can be used as an alternative for screening antiandrogen activities, but the further study is necessary to use as a recommended assay.