

Journal of Andrology, Vol 2, Issue 3 152-161, Copyright © 1981 by [The American Society of Andrology](#)

In Vivo and *In Vitro* Investigation of the Extrapituitary Antireproductive Effects of a Potent LHRH Agonist in Immature and Adult Male Rats

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Co-incubation with a potent LHRH agonist, D-Ala⁶-Des-Gly¹⁰-Pro⁹-NHEt-LHRH (Wy-18,481), did not affect testosterone or progesterone production by adult intact rat testes *in vitro*. Prior administration to adult intact rats *in vivo* (100 µg/rat/day, subcutaneously) reduced subsequent basal and hCG-stimulated testosterone production *in vitro* and dramatically increased progesterone production. Similar chronic administration of the agonist *in vivo* to adult hypophysectomized (hypx) rats also depressed testosterone production *in vitro* but had no effect on that of progesterone. Using dosages which produce marked inhibition of the weights of the testes and of accessory reproductive glands in both immature and adult intact rats, long-term (up to 28 days) treatment with Wy-18,481 slightly potentiated the atrophy of the testes and of the seminal vesicles due to hypophysectomy in the immature rat but had no apparent effect in the hypx adult. Concurrent administration of Wy-18,481 did not affect the support provided to the reproductive organs by dihydrotestosterone replacement in either immature or adult hypx rats. These results suggest that extended exposure is required to elicit direct effects of the agonist on testicular function and that these effects, which involve interference with steroidogenesis and not steroid action, differ qualitatively in the hypx animals from those occurring in the presence of the pituitary. Moreover, there appears to be an age-related difference in sensitivity to the direct effect of the agonist.

Key words: LHRH agonist, extrapituitary reproductive effects, age-dependency, hypophysectomy, testicular function *in vitro* and *in vivo*, dihydrotestosterone, male contraception

Submitted on September 3, 1980

Revised on October 28, 1980

Accepted on November 10, 1980

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