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## JOURNAL ARTICLE

# The contraceptive effects of etoprine on male mice and rats

N. S. Malik, S. A. Matlin, J. Fried, R. E. Pakyz and M. J. Consentino

Department of Biology, Millersville University, Pennsylvania 17551, USA.

We had previously found that 2,4-diaminopyrimidines affected spermatogenesis, possibly through the inhibition of testicular dihydrofolate reductase (DHFR). The current study examined the effects of etoprine, a highly lipophilic 2,4-diaminopyrimidine that is also a potent DHFR inhibitor, on the fertility of male mice at various dosages (0.1-50 mg/kg/day) for 55 days and male rats at 5 mg/kg/day for 65 days. Two other substituted diaminopyrimidines were tested at dosages of 50 mg/kg/day for 55 days. Results of breeding trials along with assessment of various parameters indicative of male fertility were noted. We found that of the compounds tested, etoprine is a potent antifertility agent that causes complete infertility at doses of  $\geq 5$  mg/kg/day in mice with a threshold of effectiveness occurring between 1 and 5 mg/kg/day. The antifertility action of etoprine may be related to its capacity to inhibit testicular DHFR and its high degree of lipophilicity.

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