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JOURNAL ARTICLE

Posttesticular antifertility action of triptolide in the male rat: evidence for severe impairment of cauda epididymal sperm ultrastructure

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A variety of active diterpene epoxides, including the triptolide (isolated from Tripterygium wilfordii) have been reported to cause infertility in male rats. Previously, we showed that oral administration of triptolide at a dosage of 100 microg/kg per body weight for 70 days completely inhibited fertility in male rats, with little or no demonstrable detrimental effect on spermatogenesis and Leydig cell function as determined by testicular light microscopic appearance and serum and intratesticular testosterone levels. Despite the apparent absence of effects on the testes, cauda epididymal sperm were abnormal, with complete cessation of sperm motility and some reduction in sperm numbers. This study was undertaken to provide additional insight into the subcellular sites and possible mechanisms of action of this compound using ultrastructural analysis of the testes and epididymidis. The most striking effect of triptolide treatment was observed in sperm in the epididymis. In rats rendered infertile with 100 microg/kg per body weight of triptolide daily for 70 days, virtually all cauda epididymal sperm exhibited complete absence of plasma membrane over the entire middle and principal piece, premature decondensation of the nuclei, and disorganization of the mitochondrial sheath with many vacuolated mitochondria. No ultrastructural differences in the epididymal epithelium were observed between control and triptolide-treated rats. The testes appeared to be mildly affected after triptolide treatment but exhibited only subtle ultrastructural defects in the germ cells. The findings of severe impairment of cauda epididymal sperm ultrastructure, along with minimal discernible abnormalities in the fine structural cytology of the testes, further suggest that the site of action of this compound is posttesticular and may be confined to the cauda epididymal sperm. However, we cannot rule out an effect of triptolide that occurs during germ cell maturation but is delayed in its manifestation or triggered at the rete testis and epididymal level.

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