

INFLUENCE OF FERUTININ ON SEXUAL BEHAVIOR OF FEMALE RATS

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Ferutinin is a daucane sesquiterpene ester from *Ferula hermonis*, a perennial herbal plant native of Lebanon. Recently we found an impairment in sexual activity of ovariectomized hormone-primed female rats following acute (30 and 60 mg/kg) or subchronic (1 and 10 mg/kg/day) oral administration of *F. hermonis* root extract [1]. In a following study we observed a reduced sexual receptivity in hormone-primed female rats acutely treated with ferutinin (2.5 mg/kg), thus demonstrating the crucial role of this compound in the negative effect of the plant extract on female sexual behavior [2]. The present experiments were designed to investigate the effect of the chronic administration of ferutinin on sexual behavior of ovariectomized hormone-primed and non hormone-primed female rats. Four groups of Sprague-Dawley female rats were ovariectomized and then submitted to the following treatments for four weeks: 1) vehicle (Tween 80 and water); 2) estradiol benzoate (EB) 1.5 µg/rat subcutaneously (s.c.) twice a week; 3) ferutinin 0.5 mg/kg/day by oral gavage; 4) ferutinin (0.5 mg/kg/day) combined with EB (1.5 µg/rat, twice a week). All animals were treated with progesterone (P) s.c., four hours before the test. Starting from the second week of treatment, receptivity (lordosis response to male stimulation) and proceptivity (hop/darts and ear wiggings) were evaluated once a week. One way analysis of variance (ANOVA) and Newman-Keuls post-test were used for statistical analysis of the data. After 14 days of treatment, a significant ($P<0.001$) increase in lordosis response was observed in EB treated rats ($LQ=77.3\pm4.7$) as well as in ferutinin treated animals ($LQ=56.4\pm8.7$), in comparison to vehicle group ($LQ=0.0\pm0.0$). On the other hand, in ferutinin combined with EB treated rats an increasing reduction in LQ in comparison with EB treated rats was clearly evident, starting from the 2nd week of treatment. The proceptive behaviors were significant and time-dependently enhanced by EB treatment, while not influenced by ferutinin alone. In ferutinin combined with EB treated rats proceptive behaviors were significantly reduced in comparison with EB treated rats. A Western blot analysis on hypothalamic extracts showed an increase in the expression of ER α receptors after the treatment with ferutinin in non hormone-primed rats, in comparison to the vehicle group. In ferutinin combined with EB treated rats, ER α expression was reduced in comparison with EB treated rats. The present results suggest a different effect of ferutinin on sexual behaviour of female rats depending on the absence or presence of estrogens in ovariectomized rats.

[1] Zanolli P., Zavatti M., Rivasi M. and Baraldi M. (2005) *Physiol Behav* 86: 69-74.

[2] Zavatti M., Montanari C. and Zanolli P. (2006) *Physiol Behav* 89: 656-661.