The Effects of D-6-Methyl-8-[β-isopropylaminoethyl] ergoline-I on the Lactation in Nursing Rats

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Summary. D-6-Methyl-8-[β-isopropylaminoethyl] ergoline-I [VÚFB-10726], beginning from the dose of 0.05 mg/kg p.o., suppresses lactation through the inhibition of prolactin secretion in nursing rats.

Suppression of lactation after administration of certain ergoline derivatives have already been reported[2]. Another compound of this type is the compound VÚFB-10726, D-6-methyl-8-[β-isopropylaminoethyl] ergoline-I *bis*- [hydrogen maleate][3]. In female rats, after unilateral ovarectomy, it enhances the secretion of total hypophyseal gonadotropins; it possesses a moderate antiserotonin activity[4] and lowers the blood pressure. In an acute toxicity test with oral administration to S-strain mice (bred at the Institute's farm Rosice), the LD_{50} was found to be 108 mg/kg (confidence limits 98–120 mg/kg).

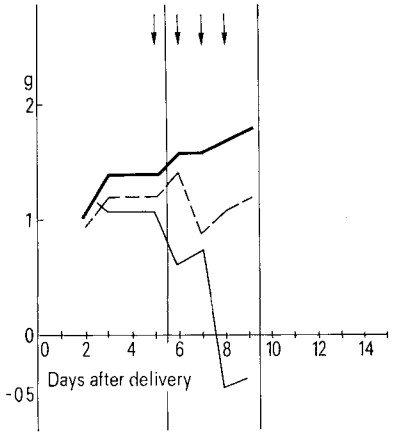

Fig. 1. Effects of VÚFB-10726 alone and combined with Luteotropin Spofa on body-weight gain in suckling rats.
———, Control; ———, VÚFB-10726 0,5 mg/kg p. o. daily per nursing mother rat; ·····, VÚFB-10726 0,5 mg/kg p.o. plus Luteotropin Spofa, 5 mg i. m. daily per nursing mother rat; ↓, days of administration.

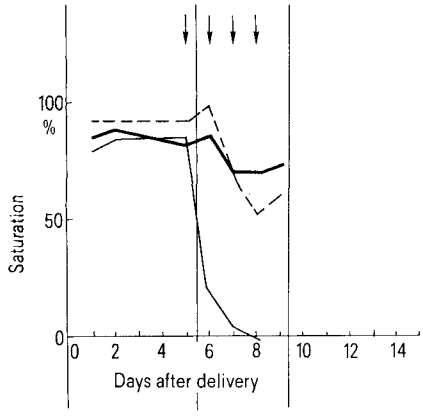

Fig. 2. Effects of VÚFB-10726 alone and combined with Luteotropin Spofa on presence of 'milk spots' in suckling rats, expressed in per cent saturation.
———, Control; ———, VÚFB-10726 0,5 mg/kg p.o. daily per nursing mother rat; ·····, VÚFB-10726 0,5 mg/kg p.o. plus Luteotropin Spofa, 5 mg i.m. daily per nursing mother rat; ↓, days of administration.

We have investigated the effects of the compound on lactation. The antilactation activity was studied by a routine method in primiparous rats (Wistar, 220–250 g, 6 young with each mother); criteria of lactation were the mean daily body weight gains of the suckling young and the presence of milk in their stomachs, detected in the form of so-called milk spots[5,6]. The compounds was administered by stomach tube in aqueous solution, in doses between 0.01 and 1 mg/kg/5ml active base. The medium effective doses were calculated for both criteria. The dependence of the antilactation effect on the inhibition of prolactin was probed by concurrent administration of the compound (0.5 mg/kg/5 ml p.o.) and prolactin (Luteotropin Spofa, from bovine hypophyses, 5 mg i.m. per rat per day).

An antilactation effect of the preparation was detectable from a daily dose of 0.05 mg/kg upwards. Doses of 0.5 and 1 mg/kg completely stopped lactation; in the females whose young did survive starvation, this effect was reversible after drug withdrawal. The medium effective dose, ED_{50}, reducing the mean values of the daily bodyweight gain of the offspring to 50% of the initial value, was 0.15 mg/kg (95% confidence limits 0.10 to 0.24 mg/kg). The ED_{50} reducing the presence of 'milk spots' to 50% was 0.06 mg/kg (0.02 to 0.10 mg/kg). Exogenous supply of prolactin prevented the antilactation effect of the compound (Figures 1 and 2).

The described antilactation activity of the compound VÚFB-10726, as evident from the results of our experiments, is directly connected with the inhibition of prolactin production as shown in experiments conducted by KREJČÍ et al.[7].

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