The present study shows that intraperitoneal administration of (+)-INPEA sensitizes the uterine tissue to the action of oxytocin and prostaglandins. This potentiating effect of (+)-INPEA is of interest in view of the therapeutic application of oxytocin and prostaglandins in the induction of labour and in the termination of pregnancy. The doses at which these agents are usually effective, often produce severe, and at times intolerable, side effects. It may allow the use of smaller doses of prostaglandins and oxytocin for induction of abortion and labour, thus limiting their side effects. Further work to evaluate its therapeutic effectiveness and the mechanism of the potentiation is in progress.

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Anti-oestrogenic activity in compounds related to ethamoxytriphetol (MER 25), clomiphene and MRL 37

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α-[4-(β-Diethylaminoethoxy)-3,4-xylyl]-α-phenyl-β-4-methoxyphenylethanol (P642), α'-[4-(β-diethylaminoethoxy)-3,5-xylyl]-4-methoxystilbene (P781), and the α-bromo-, and di-hydro-derivatives of the latter compound (P778 and P707 respectively) are analogues of ethamoxytriphetol, clomiphene and MRL 37 possessing two methyl groups ortho to the aminoethoxy side chains. They have been examined for oestrogenic and anti-oestrogenic activity using the Allen-Doisy and uterine weight tests.

In the latter test using immature mice, P778 and P781 were partial agonists showing maximal responses of 85% and 60% of that obtainable with 17β-oestradiol (0·16 μg) in total doses of 2·0 mg and 8 0 mg respectively administered s.c. in arachis oil. P642 was neither oestrogenic nor anti-oestrogenic in doses up to 4 mg s.c. but 2 mg of either P707 or P781 suppressed the uterine response to 0·06 μg of 17β-oestradiol ($P<0.001$), when hormone and antagonist were administered together (s.c.) in the same solution. When administered subcutaneously with 0·03 μg 17β-oestradiol, sub-oestrogenic doses of P778 (0·1–0·2 mg) significantly increased the uterine response.

In contrast to these results, when using the Allen-Doisy test on ovariectomized mice, P778 and P781 (2 mg s.c.; or respectively 8·0 and 4·0 μg intravaginally) were non-oestrogenic. Furthermore P707 and P781 (2 mg s.c.; or respectively 32·0 and 8·0 μg intravaginally) did not inhibit the vaginal cornification response produced by concomitantly administered 17β-oestradiol (0·03 and 0·06 μg s.c.; 2×10^{-4} and 8×10^{-4} μg intravaginally).

It appears that the different results obtained in the two test systems are unlikely to be due to differences in the uptake of P707 by the uterus and vagina, or to the suppression by P707 of the uptake of 17β-oestradiol. This was demonstrated in ovariectomized mice by determining the levels of radioactivity in skeletal muscle, blood, liver, pituitary gland, cerebral cortex, uterus and vagina at various times up to 24 h following the administration of tritium labelled P707 (0·5 mg s.c. in 0·05 ml arachis oil; specific activity 20 μC/mg) and at varying times up to 4 h following the administration of unlabelled P707 (2 mg) together with 6,7-T-17β-oestradiol (0 01 μg s.c. in arachis oil; specific activity 147 μC/mg). Assuming negligible metabolism of the labelled compounds, significantly higher levels of P707, when compared with those in skeletal muscle, were found in vagina (6–24 h) and uterus (8–24 h) but at no time were the levels in these tissues significantly different from one another. No suppression by P707 of the uptake of tritiated 17β-oestradiol was observed in any of the tissues examined.