dermally with 10 mg ovalbumin (O.A.) in Freund's complete adjuvant, and three weeks later challenging the animals intra-articularly with O.A. We have found the optimal challenge dose to be 5 mg O.A., 10 mg O.A. caused widespread deaths due to systemic anaphylaxis, while 100 μg O.A. was insufficient to produce a marked response. With this method of sensitization we have produced chronic, progressive arthritis which is characterized by synovial effusion, synovial hyperplasia, pannus formation, plasma cell infiltration, follicular lymphocyte aggregation and bone and cartilage erosions.

Monoarticular arthritis in rabbits is strain and age dependent. Old English rabbits (O.E.) gave a better response than New Zealand White (NZW) rabbits, which in turn were superior to Dutch rabbits. In addition, thirteen week-old rabbits gave a better response than nine week-old rabbits.

Cell-free synovial fluid from arthritic rabbits has been examined for the presence of prostaglandins (PG). The fluid was superfused in Krebs solution over isolated rat fundic strip and rat colon preparations. The tissues were blocked by a combination of atropine, phentolamine, methysergide and mepyramine (all 10^{-7} g/ml) and propranolol (2×10^{-6} g/ml). Prostaglandin-like activity was assayed as PGE_1 or PGE_2. In preliminary experiments in two NZW rabbits, 60–80 ng PG-like substance was found in the synovial sac of one rabbit killed 18 h post challenge and 15–18 ng PG-like substance was found in one rabbit killed 7 days post challenge. However, PG-like activity could not be detected in 8 out of 9 O.E. rabbits killed 8 weeks after challenge. The remaining rabbit from this group contained 30 ng PG-like substance. This animal also showed the highest polymorph infiltration of the group.

Similar levels of PG to those found at 18 h in monoarticular arthritis have been found by Eakins, Whitelocke, Perkins, Bennett & Unger (1972) in their study of acute immunogenic uveitis in the rabbit. Results of further investigations into the presence and importance of PG in rabbit monoarticular arthritis will be presented at the meeting.

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Effect of intraperitoneal administration of (+)-INPEA on oxytocin and prostaglandin evoked responses of the isolated rat uterus

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The effect of optical isomers of INPEA (N-isopropyl-p-nitrophenyl ethanolamine hydrochloride) on oxytocin-evoked (Saini & Sharma, 1971) and on prostaglandin-evoked (Rao & Sharma, 1972) responses of isolated rat uterus has been reported (−)-INPEA exhibited a weak antioxytocin activity but had no effect on prostaglandin-evoked responses. In contrast, (+)-INPEA potentiated the action of oxytocin and prostaglandins when added to the bath fluid at a concentration of 1×10^{-5} g/ml. In the present investigation, the effect of intraperitoneal administration of (+)-INPEA on prostaglandin (PGE_1, PGE_2, $PGF_2\alpha$) and oxytocin-evoked responses was studied on the same preparation.

Uterine strips from (+)-INPEA treated rats (10 mg/kg body weight I.P., one hour before the start of experiment) were suspended in an organ bath (10 ml) containing aerated de Jalon's solution at 29° C and equilibrated for a period of 30 min. Responses were recorded to the graded doses of each of the agonists (oxytocin, PGE_1, PGE_2 and $PGF_2\alpha$) on a potentiometric recorder. Seven experiments were performed with each drug. In all the experiments there was marked increase in the amplitude of oxytocin and prostaglandin (PGE_1, PGE_2 and $PGF_2\alpha$) evoked responses when compared to controls.

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.