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Relaxing potency of terbutaline and orciprenaline on rat uterus

The inhibitory effects of the selective β-receptor stimulating agent terbutaline (Persson & Olsson, 1970) and of orciprenaline have been compared on carbachol-induced contractions in the rat isolated uterus.

Female rats, Sprague-Dawley, 130–150 g, had 0·2 μg 17-β-oestradiole benzoate subcutaneously 24 h before being killed by a blow on the head and bled. The middle part of each uterus horn, of about 2 cm length, was put in an organ bath (25 ml) containing calcium-poor Locke solution (45 g NaCl, 2·1 g KCl, 0·3 g $CaCl_2$, 2·5 g $NaHCO_3$, 2·5 g glucose in 5 litre of glass-redistilled water) at 25° and gassed with 5% carbon dioxide in oxygen. Isometric tension changes were recorded. Dose-response measurements of carbachol-induced contractions, and a dose of carbachol (1·0–4·0 μg/ml) corresponding to about 80% of maximum contraction was then selected for use in the test of inhibitory activity of both drugs. These were administered at 0·008–0·8 μg/ml 90 s before carbachol. The decrease of carbachol-induced contraction was recorded. The dose of carbachol was then given every 8 min until a stable response again was obtained and the next β-adrenoceptor effect was evaluated.

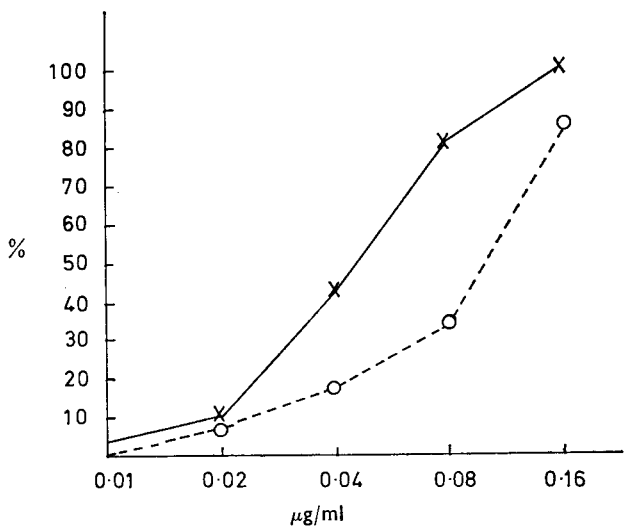

FIG. 1. The inhibition (%) of carbachol-induced contractions by different doses of terbutaline (×) and orciprenaline (○).

The effect of the β-adrenoceptor blocking agent propranolol (0·1 μg/ml) was determined by administering it to the bath 20 min before terbutaline or orciprenaline. The amounts of drugs are expressed as the bases.

Twelve preparations from nine rats were used for the calculation of relaxing potency (ED50) of terbutaline and orciprenaline [terbutaline = 1·9 ($\pm$0·1 s.d.) $\times$ orciprenaline]. Slightly more than half the total number of preparations were discarded because of variation in the response to carbachol, or too much spontaneous activity, or because less than three dose-levels of the β-adrenoceptor stimulating compounds were evaluated.

Propranolol completely prevented the effect of both drugs given in doses that otherwise produced (60–80%) inhibition of the carbachol-induced contractions. A typical dose-response curve of the effects on the same preparation is shown in Fig. 1.

Terbutaline is seen to be about twice as potent as orciprenaline in relaxing the rat uterus. This ratio is similar to that found in the lung for the two compounds by Persson & Olsson (1970) who also reported orciprenaline to be more active than terbutaline on the heart (inotropic and chronotropic activity). The finding that terbutaline is more potent than orciprenaline on uterus is not surprising since Lands, Ludena & Buzzo (1967) have characterized the β-adrenoceptors in uterus to be of the same type (β_2-receptors) as in the lung and differing from the β-adrenoceptors in the heart (β_1-receptors).

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α-Methyltryptophan increases 5-hydroxytryptamine-like material in rat brain

Previous reports from this laboratory (Sourkes, Missala & Papeschi, 1969; Sourkes, Missala & Oravec, 1970) indicated that α-methyltryptophan (AMTP) induced a decrease of tryptophan, 5-hydroxytryptamine (5-HT) and 5-hydroxyindoleacetic acid (5-HIAA) concentrations in the brain of rats. Because AMTP had been found to increase tryptophan pyrrolase activity in the liver (Sourkes & Townsend, 1955), the hypothesis was put forward that the effect on brain 5-HT was mediated by an increased flow of tryptophan in the kynurenine pathway with consequent decreased availability of substrate for 5-HT synthesis. However, the decrease of the material estimated as 5-HT after administration of AMTP was not dose-dependent; AMTP itself may also be converted to α-methyl-5-HT (AM-5-HT) in the brain, as has been reported for α-methyl-5-hydroxytryptophan (Lahti & Platz, 1969). For these reasons we re-investigated the problem by using a different method to estimate 5-HT and 5-HIAA.

Previously 5-HT was estimated according to Snyder, Axelrod & Zweig (1965) (butanol extraction-ninhydrin condensation) and 5-HIAA by the method of Giacalone & Valzelli (1966) (butyl acetate extraction-3N HCl fluorescence). I have now compared the results obtained with these methods with results obtained by the method of Ahtee, Sharman & Vogt (1970), which is based on the sequential separation of 5-HT and 5-HIAA from the same sample by column chromatography on Amberlite CG-50, type I, and Sephadex G-10. The fluorescence in 3N HCl of both compounds was read in an Aminco-Bowman spectrophotofluorometer (excitation: 295 nm;