Isoprenaline stimulates α-adrenoceptors in bovine pulmonary blood vessels

Some interest has centred recently on the cardio-respiratory pharmacology of ruminants (Eyre 1969, 1970; Alexander, Eyre & others 1967, 1970: Aitken & Sanford 1969, 1970). It seems certain that the lung is an important anaphylactic shock organ of cattle, and in addition to the liberation of histamine (Eyre, 1971a) and 5-HT (Eyre: unpublished observations), dopamine is liberated from mast cells which may also participate in the pulmonary anaphylactic responses of this species (Eyre, 1971b). It was thus necessary to study adrenergic mechanisms in the bovine pulmonary musculature as part of a wider investigation.

Pulmonary artery, vein and bronchus were removed from the lungs of cattle 20 to 60 min after slaughter. Blood vessels were cut spirally and bronchi cut into rings before mounting in the usual way at 35° in a bath of 20 ml Krebs-Henseleit (1932) solution, gassed with 5% carbon dioxide in oxygen.

The blood vessel strips contracted to (ng/ml as base) histamine 50, 5-HT 2, acetylcholine 20, noradrenaline 100, phenylephrine and dopamine 500. Isoprenaline (5–50 ng/ml) relaxed the muscle preparations which were partially contracted in the presence of histamine, 5-HT or acetylcholine and this relaxant effect of isoprenaline was inhibited by the β-adrenoceptor blocking agent propranolol (100–200 ng/ml). Concentrations of isoprenaline $>1{\cdot}0$ μg/ml contracted the pulmonary artery and vein strips in the presence of propranolol 100 ng/ml. This contractile response of isoprenaline was abolished by the α-adrenoceptor blocking agent phentolamine (200–500 ng/ml).

The bronchial muscle contracted to histamine, 5-HT and acetylcholine whereas isoprenaline and dopamine caused relaxation. Noradrenaline and phenylephrine failed to elicit any response in bronchial muscle. The relaxant action of dopamine and isoprenaline was inhibited by propranolol (200 ng/ml). However, increasing concentrations of dopamine or isoprenaline, up to 50 μg/ml failed to contract the bronchial musculature.

It would appear that bovine pulmonary artery and vein possess both α- and β-adrenoceptors and that in the presence of propanolol, isoprenaline has an affinity for α-receptors which is comparable with that of noradrenaline or phenylephrine. Flacke, Osgood & Bendixen (1970) described a weak α action of isoprenaline on peripheral resistance in the dog. It may be that α effects of so called β-adrenergic agents have not been fully recognized.

Isoprenaline showed no tendency to constrict bovine bronchial muscle. Indeed neither noradrenaline nor phenylephrine had any action on the bronchial strip and it may be that the bovine airway musculature is devoid of α-adrenoceptors in contrast to such species as guinea-pig, rat, rabbit, cat (Fleisch, Maling & Brodie, 1970).

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A study of aqueous systems of purified non-ionic surfactant by membrane osmometry

The application of the membrane osmometry to the determination of number average micellar molecular weights ($\bar{M}_n$) has been reported by Coll (1969, 1970) and Attwood, Elworthy & Kayne (1969, 1970). We report the value of $\bar{M}_n$ of a purified sample of a non-ionic surfactant of pharmaceutical interest, polysorbate 80 and show that the effect of solubilizing nitrofurazone in micelles can be studied by membrane osmometry. Further, osmotic pressure measurements on the purified sample are compared with the commercial sample as well as a sample containing a known amount of polyoxyethylene glycol 600 (PEG 600).

A commercial sample of polysorbate 80 (polyoxyethylene-20-sorbitan monooleate) B.P.C. was purified by partitioning between 5N sodium chloride solution and ethyl acetate (Weibull, 1960). Samples were dried under passage of indifferent gas for 2 h at 30°/15 mm Hg followed by 1 h at 30°/3 mm Hg. Precipitated salts were filtered off through a sintered glass filter (G 3). Removal of contaminating substances was followed by thin-layer chromatography (Thakkar, Kuhn & Hall, 1967; Cerdas, Carlier & others, 1968). The extraction procedure removed polyoxyethylene glycols or polyoxyethylated sorbitans (or both). The saponification values for the purified and non-purified polysorbate 80 were 61·1 and 48·8 respectively; the hydroxyl values were 54·6 and 74·0 respectively. The critical micelle concentration (cmc) for the purified polysorbate 80 at 25° was found by the method of Becher (1962) to be 0·11 g/litre (extrapolated value). Nitrofurazone B.P.C. was found to be solubilized to an extent of $2{\cdot}32 \times 10^{-5}$ mol/g surfactant by purified polysorbate 80 aqueous solutions at 25·0° (±0·05°).

A Melabs CSM-2 recording membrane osmometer was used in these measurements at 25·0° (±0·1°). A cellulose membrane (prepared by drying a film from a 25% solution of cellulose acetate in acetone + dimethylformamide and treating the film for about 5 min in 70° water) was used for all the measurements. The molecular weight of a protein, cytochrome-C (mol. wt. 13 400), was found from the osmometer to be 15 000, thus showing that the membrane was non-permeable to molecules larger than 15 000. The accuracy of osmometer was ±0·1 cm of solvent.

In all experiments, solutions of concentration much larger than the cmc were placed on the solution side, and the solvent side was filled with a solution of 1 g/litre (several times the cmc). The number of monomers in equilibrium with micelles in the above solutions does not significantly increase with concentration (i.e. over the cmc). Hence the osmotic pressure arising from the monomers will be expected to be negligible. Since the membrane was found to be non-permeable to molecules of weight over 15 000, we did not consider any possibility of micelle diffusion ($\bar{M}_n \gg$