UPTAKE OF AMPHETAMINE BY GUINEA-PIG LUNG IN VITRO

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Several basic drugs that exist as cations at physiological pH have been found to be concentrated in lung tissue after parenteral administration (Brandenberger-Brown, 1974). For such compounds, the lung may have an important regulatory role in relation to their plasma levels. There is evidence that the uptake of some of these drugs into the lung e.g. propranolol (Dollery & Junod, 1976) involves a saturable transport mechanism. Amphetamine has been shown to be concentrated in the lung in several species (Axelrod, 1954) and the present work describes the uptake of D-^{14}C-methylene amphetamine into guinea-pig lung in vitro.

Lung slices (30mg) were incubated with shaking at 37°C in Krebs-Ringer-Phosphate-Glucose pH 7.4 (3ml) containing labelled amphetamine. Uptake was assessed as a tissue-to-medium (T/M) concentration ratio [tissue concn. (μmol g^{-1}) ÷ medium concentration (μmol ml^{-1}) of amphetamine]. The time-course of uptake of amphetamine (1μM) was characterized by a rapid increase in T/M ratio up to 30 min. Between 30 and 90 min of incubation, the T/M increased more slowly. When the concentration of amphetamine in the medium was varied from 0.5-10.0μM, the T/M, for a 30 min incubation, decreased rapidly (from 19.9 to 6.2) suggesting saturation of a transport process. The T/M for amphetamine (1μM, 30 min incubation) was temperature-dependent and pH-sensitive, optimal values being 37°C and pH 7.4. Uptake of amphetamine (1μM) was markedly reduced by the presence in the medium of guanethidine, imipramine and KCN (all at 1μM) and by replacing Na^+ with Li^+ in the medium. The inhibitory effects of these drugs were probably exerted on a transport process because the compounds did not alter the binding of amphetamine (1μM) to homogenates of the lung. The degree of binding (88%) of amphetamine (1μM) to lung homogerates was similar to that found for guinea pig plasma (at equivalent protein concns). Thus this binding cannot be a major factor contributing to the concentration of amphetamine in lung. By means of the ^{14}C-dimethyloxazolidine dione method (Irvine & others, 1960), the apparent intracellular pH (6.3) of the guinea-pig lung was determined. The pH of guinea-pig plasma was 7.25. This pH gradient would not significantly affect the ionization of amphetamine (pKa 9.8) in the intracellular and extracellular compartments and therefore is unlikely to contribute to the uptake phenomenon.

It is concluded that an active carrier-mediated transport process is largely responsible for the relatively high concentration of amphetamine found in lung tissue.

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