

an inhibition of the re-uptake. This effect of ergot alkaloids, little known to date, might be significant for the pharmacological characterization of these substances.

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Removal of 5-hydroxytryptamine by rat isolated lung.

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5-Hydroxytryptamine (5-HT) is removed from the circulation by the lung (Axelrod & Inscoe, 1963; Gaddum, Hebb, Silver & Swan, 1953; Thomas & Vane, 1967). The isolated lungs of rat and guinea-pig perfused with Krebs solution will also remove 5-HT; we have studied this removal using the rat isolated lung.

Rats were anaesthetized with pentobarbitone and the pulmonary artery and trachea cannulated. The lungs were then dissected free, inflated and perfused via the pulmonary artery with oxygenated Krebs solution maintained at 37°C. The lung perfusate was superfused over rat stomach strips (Vane, 1957) to estimate the 5-HT present. The amount of 5-HT removed by the lungs was determined by comparing the responses of the rat stomach strip to infusions of 5-HT made directly to the assay tissues with those to infusions of 5-HT made into the pulmonary arterial cannula. Rat lungs removed 90–98% of the 5-HT passing through them, and this degree of removal was maintained when the infusions (3–5 min long) were repeated up to 4 times. The pressure in the pulmonary artery cannula averaged 10 mm Hg and during infusion of 5-HT (10–40 ng/ml) the pressure changes were minimal.

When amitriptyline (10^{-6} – 10^{-5} M) or desmethylinipramine (10^{-5} M) were infused into the lungs for 5 min before and during the infusion of 5-HT, more 5-HT (20–50%) appeared in the lung perfusate than under control conditions (2–10%). Reserpine had no effect on the disappearance of 5-HT in rat lung either when the rats were pretreated (2 mg/kg intraperitoneally 48 and 24 hr before use) or when it was infused concomitantly (10^{-5} M) with 5-HT. The monoamine oxidase inhibitors, mebanazine (10^{-5} M) and iproniazid (10^{-4} M) did not increase the peak of the contractions of the rat stomach strip which occurred during infusions of 5-HT into the lungs, but the contractions persisted for 40–50 min compared with 6–9 min during infusions into untreated lungs. All these contractions were antagonized by methysergide (10 ng/ml), suggesting that the prolonged contraction was due to 5-HT reappearing in the perfusate after the initial removal into some structure in the lungs. These two monoamine oxidase inhibitors do not affect uptake of catecholamines by rat heart (Iversen, 1965).

When tranylcypromine (10^{-6} – 10^{-5} M), a monoamine oxidase inhibitor that does block uptake, was used, both inhibition of removal of 5-HT by the lung and prolongation of the contractions of the rat stomach strips were seen.

These experiments were repeated using ^3H -5-HT and the total radioactivity, ^3H -5-HT and ^3H -metabolites appearing in the perfusate determined. There was good correlation between the amounts of biologically-active 5-HT and radioactive 5-HT in the perfusate.

We conclude that the infused 5-HT is not taken up and stored in the lungs in structures analogous to the granules in platelets or rat mast cells, because 5-HT in these storage sites is protected from enzymic inactivation. However, the initial uptake process does show similarities to amine uptake in platelets or nerve endings in that it is inhibited by amitriptyline, desmethylinipramine or tranylcypromine.

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Intracellular enzymes in local lymph after chemical¹ injury.

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It was shown earlier in cats (Lewis, 1967) and rabbits (Lewis, 1969) that after thermal injury the extent of cellular damage could be assessed by estimation of the increase in concentrations of various intracellular enzymes escaping from the injured tissue into the local lymph.

The purpose of the present investigation was to determine if the effects of chemical injury could be assessed in the same way. Dimethyl sulphoxide (DMSO) and croton oil were selected to produce mild and strong tissue injuries respectively.

Cats and rabbits were anaesthetized with pentobarbitone sodium (40 mg/kg) and lymph was collected via a polythene cannula inserted into the main femoral lymphatic as described by Lewis & Westcott (1968). After collecting a control sample of lymph, six subcutaneous injections of 0.2 ml DMSO or croton oil undiluted or diluted with corn oil were made at different sites in the hind leg. Lymph was collected continuously for a further 4–6 hr.

The concentrations in the lymph and plasma of protein potassium and six enzymes representing different intracellular compartments were estimated. The methods used were those quoted in the earlier papers and the enzyme localization was after Hess (1963).