THE ADSORPTION OF EMEPRONIUM BROMIDE BY EVERTED SACS OF RAT SMALL INTESTINE

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Physical adsorption of drug molecules at the intestinal mucosal surface as a limiting factor in their passage across the intestinal epithelial barrier has been supported by the work of Kakemi et al (1969(a), 1969(b)). Irwin et al (1969), studying the absorption of isopropamide iodide concluded that the addition of the trichloracetate anion produced an ion pair with the cation of the quaternary ammonium drug compound and this significantly promoted its pharmacological response after oral administration. The present investigation studied the adsorption by everted sacs (Kakemi et al 1969(a)) of the quaternary ammonium compound emepronium bromide and the influence of an excess of trichloracetic acid.

The adsorption of emepronium bromide from 0.015% $^{w}/_{v}$ solution at 37^{o} by everted sacs of rat intestine was measured at five different pH levels, four replicate determinations being performed at each pH. This was repeated in the presence of 0.068% $^{w}/_{v}$ trichloracetic acid which, because the solutions were buffered and the low concentration was considered to be a non-protein precipitant. Assay of the emepronium bromide was by spectrophotometric analysis at 420 nm of the bromothymol blue complex extract in chloroform (Schill & Marsh 1963). A calibration curve was determined with each experiment; the trichloracetic acid was found not to interfere with the assay.

The adsorption both in the presence and absence of trichloracetic acid showed a peak at pH 7 but the amounts adsorbed were lower in the presence of the acid; also in the absence of the trichloracetate minimum adsorption occurred at pH 9.0 whereas in its presence the minimum was at pH 4.0 (Table 1).

Table 1. Emepronium bromide (EMB) adsorption by everted sacs of rat small intestine in the presence and absence of trichloracetic acid (TCA) at different pH levels

	Mean % of original EMB adsorbed per G of wet weight tissue	
pH	EMB alone	EMB with 10x excess TCA
4	22.17	6.59
6	25.17	8.92
7	27.88	18.74
8	21.48	15.59
9	18.63	13.30

Sundwall et al (1973) have reported that 2.5-5.0% of an oral dose of emepronium bromide is absorbed in humans; since the drug is a quaternary ammonium compound and therefore fully ionised in the intestinal environment, a mechanism of absorption other than simple diffusion is suggested. If the absorption across the intestinal barrier is limited by the adsorption on the mucosal surface then the extent of the adsorption should mirror the amount of drug passing across the barrier; the results presented here would indicate a peak absorption at pH 7. If the TCA forms ion pairs with the emepronium bromide and has no direct effect on the mucosal adsorbing surface, then the lower adsorption in the presence of TCA might indicate an inhibition of drug transfer and not promotion contrary to the findings of Irwin et al (1969). Further work is necessary on the passage of drug across the everted sac wall to attempt a correlation with adsorption to the mucosal surface.

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