THE INFLUENCE OF SOME WEAK ELECTROLYTES ON TRANSMURAL POTENTIALS IN RAT SMALL INTESTINE

J.H. Collett*, H.J. Cox* and R.C. Small**, Departments of Pharmacy* and Pharmacology**, University of Manchester, Manchester, M13 9PL, U.K.

It is known that there are relationships between transmural ion fluxes and electrical measurements across the wall of the gastro-intestinal tract. Three bioelectrical parameters can be measured to characterize these electrical properties:- transmural potential difference (p.d.), short circuit current and conductance. There are reports in the literature that changes in transmural p.d. in everted rat intestine in vitro can be induced using concentrations of compounds not normally measurable by standard analytical measurements (Hardcastle and others, 1978). In this work we have measured changes of transmural p.d. when solutions of weak electrolytes were placed in the luminal fluid of everted rat jejunum.

The experimental procedure was based on that reported by Barry and Eggenton (1972). An everted segment of rat intestine bathed in Krebs buffer at 37° was gassed throughout the experiment with 95% $0_2/5\%$ 0_2 . The transmural potential was measured between serosal and mucosal electrodes connected to a Grass Pl7 high impedance probe and polygraph recorder.

In these experiments it was necessary to measure transmural p.d. in the same tissue when different concentrations of the same weak electrolyte were added to the luminal fluid. Consequently preliminary experiments were carried out to determine whether the effect of an additive on p.d. could be reversed by successive washings with Krebs solution. A resting p.d. of 2.5 (\pm 0.2) m.v. was obtained and 10.2 (\pm 0.3) m.v. in the presence of a 28 mmol solution of glucose. It was necessary to wash with six 100 ml volumes of Krebs in order to return to the resting p.d. The p.d. in the presence of glucose could be regenerated six times over a time period of 90 min. When 0.6 mmol pentobarbitone solution was added the p.d. was reduced but could be regenerated by washing six times with Krebs solution. This procedure could be repeated five times so in future experiments each tissue could serve as its own control.

Potentials were measured over a time period of up to 10 min following the addition of sodium benzoate, sodium salicylate, diphenhydramine, pentobarbitone sodium and propranolol. No effect, over the time period used, was noted when either sodium salicylate or sodium benzoate was added in concentrations up to 0.7 mmol. However when diphenhydramine, pentobarbitone sodium or propranolol was added then an exponential decline in p.d. with time was noted. The rate of decline increased with increasing concentration. Slopes of plots of

 $(\log(\frac{mv}{x})/\min)$ as a function of electrolyte concentration were:- pentobarbitone

54.4 (±11); diphenhydramine 39.8 (±2) and propranolol 35.4 (±6). These values are not directly related to the ionization of the compounds. Analysis of other workers' data (Cooke and Kienzle, 1974) shows a relationship between fall in p.d. with increasing lipophilic nature of straight chain alcohols. However their compounds were structurally related and the relationship did not hold for branched chain alcohols.

Barry, R.J.C. and Eggenton, J. (1972). J. Physiol., 227, 217-231. Cooke, A.R. and Kienzle, M.G. (1974). Gastroenterology, 66, 55-62. Hardcastle, J., Hardcastle, P.T. and Sandford, P.A. Brit. J. Pharmac., 62, 463-464P (1978).

The authors acknowledge the helpful discussions with Dr. R.J.C. Barry.