# HISTOLOGICAL AND PHYSIOLOGICAL STUDIES ON THE RAT INTESTINE EXPOSED TO POLYETHYLENE GLYCOLS

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Bryan et al (1980) related fluid gain and differential cell loss, following exposure of closed segments of rat small intestine to hypertonic solutions of polyethylene glycol 2000, to the osmotic activity of the luminal fluid. In the further investigation of the effects of drug excipients on the small intestine we have exposed close gut segments in rats to solutions of polyethylene glycol 200, 2000 and 4000 in order to assess whether or not the changes observed by Bryan et al (1980) vary with the polymer chain-length. The concentrations chosen were approximately isosmolar with the most active solution used by Bryan et al (1980). The results have been compared with those from segments filled with solutions of mannitol which behave osmotically as ideal solutions. Saline filled segments and untreated tissue were used as controls.

The PEG and mannitol solutions caused a significant reduction in villus height. PEG solutions caused goblet cell capping and a significant differential loss of enterocytes compared with control tissue, although there was no difference in the extent of mucosal damage between the segments exposed to the various PEG solutions. Goblet cell capping was also present in the mannitol-treated segments and for the 18% w/v solution cell loss was extreme and resulted in a severe disruption of the villus architecture. Figures for water flux, estimated using $^{14}C$- polyethylene glycol 4000 are shown in Table 1. An indwelling cannula permitted sampling during the course of the experiment.

TABLE 1 Luminal water flux in loop preparations

| Solution | Osmotic Pressure $mOsm\ kg^{-1}$ | % Volume change with time (Mean ± SE 2 loops per animal: 3 animals per treatment group) | | |
|---|---|---|---|---|
| | | 20 min. | 40 min. | 60 min. |
| Saline (0.9% w/v) | 310 | 0 ± 6 | 6 ± 6 | 25 ± 25 |
| Mannitol (18% w/v) | 1470 | 131 ± 13 | 231 ± 13 | 338 ± 19 |
| Mannitol (8.5% w/v) | 820 | 106 ± 16 | 159 ± 25 | 194 ± 22 |
| PEG 400 (17% w/v) | 810 | 78 ± 19 | 164 ± 12 | 147 ± 16 |
| PEG 2000 (30% w/v) | 800 | 69 ± 6 | 113 ± 6 | 144 ± 9 |
| PEG 4000 (33% w/v) | 805 | 38 ± 6 | 69 ± 9 | 81 ± 9 |

It is concluded that the mucosal damage observed resulted from disruption of the normal osmotic gradient. However, the degree of water movement was not directly related to the osmotic pressure of the PEG solutions, but rather it varied inversely with the length of the polymer chain i.e. their molecular weight. This anomalous behaviour with respect to osmolarity is exemplified by the difference in water flux between the different PEG solutions and the 8.5% mannitol solution.

The authors gratefully acknowledge gifts of polyethylene glycol from Hoechst Pharmaceuticals, Milton Keynes, Bucks.

Bryan, A.J. et al (1980) Int. J. Pharm. 7: 145-56

0022-3573/81/120037P-01$02.50/0