ENHANCEMENT OF ABSORPTION OF SODIUM CROMOGLYCATE ACROSS THE NORMAL AND REGENERATING RAT RECTUM

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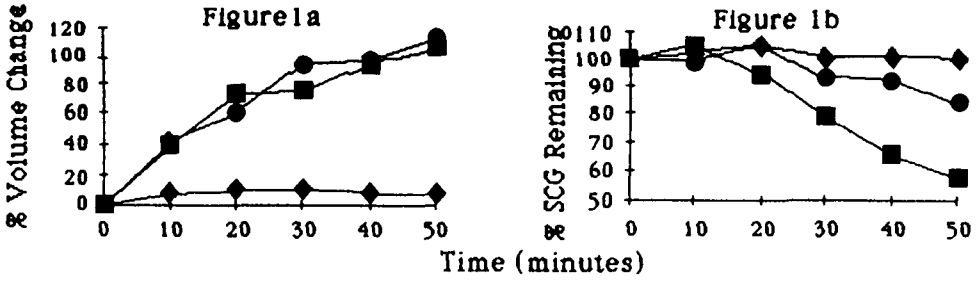
Previous studies in our laboratories have shown that the regeneration of the rectal mucosa after ulceration with suppositories of polyoxyethylene (23) lauryl ether is rapid and complete within one week (Holyhead et al 1983). During the period of regeneration, the absorption of prednisolone from rectal enemas is reduced, but may be increased by coadministration of sodium salicylate (Whiston et al 1985). In the present studies the effect of sodium salicylate on the absorption of sodium cromoglycate (SCG) has been investigated in the normal and damaged bowel models.

All microenemas were made up in a modified Krebs buffer (pH 7.6) containing sodium salicylate (5% w/v) or mannitol (10.5% w/v). Final osmolarities were 290 mOsm/kg for control solution and 870 mOsm/kg for salicylate and mannitol. 1.0 ml volumes of the microenema containing 0.1% (w/v) SCG as either 14C-labelled (1.8 uCi) or 3H labelled compound (2.4 uCi) and 0.2uCi 3H PEG 4000 (non-absorbed marker) with or without 5% sodium salicylate or 10.5% mannitol were administered to groups of anaesthetised rats prepared with a rectal in situ loop as described by Thomas et al (1984). For the damaged rectum group, rats were pretreated with a BRIJ 35 suppository 24 hours prior to the experiment. Tail tip and luminal samples were taken at intervals throughout the experiment and assessed for fluid flux (Figure 1a) and drug uptake (Figure 1b).

FIGURE 1. Effect of 5% sodium salicylate (■) and 10.5% mannitol (●) on luminal water flux and absorption of SCG. Krebs buffer was the control (◆). All measurements represent the mean of at least six animals. Standard deviations are covered by the data points.



5% salicylate and 10.5% mannitol produced a similar fluid flux into the lumen. Salicylate produced a greater effect on absorption of SCG than mannitol and approximately 2% of the dose was detected in the bladder urine when the animals were killed. In the damaged gut preparation, salicylate produced a similar increase in absorption of the cromone.

Hyperosmotic solutions are known to increase the membrane permeability of substances with a molecular weight less than 700. The mechanism appears to function by opening up the intercellular spaces (tight junctions) and is associated with an altered epithelial morphology. Since mannitol does not significantly increase the permeability to the cromone it is suggested that salicylate is able to interact with a deeper epithelial barrier made accessible by the hyperosmolarity of the solution.

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Holyhead et al., (1983) Br. J. Exp. Path. 64: 456-461.
Thomas N W et al., (1984) Int. J. Pharmaceut. 20:163-169.
Whiston R J et al., (1985) Int. J. Pharmaceut. 23:247-254