36P

THE HISTOLOGICAL EFFECTS OF SUPPOSITORY BASES UPON THE RECTAL EPITHELIUM OF THE RAT

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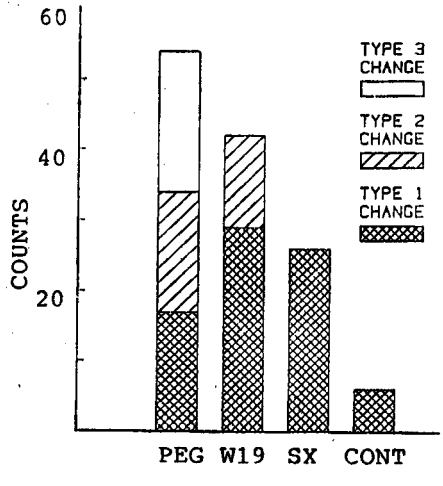
During the period of suppository liquefaction or melting, a small region of the rectal lining is subjected to an acute insult because of its intimate contact with the vehicle and high concentrations of the drug. Most bases, particularly hard fats are regarded as inert, but some water soluble macrogols may cause slight irritancy because of their dehyrating effect on the mucous membrane (Senior 1974). We have quantified histologically the acute response of the rectal epithelium in rats to suppositories of PEG 1500, Witepsol H19 and Suppocire OS1X. Groups of 180-200g male Wistar rats (n=5) were fasted overnight with water ad libitum. Animals were anaesthetised with pentobarbitone sodium ip (75mg/kg body weight) and treated with small suppository (6.5mm x 4.0mm). After 1 hour control and treated animals were killed, the anal canal and lower rectum removed and processed by conventional techniques for histological examination. From each animal four randomly selected sections through longitudinal profiles of the rectal mucosa were analysed. Counts were made between the anorectal junction and the 100th gland of the interglandular sites showing the following changes. Type 1, presence of detached cells or cells in the process of detachment; type 2, reduction in epithelial cell height consequent upon cell loss; type 3, exposed basal lamina following complete loss of surface epithelium. Data were screened using the Kruskal-Wallis one way analysis for nonparametric data and differences between treatments was assessed using the Mann-Whitney U test.

Fig.1 Stacked bar chart illustrating mean counts from 5 rats/treatment for the three types of changes identified in the rectal epithelium between the rectoanal junction and the 100th gland after suppository treatment. Cont - Untreated animals: SX - Suppocire OS1X treated: W19 - Witepsol 19 treated: PEG - PEG 1500 treated.



Local effects were produced by all three bases; type 1 changes following each treatment were statiscially significant. The changes represented a spectrum in the response of the rectal epithelium to increased cell loss. Initially changes in cell dimension were able to compensate for cell loss but eventually this process was unable to prevent ulceration. Normal structure is likely to be restored rapidly following type 1 and 2 changes. However, the production of localized ulcers, although capable of rapid repair (Holyhead et al 1983), may influence absorption of both drug and other materials from the lumen of the large bowel. Clearly local histological changes to occur at the site of suppository insertion, even with so called inert bases, and these should be investigated during formulation development.

Holyhead, E.M. et al (1983) Br. J. Exp. Path. 64 : 456-461.
Senior, N. (1974) Adv. Pharm. Sci. 4 : 363-435 Eds. Bean, H.S., Beckett, A.H. and Careless, J.E. Academic Press, London & New York.

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