THE EVALUATION OF SWELLING AND SOLUTE TRANSPORT IN MODIFIED POLY-(ACRYLIC ACID) FOR MUCOADHESIVE CONTROLLED RELEASE APPLICATIONS

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Current work centres on the combination of controlled release and mucoadhesive properties in a single dosage form. Poly(acrylic acid), (PAA), previously identified as possessing mucoadhesive properties (Smart et al, 1984), dissolves and disperses relatively rapidly in contact with wet mucus membranes. By crosslinking the PAA a hydrogel is obtained exhibiting structural strength, mucoadhesion, and controlled release properties.

Crosslinked PAA systems were prepared by solution casting formulations of PAA and glycerol (or polyalkylene glycol) into glass rings, drying, and curing at 110°C for 4 hr. The dry, cured gels were swollen in pH7 buffer solution, and the swelling ratios calculated using the equation:

$$S.R. = (Dt-Do)/Do \qquad \text{where;} \quad Do = \text{diameter at time} = 0, \quad Dt = \text{diameter at time} = t$$

The fully swollen hydrogel films were placed in a two-chambered Kreevoy diffusion cell and the rates of diffusion of an anionic solute brilliant yellow (m.w. 624.56) determined through the gels at pH7, by U.V. assay of the receptor solution. The mucoadhesive capacity was measured by lifting samples of the swollen hydrogels (40mm diam.) at a rate of 1.53 mm/s from fresh mucosal tissue samples (40mm diam.) placed on an electronic balance. The weight measured was recorded by a micro-computer as the gel and tissue separated. The maximum detachment force was compared to that obtained by Robinson (Robinson et al, 1985) for polycarbophil (Table 1.).

Swelling ratios increased with increasing pH, varying from 1.0 to 17.5 for lightly crosslinked polymers, and from 1.0 to 7.0 for more highly crosslinked polymers, as the pH was changed from 3 to 7. Little change in solute transport was observed, probably due to the large size of the diffusing molecule, as the glycerol concentration was altered (Fig.1), despite considerable differences in swelling ratios (Fig.2). An increase in swelling ratio with crosslinker concentration was observed for glycerol, but a decrease for the polyalkylene glycol, possibly due to a higher degree of intramolecular reactions with the glycerol molecules, giving fewer PAA molecules bound into the gel.

Table 1: Maximum detachment force for Polycarbophil and crosslinked PAA.

Polymer	Detachment weight/g	Force/Area $x10^{-6}Nm^{-2}$	Polymer	Detachment weight/g	Force/Area $x10^{-6}Nm^{-2}$
Polycarbophil	0.855	1.061	PAA(0.75%glyc)	75.89	5.920
PAA(0.35%glyc)	15.57	1.215	PAA(1.00%glyc)	20.68	1.614
PAA(0.50%glyc)	40.12	3.130			

FIG.1. DIFFUSION OF BRILLIANT YELLOW DYE

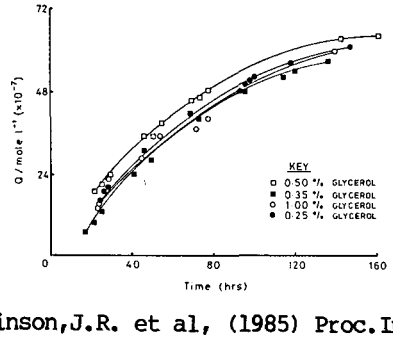
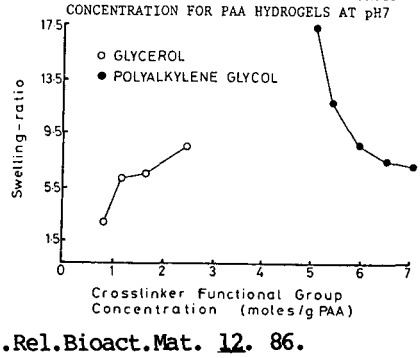


FIG. 2. SWELLING RATIO VERSUS CROSSLINKER GROUP CONCENTRATION FOR PAA HYDROGELS AT pH7



Robinson,J.R. et al, (1985) Proc.Int.Symp.Cont.Rel.Bioact.Mat. 12. 86.
Smart,J.D. et al, (1984) J.Pharm. Pharmacol. 36. 295.