IN VITRO TECHNIQUES FOR MEASURING MUCOADHESION

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Recent interest has been expressed in the delivery of drugs to, or via, mucus membranes by 'adhesive' particles. In vivo techniques were employed in previous studies, e.g. Chen & Cyr (1970), whereas this work will relate to the development of in vitro models. The surface of the mucus membranes consists of epithelial cells covered with a continuous mucus layer. Because of the relative complexity of this surface, our initial investigations used models incorporating biological tissues. Test systems were developed where suspensions of ion exchange resin particles flowed over the inner mucosal surface of a section of guinea pig intestine, and the weight adhering determined. These methods were soon found to be of limited value due to fairly rapid degeneration and biological variation of the tissue, which resulted in poor data reproducibility.

However, it was possible to demonstrate the effect of particle size and charge on 'adhesion' after 5 min contact with everted intestine. Sieve size fractions 75-53 μm and <32 μm were not significantly different, but a larger size fraction (178-63 μm) showed a significant increase in the weight adhering. A positive surface charge was seen to favour 'adhesion' when various resin particles with similar physical characteristics were tested, and a relationship between the weight adhering and the electrophoretic mobility demonstrated. The relevance to in vivo conditions, where the adsorption of proteins and other materials would be expected to negate any surface charges, is questionable.

Penetration of, or adhesion to, the outer mucus layer is a requirement for adhesion to mucus membranes. Mucoadhesion was investigated in a second in vitro system by measuring the maximum force recorded when a polymer coated glass plate was slowly pulled from 1 ml of 'homogenised' guinea pig intestinal mucus gel after 7 minutes contact. Results were expressed as a percentage of the clean plate force. Polymers reported by Chen & Cyr (1970) to have varying degrees of short-term adhesiveness to oral mucosa were investigated, and the results compared. The rank order correlation between the results suggests that materials that adhere to an isolated mucus gel will also adhere to oral mucosal membranes. Polymers with molecular weights >100,000 exhibited maximum adhesion. Hydration of the polymer coat to form a 'tacky' film, rather than a slippery mucilage, was necessary for adhesion, and the probable role of van der Waal interactions, and interprenetration of polymer chains with the mucus gel network is currently under investigation.

Polymer coat	*Mean % Force	Standard Deviation	†Chen & Cyr assessment
Sodium carboxymethylcellulose	192.4	12.0	Excellent
Tragacanth	154.4	7.5	
Sodium alginate	126.2	12.0	
Karaya gum	125.2	4.9	Satisfactory
Gelatin	115.8	5.6	Fair
Pectin	100.0	2.4	
Polyvinylpyrollidone	97.6	3.9	Poor
Acacia	97.6	5.9	
Polyethylene glycol 6000	96.0	7.6	

*Mean value from 3 plates coated with the test hydrocolloid, each result expressed as a percentage of the clean plate force.

†Chen & Cyr in vivo subjective assessment of the performance of adhesive intraoral discs containing 60% test hydrocolloid.

Chen, J.L. & Cyr, G.N. (1970) Adhes. Biol. System. 163-180 (ed. R.S. Manly), Academic Press

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