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A novel in-vitro apparatus for evaluating the mucoadhesion of liquid and semi-solid formulations

SIMON A. YOUNG AND JOHN D. SMART

School of Pharmacy and Biomedical Sciences, University of Portsmouth, White Swan Road, Portsmouth PO1 2DZ

Mucoadhesive liquid or semi-solid formulations are desirable to enhance the delivery of drugs to treat local conditions of the mouth and oesophagus, to optimize the bioavailability of drugs absorbed through these mucosa and to provide mechanical protection to inflamed or damaged tissue. In order to establish the mucoadhesive performance of potential formulations a more advanced test system than the "falling film" method [Teng & Ho, 1987] or the "modified viscometer" method [Bremeker, 1983] is required.

The porcine oesophageal mucoadhesion test system comprises a test cell constructed from Perspex™ into which a previously isolated mucosa approximately 150mm long was clamped to yield a test plane 120mm in length and 15mm wide, inclined at 30° to the horizontal. Once clamped, the underside of the tissue was exposed to a modest vacuum applied through a series of fine peripheral drillings, which, whilst being inadequate to draw fluid through or from the tissue, was sufficient to pull the elastic mucosa into a flat plane, without distorting the epithelial surface.

Isolated porcine epithelial tissue was prepared by the dissection of outer musculature from whole oesophagi of freshly sacrificed animals, to yield the cylindrical submucosa and epithelium only: These were rapidly frozen by immersion in liquid nitrogen and subsequently stored at -20°C until required. Once thawed in normal saline at room temperature, an epithelium was mounted in the test cell and maintained at 37°C. Surface dessication was prevented by the supply of warm humidified air and the flow of artificial salivary eluant applied at the top of the test plane and removed from the collection nozzle by a fraction collector.

After equilibration, a 1g sample of test formulation incorporating both thymol phthalein (soluble) and a suspension of fluorescein free acid was applied at the top of the test plane. Resultant eluant fractions were assayed by absorbance and fluorescence to determine the recovery of these validated marker systems, locating a model water soluble drug and the structure of the formulation respectively.

For both 0.5% Carbopol 934P and 0.5% Polycarbophil aqueous gels (figure 1) the retention of formulation by the test tissue may be adequately modelled by an exponential decay function, yielding significantly different elimination half-lives of 5.19 (± 1.32) mins and 2.74 (± 0.14) mins respectively. No significant difference in recovery of soluble and insoluble markers was observed.

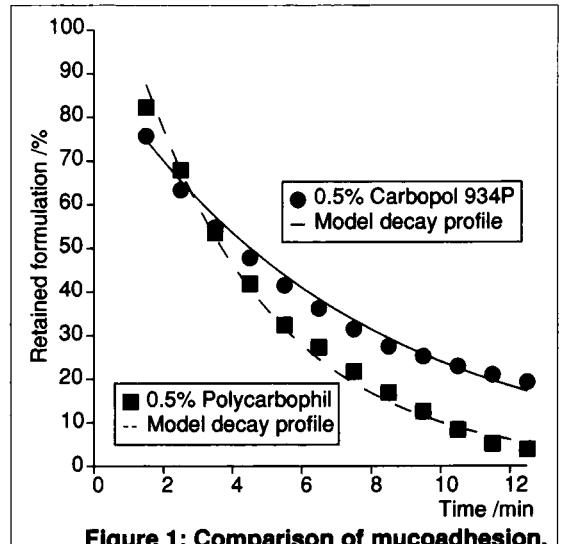

Figure 1: Comparison of mucoadhesion.

The porcine oesophageal mucoadhesion test system presented here has proven capable of differentiating closely related polymer formulations for the clinically relevant [Heliwell, 1993] duration of adhesion.

References:

Bremeker KD (1983), Pharm. Ind. 45, 417- 425.

Helliwell M (1993), Adv. Drug Delivery Rev. 11(3), 221-251.

Teng CLC and Ho NHF (1987), J. Control Release 6,133-145.