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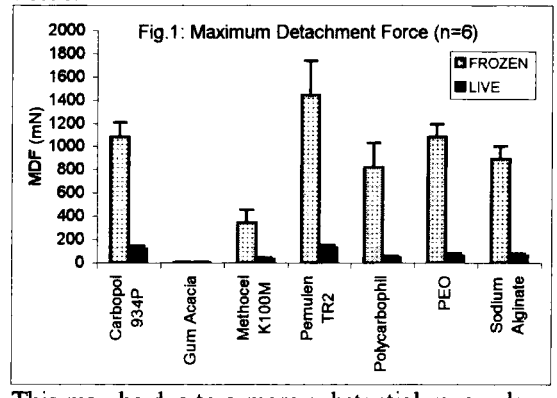
Tensile studies comparing the use of frozen and live viable rat small intestine as model mucosal surfaces

M. M. PATEL, S. ARKLE AND J. D. SMART

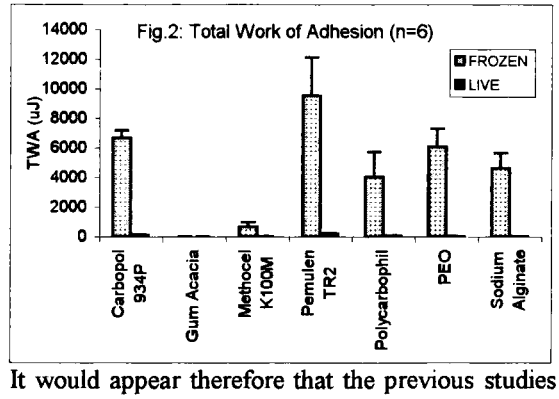
School of Pharmacy and Biomedical Sciences, University of Portsmouth, White Swan Road, Portsmouth PO1 2DT

The overall aim of this investigation is to produce a test system that allows the full characterisation of a mucoadhesive material, prior to *in vivo* testing. In previous work (Mortazavi and Smart 1995) the effect of applying tensile stresses to a mucoadhesive joint was evaluated, using a modified tensiometer. This study describes a technique that allows the use of live mucous-producing tissue, hence simulating *in-vivo* conditions more closely.

Flat-faced compacts were produced, with a diameter of 6mm, containing 50mg of various putative mucoadhesive materials. These were tested for their adhesive properties using tensile stresses, and live and 'flash frozen' rat small intestine as the model mucosal surface. In the 'live' tissue study, fresh rat small intestine was paralysed by placing in aerated De Jalons physiological buffer pH 7.4 at 37°C. An assay was developed to test for the presence of lactate dehydrogenase (LDH), so as to identify the onset of cell death in the small intestine. In the second study, fresh rat small intestine was flash frozen in liquid nitrogen (20 s) and stored at -20°C. This was then allowed to thaw at room temperature for 10 min. Both mucosae were then used in tensile studies using a modified tensiometer similar to that described by Mortazavi and Smart (1995). The model mucosal surface was clamped into place on a movable platform, within a water bath containing the De Jalons buffer. Each compact was attached to 1.5g weight, which was suspended from the underside of a balance linked to a microcomputer for data collection. This was then placed into contact with the exposed mucosa and after 2 min, the platform was lowered at a rate of 2 mm min^{-1} until adhesive joint failure occurred. The strength of the adhesive joint was calculated in terms of the maximum detachment force (MDF, the force required to break the adhesive joint in mN) and total work of adhesion (TWA, the area under the force elongation curve measured in μJ). Seven test materials were evaluated using both systems, with each experiment being completed six times. From this study it is apparent that stronger adhesion, in terms of both MDF's (Fig. 1) and TWA (Fig. 2) was achieved using the flash frozen tissue.



This may be due to a more substantial mucus layer being present on the viable tissue, and indeed mucus secretion may be stimulated during adhesive joint formation. Non-uniformity of the viable tissue surface may also have an effect on the adhesive joint strength, producing the greater variation in the results obtained.



It would appear therefore that the previous studies using only frozen tissue may not be representative of the *in vivo* situation.

Mortazavi, S.A., and Smart, J.D. (1995) Int. J. Pharm., 116, 223.