THE EFFECT OF TEMPERATURE AND TIME ON THE IN-VITRO ADHESION OF PUTATATIVE MUCOADHESIVES TO MUCUS

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The search for bioadhesive polymers as platforms for controlled drug delivery is increasing due to the possibility of improving bioavailability by prolonging the residence time of the dosage form in the gastrointestinal tract. The ability of materials to adhere to mucus has largely been assessed in vitro owing to experimental difficulties encountered in vivo. The surface tensiometer technique is commonly used for in vitro mucoadhesion studies since it offers good reproducibility (Kellaway, 1989). However, key features of the methodology are often poorly described or omitted, especially regarding the environmental conditions to which the mucus is subjected. To address this fact, the purpose of this study was to determine the effect of temperature and time on the mucoadhesion of sodium carboxymethylcellulose (SCMC), poly(acrylic acid) [PAA], gelatin-acacia microcapsules (GM) and acacia. The changes in mucus dry weight concentration with time were also monitored.

Gelatin-acacia microcapsules were prepared by the complex coacervation of acid gelatin and acacia at pH 4.1 as reported by Helliwell et al (1989). PAA was synthesised from acrylic acid using benzoyl peroxide as the initiator (Ch'ng et al, 1985). The washed polymer was dried at 90°C for 12h before being ground to the required size (250-500 μm). Microcapsules or powdered polymer were coated onto rubber discs and fixed by an adhesive resin.The rubber disc was mounted on a glass rod which in turn was suspended from a 5g torsion balance (Model O, White Elec. Inst. Co. Ltd.). Pig stomachs obtained at slaughter were washed and frozen until required. After thawing, the mucus was gently scraped from the mucosa, pooled and diluted with distilled water to give a dry weight content of 4.27%. The diluted mucus was transferred to a jacketed beaker and raised slowly until contact with the coated disc was made. After an equilibration time of 10 min for the SCMC and 5 min for the other materials, the disc was raised at a rate corresponding to 50 mg/s. Control experiments were carried out in an identical manner using adhesive resin-coated discs. The procedure was performed at 9, 22, and 37°C; mean detachment forces expressed as a percentage of the control are shown in Table 1. The force required to detach coated discs, immediately after contact with mucus equilibrated at 9, 22, and 37°C, was measured at 0 and 2 h; the percentage change in detachment force after 2 h is shown in Table 2.

Table 1 Mean Detachment force as a % of control

Mucoadhesive	Temp (°C)		
	9	22	37
SCMC	163	150	145
PAA	151	139	136
GM	127	124	118
Acacia	111	104	96

Table 2 Percentage change in force required to detach coated discs from mucus after 2h

Mucoadhesive	Temp (°C)		
	9	22	37
SCMC	0.0	2.9	17.2
PAA	2.2	0.0	8.0
GM	1.7	0.8	7.2
Acacia	0.0	1.7	-1.9

The mean detachment force, when compared to the control, for each mucoadhesive (MA) decreased as the mucus temperature increased. There was a two fold increase in the percentage dry weight concentration of mucus equilibrated at 37°C compared to mucus equilibrated at 9 or 22°C (after 2 h). Each MA, with the exception of acacia, showed an increase in adhesiveness to mucus (37°C) after 2 h. This increase, however, was not observed with the control disc. The use of a physiologically relevant temperature has introduced limitations to the technique and this has important implications especially when the tensiometer is being used to rank putative MAs. The results obtained suggest that experimental conditions must be fully documented before one can compare data from the tensiometer technique.

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