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The bioadhesive properties of hydrophobized polyvinylpyrrolidone

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We have recently reported that the introduction of hydrophobic caprolactone end blocks onto polyoxyethylene glycol (molecular weight 4,000) increases its bioadhesion (Martini et al 1995). We now report that the introduction into the hydrophilic polymer, polyvinylpyrrolidone (PVP) of a hydrophobic chain also increases its bioadhesive properties.

PVP, of molecular weight of around 10,000, was hydrophobized by the attachment of C12 hydrocarbon chains at nominal C12 hydrophobe to vinyl pyrrolidone ratios of 1:10, 1:25, 1:50,1:75,1:100. The hydrophobized derivatives of PVP are described by the designation C_{12}PVP1:n where n is the nominal number of PVP units per hydrophobe.

Matrices of PVP (control) and the various hydrophobicized PVP derivatives were produced by direct compression using an IR press. Force-elongation curves were determined using a modified tensile stress tester, for matrices in contact with rabbit mucosal tissue freshly removed from duodenum. The matrix was uniformally wetted with distilled water (15µl) before being brought into contact with the mucosal tissue at an initial compression force of 0.5N. The adhesion force was measured at an elongation rate of 0.0125 cm min^{-1} after a pre-swelling time of 10 min. The mean work of adhesion (W_A) was calculated from the area under the curves (mean of at least 3, generally 6 individual experiments) while the mean force of detachment (F_D) was calculated from the peak of the elongation curve. The results of the experiment are given in the Table. For reference the values obtained for pectin and Carbopol 934 are also included.

Bioadhesive properties of hydrophobicized PVP

Matrix Material	Mean W_A 10^3 mJ	Mean F_D N
C_{12}PVP1:10	18.3	0.44
C_{12}PVP1:25*	19.3	0.50
C_{12}PVP1:50	20.9	0.63
C_{12}PVP1:75	20.4	0.56
C_{12}PVP1:100	16.3	0.28
PVP	13.4	0.33
Pectin	16.6	0.24
Carbopol 934	56.4	0.65

n = 6, except for * where n = 3

It is worth noting that for all samples tested, including unmodified PVP, the presence of a thin layer of tissue on the surface of the matrix was evidence that, at the detachment of the matrix, rupture occured within the mucosal tissue rather than at the polymer-mucus-interface.

It can be seen from the Table that the PVP derivatives all demonstrate a slightly higher bioadhesive nature than the original PVP molecule and that this increase in bioadhesiveness is dependent upon the ratio of hydrophobe to PVP units with PVP derivatives containing very low and high amounts of C12 hydrophobe present exhibiting the least bioadhesion.

These results suggest that the presence of the hydrophobe alters the conformation of the polymer chain in such as way as to make the amide linkages present on the heterocyclic ring more accessible for interaction with the mucus. This study supports the observation of Martini et al (1995) that hydrophobizing a short chain hydrophilic polymer may increase its bioadhesive nature

Martini L, Attwood D, Collet JH, D'Emanuele A
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