J. Pharm. Pharmacol. 1998, 50 (Supplement): 66

Rheological analysis of poly (methyl vinyl ether–maleic anhydride) gels

M. S. LAWLOR, D. S. JONES AND A. D. WOOLFSON

Pharmaceutical Devices Group, School of Pharmacy, The Queen's University of Belfast, Medical Biology Centre, 97 Lisburn Road, Belfast BT9 7BL

It is accepted that the retention of conventional formulations, e.g. mouthwashes, within the oral cavity is poor, and, as a result, the clinical efficacy of such formulations is severely compromised. Mucoadhesive polymers, when used as drug delivery platforms, have been reported to both enhance the retention of topical formulations within the oral cavity, and in some cases, provide controlled drug release to specific sites. (Jones et al 1997). Following application to the oral cavity, formulations are subjected to oscillatory shearing forces, such as swallowing, chewing, breathing, etc., which affect their rheological properties and thus clinical performance. (Jones et al, 1998) The bioadhesive copolymer poly (methyl vinyl ether- maleic anhydride) (Gantrez®) has been previously used in drug delivery systems designed for use in the oral cavity however, there is little information available concerning the effects of oscillatory stresses on the rheological properties of Gantrez® gels. Therefore, this study examined the rheological properties of Gantrez® gels using oscillatory rheometry.

Gantrez (10, 15% w/w) was initially dissolved in distilled water using mechanical stirrer. Following this, PVP (3, 6, 9% w/w) and glycerol (0, 7.5% v/w) were added and the gels neutralised using NaOH solution (30%). Gels were stored at room temperature for at least 24 h prior to analysis.

The viscoelastic properties of the gels were measured using a Carri-Med CSL^2-100 stainless steel parallel plate rheometer with a 6cm diameter geometry. Rheograms were produced in triplicate over a frequency range of 0.01 to 1.0Hz at a constant temperature of 20°C and constant strain ($1x10^{-3}$).

The effects of increasing concentrations of Gantrez, PVP and glycerol on the storage modulus (G'), loss modulus (G"), the loss tangent (tan δ) and the dynamic viscosity (η'), at representative frequencies, were statistically evaluated using a three way Analysis of Variance (ANOVA, $p<0.05$ denoting significance). For all analyses, the c.v. < 10%.

For all formulations, G' and G" increased significantly with increasing oscillatory frequency, while the loss tangent decreased. As the concentration of PVP was increased, the G' and G'' increased significantly, while the loss tangent significantly decreased. G' and G'' also increased as a function of increasing Gantrez® concentration. All formulations show greater elastic characteristics at high frequency. Increased glycerol concentration significantly increased G', G'' and η' and decreased the loss tangent in the presence of 10% Gantrez®. However, in the presence of 15% Gantrez® and PVP, the opposite effects were observed. The gels with higher PVP and Gantrez® concentrations exhibited greatest elasticity.

Table 1: Rheological Parameters at a frequency of 0.68Hz

Formulation	G' (Pa)	G" (Pa)	tan (δ)	η'
10%Gantrez				
0 gly, 3 PVP	28.72	84.87	2.962	19.65
0 gly, 6 PVP	104.7	213.2	2.037	49.37
0 gly, 9 PVP	175.7	300.8	1.712	69.65
7.5gly,3PVP	73.06	166.9	2.282	38.65
7.5gly,6PVP	198.6	346.8	1.747	80.30
7.5gly,9PVP	244.8	407.7	1.670	94.39
15% Gantrez				
0 gly, 3 PVP	629.5	821.7	1.305	190.3
0 gly, 6 PVP	2405	2445	1.016	566.3
0 gly, 9 PVP	3930	3681	0.937	852.3
7.5gly,3PVP	619.4	835.2	1.349	193.4
7.5gly,6PVP	1485	1706	1.149	395.1
7.5gly,9PVP	1928	2072	1.075	479.9

Increased elasticity, associated with increased concentrations of Gantrez® and PVP may be attributed to greater entanglement of the polymer chains. In addition, such entanglements enhanced η' of these formulations. Given the reported relationship between elasticity (G') and mucoadhesion (Tamburic and Craig 1995; Jones et al. 1997), formulations containing highest concentrations of Gantrez® and PVP and in the absence of glycerol, should exhibit greater mucoadhesive properties. Indeed, the rheological properties of these formulations would also be expected to promote controlled topical delivery of therapeutic agents, e.g. chlorhexidine (Jones et al. 1998). This study has further highlighted the use of oscillatory rheometry for the characterisation of topical systems.

Jones D.S. et al (1998) Pharm. Res. in press

Jones D.S. et al (1997) Int. J. Pharm. 151:223-233.

Tamburic S. et al (1995) J. Control. Release 37: 59-68.