J. Pharm. Pharmacol. 1998, 50 (Supplement): 157

The effect of alcoholic solvents on the rheological properties of gels composed of cellulose derivatives

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Cellulose ethers are widely used as suspending and thickening agents in the formulation of liquid and semisolid drug delivery systems. However, little is known about the effect of alcoholic excipients on their rheological properties. In this study we investigate the viscoelastic properties of gels made from commonly used cellulose ethers in water and alcohol co-solvents.

HEC, CMC and HPMC gels were made using concentrations of 3, 10 and 5%w/w respectively. In water, these concentrations produce semisolid gels of similar consistency. For each material, gels were made using co-solvents composed of water and alcohol (ethanol, propylene glycol or glycerol) in various proportions. Gels were made by rapid addition of the polymer to the solvent mixture under high speed stirring. They were stored in sealed containers at 4°C for 24 hours to allow complete wetting / dissolution before testing. Oscillatory analyses were performed using a Carri-Med CSL^2-100 rheometer with a 4cm diameter parallel plate geometry and a 1000µm gap. A strain of 6.5×10^{-3} was found (by torque sweep) to lie within the linear viscoelastic region for all samples and was used for frequency sweep analyses. These were performed at 20°C over a frequency range from 0.01 to 1.0 Hz.

Tables 1, 2 and 3 show the storage modulus (G') for each system at a frequency of 1.0Hz.

	Ethanol	Prop.Glycol	Glycerol
0%	354.2 ± 6.2	354.2 ± 6.2	354.2 ± 6.2
10%	427.3 ± 3.3	401.83 ± 44.2	446.9 ± 8.4
20%	459.5 ± 41.7	462.6 ± 14.9	557.7 ± 9.2
30%	470.2 ± 33.4	532.6 ± 6.8	677.1 ± 11.6
40%	449.2 ± 11.9	617.7 ± 17.9	745.1 ± 34.0
50%	400.4 ± 16.0	667.9 ± 8.7	919.3 ± 25.6
60%	229.5 ± 4.9	724.2 ± 19.8	933.8 ± 25.0
70%	-	609.7 ± 15.6	635.2 ± 1.0
80%	-	60.8 ± 0.5	342.7 ± 0.7

Table 1. G' at 1.0Hz for HEC 3% in various solvents.

In each case, loss modulus and dynamic viscosity were also increased then decreased with increasing concentrations of alcoholic solvents. These trends were observed over the full range of frequency observed.

	Ethanol	Prop.Glycol	Glycerol
0%	432.9 ± 3.9	432.9 ± 3.9	432.9 ± 3.9
10%	802.5 ± 16.0	516.0 ± 1.5	642.7 ± 8.2
20%	1024.7 ± 19.3	720.2 ± 3.5	793.3 ± 10.0
30%	1186.3 ± 11.0	1389.3 ± 7.6	1315.0 ± 3.5
40%	671.5 ± 7.5	1845.3 ± 8.6	1969.0 ± 9.5
50%	-	2438.7 ± 24.1	2593.3 ± 37.5
60%	-	3289.7 ± 27.0	3657.7 ± 34.8
70%	-	5339.0 ± 23.9	5033.3 ± 39.8
80%	-	16.9 ± 1.5	33.2 ± 1.7

Table 2. G' at 1.0Hz for CMC 10% in various solvents.

	Ethanol	Prop.Glycol	Glycerol
0%	300.2 ± 8.7	300.2 ± 8.7	300.2 ± 8.7
10%	326.1 ± 1.5	430.3 ± 12.1	427.4 ± 4.6
20%	407.0 ± 8.6	492.7 ± 15.0	521.3 ± 12.5
30%	379.5 ± 25.3	625.5 ± 24.3	390.7 ± 4.7
40%	378.2 ± 12.9	912.3 ± 36.1	243.8 ± 8.1
50%	393.6 ± 11.7	967.9 ± 27.7	-
60%	389.3 ± 17.8	1041.7 ± 35.8	-
70%	355.6 ± 16.4	769.1 ± 14.1	-
80%	300.4 ± 9.5	15.6 ± 0.9	-

Table 3. G' at 1.0Hz for HPMC 5% in various solvents

For each of the polymers investigated, increases in the alcohol content of the co-solvent produced increases in gel consistency up to a maximum, after which further increases reduced the consistency or, in some cases, completely destroyed the gel. With small amounts of ethanol these polymers remain completely soluble. Increases in consistency may be due to the increase in polymer concentration relative to the water content. With larger amounts of ethanol they are only partially soluble and the consistency is reduced. In propylene glycol or glycerol the polymers do not dissolve but exhibit swelling, leading to increased consistency. Swelling increases with increased proportions of these solvents until maximal swelling is achieved. Further increases in the proportion of these solvents causes dilution and a reduction in consistency.

In conclusion, the incorporation of alcoholic solvents in cellulose ether gels may have dramatic effects on their viscoelastic properties which will influence both the clinical and non-clinical use of such systems..