

Rheological analysis of carbopol/hydroxyethylcellulose gels as platforms for topical drug delivery

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Carbopol (PAA) forms low viscosity acidic solutions in water that transform into gels as the solution pH is increased. The viscosity of such gels can be further modified by the addition of suitable viscosity-enhancing polymers. The rheological properties of such bicomponent systems may be more accurately controlled and, also, may be designed to offer a wider range of viscoelastic properties by the formation of physical networks (Jones et al. 1997). The objective of this study was to characterise the rheological properties of gels composed of PAA and hydroxyethylcellulose (HEC), a viscosity enhancing polymer, and, to examine the presence of network formation between these two polymers.

Aqueous gels of PAA (Carbopol ETD-2050; 0.5-1.5% w/w) were prepared by gradually adding the required quantities of PAA solid to distilled water with stirring. Aqueous HEC gels (0.5%-1.5%) were prepared in a similar fashion. Gels containing both PAA and HEC (PAA 0.5%:HEC 0.5%; PAA 0.5%:HEC 1.5%; PAA 1.5%:HEC 0.5%; PAA 1.5%:HEC 1.5%) were prepared by dispersing the required amounts of PAA and HEC solids into distilled water with stirring. The pH of each sample was adjusted to either 7.5 ± 0.2 or 4.0 ± 0.1 (following dissolution of each polymer) by the addition of measured volumes of 0.2M NaOH solution. All gels were stored at room temperature for at least 24h prior to analysis. Oscillatory properties of each film were investigated using a Carri-Med CSL²-100 rheometer in conjunction with a parallel plate geometry (4cm diameter, 1.0mm plate separation). Frequency sweep analysis was performed at 20°C under controlled strain (5.00×10^{-2}) over a frequency range of 0.1 - 1.0Hz. Oscillatory parameters investigated included; storage modulus (G'), loss modulus (G''); dynamic viscosity (η') and tan (δ). The effects of formulation on the rheological properties of resulting gels were statistically evaluated using a one-way ANOVA ($p < 0.05$).

Table 1. Viscoelastic properties of gels composed of PAA, HEC or PAA and HEC (pH 7.5) at a representative frequency of 0.4791Hz.

%PAA	%HEC	G' (Pa)	G'' (Pa)	Tan (δ)
0.0	1.0	8.48±0.20	10.55±0.58	1.244±0.09
0.0	1.5	28.42±2.15	27.49±1.27	0.968±0.02
0.5	0.0	64.36±8.22	17.87±8.86	0.288±0.17
1.0	0.0	46.61±1.53	10.22±0.11	0.219±0.01
1.5	0.0	66.46±2.60	12.24±0.44	0.184±0.01
0.5	0.5	53.64±5.18	22.86±1.11	0.427±0.02
0.5	1.5	286.7±10.5	116.0±7.85	0.404±0.01
1.5	0.5	76.03±4.41	35.49±1.25	0.467±0.01
1.5	1.5	288.80±5.2	118.4±1.63	0.409±0.00

Increasing concentrations of either PAA or HEC significantly enhanced G' , G'' , η' yet decreased the loss tangent of the gels under examination. Increasing oscillatory frequency significantly increased G' , G'' and decreased η' of all gels. Notably, the viscoelastic properties of HEC gels were significantly more dependent on frequency than those of PAA gels of the same concentration, primarily due to the cross-linked nature of the latter polymer. Interestingly, the elastic properties of mixed gels in which neutralisation of PAA (to pH 7.5) occurred in the presence of HEC were significantly greater than in gels containing identical concentrations of each polymer and prepared by admixing. These phenomena were also observed at pH 4, however, were more enhanced at pH 7. This suggests that a network is formed between PAA and HEC during the process of neutralisation and swelling of adjacent chains of PAA. Hence the propensity for chain entanglement between PAA and HEC is enhanced, resulting in a synergistic effect on formulation elasticity.

This study has shown that the rheological properties of PAA or HEC gels may be significantly enhanced by the incorporation of polymer gel networks between these two polymers. These observations have direct implications for the formulation of topical formulations.

Jones, D.S., Woolfson, A.D., Bonner M. 1997. *J. Pharm. Pharmacol* 49: 125