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Molecular weight dependence of the properties of ethyl cellulose and hydroxypropyl methylcellulose films

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Summary

The molecular weight dependence of the mechanical and other properties of ethylcellulose and hydroxypropyl methylcellulose has been studied using the Flory equation: property = $A + B/M$ where M is the molecular weight and A and B are constants. B values for the mechanical properties were negative and, when corrected for degree of polymerisation, comparable to those for cellulose acetate but an order of magnitude lower than those for polystyrene and polypropylene. B values have also been used to investigate the molecular weight dependence of permeability, release rate and incidence of cracking of film coatings. Use of B values in investigating possible mechanisms for the deleterious effect seen on the addition of titanium dioxide to hydroxypropyl methylcellulose has been proposed.

Introduction

The relationship between the mechanical properties of a polymer and its molecular weight is qualitatively the same for all polymers. Low molecular weight polymers are usually relatively weak but the properties increase to asymptotic maxima at high molecular weight (Alfrey, 1965). Quantification of the relationship stems from the work of Flory (1945) in his attempt to reconcile the experimental findings of Sookne and Harris (1945) on the molecular weight dependence of the tensile strength and elongation of cellulose

acetate. The equation derived fitted the experimental results well:

$$P = A + \frac{B}{M} \quad (1)$$

where P is the mechanical property, M denotes the number average molecular weight, M_n , for heterogeneous polymers and A and B are constants.

In later work on polystyrenes of both broad and narrow molecular weight distributions (measured by sedimentation), McCormick et al. (1959) disputed the use of M_n , suggesting that M_n should be replaced by some value of the molecular weight between M_n and the weight average molecular weight, M_w . In more recent work on commercial polypropylenes (measured by gel permeation

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chromatography), Ogawa (1992) suggested the adoption of the geometric mean molecular weight, i.e., $(M_n \cdot M_w)^{1/2}$. He also hypothesised that B has value in comparing the difference of molecular weight dependence among polymer species.

In this paper, these concepts have been applied to the properties, both mechanical and others, of the cellulose ethers, ethylcellulose and hydroxypropyl methylcellulose, commonly used in the film coating of oral dosage forms.

Results and Discussion

In all cases, M has been taken as the peak molecular weight determined using gel permeation chromatography (Rowe, 1980, 1982).

Mechanical properties of ethylcellulose and hydroxypropyl methylcellulose

Using data on the mechanical properties, tensile strength and elongation to break, for both polymers (Rowe, 1980, 1982, 1986b) it is possible to show:

(a) For ethylcellulose:

Tensile strength (MPa)

$$= 77.70(\pm 2.13) - \frac{7.01(\pm 0.70) \times 10^5}{M}$$

$$r^2 = 0.9529$$

Elongation (%)

$$= 42.72(\pm 1.40) - \frac{6.65(\pm 0.46) \times 10^5}{M}$$

$$r^2 = 0.9768$$

(b) For hydroxypropyl methylcellulose:

Tensile strength (MPa)

$$= 52.40(\pm 0.98) - \frac{5.35(\pm 0.55) \times 10^5}{M}$$

$$r^2 = 0.9790$$

Elongation (%)

$$= 28.67(\pm 1.27) - \frac{9.38(\pm 0.73) \times 10^5}{M}$$

$$r^2 = 0.9882$$

where the figures in parentheses are the standard errors.

The negative values of B show that the mechanical properties increase with molecular weight. The regression coefficients are exceptionally high considering the number of samples (seven for ethylcellulose, four for hydroxypropyl methylcellulose) and the known inaccuracies in measuring the mechanical properties of thin films by tensile testing. The similarity of the B values for each polymer implies the same molecular weight dependence on both properties.

TABLE 1

Comparison of the molecular weight dependence of the mechanical properties of a variety of polymer (B calculated in terms of DP)

Polymer	Properties	B (\pm SE) ($\times 10^3$)	Reference
Ethylcellulose	tensile strength	-3.05 ± 0.30	this work
Ethylcellulose	elongation	-2.89 ± 0.20	this work
Hydroxypropyl methylcellulose	tensile strength	-2.76 ± 0.28	this work
Hydroxypropyl methylcellulose	elongation	-4.84 ± 0.38	this work
Cellulose acetate	tensile strength	-4.98 ± 0.34	Sookne and Harris (1945)
Polypropylene	tensile strength ^a	-89.9	Okawa (1992)
Polypropylene	elongation ^a	-67.4	Okawa (1992)
Polystyrene	tensile strength	-31.5	McCormick et al (1959)

^a At yield measurements – mean value of measurement at 45 and 60°C

In order to compare the molecular weight dependence of the mechanical properties of different polymers, it is first necessary to redefine M in Eqn 1 in terms of DP, the degree of polymerisation. If this is done for ethylcellulose and hydroxypropyl methylcellulose using values for the molecular weight of each monomer unit of 230 and 194, respectively, then B decreases proportionately (Table 1).

A comparison of the values for B for various polymers is shown in Table 1. The value calculated for the two cellulose ethers in this work is comparable to that determined for cellulose acetate using the data generated by Sookne and Harris (1945) but is an order of magnitude less than those for polypropylene and polystyrene. This cannot be due to changes in crystallinity as suggested by Okawa (1992), since all the cellulose derivatives are amorphous comparable to polypropylene. The differences in the value of B for these two sets of polymers may instead be due to the differences in the interaction between the polymer chains within the film. In the cellulose derivatives this will be through a mixture of van der Waals forces and hydrogen bond formation while in polypropylene and polystyrene it will be predominantly through van der Waals forces.

Pigment addition to hydroxypropyl methylcellulose films

It is well known that the addition of pigments to films can have a deleterious effect on the resultant mechanical properties (Gibson et al., 1988b). However, it is also generally assumed that the underlying beneficial effect of increasing the molecular weight of the polymer will be independent of the pigment concentration provided it does not exceed the critical volume concentration. Use of B values for a system where both molecular weight and pigment concentrations have been varied should provide a means of investigating this specific effect.

Using data on the mechanical properties of hydroxypropyl methylcellulose films prepared from three samples of polymer of increasing molecular weights and containing increasing concentrations of titanium dioxide (Shin Etsu Chemical Co. Ltd, 1990), it is possible to calculate B

TABLE 2

Effect of concentration of titanium dioxide for hydroxypropyl methylcellulose ($n = 3$)

Property	Pigment concentration (% w/w)	$B (\pm SE) (\times 10^5)$	r^2
Tensile strength	0	-6.00 (± 0.73)	0.9856
Tensile strength	10	-17.39 (± 6.95)	0.8621
Tensile strength	20	-18.81 (± 5.61)	0.9115
Elongation	0	-10.48 (± 2.40)	0.9994
Elongation	10	-10.48 (± 2.19)	0.9604
Elongation	20	-11.54 (± 3.03)	0.9337

values for both tensile strength and elongation to break (Table 2). In both cases, the concentrations of titanium dioxide are well below the critical pigment volume concentration of this polymer (Gibson et al., 1988a).

It can be seen that the addition of titanium dioxide causes an immediate 3-fold increase in the value of B for tensile strength but has little or no effect on the value for elongation. The reason for this can only be hypothesised. It is now accepted that fracture in a polymer originates from points in the polymer matrix where chain ends are concentrated either due to the film formation process or as a result of molecules slipping along one another whereas elongation stems from the uncoupling of the intermolecular interactions along the chains. Hence, the interaction of titanium dioxide with the polymer must be via the chain ends rather than between the chains. Evidence for such an interaction, albeit in an aqueous solution of the polymer has already been shown (Gibson et al., 1988c).

Moisture permeability and cracking in hydroxypropyl methylcellulose films

Increasing the molecular weight of hydroxypropyl methylcellulose is known to cause a decrease both in the incidence of cracking/edge splitting in film coated tablets (Rowe and Forse, 1980) and in the moisture permeability of free films (Shin Etsu Chemical Co., Ltd, 1990) – both properties decreasing to an asymptotic minimum at high molecular weights. Application of Eqn 1 to the data yields values of B of $+1.67 (\pm 0.56) \times 10^6$ ($r^2 = 0.7482$, $n = 5$) and $+1.13 (\pm 0.45) \times 10^6$

TABLE 3

Release rate data for ethylcellulose films ($n = 5$)

Time (h)	$B (\pm SE)$ ($\times 10^6$)	r^2
1/2	0.86 (± 0.33)	0.6919
1	1.51 (± 0.50)	0.7512
2	2.04 (± 0.50)	0.8465
3	2.09 (± 0.35)	0.9244
4	2.02 (± 0.33)	0.9272
5	1.84 (± 0.28)	0.9357

($r^2 = 0.8641$, $n = 3$) for cracking and moisture permeability, respectively. Although the correlations are not as good as those obtained with the mechanical properties the results are significant. Despite the fact that both values of B are positive, as expected, they are some 2–3-times higher than those for the mechanical properties.

Drug release from spherical granules coated with ethylcellulose

In work on the effect of molecular weight of ethylcellulose on the release of a drug from spherical granules coated with a film formulation consisting of 90% ethylcellulose with 10% hydroxypropyl methylcellulose, Rowe (1986a) showed that the amount of drug released at a specific time decreased with increasing molecular weight of ethylcellulose reaching an asymptotic value at molecular weights greater than 35 000. It was suggested that this was caused by the presence of micro cracks/flaws in the films prepared from the low molecular weight polymers. Application of Eqn 1 to the release data at time intervals from 0.5 to 5 h yields positive values of B with good correlation although 2–3-times greater than those obtained for the mechanical properties (Table 3). There is also a trend to constant values of B after 2 h. This result implies a change in mechanism of release at short times leading to a steady-state condition after approx. 2 h.

Conclusions

It can be seen from the data presented that Eqn 1, although highly simplified, can be used to

investigate the molecular weight dependence of a relatively wide range of properties for cellulose ethers used in the film coating of oral dosage forms. Provided data are available, it can also be used to investigate possible mechanisms for specific effects. It could possibly be used to predict the properties of a film prepared from a polymer of different molecular weight for inclusion in formulation expert systems.

References

- Alfrey, T., The mechanical properties of high polymers. *High Polymers*, Vol VI, Interscience, New York, 1965
- Flory, P.J., Tensile strength in relation to molecular weight of high polymers *J Am Chem Soc*, 67 (1945) 2048–2050
- Gibson, S.H.M., Rowe, R.C. and White, E.F.T., Determination of the critical pigment volume concentrations of pigmented film coating formulations using gloss measurement. *Int J Pharm*, 45 (1988a) 245–248.
- Gibson, S.H.M., Rowe, R.C. and White, E.F.T., The mechanical properties of pigmented tablet coating formulations and their resistance to cracking. I Static mechanical testing *Int J Pharm*, 48 (1988b) 63–77.
- Gibson, S.H.M., Rowe, R.C. and White, E.F.T., Quantitative assessment of additive-polymer interaction in pigmented hydroxypropyl methylcellulose formulations using immersion calorimetry. *Int. J Pharm*, 48 (1988c) 113–117.
- McCormick, N.W., Brower, F.M. and Kin, L., The effect of molecular weight distribution on the physical properties of polystyrene *J Polym. Sci*, 39 (1959) 87–100
- Ogawa, T., Effects of molecular weight on mechanical properties of polypropylene *J Appl Polym Sci*, 44 (1992) 1869–1871
- Rowe, R.C., The molecular weight and molecular weight distribution of hydroxypropyl methylcellulose used in the film coating of tablets *J Pharm Pharmacol*, 32 (1980) 116–119
- Rowe, R.C., Molecular weight studies on ethyl cellulose used in film coating *Acta Pharm. Suec*, 19 (1982) 157–160
- Rowe, R.C., The effect of the molecular weight of ethyl cellulose on the drug release properties of mixed films of ethyl cellulose and hydroxypropyl methylcellulose *Int J Pharm*, 29 (1986a) 37–41
- Rowe, R.C., A scientific approach to the solution of film splitting and bridging of the intagliations on film coated tablets *STP Pharma*, 2 (1986b) 416–421
- Rowe, R.C. and Forse, S.F., The effect of polymer molecular weight on the incidence of film cracking and splitting on film coated tablets *J Pharm. Pharmacol*, 32 (1980) 583–584
- Sookne, A.M. and Harris, M., Polymolecularity and mechanical properties of cellulose acetate *Ind Eng Chem*, 37 (1945) 475–482