International Journal of Pharmaceutics, 31 (1986) 175–177
Elsevier

IJP 01034

The solubility parameters of some cellulose derivatives and polyethylene glycols used in tablet film coating

P. Sakellariou [1], R.C. Rowe [2] and E.F.T. White [1]

[1] *Department of Polymer Science and Technology, University of Manchester Institute of Science and Technology, Manchester M60 1QD and* [2] *ICI Pharmaceuticals Division, Alderley Park, Macclesfield, Cheshire SK10 2TG (U.K.)*

(Received January 16th, 1986)
(Accepted February 3rd, 1986)

Key words: solubility parameter – cellulose derivatives – polyethylene glycols

Summary

The solubility parameters of ethyl cellulose, hydroxypropyl methylcellulose, hydroxypropyl cellulose, hydroxypropyl methylcellulose phthalate, cellulose acetate phthalate and the polyethylene glycols of molecular weight 200–6000 $g \cdot mol^{-1}$ have been calculated using group molar attraction constants. The calculated values are, with the exception of those calculated using the group molar attraction constants given by Small (1953), in close agreement with those observed experimentally.

A knowledge of the compatibility characteristics and solubility of polymers and plasticizers used in film coating is important in the optimization of both the film formulation and the processing conditions (Rowe, 1984). In this respect polymer scientists have tended to use the solubility parameter approach based on the regular solution theory of Hildebrand and Scott (1950) who defined the solubility parameter (δ) of a substance as the square-root of its cohesive energy density or energy of vaporization per unit volume. Although it is relatively easy to directly measure the solubility parameter of volatile substances, the method is not applicable to non-volatile polymers. Solubility parameters for these materials can only be determined indirectly by studying polymer–solvent interactions which are assumed to be a maximum when the solubility parameter of the polymer is equal to the solubility parameter of the solvent. These methods, which usually involve viscosity or polymer swelling measurements, can be laborious and time consuming and a more rapid approach is sometimes necessary. In this respect, it is possible to calculate the solubility parameter of a polymer from its molecular structure from the summation of the group molar attraction constants (F) present in the molecule using the formula:

$$\delta = \frac{\Sigma F}{V}$$

where V is the molar volume of the polymer (Small, 1953).

This approach has been applied in this work to both the cellulose derivatives and polyethylene glycols used in tablet film coating.

The film formers studied were ethyl cellulose and hydroxypropyl cellulose (EC and HPC; Hercules Powder Co., Wilmington, DE, U.S.A.); hy-

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Correspondence: R.C. Rowe, ICI Pharmaceuticals Division, Alderley Park, Macclesfield, Cheshire SK10 2TG, U.K.

droxypropyl methylcellulose and hydroxypropyl methylcellulose phthalate (HPMC and HPMCP; Shin-Etsu, Chemical Co., Tokyo, Japan) and cellulose acetate phthalate (CAP; Eastman Chemical Products, Kingsport, TN, U.S.A.). The polyethylene glycols (PEG) with nominal molecular weights of 200, 400 600, 1000, 4000 and 6000 $g \cdot mol^{-1}$ were obtained from BDH Chemicals, Poole, U.K. Densities of the cellulose derivatives were determined using helium pycnometry (model 930, Beckman Instruments, Glenrothes, Fife, Scotland). The number average molecular weights of the polyethylene glycols were determined using gel permeation chromatography with tetrahydrofuran as carrier solvent. The solubility parameters for the cellulose derivatives were calculated by dividing the sum of the group molar attraction constants for one representative structural unit by the molar mass of that unit and multiplying by the polymer density. Those for the polyethylene glycols were calculated from the entire molecule. The group molar attraction constants were obtained from tables given by Small (1953), Hoy (1970) and van Krevelen and Hoftyzer (1976).

The results together with experimental data from the literature are given in Table 1. It can be seen that, for the cellulose derivatives for which experimental data are available, there is good agreement between the solubility parameter calculated using the group molar attraction constants given by Hoy (1970) and van Krevelen and Hoftyzer (1976) and that determined experimentally. However, the solubility parameters calculated using the group molar attraction constants given by Small (1953) are much smaller. This discrepancy is due, in the main, to the somewhat arbitrary molar attraction constant assigned by Small to the hydroxyl group present in relatively

TABLE 1

CALCULATED SOLUBILITY PARAMETERS TOGETHER WITH LITERATURE EXPERIMENTAL DATA FOR THE CELLULOSE DERIVATIVES AND POLYETHYLENE GLYCOLS (DATA AT 25°C UNLESS STATED)

	Solubility Parameter ($MPa^{\frac{1}{2}}$)			
	Small	Hoy	van Krevelen	Literature
EC	16.1	19.0	20.6	19.4–19.7 (Kent and Rowe, 1978) 21.1 (Burrell, 1975)
HPMC	16.1	21.5	24.4	20.7–25.6 (Aulton et al., 1985)
HPC	17.0	21.1	24.9	21.7–23.6 (Roberts and Thomas, 1978)
HPMCP	17.2	22.4	26.4	–
CAP	21.7	24.1	27.2	–
PEG 200	19.1	20.2	26.1	23.7 (Vaughan, 1985)
PEG 400	18.4	20.2	23.1	18.0 [a] (Takamiya et al., 1959) 23.2 (Vaughan, 1985)
PEG 600	18.0	19.7	22.5	20.5 [b] (Kawakami et al., 1976)
PEG 1 000	19.1	21.5	23.4	20.1 [b] (Kawakami et al., 1976)
PEG 4 000	18.9	21.1	22.5	19.4 [b] (Kawakami et al., 1976) 23.7 (Otozai and Tohyama, 1976) 22.1–24.6 [c] (Burrell, 1975)
PEG 6 000	18.8	21.2	22.4	23.7 (Otozai and Tohyama, 1976)

[a] Measured at 100°C.

[b] Measured at 67.3°C.

[c] Mid range values for poorly, moderate and strongly hydrogen bonding solvents.

large numbers in all the polymers (348 $MPa^{\frac{1}{2}} \cdot cm^3 \cdot mol^{-1}$ the sum of 205 for the hydrogen and 143 for the ether oxygen) compared to those constants determined by Hoy (462 $MPa^{\frac{1}{2}} \cdot cm^3 \cdot mol^{-1}$) and van Krevelen and Hoftyzer (754 $MPa^{\frac{1}{2}} \cdot cm^3 \cdot mol^{-1}$). Tables comparing the constants determined by all these workers are given in Barton (1983). The high values for the solubility parameters calculated for cellulose acetate phthalate are consistent with those observed for the closely related cellulose acetate polymer (27.1–27.8 $MPa^{\frac{1}{2}}$ — Burrell, 1975).

A similar explanation to the one given above can be used for the differences between the solubility parameters calculated for the polyethylene glycols but here the discrepancy is not so marked since there are only two hydroxyl groups per molecule. The effect of these hydroxyl groups on the solubility parameter will decrease with increasing molecular weight, hence the slight decrease in the calculated solubility parameters with increasing molecular weight consistent with that observed in practice (Kawakami et al., 1976; Otozai and Tohyama, 1976; Vaughan, 1985). The distinct break in the trend occurring between PEG 600 and PEG 1000 is due to the simple fact that the former is a liquid and the latter is a solid and that different density values were used in the calculations — 1.12 $g \cdot cm^{-3}$ for the liquid polyethylene glycols and 1.20 $g \cdot cm^{-3}$ for the solid polyethylene glycols. The effect of variable density is the reason for the relatively low values of the solubility parameter determined by Takamiya et al. (1959) and Kawakami et al. (1976) since both groups of workers made measurements in excess of the melting points of the solid polyethylene glycols. If the calculated solubility parameters are corrected for the changes in density at these temperatures (1.09 $g \cdot cm^{-3}$ at 67.3°C and 1.06 $g \cdot cm^{-3}$ at 100°C) then the agreement between the calculated and observed values is much better.

In conclusion it can been seen that the use of group molar attraction constants, especially those given by both Hoy (1970) and van Krevelen and Hoftyzer (1976) provides a rapid and realistic value for the solubility parameters of both the cellulose derivatives and polyethylene glycols used in tablet film coating.

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