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HANSEN SOLUBILITY PARAMETERS FOR SELECTED CELLULOSE ETHER DERIVATIVES AND THEIR USE IN THE PHARMACEUTICAL INDUSTRY

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ABSTRACT

The paper describes a laboratory method used for determining the partial solubility parameters of five METHOCEL* and six ETHOCEL* cellulose ether products. A simple computer spreadsheet has also been devised to calculate the partial solubility parameters from the laboratory data. These new laboratory derived values extend the data base of solubility parameters that have been used to explore certain cellulose ether applications. The cellulose ethers are characterized in terms of non-polar, polar, and hydrogen bonding behavior. METHOCEL A, E, F, K and J cellulose ethers all have similar solubilities and are thus assigned solubility parameters in the range of non-polar (δ d) = 17.4 - 18.2, polar (δ p) = 14.6 - 16.5, hydrogen bond (δ h) = 15.5 - 19.4 with a radius of interaction of 10.3

More organic like solubility is shown by the six ethoxy cellulose ether derivatives. The range of Hansen partial solubility parameters are non-polar (δd) = 16.6 - 17.3, polar (δp) = 6.6 - 8.3, and hydrogen bond (δh) = 8.5 - 10.0.

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INTRODUCTION

Cellulose ethers are linear polymers of condensed anhydro-glucose rings forming a carbohydrate skeleton to which methyl and hydroxypropyl groups are attached by an ether linkage. These polymers are used in the pharmaceutical industry for a variety of applications including tablet coating and wet granulation binders. The solubility profiles of several cellulose ether products have been determined. The solubilities are characterized in terms of non-polar, polar, and hydrogen bonding components. Rowe (1) has used solubility parameters to examine certain pharmaceutical uses of cellulose ethers like a hydroxypropyl methylcellulose, a hydroxypropyl cellulose and ethyl cellulose. The three Hansen solubility parameters for microcrystalline cellulose have been determine by a gas-solid chromatography method (2). A similar study by Phuoc (3) determined the solubility parameters of lactose.

Ethyl cellulose and cellulose acetate membranes have been characterized by solubility parameter profiles (4,5). Solubility studies on ethyl cellulose used in tablet film coating have been reported (1,6,7,8). The solubility profiles of several ETHOCEL* cellulose products (ethoxy cellulose ether structures) as determined in our laboratory will be detailed in the paper.

This paper will include a short review of solubility parameter theory; comments on literature cited solubility work with cellulose derivatives and a description of our laboratory work that gave the partial Hansen solubility parameters for five METHOCEL* (methoxy and hydroxypropyl substituted) cellulose ethers and six ETHOCEL cellulose ethers. Solubility profiles of five low viscosity grades of METHOCEL ethers in several alcohol/water solvent blends are also reported.

Solubility Parameter Theory:

The concept that solubility is related to the internal energy of solvents and solutes (eg. polymers) was first proposed by Hildebrand in 1916. Molecules subject to the same internal pressure are most effective in attracting and interacting with each other. Internal pressure is the energy required to vaporize 1 cubic centimeter of a

material. The internal energy/molar volume ratio E/V, (where V=mol. wt./density) is referred to as the cohesive energy density (CED). By definition the solubility parameter is the square root of the CED value.

$$\delta = (CED)^{1/2} = \left(\frac{\Delta E}{V}\right)^{1/2} = \left(\frac{\Delta H\text{-}RT}{V}\right)^{1/2}$$

Here, T = absolute temperature, R = gas constant, V = molar volume, H = enthalpy of vaporization, and E = the energy of vaporization. The cohesive energy density (CED) is the energy that binds the molecules in 1 cc. of solvent or solid. Solubility theory predicts that dissolution occurs when a solute (polymer) is surrounded by a solvent of similar CED value. The δ value has the unit dimensions of $(calories/cc)^{1/2}$ and are designated as a Hildebrand (H). Current usage favors the SI units where 1 $calorie^{1/2}/cc^{3/2} = 2.05\ MPa^{1/2}$ (megapascal).

Hansen (9) has pioneered the concept that the total cohesive energy term and thus the total solubility parameter (δ T) arises from a nonpolar interaction (δ d), a polar interaction (δ p), and a hydrogen bonding component (δ h). The three partial solubility parameters are related by the expression (1).

$$\delta T = (\delta d^2 + \delta p^2 + \delta h^2)\,1/2 \qquad (1)$$

The solubility parameters of a great number of solvents are known and tabulated (10). Solubility parameters of solvent mixtures can be calculated from the equation (2).

$$\delta(\text{mixture}) = \phi_1 \delta_1 + \phi_2 \delta_2 + \ldots \qquad (2)$$

where ϕ is the volume fraction of a mixture component.

The solubility parameters of selected solids or polymers are available in standard references like Barton's handbook on solubility parameters (10). Estimates of the polymer solubility parameters as determined from a group contribution theory based on the chemical structure is also described in Barton's book. The most exact solubility parameter determination uses the solubility behavior of the polymer in a series of solvents with varying degrees of polarity and hydrogen bonding ability. Solubility behavior of five types of METHOCEL ethers in a series of solvents were used to determine the METHOCEL solubility parameters reported in this study.

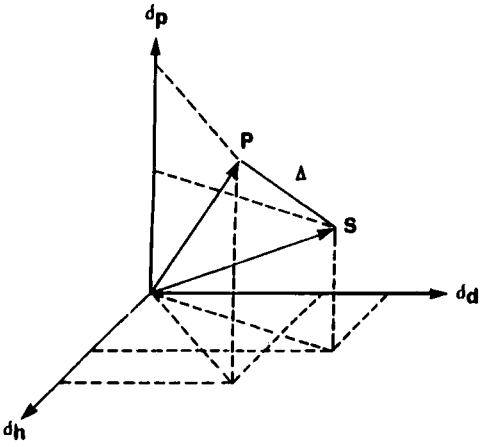

FIGURE 1

3D Display of
Solubility Parameters

The total solubility parameter of a material is a point located in three dimensional space where the three partial solubility parameter vectors meet as shown in Figure 1. The distance between the two total solubility points (S is for solvent and P is for polymer) determines the degree of interaction and solubility for the solvent and polymer. Higher solubilities are expected as the distance between points P and S decreases.

The distance in space between two sets of parameters (i.e., how closely they are matched) can be represented by the term, radius of interaction, or ${}^{ij}R$ and calculated by equation (3).

$$ {}^{ij}R = (4({}^{i}\delta d - {}^{j}\delta d)^2 + ({}^{i}\delta p - {}^{j}\delta p)^2 + ({}^{i}\delta h - {}^{j}\delta h)^2)^{1/2} \qquad (3) $$

In equation (3), the "j" terms correspond to the parameters of the solute and the "i" terms to the parameters of the solvent. The radius of interaction terms will be used later to calculate the solubility parameters for the METHOCEL and ETHOCEL ether derivatives. If the value from equation (3) is less than the radius of interaction for the polymer itself (${}^{ij}R < {}^{j}R$), the solvent or solvent blend will dissolve the polymer.

TABLE 1

Hansen Solubility Parameters for Cellulose Derivatives

Material	Molar Vol.	Solubility Parameters $(MPa)^{1/2}$ δt	δd	δp	δh
Microcrystalline Cellulose	216	39.3	19.4	12.7	31.3
Cellulose Acetate	860	25.1	18.6	12.7	11.0
Ethyl Cellulose	750	20.6	16.7	2.9	11.7
Lactose	237	39.9	19.6	26.2	23.2

LITERATURE REFERENCES TO CELLULOSE DERIVATIVES

Rowe (11) has used solubility parameter theory to study the adhesion of film coatings to tablet surfaces in the pharmaceutical industry. A summary of the Hansen solubility parameters from Rowe's paper for a series of cellulose derivatives is given in Table 1. Rowe (12) used solubility parameter relationships to help explain the cohesion and adhesion forces between substrate and polymeric binder, eg. cellulose ether, in a wet granulation process.

The partial solubility parameters of lactose (3) were determined by using lactose as the stationary phase in a gas-solid chromatography experiment. The behavior of liquids of known physical properties on this solid support and use of the Snyder/ Karger-Hansen interaction model gave the solubility parameters listed in Table 1.

Rowe (1) has published a two dimensional solubility map for ethyl cellulose(EC), hydroxypropyl methylcellulose(HMPC) and a hydroxypropyl cellulose(HPC) using polarity and hydrogen bonding data furnished by several literature solubility studies. The solubility envelopes shown in Figure 2 were constructed by plotting the position of various test solvents that dissolved or did not dissolve the particular cellulose derivative. A plus (+) mark indicates a solvent for the HPC and HPMC derivatives, while a circle (O) mark indicates solubility for only the ethyl cellulose moity. The HPMC envelope is slightly smaller than the HPC solubility area. The ethyl cellulose

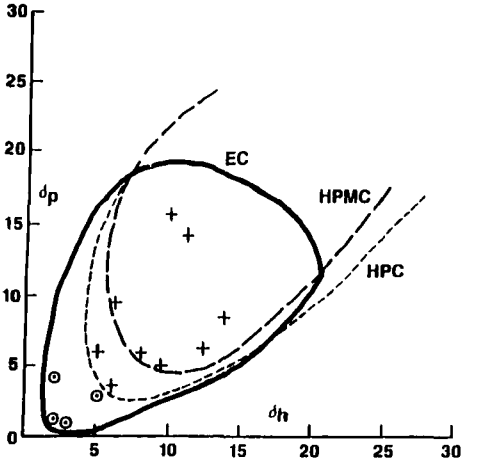

FIGURE 2

SOLUBILITY MAP FOR ETHYL CELLULOSE (EC), HYDROXYPROPYL METHYLCELLULOSE (HPMC) AND HYDROXYPROPYL CELLULOSE (HPC)

envelope supports the known fact that solvents with little polarity and hydrogen bond character can be good solvents for ethyl cellulose derivatives. Solubility studies in our laboratory with HPMC derivatives support and extend the knowledge that Rowe's study supplies.

Blends of ethyl cellulose with either a HPMC or HPC derivative are used for delayed or sustained release films on tablets. Solubility envelopes have also been used to predict interaction of these films with various film plasticizers (6,7,8).

EXPERIMENTAL

Solubility Parameter Determination:

An array of 39 solvents with varying solubility parameters were used to determine the solubility profile of the METHOCEL and ETHOCEL cellulose ether samples. The solubility behavior of the test substance was judged as soluble (S), partial solution/ hazy (H), or insoluble (I) after contacting the cellulose ether sample with a solvent for

some 18 hours (overnight). Tests used 0.25 grams of sample in a 5 dram (2 1/4 inch ht., 27.5 mm diameter) bottle equipped with a polyseal cap that contained 10 mls. of test solvent. The test bottles were placed in a large ball mill jar with adequate padding and the jar placed on a roller overnight. Placement of the vertical axis of the bottles 90 degrees to the top/bottom axis of ball mill jar allows the test bottle contents to tumble as the mill jar rolls. After the test period the samples were judged for solubility behavior with a rating of S, H or I. Areas of product solubility were then plotted and the data used to calculate the partial solubility parameters for the particular cellulose ether.

Alcohol/Water Solubility Profiles:

An array of thirty binary solvent blends with varying polarity were used to determine the solubility profiles of the low molecular weight HPMC samples. Twenty of the blends listed in Table 2 consisted of n-propanol, isopropanol and ethanol with water. Additionally, ten blends of methylene chloride and ethanol were included in the study. The alcohol/water study used the same experimental procedure as outlined above and used METHOCEL ether concentrations of 3, 6 and 10 weight percent.

RESULTS

The solubility data was evaluated using a spreadsheet, i.e. "Lotus 123**". Shareef (13) in a recent paper characterized four inorganic pigments in terms of partial solubility parameters. Shareef's data treatment method was simplified and transferred to a Lotus 123 spreadsheet that served as a basis for our calculations of partial solubility parameters. The evaluation critique requires one to find the center and radius of the sphere whose volume is minimum and which best encloses all of the given points (solvents showing soluble or partial soluble behavior). The center of this sphere as determined by the nonpolar, polar and hydrogen bond vectors represents the partial solubility parameters of the test polymers.

The intention of our spreadsheet calculations was to determine the distance(Dij) between two points in the sphere of influence. The Dij between two points is equal to:

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TABLE 2

SOLUBILITIES OF ***METHOCEL*** CELLULOSE ETHERS IN BINARY SOLVENT MIXTURES

BLEND NUMBER	SOLVENT NAME	VOLUME FRACTION SOLVENT #1	VOLUME FRACTION SOLVENT #2	SOLUBILITY PARAMETERS OF BINARY SOLVENT PAIR DELTA D	DELTA P	DELTA H
1	n-PROPYL ALCOHOL	0.2	0.8	18.8	15.6	17.6
2	WATER	0.8	0.2	16.7	9.0	17.4
3	n-PROPYL ALCOHOL	0.3	0.7	18.4	14.5	17.5
4	WATER	0.7	0.3	17.1	10.1	17.5
5	n-PROPYL ALCOHOL	0.4	0.6	18.1	13.4	17.5
6	WATER	0.6	0.4	17.4	11.2	17.5
7	ISOPROPANOL	0.2	0.8	18.8	15.5	17.4
8	WATER	0.8	0.2	16.5	8.4	16.6
9	ISOPROPANOL	0.3	0.7	18.4	14.3	17.2
10	WATER	0.7	0.3	16.9	9.6	16.8
11	ISOPROPANOL	0.4	0.6	18.0	13.1	17.1
12	WATER	0.6	0.4	17.3	10.8	16.9
13	ETHANOL: (anhydrous)	0.4	0.6	18.0	14.2	18.3
14	WATER	0.6	0.4	17.3	12.4	18.7
15	ETHANOL (anhydrous)	0.1	0.9	19.1	16.9	17.8
16	WATER	0.9	0.1	16.2	9.7	19.2
17	ETHANOL (anhydrous)	0.2	0.8	18.8	16.0	18.0
18	WATER	0.8	0.2	16.5	10.6	19.0
19	ETHANOL (anhydrous)	0.3	0.7	18.4	15.1	18.1
20	WATER	0.7	0.3	16.9	11.5	18.9
21	METHYLENE CHLORIDE	0.1	0.9	16.0	8.5	18.1
22	ETHANOL (anhydrous)	0.9	0.1	18.0	6.5	7.4
23	METHYLENE CHLORIDE	0.2	0.8	16.3	8.3	16.7
24	ETHANOL (anhydrous)	0.8	0.2	17.7	6.8	8.8
25	METHYLENE CHLORIDE	0.3	0.7	16.5	8.0	15.4
26	ETHANOL (anhydrous)	0.7	0.3	17.5	7.0	10.1
27	METHYLENE CHLORIDE	0.4	0.6	16.8	7.8	14.1
28	ETHANOL (anhydrous)	0.6	0.4	17.2	7.3	11.4
29	METHYLENE CHLORIDE	0.5	0.5	17.0	7.5	12.7
30	ETHANOL (anhydrous)	0.5	0.4	17.1	7.4	12.1

$$Dij = [(Xi-Xj)^2 + (Yi-Yj)^2 + (Zi-Zj)^2]^{1/2} \qquad (4)$$

All combinations of the solvents yielding a soluble or partial soluble behavior are calculated so as to arrive at the largest Dij values. The vector between two points giving the maximum separation distance can be considered the diameter of the sphere and the radius denoted as the radius of interaction is $C_R = \frac{Dij\ (max)}{2}$.

The coordinates of the center of the sphere are:

$$Cx = \frac{Xi + Xj}{2}; Cy = \frac{Yi + Yj}{2} \text{ and } Cz = \frac{Zi + Zj}{2}$$

These coordinates are the three partial solubility parameters for the test polymers. Table 3 lists the solubility parameters for five types of METHOCEL ether products as derived by the method just described. As one proceeds from "A" chemistry to "J" chemistry the number of solvents showing solubility for the METHOCEL increases. METHOCEL A shows solubility in only three solvents, dimethyl sulfoxide, benzyl alcohol and water. METHOCEL E, F, K shows solubility in formamide and the three solvents listed for METHOCEL A. The higher hydroxypropyl substitution of METHOCEL J allows the addition of Methyl Cellosolve*** solvent to the list of four soluble solvents. The degree of methoxy and hydroxypropyl ether substitution in the different types of the METHOCEL cellulose ether products is detailed in Table 4.

The use of the Lotus spreadsheet to calculate the partial solubility parameters for METHOCEL or ETHOCEL derivatives is simple and straight forward as described here: (1) Basis for these calculations is the soluble and partial soluble behavior of cellulose ether in the test solvents. (2) In order to calculate the solubility parameters one uses equation 4 to calculate Dij value or the distance in 3D space between each solvent or partial solvent. The next task is to search the columns of Dij calculations in the Lotus 123 spreadsheet for maximum values, eg. > 11.0. For example, twenty-seven binary solvent combinations with large Dij values were selected in the J4M study to calculate the radius of interaction and the center of the sphere. The final values for METHOCEL J4M cellulose ether were taken as the average of each of the twenty-seven Dij values listed for the solvent pairs.

A summary of Hansen solubility parameters for different types of cellulose derivatives is detailed in Table 5. The term "Delta A" which combines the polar and hydrogen bonding components is used to sort the derivatives from most "water like" to

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TABLE 3

Summary of Solubility Parameters for Several Types of Cellulose Ethers

	Solubility Parameters MPa 1/2			
METHOCEL ETHER	NONPOLAR	POLAR	HYDROGEN BONDING	RADIUS INTERACTION
A4M	18.0	15.3	19.4	8.2
E4M and E6	17.4	14.9	19.3	7.6
F4M	18.2	16.5	15.5	7.7
K4M	18.0	15.3	19.4	8.2
J4M	17.6	14.6	18.2	7.8

TABLE 4

Profile of METHOCEL Cellulose Ethers
%Methoxy and Hydroxypropyl

METHOCEL TYPE	METHOXY SUBST.	HYDROXYPROPYL
A4M	27.5 - 31.5	-----
E4M	28.0 - 30.0	7.0 - 12.0
F4M	27.0 - 30.0	4.0 - 7.5
K4M	19.0 - 24.0	7.0 - 12.0
E6 PREM.	28.0 - 30.0	7.0 - 12.0
J4M	16.5 - 20.0	23.0 - 32.0

TABLE 5

Hansen Solubility Parameters for Cellulose Derivatives

Solubility Parameters in MPa1/2

Material	Total	Non-Polar	Polar	Hydrogen Bond	Delta A*
Lactose	39.9	19.6	26.2	23.2	35.0
Microcrystalline Cellulose	39.3	19.4	12.7	31.3	33.8
METHOCEL A, E, F, K, or J	29.0 - 30.6	17.4 - 18.2	14.6 - 16.5	15.5 - 19.4	22.6 - 24.7
Cellulose Acetate	25.1	18.6	12.7	11.0	16.8
Ethyl Cellulose	20.6	16.7	2.9	11.7	12.0

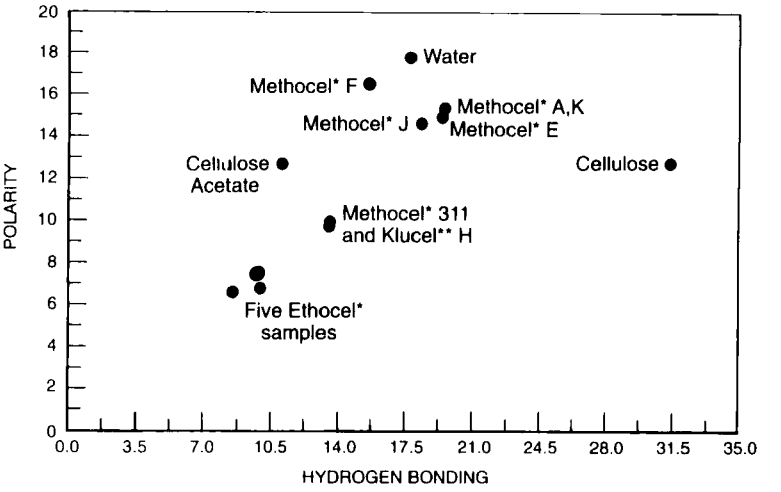
Note* Delta A is equal to the square root of the sum of the squares of the polar and hydrogen bond components.

TABLE 6

Hansen Solubility Parameters for ETHOCEL Ethoxy Cellulose Derivatives

Partial Solubility Parameters in MPa 1/2

ETHOCEL Material	Total	Non-Polar	Polar	Hydrogen Bonding	Delta A	Ethoxyl Content (%)
MED. 50	21.0	17.2	6.9	9.9	12.1	45 - 46.5
STD. 10	20.9	16.6	8.3	9.7	12.8	48 - 49.5
STD. 45	21.0	17.0	7.7	9.6	12.3	48 - 49.5
STD. 100	21.0	17.0	7.7	9.6	12.3	48 - 49.5
HE 45	20.4	17.3	6.6	8.5	10.8	49.5 - 52
HE 350	21.0	17.3	6.6	10.0	12.0	49.5 - 52



*TRADEMARK OF THE DOW CHEMICAL COMPANY
**TRADEMARK OF AQUALON INC.

FIGURE 3

HANSEN SOLUBILITY PARAMETERS FOR CELLULOSE DERIVATIVES

the least "water like." METHOCEL A, E, F, K or J with the partial reaction of hydroxyl groups falls below cellulose and considerably above the less polar cellulose acetate. As expected, the ethyl cellulose reported by Rowe (11) has the least combined polarity and hydrogen bond character.

A summary of the Hansen solubility parameters for six ETHOCEL cellulose ether derivatives is given in Table 6 where increasing hydroxyl substitution gives decreasing polar and hydrogen bonding character as shown by the Delta "A" values.

The ETHOCEL partial solubility parameters were derived in a manner identical to the METHOCEL derivatives. The ETHOCEL products have more hydrophobic solubility (organic like) than cellulose acetate derivatives which are inturn more hydrophobic than the methyl and hydroxypropyl ether derivatives of cellulose.

A representation of the hydrogen bond and polar character of various cellulose derivatives is detailed in Figure 3. The progression from a high hydrogen bonding and polar character of cellulose to the methyl and hydroxypropyl ether structures with water-like solubility to the further capping of the hydroxyl groups with acetate groupings is shown in the figure. Further organic-like solubility is obtained in the ethoxy cellulose structures that do not have any water-like solubility.

Solubility summaries of the five low viscosity grades (low molecular weight) METHOCEL products in the thirty binary solvent blends are detailed in Tables 7 and 8.

DISCUSSION

None of the METHOCEL ether types exhibited significant solubility in any of the pure alcohols or pure methylene chloride. Only upon the addition of 20 % water to the alcohol does one see any appreciable solubility. The METHOCEL A15LV-P shows the least solubility in the alcohol/water blends, while E5-P shows the largest range of solubility in the alcohol/water blends.

None of the METHOCEL products tested showed any significant solubility in the ten methylene chloride/ethanol solvent blends. There are however, many samples showing a partial solubility (a "H" rating), indicating that some material dissolved at room temperature. In some applications this level of solubility may be adequate.

The n-propanol/water blends show the best solubility for the METHOCEL products tested. Likewise, METHOCEL E5-P and F4-P ethers give the most consistent solubility response with all three alcohol/water solvent pairs in the concentration range of 3-10 %. The isopropanol/water blends show less solubility for higher concentrations of all the METHOCEL types tested as compared to the better solvency of the blends of n-propanol or ethanol with water.

The work reported here has characterized METHOCEL A, E, F, K and J ethers in terms of non-polar, polar, and hydrogen bonding behavior. The solubility study with a series of selected solvents shows that METHOCEL A, E, F, K and J all have similar solubilities and are thus assigned solubility parameters in the range of non-polar (δ d) = 17.4 - 18.2, polar (δ p) = 14.6 - 16.5, and hydrogen bond (δ h) = 15.5 - 19.4 with a radius of interaction of 10.3.

TABLE 7

Solubility Summary for ***METHOCEL*** A15LV-P, E15LV-P, E5-P, F4-P, K3-P Cellulose Ethers in Water/Alcohol Solvent Blend

PRODUCT DESCRIPTION	A15LV-P 3 WT. %	A15LV-P 6 WT. %	E15LV-P 3 WT. %	E15LV-P 6 WT. %	E15LV-P 10 WT.%	E5-P 3 WT. %	E5-P 6 WT. %	E5-P 10 WT.%	F4-P 3 WT. %	F4-P 6 WT. %	F4-P 10 WT.%	K3-P 3 WT.%	K3-P 6 WT.%	K3-P 10 WT.%
ALCOHOL/WATER /BLENDS														
100% Water	S	S	S	S	S	S	S	S	S	S	S	S	S	S
0.8 H2O/0.2 NPA	S	H	S	S	S	S	S	S	S	S	S	S	S	S
0.7 H2O/0.3 NPA	S	S	S	S	S	S	S	S	S	S	S	S	S	S
0.6 H2O/0.4 NPA	S	S	S	S	S	S	S	S	S	S	S	S	S	S
0.4 H2O/0.6 NPA	S	S	S	S	S	S	S	S	S	S	S	S	S	S
0.3 H2O/0.7 NPA	H	H	S	S	S	S	S	S	S	S	S	S	S	S
0.2 H2O/0.8 NPA	H	H	S	S	S	S	S	S	S	S	H	H	H	H
100% NPA	H	H	I	I	I	I	I	I	I	I	I	I	I	I
0.8 H2O/0.2 IPA	H	H	S	S	H	S	S	S	S	S	S	S	S	S
0.7 H2O/0.3 IPA	S	H	S	S	H	S	S	S	S	S	S	S	S	S
0.6 H2O/0.4 IPA	S	H	S	S	H	S	S	S	S	S	S	S	S	S
0.4 H2O/0.6 IPA	H	H	S	S	H	S	S	S	S	S	S	S	S	S
0.3 H2O/0.7 IPA	H	H	S	H	H	S	S	S	S	S	H	H	H	H
0.2 H2O/0.8 IPA	I	I	S	H	H	S	S	H	H	H	H	H	H	H
100 % IPA	I	I	I	I	I	I	I	I	I	I	I	I	I	I
0.9 H2O/0.1 ETOH	S	H	S	H	S	S	S	S	S	S	S	S	S	S
0.8 H2O/0.2 ETOH	S	H	S	S	H	S	S	S	S	S	S	S	S	H
0.7 H2O/0.3 ETOH	H	H	S	S	H	S	S	S	S	S	S	S	S	S
0.6 H2O/0.4 ETOH	S	H	S	S	S	S	S	S	S	S	S	S	S	S
0.4 H2O/0.6 ETOH	H	H	S	S	S	S	S	S	S	S	S	S	S	S
0.3 H2O/0.7 ETOH	H	H	S	S	S	S	S	S	S	S	S	S	H	H
0.2 H2O/0.8 ETOH	I	H	S	H	H	S	S	S	H	H	H	H	H	I
0.1 H2O/0.9 ETOH	I	I	H	H	H	H	H	H	H	H	I	I	I	I
100% ETOH	I	I	I	I	I	I	I	I	I	I	I	I	I	I

NOTE: NPA = n-PROPANOL, IPA = ISOPROPANOL and ETOH = ETHANOL

SOLUBILITY RATINGS: S = SOLUBLE, H = HAZY OR PARTIAL SOLUBILITY, AND I = INSOLUBLE

TABLE 8

Solubility Summary for ***METHOCEL**** A15LV-P, E15LV-P, E5-P, F4-P, K3-P Cellulose Ethers in ETHANOL/MECL2 Solvent Blend

PRODUCT DESCRIPTION	A15LV-P 3 WT. %	A15LV-P 6 WT. %	E15LV-P 3 WT. %	E15LV-P 6 WT. %	E15LV-P 10 WT.%	E5-P 3 WT. %	E5-P 6 WT. %	E5-P 10 WT.%	F4-P 3 WT. %	F4-P 6 WT. %	F4-P 10 WT.%	K3-P 3 WT.%	K3-P 6 WT.%	K3-P 10 WT.%
100% ETOH	I	I	I	I	I	I	I	I	I	I	I	I	I	I
0.1 MECL2/0.9 ETOH	I	I	I	I	I	I	I	I	I	I	I	I	I	I
0.2 MECL2/0.8 ETOH	I	I	I	I	H	H	H	I	I	I	I	I	I	I
0.3 MECL2/0.7 ETOH	I	I	H	H	H	H	H	H	I	I	I	I	I	I
0.4 MECL2/0.6 ETOH	I	I	H	H	H	H	H	H	H	H	H	I	H	I
0.5 MECL2/0.5 ETOH	H	H	S	H	H	H	H	H	H	H	H	H	H	I
0.55 MECL2/0.45 ETOH	H	H	S	H	H	H	H	H	H	H	H	H	H	I
0.6 MECL2/0.4 ETOH	H	H	H	H	H	H	H	H	H	H	H	H	H	I
0.7 MECL2/0.3 ETOH	H	H	H	H	H	H	H	H	H	H	H	H	H	I
0.8 MECL2/0.2 ETOH	H	H	H	H	H	H	H	H	H	H	H	H	H	I
0.9 MECL2/0.1 ETOH	H	H	H	H	H	H	H	H	H	H	H	I	I	I
100 % MECL 2	I	I	I	I	I	I	I	I	I	I	I	I	I	I

NOTE: MECL2 = METHYLENE CHLORIDE and ETOH = ETHANOL

SOLUBILITY RATINGS: S = SOLUBLE, H = HAZY OR PARTIAL SOLUBILITY, and I = INSOLUBLE

TABLE 9

Partial Solubility Parameters Determined From Binary Solvent Study

Average of Solvent Parameters Showing Good Solubility for ***METHOCEL**** (Rating of "S") Cellulose Ethers

METHOCEL	WT. %	SOLUBILITY PARAMETERS (MPa 1/2) TOTAL	NON-POLAR	POLAR	HYDROGEN BONDING	DELTA "A"
F4 - P	10	28.7	18.0	13.6	17.7	22.3
K3 - P	10	28.7	18.1	13.7	17.6	22.3
E5 - P	10	28.1	17.8	12.8	17.6	21.8
A15LV - P	6	28.3	18.0	13.0	17.5	21.8
E15LV - P	10	27.9	17.7	12.7	17.4	21.5
Solubility Parameters of Higher Molecular Weight ***METHOCEL*** Products (Data from Table 3)						
A4M	--	30.6	18.0	15.3	19.4	24.7
K4M	--	30.6	18.0	15.3	19.4	24.7
E4M/E6	--	30.0	17.4	14.9	19.3	24.4
F4M	--	29.0	18.2	16.5	15.5	22.6

Solubility studies with ETHOCEL derivatives have given Hansen partial solubility parameters in the range of non-polar (δ d) = 16.6-17.3, polar (δ p) = 6.6-8.3, and a hydrogen bond (δ h) value of 8.5-10.0. The ethoxy cellulose derivatives have more organic solubility than cellulose acetate which is, in turn, more hydrophobic than the methyl and hyroxypropyl ether derivatives.

The Hansen solubility parameters for the five METHOCEL products as determined from the binary solvents used in the study are listed in Table 9. The individual solubility parameters for the METHOCEL ether samples were taken as equal to the average of the parameters of the binary solvent blends that gave a "S" rating for the particular METHOCEL ethers. This simplified method can be justified since the Hansen parameters for all the alcohol/water blends fall into a narrow range. The solubility parameters determined in this manner are comparable to the values given in Table 3 for similar METHOCEL products of somewhat higher molecular weight.

The largest differences in the partial solubility parameters of the low viscosity grades listed in Table 9 is seen in the polarities of the METHOCEL products. Based on polarity the order is K3-P > F4-P > A15LV-P > E5-P > E15LV-P (the lowest value).

SUMMARY

Solubility parameter theory has been used previously to explore certain cellulose ether applications. Film coating work by Rowe (1,6,7,8,11,12) in the pharmaceutical industry is one example. Partial characterization of a HEC and a HPMC derivative in terms of solubility parameter values has been reported by Rowe in his pharmaceutical film work.

Our work has characterized METHOCEL A, E, F, K and J cellulose ethers in terms of non-polar, polar, and hydrogen bonding behavior. A solubility study with a series of selected solvents shows that METHOCEL A, E, F, K and J ethers all have similar solubilities and are thus assigned solubility parameters in the range of non-polar (δ d) = 17.4-18.2, polar (δ p) = 14.6-16.5, and hydrogen bond (δ h) = 15.5-19.4 with a radius of interactions of 10.3.

Solubility studies with ETHOCEL derivatives have given Hansen partial solubility parameters in the range of non-polar(δ d) = 16.6-17.3 , polar(δ p) = 6.6-8.3

and a hydrogen bond(δ h) value of 8.5-10.0. The ethoxy cellulose derivatives have more organic solubility than cellulose acetate which is inturn more hydrophobic than the methyl and hyroxypropyl ether derivatives.

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