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RELATIVE HYDROPHOBICITY OF SYNTHETIC MACROMOLECULES

II*. POLY(VINYL ALCOHOL) WITH VARIOUS DEGREES OF ACETYLA- TION

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SUMMARY

Partitioning of poly(vinyl alcohol) (PVA) of various molecular weights and degrees of acetylation (from 1% up to 18%) in the aqueous Ficol-400-dextran-70 two-phase system was studied at pH 7.4 at varied ionic compositions of the system. The relative hydrophobicity of the polymers was estimated. It was established that the relative hydrophobicity of PVA depends on the degree of acetylation of the polymer but not on the molecular weight of PVA in the range from $2 \cdot 10^4$ to $1 \cdot 10^5$. The results obtained are considered in comparison with those reported previously for polyethylene glycols, polyacrylamides and polyvinylpyrrolidones. The effect of the macromolecular nature of a compound on its hydrophobic character is discussed.

INTRODUCTION

It has been shown earlier¹ that the relative hydrophobicity of synthetic macromolecules can be estimated by the partition technique as well as that of biopolymers^{2,3}. It has been particularly established¹ that the hydrophobic character of macromolecules depends on their chemical nature.

The partition technique was used in this work to study the relative hydrophobicity of poly(vinyl alcohol) (PVA) of various molecular weights and of different degrees of acetylation. The results obtained are discussed in comparison with the estimates of the relative hydrophobicity of polyethylene glycols, polyacrylamides and polyvinylpyrrolidones reported previously¹.

* For Part I, see ref. 1.

EXPERIMENTAL

Materials

Ficoll-400 (lot 19069) was obtained from Pharmacia (Upssala, Sweden) and dextran-70 (lot 680480) under the trade name Polyglucinum from Minmedprom (U.S.S.R.).

Samples of PVA containing 1% (PVA-I), 6% (PVA-II), 12% (PVA-III) and 18% (PVA-IV) of acetate groups were obtained, fractionated and characterized as described earlier⁴.

Methods

Tritium labelling of the PVA samples was carried out as described earlier¹.

The aqueous polymeric two-phase systems were prepared as described¹ and had the following composition: 12.0% (w/w) Ficoll-400, 11.0% (w/w) dextran-70 and amounts of sodium chloride and sodium phosphate buffer (pH 7.4) according to the relationship

$$C_{\text{buffer}} = 0.11 - 0.67C_{\text{NaCl}}$$

where C_{buffer} is the concentration of the buffer, varying from 0.01 *M* to 0.11 *M*, and C_{NaCl} is the concentration of sodium chloride, varying from 0 to 0.15 *M*.

The partition experiments were carried out as described previously¹⁻³. The phases of the two-phase system were allowed to settle for 21-24 h at 25°C, then aliquots of both phases were pipetted from the system and used for the solute concentration measurements.

The concentrations of the PVA samples examined were determined by radioactivity measurements as described in detail elsewhere⁵.

The partition coefficient of a polymer, *K*, is defined as the ratio of the polymer concentration in the Ficoll-rich phase to that in the dextran-rich phase. The *K* values were measured for each solute over approximately 10-fold concentration ranges and were found to be independent of the solute concentration under all the conditions employed. Each partition coefficient was determined as the mean of three measurements on four different dilutions of each partition experiment carried out three or four times at a given ionic composition of the two-phase system. Deviations from the mean *K* value did not exceed 3% for any of the polymers examined.

RESULTS

It has been shown previously² that the estimates of the hydrophobic character of solutes depend on the particular two-phase system used. As the system containing 12.5% (w/w) Ficoll-400 (lot 11069, Pharmacia) and 10.8% (w/w) dextran-70 (lot 580870, Minmedprom) has been chosen as the reference system², the results obtained in this work were converted to the reference system according to the equation

$$\ln K_0 = a_i \ln K_i + b_i \quad (1)$$

where K_i is the partition coefficient of a solute in the two-phase system employed, K_0

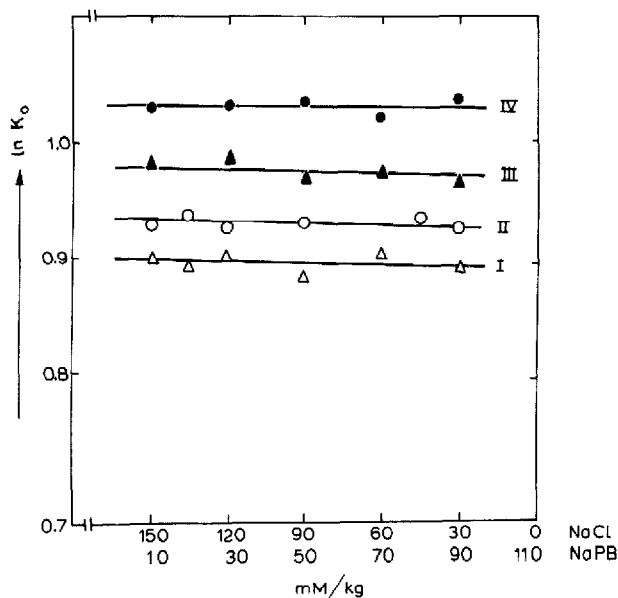


Fig. 1. Logarithm of the partition coefficient of PVA with different percentages of acetate groups as a function of the ionic composition of the Ficoll-400-dextran-70 two-phase system. 1 = PVA with 1% of acetate groups; 2 = PVA with 6% of acetate groups; 3 = PVA with 12% of acetate groups; 4 = PVA with 18% of acetate groups. NaPB = sodium phosphate buffer (pH 7.4).

is the partition coefficient of the solute in the reference system and a_i and b_i are constants. The a_i and b_i values determined as described earlier¹ were found to be 1.416 and -0.139 , respectively, and to be independent of the ionic composition of the systems compared under the conditions used.

It has been shown⁶ that the partition coefficient of a non-ionic solute can be described by the equation

$$\ln K = n^{\text{CH}_2} E \quad (2)$$

where E characterizes the difference in the hydrophobic character of the two phases of the system (according to the equation $\Delta G_{\text{tr}}^{\text{CH}_2} = -RTE$, where $\Delta G_{\text{tr}}^{\text{CH}_2}$ is the free energy of transfer of a CH_2 group between the phases^{2,6}, and n^{CH_2} is the equivalent number of CH_2 groups that characterizes the intensity of the interactions of the

TABLE I

HYDROPHOBIC CHARACTER OF PVA WITH VARIOUS DEGREES OF ACETYLTATION

The hydrophobic character of the polymers is independent of the molecular weight of the polymers in the range $2 \cdot 10^4$ – $1 \cdot 10^5$.

Percentage of acetate groups	$n^{\text{CH}_2} \pm S.D.$
1.0	33.4 ± 1.0
6.0	34.8 ± 0.8
12.0	36.4 ± 0.8
18.0	38.2 ± 1.0

solute with an aqueous environment relative to that of a CH_2 group, *i.e.*, it is a measure of the relative hydrophobicity of the solute under the given conditions of the aqueous medium^{1-3,5,6}.

E is independent of the ionic composition of the Ficoll-dextran two-phase system under the conditions used^{2,6}. Some of the typical relationships between the logarithm of the partition coefficient of the polymers examined and the ionic composition of the system are presented in Fig. 1. It can be seen that all the relationships established are in agreement with eqn. 2. The n^{CH_2} values for the polymers examined are given in Table I.

DISCUSSION

The results in Table I indicate that the relative hydrophobicity of PVA depends on the degree of acetylation of the polymer according to the equation

$$n^{\text{CH}_2} = 33.1 + 0.28N \quad (r^2 = 0.999) \quad (3)$$

where n is the percentage of acetate groups in PVA, varying from 1% up to 18%, and r^2 is the correlation coefficient.

It should be noted that it has been observed earlier⁴ that both coefficients K_η and α_η in the Mark-Houwink viscosity equation $[\eta] = K_\eta M^{\alpha_\eta}$ depend on the percentage of acetate groups in PVA. This fact and eqn. 3 seem to indicate that there is a relationship between both K_η and α_η and the relative hydrophobicity of the polymer, n^{CH_2} . This seems to imply that both coefficients in the Mark-Houwink equation are related to the intensity of the macromolecule-solvent interactions. It should be noted, however, that an examination of the hydrophobic character values reported for polyethylene glycol, polyacrylamide and polyvinylpyrrolidone¹ in comparison with the K_η and α_η values for these polymers shows that there is no general relationship between the above characteristics. Hence, it is possible to conclude that the intensity of the macromolecule-solvent interactions only partially affects the K_η and α_η values.

TABLE II

CHARACTERISTICS OF THE EFFECT OF THE MOLECULAR WEIGHT OF POLYMERS ON THEIR RELATIVE HYDROPHOBICITY

The effect is described by $n^{\text{CH}_2} = \alpha p^\beta$ (eqn. 4), where p is the degree of polymerization.

Polymer	M_w range	α	β
Polyethylene glycol	$1.5 \cdot 10^3 - 4 \cdot 10^4$	170	0
Polyvinylpyrrolidone	$5 \cdot 10^3 - 1.8 \cdot 10^5$	201.1	-0.190
Polyacrylamide	$1 \cdot 10^4 - 5 \cdot 10^5$	-17.31	0.217
Poly(vinyl alcohol):			
1% Ac*	$2 \cdot 10^4 - 1 \cdot 10^5$	33.4	0
6% Ac	$2 \cdot 10^4 - 1 \cdot 10^5$	34.8	0
12% Ac	$2 \cdot 10^4 - 1 \cdot 10^5$	36.4	0
18% Ac	$2 \cdot 10^4 - 1 \cdot 10^5$	38.2	0

* Ac = acetate groups.

The observed independence of the relative hydrophobicity of PVA with a given degree of acetylation of the molecular weight (M_w) of the polymer (in the M_w range $2 \cdot 10^4$ – $1 \cdot 10^5$) seems to support the assumption⁴ that the relative intensity of the PVA–water interactions is governed by some part of the polymer's groups that is capable of participating in these interactions and not engaged in the intramolecular interactions. It should be noted that the results reported earlier⁴ and those presented in Table I appear to indicate that there is a relationship between the relative hydrophobicity of macromolecules and their capability of altering the thermodynamic properties of an aqueous solution. This assumption is under study at present.

The estimates of the hydrophobic character of PVA with different degrees of acetylation are presented in Table II together with those for polyvinylpyrrolidone (PVP), polyethylene glycol (PEG) and polyacrylamide (PAAm) reported previously¹. The relative hydrophobicity of PVP and PAAm depends on the molecular weight of the polymer¹ according to the equations given in Table II. The equations are presented in a form representing the effect of the degree of polymerization, p , on the hydrophobic character of a given polymer:

$$n^{\text{CH}_2} = \alpha p^\beta \quad (4)$$

where α and β are constants specific for a given polymer. From eqn. 4, it is clear that α can be considered as a measure of the relative hydrophobicity of a monomeric unit of the polymer chain in question. An examination of the α values in Table II, however, indicates complete disagreement between these values and the estimates reported in the literature^{7,8} for the hydrophobic character of the monomeric units of the polymers under consideration. It seems likely that this disagreement is due to the effect of the macromolecular nature of a substance on its physico-chemical characteristics. It is known⁹ that the hydrophobic character of a particular group often depends on the nature of the neighbouring groups and on the conformation of the molecule. Hence, it seems possible that monomeric units of a given polymeric chain are different in relation to the macromolecule–solvent interactions.

As a first approximation it can be assumed that there are only two different types of the monomeric units in a given polymeric chain. The first type includes the so-called non-effective units, which make no contribution to the interactions of the polymeric chain with the solvent. The second type includes the so-called effective units, which are assumed to be characterized by equal contributions to the macromolecule–solvent interactions. It can be also assumed that all the monomeric units of the polymeric chain with a length of less than 50 units are equally effective. If this is so, it is possible to estimate the relative hydrophobicity of the polymer's effective monomeric unit using the n^{CH_2} values obtained for the polymers with a degree of polymerization $p \leq 50$.

The values of $n_{\text{eff}}^{\text{CH}_2}$ obtained for the effective monomeric units of PEG and PVP are presented in Table III. These values are of the same order as those obtained by using the Hansch hydrophobic substituent constants⁸. From the $n_{\text{eff}}^{\text{CH}_2}$ values and the experimentally determined estimates of the relative hydrophobicity of PEG and PVP of different chain lengths, it is possible to calculate the number of effective monomeric units, p_{eff} , for the polymers under examination. The calculated p_{eff} values are given in Table III. It can be seen from Fig. 2 that the relationship between the degree of

TABLE III
CHARACTERISTICS OF POLYMER-SOLVENT INTERACTIONS

Polymer	p	n^{CH_2}	p_{eff}	$n_{\text{eff}}^{\text{CH}_2}$	p_{eff}/p	f^*	k^*	p_0
Polyethylene glycol	34	170	34	5.0	1.0	1.535	-1.002	34.3
	136	170	34		0.25			
	454	170	34		0.075			
	909	170	34		0.037			
Polyvinylpyrrolidone	45	102.5	45	2.8	1.0	1.905	-1.177	80.4
	108	75.8	33		0.305			
	153	71.0	31		0.203			
	450	64.8	27		0.060			
	1622	49.3	23		0.014			
Polyacrylamide	149	-51.0	25	-2.04	0.168**	0.930	-0.784	8.5
	937	-76.4	38		0.040**			
	6394	-106.3	51		0.008**			
	6901	-126.8	62		0.009**			
Poly(vinyl alcohol): 1% Ac***	454	33.4	34	0.98	0.075**	1.474	-0.982	29.8
	909	33.4	34		0.037**			
	1363	33.4	34		0.025**			
	1818	33.4	34		0.019**			
	2273	33.4	34		0.015**			
6% Ac [§]				1.02				
12% Ac [§]				1.07				
18% Ac [§]				1.12				

* f and k are constants in eqn. 5.

** Values calculated as described in the text.

*** Ac = acetate groups.

§ For PVA with 6%, 12% and 18% of acetate groups, only the characteristics unlike those for PVA with 1% of acetate groups are given.

polymerization, p , and the relative number of effective monomeric units, p_{eff}/p , is given by

$$\log (p_{\text{eff}}/p) = f + k \log p \quad (5)$$

where f and k are constants.

There was no available fraction of PVA with a degree of polymerization less than 50. Therefore, the p_{eff} and p_{eff}/p values for PVA given in Table III were calculated assuming that the p_{eff}/p value for PVA with a p value of 909 is 0.037, as for PEG. This assumption is clearly a rough approximation. It is based on the observed common character of the curve in Fig. 2 for PEG and PVP. An indirect confirmation of the assumption is considered below. The same assumption was used when considering the results obtained for PAAM. The p_{eff}/p and $n_{\text{eff}}^{\text{CH}_2}$ values for PVA and PAAM are presented in Table III.

It follows from the data in Table III that the relative hydrophobicity of an effective monomeric unit of PVA with 1% of acetate groups is equivalent to that of

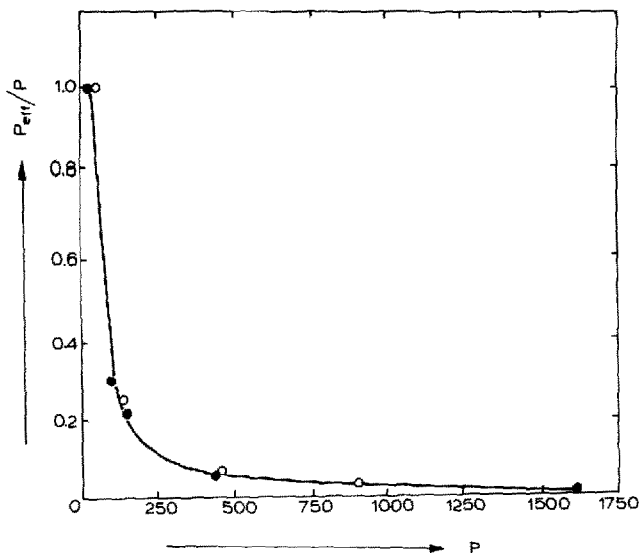


Fig. 2. Relative number of effective monomeric units in the polymeric chain, p_{eff}/p , as a function of the total number of units, p , for PEG (O) and PVP (●).

0.98 CH_2 group and that of the unit of PVA with 18% of acetate groups is equivalent to that of 1.12 CH_2 . It follows from these estimates that the relative hydrophobicity of an effective monomeric unit of PVA without acetate groups is equivalent to that of 0.97 CH_2 groups and the relative hydrophobicity of the monomeric unit of poly(vinylacetate) is equivalent to that of 1.97 CH_2 groups, *i.e.*, the latter unit is more hydrophobic than the former by 1.0 equivalent CH_2 groups. It should be noted that the difference between the relative hydrophobicities of the above units estimated from the results reported by Leo *et al.*⁸ amounts to 0.84 equivalent CH_2 groups. Hence, the estimates of the hydrophobic character of the units under consideration obtained on the basis of the above assumptions are in good agreement with those reported in the literature^{7,8}.

The values of the constants f and k in eqn. 5 determined for the polymers under study are given in Table III. It is clear that eqn. 5 can be expressed in the form

$$p_{\text{eff}} = p_0 p^m \quad (6)$$

where p_0 and m are constants: $m = k + 1$ and $p_0 = 10^f$. It is evident that formal considerations allow one to put any p value in eqn. 6. If $p < p_0$, however, the p_{eff} value will exceed that of the total degree of polymerization, p , which is physically impossible. The p_{eff} value is equal to or less than p only when the p value is equal to or exceeds p_0 . Therefore, it seems reasonable to suggest that the p_0 value characterizes the ultimate number of monomeric units in the polymeric chain under which all the units give similar contributions to the total relative hydrophobicity of the macromolecule. When the polymeric chain length, p , exceeds the ultimate number p_0 , only part of the units participate in the polymer-solvent interactions, *i.e.*, the macromolecular effect is observed. The p_0 values given in Table III appear to be of a similar

order to that of Kuhn segments which are representative of the hydrodynamic properties of the macromolecules.

It seems that a study of the p_0 values for various synthetic and biological macromolecular compounds may be useful in obtaining a better insight into the mechanisms of polymer-solvent interactions. Further studies are in progress at present.

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