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Size-exclusion chromatographic and viscometric study of polymer solutions containing nicotine or silicic acid

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Abstract

Preferential interactions of polymers with low-molecular-mass compounds were investigated regarding mainly the preferential solvation parameter and the intrinsic viscosity of ternary polymer solutions. Well characterized poly(vinylpyrrolidone) and poly(4-vinylpyridine) as macromolecular components in the presence of pure water or buffered solutions of nicotine or silicic acid served to formulate several ternary systems. Measurements included size-exclusion chromatography (SEC) and viscometry (off-line) at the appropriate concentration ranges, in order to obtain a linear response of the SEC detector and to describe the concentration dependence of the reduced viscosity by means of the Huggins equation for dilute polymer solutions. The former technique allows the so-called vacant peak to be attained, closely related to the preferential solvation parameter, which was directly monitored by means of a refractive index detector. Numerical evaluation of the preferential solvation parameter and intrinsic viscosity was used to account for overall interactions between linear vinyl polymers and nicotine and silicic acid as precursors of toxic agents.

1. Introduction

Polymers dissolved in a binary mixture of two low-molecular-mass molecules can often exhibit preferential solvation phenomena. In other words, the concentration of the solution in the close vicinity of the macromolecules is different from that in the bulk solution. Theoretical and experimental aspects of preferential solvation have been reported in the past mainly concerning synthetic polymers in binary organic and inorganic mixtures [1–4]. The first concerns to both Flory–Huggins and Flory–Prigogine–Patterson theories of polymer solutions, where complex expressions dealing with this phenomena have been reported [5,6]. From an experimental viewpoint over the past two decades, there has been increasing interest in incorporating new techniques and in developing the corresponding theoretical background. The pioneering experimental techniques available include equilibrium dialysis in conjunction with differential refractometry and light scattering, which are now employed fairly widely [7–9]. Others developed more recently include ultracentrifugation [10], differential densitometry and NMR, infrared and fluorescence spectroscopy [11–14]. Despite the important progress in experiment and theory, gaps in our knowledge still exist

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regarding multi-component polymer solutions [15–18].

In 1976, Berek *et al.* [19] reported a method based on the so-called "vacant peak" for polymer–mixed solvent systems, which was monitored by high-performance size-exclusion chromatography (HPSEC), assuming proportionality between the amount of polymer injected and the area of this singular peak. Since then, this assumption has made amenable the direct determination, rapidly and accurately, of the preferential solvation parameter, λ, by means of the SEC technique. Full details of the operational procedure and theoretical basis of this method have been given elsewhere [20–22]. Liquid chromatography has become one of the most widely used techniques for the evaluation of λ using size-exclusion and reversed-phase separation mechanisms [23,24].

We present in this paper a study of preferential solvation for poly(vinylpyrrolidone) (PVP) and poly(4-vinylpyridine) (P4VPy) in binary aqueous solutions of a toxic agent such as nicotine (NIC) or silicic acid (SA). PVP was selected because of its biocompatible character, so that it is suitable for use in injections and other parenteral applications. Moreover, the polymer is supplied in various molecular mass grades, including specially purified grades for pharmacological applications [25–27]. Nicotine is a highly toxic alkaloid which was first isolated in 1828 from tobacco, being present in amounts of 0.5–8.0% by mass. It exists as a tertiary amine with one chiral carbon located at the 2′-position of the N-methylpyrrolidine ring. Nicotine and other related metabolites can be found in the urine and hair of smokers and most non-smokers [28,29]. Moreover, the salt form has been used as a natural insecticide [30], and the free base as an anthelmintic agent in medicine [31] and as an experimental drug in the treatment of Parkinson's and Alzeimer's diseases [32,33]. Numerous gas chromatographic (GC) and liquid chromatographic (LC) [29,34,35] methods for assaying nicotine have been reported. The last low-molecular-mass component involved in this work is the (macro) silicic acid, $Si(OH)_4$, which was selected because of the toxicological character of silica dust [36]. Silica dissolves in water to form monosilicic acid. It has been found that the toxic effects of silica are due to the capacity of silicic acid to act as a hydrogen donor in the formation of hydrogen-bonded complexes with active groups such as phospholipids or secondary amide groups of proteins [37–39].

We formulated the following ternary polymer systems: water–nicotine–PVP and water or buffer solution–PVP–silicic acid, the two first components being considered as a binary solvent and the third as the solute. In choosing these compounds for study we were guided by the desire to correlate macroscopic physico-chemical properties of the polymer, represented by the preferential solvation parameter and the intrinsic viscosity, with the protective effects of some polymers on the toxicity exhibited by some low-molecular-mass substances, of which nicotine or silicic acid were selected in this work owing to their organic and inorganic nature, respectively.

2. Experimental

2.1. Chemicals and reagents

HPLC-grade water was produced by a Milli-Q water-purification system (Millipore, Bedford, MA, USA), consisting of prefilter, charcoal, ion-exchange and Organex cartridges. Buffer solutions were prepared using different reagents such as $NaHCO_3$, NaOH, $NaCH_3COO \cdot 3H_2O$ and CH_3COOH and Milli-Q-purified water. All reagents were of analytical-reagent grade from Merck (Darmstadt, Germany). Dextran samples obtained from Pharmacia (Uppsala, Sweden) of nominal molar masses 10, 17.7, 40, 66.9, 83.3, 170 and 500 kg mol^{-1} were used as standards for SEC column calibration. Poly(vinylpyrrolidone) of two molecular mass grades, 10 and 40 kg mol^{-1}, were obtained from Fluka (Darmstadt, Germany). Nicotine (NIC) and silicic acid (SA) were of puriss reagent grade from Merck. All reagents were used as obtained from the supplier. A poly(4-vinylpyridine) (P4VPy) sample was obtained by ultrafiltration of a commercial

sample of nominal molecular mass 40 kg mol^{-1}, supplied by Polysciencies (Washington, PA, USA). Ultrafiltration was carried out with a Millipore 142-mm diameter HI-FLUX UF cell.

2.2. Chromatographic measurements

A Waters Model ALC/GPC 202 liquid chromatograph equipped with an M-45 solvent-delivery system, a U6K universal injector and an R-410 refractive index detector was used. All chromatograms were recorded on a Spectra-Physics Model 4290 computing integrator, which was set at an attenuation of 4 or 8 for experiments involving SA or NIC, respectively. A Spherogel TSK PW 4000 column with 500 Å nominal pore size was used. The interstitial packing volume and total pore volume were 5.15 and 10.40 ml, as measured with high-molecular-mass dextran and ^2H_2O, respectively. The mobile phase flow-rate was adjusted to 1.0 ± 0.02 ml and thermostated at 25.0 ± 0.1°C in all experiments.

Two sets of experiments were performed. In those involving PVP as solute, the mobile phases were dilute solutions of NIC in pure water; in those involving SA as solute, the following mobile phases were prepared: solution of PVP-10 in a $NaHCO_3$–NaOH buffer (pH 10.0), solution of PVP-40 in the same buffer, PVP-10 in pure water, PVP-40 in pure water and P4VPy in NaOAc–CH_3COOH buffer (pH 4.0). The mobile phase compositions and the solute concentrations (PVP or SA) will be indicated in the next section.

The column was equilibrated overnight before injection of the analyte solution, which was always prepared using the corresponding mobile phase as solvent. Eluents and solutions injected were degassed and filtered, in all instances, through regenerated cellulose 0.45-μm pore diameter filters from Micro Filtration Systems (Dublin, CA, USA). The calibration graph for TSK PW 4000, using dextrans as standards, was obtained by extrapolation to zero concentration of peak elution volumes obtained for at least three injected concentrations.

2.3. Viscosities

Viscosity measurements were performed with an AVS 440 automatic Ubbelohde-type capillary viscometer from Schott Geräte (Hofheim, Germany). The instrument was equipped with a Model CT 1450 thermostated bath and with a Model T80.20 piston burette, moved by a microprocessor-controlled stepping motor for sample autodilution. For each solution, a 15-ml sample was loaded into the viscometer and placed in the thermostated bath. Measurements were initiated after an equilibration time of *ca.* 5–10 min and were continued until several elution time readings agreed to within 0.5%. All the viscosity measurements were performed at 25.0 ± 0.1°C. The viscosity η follows from $\eta = A\rho t - B\rho/t$, ρ being the solution density, t the elution time and A and B calibration constants. Elution times were determined as the average of several readings and the values obtained for the calibration constants were $A = 4.943 \cdot 10^{-5}$ cm^2 s^{-2} and $B = 1.783 \cdot 10^{-2}$ cm^2.

3. Results and discussion

Table 1 lists the polymer–toxic agent systems studied. Sample codes in the first column with N and S refer to those containing nicotine and silicic acid, respectively The probes (second column) were PVP for N-systems and SA for S-systems. Note that in the first set of systems, the toxic agent (NIC) exists as a component of the solvent, whereas the polymer probes act as the solute. In contrast, in the second set of systems PVP exists as a component of the binary solvent whereas the SA probe acts as the solute. The reason for using the systems in this particular form was the low solubility of SA in pure water [39], whereas its solubility increases when binary aqueous solutions, as shown in Table 1, are used instead of pure water.

As outlined in the Introduction, we explored the polymer–toxic agent interactions by means of SEC and viscometric (off-line) techniques. The proposed analysis is based on the evaluation of the preferential solvation parameter, λ, and of

Table 1
Polymer–toxic agent systems studied in different aqueous media, with the range of concentrations covered by each component, expressed as % (w/v), for λ determination in parentheses

Code	Probe	Binary eluent
N1	PVP-10 (0.1–0.8)	Water + nicotine (0.20–0.45)
N2	PVP-40 (0.4–1.7)	Water + nicotine (0.20–0.45)
S1	SA (0.016–0.035)	Water + PVP-10 (0.25–0.40)
S2	SA (0.010–0.030)	Water + PVP-10 (0.20–0.40)
S3	SA (0.015–0.045)	Buffer (pH 10) + PVP-10 (0.20–0.45)
S4	SA (0.015–0.045)	Buffer (pH 10) + PVP-40 (0.20–0.45)
S5	SA (0.005–0.035)	Buffer (pH 4) + P4VPy (0.10)

the reduced viscosity (η_{sp}/c). Next, we outline briefly the theoretical background for ternary polymer systems, dealing with the above parameters. Thus, for convenience, we begin by reproducing some of the previously derived equations because they are required for the discussion.

(a) When a solvent (1) is preferentially adsorbed by a polymer in a ternary system S(1)–S(2)–polymer(3), λ can be defined as the change in the volume fraction of component 1 with respect to the polymer concentration at infinite dilution. Thus, the expression for λ would be [20]

$$\lambda = \frac{\Delta\nu_1^0}{c_3} \cdot \frac{A_2}{A_1(+,-)} \tag{1}$$

c_3 being the concentration of the component designated the probe in Table 1 and $\Delta\nu_1^0$ refers to the difference in the volume fraction of the solute between the solution and the mixture (binary eluent), being related to the peak area obtained in the calibration (*i.e.*, NIC) A_1. Subsequent injection of a ternary system will give a vacant NIC peak area, A_2. Thus, the preferential interaction parameter, λ, can be calculated from the experimentally observed parameters through Eq. 1.

(b) The viscosity of binary polymer solutions at low concentrations can be expressed as

$$\eta(c) = \eta_s(1 + [\eta]c + k_H[\eta]^2c^2 + \cdots) \tag{2}$$

where η_s is the solvent viscosity, $[\eta]$ the intrinsic viscosity of the polymer and k_H the Huggins coefficient.

Rearrangement of Eq. 2 yields

$$\frac{\eta_{sp}}{c} = [\eta] + bc \tag{3}$$

where $b = k_H[\eta]^2$ and

$$\frac{\eta(c) - \eta_s}{\eta_s c} = \frac{\eta_{sp}}{c} \tag{4}$$

The same functionality can be assumed for ternary systems, here PVP in a binary mixture composed of pure water or buffered solution in the presence of NIC or SA. In this way, the viscosity of a ternary solution at low concentrations can be similarly expressed as

$$\left(\frac{\eta_{sp}}{c}\right)_m = [\eta]_m + b_m c_m \tag{5}$$

where the subscript m denotes the polymer–toxic agent mixture. A plot of Eq. 5 will yield $[\eta]_m$ and b_m from the intercept and the slope, respectively. In the light of this equation, two features can be examined: the dimension of the PVP coils, as evidenced by $[\eta]_m$, and the polymer–toxic agent interaction, as evidence by b_m.

3.1. Calibration of RID response

Before injecting a ternary solution formed by the probe in a binary solvent, as listed in Table 1, an NIC solution of known concentration in a given solvent mixture was injected. The difference in the volume fraction of NIC between the above solution and the mixture, $\Delta\nu_1^0$, was related

to the area of the NIC peak, A_1. Subsequent injection of a ternary system will give a vacant NIC peak area, A_2. The application of Eq. 1 with the above parameters as input data allows us to obtain the λ values for both the N- and S-systems listed in Table 1.

Fig. 1 displays the detector response on injection of diverse aqueous NIC solutions, with [NIC] ranging from 0.06 to 0.34% (w/v). The baseline corresponds to a 0.20% aqueous solution of NIC. A derivative-shaped signal was observed on injection of NIC solutions at concentrations other than 0.20%. Hence, when the values of [NIC] are greater than 0.20%, the direction of this signal first shows an increase, denoted by (+). In contrast, when the contrary occurs, the signal obtained then decreases (−) in the relative transmittance. Fig. 2 depicts the plot of the deviation of [NIC] with respect to the reference binary eluent, [NIC] = 0.20% as indicated above, against the area of the deflection peaks shown in Fig. 1. A good linear correlation was found for both the positive N(+) and negative N(−) directions of signal deflection for

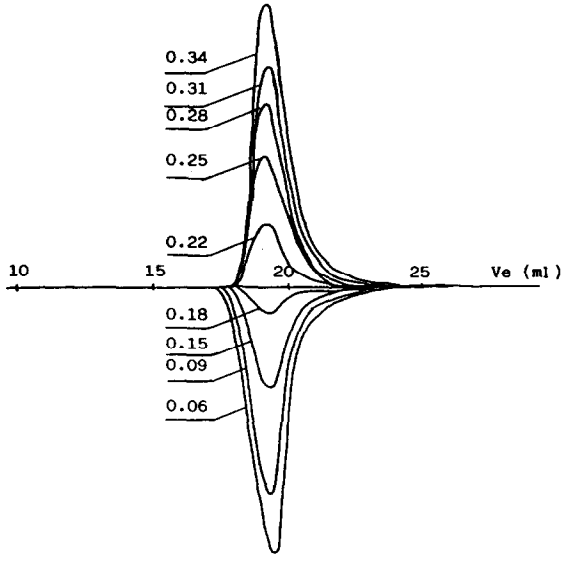

Fig. 1. Positive (●) and negative (○) signal deflections from refractive index detector on injection of 500 μl of nicotine solutions. Baseline corresponds to a mobile phase composition of 0.20% aqueous solution of nicotine and the detector attenuation is fixed at 8.

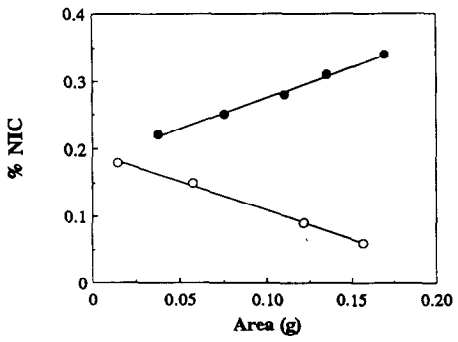

Fig. 2. Calibration graph for the deflection peaks obtained from different nicotine solutions. Symbols [○ = N(−); ● = N(+)] refers to experimental data and lines to a linear regression fit. Mobile phase composition corresponds to a 0.20% aqueous solution of nicotine.

nicotine-containing eluents. The same procedure was applied to calibrate the silicic acid-containing systems. The linear regression equations and their correlation coefficients are given in Table 2 for all the systems studied; $A(+,-)$ denotes the area of the deflection peak in both directions.

3.2. Evaluation of λ

We next proceeded to obtain the elution profile of diverse ternary polymer systems constituted by a probe in a binary eluent as specified in Table 1. When size exclusion is the main factor governing the separation mechanism in LC, the first peaks correspond to macromolecular species whereas the last peak or "vacant peak" denotes preferential interaction of the polymer, PVP or P4VPy, with one of the remaining components. As an example, Fig. 3 shows the elution profile of PVP-10 (0.30%) in an eluent formed by a dilute aqueous solution of NIC (0.20%). The amount of NIC preferentially solvated by PVP can be evaluated from the area of the last peak in conjunction with the calibration $A(-)$ equation from Table 2 for the nicotine-containing systems, and Eq. 1 for λ determination. Fig. 4 shows λ values as a function of both PVP and NIC concentrations. From Fig. 4a, there was no clear dependence of λ for PVP-10 on the above parameters because a gross scatter of data has been found. Fig. 4b shows the same plot for

Table 2
Calibration equations of the detector response on injection of diverse binary mixtures at different compositions

Mobile phase[a]	Code	Calibration equation[b]	Correlation coefficient
Water + NIC (0.20)	N1, N2	$A(+) = 0.1823 + 0.9242$ [NIC]	0.9977
	N1, N2	$A(-) = 0.1954 - 0.8594$ [NIC]	0.9986
Water + PVP-10 (0.20)	S1	$A(-) = 0.2025 - 0.2327$ [PVP-10]	0.9979
Water + PVP-40 (0.25)	S2	$A(-) = 0.2456 - 0.4637$ [PVP-40]	0.9978
Buffer (pH 10) + PVP-10 (0.20)	S3	$A(+) = 0.2237 + 0.4334$ [PVP-10]	0.9872
	S3	$A(-) = 0.2094 - 0.6273$ [PVP-10]	0.9950
Buffer (pH 10) + PVP-40 (0.20)	S4	$A(+) = 9.8847 + 0.2621$ [NaOH]	0.9761
	S4	$A(-) = 9.9021 - 0.1235$ [NaOH]	0.9993
	S4	$A(-) = 25.378 - 61.337$ [$NaHCO_3$]	0.9912
	S4	$A(+) = 0.1949 + 0.0013$ [PVP-40]	0.9996
	S4	$A(-) = 0.1900 - 0.0019$ [PVP-40]	0.9996
Buffer (pH 4) + P4VPy (0.10)	S5	$A(-) = 0.1003 - 0.3097$ [P4VPy]	0.9970

[a] Values in parentheses are concentrations of the second component (%).
[b] $A(+/-)$ refers to the area of the signal deflection when the direction shows an increase or a decrease in the relative transmittance.

PVP-40, the scatter of points being more pronounced and the λ values lower than those for the preceding systems. It is clear that the values of λ are strongly dependent on the PVP molar mass, being more pronounced as the latter decreases. In contrast with most polymer–mixed solvent systems, where the value of the preferential interaction parameter changes from positive to negative or *vice versa*, going through a maximum (or minimum) depending on the cosolvent or co-non-solvent behaviour of the binary solvent mixture [15–18], for the N-systems studied here the condition $\lambda = 0$ was not reached, at least in the range of NIC concentrations assayed.

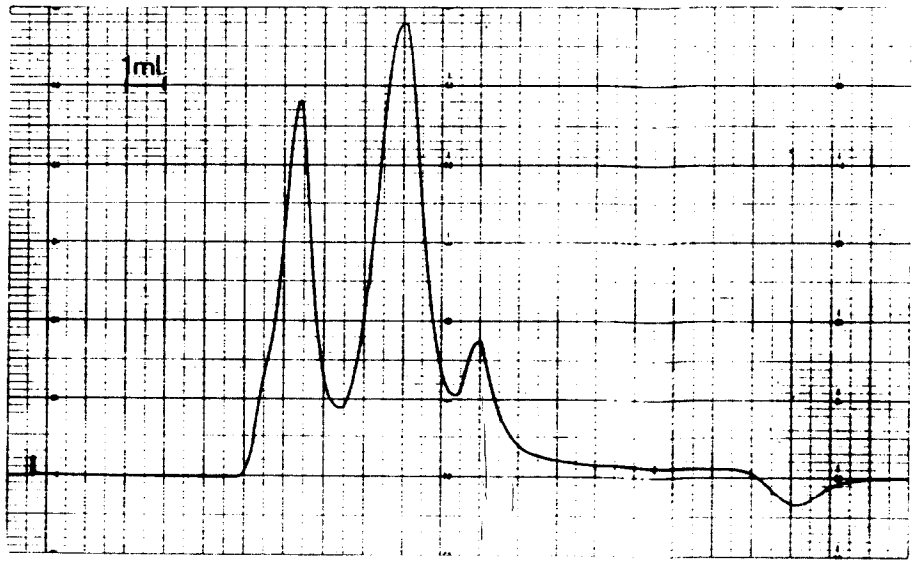

Fig. 3. Elution profile of poly(vinylpyrrolidone) (M_r 10^4) at 0.30% in a 0.20% solution of nicotine as eluent. The last signal corresponds to vacant peak.

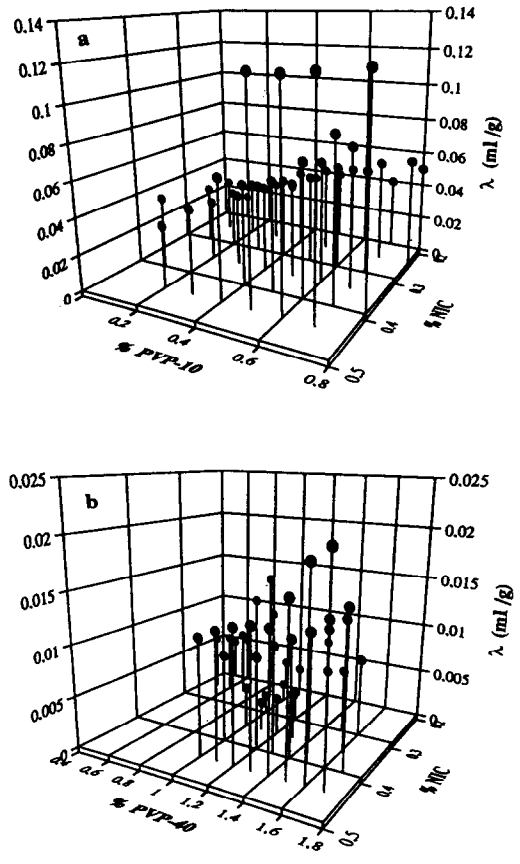

Fig. 4. Dependence of the experimental preferential interaction parameter λ (from Eq. 1) on nicotine and poly(vinylpyrrolidone) concentrations. PVP molar mass: (a) 10^4 and (b) $4 \cdot 10^4$ g/mol.

Moreover, a positive value of the preferential solvation parameter at low NIC concentrations means that these are more nicotine molecules in the vicinity of PVP because of the high affinity of nicotine for this polymer. The affinity of PVP for diverse co-solute molecules has been explained in depth by Molyneaux and Vekavakayanondha [40], but from our experimental measurements nothing can be inferred about these specific interactions.

Fig. 5a and b illustrate plots of the dependence of λ on SA and PVP concentrations in aqueous buffer (pH 10.0) media, corresponding to systems S3 and S4 in Tables 1 and 2, respectively. The same methodology as detailed above for N-systems was used for the evaluation of λ. From Fig. 5a, it can be seen that the λ values become higher at lower contents of both SA and PVP-10 components. A sudden increase in λ close to [PVP-10] = 0.25% and [SA] < 0.03% is observed, being positive in all instances. The positive values of λ at low SA concentrations mean that there are more SA molecules in the vicinity of PVP-10 as a consequence of the high affinity between both components under the adopted conditions. The same arguments can be used to explain the evolution of λ values for S-systems containing PVP-40, showed in Fig. 5b. However, in the latter system the λ values increase smoothly as both SA and PVP-40 concentrations decrease, being 50% lower than those obtained for the system in Fig. 5a.

In order to explore the effect of the aqueous media on λ, we applied two systems referred to as S1 and S2 in Tables 1 and 2, with the same polymer–toxic agent pairs dissolved in pure water instead of the above buffered solution. All details of the compositions and the calculation of the $A(+,-)$ parameter, necessary to apply Eq. 1, are also included in Tables 1 and 2. Fig. 6 depicts λ values as a function of both SA and PVP concentrations; the lines connecting points were drawn for the sake of visualization. Thus, for systems S1 and S2, positive λ values were always obtained, increasing as the SA and NIC concentrations decreased. The same trend was observed for systems S3 and S4 (see Fig. 5). An interesting observation from Fig. 6 is that λ increases as the PVP molar mass increases, in contrast with that observed in Fig. 5, where the opposite trend was found. The reason for this behaviour is not understood. In addition, from comparison of the λ values plotted in Figs. 5 and 6, it is clear that the data from the former are, in all instances, higher than those in the latter. For example, choosing as a representative value from each figure the top value for λ, we can see that 0.08 and 0.1 correspond to systems S1 and S2 where pure water is the bulk solvent, whereas for systems S3 and S4 where the bulk solvent is buffer (pH 10.0) solution, λ values of 0.6 and 0.3, greater than the preceding ones, were obtained. In the light of these results, it can be inferred that the change in the bulk water

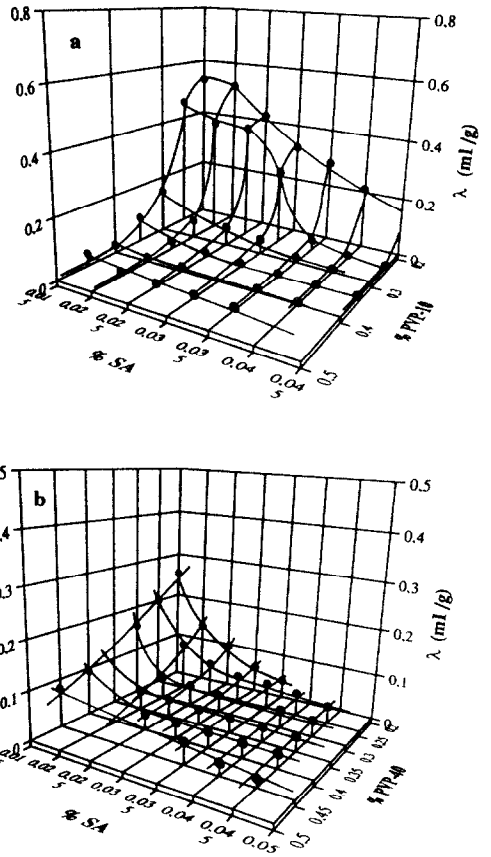

Fig. 5. Dependence of the experimental preferential interaction parameter λ (from Eq. 1) on silicic acid and poly(vinylpyrrolidone) concentrations. The bulk solvent is a buffer solution of pH 10.0.

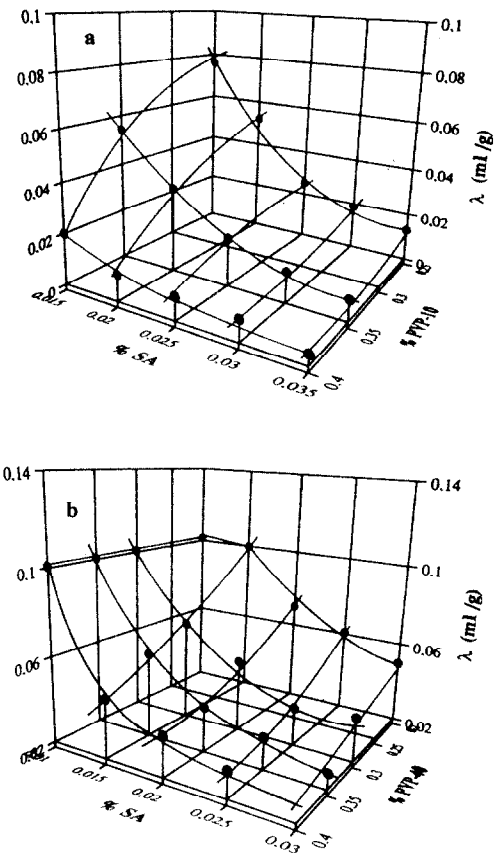

Fig. 6. Dependence of the experimental preferential interaction parameter λ (from Eq. 1) on silicic acid and poly(vinylpyrrolidone) concentrations. The bulk solvent is pure water.

structure on addition of electrolytes, as for systems S3 and S4, plays an important role in facilitating the diffusion of SA molecules in the vicinity of the polymer coil.

Lastly, we conducted exploratory experiments on a polymer containing pyridine rings instead of pyrrole in order to discuss the effect of the functional group on λ. A 0.10% solution of P4VPy in buffer (pH 4.0) as eluent and SA solutions as solute were used in SEC experiments. This system is denoted S5 and the concentration range covered by the SA is given in Table 1. The $A(-)$ values necessary to apply Eq. 1 were also obtained from a linear regression fit and the corresponding equation is reported in Table 2. The λ values obtained for this system are depicted in Fig. 7, where a unique mobile phase composition was applied. This plot reveals that λ follows a similar trend to that observed for the already discussed S-systems. As the molar masses of PVP-40 and P4VPy are the same, it seems reasonable to compare the λ values obtained for the systems where both polymers are involved. This comparison can easily be done by inspection of Figs. 5b, 6b and 7b, and it is concluded that the dependence of λ on P4VPy and SA concentrations follows qualitative and quantitatively the same trend as in S-systems.

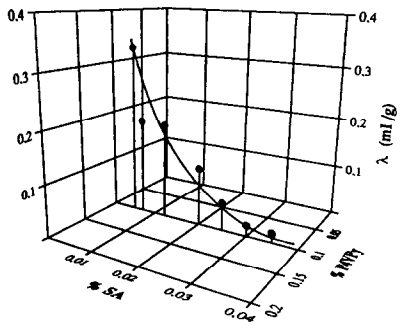

Fig. 7. Dependence of the experimental preferential interaction parameter λ (from Eq. 1) on silicic acid concentration, using a 0.1% solution of poly(4-vinylpyridine) in buffer of pH 4.0 as eluent.

3.3. Viscosity from ternary solutions

Results from binary and ternary solutions were compared to determine if the interaction between the polymer and the toxic molecules produces some additional effects. Two features were analysed: the dimension of the polymer coil, as evidenced by $[\eta]_m$, and the polymer–toxic agent interaction, quantified by the parameter b_m from Eq. 5.

The intrinsic viscosities and Huggins coefficients for binary systems, such as PVP-10, PVP-40 and P4VPy in pure water, buffer (pH 10.0) and buffer (pH 4.0), were determined from the dilute binary solution data, not reported here for simplicity. Plotting these data according to Eq. 3 produced $[\eta]$ and b from the intercept and slope, respectively. Table 3 gives these data along with the correlation coefficient, yielding fair linear fits, as expected.

The ternary solution viscosities were plotted according to Eq. 5. The intercepts $[\eta]_m$, the slopes b_m and the correlation coefficients are also given in Table 3. The nicotine-containing systems exhibit a concentration dependence of the reduced viscosity with two zones clearly delimited by a crossover concentration, $c_m^* = 0.15 \cdot 10^{-3}$ g ml^{-1}. At $c_m < c_m^*$, the reduced viscosity shows a reasonable linear behaviour, indicating that Eq. 5 is an adequate representation of the viscosity; however, at $c_m > c_m^*$, both $[\eta]_m$ and b_m are not dependent on concentration, at least in the concentration range measured. In Table 3 the data obtained for the intercept and slope of Eq. 5 for the PVP-10 + NIC and PVP-40 + NIC systems in pure water are also given. Comparison of the intercept values for binary PVP-10 + pure water and ternary PVP-10 + NIC + pure water systems at $c_m < c_m^*$, indicates that there is a

Table 3
Viscosity data at 25°C for pure polymer (Eq. 3) and for polymer–toxic agent mixtures (Eq. 5) in different aqueous media

Solute	Solvent	Intercept (ml g^{-1})	Slope	Correlation coefficient
PVP-10	Pure water	7.90	0.019	0.987
PVP-40	Pure water	21.6	0.136	0.997
PVP-10	Buffer (pH 10.0)	5.71	0.146	0.998
PVP-40	Buffer (pH 10.0)	18.7	0.351	0.998
P4VPy	Buffer (pH 4.0)	149.8	2.184	0.985
PVP-10 + NIC	Pure water	6.21	−0.058	–
		11.0	−4.210	–
PVP-40 + NIC	Pure water	12.7	−0.056	–
		15.8	−1.479	–
PVP-10 + SA	Pure water	5.54	0.309	0.996
PVP-10 + SA	Buffer (pH 10.0)	4.04	0.674	0.987
PVP-40 + SA	Pure water	16.6	1.290	0.996
PVP-40 + SA	Buffer (pH 10.0)	16.5	0.756	0.996
P4VPy + SA	Buffer (pH 4.0)	154.1	0.371	0.992

considerable increase ranging from 7.902 to 11.019 ml g^{-1}, which denotes an expansion of the PVP-10 random coil itself or an increase in the hydrodynamic size as a consequence of the preferential binding of the NIC molecules to the polymer. In contrast, at $c_m > c_m^*$ the intrinsic viscosity decreases from 7.902 to 6.207 ml g^{-1}, which means a coil contraction, probably due to the NIC + pure water being a poor solvent for PVP-10 compared with pure water. This argument can also be used to explain the viscosity of PVP-40 + NIC + pure water. From the comparison of the intercept values for ternary and binary systems, we obtain 15.8 ml g^{-1} at $c_m < c_m^*$ and 12.7 ml g^{-1} when $c_m > c_m^*$, both values being lower than the 21.6 ml g^{-1} corresponding to the PVP-40 + pure water binary system.

Analysis of the S-containing systems indicates that the intercepts for ternary solutions are always lower than those corresponding to binary solutions, independent of the bulk solvent composition. This shows that the polymer coil contracts, owing to the presence of SA in the system. In the light of these results, nothing can be inferred about the possible PVP–SA association. However, as claimed by other workers [36–39], similar macromolecular compounds can associate with SA molecules via hydrogen bonding. When P4VPy is incorporated instead of PVP in a ternary system, an increase from 149.8 (binary) to 154.1 (ternary) is detected. The increment in $[\eta]_m$ supports, on the one hand, the idea of a coil expansion and, on the other, a considerable increase in the hydrodynamic size, probably because SA has a proton-donating ability strong enough to form a hydrogen bond with the nitrogen of the pyridine ring placed on the polymer.

The second feature analysed was the solute–solvent interactions by comparison of the slopes obtained for binary (see Eq. 3) and ternary systems (see Eq. 5), with the data summarized in Table 3. Considering the N-containing systems, the slope values obtained for the ternary systems are, in all instances, lower than those for the corresponding binary systems. This behaviour could be attributed to the hydrophobic nature of the NIC molecules preferentially solvated in the vicinity of the PVP coil rather than a true association between PVP and NIC (macro)molecules. In contrast with the above behaviour, the values of the slopes for S-containing systems are larger for ternary than for binary systems. A possible argument to justify this trend could be the weak hydrophobicity displayed by the SA bound to PVP. In this context, and as pointed out by other workers [37–39], the capability of SA to bind PVP is supported by the proton-donating ability of SA to create hydrogen-bonded links with carbonyl groups from pyrrole rings of PVP.

Fig. 8 shows an example of the reduced viscosity for S-containing systems in a buffer (pH 10.0) as a function of the solute concentration. For binary systems, the polymer samples PVP-10 [(a), open symbols] and PVP-40 [(b), open symbols] must be considered as solutes. For ternary systems, the solute consists of a binary mixture of PVP + SA [(a) and (b), closed symbols]. The good linear correlation fits in all experiments depicted in Fig. 8 support the idea

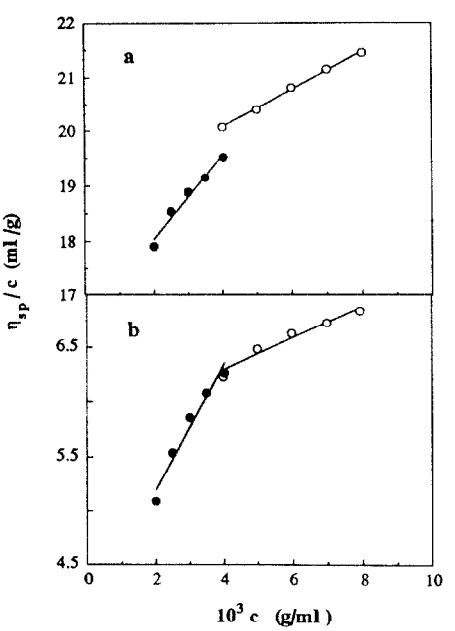

Fig. 8. Concentration dependence of the reduced viscosity for binary (open symbols) and ternary (closed symbols) silicic acid-containing systems in a buffer solution of pH 10.0. (a) ○ = PVP-40, ● = PVP-40 + SA; (b) ○ = PVP-10, ● = PVP-10 + SA.

that Eqs. 3 and 5 are adequate representations of the viscosity data over the concentration range studied. The same is true of the remaining S-systems, not plotted here for simplicity. The last system in Table 3 concerns a sample of P4VPy dissolved in a buffer solution (pH 4.0) for a binary system, and P4VPy + SA in the same buffer for a ternary system. The slope values for the two systems were 2.184 and 0.371, respectively. Note that this trend is contrary to the above-mentioned conclusion drawn for PVP + SA systems. However, in the present instance the experiments were carried out at pH 4.0 and taking into account that the pK_a of the silicic acid is 9.8, hence it will be in a fully protonated form. Moreover, it can be assumed that the pyridine ring of P4VPy will adopt a partially protonated form, at the same pH. Consequently, the existence of ionic repulsion between the two species could explain the above decrease in the slope value for both systems. The apparent affinity between the P4VPy and SA, supported by the λ values and corroborated by the intercept value derived from viscosity measurements, is clearly in disagreement with the above arguments. Regarding this unsolved question, additional experiments using other techniques must be done. We think, however, that our explanations open up a new approach to the study of polymer–toxic agent affinity.

4. Conclusions

The techniques used here, SEC and capillary viscometry, have been valuable in the study of preferential binding to polymers in dilute aqueous solutions of toxic agents. From the analysis of the vacant peaks obtained from SEC experiments for PVP and P4VPy samples in the presence of NIC or SA, as low-molecular-mass toxic agents, accurate information regarding the preferential solvation parameter, λ, has been obtained in addition to its concentration dependence on both polymer and toxic agent.

For PVP + NIC + pure water ternary systems, no correlation of λ with polymer molar mass and/or concentration of NIC was found. In contrast, for PVP + SA + pure water (or buffer pH 10.0), a clear dependence of λ on the above parameters was established, as can be seen in Figs. 5 and 6. The results obtained for λ reveal that the ability of NIC to solvate PVP is much less than that for SA, probably owing to the hydrophobic character of the former compound. In addition, a short series of experiments under the same experimental conditions but using P4VPy instead of PVP was carried out in order to analyse the effect of the pyridine ring on the preferential interaction. For this system, the effects on λ remain unaltered, ranging over the same order as for PVP-containing systems. Complementary information about the preferential interaction concerning polymers and a toxic agent was obtained from capillary viscosity measurements. Over the concentration range assayed, the experimental data on the reduced viscosity show a linear dependence on total concentration, allowing us to accommodate experimental data in conventional equations dealing with the viscosity of uncharged dilute polymer solutions (see Eqs. 3 and 5). Two main features were explored regarding the above equations, the intrinsic viscosity and the solute–solvent interaction. The conclusions obtained from the viscosity experiments support the behaviour of λ; however, some contradiction arguments derived from the interpretation of the viscosity data for P4VPy + SA system demand additional experiments to understand in depth the nature of these interactions. A complete description of the specific interactions is complicated and beyond the scope of this paper.

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