

About phase separation of aqueous polymeric two-phase dextran-polyvinylpyrrolidone systems

E.A.Masimov, S.R.Bagirova, Kh.T.Hasanova

Baku State University, 23 Z.Khalilov Str., AZ-1148 Baku, Azerbaijan

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The effect of the polyvinylpyrrolidone molecular weight on the phase separation of an aqueous two-phase dextran-PVP system has been studied. Mathematical expressions of concentration dependences C_{PVP} versus C_{Dex} for the two-phase systems formed by dextran and polyvinylpyrrolidone of various molecular weights are obtained. It is shown that all these dependences are described by the generalized equation $C_{PVP} = K \cdot e^{-\alpha C_{Dex}}$ which makes it possible to construct binodal curves of these systems without experiments. It has been established that for polyvinylpyrrolidones with high molecular weights, phase separation in the systems occurs at lower concentrations of phase-forming components. Thus, the results of the study confirm the fundamental role of water in the processes of phase separation of the polymer-polymer-water system. To elucidate the mechanism of the influence of various external factors on the compatibility of polymers in a common solvent, the influence of temperature on phase separation in the dextran-PVP-water two-phase system has been studied. The interaction parameters between the components of the system are calculated, the differences between these parameters ($\Delta\chi = \chi_{P_1-H_2O} - \chi_{P_2-H_2O}$) are determined, and the dependence of the effect on temperature is studied. With increasing temperature, the effect decreases and at the same time, the compatibility of polymers in aqueous solution improves.

Keywords: dextran, polyvinylpyrrolidone, water-polymer two-phase systems, phase separation, interaction parameter.

Про фазовий поділ водних полімерних двофазних систем декстран-полівінілпіролідон. *Є.А.Масімов, С.Р.Багірова, Х.Т.Гасанова*

Досліджено вплив молекулярно маси полівінілпіролідону на фазовий поділ водної двофазної системи декстран-РВП. Отримано математичні вирази концентраційних залежностей C_{PVP} від C_{Dex} для двофазних систем, утворених декстраном і полівінілпіролідонем з різною молекулярною масою. Показано, що всі ці вирази описуються узагальненим рівнянням $C_{PVP} = K \cdot e^{-\alpha C_{Dex}}$, яке дає змогу побудувати бінодальні криві цих систем без експериментів. Встановлено, що для полівінілпіролідонів з високою молекулярною масою поділ фаз у системах відбувається при менших концентраціях фазоутворюючих компонентів. Таким чином, результати дослідження підтверджують фундаментальну роль води в процесах фазового поділу системи полімер-полімер-вода. Для з'ясування механізму впливу різноманітних зовнішніх чинників на сумісність полімерів у загальному розчиннику досліджено вплив температури на фазовий поділ у двофазній системі декстран-ПВП-вода. Розраховано параметри взаємодії між компонентами системи, визначено відмінності між цими параметрами ($\Delta\chi = \chi_{P_1-H_2O} - \chi_{P_2-H_2O}$) та досліджено залежність ефекту від температури. Зі збільшенням температури ефект зменшується і в той же час покращується сумісність полімерів у водному розчині.

1. Introduction

It is known that a mixture of aqueous solutions of two polymers separates into two coexisting phases at concentrations of polymers above a certain critical value. When a substance is introduced into such a system, an uneven distribution of this substance occurs, which is characterized by a distribution coefficient, i.e. the ratio of its concentration (weight) in the coexisting phases of the system [1–8].

A number of works [9–16] show the promise of using such systems in biotechnology, medicine, and pharmacology, in particular, for the separation and purification of mixtures of chemical compounds, including mixtures of particles of biological origin (proteins, viruses, cells, etc.)

As is known, a 0.5 % aqueous solution of PVP with a molecular weight of $M \approx 12000$ is used as a blood substitute and antioxidant [17]. Dextran, like PVP, is widely used in medicine as a blood thinner and antithrombotic agent, as well as a blood substitute for massive blood loss. The study of two-phase systems formed by PVP and dextran in water can serve as a model for studying biochemical processes in living organisms, which are multi-phase, multicomponent systems [18].

It should be noted that in scientific publications there are often conflicting opinions about the mechanism of incompatibility of two polymers in water. Some authors have brought to the fore the idea of the fundamental role of the polymer components of the system in the process of separating the system into two phases, believing that if two polymers are incompatible in one solvent, then they must be incompatible in other solvents. In this case, the decisive role in the separation is played by the interaction of polymers with each other, and the role of the solvent is reduced to screening these interactions [9]. The authors of [2, 3, 8, 19–25] analyzed the contradictory results obtained by different authors on the incompatibility of polymers in water and put forward a hypothesis about the fundamental role of water in the formation of two-phase systems. In their opinion, when the system is separated, two aqueous phases are formed that do not dissolve in each other and have a different structure. Subsequently, this hypothesis was confirmed experimentally by the authors [2, 8, 20–23].

Gupta [18], referring to the works of B.Zaslavsky et al. [24, 25], showed that the

structure of water modified with a polymer plays a central role in the phase separation of a two-phase polymer system.

The present work is a continuation of our studies of two-phase aqueous systems PVP-dextran [26–28]. In this paper, we consider the results of the analysis of binodals of phase diagrams of aqueous polymeric systems dextran-polyvinylpyrrolidone (PVP)-water according to the Flory-Huggins theory, as well as the results of the analysis of these phase diagrams using a new approach recently proposed in the literature for the thermodynamic description of aqueous polymeric two-phase systems.

2. Theoretical background

Although Flory-Huggins theory [29–31] was intended for non-polar solvents, it has been shown that it can be applied to polar solvents, i.e. to aqueous solutions of polymers. As you know, water, due to hydrogen bonds between molecules, has certain structures, called clusters, and polymeric properties. As the size increases, the clusters approach the size of the polymer molecule. In this case, the polarity of water as a whole decreases. Thus, the conditions accepted in the Flory-Huggins theory (non-polarity of the solvent and the coincidence of the sizes of the polymer and the solvent molecule) are satisfied [32, 33].

There are limitations that prevent the use of the classical Flory-Huggins theory for the thermodynamic description of phase separation in three-component systems in which water is the solvent [34, 35]. Nevertheless, taking into account the characteristics of water as a solvent, an attempt to apply this theory to the analysis of phase separation in aqueous polymer systems seems justified. Such an attempt is now all the more necessary now, that in a number of recent works [35], the Flory-Huggins theory serves as the basis for creating theoretical concepts not only about the mechanism of phase separation in aqueous polymer systems, but also about the mechanism of the processes of distribution of biological macromolecules between equilibrium coexisting phases of such systems.

A number of works [9, 28, 36] describe methods for estimating the parameters of thermodynamic interaction. For the present work, the most important is the so-called Allen method, according to which the parameter of the thermodynamic interaction of polymers polymer P_1 -polymer P_2 is determined from the polymer composition of co-

existing phases in delaminated three-component systems polymer P_1 -polymer P_2 -solvent.

Authors of [37, 38] for the first time calculated the effective parameters χ_{12}^{eff} of polymer interaction using the Flory-Huggins theory for aqueous mixtures of two polymers in a common solvent. The following simplified approaches have been adopted: the ratio of the molar volumes of polymers to the molar volume of solvent and the molecular weights of the polymers are the same. In this case:

$$\chi_{12}^{eff} = \chi_{12}(1 - \varphi_0), \quad (1)$$

where χ_{12} is the parameter of interaction between polymers without a solvent, φ_0 is the volume fraction of the solvent. As can be seen from equation (1), at $\varphi_0 \rightarrow 1$, the effective parameter of the interaction of polymers approaches zero ($\chi_{12}^{eff} \rightarrow 0$), and the system becomes single-phase. According to this theory, with an increase in the molecular weights of the phase-forming polymers, the critical values of the volume fraction of the solvent φ_{kr} and the effective parameter of polymer interaction χ_{12} decrease, i.e. polymer incompatibility (phase separation) occurs at lower values of the polymer interaction parameter χ_{12} . The common solvent of the system reduces the number of contacts of polymer molecules with each other and the parameter decreases. This theoretical result is confirmed in [39].

Some authors emphasize the key role of the solvent in the process of phase separation of the solution and its thermodynamics [2, 8]. The thermodynamic properties of polymer pairs in different solvents were studied. It was shown that even for small positive values of the interaction parameters χ_{12} and at very different values χ_{10} ; χ_{20} , the incompatibility of polymers in the system occurs. As is known, the parameter α in the Mark-Kuhn-Houwink [40] equation characterizes the polymer-solvent interaction and is related to the intrinsic viscosity $[\eta]$ of the polymer solution by the following equation:

$$[\eta] = KM^\alpha, \quad (2)$$

where M is the molecular weight of the polymer.

It was shown that the critical concentrations for the phase separation of polymers

are inversely proportional to the difference between the parameters α ($|\alpha_1 - \alpha_2|$). Since the parameter α , as well as the χ_{10} and χ_{20} parameters characterize the polymer-solvent interaction, the authors of [31] came to the conclusion that the critical concentrations for the phase separation of polymers in the solvent are related to the $|\chi_{10} - \chi_{20}|$ difference, and the incompatibility of polymers decreases with increasing this difference. It was theoretically shown that if the interactions of polymers with a solvent differ $\Delta\chi = |\chi_{10} - \chi_{20}| \neq 0$, then even compatible polymers without solvents ($\chi_{12} < 0$) in a given solvent become incompatible.

3. Experimental

In the work, the molecular weight of dextran was maintained constant ($M \approx 70000$), and the molecular weight of the used PVP (purchased from the German company "Applichem") were $M \approx 10000$, 30000, 40000, and 54000 r.a.m. Water was double distilled in a quartz tube.

Dry dextran was dissolved in water for several hours to swell. Then the solution was heated to the boiling point, but not boiled, and after cooling it was passed through a filter with a pore size of 16 μm .

The phase diagrams of the systems under study were determined by preparing a series of two-phase systems with different concentrations of the two polymers.

The upper and lower phases were analyzed for their contents of the phase polymers. All the phase diagrams were plotted in the 23–25°C temperature range.

The phases of the two-phase system were kept for 21–24 h. The dextran concentrations in both phases were determined by the method of polarimetry. The PVP concentrations in the phases were calculated from the dry weight measurements [9].

4. Results and discussions

The binodal curves and connecting lines of the studied systems were constructed according to the well-known technique [9, 40]. The results obtained are presented in Fig. 1.

As follows from Fig. 1, with an increase in the molecular weight of PVP, the binodal line of the system shifts towards the origin of coordinates; this indicates an increase in the heterogeneous region of the phase diagram. In other words, with an increase in the molecular weight of one of the polymers (at $M_{Dex} \sim const$), phase separation (an incompatibility of polymers in water) occurs

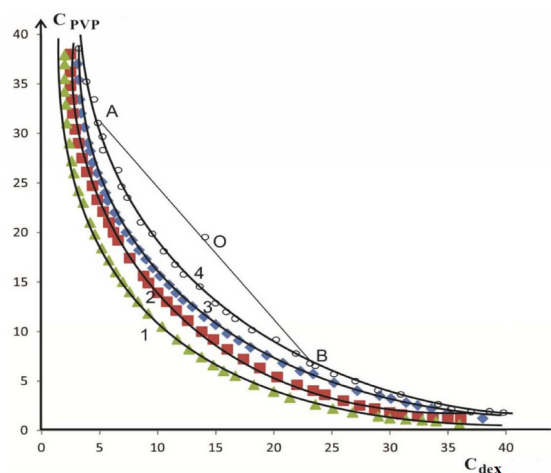


Fig. 1. Influence of PVP molecular weight on the phase diagram of the dextran-PVP-water system: 1 — $M \approx 54000$ r.a.m.; 2 — $M \approx 40000$ r.a.m.; 3 — $M \approx 30000$ r.a.m.; 4 — $M \approx 10000$ r.a.m.

at lower concentrations of polymers. Binodal mixing occurs because helical PVP molecules with a lower molecular weight are more likely to open more completely and, accordingly, hydration increases. As a result, polymer molecules with their aqueous environment become more compatible with water-salt environments. This compatibility should decrease as the molecular weight of the PVP increases and decomposition occurs at lower polymer concentrations.

For the binodal curves of the studied systems, the following expressions were obtained:

$$\begin{cases} y_1 = 36.641e^{-0.113x}, \\ y_2 = 40.466e^{-0.102x}, \\ y_3 = 40.259e^{-0.08x}, \\ y_4 = 37.722e^{-0.065x}, \end{cases} \quad (3)$$

where $y = C_{PVP}$ and $x = C_{Dex}$ are the concentrations of PVP and dextran polymers, respectively. The generalization of these equations leads to the expression

$$y = ke^{-\alpha x}, \quad (4)$$

where k is α preexponential coefficient independent of molecular weight and is the inverse of the dextran concentration at which the PVP concentration must decrease by a factor of e for separation to occur. In other words, α shows the rate of the PVP concentration decrease with an increase of the dextran concentration on the equilibrium curve

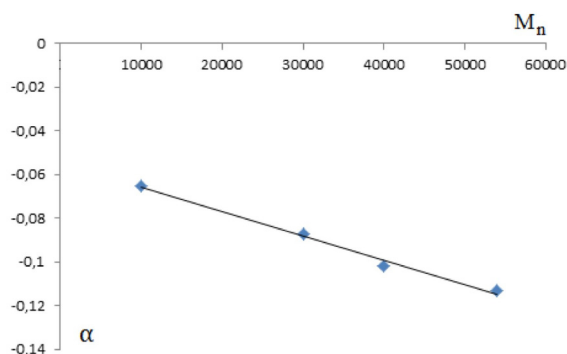


Fig. 2. Dependence of the inverse concentration of dextran on the molecular weight of PVP.

"homogeneous phase — heterogeneous phase". Obviously, changes in α reflect a change in the shape of the binodal curves. The change in the degree of hydration with increasing molecular weight can also explain the dependence of the slope of the connecting lines

$$\text{tg} = \frac{C_{PVP}^{up} - C_{PVP}^{dn}}{C_{Dex}^{dn} - C_{Dex}^{up}} \quad (5)$$

of the binodals on the molecular weight of PVP, the values of which are given in the Table. The Table lists also the polymer compositions of the initial system and the phases of the system.

The value of $\text{tg}\beta$ in the Table is the slope coefficient connecting the lines of the two-phase system dextran-PVP-water. This value makes it possible to compare the volumes of phases in a two-phase system corresponding to an arbitrary point taken in an inhomogeneous region. This value is a constant for a given polymer pair at a given temperature and pressure. The value of $\text{tg}\beta$ may vary depending on the molecular weight of the phase-forming polymers, the temperature of the solution.

As follows from (4), there is some correlation between the values of the coefficient α and the molecular weight of PVP.

$$\alpha = e^{-0.6M_n} - 0.054. \quad (6)$$

This dependence is shown in Fig. 2. As follows from the results obtained, for any two-phase system dextran-PVP-water, with a change in the molecular weight of PVP, it is possible to obtain the values of α and plot a curve $y(x)$ without experiments, i.e., to plot a binodal curve of this system for a given molecular weight of PVP.

Table. Polymer compositions of the initial system and the phases of the system

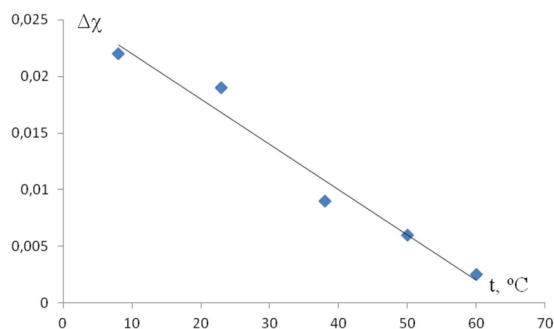
Initial system		Upper phase		Lower phase		tg β
$C_{PVP, \%}$	$C_{Dex, \%}$	$C_{PVP, \%}$	$C_{Dex, \%}$	$C_{PVP, \%}$	$C_{Dex, \%}$	
23.0	9.1	27.1	4.6	7.9	24.5	-0.97
24.0	9.0	28.5	4.4	6.1	27.7	-0.96
24.0	10.1	29.5	4.3	6.1	28.1	-0.98
22.1	11.1	28.5	4.4	6.1	27.7	-0.96

Thus, the study of the phase diagrams of the two-phase system dextran-PVP-water showed that with an increase in the molecular weight of PVP, the binodal curve of the system shifts towards a decrease in the compatibility of polymers in water, which is associated with a change in the degree of polymer hydration, a decrease in the number of free water molecules, which leads to stratification of the system and the formation of two aqueous phases of different structure..

It was shown that with an increase in the molecular weights of polymers, the incompatibility of polymer pairs in a common solvent (in water) increases. This can be explained by the fact that many functional groups (ionogenic groups, carboxyl groups, etc.) contained in polymers facilitate the interaction of polymer macromolecules with water, and as a result, the number of free water molecules in the system decreases, and phase separation occurs at lower concentrations of phase-forming components. In such cases, exothermic mixing ($\Delta H_{mix} < 0$) occurs and this leads to incompatibility of the polymers in water.

The χ_{10} and χ_{20} dependencies of PVP on external factors (for example, on temperature) determine the main role of the polymer-solvent interaction. It should be noted that the value $\Delta\chi$ and nature of the solvent also affect the χ_{12} parameter. When $\Delta\chi$ is constant, even for small χ_{12} values, the $\Delta\chi$ has more influence on $\Delta\chi_{12}$. In [30, 31], the role of the $\Delta\chi$ value as the main parameter characterizing the incompatibility of a polymer in a common solvent was experimentally confirmed.

Thus, both the analysis of the classical Flory-Huggins theory and experimental results show that the compatibility of polymers in a common solvent is mainly determined by the $\Delta\chi = |\chi_{10} - \chi_{20}|$ parameter. And the temperature dependence of the $\Delta\chi$

Fig. 3. Temperature dependence of $\Delta\chi$ in the dextran-PVP-water system.

parameter is associated with the temperature dependences of the χ_{10} and χ_{20} parameters separately [29, 30].

The calculated values of the $\Delta\chi$ parameters for different temperatures in the two-phase system dextran-PVP-water are shown in Fig. 3. As can be seen from Fig. 3, with increasing temperature the $\Delta\chi$ value decreases and the compatibility of polymer pairs in water increases.

Thus, using the Flory-Huggins theory for aqueous solutions of polymers, one can calculate the thermodynamic parameters of polymer-polymer and polymer-solvent interactions, and by analyzing the value of the $\Delta\chi$ difference, one can determine the direction of phase separation in two-phase polymer-polymer-water systems. The possibility of using the Flory-Huggins theory for aqueous solutions of polymers, as noted above, is explained by the fact that large $(-H_2O)_n$ clusters are formed due to hydrogen bonds in water. In this case, with an increase in the degree of polymerization (n), the average value of the total dipole moment decreases and the polarity of the solvent decreases and the sizes of the clusters and macromolecules become comparable.

As the temperature increases, the hydrogen bonds formed between polymer molecules and water molecules in solution weaken, the number of free water molecules in the environment increases, solubility improves, which reduces the value of the interaction parameter. This once again confirms the role of water in explaining the mechanism of phase formation.

The foregoing, in our opinion, makes it possible to apply the Flory-Huggins theory to the aqueous solutions of polymers.

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