Chitosan and Poly(vinyl pyrrolidone): Compatibility and Miscibility of Blends

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Summary: The miscibility of chitosan and poly(vinyl pyrrolidone) –PVP- has been studied by viscosity measurements, differential scanning calorimetry (DSC) and Fourier transform infrared spectroscopy (FTIR). For chitosan/PVP blends in solid state (thin films) interaction were found by FTIR and DSC methods. After blending PVP with chitosan the glass transition temperature Tg was altered, this may be a result of hydrogen bonds between the synthetic and biological component. It was found that solution of chitosan and PVP are immiscible, viscosimetry methods showed that interactions between chitosan and PVP are to small for the predictions of miscibility, due to the high affinity of the two polymers for the solvent. The study of blends with bespoke structural and properties will be essential for the development of a new generation of biocompatible stimuli-sensitive hydrogels.

Keywords: biocompatibility; chitosan; differential scanning calorimetry (DSC); miscibility; poly(vinyl pyrrolidone)

Introduction

Blends of synthetic and natural polymers represent a new class of materials with better mechanical properties and biocompatibility than those of the single components. In particular blends between mesogenic and flexible polymer have received considerable attention to verify the possibility that disordered chains of a conventional polymer can be induce to present an ordered structure directed by a liquid crystalline polymer.[1] Interest in the biomaterial properties of chitosan mixed with synthetic polymers, and with natural polymers has increased.[2] The work presented here is to investigate the properties of new materials based on the blends of chitosan and poly(vinyl pyrrolidone) with a specific focus on the all important molecular interactions between these two components. Both polymers are

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frequently used in the field of biomaterials and their specific properties may be used to produce blends with unique structural and mechanical properties especially for the development of a new generation of hydrogels. Chitosan is a natural cationic polyelectrolyte copolymer of glucosamine and N-acetylglucosamine derived from chitin, a polysaccharide found in the exoskeleton of shellfish like shrimp or crabs. Chitin is a homopolymer comprised of 2-acetamido-2-deoxy-β-D-glucopyranose units; however, some units exist in the deacetylated form as 2-amino-2-deoxy-β-D-glucopyranose. When chitin is deacetylated to at least 50 %, it becomes soluble (depending on the molecular weight) in dilute acids and is referred to as chitosan. Chitosan possesses many of the properties as cellulose based dietary fibre, however unlike plant fibre, it has the ability to significantly bind fat, acting like a "fat sponge" in the digestive tract.[3] Recently it has attracted great attention because the range of its applications has been extended to medical,[4] wastewater treatment,[5] biomembranes[6] and hydrogel development.[7] It has been reported that chitosan is a potentially useful pharmaceutical material owing to its biocompatibility and low toxicity.[8] For this reason it can be used in many applications in the formulations employed in drug delivery. Furthermore the macromolecular chain of chitosan is stiff enough to stabilise a liquid crystalline phase in acetic acid solution, where the persistence length is reported to be between to 190 Å[9] to 300 Å[10] depending on the acetylation degree (d.a.). According to the molecular model of Minke et al.[11] the formation of hydrogen bonds between the CH_2OH of one residue and an O-Ac group of an adjacent residue could stabilise the extended conformation around the glucosidic linkage. Therefore, as d.a. increases, the rigidity of the chain increases. Ogura et al.[12] found that concentrate solutions (30-90 %) of chitosan (d.a. 10 %) in aqueous 10 % acetic acid showed a characteristic texture of a liquid crystalline cholesteric phase. Terbojevich et al.[9] reported evidence for the presence of liquid crystalline phase of chitosan at higher d.a. 15-42 % in 10 % acetic acid solution. The critical concentration (Cp') for the appearance of the anisotropic phase, at concentration of 10-25 % wt/wt in acetic acid, is inversely proportional to the molecular weight of the samples. Poly(vinyl pyrrolidone) because of its outstanding absorption and complex formation abilities is widely employed in pharmacy and medicine. Uses of PVP range from the preparation of synthetic blood plasma, construction of hydrogels by radiation methods and to creations thromboresistant of hydrophilic gels.[13] The primary objective of the project was to study the interaction between synthetic polymer PVP and

chitosan. The miscibility of the two components has been verified by DSC analysis, using the variation of the glass transition temperature (Tg) of the blends versus the blend ratio by FTIR, as well as viscosimetry measurements of blends in solution.

Materials and Methods

Pure PVP (Mw = 360000) was supplied by Fluka. Chitosan (Mw = 200000) was obtained by hydrolysys of a sample of commercial chitosan from Rybex Kryll, Euphasia superba (Fisheries Central Board, Szczecin, Poland). The d.a. specified by the producer and confirmed by ^{1}H NMR was 42 %.[9] Acetic acid (Aldrich) and deionised water were used throughout the work. Polymer blends were prepared by mixing different suitable volumes of PVP and chitosan aqueous solutions (1 % wt of polymers on acetic acid 0.1 mol) in order to obtain mixtures with the following ratios: chitosan/PVP 80/20 % wt, 60/40 % wt, 50/50 % wt, 40/60 % wt and 20/80 % wt. Thin films were obtained by casting solutions onto glass plate, covered by polyethylene. After solvent evaporation, the samples were dried in vacuum at room temperature. Viscosity measurements of chitosan, PVP and chitosan/PVP solution were performed at 20°C in 0.4 M acetic acid using a quartz Ubbelohde viscometer. The IR spectra were obtained using spectrophotometer Mattson Genesis II. Thin films were analysed by casting solutions onto CaF_2 spectrophotometer windows. Samples were analysed with transmission measurements, i.e. by registering their absorbance. TA Instrument DSC Modulated 2920 was used for analysis of Tg. The samples were cycled 10°C/min. from 20°C to 300°C, cooling 20 °C/min. from 300°C to –80°C, and heating again 10 °C/min from -80 °C to 300 °C. First cycle has been run in order to eliminate the effects deriving from earlier thermal histories and to eliminate the residual water, the second heating cycle has been always considered to determinate the Tg. A third heating has been carried out on some samples and any differences, in comparison with the second heating, have been observed on DSC profiles.

Results and Discussion

When chitosan is blended with a PVP, the miscibility between their molecules is a very significant factor in determining the mechanical property of the blend. In order to estimate the miscibility we used the variation of the glass transition temperature Tg of the blends as function of the blend ratio. For this reason at first we estimated Tg for chitosan (previous

studies report only one Tg for chitosan,[2] were the value 203 °C). The Tg of chitosan in our conditions was determined to be at 225°C based on the careful second cycle DSC measurement. The difference between the two Tg depends on the different acetylation degree. The Tg reported by Sakurai et al. is lower because the chitosan has a very low d.a. (4 %) in comparison with the one used in this work and therefore the material is more flexible.[13]

As shown in Figure 1, for all compositions the blends are characterised by only one glass transition, in which the Tg is intermediate between those of the pure components and increases with the weight fraction of chitosan: this effect should be considered an evidence of the compatibility between chitosan and PVP and therefore some interactions are present in the solid state in the whole concentration range.

Moreover to predict the experimental behaviour the experimental Tg in function of the compositions were compared with those of theoretic equations of:

- Flory-Fox[14] $1/Tg = W_1 / Tg_1 + W_2 / Tg_2$

where W_1 and W_2 are the weight fractions of the two polymers 1 and 2; Tg_1 and Tg_2 are respectively their glass transition temperatures.

- Gordon-Taylor[15] $Tg = (W_1 Tg_1 + K W_2 Tg_2) / (W_1 + K W_2)$
- Utracki[16] $\ln Tg = (W_1 \ln Tg_1 + K W_2 \ln Tg_2) / (W_1 + K W_2)$

K in the last two equations is a parameter that derives from the ratio of the difference between the thermal expansion coefficients of the pure rubber (l) and the glassy (g) components (1 and 2 respectively): $K = \alpha_{l,2} - \alpha_{g,2} / \alpha_{l,1} - \alpha_{g,1}$

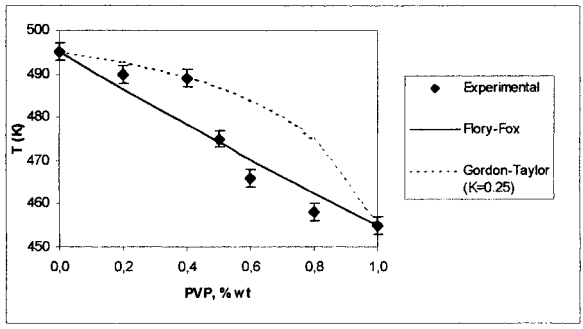

Figure 1. Calculated and experimental Tg values for the chitosan / PVP mixtures.

Figure 1 shows the experimental outline of the Tg vs. the composition of the mixture and the behaviour is compared with those of theoretic equations of Flory-Fox and Gordon-Taylor (assuming the empirical parameter K = 0,25). As shown, there is good agreement of the experimental data with low percentage of PVP with the Gordon-Taylor equation with K = 0,25 and for high percentage of PVP with the Flory-Fox (and Gordon-Taylor and Utracki equations with K = 1 even the curves are not reported). It is well known that the theoretic equations have been proposed for flexible polymers and therefore the reason why the experimental values follow a sigmoid trend and do not fit completely with the theoretic curves is that the chitosan is characterized by a good stiffness. FTIR is a very powerful technique to detect the inter-molecular interactions between two polymers. The FTIR spectra of chitosan depict characteristic absorption bands at 3362, 2932, and 2887, 1635 and 1384 cm^{-1} which represent the presence of –OH group, $-CH_2$ and $-CH_3$ group (aliphatic group), -C=O group and C-O stretching of primary alcoholic group ($-CH_2$-OH, considered to be a potential site for cross-linking), respectively.

The amino group has a characteristic absorption band in the region of 3400-3500 cm^{-1}, which is masked by the absorption band due to –OH group. The presence of significant peaks at 1635 cm^{-1} (due to CH_3-C=O group denoting the presence of acetyl group) and 3362 cm^{-1} (representing the presence of $-NH_2$ group), confirms that chitosan is a partially deacetylated product, unlike its parent molecule chitin which is a completely acetylated moiety.[17] The C=O of PVP at 1660 cm^{-1} is very evident and present in every blends. The inter-molecular interaction through hydrogen bonding can be characterised by FTIR, because the specific interaction affects the local electron density and the corresponding frequency shift can be observed. The miscibility, verified by DSC analysis, has been confirmed by FTIR spectra of chitosan, PVP, and chitosan/PVP blends (see Figure 2a and b). The position of characteristic bands of chitosan at 3362 and 1635 cm^{-1} are shifted in blends to higher frequencies (3400 and 1659 cm^{-1} respectively for the blend with composition 50/50). It suggests interaction between chitosan and PVP by hydrogen bonds. Chitosan, which is a hydrogen donor, forms hydrogen bond with carbonyl group from PVP. The pyrrolidone rings in PVP contain a proton-accepting carbonyl moiety, while chitosan presents hydroxyl and amino groups as side groups. Therefore, a hydrogen-bonding interaction may take place between these two chemical moieties in blend of chitosan and PVP. The formation of hydrogen bonds between

two different macromolecules competes with the formation of hydrogen bonds between molecules of the same polymer.

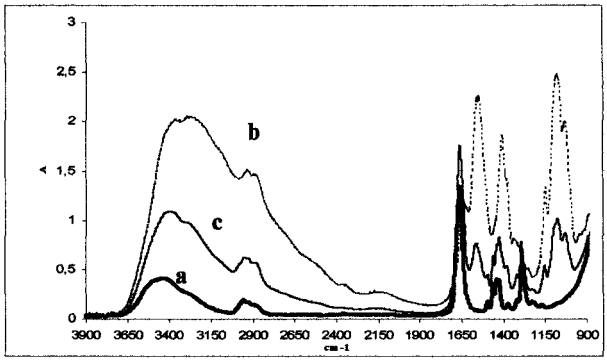

Figure 2a. FTIR spectra of PVP (a —), chitosan (b---), and chitosan / PVP 50/50 (c—).

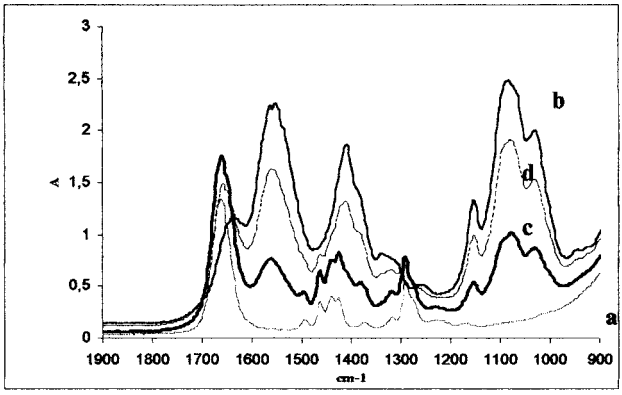

Figure 2b. FTIR spectra of PVP (a—), chitosan (b—), chitosan / PVP 50/50 (c—), and chitosan / PVP 80/20 (d---).

Dilute solution viscometry has been frequently employed in compatibility characterization.[18] The simplest technique consists in the analysis of the viscosity trend in function of blend composition. More sophisticated method, starting from the experimental determination of the Hugging coefficient, calculate a parameter, Δb, correlated to the differences between polymer chain interactions, experimentally determine, and interactions in ideal mixture, theoretically evaluated. Various are the criterion to determine Δb, we used the method reported in

literature.[19] The parameter Δb is calculated according to the relation: $\Delta b = b_{23} - \sqrt{b_{22} b_{33}}$ where b_{22} and b_{33} are specific interaction coefficients of components 2 and 3 in single polymer solution and b_{23} represents the interaction between different type polymer molecules in mixed polymer solution. Polymer mixtures might exhibit positive or negative deviations from the defined ideal behaviour because of the existence or absence of interaction. When the parameter $\Delta b > 0$ the two polymer are miscible.[20] According to the classical Huggins equation, from the intercept and slope of the plots of η_{sp}/c vs c, $[\eta]$, b_{22}, b_{33} and b_m are obtained. Where $b_m c^2$ represent the total polymer–polymer interaction in the ternary system. The specific interaction parameters between the two polymers, b_{23}, are obtained by substituting all the experimentally evaluated terms in the equation:

$b_{23}=(b_m c^2 - b_{22}c_2^2 - b_{33}c_3^2)/ 2c_2 c_3$

Table 1 lists viscometric data obtained for binary blends containing chitosan and PVP. The viscosity measurements shows that $[\eta]$ of chitosan rapidly decreases in the presence of small amount of PVP probably due to the weaker interaction between chitosan and PVP respect to chitosan-solvent. The negative values of Δb were observed for all the mixture and indicate immiscibility of these two components.

Table 1. Viscometric data for binary blends containing chitosan and PVP.

% wt PVP	[η]	Δb	% wt PVP	[η]	Δb
0	2,915		60	0,447	-1.841
10	1,735	-14.339	70	0,340	-1.055
20	2,585	-2.316	80	0,286	-0.815
30	0,639	-5.774	90	0,189	-0.470
40	0,545	-3.830	100	0,088	
50	0,569	-2.754			

To calculate the theoretical ternary phase diagram for a system composed by a rigid and a flexible polymer it is necessary to know the axial ratio of the rigid (X_2) polymer and the flexible (X_3) one. For chitosan sample the axial ratio can be evaluated indirectly knowing the critical concentration for the appearance of the anisotropic phase. In our case, chitosan with MW = 200000 and d.a. = 42 % has a Cp' value equal to 25 % wt/wt, as reported in literature;[9] then assuming the additivity of the specific volumes of the polymer (0.76 mL/g) and the solvent (1 mL/g) the polymer volume fraction can be determined (Vp' = 0.20).

According to Flory's lattice theory: [21]

$$Vp' = \frac{8}{X_2}\left(1 - \frac{2}{X_2}\right)$$

where X_2 is the axial ratio of the Kuhn segment: $X_2=2q/d$, q is the persistent length and d the diameter of the chain, the axial ratio $X_2 = 38$ has been calculated.

For the PVP flexible polymer the axial ratio ($X_3 = 444$) can be calculated from the ratio between the length of the completely extended chain and the diameter according to the equation: $X_3= (Mw/Mo)\ Lo\ (1/d)$

where Mo is the molar mass of the repeating unit (Mo = 109) and Lo the projection of the repeating unit length on the chain axis (Lo=1.25 Å). The diameter was taken as 9.3 Å as obtained from the relationship:[21] $d=(Mo/\delta N_a Lo)^{1/2}$

where δ is the polymer density, taken as 1.66 g/mL and N_a is the Avogadro number (alternative calculation of X_3 produce no significant variation of final results).[22]

Figure 3 shows the theoretical phase diagram calculated according to the Flory theory[23] using the axial ratio $X_2 = 38$ and $X_3 = 444$ and an interaction parameter $\chi_{23} = 0$. A complete exclusion of the flexible polymer PVP from the mesophase due to an entropic effect related to the interference of random coil with the mutual orientation of the rodlike molecules is predicted for overall volume fraction higher than 0,2-0,33 and no homogeneous phase are possible at the solid state between the two polymers.

The viscometric results, immiscibility between the two polymers, agree with the theoretical results, DSC and FTIR results show instead a good miscibility between the two polymers at the solid state. Complete compatibility at the solid state and immiscibility in solution has been theoretically predicted for flexible polymers.[24,25] This may happen when the interactions between the two polymers are totally favourable or, at least, not unfavourable ($\chi_{23} \leq 0$ or slightly < 0) to exceed the entropic gain due to the blending and the interaction between the polymer and the solvent are very strong (χ_{12} and $\chi_{13} < 0$). In such a case the adding of a solvent to the homogeneous blend of the two polymers leads to a separation in two phases, each stabilised by polymer-solvent interaction, that is stronger than the one between the macromolecules compound. This could be the case of chitosan and PVP, in fact the results of FTIR and DSC seem to indicate some polymer-polymer interactions, furthermore the χ_{12} and χ_{13} for chitosan-ac. acid and PVP-ac. acid should also be less than zero due to the strong

interactions between chitosan or PVP and ac. acid/water solution. In fact the viscosity measurements shows that [η] of chitosan rapidly decreases in the presence of small amount of PVP probably due to the stronger interaction between chitosan and solvent respect to chitosan-PVP. It is thus supposed that in a chitosan/PVP/ac. acid system a situation similar to that theoretical predicted for flexible polymers is established: there is a complete compatibility in the solid state whereas in diluted solution an incompatibility between the polymers appears, not only due to the high affinity of the two polymers for the solvent, but also for the formation of a liquid crystalline phase, that contribute to the incompatibility. Similar results was observed for blends based on cellulose and chitin,[26] where a phase separation appears in the diluted dimethylacetamide- LiCl solution, with Cp higher than 10 % wt, whereas a good compatibility at the solid state is confirmed by infrared measurements on films. The viscometer data showing immiscibility between the polymers could be heavily affected by the strong interaction between chitosan and PVP with the solvent. As a consequence, we can imagine the two polymeric molecules to be surrounded by a 'shell' of solvent strictly bonded to the chain. This could be one of the main reasons for the lack of short-range interaction between the units of dissimilar chains.

Conclusions

The miscibility of chitosan and poly(vinyl pyrrolidone) PVP depends on the physicval state of the blend. For the blends in solution it were found that chitosan and PVP are immiscible when we have these two components in third component as solution. Viscosimetry methods showed that interactions between chitosan and PVP in solvent are to small for the predictions of miscibility, due to the high affinity of the two polymers for the solvent. For chitosan/PVP blends in solid state (thin films) some interaction were found by FTIR and DSC methods. After blending PVP with chitosan the glass transition temperature Tg was altered. The interaction may be a result of hydrogen bonds between the synthetic and biological component. However, a hydrogen-bonding interaction may take place between these two chemical moieties in blend of chitosan and as well as between molecules of the same polymer. The study of blends with selected structural properties has been useful for the development of a new generation of biocompatible stimuli-sensitive hydrogels.

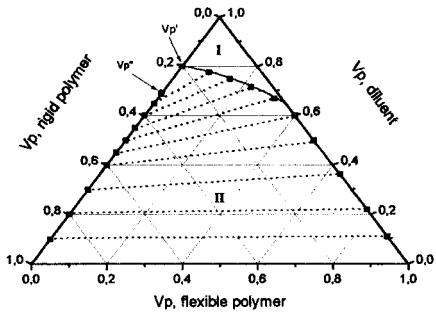

Figure 3. Theoretical phase diagram for athermal system: rigid polymer (chitosan) / flexible polymer (PVP) / diluent. Axial ratio of rigid chain = 38, contour length of flexible chain = 444. **I)** homogeneous isotropic phase – **II)** biphasic phase: anisotropic + isotropic. The dotted lines show the tie line between the conjugated phases. Vp' (Vp'') are the critical volume fraction for the appearance (stability) of the liquid crystalline phase.

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