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ADJUSTING DRUG RELEASE BY USING MISCIBLE POLYMER BLENDS AS EFFECTIVE DRUG CARRIES

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In the present study PVP/HPMC and PVP/Chitosan polymer blends were prepared by using the solvent evaporation technique. From DSC studies were revealed that both blends are completed miscible in the entire composition range since only one glass transition temperature was detected. Miscibility can be attributed to the strong interactions evolved between the carbonyl group of PVP, which acts as strong proton acceptor, with hydroxyl and amino-groups of HPMC and Chitosan, which are proton donors. Thus hydrogen bonds are easily formed, as was verified by FTIR, producing miscible blends. However, the extent of interactions depends from polymer composition and mainly from the ratio and the kind of reactive groups. In PVP/HPMC blends a negative variation of T_g is recorded while in PVP/Chitosan the variation has a sigma form. The miscibility of these systems creates matrixes with completely different physical properties in order to use as effective drug carriers. PVP/HPMC blends can be used as pulsatile chronotherapeutics systems adjusting exactly the time of the drug release while PVP/Chitosan blends can be used to control the release profile of a poorly water soluble drug. In these blends HPMC and Chitosan respectively are the control factors for the corresponding applications.

Keywords: *chitosan, drug carriers, felodipine, hydroxypropyl methylcellulose, miscible blends, poly(vinyl pyrrolidone)*

Introduction

During the last decade several studies have been carried out regarding the effect of circadian rhythmicity to the symptomatology of several diseases. Pulsatile release formulations have already been investigated in order to adjust the initiation of the release of the drugs for a definite period of time. The simplest pulsatile formulation corresponds to the press-coated tablets comprising of two layers. The internal layer contains the active pharmaceutical ingredient while the external one is composed of a polymer, which adjusts the initiation of the release by its rupture. The disadvantage of such formulations is that the rupture time cannot be adjusted as it is strongly correlated with the physicochemical properties of the polymer. Very commonly two or more polymers can be used to develop an acceptable product regarding the efficient control release of the active compound. In some cases miscible polymer blends seem to be the most effective drug carrier for pulsatile chronotherapeutics. However, due to thermodynamic restrictions the majority of the polymer blends are immiscible containing two or more different phases.

The use of physical mixtures of polymers is inappropriate due to the different erosion rates of the substances, which lead to channeling creation and unrepeatable rupture times. In order to prepare miscible blends the free energy of mixing, which includes both entropic and enthalpic terms, must obtain a negative value ($\Delta G_{mix}=\Delta H_{mix}-T\Delta S_{mix}$). Specific interactions between the polymeric components can give rise to negative free energy of mixing in spite of the high molecular mass of polymers which means high entropy. The most common interactions that are involved in blends and enhance miscibility are hydrogen bonding, charge transfer complexes, ionic and dipole interactions and π-electrons [1]. One other advantage is that the release profile of a drug formulation can be controlled through the use of polymer blends [2, 3]. The presence of strong intermolecular forces, especially hydrogen bonds may result in different physico-chemical characteristics compared to the initial polymers. This capability exists mainly in polymer blends, which are fully miscible. Such polymer blends, like PEG/polysorbate 80, were used successfully to enhance the dissolution rate of poorly-water soluble drugs [4]. The solubility reaches its highest

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value in compositions with a 3:1 analogy. After exposure to aqueous media the two polymers can completely dissolve and the drug disperses in a very finely subdivided form. Furthermore, adjusting the composition of these polymers and the polymer drug interactions the release profile of a drug formulation can be controlled [5].

The aim of the present study was to prepare miscible polymer blends composed by polyvinylpyrrolidone (PVP) and hydroxypropyl-methyl cellulose (HPMC) as well as PVP/Chitosan. These blends are investigated in order to create an adjustable system based on the high release rate of PVP and the respective low one of HPMC and Chitosan. PVP/HPMC blends are for first time prepared and studied. Furthermore, HPMC and Chitosan are two of the most effective mucoadhesive polymers and for this reason are appropriate for the production of chronotherapeutics. From our previous study it was found that the mucoadhesive force of HPMC was enhanced when it was blended with PVP [6].

Polyvinylpyrrolidone (PVP) is a water-soluble tertiary amide and a strong Lewis base and since it possesses good biocompatibility it has found many applications in pharmaceutical technology. Because of its polar groups, it is a strong proton acceptor and can easily exhibit hydrogen bond interactions with other polymers or small molecules, given the latter being proton donors. This effect enhances polymer miscibility since hydrogen bonding induces a negative, favorable enthalpic contribution to the Gibbs free energy of mixing. Ford has demonstrated that PVP can inhibit the crystallization of drugs, producing amorphous solid dispersions with increased drug dissolution rates [7].

Hydroxypropyl methylcellulose (HPMC) has been used extensively as a drug carrier and for the enhancement of the dissolution behavior of poorly water-soluble drugs as well [8–10]. It is a hardly water soluble polymer carrier with the ability to swell on contact with aqueous solutions creating a hydrocolloid gel mass on its external surface. This mass gradually dissolves with time. Therefore, from such systems, the release of active ingredients is expected to be controlled by the dissolution rate of the polymer gel. HPMC was found to promote the dissolution rate of Felodipine, which is a poorly water soluble drug, via solid dispersion [11]. Compared with PVP solid dispersions, HPMC systems have a slower drug release rate, which can be characterized as retarded release.

Chitosan is produced from the deacetylation of chitin in the presence of 40 mass% NaOH and at a temperature of 120°C for 1–2 h, and exhibits completely different properties from chitin [12]. Chitosan has found a vast number of applications in recent years and it is considered one of the most significant materials from the point of view of potential applications. This is attributed to the high nitrogen content (6.89%) and the fact that it is a completely biodegradable polymer, biocompatible, non toxic, with a high adsorption capability. Furthermore, it can relatively easily form films or fully miscible blends with other polymers having multiple applications, since it is soluble in weak acids such as acetic acid [13, 14]. Most natural polysaccharides, such as cellulose, starch, dextrin etc., exhibit a weak acid and mainly neutral behavior whilst chitosan, due to the presence of the amino groups, constitutes a unique example having a weak basic character.

The aim of this study is the investigation of the miscibility and the physicochemical characteristics of the polymer blends as well as their ability to be used as effective drug carriers. The dissolution enhancement of a poorly water soluble drug like Felodipine and the ability of these miscible blends to control the drug release profile are also studied.

Experimental

Materials

Polyvinylpyrrolidone (PVP) type Kollidon K30 with a molecular weight of 50,000 to 55,000 was obtained from BASF. HPMC type METHOCEL K4M was supplied from Colorcon. Chitosan with a low molecular mass was supplied from Aldrich chemicals. Felodipine (FELO) with an assay of 99.9% was obtained from PCAS (Longjumeau, France) having a melting point of 143–145°C and solubility in water approximately 0.5 mg L^{-1} while it is freely soluble in ethanol. Ethanol absolute was obtained from Merck. All the other materials and reagents were of analytical grade of purity.

Preparation of polymer blends and drug dispersions

Polymer blends were prepared using the solvent method. PVP immediately dissolved in distilled water, while HPMC was first immersed in water for 1 week to swell and complete dissolution was achieved with gentle heating at 60°C. Chitosan was dissolved in an acetic acid solution 2 mass%. The solutions were mixed at different amounts preparing PVP/HPMC and PVP/Chitosan blends with concentrations 10/90, 20/80, 30/70, 40/60, 50/50, 60/40, 70/30, 80/20 and 90/10 mass/mass. Water was removed from the solutions at room temperature and the blends were received as cast films. For complete film drying the samples were placed in a vacuum oven for 24 h at 80°C.

Drug polymer dispersions containing 10 mass% FELO were prepared in a similar manner. The drug substance (freely soluble in ethanol) and the polymers were dissolved in appropriate quantities of absolute ethanol (PVP) or water (1 mass% acetic acid for chitosan) and the solutions after mixing were sonicated for 15 min. To prepare the PVP/FELO and (PVP/Chitosan)/FELO dispersions the solutions were maintained at 40°C for 48 h in order to slowly evaporate the solvent. The drug polymer dispersions were taken in the form of thin films.

Instrumentation methods

Thermal analysis

Thermal analysis of the samples was carried out using a PerkinElmer, Pyris 1 differential scanning calorimeter (DSC). The calorimeter was calibrated with indium and zinc standards. For each measurement a sample of approximately 6 mg was used, placed in aluminum seal and heated up to 135°C with a heating rate of 20°C min^{-1}. The sample remained at this temperature for 15 min in order to remove remaining moisture traces from the polymers. Afterwards, the samples were cooled to 0°C with a cooling rate of 20°C min^{-1} and scanned again up to 200°C using the previous heating rate. From this second scan the glass transition temperature of the blends (T_g) was measured.

Fourier transformation-Infrared Spectroscopy (FT-IR)

FTIR spectra were obtained using a Perkin-Elmer FTIR spectrometer, model Spectrum 1. The IR spectra, in absorbance mode, were obtained in the spectral region of 450 to 4000 cm^{-1} using a resolution of 4 cm^{-1} and 64 co-added scans. The spectra presented are baseline corrected and normalized.

Scanning Electron Microscopy (SEM)

The morphology of the prepared blends as well as of the initial materials, were examined using a scanning electron microscope (SEM), type Jeol (JMS-840). For this examination the fractured samples of solid dispersions, prepared under liquid nitrogen, were used. All the studied surfaces were coated with carbon black to avoid charging under the electron beam.

X-Ray Diffraction (XRD)

XRD analysis was performed on randomly oriented samples, scanned over the interval of 5–55° 2θ, using a Philips PW1710 diffractometer, with a Bragg-Brentano geometry (θ, 2θ) and a Ni-filtered CuK_α radiation.

Mechanical properties

Tensile strength and elongation at break of the prepared PVP/Chitosan blends were studied on relatively thin films, which were prepared by the solvent method as described before. Dumbbell-shaped tensile-test specimens (central portions, ~5 X 1.5 mm thick; gauge length, 22 mm) were cut from the sheets in a Wallace cutting press and conditioned at 23°C and 55–60% relative humidity for 48 h. The stress-strain data were received by using an Instron tensile testing machine model 1122 in accordance to ASTM D 1708-66. At least five specimens were tested for each sample and the average values were reported. Typical standard deviation values were found for all samples.

In vitro release profile

The release of Felodipine from the polymer dispersion systems was measured by a modified dissolution apparatus II (paddles) USP. A stationary disk was used in order to achieve hydrodynamic equilibration. The disk has been prepared by Pharmathen S. A., Pharmaceutical Industry. It is a circular stainless 8 mesh grid with a diameter of 53 mm. It was placed at the bottom of the dissolution vessel and above the tablets in order to avoid tablet irregular revolution and achieve hydrodynamic equilibration. The test was performed in 37±1°C with a rotation speed of 100 rpm using 500 mL of a 0.1 M phosphate buffer with a pH value of 6.5 containing 2% Polysorbate 20 as a dissolution medium. The tests were performed in triplicate. The instrumentation used for the dissolution test was an apparatus type DISTEK 2100B equipped with an auto sampler.

Results and discussion

Characterization of the prepared blends

The prepared PVP/HPMC and PVP/Chitosan blends are transparent at the whole composition range indicating that these blends may be miscible. Surface examination of the liquid nitrogen fractured blends revealed that the morphology of the blends depends on their composition. In blends with a low PVP content, 10 and 20 mass%, the existence of small spheres is observed, which are uniformly scattered over the whole surface of the samples. Thus, one could say that these blends are probably consisted of two different phases and that the small spheres represent the dispersed phase. As the PVP concentration is increased the small spheres tend to disappear, leading to a more homogenous surface and only one smooth surface is observed on the samples with a concentration

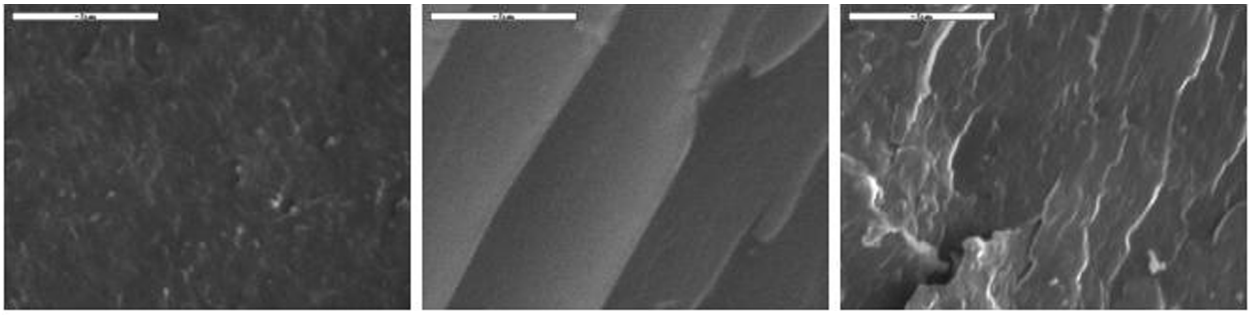

Fig. 1 SEM micrograph of liquid nitrogen fractured surfaces of PVP/Chitosan blends with different composition ranges; a – 20/80 mass/mass, b – 50/50 mass/mass and c – 80/20 mass/mass

of 40–60 mass%, a fact that indicates complete miscibility of the particular blend. In blends with a PVP concentration higher than 70 mass%, the surface becomes rough and coarse. Remarkable is the fact that the morphology in both blends (PVP/HPMC and PVP/Chitosan) is almost similar without significant differences being observed.

Miscibility examination of the blends was carried out through the use of DSC and in Fig. 2 the thermographs of both blends are presented. HPMC has a T_g value of about 202°C, and PVP exhibits one at a lower temperature, at 167°C. Even thought this difference is very small it proves that differential scanning calorimetry is a sensitive technique for the miscibility study of such blends [15]. As can be seen in all compositions there is only one T_g, which ranges between the glass transition temperatures of the two initial polymers and is concentration dependent. This is a much more valid criterion with which to substantiate that PVP/HPMC blends are fully miscible. However, the blends showed broader glass transition temperatures than the homopolymers, as a result of higher microheterogeneity in the system caused by hydrogen bonding interactions. The glass transition temperature width reflects the extent of the microrelaxations responsible for the transition.

Similar are also the results from the examination of PVP/Chitosan thermographs where only one T_g is detected, even thought the enthalpy relaxation of Chitosan is very small and thus hard distinguished (Fig. 2b). For this reason DSC thermographs of all blends were repeated for more than three times. The recorded T_g of Chitosan is 157°C and is very close to that mentioned in literature (140–150°C), which was determined by using four different techniques [16]. However, it should be mentioned that there are major arguments as far as the accurate determination of the glass transition temperature is concerned and completely different values have been reported [17]. This is something that should not be considered incorrect since there is a strong dependency from the deacetylation degree, molecular mass and degree of crystallinity [18]. A particularity of the prepared blends is that the T_g value does not alterate in a prescribed manner, as is the case in the PVP/HPMC blends, but rather exhibits a peculiar behavior. In blends with low PVP concentrations a positive deviation from the linear behavior appears, whereas in blends with high concentrations the temperatures are lower, even from the original polymers. A similar behavior was mentioned just recently for PVP/Chitosan blends [19] while in a previous study

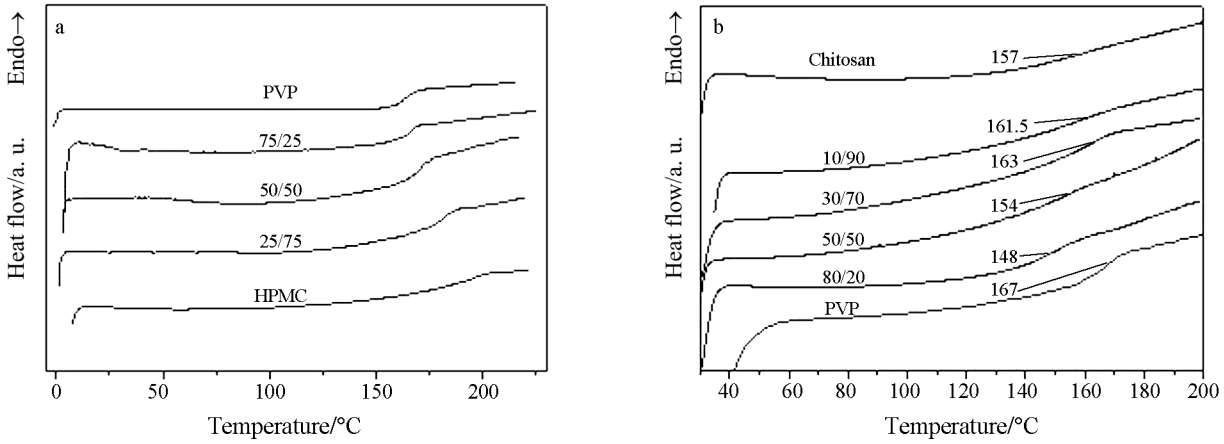

Fig. 2 DSC curves of a – PVP/HPMC and b – PVP/Chitosan blends

T_g was varied almost linearly between the T_g temperatures of the initial polymers [20].

During time several theoretical and empirical equations have been proposed to adequately describe the dependence of the glass transition temperature of a miscible blend from the mass fractions and the glass transition temperatures of the initial polymers. Among those, T_g/composition relationships can be evaluated by the Fox equation that was one of the first proposed [21]

$$1/T_g=w_1/T_{g1}+w_2/T_{g2} \quad (1)$$

where T_g is the glass transition temperature of the blend, w_1 and w_2 are the mass fractions of the initial polymers that constitute the blend and T_{g1}, T_{g2} are their glass transition temperatures. Gordon-Taylor proposed an equation taking into account the evolved interactions that can not be predicted by the Fox equation [22]

$$T_g=(w_1T_{g1}+kw_2T_{g2})/(w_1+kw_2) \quad (2)$$

where k is a constant representing a semi-quantitative measure of the interaction strength between the reactive groups. If k takes values close to 1 or above then it is suggested that strong interactions take place as in the case of PVP/PVAL and PVP/phenoxy blends [23, 24]. These classical equations predict that T_g can continuously and monotonically increase with blend composition. However, in several polymer blend systems it was observed that such a variation is not always the case. For this reason Couchman examined the thermodynamic behaviour of both polymers in order to obtain a more accurate prediction of the T_g-composition dependence [25]

$$\ln T_g= [(w\Delta C_p\ln T_g)_1+(w\Delta C_p\ln T_g)_2]/[(w\Delta C_p)_1+(w\Delta C_p)_2] \quad (3)$$

where w is the mass fraction of each component and ΔC_p represents the heat capacity change at the T_g temperature.

By using the above equations, as can be seen in Fig. 3, only the Gordon-Taylor and Couchman-Karasz fits well with the experimental data. The Fox equation gives results that are just a little lower than the linear variation of the T_g temperature of the initial polymer and deviates significantly from the experimental values. For this reason it is not appropriate for the study of PVP/Chitosan blends. By applying the Gordon-Taylor equation with k=0.25, a very well correlation with the experimental data is obtained. This value is inferior to 1, implying that the interaction between the hydroxyl groups of HPMC and the carbonyl groups of PVP are rather weak. However, this small value does not exclude the formation of completely miscible blends. Such a small value (k=0.41) was calculated for PVP/PAN

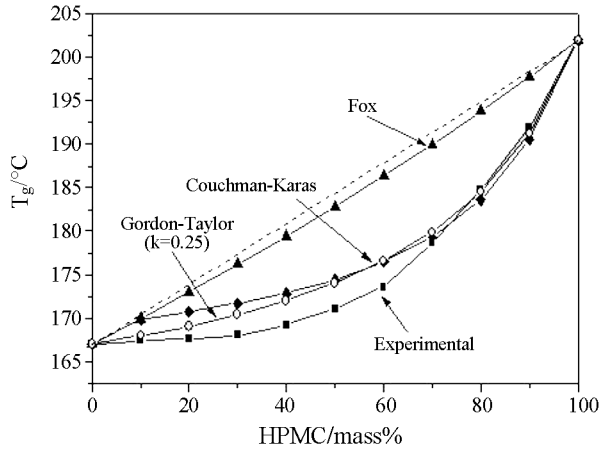

Fig. 3 Prediction of T_g-composition dependence in PVP/HPMC blends by using several equations

blends, which are miscible as well [26]. The Couchman-Karasz equation gives similar fittings by using 0.37 and 0.07 J g^{-1} K^{-1} as the ΔC_p values for PVP and HPMC respectively. These values were calculated from the thermographs of both polymers obtain by DSC measurements, in the glass transition temperature range. Thus, it can be concluded that both equations outline the large negative T_g deviations from the mass average values calculated from the DSC curves.

The above equations can successfully describe polymer blends that exhibit only negative deviations with regard to the linear mixing rule, as in our prepared blends. However, they are inappropriate for the study of PVP/Chitosan blends in which an S-form variation is observed (Fig. 4), which is common in miscible PVP blends [27–29]. Glass transition temperature shows a positive variation for compositions in which Chitosan predominates, indicating that strong intermolecular interactions, probably hydrogen bonding, are taking place between the two components. By increasing the PVP content in the blends, the variation becomes negative with recorded T_g values, even lower than those of the initial polymers. However, this negative variation does not exclude the formation of completely miscible blends. In these compositions it seems that week interactions are evolved and Chitosan has a plasticizing effect to the PVP macromolecules. Kwei has extended the Gordon-Taylor equation by introducing a further factor (q) as a measurement of the number of specific interactions (Eq. (4)). For this reason the proposed equation is appropriate for polymers blends for which positive values are recorded than the linear deviations [30]. However, using values of k=0.01–0.05 and q=30, an accurate prediction can be obtained but only for the positive variations. For concentrations higher

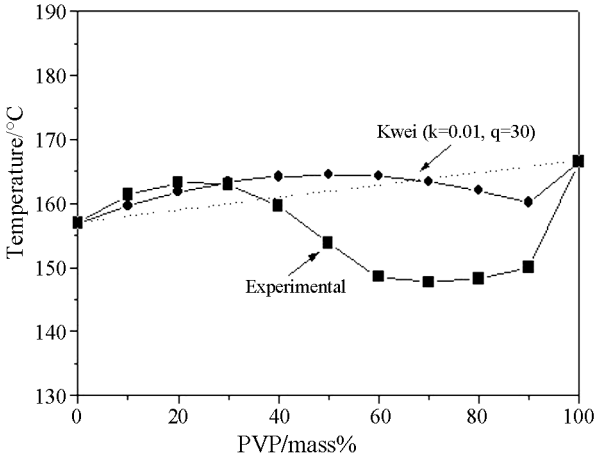

Fig. 4 Variation of T_g in PVP/Chitosan blends

than 40 mass% PVP the Kwei equation can not be satisfactorily used.

$$T_g=(w_1T_{g1}+kw_2T_{g2})/(w_1+kw_2)+qw_1w_2 \qquad (4)$$

Particular sensation is incurred from the fact that the transition diagram of the mechanical properties ensues an analogous behavior with that of the T_g value as well. Both homopolymers according to the stress strain data could be characterized as strong materials since their tensile strength is very high. However, they break before the appearance of the yield point and have a very low elongation at break. For this reason both polymers can be safely characterized as brittle and strong materials. Chitosan has a tensile strength of about 51 MPa, whilst PVP has a somewhat higher strength, close to 65 MPa (Fig. 5). In blends with 10 and 20 mass% PVP content a positive deviation from the linear behavior is observed, between the properties of the original polymers. This could be attributed to the existence of strong interactions between the reactive groups of chitosan and PVP, which could lead to the formation

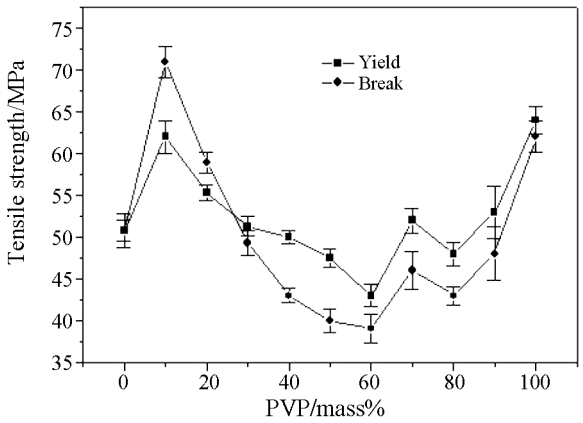

Fig. 5 Tensile strength at yield point and at break point of the prepared PVP/Chitosan blends containing different compositions of each one polymer

of a stronger matrix due to the physical crosslinking. This is supported by the capability of a complex formation between the two polymers, inducing a significant improvement over the mechanical properties of the prepared blends as well. However, in blends with a 60 mass% PVP content, the lowest tensile strength value is observed, a characteristic that is only observed in immiscible blends. In immiscible blends tensile strength exhibits a minimum value, which in most cases appears in blends containing equal amounts (50/50 mass/mass) of each polymer. Furthermore, this minimum value could be even lower than the tensile strength of either one of the initial polymers. This is observed because when equivalent amounts of both polymers are used, especially large phases of each one are formed, resulting in the final sample being particularly brittle. Nevertheless, in our case, as is already confirmed by DSC measurements and SEM observations, the blends are miscible over the entire composition range and therefore this behavior should be attributed to other factors.

In the chitosan spectrum, the peaks at 3461 and 3237 cm^{-1} are attributed to the –OH and $–NH_2$ groups respectively. These peaks in blends with PVP were found to shift, the foremost towards lower frequencies whilst the latter towards higher ones (Fig. 6). Furthermore, the shift of the hydroxyl groups seems to reach a maximum value in blends with equal amounts of the polymers (50/50 mass/mass), whereas the –OH peak is detected at 3435 cm^{-1}, which is a significant shift. However, because the $–NH_2$ peak is recorded as a shoulder, its shift isn't of particular distinctness, although a small shift of 1–10 cm^{-1} to higher wavenumbers is observed. It seems that both reactive groups exhibit interactions with PVP because the corresponding frequencies, and thus electron densities, of the particular groups have been altered in the blends. Both the reactive groups of chitosan are electron donors and can form hydrogen bonds with the carbonyl groups of PVP ensuring miscibility of the prepared blends. This is confirmed from the observable shift of the carbonyl groups of PVP, which shift from 1664 to 1659 cm^{-1}, whilst in blends with a chitosan content of 70–90 mass% a second peak seems to be recorded with a maximum at 1647 cm^{-1}. These shifts constitute a confirmation of the strong interactions that evolve between the amino or hydroxyl groups of chitosan and the carbonyl groups of PVP, and result in the miscibility of the polymers. Similar hydrogen bonds are formed between the carbonyl groups of PVP and the hydroxyl groups of HPMC contributing in the miscibility of the system. Due to the formation of such hydrogen bonds PVP can create miscible blends with other polymers

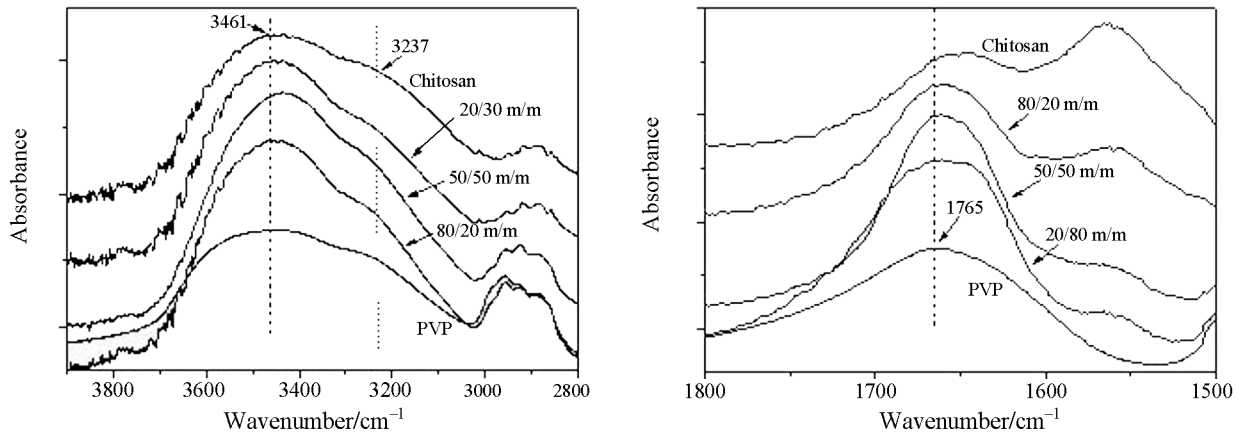

Fig. 6 FTIR spectra of PVP, Chitosan and the studied blends

containing electron donor groups [31–34]. The extent of the interactions seem to be dependent on the concentration of the two polymers and, thus, from the analogy of the reactive groups. Moreover, it seems to be greater in blends with concision close to an equal amount of each polymer, as it can be seen from Fig. 6. This, however, in the case of the PVP/Chitosan blends is not in agreement with the results of the mechanical properties and the variation of the glass transition temperature as well, where at the aforementioned concentrations the respective minimum values are observed.

Examination of the samples with XRD could provide some explanations relatively to this behavior. As is ascertained from the XRD patterns, pure Chitosan is a semi-crystalline polymer with characteristic peaks at 2θ 11.5, 15.12 and 18.5. Also semi-crystalline are the blends with a low concentration of PVP, mainly at 10–20 mass% content, whilst as the concentration of PVP increases, the blends become more amorphous. In particular, from the Chitosan/PVP 60/40 mass/mass blend and thereafter the samples are completely amorphous. The crystallinity of the blends with a low PVP content can explain the augmented mechanical properties exhibited by the blends, as well as the higher glass transition temperatures. It is a well known fact that the degree of crystallinity has a positive effect on both of them.

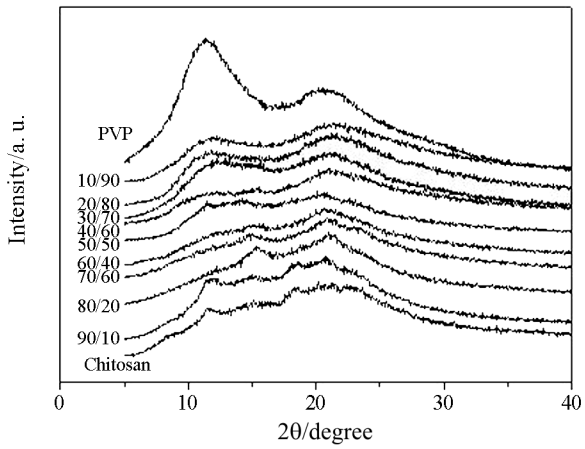

Fig. 7 XRD patterns of PVP, Chitosan and their prepared blends

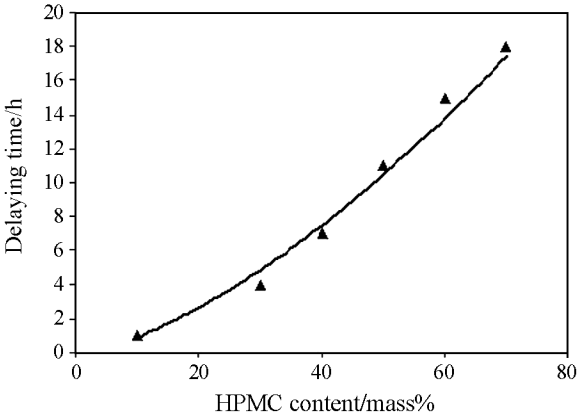

Fig. 8 Delaying time (*h*) of the tablets prepared with different PVP/HPMC blends *vs*. HPMC content (mass/mass)

Ability of the prepared blends used as effective drug carriers

The advantage of the above blends is that they are prepared from polymers that exhibit completely different physical properties, but mainly that they have different dissolution rates. Thus, matrixes are prepared with a completely different behavior compared with the original polymers when they come in contact with water solutions. For example, PVP/HPMC blends combine the high solubility of PVP with the insolubility of HPMC, which, of course, swells when it comes in contact with water and causes an explosion of the tablet or the capsule, in which it has been formed. These blends are ideal in order to

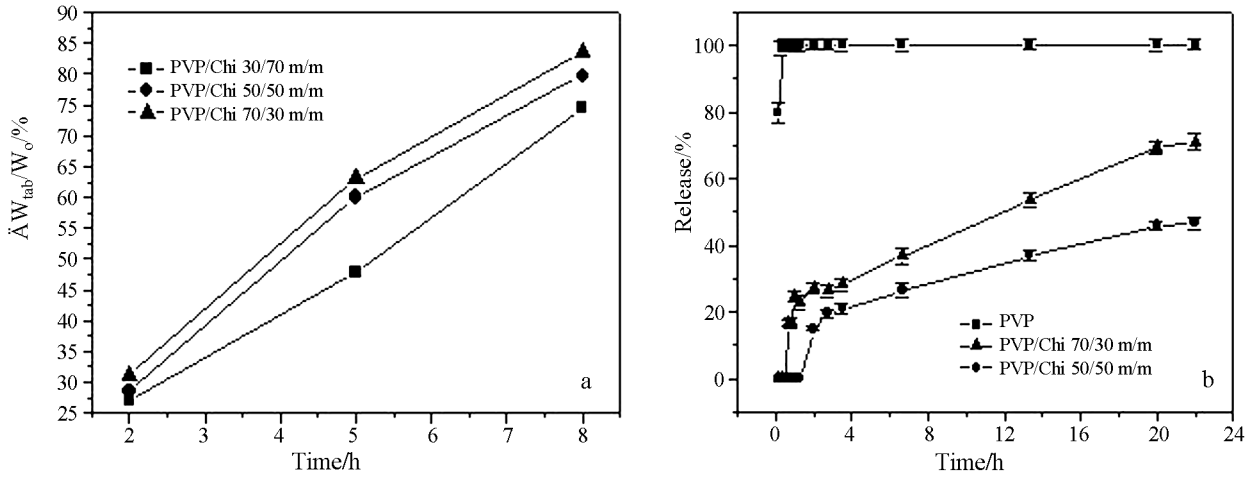

Fig. 9 a – Erosion rate of tablets prepared using PVP/Chitosan blends and b – release rate of the drug Felodipine from these mixtures

create an adjustable pulsatile system based on the high release rate of PVP and the respective low one of HPMC. To examine this, two-layer tablets were prepared by using an IR press. The coated layer had a thickness of 1 mm and it was composed from the PVP/HPMC blends at different concentrations (inactive layer), while the intermediate layer consisted from PVP/FELO 90/10 mass/mass solid dispersion in a thickness 2 mm. For their preparation a compression force of 500 Kp was applied and their resistance to crashing (hardness) was found to be more than 60 Nt. From the dissolution studies it was found that FELO releases from the active core at different times, strongly depending from the composition of coating layer. In Fig. 8 the delaying profiles of FELO release from these prepared tablets are presented. As it can be seen, by increasing the HPMC amount, the delay time is shifted to higher values. As delaying time it was defined the time that FELO will start to release from the active core, measured during dissolution of the tablets. This is very important in the case in which a drug must be released in a pulsatile manner. In the studied tablets the delaying time of FELO release can be decisively adjusted during time by varying the PVP/HPMC concentrations.

The PVP/Chitosan blends were studied for different applications such as controlled released systems of FELO in the form of single tablets with 10 mm diameter. These tablets contains 10 mass% FELO and were prepared with a compression force of 500 Kp. Hardness was found about 70 Nt. In Fig. 9 the mass loss of the tablets is presented with regard to the dissolution time. In order to measure the erosion rate, the tablets were added in 500 mL of a 0.1 M phosphate buffer with a pH value of 6.5 containing 2% Polysorbate 20 using 100 rpm agitation and the remaining mass after 2, 5 and 8 h was measured until constant mass (drying at 100°C). As it can be observed, increasing the PVP content, the erosion rate of the tablet becomes higher. This is attributed to the higher solubility of PVP compared to Chitosan which does not dissolve but adsorbs water and form a gel. Thus, the tablets prepared by these mixtures degrade gradually releasing the effective substance from the polymeric matrix.

This behavior seems to have a significant effect on the release rate of the pharmaceutical substance Felodipine, which is a poorly water soluble drug and is used in this study as a model substance. From our previous study it was found that its dissolution rate and thus its biocompatibility can be enhanced by preparing solid dispersions in a PVP matrix [35]. However, its release takes place immediately, during the first 30 min (Fig. 9b). Using different PVP/Chitosan blends the drug release can be controlled with regard to the elapsed time while Chitosan is the main factor controlling the release rate. As the amount of Chitosan decreases the release rate becomes higher.

Conclusions

From the above study of the prepared blends it can be concluded that PVP can create completely miscible blends with HPMC and Chitosan. In the case of PVP/HPMC blends, hydrogen bonds between carbonyl groups of PVP and hydroxyl groups of HPMC are responsible for the miscibility. However these interactions are rather week and the T_g value variation exhibits a negative deviation from the respective linear one. In PVP/Chitosan blends the T_g variation depends on the polymer composition and takes an S-shape form.

Both blends can be used for completely different applications in pharmaceutical technological applications.

PVP/HPMC blends can be used as effective coating layers of pulsatile systems in the form of two-layer tablets, in the case that the therapeutic effect of the drug appears to have circadian dependency and the drug has to be delivered to the body after a definite period of time. The amount of HPMC in the blend can precisely adjust the time of the drug release.

In the case of PVP/Chitosan blends the release profile of a drug can be controlled by the amount of used Chitosan in the blend.

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