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Poly(vinyl alcohol) Functionalized β-Cyclodextrin as an Inclusion Complex

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Hydrophilic poly(vinyl alcohol) functionalized β-cyclodextrin polymers were synthesized by copolymerization through a mixture of β-cyclodextrin (β-CD) and epichlorohydrin (Epi) in the presence of poly(vinyl alcohol) (PVA). The water soluble or hydrogel polymers were obtained depending on the β-CD/Epi molar ratios used in the polymerization. The structures of polymers were characterized by FT-IR, ^{1}H-NMR, ^{13}C-NMR, XRD, TGA, and DSC, respectively. The results demonstrated that the copolymerization between PVA and β-CD indeed occurred. The number of cyclodextrin units grafted on PVA chain calculated from ^{1}H-NMR spectra are 37, 41 and 73 mole β-CD per 1000 mole PVA units in PVA-β-CD1, PVA-β-CD2 and PVA-β-CD3 polymers, respectively. The contents of β-CD in polymers increased with the increase of Epi/β-CD molar ratio in the reactions. *In vitro* release of aspirin (Asp) suggested that all polymers performed sustained-release of Asp, especially, PVA-β-CD3 showed nearly linear release of Asp for 24 h. The half lifetime of an Asp tablet made from PVA-β-CD 1∼5 is 13, 7, 13, 8, and 8 h, respectively. The 3-hydroxy-2-naphthoic acid (3H2NA) was used to study the interaction between drug and polymers. Fluorescence emission spectra analysis demonstrated that cyclodextrin units grafted on polymers keep the ability of forming inclusion complex with 3H2NA by supermolecular interactions. The regression of experimental data showed that 1:1 stoichiometry for the inclusion complex between β-CD and 3H2NA, and the association constant for PVA-β-CD1, PVA-β-CD2 and PVA-β-CD3 are 305, 97 and 354 mL·g^{-1}, respectively, which increased with the increase of the content of β-CD in PVA-β-CD polymers.

Keywords: Poly(vinyl alcohol), β-cyclodextrin, inclusion complex, supermolecular interaction, crosslinking, aspirin, 3-hydroxy-2-naphthoic acid, functional polymers

1 Introduction

Poly(vinyl alcohol) (PVA), a water-soluble polyhydroxyl polymer, has been frequently used in biomedical applications such as implants (1), soft contact lenses (2), and artificial organs (3). The large applicability of PVA depends on its low price, easy availability, excellent mechanical strength, biocompatibility, and nontoxicity (4). Those characteristics come jointly with a remarkable chemical versatility due to the presence of the hydroxylic moiety, which makes feasible a number of grafting modifications and of crosslinking reactions of the polymer backbone. Beside its hydrophilic character, PVA forms hydrogels that are widely used in pharmaceutics as a drug delivery matrix. However, the interactions between PVA and drugs are based on polymer matrix, and do not have selectivity for drugs. In recent years, the drug delivery system based on host-guest interaction is widely developed for its controlling release and selectivity.

Cyclodextrins (CDs) are well known host molecules for their ability to form inclusion complexes (host-guest type) with several classes of compounds including drugs. The classical cyclodextrin series are constituted of six (α-CD), seven (β-CD), or eight (γ-CD) D-glucopyranoside units linked by R-1,4 bonds. CDs have a torus-shaped, apolar and electron-rich hydrophobic cavity with an internal diameter of 5.7, 7.8 and 9.5 Å, respectively (5). Due to this inherent property, CDs are used widely in pharmaceutical science to improve drug stability, dissolution rates, and bioavailability (6). Owing to the excellent characters of CDs, much work has focused on modifying polymers with CDs (7, 8) and the applications as an adsorbent for adsorption of dyes (9–11). PVA modified with CDs also has been applied. Sreenivasan (12) found that the release of salicylic acid from PVA matrix in the presence of β-CD prolonged

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considerably the release of the profile of the drug from the PVA gel. However, the material is just a mixture of PVA and CD. Thus, many crosslinked CD/PVA materials have been prepared in the literature. PVA microspheres containing CD were obtained by chemical crosslinking with glutaraldehyde of an acidified mixture solution of PVA and α-,β- or γ-CD (13). Poly(vinyl alcohol)-based hollow (air-filled) microparticles with surface chemical coupling with β-CD is also prepared (14). Moreover, PVA containing CD can be used in chiral selective cation-exchange membrane and chiral selective anion-exchange membrane (15). However, aldehydes crosslinking reagents may lead to a decrease in hydrophilicity of materials. Therefore, some other reagents should be applied to increase or retain the hydrophilicity of PVA. Epichlorohydrin (Epi) is a common crosslinking reagent, which reacts with hydroxyl groups in alkaline media, and the product is glycidol ether, which is a hydrophilic and biocompatible polymeric material. In the present work, Epi was used as a crosslinking reagent, a series of hydrophilic poly(vinyl alcohol) crosslinked β-cyclodextrin polymers (PVA-β-CD), i.e., three water soluble polymers and two hydrogels were obtained. The products were characterized by FT-IR, ^{1}H-NMR, ^{13}C-NMR, TGA, DSC and XRD. *In vitro* release of aspirin (ASP) results suggested that all polymers performed sustained-release of Asp, especially, PVA-β-CD3 showed nearly linear release of Asp for 24 h. The half lifetime of Asp tablet made from PVA-β-CD 1$\sim$5 is 13, 7, 13, 8, and 8 h, respectively. Inclusion properties of these synthesized polymers were investigated by fluorescence spectra using 3-hydroxy-2-naphthoic acid (3H2NA) as a fluorescence guest at different 3H2NA concentrations and pH. The results demonstrated that β-CD was just linked on PVA chain, and β-CD units retained the ability of forming an inclusion complex with small molecules by supermolecular interactions, other than filled with PVA chains resulting in a loss of its character of being a host molecule.

2 Experimental

2.1 Materials

PVA (LR, Average polymerization degree of 1750 $\pm$ 50) was purchased from Tianjin NO. 6 Chemical Reagent Factory. β-CD, Epi, salicylic acid (SA), and 3H2NA were analytical reagents purchased from Tianjin Kermel Chemical Reagents Development Center. Dialysis bag (cellulose membrane, M_W cut-off 8000) purchased from Sigma-Aldrich. Asp (BP/CP/USP/) was purchased from JQC (Huayin) Pharmaceutical Co. Ltd.

2.2 Methods

IR spectra were recorded on Nicolet 870 using KBr pellets. ^{1}H-NMR and ^{13}C-NMR spectra were recorded on AVANCF 300MHz super-conducting Fourier Digital NMR spectrometer (with TMS as an internal standard, D_2O was used as a solvent). Fluorescence emission spectra were measured with a 970CRT fluorescence spectrophotometer (λ_{ex} = 350 nm, S_{em} = 10 nm/ S_{ex} = 10 nm (at 25°C)). The XRD measurements were recorded on a Rigaku D/max-3c apparatus at room temperature with Cu $K\alpha$ radiation (λ = 0.154 nm) in a range of 5–40° (2θ), operated at 40 kV and 100 mA. The TGA measurements were performed on a Thermoanalyzer System, model Q600SDT (TA Co. Ltd. USA). Samples of about 5 mg, placed in a pan, were heated from 50 to 550°C at a scanning rate of 20°C/min, under a constant flow of dried nitrogen. The differential scanning calorimetry (DSC) of the selected samples was conducted on a TA-Q1000 under the atmosphere of flowing nitrogen and at a heating rate of 20°C·min^{-1}.

UV-Vis spectra were recorded on TU-1901 UV-Vis spectroscopy (Beijing Purkinje General Instrument Co. Ltd.)

2.3 Synthesis of Poly(vinyl alcohol) Crosslinked β-cyclodextrin Polymers

A typical synthesis procedure for PVA-β-CD is described as following: A mixture of 3.0 g PVA, 10.0 g β-CD and 40 mL water was stirred at 95°C until all reagents dissolved in water, when the solution temperature cooled down to 60°C, 30 mL of 30% NaOH aqueous solution was slowly added dropwise under stirring. Then the calculated amount of Epi was added directly. The polymerization was kept at 60°C for 12 h, then the reaction was stopped by the addition of acetone. Finally, acetone was removed and a pale yellowish hydrogel was obtained. The gel was neutralized by hydrochloric acid and washed liberally with 70% alcohol/water solution until no chloride ion in aqueous solution was detected, and then vacuum freeze-dried. A pale yellowish PVA-β-CD was obtained.

2.4 Preparation of Asp Tablet

An amount of 0.275 g polymer synthesized and 0.025 g Asp were grinded for 30 min in an agate mortar, afterwards, 3 mL of 20% ethanol were added, and kept at room temperature for 24 h, then vacuum freeze-dried for 48 h. The tablet was prepared at 5 MPa for 2 min. T1$\sim$T5 are made from PVA-β-CD1$\sim$5, respectively.

2.5 *In vitro* Drug Release

The *in vitro* drug release study was conducted using a dialysis bag. 0.1g of the drug-loaded tablet were put into 10 mL of a phosphate buffer solution (pH 6.8) inside a dialysis bag. The dialysis bag was placed in 30 mL of the buffer solution at 37°C. At successive time intervals, aliquots (5 mL) of the release medium were collected and replaced

with a fresh buffer solution. The collected sample was next analyzed using the UV-Vis spectroscopy.

2.6 Inclusion Property of PVA-β-CD

A series of aqueous solutions of 3H2NA, mixed with hydrosoluble PVA-β-CD, were prepared and kept at room temperature for 24 h, the concentration of 3H2NA is 1.00×10^{-5} mol·L^{-1} and PVA-β-CD are 0, 3.528×10^{-4}, 5.880×10^{-4}, 7.350×10^{-4}, 2.940×10^{-3}, 5.145×10^{-3}, 7.350×10^{-3}, 1.29×10^{-2} g·mL^{-1} respectively. Fluorescence emission spectra were measured with a 970CRT fluorescence spectrophotometer ($\lambda_{ex} = 350$ nm, $S_{em} = 10$ nm/$S_{ex} = 10$ nm). Double reciprocal plots (16) between $(F - F_0)^{-1}$ and $C^{-1}_{\beta\text{-CD}}$ were obtained, where F_0 is the fluorescence intensity of 3-hydroxy-2-naphthoic acid in aqueous solution and F is the intensity of 3-hydroxy-2-naphthoic acid in the presence of PVA-β-CDs.

3 Results and Discussion

3.1 Synthesis and Characterization

Most modifications of polyhydroxyl polymer, such as starch, cellulose and chitosan are applied in an alkaline media. PVA is a polyhydroxyl polymer, however, PVA will form a thick colloid material in a strong alkaline aqueous media, and therefore, most modifications of PVA are applied in acidic media or in organic solvents. It is interesting that PVA can dissolve in a strong alkaline aqueous solution in the presence of β-CD. The possible reason is that β-CD accepts base and prevents PVA chains to reunite. Thus, β-CD modified PVA is obtained by using Epi as crosslinked reagents in an alkaline aqueous solution (Table 1). With the increase of the molar ratio of Epi/β-CD, the water solubility of products decreased. Water soluble PVA-β-CD1, PVA-β-CD2, and PVA-β-CD3 were obtained when 10 g β-CD dissolve together with 3 g PVA and the molar ratios of β-CD/Epi are 1/1, 1/2 and 1/4, respectively. However, when the molar ratios of β-CD/Epi are 1/7 and 1/10, hydrogels of PVA-β-CD4 and PVA-β-CD5 are obtained.

Figure 1 shows FT-IR spectra of PVA-β-CDs, PVA and β-CD. The similar peak-shaped vibration of polymers and β-CD implies that polymers keep the original characteristic structure of β-CD. The characteristic bands of -OH strongly appear at near 3440 cm^{-1}(O-H of stretching) and 1640 cm^{-1} (O-H of plane bending). The characteristic bands of CD are also observed at 1028–1159 cm^{-1}(C-O and C-O-C of stretching). Compared with β-CD, the absorption of the polymers is wider and weaker and demonstrated that new ether bonds existed and resulted in the polarity decrease.

Table 1. Conditions for synthesis of PVA-β-CDs

β-CD/Epi[a]	*β-CD (g)*	*PVA (g)*	*Polymer*
1/1	10.0	3.0	PVA-β-CD1
1/2	10.0	3.0	PVA-β-CD2
1/4	10.0	3.0	PVA-β-CD3
1/7	10.0	3.0	PVA-β-CD4
1/10	10.0	3.0	PVA-β-CD5

[a]Molar ratio.

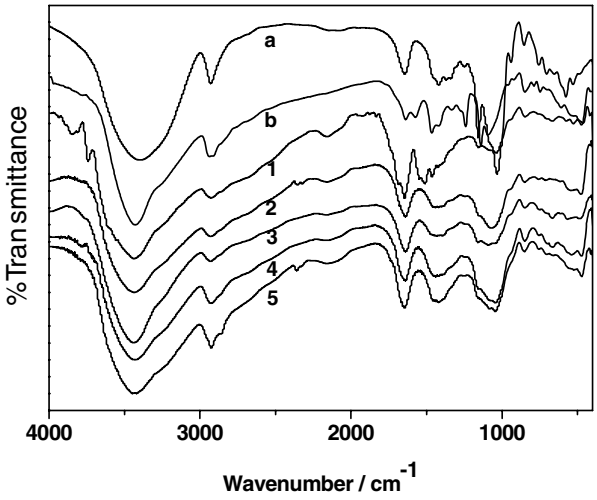


Fig. 1. IR spectra of β-CD(a), PVA(b) and PVA-β-CD1∼5.

Figure 2 shows ^{1}H-NMR spectra of PVA-β-CD1∼3. The peak near 5 ppm is assigned to the anomeric proton attached to the C-1 of the glucose unit; and two broadened peaks between 3 and 4 ppm correspond to the protons in pyranose rings, the protons attached to C-1 of the PVA units and the protons of glycerol ether units. Peaks near 1.5 ppm are assigned to the proton attached to the C-2 of the PVA units. ^{1}H-NMR spectra demonstrated that PVA and β-CD are successfully crosslinked by Epi. According to the integral area ratio of near 5 to 1.5 ppm, the amounts of

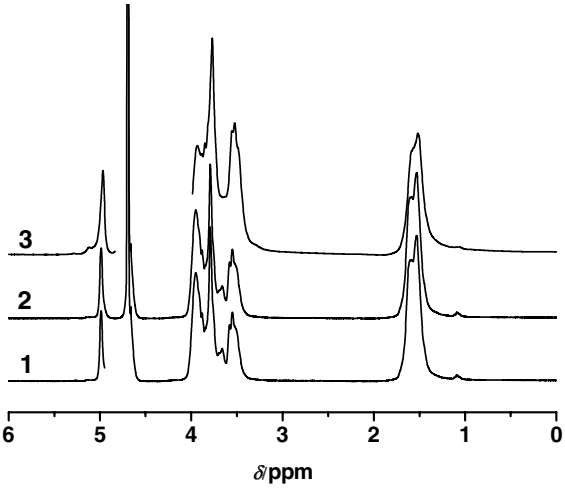


Fig. 2. ^{1}H-NMR spectra of PVA-β-CD1, 2, and 3 in D_2O.

Table 2. [1]H-NMR analysis of polymers

Samples	*Integral area* ~ 5*ppm*	~ 1.5*ppm*	*CD units per 1000 PVA units*
PVA-β-CD1	1.00	7.64	37
PVA-β-CD2	1.00	6.84	41
PVA-β-CD3	1.00	3.87	73

cyclodextrin units linked on PVA chain can be calculated. There are about 37, 41 and 73 mole β-CD per 1000 mole PVA units in PVA-β-CD1, PVA-β-CD2 and PVA-β-CD3, respectively (Table 2). In other words, with the increase of Epi in reaction, the amounts of β-CD linked on PVA increase as well.

To investigate the structure of polymers, ^{13}C-NMR spectra of PVA-β-CD1, 2, and 3 in D_2O are given in Figure 3. The peaks at 68, 66, 64 and 43 ppm are assigned to carbons in PVA chains. The peaks at 101, 80, 72, and 59 ppm are assigned to C-1, C-4, C-3, and C-6 of the glucose units in cyclodextrin, respectively. At 71 ppm, the peak is assigned to C-2 and C-5 of the glucose units, signals of C-2 and C-5 which overlay each other suggest that the products are polymers. There is no any signal ranging from 72 to 80 ppm attributed to the resonance of C-2 and C-3, suggesting the substitution did not occur on C-2 and C-3. Signals at 67 and 62 ppm are attributed to the carbons of glycidol chains, from PVA-β-CD1 to PVA-β-CD3, the intensity increased, and suggested that the crosslinked degree of polymers increased with the increase of Epi in reaction.

3.2 Crystallinity

The X-ray diffraction measurements were performed to examine the crystalline nature of PVA-β-CDs. Figure 4 shows the X-ray diffraction scans for PVA-β-CD1~5. From Figure 4, it indicated that there was only one peak around

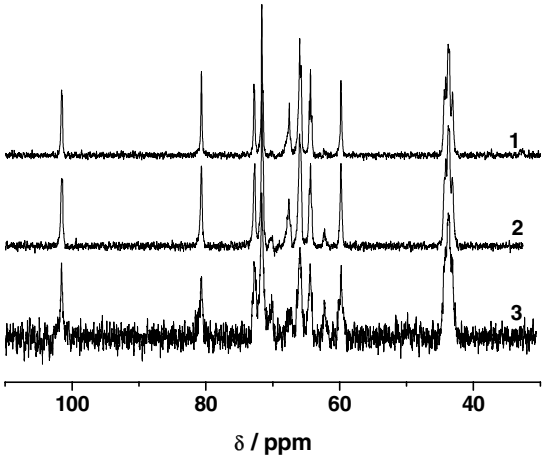


Fig. 3. ^{13}C-NMR spectra of PVA-β-CD1, 2, and 3 in D_2O.

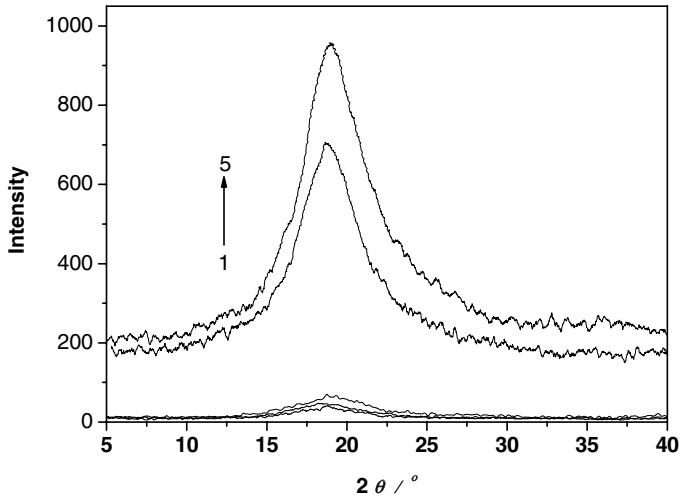


Fig. 4. The X-ray diffraction measurement for PVA-β-CD1~5.

2θ of 19°. From PVA-β-CD1 to PVA-β-CD5, the peak intensity of the diffractions increased significantly. The crystallinity of products increased with the increase of the Epi amounts in reaction systems as well. In comparison with PVA-β-CD4 and PVA-β-CD5, the peak intensity of PVA-β-CD1~3 is very low, the possible reason is that the crosslinking degrees in PVA-β-CD1~3 polymers are lower, and they are also water soluble.

3.3 TG Analysis

From room temperature to 550°C, there were three weight loss stages for PVA-β-CD1~5 as shown in Figure 5. The first transition temperature ranged from room temperature to 180°C, which is corresponding to the loss of water. The following transition temperature ranged from 180 to 350°C is attributed to the degradation of polymer, and the final

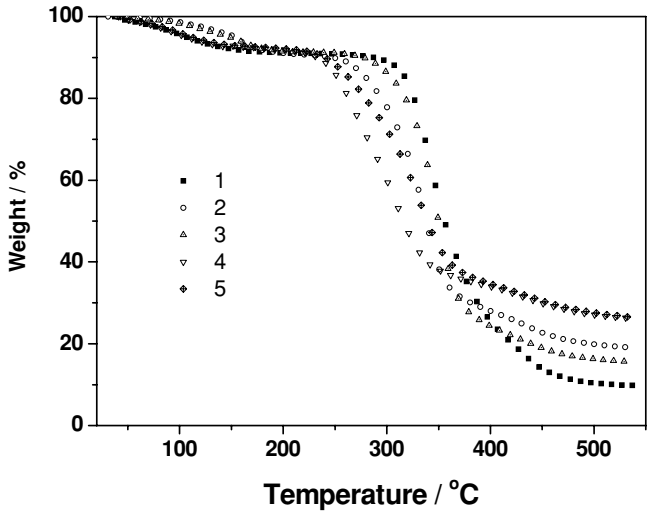


Fig. 5. TG curves of PVA-β-CD1~5.

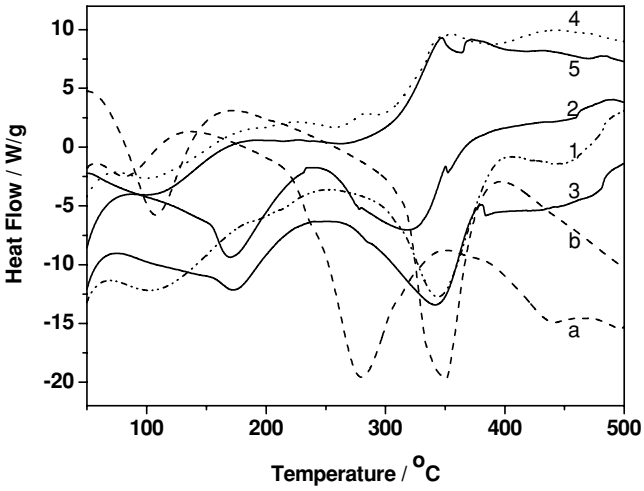


Fig. 6. DSC curves of PVA (a), b-CD (b), PVA-b-CD1 (1), PVA-b-CD2 (2), PVA-b-CD3 (3), PVA-b-CD4 (4), PVA-b-CD5 (5).

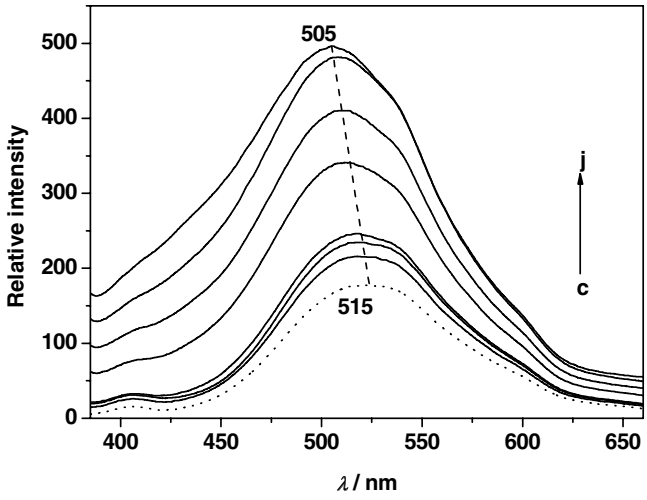


Fig. 7. Fluorescence emission spectrum of 3H2NA 1.00×10^{-5} mol·L^{-1} in the presence of different concentrations of PVA-β-CD1 in solution. PVA-β-CD1 concentrations, c-j: 0, 3.528×10^{-4}, 5.880×10^{-4}, 7.350×10^{-4}, 2.940×10^{-3}, 5.145×10^{-3}, 7.350×10^{-3}, 1.29×10^{-2} g·mL^{-1} respectively.

transition above 400°C is ascribed as the degradation of polymer fragments. In the main weight loss processes, the starting weight loss temperatures tend to lower from PVA-β-CD1 to PVA-β-CD5. The possible reason is that with the increase of the Epi/β-CD molar ratio, the polymers tend to crosslink each other, and the content of PVA and glycidol chain increased, both of them tend to degrade at low temperature. In the final degradation processes, the amounts of residual materials that did not degrade increased from PVA-β-CD1 to PVA-β-CD5, the possible reason is that the content of PVA and glycidol chains increased, and the oxygen content of them was smaller than cyclodextrin, so the amounts of carbonization increased as well.

From Figure 6, the first endothermic processes from ambient temperature up to 200°C are similar for PVA-β-CD1, PVA-β-CD4 and PVA-β-CD5 to that of the β-CD, and the endothermic peaks appeared at 110°C. However, endothermic peaks of PVA-β-CD2 and PVA-β-CD3 appeared at 170°C, the peak position is lower than the thermal degradation of PVA and β-CD, but higher than the water loss process of PVA and β-CD. The other endo or exo process is thermal degradation that occurs above 300°C and peak at 350°C, for PVA-β-CD1, PVA-β-CD2, and PVA-β-CD3. These processes are an endothermic process, and the results are similar with that of the β-CD. However, for PVA-β-CD4 and PVA-β-CD5, the thermal degradation changes to exothermic processes. The results indicate that PVA-β-CD4 and PVA-β-CD5 polymers are different with the other samples, β-CD and PVA chains are remarkably crosslinked by glycidyl ether in PVA-β-CD4 and PVA-β-CD5 polymers.

3.4 Inclusion Property

3H2NA is a fluorescence reagent containing an intramolecular hydrogen bond and has a similar structure with salicylic acid (17). 3H2NA was used to study the inclusion behaviors of β-cyclodextrin polymers (18) and the inclusion property between PVA-β-CD and guest in solution. A great increase in the fluorescence relative intensity and a blue shift from 515 to 505 nm are observed in Figure 7, suggesting the lower polarity of species in the CD cavity. Obviously, the reasonable explanation is that the shielding effect of CD makes self-quenching reduce when 3H2NA enters the CD cavity. The blue shift occurrence is an indication of the host-guest interaction. These results suggest that cyclodextrin is just linked on the PVA chain; cyclodextrin units keep the ability of forming inclusion complex with small molecules by supermolecular interaction, other than filled by PVA chains, which result in loss of its character of being a host molecule.

The fluorescence relative intensity increases with the increase of PVA-β-CD concentration in an aqueous solution when 3H2NA remains in the same concentration under the same conditions. According to the method reported by Bright et al. (16), for a simple 1:l (host-guest) complex:

$$C_S/F_{SB} = (K k_{SB} Q_{SB})^{-1} (C_B)^{-1} + (k_{SB} Q_{SB}^{-1}) \qquad (1)$$

where K is the equilibrium constant, C_s is the analytical concentration of the fluorescent substrate, C_B is the analytical concentration of the β-CD, Q_{SB} is the quantum yield for inclusion complex, F_{SB} is the fluorescence intensity of inclusion complex, and k_{SB} is an instrumental constant. Thus, a reasonable estimation of K can be obtained from a plot of $1/F_{SB}$ vs. $1/C_B$, by simply dividing the intercept by the slope. Plots of this type are referred to as double reciprocal plots. Figure 8 illustrates the double reciprocal plot for 3H2NA and PVA-β-CDs complex. The completely linear regression for this plot is an indication of 1:l complexation. Those results show that the inclusive ratio

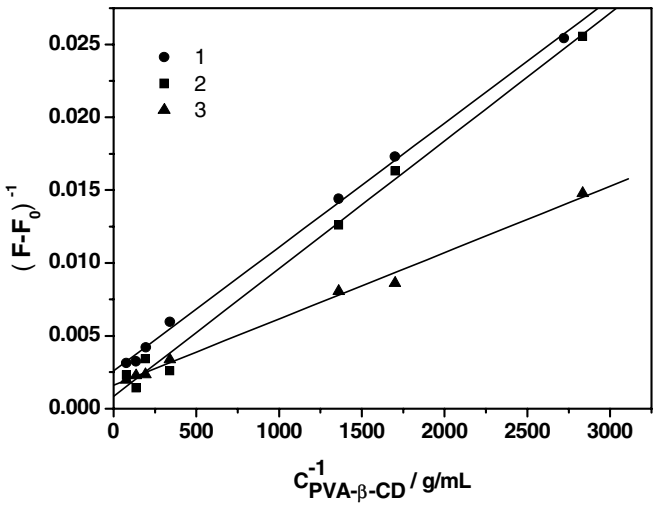


Fig. 8. Double reciprocal plot for 3H2NA and PVA-β-CDs complex. (●PVA-β-CD1 ■PVA-β-CD2 ▲PVA-β-CD3).

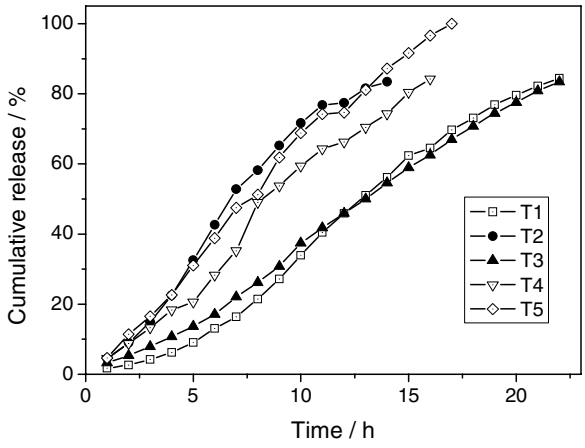


Fig. 10. Asp release behavior of T1 ~ T5.

of the CD to 3H2NA is really the same for PVA-β-CD1 to PVA-β-CD3. Furthermore, the formation constants of PVA-β-CD1, PVA-β-CD2 and PVA-β-CD3 are 305, 97 and 354 $mL \cdot g^{-1}$, respectively. The results indicated that with the increase of β-CDs content in PVA-β-CDs, the stability of the inclusion complex between PVA-β-CD and 3H2NA increased.

3.5 *In vitro* Release of Asp

Asp was used as a model substance to study the delivery property of synthesized polymers. Figure 9 shows the UV-Vis spectra of release medium for different tablets. T1 and T3 have obvious absorbance at 265 nm, and indicated that some of drug molecules are released as the Asp, but for T2, T4, and T5, almost all drug molecules are released as SA.

Results of the drug release are shown in Figure 10. The half lifetime of T1 ~ T5 is 13, 7, 13, 8, and 8 h, respectively. All tablets performed sustained-release of Asp. T3 made from PVA-β-CD3, shows nearly linear release of Asp for 24 h, and the half lifetime is longer than others. T1 released slowly at the initial stage, but a little faster at the last stage. The release tendency and half lifetime of T1 are similar to T3. However, for T2, it is very interesting that almost all drug molecules are released as SA, not Asp, also released more quickly than T1 and T3. For T4 and T5, the half lifetime is shorter than T1 and T3. With the increase of Epi in reaction, more –OH groups on CD ring participate in the reaction, those polymer chains delayed Asp from entering into a β-CD cavity to form an inclusion complex and led the hydrolyzation of Asp, so T4 and T5 released the drug as SA. The hydrolyzation of Asp not only occurred in the release stage, but also in the preparation of the tablet process, many Asp molecules were hydrolyzed during the swelling process with 20% ethanol.

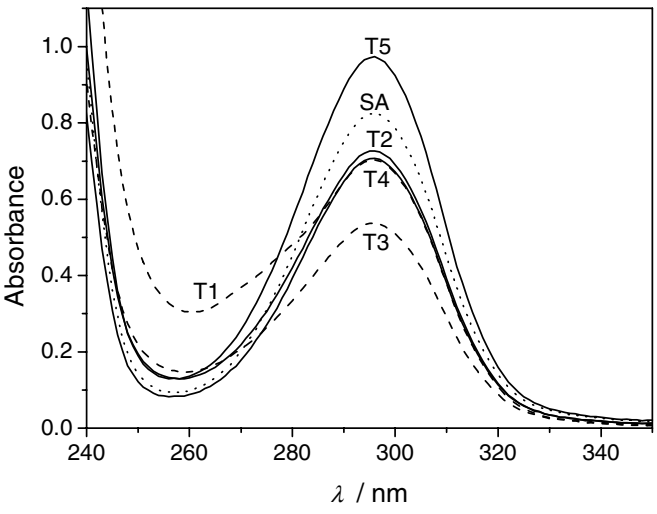


Fig. 9. UV-vis spectra of T1 ~ T5 and SA.

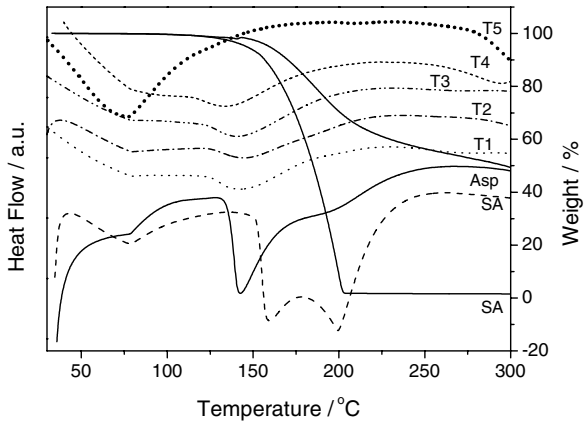
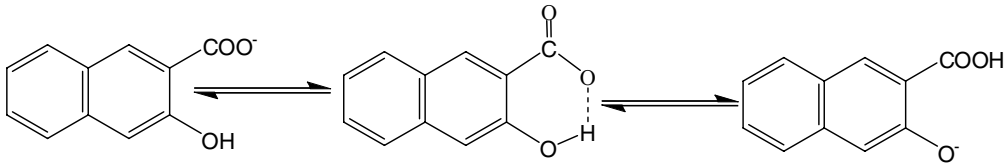


Fig. 11. DSC curves of T1 ~ T5, TG/DSC curves of SA and Asp.

mixture.



Sch. 1. Effect of pH on acid-base balance of 3H2NA

3.6 Thermal Analysis

We used DSC and TG to characterize the physical properties of the drugs in the polymer (Figure 11). Asp shows a melting endothermic peak at 142°C as shown in the DSC curve of Asp. The melting process is a decomposition process and leads to about 20% weight loss. SA shows a melting endothermic peak at 159°C. The TG curve of SA shows an almost complete weight loss, because SA will volatilize immediately after melted. T1 ~ T4 samples show endothermic peaks at nearly 140°C, indicating that Asp is embedded by polymers successfully. No peak at the temperature range from 140 to 160°C for the T1 ~ T4 was detected, suggesting that SA dispersed well in polymers. No peak is observed at the temperature range from 120 to 200°C, indicating that little Asp existed in T5 because all Asp molecules have been hydrolyzed into SA during the swelling process of preparing the tablet.

3.7 Effect of pH on the Fluorescence of 3H2NA and 3H2NA/PVA-β-CD1 Mixture

The effects of pH on the fluorescence of 3H2NA and 3H2NA/PVA-β-CD1 mixture were studied (Figure 12). When the pH is lower 7, blue shifts of the fluorescence maxima emission are observed, and red shifts while pH is greater 7 with the presence of PVA-β-CD1. When pH = 1.4, the fluorescence intensity of 3H2NA is very low, and great increases are observed in the presence of PVA-β-CD1. When pH ranges from 4 to 11, an obvious blue shift and great increase fluorescence intensity are observed in the presence of PVA-β-CD1. When pH = 13, the fluorescence intensity of 3H2NA is very strong, and an obvious increase is observed in the presence of PVA-β-CD1. The fluorescence behaviors of 3H2NA are affected by pH because it is a fluorescence reagent containing an intramolecular hydrogen bond (19). A similar phenomenon is observed in the presence of PVA-β-CD1, which indicates that the phenolic hydroxyl and carboxyl group of 3H2NA are outside of the cavity of β-CD units. The increase in fluorescence intensity demonstrates that the inclusion process indeed occurred, combining the results of the double reciprocal plot for 3H2NA and PVA-β-CDs complex (Figure 8), we can conclude that the inclusion complex formed: one naphthalene ring of 3H2NA enters into one of the cavity of β-CD units on polymer and the hydrophobic interactions and hydrogen bonding play an important role in the formation of the inclusion complex (Scheme 1).

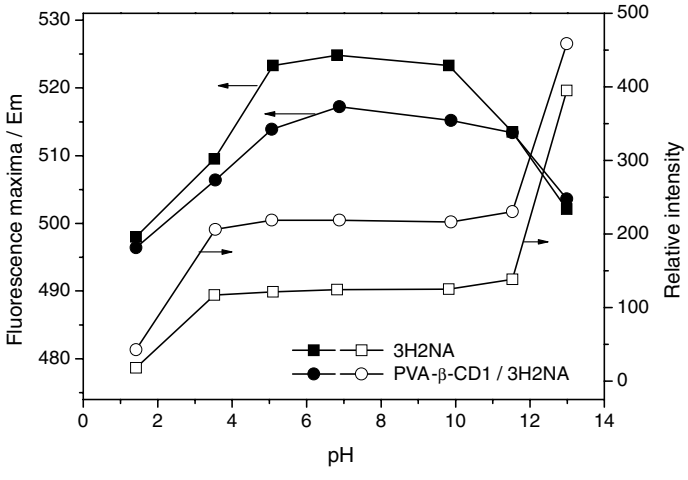


Fig. 12. The effect of pH values on the fluorescence of 3H2NA and 3H2NA/PVA-β-CD1 mixture.

4 Conclusions

We found that poly(vinyl alcohol) can dissolve in strong alkaline aqueous media in the presence of β-cyclodextrin, which makes the crosslinking between PVA and β-CD possible. In the present study, hydrophilic poly(vinyl alcohol) grafted β-cyclodextrin polymers with varieties of β-CD units in the grafted PVA-β-CD polymers were synthesized. The grafted polymers were confirmed by FT-IR, UV-Vis, XRD, NMR, IR, TGA, and DSC. The cyclodextrin units on grafted polymers retain the ability of forming inclusion complex with a small molecule by supermolecular interactions. The fluorescence results indicated that the inclusive ratio of β-CD to 3H2NA is 1:1 for PVA-β-CD1~3, and the association constants increased with the increase of β-CD content in PVA-β-CDs, so the stability of the inclusion complex between PVA-β-CD and 3H2NA increased with the increase of the β-CD content in PVA-β-CDs. Aspirin was selected as a drug model to embed with PVA-β-CDs. The vitro release of Asp suggested that all polymers performed sustained-release of Asp, especially, PVA-β-CD3 showed nearly linear release of Asp for 24 h. The half

lifetime of the Asp tablet made from PVA-β-CD 1∼5 is 13, 7, 13, 8, and 8 h, respectively. The titled method may be useful to the pharmaceutical industry for improving the solubility and stability of drugs.

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