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An investigation of the thermodynamic miscibility between VeTPGS and polymers

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Abstract

Within the past decade, more than half of the drug candidates generated are poorly water soluble and therefore overcoming the low aqueous solubility of drug candidates becomes critical for product development. Vitamin E TPGS (VeTPGS), a non-ionic surfactant, has been used in both liquid and solid dosage forms to solubilize compounds and improve their bioavailability. To prepare solid dosage forms using VeTPGS, VeTPGS is often mixed with other excipients, mostly polymers. However, there is still a lack of understanding of miscibility between VeTPGS and polymers from a thermodynamic point of view. In this paper, the miscibility of VeTPGS with polymers has been studied in the light of the Flory–Huggins (F–H) theory with an objective to understand the effect of dispersion forces (solubility parameter) and nondispersive interactions on the miscibility between VeTPGS and polymers. A series of polymers with similar solubility parameters and structure similarity were selected. Binary blends of polymers and VeTPGS were prepared using a vapor evaporation technique followed by XRPD, DSC, and SEM characterization. Results suggest that the miscibility between VeTPGS and PMMA is very likely due to a specific interaction between the hydrophobic portion of VeTPGS (Vitamin E) and PMMA.

Keywords: Vitamin E TPGS; Solid dispersion; Flory–Huggins theory; F–H interaction parameter; Miscibility and modified F–H theory

1. Introduction

In the last decade, the implementation of high throughput techniques for screening new compounds for pharmacological activity has generated a significant number of new drug candidates with good permeability, but poor aqueous solubility (Van de Waterbeemd et al., 2003). This class of compounds is typically identified as "Class 2" according to the biopharmaceutical classification systems (BCS) (Amidon et al., 1995; Dressman et al., 1998; Yu et al., 2002). The poor solubility of these compounds is the rate-limiting step for absorption. Consequently, this lack of aqueous solubility imposes a significant challenge for scientists in drug development to improve product bioavailability by increasing solubility or dissolution rate. To increase the bioavailability of BCS Class II compounds and thereby the efficacy of the drugs, a few approaches have been taken, including: particle size reduction (Hu et al., 2004), lipid-based drug delivery systems such as SEDDs (Pouton, 2006), drug–polymer solid dispersion (amorphous systems) (Habib, 2000), and other solubilization methods (Yalkowsky, 1998). Although particle size reduction, which is to increase the dissolution of particles by increasing the overall surface area (Noyes–Whitney Equation), is the most common method used in industry, it often has limited value at high dose (Carstensen, 1973). For lipid-based delivery systems, solubilizers and stabilizers are often needed (Pouton, 2000). In the case of preparing drug–polymer solid dispersions, a surface active agent is often added to enhance the bioavailability (Wulff and Alden, 1995). Vitamin E d-alpha tocopheryl polyethylene glycol 1000 succinate (VeTPGS), a non-ionic surfactant, is often used in both liquid and solid dosage forms for increasing solubility and bioavailability (Yu et al., 1999; Damian et al., 2002). Chemically, VeTPGS is made of PEG1000 and Vitamin E (see Fig. 1). VeTPGS has been used in liquid formulations to enhance bioavailability (Yu et al., 1999). VeTPGS was also used in a solid dispersion formulation (Damian et al., 2002; Rajebahadur et al., 2006). To incorporate VeTPGS into

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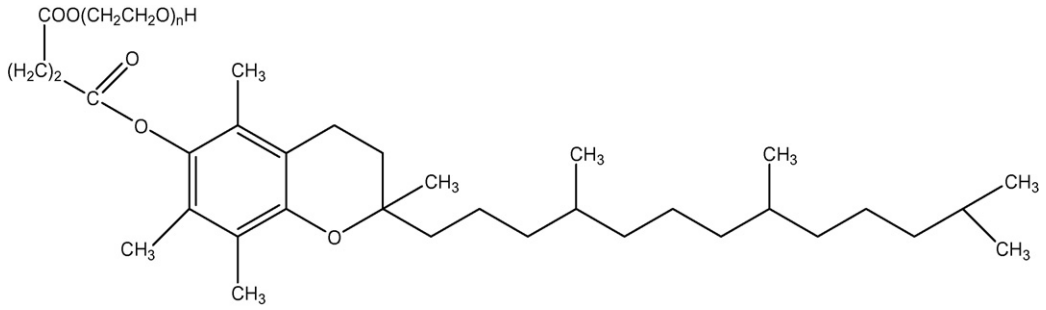

Fig. 1. Chemical structure of VeTPGS.

solid dosage forms, either a conventional solid or a solid dispersion, VeTPGS needs to be mixed with polymers or other materials to overcome its waxy nature due to its low melting point through adsorption or increasing its glass transition temperature. However, the miscibility of VeTPGS with polymers is still not well understood. This research addresses the miscibility of VeTPGS with polymers from the thermodynamic point of view. Polymers including PMMA, PEO, and PEG1000, having a similar solubility parameter (δ), or similar structure, were selected to study their miscibility with VeTPGS. X-ray powder diffraction (XRPD), DSC, and SEM have been used to characterize VeTPGS-polymer blends. The Flory–Huggins (F–H) theory serves as a frame to discuss their miscibility (Flory, 1942; Huggins, 1942).

2. Materials and methods

2.1. Materials

Carbowax Sentry Polyethylene Glycol 1000 NF, FCC Grade (PEG1000) was obtained from Union Carbide Chemicals Inc. (Danbury, CT). Poly(methyl methacrylate) (PMMA), Vitamin E, and polyethylene oxide (MW 100,000 and 200,000) (PEO100 and PEO200, respectively) were purchased from Sigma–Aldrich Chemicals Inc. (St. Louis, MO). Vitamin E d-alpha tocopheryl polyethylene glycol 1000 succinate (VeTPGS) was purchased from Eastman Chemicals Inc. (Kingport, TN). The solvents used to dissolve the polymers or Vitamin E TPGS or Vitamin E were ethyl alcohol (200 Proof) purchased from Aaper (Shelbyville, KY). Acetone and chloroform were obtained from EM Sciences (Norwood, OH). All solvents used were HPLC grade or equivalent.

2.2. Sample preparation

Each blend was prepared in four, separate, exact gram ratios of 1:1, 1:2, 1:3, and 1:4. The polymer pairs or VeTPGS or Vitamin E and polymers were dissolved in 100 mL of solvent (neat). For the PEG1000-PMMA, PEO100-PMMA, and PEO200-PMMA blends, all materials in the exact gram ratio as mentioned above were dissolved in acetone. The solutions were placed on a stir plate followed by slight heating for 15 min until the solutions were clear and colorless. To prepare the VeTPGS-PMMA blends, all materials in the exact gram ratio were dissolved in chloroform followed by stirring for 1.5 h. The resulting solutions were clear and colorless except for the VeTPGS-PMMA solution in the 1:1 ratio, which was translucent gray. The Vitamin E-PMMA blend was prepared by dissolving Vitamin E and PMMA in chloroform, followed by a 10-min stirring. The ratio of the Vitamin E and PMMA was equivalent to the 1:3 ratio of VeTPGS-PMMA. The resulting solution was clear with a yellowish-brown color. All polymer blend solutions were poured into Teflon-coated Petri dishes (Chemware PFA Petri Dish, 100 mL), and allowed to evaporate in a fumehood overnight. The air-dried samples were then placed in a vacuum oven to further remove any residual solvent.

2.3. DSC measurement

Thermal analysis experiments were performed using a TA Instruments Q1000 DSC with a refrigeration cooling system (RCS) in a standard mode. In-house dry nitrogen was used as the purge gas at a flow rate of 50 mL/min. The scanning rate used was 10 °C/min. A typical scanning temperature range was from −70 to 250 °C. Typically, a 5–10 mg sample was cut from one of the prepared polymer films followed by transferring into an open, aluminum pan. The sample pan was then transported to the instrument carousel for measurement. Determination of the glass transition temperature (T_g) at the reflection point, and the melting point temperature (T_m) at the onset point was obtained using TA Instruments' standard extrapolation programs.

2.4. XRPD measurement

X-ray powder diffraction (XRPD) patterns of all samples used in this work were taken at ambient temperature using a Bruker AXS X-Ray Powder Diffractometer (Model D8 Advance, Serial No. 001983) at 40 mA and 40 kV with Cu Kα radiation (1.54 Å) in parallel beam mode with a Gobel Mirror, and a LiF monochromator. A scintillation detector was employed for XRPD acquisition. All XRPD patterns were acquired using a scan type detector at a tube angle of 1° (2θ). A typical scan range was from 1° to 35° (2θ) with a step size of 0.05° (2θ), and a counting time of 4 s. Samples for XRPD measurement were prepared by cutting approximately a 1 cm^2 from each of the polymer films and transferring the representative sample to a nickel-plated sample holder, followed by placement of the holder into the instrument.

2.5. Scanning electron microscopy (SEM) characterization

Two preparations for each polymer film were made as follows:

(i) Preparation 1: Pieces of each polymer film were cut with a razor blade to expose a cross-sectioned surface. The films were cut at room temperature. The cross-sections were trimmed to an approximate size of 10 mm × 2 mm, and mounted on edge to an aluminum pin mount secured with carbon conductive tabs. The cross-sections were sputter coated with approximately 12 nm of platinum using an Edwards Model XE 200 Xenosput.

(ii) Preparation 2: Pieces of each polymer film were bent until they fractured to expose a cross-sectioned surface at room temperature. The cross-sections were trimmed to an approximate size of 10 mm × 2 mm, and mounted on edge to an aluminum pin mount secured with carbon conductive tabs. The cross-sections were sputter coated with approximately 12 nm of platinum using an Edwards Model XE 200 Xenoput.

The polymer films were imaged as follows:

(iii) Cross-sections of the films were photographed using an Olympus stereo microscope (model SZH) equipped with a DF PLANAPO 1X lens before sputter coating. The magnifications were not calibrated.

(iv) The sputter coated cross-sections were then photographed using a Hitachi S-4000 scanning electron microscope at various stage angles with 2 kV accelerating voltage, and 15 mm working distance.

3. Results

Materials with either similar solubility parameters (VeTPGS, PEO, and PMMA) or structure similarity (VeTPGS, PEG1000, and PEO100) were selected to investigate their miscibility. The solubility parameter difference for these polymers are listed in Table 1 (Schick, 1987; Colby, 1989; Bicerano, 1996; Van Krevelen, 1997; Utracki and Simha, 2004; Adamska and Voelkel, 2006). For VeTPGS, the aqueous solubility ratio of PEG1000 to Vitamin E is about 5000, therefore, it can be reasonably assumed that PEG1000 contributes significantly to aqueous solubility. Based on the group contribution method proposed by Van Krevelen (1997), the calculated solubility parameter for PEG1000 and Vitamin E is similar (about 20 $(J/cm^3)^{1/2}$). They are similar to other polymers.

Table 1
Solubility parameter difference, F–H interaction parameter and miscibility for PEG 1000/PMMA, PEO100/PMMA, PEO200/PMMA AND VeTPGS/PMMA binary blends[a]

Polymer pair	Miscible (yes/no)	$\delta 1 - \delta 2$	χ	Detectiontechnique
PEG1000/PMMA	No	Small	Na	DSC and XRPD
PEO100/PMMA	No	∼0	∼0	DSC and XRPD
PEO200/PMMA	No	∼0	∼0	DSC and XRPD
VeTPGS/PMMA	Yes	Small	Na	DSC and XRPD

Na, not available; $\delta 1 - \delta 2$, solubility parameter difference; χ, Flory–Huggins interaction parameter.

[a] The experimental value for solubility parameter of PMMA ranges from 18.6 to 26 $(J/cm^3)^{1/2}$ and the solubility parameter value for PEO type polymer is around 20 $(J/cm^3)^{1/2}$.

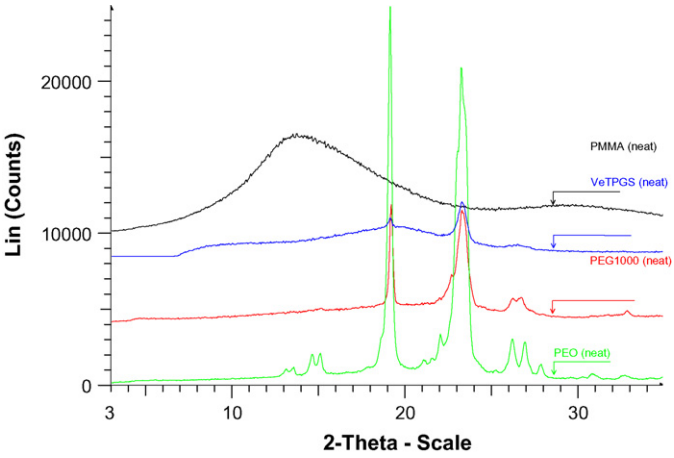

Fig. 2. XRPD patterns of neat polymers including (from bottom to top) PEO100, PEG 1000, VeTPGS and PMMA.

3.1. XRPD and DSC characterization of both neat polymers and binary blends

Fig. 2 shows the XRPD patterns of neat polymers, including PEO100, PMMA, PEG1000, and VeTPGS. As indicated in Fig. 2, VeTPGS, and all polymers studied with the exception of PMMA, are crystalline with two major Bragg reflections at two theta angles of ∼19° and 23°. Neat PMMA polymer is amorphous in nature (Van Krevelen, 1997). It is also noted that PEO100 and PEG1000 have other minor Bragg reflections other than the two major ones at 19° and 23°. PEO200 is similar to PEO100. These are also confirmed by thermal analysis data shown in Table 2 where melting points and glass transition temperatures of the above materials are listed. Fig. 3 shows the XRPD patterns of binary blends at a (w/w) ratio of 1 to 3 for PEG1000/PMMA, PEO100/PMMA, PEO200/PMMA, VeTPGS/PEO100 and VeTPGS/PMMA. Since blends of other weight ratios have similar behavior as the blends with a weight ratio of 1:3, the blends with a weight ratio of 1:3 are chosen to be presented here. The Bragg reflections are observed for PEG1000/PMMA, PEO100/PMMA, PEO200/PMMA and VeTPGS/PEO100 blends whereas the VeTPGS/PMMA blend exhibits an amorphous structure, indicating that all blends

Table 2
Melting points and glass transition temperatures of PEO100, PEO200, PEG100, VeTPGS and PMMA polymers

Polymer	T_g (°C)	m.p. (°C)
PEO100	∼−67	∼60
PEO200	Same as PEO100	Same as PEO100
PEG1000	–	∼37–40
VeTPGS	–	∼37–41
PMMA	∼105	–

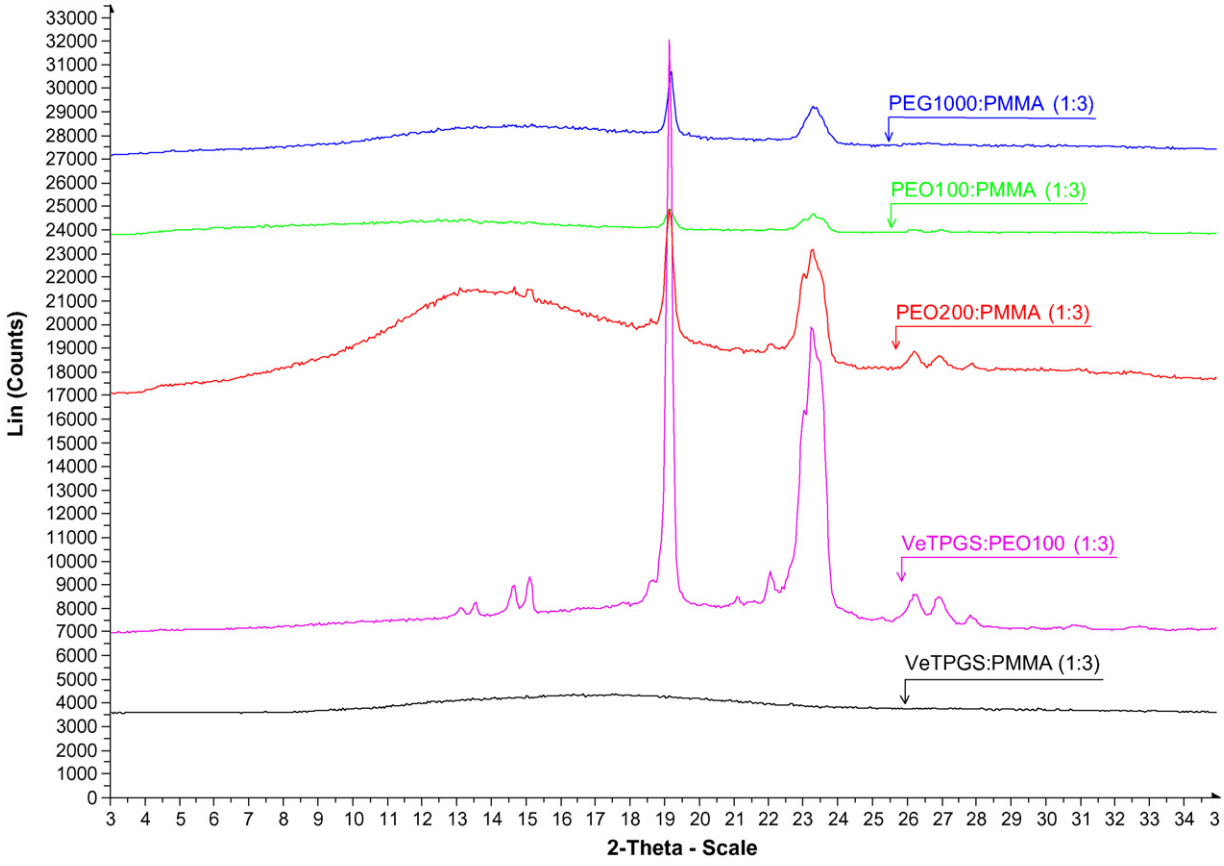

Fig. 3. XRPD patterns of (1:3 ratio) binary blends of VeTPGS/PMMA, VeTPGS/PEO100, PEO200/PMMA, PEO 100/PMMA and PEG 1000/PMMA.

except VeTPGS/PMMA were phase separated. It formed a miscible, amorphous phase. In Fig. 4, DSC thermograms of PEO100/PMMA, VeTPGS/PMMA, PEO200/PMMA, PEG1000/PMMA, and VeTPGS/PEO1000 blends in a 1 to 3 ratio (w/w) are displayed. The melts of PEO100 and PEO200 in their blends with PMMA are observed (left thermogram). As indicated by XRPD, for VeTPGS/PMMA blends, the melting of VeTPGS is not seen. A glass transition is detected instead, indicating the formation of an amorphous phase. The melts of VeTPGS and PEG1000 were observed for VeTPGS/PEO100 and PEG1000/PMMA blends (right thermogram), and a glass transition at ~40 °C was detected for the VeTPGS/PMMA blend. For the VeTPGS/PEO100 blend (1:3 ratio), two melting points were observed. The first melting endotherm is attributed to VeTPGS and the second is attributed to PEO, indicating that VeTPGS and PEO are phased separated. They exist as a crystalline state. This observation is consistent with the corresponding XRPD result. Fig. 5 shows SEM micrographs of a VeTPGS/PMMA blend (left image) and a PEO100/PMMA blend (right image). A uniform structure can be seen for the image on the left whereas the image

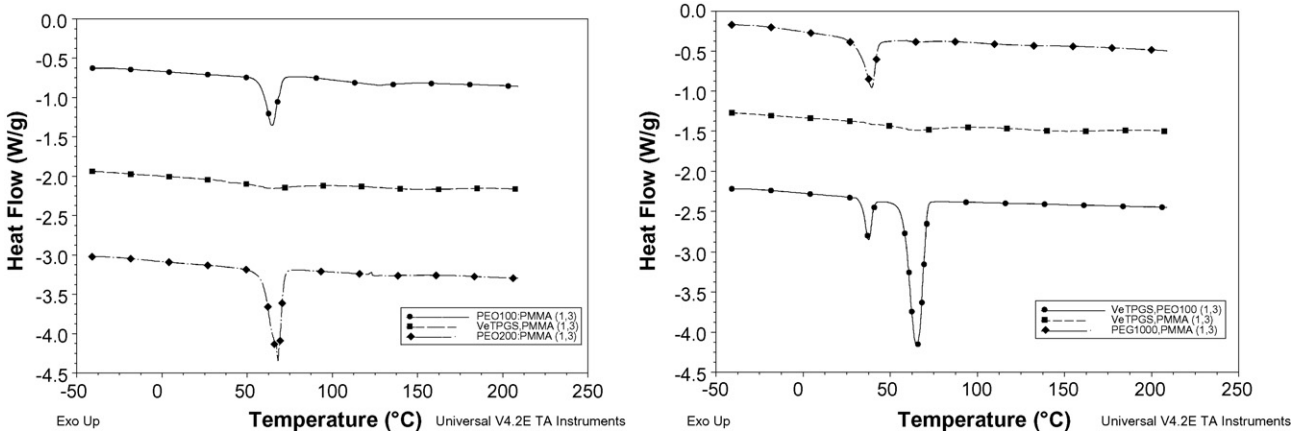

Fig. 4. DSC thermograms of (1:3 ratio) binary blends: (left, from bottom to top) PEO200/PMMA, VeTPGS/PMMA and PEO100/PMMA; (right, from bottom to top) VeTPGS/PEO100, VeTPGS/PMMA, and PEG 1000/PMMA.

Fig. 5. SEM micrographs of VeTPGS/PMMA blend (left) and PEO100/ PMMA blend (right) in 1:3 (w/w) ratios.

on the right shows a non-uniform structure, indicating a phase separation.

3.2. Characterization of VeTPGS/PMMA blends with various weight ratios

Fig. 6 shows the XRPD patterns of VeTPGS/PMMA blends whose weight ratio varied from 1:1 to 1:4. As seen in Fig. 6, the VeTPGS/PMMA blend with a weight ratio of 1:1 was phase separated where Bragg reflections of VeTPGS at 19° and 23° were observed, indicating that VeTPGS in this blend was crystallized out. Also seen in Fig. 6, the blends of VeTPGS/PMMA with a weight ratio from 1:2 to 1:4 remains amorphous where the Braggs reflections for VeTPGS were not observed. In Fig. 7, DSC thermograms of VeTPGS/PMMA blends of various weigh ratios are shown where the melting of VeTPGS was observed for the VeTPGS/PMMA blend with a weight ratio of 1:1, which is consistent with the XRPD observation. For the VeTPGS/PMMA blends of other weight ratios, the glass transition was observed, indicating that the two materials formed a miscible phase. In the case of the 1:2 ratio blend, a little residual melting of VeTPGS was also observed. However, the vast majority of VeTPGS formed an amorphous phase with PMMA.

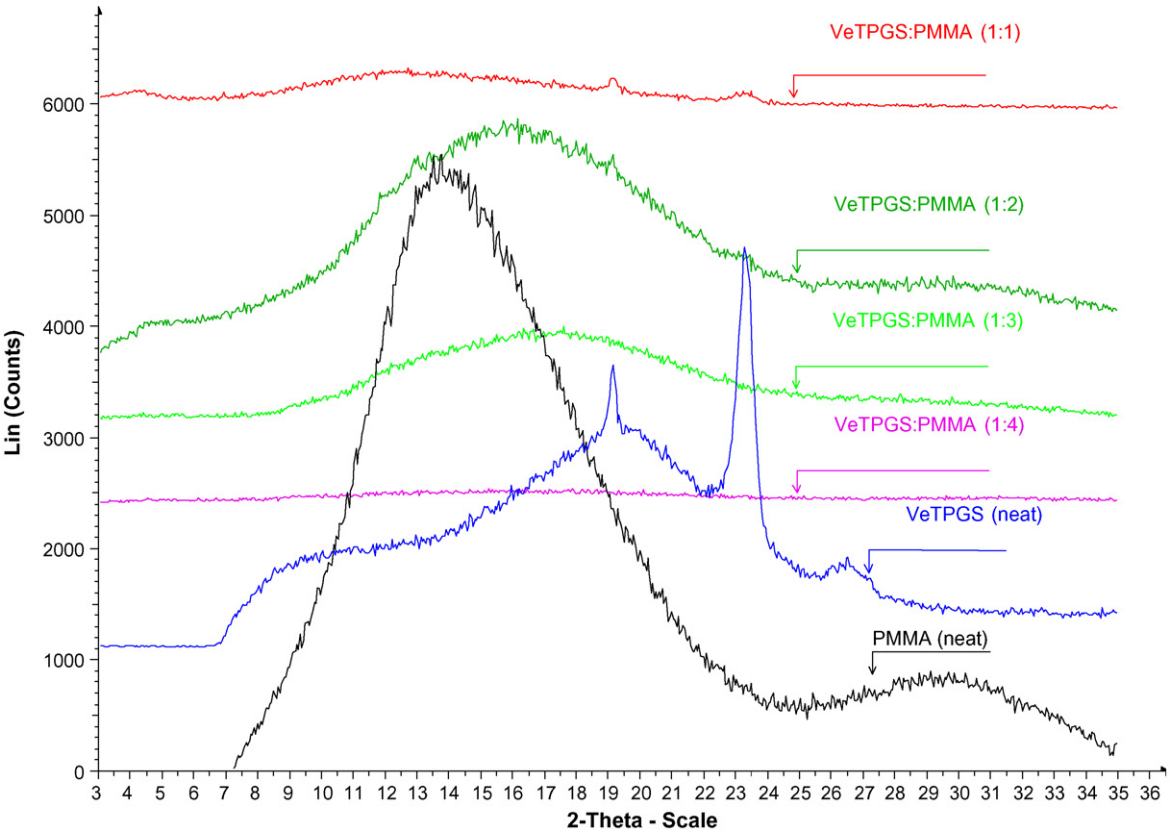

Fig. 6. XRPD patterns of neat PMMA, neat VeTPGS and VeTPGS/PMMA blends with weight ratio varied from 1:4 to 1:1 (from bottom to top).

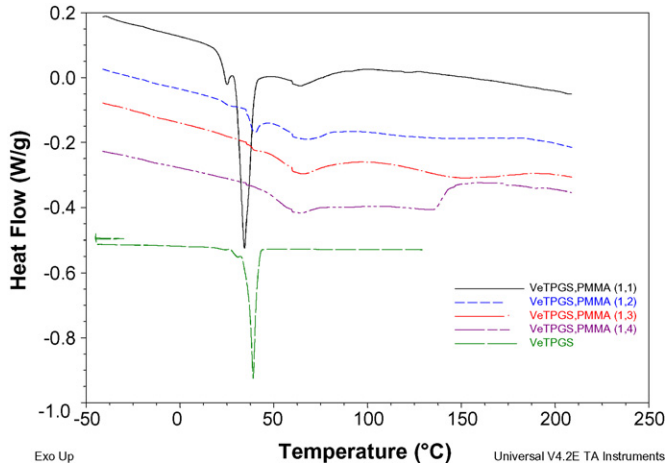

Fig. 7. DSC thermograms of Neat VeTPGS and VeTPGS/PMMA blends with weight ratio varied from 1:4 to 1:1.

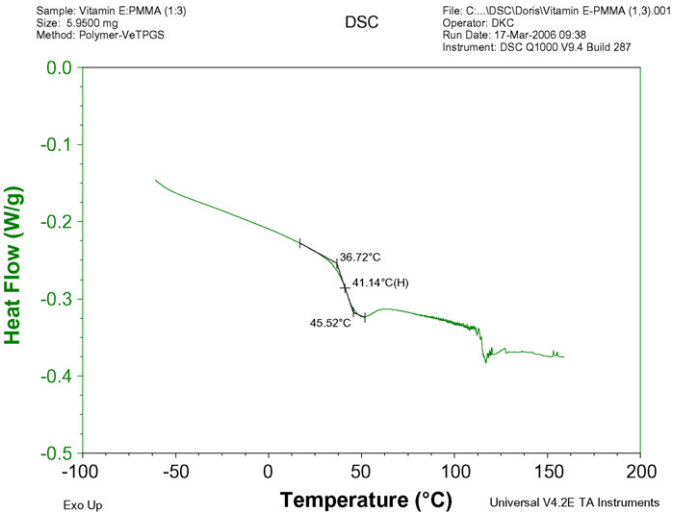

Fig. 8. A DSC thermogram of a Vitamin E/PMMA blend in a weight ratio equivalent as 1:3 for VeTPGS/PMMA blend.

3.3. Miscibility characterization of Vitamin E with PMMA

To verify the contribution of Vitamin E to the formation of an amorphous phase between VeTPGS and PMMA in the VeTPGS/PMMA blend, a blend of Vitamin E/PMMA in the same ratio as 1:3 (w/w) VeTPGS/PMMA blend was made. Fig. 8 shows the DSC thermogram of Vitamin E/PMMA blend in a weight ratio equivalent to the VeTPGS to PMMA weight ratio of 1:3. As indicated, a glass transition was observed for the Vitamin E/PMMA blend where the T_g is around 41 °C.

4. Discussion

4.1. Theoretical background

(i) Flory–Huggins theory for binary mixtures (F–H).

Based on the thermodynamics of mixing for regular solutions with consideration of losing freedoms in polymers due to bonds between monomers, Flory (1942) and Huggins (1942) derived the following equation independently. This equation served as the thermodynamic framework for the formation of blends (Coleman et al., 1991; Paul and Bucall, 2000).

$$\frac{\Delta G_m}{RT} = \frac{\Phi_A}{N_A}\ln \Phi_A + \frac{\Phi_B}{N_B}\ln \Phi_B + \Phi_A \Phi_B \chi \quad (1)$$

where Φ_A, Φ_B, N_A, N_B and χ are the volume fractions, degree of polymerization of polymer A and B, and the Flory–Huggins interaction parameter, respectively.

According to the Hilderbrand solubility relation,

$$\chi \propto (\delta_A - \delta_B)^2 \quad (2)$$

In Eq. (1), the first term, $(\Phi_A/N_A)\ln \Phi_A + (\Phi_B/N_B)\ln \Phi_B$ is the entropy of mixing and the second term is predominantly enthalpic. For polymer systems, the entropy of mixing is close to zero, and the free energy of mixing is determined by the second term, enthalpy. Since the F–H theory only considers non-specific dispersion force interactions, polymers with hydrogen bonding interaction, and other interactions, an extra free energy term, $\Delta G_H/RT$ is added to the F–H theory. This is often referred to as the modified F–H theory (see Eq. (3)).

(ii) Modified Flory–Huggins theory for binary mixtures (Coleman et al., 1991).

Considering specific interactions, Eq. (1) can be written as:

$$\frac{\Delta G_m}{RT} = \frac{\Phi_A}{N_A}\ln \Phi_A + \frac{\Phi_B}{N_B}\ln \Phi_B + \Phi_A \Phi_B \chi + \frac{\Delta G_H}{RT} \quad (3)$$

The last term in Eq. (3) represents the free energy corresponding to specific interactions.

For polymers, the entropy of mixing is very small (close to zero). The enthalpy of mixing, which is proportional to χ, and specific interactions (ΔG_H) determine the miscibility of two polymers. In this paper, VeTPGS is treated as a polymer since one segment of VeTPGS is PEG1000. A rough estimate using the F–H theory indicates the entropy for mixing VeTPGS with PMMA in a 1:3 ratio is close to zero. Therefore, in the following text, our discussion for VeTPGS/PMMA blends and other polymer blends will focus on enthalpy and other interactions.

4.2. Miscibility based on solubility parameters (χ) and structure similarity

Table 1 summarizes the solubility parameter differences ($\Delta\delta$), the related Flory–Huggins interaction parameter (χ) values, and the miscibility for the polymer pairs examined. The solubility parameter difference between PEO and PMMA is reported to be close to zero. For PEG1000/PMMA pairs, it is indicated from literatures that the difference is very small (Schick, 1987; Colby, 1989; Adamska and Voelkel, 2006). In the case of VeTPGS/PMMA, assuming the molecule is more PEG1000-like, the solubility parameter difference between VeTPGS and PMMA is also very small. As seen in Table 1, polymer pairs with similar solubility parameters such as PEO/PMMA, where $\chi = 0$ based on the Hilderbrand relation

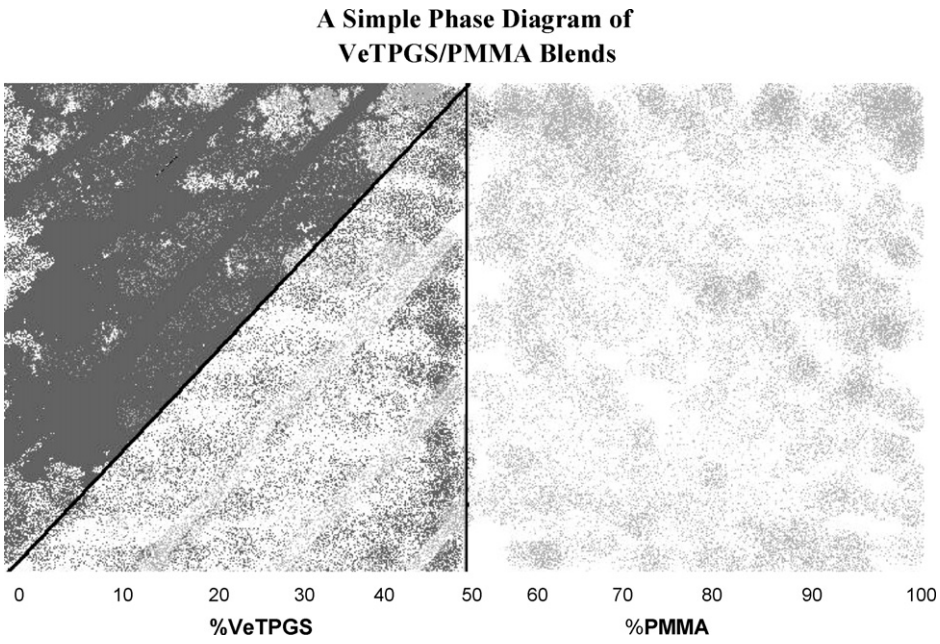

Fig. 9. A diagram showing the miscibility window of VeTPGS/PMMA blends.

shown in Eq. (2), do not form miscible blends. In this case, the free energy for mixing, according to the F–H theory, should be close to zero. As demonstrated by experimental results in this paper, $\Delta G \approx 0$ cannot ensure miscibility between two materials. This confirms the observation for many polymer pairs reported in literature (Schmidt-Rohr and Spiess, 1994). It is reported in literature that PEO/PMMA is marginally miscible or miscible in liquid state (Colby, 1989; Pedemonte et al., 1994). A recent study showed that two glass transition temperatures were observed for the PEO/PMMA system (Lodge et al., 2006). As seen in Table 1, PEO/PMMA is not miscible at room temperature in the composition range studied. However, for the blends of VeTPGS/PMMA with a weight ratio above 1:2, a miscible system was observed based on both X-ray and DSC measurements, and SEM micrographs. Considering VeTPGS is made of two segments: PEG1000 (hydrophilic) and Vitamin E (hydrophobic), blends of these two segments with PMMA were prepared. The blend of PEG1000/PMMA is phase-separated according to our experimental results whereas the blend of Vitamin E and PMMA forms a miscible system (Fig. 8). Based on these results, it appears that the miscibility between VeTPGS and PMMA is likely due to an interaction between the Vitamin E portion of VeTPGS and PMMA. Since Vitamin E, which is sparingly soluble in water, is hydrophobic, this interaction is referred to as a "hydrophobic interaction" in this paper. One could argue that this "hydrophobic interaction" gives a negative free energy which ultimately makes the overall free energy change for mixing negative. It also suggests that the PEG1000 portion of VeTPGS plays a less important role for mixing since VeTPGS does not form a miscible blend with PEO even though there is similarity between the PEG1000 portion of VeTPGS and PEO. The results suggest that the hydrophobic moiety (Vitamin E) of VeTPGS strongly associates with hydrocarbon chain of PMMA. The same moiety contributes the surfactant property of VeTPGS to solubilize hydrophobic compounds. More studies are needed to investigate the specific nature of this interaction. When the molecular weight of PEO varies from 100 to 200 K, the trend for miscibility does not change even though changing molecular weight (degree of polymerization) would effectively change the miscibility window according to Eq. (4):

$$\chi_c = \frac{1}{2}\left(\frac{1}{\sqrt{N_A}} + \frac{1}{\sqrt{N_B}}\right)^2 \quad (4)$$

where χ_c, N_A and N_B are critical miscibility interaction parameters, and degrees of polymerization for polymers A and B. This is probably due to the fact that at a molecular weight of 100 K, χ_c is close to zero and there is little change for χ_c when the PEO molecular weight increases from 100 to 200 K. Finally, the miscibility window of VeTPGS/PMMA is explored. As demonstrated from the experimental data, at an approximate weight/weight ratio above 1:2, VeTPGS and PMMA form miscible blends at room temperature as shown in Fig. 9. The glass transition temperatures of these blends were also measured and compared with the estimated values (see Table 3). Their esti-

Table 3
Measured glass transition temperatures for VeTPGS/PMMA blends with weight ratio from 1:2 to 1:4 vs. the estimated values using Fox equation

Sample (VeTPGS:PMMA)[a]	T_g (experimental) (K)	T_g (calculated) (K)[b]
1:2	24	22
1:3	38	39
1:4	54	50

[a] w/w ratio is used here.
[b] T_g of blends was calculated using a T_g of 210 K (VeTPGS), which is estimated independently, for calculation.

mated T_g values (see Table 3) were calculated based on the Fox equation (Fox, 1956) (see Eq. (5)).

$$\frac{1}{T_g} = \frac{w_1}{T_{g1}} + \frac{w_2}{T_{g2}} \quad (5)$$

where T_{g1} and T_{g2} are the individual glass transition temperatures of PMMA and VeTPGS, and w_1 and w_2 are the weight fractions of these two components. A T_g value of 210 K for VeTPGS, estimated independently using Eq. (5), was used for estimating the glass transition temperature of the blends. As seen in Table 3, the experimental glass transition temperatures for VeTPGS/PMMA blends of varied weight ratios of 1:2 to 1:4 are similar to those estimated based on Eq. (5), further supporting that VeTPGS/PMMA form miscible blends. Based on the results in this paper, it is hypothesized that the Vitamin E portion of VeTPGS strongly interacts with PMMA. This interaction enables VeTPGS to mix well with PMMA.

5. Conclusions

In this paper, it has been demonstrated that polymer pairs with a similar solubility parameter do not form a miscible phase, indicating that a similar solubility parameter cannot ensure a completely miscible phase. VeTPGS, a nonionic surfactant, forms a miscible system with PMMA as shown by XRPD, DSC, and SEM. The miscibility window for VeTPGS/PMMA is approximated to be at a ratio >1:2. As demonstrated by the miscibility data of the blends made from PEG1000/PMMA and Vitamin E/PMMA, the major contribution for VeTPGS/PMMA miscibility is the interaction between Vitamin E and PMMA. Furthermore, even though the PEG1000 portion of VeTPGS has structure similarity to PEO100, they do not form a miscible blend, further demonstrating the importance of the Vitamin E contribution in these blends. The results in this paper can be used as a guide when VeTPGS is used in various formulations. More experimental work is needed to illustrate the effect of temperature on VeTPGS/PMMA blends.

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