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Asymmetric porous membranes formed by coagulation-induced phase separation in poly(ether sulfone)/poly(vinyl pyrrolidone)/genistein blends

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ABSTRACT

Development of asymmetric channel morphology driven by coagulation-induced phase separation of genistein (G) modified poly(ether sulfone)/poly(vinyl pyrrolidone) (PES/PVP) blends has been examined in relation to their miscibility phase diagram. PES/G pairs turned out to be miscible in the amorphous state, whereas solid–liquid phase separation occurred at high genistein compositions. The solid–liquid phase diagram involving the liquidus and solidus lines were computed self-consistently in the framework of the combined free energy of Flory-Huggins for liquid–liquid phase separation and phase field free energy for crystal solidification. The ternary phase diagram of PES/PVP/G blends was subsequently established that consisted of various coexistence regions. The actual amounts of genistein incorporated in the PES/PVP membranes were determined as a function of weight percent of genistein in feed. On the basis of UV-vis spectroscopy, the extent of genistein leaching during incubation in human blood was evaluated in conjunction with the PVP leaching from the blend membrane.

1. Introduction

Hemodialysis (HD) is a blood purification process for treating end stage renal disease (ESRD) patient having kidney impairment. A hemodialyzer is generally employed as an artificial kidney in the HD treatment, whereby patient blood is circulated through a bundle of hollow synthetic fibers having percolated channels across the fiber walls. The dialysates including uremic toxins are filtered out through the semicro-channels while the purified blood is pumped back to the vein. Such HD treatment lasts for an average of about 3 h per session and 3 to 4 sessions per week for ESRD patients. The prolonged contact of blood with the synthetic membranes creates long term complications such as dialysis induced oxidative stress (DIOS) [1,2] and membrane induced inflammation (MII) [3,4]. DIOS occurs when the excessive reactive oxygen radicals produced by neutrophils overpower the natural antioxidant defense mechanism of the patient body. Likewise, MII is caused by undesirable immune response due to the interaction between blood and the synthetic HD membranes [4].

To alleviate the aforementioned DIOS and MII complications, multi-functional HD membranes have been heavily sought by modifying hydrophilic/hydrophobic polymer blends with vitamin E or phytochemicals (i.e., plant derived chemicals) such as soybean-derived compound called genistein(4′,5,7-trihydroxy isoflavone). Vitamin E modified HD membrane can be found in market place, albeit marginally improved anti-oxidant property [5,6]. On the other hand, neat genistein appears to possess many pharmaceutical benefits with remarkable anti-oxidant and anti-inflammatory properties [7–9],thereby making it a desirable candidate for incorporating into HD membranes.

In our previous study [10], we reported that the genistein modification of poly(amide)/poly(vinyl pyrrolidone) (PA/PVP) blends exhibited excellent cell viability, improved suppression of both reactive oxygen species and cytokine levels as compared to the unmodified blend membranes. In the present study, poly(ether sulfone) (PES) was chosen in lieu of PA as the hydrophobic matrix because of its outstanding thermal resistance and hydrolytic stability. More importantly, the mechanical strength and integrity of

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the PES membrane can be sustained at high temperature and high humidity environment [11,12]. Which makes the PES to be a preferred candidate in the development of multifunctional HD membrane for longer genistein depot. Furthermore, anti-fouling and anti-platelet adhesion of the PES membrane can be improved via blending with hydrophilic PVP [13–16]. By virtue of the aforementioned profound improvement in mechanical and adhesion properties, PES/PVP pairs have been chosen as the polymer matrix in this study.

To enhance the in-depth understanding, it is of paramount importance to examine the role of molecular interaction in the miscibility behavior of various polymer/genistein mixtures. We have conducted the miscibility characterization in relation to the binary PES/genistein (PES/G) blends using differential scanning calorimetry (DSC), Fourier transform infrared spectroscopy (FTIR), and polarized optical microscopy (POM). To improve understanding of all over phase behavior, a theoretical phase diagram of the PES/G blend was computed in the context of the combined free energies of Flory-Huggins for liquid–liquid phase separation and of phase field theory for crystal solidification [17]. On the basis of FTIR, the specific intermolecular interactions such as hydrogen-bonding and/or dipole–dipole interaction were investigated at various coexistence regions within the ternary phase diagram of the PES/PVP/genistein (PES/PVP/G)blends. Scanning electron microscopy (SEM) was utilized to investigate the surface and cross-sectional morphologies of the unmodified versus modified membranes. UV-vis spectroscopy was employed to determine PVP and genistein leaching during incubation in blood plasma.

2. Materials and methods

PES (Ultrason E 6020P) utilized in the present study was an amorphous polymer kindly provided by BASF Corp. (Wyandotte, MI). PVP was purchased from Sigma–Aldrich (St. Louis, MO) whereas genistein was bought from MDidea Exporting division (YinChuan, China) having over 98% purity. The individual polymer and genistein solution was prepared by dissolving separately in dimethyl sulfoxide (DMSO) (from Sigma–Aldrich having a purity >99.9%) and then mixed in desired proportions. The chemical structures of PES, PVP and genistein are shown in Fig. 1.

PES and PVP pellets were vacuum-dried at 100 °C for 24 h and subsequently dissolved in DMSO individually to a 5 wt% solution. Likewise, genistein was dissolved in DMSO, then added to the PES and PVP solutions in desired proportions and mixed by mechanically stirring for 48 h. The homogeneous solutions were then cast on a pre-cleaned glass slide to form a film of pre-determined thickness. The solutions on the glass plates were then immersed into non-solvent (i.e., reverse osmosis grade water) at room temperature for 5 min. After peeling off from the glass slide, the coagulated membranes were washed with deionized water to remove excess material on the surface and then vacuum dried at room temperature.

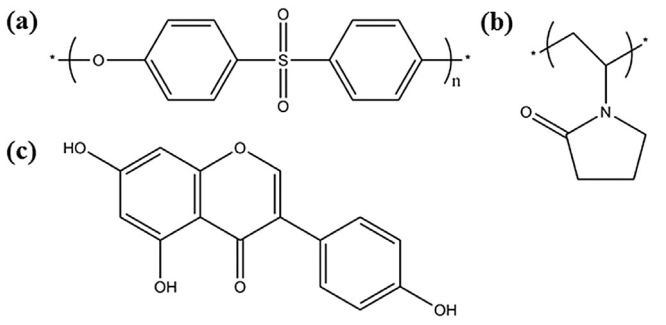

Fig. 1. Chemical structures of (a) PES, (b) PVP, and (c) genistein.

The glass transition and the crystal melting temperatures of the binary PES/PVP, PES/G and PVP/G blends as well as of the ternary PES/PVP/G blends were determined by DSC (Model 2920, TA Instruments). Temperature and enthalpy calibration were performed using an indium standard. For the DSC experiments, homogeneous solutions of neat components and their blends first were prepared by dissolving in DMSO. The solvent cast films were dried under vacuum at 150 °C for 24 h for removing any residual solvent. Approximately 5 mg of the samples was used for each DSC run. In the first heating cycle, the DSC thermograms were obtained by ramping from room temperature to 230 °C at a rate of 10 °C/min and then cooled down by simply turning off the machine. The DSC second cycle was carried out by ramping at the same rate to 310 °C.

For the FTIR analysis, the film samples were prepared from the 5 wt % DMSO solution by casting directly on the potassium bromide (KBr) disks. These films were dried under vacuum at 150 °C for 24 h. Infrared spectrum was acquired on a FTIR spectrometer (Thermo Scientific Nicolet 380) having a spectral resolution of 4 cm^{-1} by averaging over 32 scans. The FTIR spectra of the blend samples were acquired at 100 °C inside a temperature regulated chamber to alleviate the problem of moisture absorption.

The samples for POM experiments were prepared under the same conditions with those of DSC and FTIR, except that the films were cast from the 5 wt% DMSO solutions directly onto the glass substrates. An optical microscope (BX60, Olympus) attached with a 35 mm digital camera (EOS 400D, Canon) and a hot stage (LTS 350, Linkam) was used for taking the POM micrographs.

To examine the surface and cross-sectional morphology, scanning electron microscopy (SEM, JEOL-JSM-7401F) was utilized. The dried cast films were fractured in liquid nitrogen and subsequently sputtered with silver using a sputter coater (Emitech, Model K575X).

Regarding the determination of the genistein leaching during incubation with blood plasma (BP), several small circular disks having the area of 0.4 cm^2 were punched out from the cast films and then crimped to provide maximum contact with blood. After incubation, the blood plasma was collected and tested using a UV-vis apparatus (HP 8453, Hewlett Packard). The peak height of the genistein signature UV absorbance peak was analyzed as a function of genistein concentration to establish a calibration curve. The signature UV peaks of blood plasma and genistein were analyzed on a series of samples of BP containing various concentrations of genistein and the actual amount of genistein leaching during incubation was determined.

3. Results

In our previous paper [18], we reported that the PES/PVP blend films were transparent to the naked eye and also showed no identifiable domains under POM, which are expected for a miscible blend, although by no means a proof. In the DSC experiments, the systematic movement of the single glass transition with composition was observed, which in turn suggested that the amorphous PES/amorphous PVP blends are probably miscible over the entire composition range. Given the spectral resolution of 4 cm^{-1}, there is little or no movement of the FTIR spectra in the PES/PVP blends, suggesting the lack of strong specific interactions. According to Lafreniere and co-workers [19], the miscibility of PES/PVP blends may be attributed to a weak dipolar interaction between the O=S=O groups of PES and the N–C=O tertiary amide group of PVP, and/or the interaction of donor-acceptor nature between the aromatic ring and the N–C=O tertiary amide group PES and PVP.

In the DSC investigation of PVP/genistein (PVP/G) blends, a single T_g was evident in all PVP-rich compositions that