

Preparation and Physicochemical Properties of Hydroxyapatite/ Polyurethane Nanocomposites*

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Abstract In this study, nanohydroxyapatite/polyurethane (nHA/PU) composites with various contents of methoxy-poly(ethylene glycol) modified nHA (0 wt%, 10 wt%, 20 wt% and 30 wt%) were prepared by solution blending process. The physicochemical properties of the composite membranes were investigated by Fourier transform infrared spectroscopy (FTIR), X-ray diffraction (XRD), Transmission electronic microscopy (TEM), Differential scanning calorimetry (DSC), Thermo gravimetric analysis (TGA) and tensile tests. TEM photos of the nanocomposites showed that the nHA was uniformly dispersed in the polymer matrix. The membrane with 10 wt% nHA showed the highest tensile strength which was about 75% higher than that of the pure PU membrane. However, the tensile strength decreased when high content (above 20 wt%) fillers were added, which was still higher than that of pure PU. TGA measurements suggested that the thermal stability of the membranes was improved owing to nHA fillers. XRD and DSC results illustrated that the crystallinity of PU soft segments decreased with the increasing content of nanoparticles in the composites.

Keywords: Biodegradable polyurethane; Nanohydroxyapatite; Composites; Physicochemical properties.

INTRODUCTION

Hydroxyapatite [$\text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2$] nanoparticles (nHA) have been widely used as fillers of polymer matrices to prepare bone-like nanocomposites due to their favorable bioactivity, osteoconductivity and bone bonding ability^[1]. The nanoparticles dispersed in the polymer matrix not only enhance the mechanical properties of the nanocomposites, but also provide a favorable environment for osteoconduction, protein adhesion and osteoblast proliferation^[2]. Many polymer/nHA composite biomaterials have been synthesized to reduce the brittleness of HA as well as to increase the bioactivity of the polymers^[3, 4].

It is well known that homogeneous dispersion of fillers in polymer matrices and the strong interfacial adhesion between inorganic fillers and organic polymer matrices are two key factors in generating composites with good mechanical properties and bioactivities^[5]. Therefore, in order to improve the interfacial adhesion, the surface of HA nanocrystals has been modified with a diverse class of coupling agents and polymers through the chemical reaction with hydroxyl groups on HA surface^[6–8]. However, the nHAs may have agglomerated before the surface modification process. As an attempt to solve this problem, we prepared MPEG/HA hybrid

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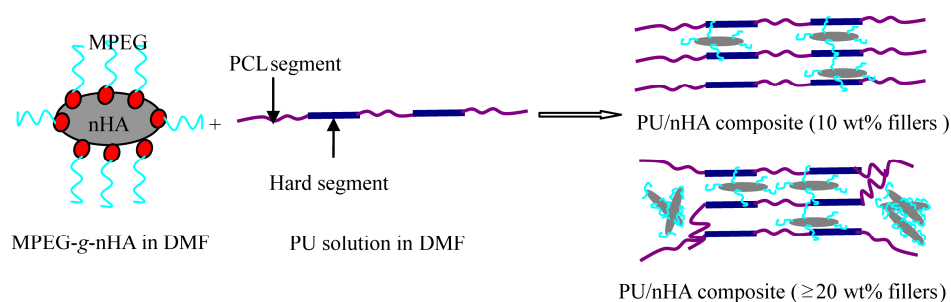
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nanoparticles (MPEG-g-nHA) by using α -methoxy- ω -dihydrogen phosphate-poly(ethylene glycol) as a steric hindrance and surface modification agent. The MPEG-g-nHAs could be dispersed in both aqueous and organic solvents, suggesting that this hybrid nanoparticles can be used as fillers to improve mechanical and bioactive properties of polymer matrices^[9].

Polyurethanes, a family of versatile multi-segment copolymers with tailorable properties, have been widely used in biomedical field due to their excellent physical properties and good biocompatibility^[10–13]. In addition to non-degradable polyurethanes, non-toxic and biodegradable polyurethanes have also been developed by reacting polyester diols, *e.g.*, poly(ϵ -caprolactone) diol (PCL), as the soft segment with aliphatic or lysine based diisocyanates^[14]. Biodegradable polyurethane/nHA composites were prepared and their physicochemical/biological properties, biodegradation and biocompatibility were also studied^[15, 16]. Porous polyurethane support coated with hydroxyapatite thin layers by using a biomimetic technique at the presence of vitamins (A and D₂) was also reported recently^[17]. In order to enhance mechanical properties and bioactivity of PU, several studies prepared polyurethane/nHA composites by *in situ* polymerization in the presence of nHA. Zhao *et al.*^[18] prepared waterborne polyurethane (WBPU)/HA nanocomposites and found that the tensile strength of 2.0 wt% WBPU/HA nanocomposite increased (17 MPa) by about 54%, compared with that of pure WBPU (11 MPa). Li *et al.*^[19] prepared nHA/polyurethane by adding nHA *in situ* during the polymerization reaction. The results revealed that as the HA content rose from 0 wt% to 30 wt%, the tensile strength of nHA/PU membranes increased from 4.91 MPa to 14.04 MPa, showing an improvement by 186%. When the nHA content was higher than 30 wt%, however, both the tensile strength and elongation-at-break presented a trend of decrease. Because the PU matrix used in these two studies was very weak, the maximum tensile strength of the prepared nanocomposites was less than 20 MPa. Meanwhile, to the best of our knowledge, there were seldom reports on preparing PU/nHA nanocomposites by solution blending between surface modified nHA fillers and PU matrices.

In the present work, biodegradable polyurethane was synthesised by using poly(ϵ -caprolactone) diol (PCL, $M_w = 2000$ Da) as soft segments, isophorone diisocyanate (IPDI) and lysine ethyl ester as hard segments. Afterwards, MPEG-g-nHA was incorporated into the PU matrix to prepare the nHA/PU nanocomposite membranes through a simple solution blending method. Improved mechanical and bioactive properties of the nanocomposites could be expected as the MPEG-g-nHA hybrid nanoparticles could facilitate the dispersion and improve the interfacial adhesion between the fillers and the PU matrix as shown in Scheme 1. The physicochemical properties of the nHA/PU nanocomposite membranes were investigated by FTIR, TEM, DSC, TGA and tensile tests in this study. It is worth noting that nanocomposites prepared in this study can be redispersed into solvent and show the maximum tensile strength above 40 MPa.



Scheme 1 Schematic illustration for preparation and supposed microstructure of PU/MPEG-g-nHA nanocomposites

EXPERIMENTAL

Materials

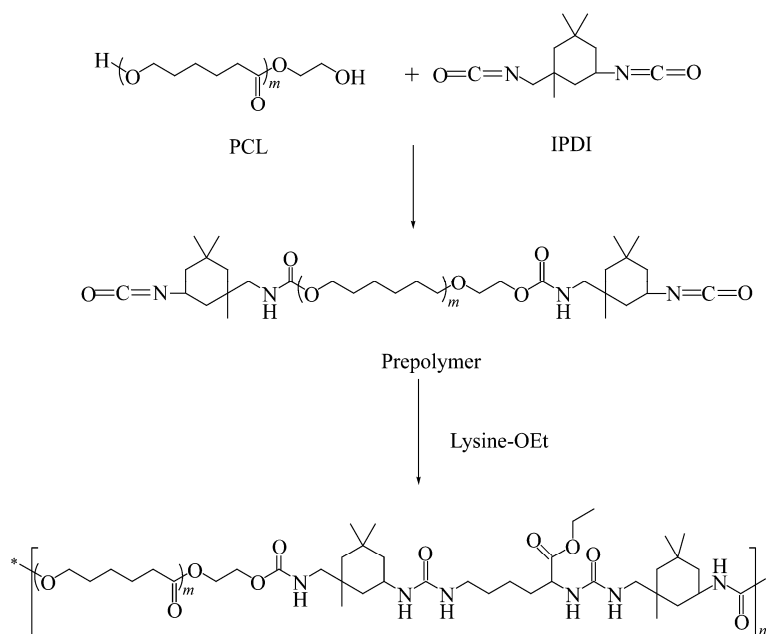
MPEG/HA hybrid nanoparticles (MPEG-g-nHA) were prepared previously with α -methoxy- ω -dihydrogen phosphate-poly(ethylene glycol) (MPEG-OPO₃H₂, $M_w = 280$ Da.) as a steric hindrance and surface modification agent^[9]. Poly(ϵ -caprolactone) diol (PCL, $M_w = 2000$ Da) was dehydrated at 100–110 °C under vacuum for 10 h

prior to use. Dimethylformamide (DMF) was dehydrated with CaH_2 and distilled under reduced pressure. Isophorone diisocyanate (IPDI) was restored in a refrigerator.

Other chemical reagents such as aqueous ammonia (25 wt%), $\text{Ca}(\text{NO}_3)_2 \cdot 4\text{H}_2\text{O}$, $(\text{NH}_4)_2\text{HPO}_4$, $\text{Sn}(\text{Oct})_2$, lysine ethyl ester (Lys-OET), as well as organic solvents were analytical reagent grade and used without further purification. All of them were purchased from Chengdu Kelong Chemical Reagent Company, China.

Synthesis of Biodegradable Aliphatic Polyurethane

Aliphatic polyurethane was synthesized using a two-step solution polymerization method as shown in Scheme 2. The synthesis was carried out in a 500 mL three-necked flask under a dry nitrogen atmosphere with a mechanical stirrer. First, 20 g of PCL (10 mmol), 6.66 g of IPDI (30 mmol) and 100 mL of dry DMF were added into the flask. The mixture reacted at 70 °C for 4 h in the presence of 0.01 wt% $\text{Sn}(\text{Oct})_2$ as a catalyst. Subsequently, 3.48 g of Lys-OET (20 mmol) was added to the mixture for further reaction at 80 °C for 3 h. The reaction mixture was cooled to room temperature and was precipitated with distilled water for 3 times to remove the unreacted compounds with low molecular weights. Finally, the polymer was dried at 80 °C for 24 h.



Scheme 2 Synthesis route of biodegradable PU

Synthesis of MPEG grafted Nano-hydroxyapatite (MPEG-g-nHA)

A transparent light blue hydrocolloid MPEG-g-nHA was obtained *via* a wet-chemical precipitation reaction according to our previous report^[9]. On the other hand, another HA prepared under the same conditions but without MPEG- OPO_3H_2 was used as the control. The MPEG-g-nHA colloid was concentrated by a rotary evaporator at 55 °C and then dialyzed through a cellulose tubular membrane with a molecular weight cut-off of 10 kDa against water for 3 d before solvent exchange with DMF.

Preparation of PU/nHA Composites

The MPEG-g-nHA/PU nanocomposites were prepared using a solution blending method. First, 2 g of PU was dissolved in 20 mL of DMF to form a transparent and viscous polymer solution. Secondly, the water in aqueous dispersions of known amounts of MPEG-g-nHA (0 wt%, 10 wt%, 20 wt% and 30 wt% of PU) was replaced by DMF through rotary evaporating at 55 °C and the dispersion was filtered to remove any aggregates. Thirdly, the filtrate was added to the viscous PU solution under stirring at room temperature for 24 h. Finally, the mixture was cast into a customized cylindrical Teflon mold and dried at 80 °C at ambient pressure for 3 d to remove most of the solvents. Afterwards, the samples were further dried under vacuum for another 48 h. The samples

with 0 wt%, 10 wt%, 20 wt%, 30 wt% of MPEG-g-nHA were designated as PU, PU10, PU20 and PU30 respectively. For better comparison, nHA (10 wt% of PU) prepared using conventional methods without surface modification was added into PU matrix which was designated as PU10 (normal) and used as a control.

Characterization

XRD analysis

XRD measurements were performed with a DX-1000 X-ray diffractometer (Dandong Fangyuan Co. Ltd, Dandong, Liaoning, China) using Cu K α radiation ($\lambda = 0.154$ nm) operated at 40 kV and 25 mA. The 2θ scanning range was from 10° to 70° .

FTIR analysis

The FTIR spectra were obtained using a Nicolet IR 2000 spectrophotometer (Thermo Nicolet, USA). The spectra were recorded between 4000 cm^{-1} and 400 cm^{-1} with 32 scans at 4 cm^{-1} resolution.

Transmission electron microscopy

Several droplets of MPEG-g-nHA dispersions in DMF or redissolved PU10 in DMF were dripping onto a carbon-coated copper grid and air dried at room temperature before observation under an H-600IV transmission electron microscope (Hitachi, Japan).

Mechanical properties

Tensile tests were carried out with dumbbell-shaped samples cut from the centre of films using a punch. The thickness of each specimen was measured using a micrometer. The tensile strength and elongation-at-break were measured by an Instron 5561 (Instron Corp., USA) testing machine at a cross-head speed of 250 mm/min. The maximum stress at failure is taken as the tensile strength. The elongation at break is calculated according to the distance between the gauges. All the given values were the means of five measurements.

Thermal gravimetric analysis (TGA)

Thermal stability of the nHA/PU composites was tested on a TG 209 F1 thermogravimetric analyzer (Netzsch Group, Germany). The measurements were carried out under a nitrogen atmosphere from 20°C to 600°C at a heating rate of 10 K/min .

Differential scanning calorimetry

Thermal transitions of PU and the composites were analyzed with a DSC 204 F1 differential scanning calorimeter (Netzsch Group, Germany) from -100°C to 100°C at a heating rate of 10 K/min under N_2 atmosphere.

RESULTS AND DISCUSSION

Colloidal Stability and Dispersion of the Nanocomposites

Most methods for preparation of organic-inorganic nanocomposites are based on solution process. Thus, the improvement of dispersion properties and colloidal stability of HA particles in polymer solution is one of the important issues^[2]. We have previously prepared MPEG grafted nHA which dispersed uniformly in organic solvents such as methanol and DMF, forming stable colloids. In this study, MPEG-g-nHA was added into the PU (10 wt%) solution in DMF and the dispersions of PU10, PU10 (normal) and PU solution are shown in Fig. 1. The mixture of MPEG-g-nHA and PU solution became a colloid which remained stable for several days while the mixture of unmodified HA and PU solution (PU10 normal) did not maintain the stability and precipitated within a couple of minutes.

The MPEG-g-nHA colloid in DMF and the redissolved MPEG-g-nHA/PU nanocomposite membranes with 10 wt%, 20 wt% and 30 wt% of MPEG-g-nHA in DMF were subjected to TEM observation, whose microphotographs are shown in Fig. 2.

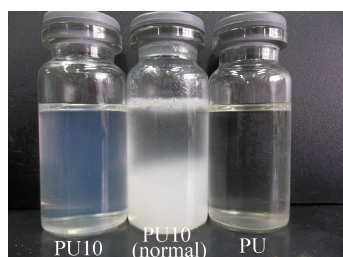


Fig. 1 Colloidal stability of PU10 and PU10 (normal) in DMF

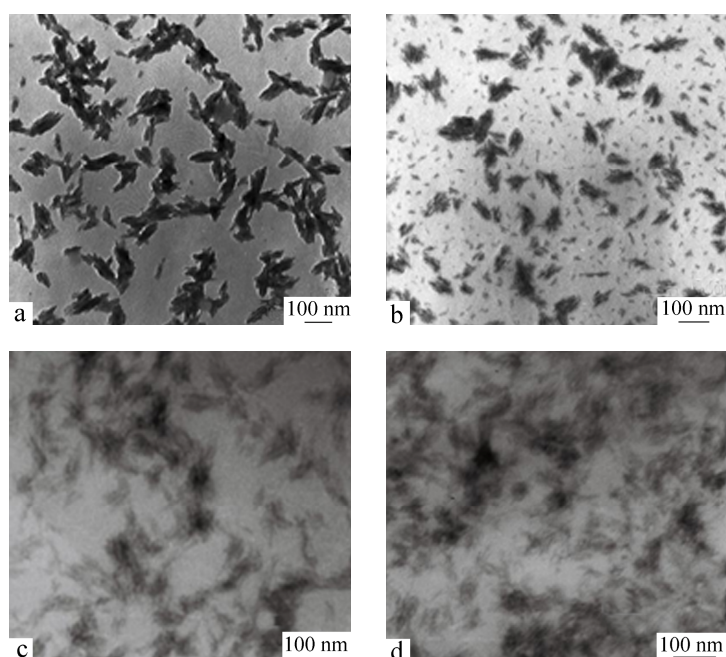


Fig. 2 TEM micrographs of MPEG-g-nHA (a) , MPEG-g-nHA/PU composite with 10 wt% MPEG-g-nHA (b), 20 wt% MPEG-g-nHA (c) and 30 wt% MPEG-g-nHA (d)

MPEG-g-nHA particles are acicular crystals with about 110 nm in length and 30–50 nm in width. The crystals were dispersed uniformly without severe agglomeration. Therefore, it is possible to prepare a uniform MPEG-g-nHA/PU composite by solution mixing. Because the MPEG molecules are ionic bonded onto the nHA surface, good compatibility is expected between the nHA fillers and polymer matrix.

The TEM images of the nanocomposites with 10 wt%, 20 wt% and 30 wt% MPEG-g-nHA particles are shown in Figs. 2(b), 2(c) and 2(d) respectively. It can be seen from Fig. 2(b) that after being dispersed into the PU matrix the MPEG-g-nHA crystals are mixed into the PU matrix and most of the filler particles were distributed uniformly at nanoscale in PU10 nanocomposite. However, when higher contents of MPEG-g-nHA fillers (*i.e.* 20 wt% and 30 wt%) were added into polyurethane matrix, some fillers tended to agglomerate into clusters (Figs. 2c and 2d) which resulted in lower reinforcement of the PU matrix, compared to the case of 10 wt%. In a word, the nanocomposites produced *via* a solution process showed enhanced colloidal stability and homogenous dispersion which facilitate the improvement of the mechanical and biological properties of the composites.

FTIR

The FTIR spectra of MPEG-g-nHA powder, pure PU and nHA/PU nanocomposite membranes containing 10 wt%, 20 wt% and 30 wt% of MPEG-g-nHA are shown in Fig. 3. In the spectrum of pure PU, the absorption bands around 3334 cm^{-1} was assigned to N—H stretching vibrations of urethane. The absorption bands at *ca.* 1700 cm^{-1} and 1730 cm^{-1} were assigned to —C=O stretching vibrations of the urethane and ester carbonyl groups which showed negligible difference between the pure PU and the nanocomposites, suggesting the similar microstructure of the carbonyl group in these materials. In the spectrum of MPEG-g-nHA (Fig. 3, HA), the absorption band at 3570 cm^{-1} was assigned to the hydroxyl groups (—OH) stretching vibrations in crystal lattice of nHA. The bands at $564.6\text{ (v}_4\text{)}$, $962.0\text{ (v}_1\text{)}$, and $1027.8\text{ (v}_3\text{)}\text{ cm}^{-1}$ were attributed to PO_4^{3-} groups. Besides the described absorption peaks, a weak absorption band at $2800\text{--}3000\text{ cm}^{-1}$ was attributed to the MPEG anchored on HA particle surfaces. The spectra of nHA/PU nanocomposites with 10 wt%, 20 wt% and 30 wt% of MPEG-g-nHA are also shown in Fig. 3. The main characteristic absorption bands of PU and nHA were observed in the composite membrane. It is worthy noting that the N—H stretching vibrations of urethane in pure PU (approximate 3334 cm^{-1}) shifted towards lower frequencies to around 3321 cm^{-1} when nHA fillers were added, indicating an improvement in hydrogen bonding^[15] between nHA particles and PU hard segment, as illustrated in Scheme 1.

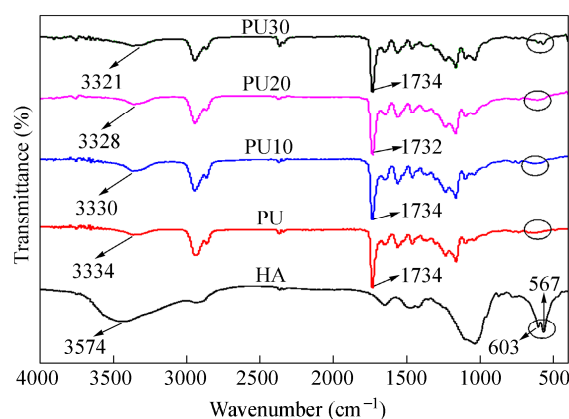


Fig. 3 FTIR spectra of nHA, PU and PU/nHA composites

XRD

X-ray diffraction profiles of MPEG-g-nHA powder, PU and nHA/PU composite membranes are shown in Fig. 4. MPEG-g-nHA powder (Fig. 4, nHA) exhibited several peaks at 26° (002), 32° (211), 40° (310) and 46.8° (222), which were the characteristic diffraction peaks of HA nanoparticles. In the pattern of PU membrane (Fig. 4, PU), two strong peaks were seen at 21.4° and 23.8° , which were the crystalline peaks of PCL soft segments of PU^[2]. The other curves in Fig. 4 show the diffraction patterns of nHA/PU composite membranes in which all the characteristic diffraction peaks of PU and nHA were observed at the same location as those of the two phases. In addition, the diffraction peaks of PU soft segments at 21.4° and 23.8° decreased with the increasing amounts of nHA fillers, suggesting the decreased crystallinity of PCL soft segment. The explanation is that more content of nHA fillers was located in the domain of soft segments when higher amount ($\geq 20\text{ wt\%}$) of nHA fillers were added and the hydrophilic MPEG-g-nHA particles tended to agglomerate in the hydrophobic PCL matrix, as shown in Scheme 1.

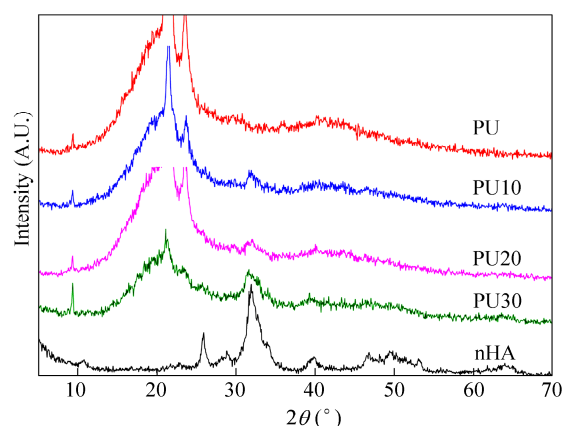


Fig. 4 XRD patterns of nHA, PU and PU/nHA composites

Mechanical Tests

Mechanical behaviors of the pure PU and MPEG-g-nHA/PU membranes were measured by tensile test, and the results are summarized in Table 1. The addition of MPEG-g-nHA into the PU matrix increased the tensile strength and decreased the elongation at break. It is of great interest to note that the nanocomposite containing 10 wt% of MPEG-g-nHA exhibited the most significant improvement in the tensile strength, which increased from 23.67 MPa to 41.5 MPa with a gain of 75% compared to pure PU. Two reasons may account for the massive improvement of the mechanical properties of nanocomposites. One was the excellent dispersibility of MPEG-g-nHA and thus the improved interfacial adhesion between organic PU matrix and inorganic HA nanocrystals due to the entanglement between MPEG on the surface of nHA and the PU matrix. Another was that hydrophilic MPEG-g-nHA was inclined to locate on the more hydrophilic hard segment of PU and formed hydrogen bonds with the N—H of urethane as proven by FTIR. The H-bond between the nHA and the —NH of urethane in the hard segment was also suggested by Li *et al.*^[18] For the sample PU10, most of the nanoparticles located in the hard segment and formed hydrogen bonds with —NH which resulted in the highest reinforcement as illustrated in Scheme 1. However, when the content of MPEG-g-nHA is higher than 10 wt%, *e.g.*, 20 wt% or 30 wt%, the tensile strength decreased with the increase of HA contents. As shown in Scheme 1, for samples with higher content of MPEG-g-nHA, more nHA powder was dispersed in the soft segment and tended to aggregate, thus decreasing the crystallinity of the PCL, which was also proven by XRD. The composites may have a defect structurally due to the aggregated nHA in the PU matrix. Therefore, it is likely that the stress concentration around the nHA aggregates resulted in early failure and fracture^[2] which caused a decrease in tensile strength.

Table 1. Mechanical properties of PU and PU/nHA membrane

Sample	Tensile strength (MPa)	Elongation at break (%)	Tensile modulus (MPa)
PU	23.7 ± 1.3	1050 ± 18	7.06 ± 0.25
PU10	41.8 ± 2.0	1007 ± 10	8.67 ± 0.31
PU20	27.7 ± 1.8	970 ± 23	10.33 ± 0.12
PU30	27.6 ± 2.2	943 ± 38	12.67 ± 0.20

Thermogravimetric Analysis (TGA)

The thermal degradation of pure PU and nHA/PU nanocomposite films with various content of nHA was studied by thermogravimetric analysis. Figure 5 shows the weight as a function of the increasing temperature (TG curves).

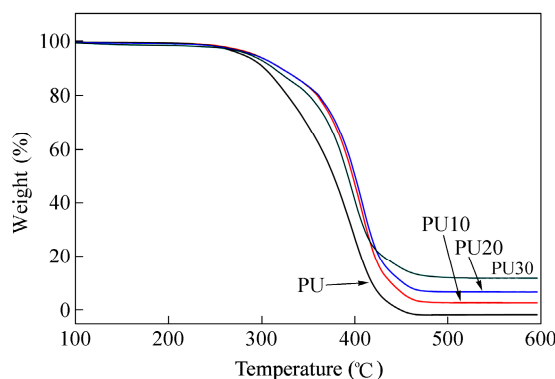


Fig. 5 TGA curves of PU and PU/nHA composites

It can be observed from Fig. 5 that the thermal stability of the nHA/PU composites was improved slightly compared to the pure PU. However, the thermal stability of the nanocomposites did not increase continuously with increasing loading levels of nHA. This slight increase indicated the positive effect of nHA on the thermal stability of the nano-composites, which was also confirmed by Li *et al.*^[19]. They ascribed the improvement of thermal stability partly to the formation of crosslinks through hydrogen bonds between the urethane groups of PU and the hydroxyl groups of nHA.

Differential Scanning Calorimetry (DSC)

DSC curves of pure PU membrane and nHA/PU hybrid membranes with different contents of MPEG-g-nHA particles are illustrated in Fig. 6. The data of glass transition temperature (T_g), melting temperature (T_m) and the melting enthalpy (ΔH_m) of soft segments calculated based on the DSC curves are listed in Table 2.

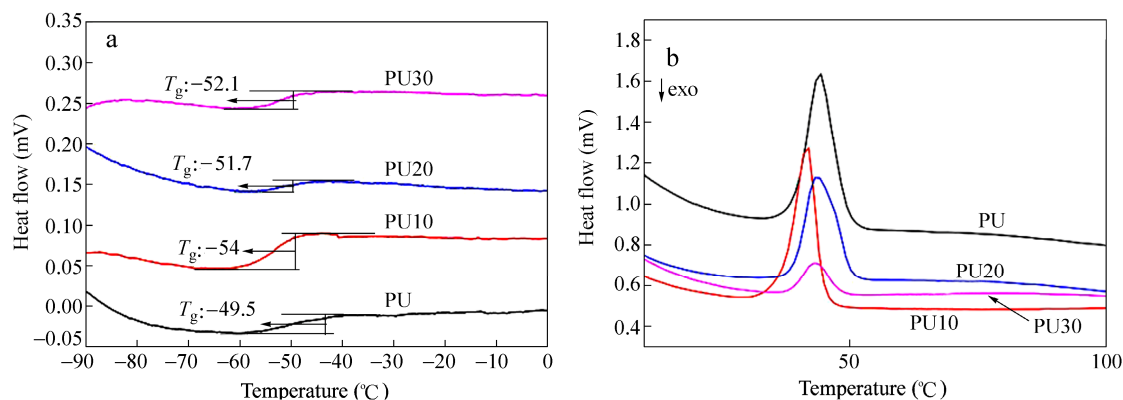


Fig. 6 DSC curves of PU and PU/nHA composites from $-90\text{ }^{\circ}\text{C}$ to $0\text{ }^{\circ}\text{C}$ at a cooling rate of -10 K/min (a) and from $0\text{ }^{\circ}\text{C}$ to $80\text{ }^{\circ}\text{C}$ at a heating rate of 10 K/min (b)

Table 2. Thermal properties of PU and nanocomposites determined by DSC

Sample	T_g ($^{\circ}\text{C}$)	T_m ($^{\circ}\text{C}$)	ΔH_m (J/g)
PU	-49.5	44.1	25.24
PU10	-54	41.6	22.51
PU20	-51.7	43.7	20.0
PU30	-52.1	43.4	5.4

All the samples showed glass transition within the temperature range from $-55\text{ }^{\circ}\text{C}$ to $-45\text{ }^{\circ}\text{C}$. Only an endothermic peak was observed in the heating process for all samples, which was ascribed to the melting of PCL domains of PU. All the nanocomposites showed lower T_g than pure PU due to the strong interaction between the

nanoparticles and the hard segments of PU. The composite with 10 wt% of nanoparticle fillers (PU10) showed the lowest T_g of $-54\text{ }^{\circ}\text{C}$. When the content of fillers in the composites exceeded 10 wt%, however, the T_g of PU matrix began to increase. It can be seen from Table 2 that the melting enthalpy (ΔH_m) of the PCL soft segments decreased with the increasing amount of the nHA fillers and the melting points (T_m) of nanocomposites were lower than that of pure PU, which suggested that more MPEG-g-nHA fillers located in the soft segment regions and decreased the crystallinity of PCL when higher amount of nHA particles were added. The result was consistent with the XRD studies as illustrated in Scheme 1.

CONCLUSIONS

In this work, nHA/polyurethane nanocomposites with various amounts of nanoparticle fillers were prepared by a simple solution blending method. HA nanoparticles were surface modified by MPEG which facilitated the dispersion of nanoparticles in both organic solvents and PU matrix. It was revealed that the mechanical properties and thermal stabilities of PU matrix were improved by the incorporation of nHA due to strong interfacial interaction and relatively uniform dispersion of nHA in the PU matrix. It is worth noting that the tensile strength of the nanocomposite membrane increased by 75% due to incorporating 10 wt% MPEG-g-nHA in the PU matrix compared with the corresponding pure PU film. When higher amounts of fillers were added, *i.e.* 20 wt% and 30 wt%, more particles tended to locate and aggregate in the soft segment region of PU which decreased the crystallinity of PCL, as proven by XRD and DSC measurements. These results suggest that the MPEG-g-nHA/PU nanocomposites with improved mechanical properties, thermal stability will certainly find their use in biomedical applications.

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