Research Article

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Preparation and characterization of thermoresponsive poly(*N*-isopropylacrylamide) copolymers with enhanced hydrophilicity

<https://doi.org/10.1515/epoly-2020-0061>

received August 30, 2020; accepted September 22, 2020

Abstract: The poly(*N*-isopropylacrylamide) copolymers with the enhanced hydrophilicity were synthesized by free radical polymerization from a mixture of the monomers *N*-isopropylacrylamide (NIPAAm), *N*-vinyl pyrrolidone (NVP), hydroxypropyl methacrylate (HPM) and 3-trimethoxysilypropyl methacrylate (TMSPM) at different feeding ratios. The attenuated total reflectance-Fourier transform infrared spectrometry (ATR-FTIR), nuclear magnetic resonance (¹H-NMR) and gel permeation chromatography (GPC) were applied to characterize the resultant copolymers. The lower critical solution temperature (LCST) of the copolymers was determined via dynamic light scattering (DLS). By alternating the molar ratios of NIPAAm and NVP, the copolymers were synthesized to have their own distinctive LCST from 25°C to 40°C. Regardless of the starting feed ratio used, the final copolymers had the similar monomeric ratio as planned. The copolymer films were then formed on platinum wafers by drop coating and thermal annealing owing to 3-trimethoxysilyl cross-linking and reacting with hydroxyl groups. The surface wettability and morphology of the specimens were observed using contact angle measurements and scanning electron microscopy (SEM), respectively. The results demonstrated that with the increase of the NVP content, the film surface became more hydrophilic. The surface microstructure of the thermoresponsive films varied depending on the copolymer composition and ambient temperature. The experimental results indicated that the addition of NVP not only increased the LCST of copolymers but also improved the hydrophilicity

of the products derived from the copolymers. This ability to elevate the LCST of the polymers provides excellent flexibility in tailoring transitions for specific uses, like controlled drug release and nondestructive cell harvest.

Keywords: poly(*N*-isopropylacrylamide) (PNIPAAm), *N*-vinyl pyrrolidone (NVP), lower critical solution temperature (LCST), dynamic light scattering (DLS), hydrophilicity

1 Introduction

Thermoresponsive systems have attracted considerable interests for their ability to change the swelling behaviors and network structures dramatically in response to temperature stimuli, which have potential applications in biomedical and biochemical fields such as drug delivery, protein separation and cell detachment (1–3). Poly(*N*-isopropylacrylamide) (PNIPAAm) is one of the most attractive thermoresponsive polymers. PNIPAAm in aqueous solutions exhibit a lower critical solution temperature (LCST) in the vicinity of 32°C (4,5). Below LCST, PNIPAAm is extremely soluble in water, whereas it becomes hydrophobic and readily precipitates from the aqueous solution when the temperature is above its LCST. It is widely believed that the thermoresponsive behavior of PNIPAAm in aqueous solutions is closely correlated with the destabilization of hydrogen bonds between water molecules and amide linkages with the increase of temperature, probably caused by the presence of hydrophobic isopropyl groups (6).

As already discussed, PNIPAAm homopolymers have the LCST of about 32°C, but this transition temperature cannot meet the requirements of various applications. If PNIPAAm is used as smart substrates of cell culture, it is required to increase the LCST to actually somewhat lower than physiological temperature, which can not only

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satisfy readily cell adhesion at 37°C but also realize speedy cell detachment below LCST through rapid hydration of thermoresponsive substrates (7,8). Thermoresponsive hydrogels are designed to have a LCST slightly above the body temperature, so that the hydrogels will be swollen in the resting state *in vivo* to maximize diffusion of drug (9,10). A carrier constructed with pure PNIPAAm is difficultly modulated by temperature changes under physiological conditions, and thus, it is essential to tailor the LCST of PNIPAAm-based materials, especially to increase the transition temperature (11), which is helping to expand the potential for future marketable applications. Previous studies have demonstrated that the addition of hydrophilic comonomers leads to the increase of LCST of thermosensitive polymers, while the incorporation of hydrophobic comonomers generally results in the decrease of LCST (6,9,11–13). Therefore, the LCST of thermosensitive polymers could be controlled by adjusting their relative hydrophobicity/hydrophilicity. Poly(*N*-vinyl pyrrolidone) (PVP) is a well-known hydrophilic and nontoxic polymer with good biocompatibility (6,11,14). It is evident that with the increase of NVP moieties in the synthesized copolymers, the LCST of PNIPAAm copolymers exhibits an increasing trend (9,11,15). A reasonable explanation is that upon increasing the NVP contents, more linear side chains in copolymers lead to an enhancement in the area of hydrophilic groups, consequently rendering LCST drop (14).

Although studies have shown that the addition of NVP can significantly increase the LCST of thermosensitive copolymers, the low participation rate of NVP can be generally found in copolymer synthesis, which may be due to the lower reactivity of NVP than NIPAAm (13,14,16). It can result in potentially wasting a lot of NVP, greatly improving the production cost. Furthermore, the synthesis process is difficult to control, and the variables acting on it are random. Therefore, it is necessary to improve the utilization rate of NVP for increasing the LCST of the thermosensitive copolymers (the hydrophilicity of end products). In this study, the synthesis of PNIPAAm copolymers with the enhanced hydrophilicity was carried out by free radical copolymerization, and then fabrication of copolymer films was conducted by drop coating and thermal annealing. It focused on the thermal properties of random copolymers bearing NIPAAm, NVP, HPM, and TMSPM over a range of temperatures, investigating the effect that temperature and NVP content had on the LCST of the copolymers and the hydrophilicity of the copolymer films. The participation rate of NVP in the synthesis process would also be concerned in this study.

2 Materials and methods

2.1 Materials

N-Isopropylacrylamide (NIPAAm), 3-trimethoxysilypropyl methacrylate (TMSPM), hydroxypropyl methacrylate (HPM), *N*-vinyl pyrrolidone (NVP) and 2-azobisisobutyronitrile (AIBN), absolute ethanol, acetone, *n*-hexane and tetrahydrofuran (THF) were supplied by Sigma. NIPAAm and AIBN were fully recrystallized from *n*-hexane and absolute ethanol, respectively, and then lyophilized using freeze dryer. Other reagents were used as received.

2.2 Synthesis of PNTHV copolymers

P(NIPAAm-co-TMSPM-co-HPM-co-NVP) (PNTHV for short thereafter) copolymers were synthesized by free radical polymerization according to our previous studies with some modifications (17,18). Briefly, four kinds of reactants, NIPAAm, TMSPM, HPM and NVP, with different feeding molar ratios (see Table 1) were placed into a three-necked flask with a condenser and subsequently purged with nitrogen for 10 min. Then, AIBN was used as an initiator and was added into the mixture solution with absolute ethanol as a solvent. The mixture was heated and stirred at 60°C for 12 h under nitrogen protection. After polymerization, a small amount of acetone was dropped into the remaining sample to dissolve it, and abundant *n*-hexane was then added for precipitating the raw product. The precipitation process was repeated at least three times to purify the samples. Finally, the end product was dried at –101°C in a ScanVac vacuum freeze dryer (Coolsafe 110-4 Pro, Labogene, Denmark) for 24 h and then stored in a refrigerator for further use.

2.3 Identification of PNTHV copolymers

2.3.1 Molecular composition

The attenuated total reflectance-Fourier transform infrared spectrometry (ATR-FTIR) spectra were used to analyze the functional groups of PNTHV copolymers via Bruker TENSOR27 spectrometer (BRUKER OPTIK GmbH) in the wavenumber range of 4,000–500 cm^{–1}. The nuclear magnetic resonance (¹H-NMR) spectra were applied to identify the molecular compositions of the compounds through Bruker AV 400 NMR spectrometer (Bruker Corporation, Switzerland).

Table 1: Composition ratios and molecular weights of PNTHV copolymers.

Sample	Feeding molar ratios	Actual molar ratios ^a	Weight-average molecular weight ^b (M_w , kDa)	Number-average molecular weight ^b (M_n , kDa)	M_w/M_n ^b
PN ₁₀₀ T ₅ H ₅	100:5:5:0	100:4.0:4.0	72.6	34.3	2.12
PN ₁₀₀ T ₅ H ₅ V ₅ ^c	100:5:5:5	100:4.3:4.9:5.0	65.7	33.6	1.96
PN ₁₀₀ T ₅ H ₅ V ₁₀	100:5:5:10	100:4.0:4.8:9.9	61.4	33.0	1.86
PN ₁₀₀ T ₅ H ₅ V ₂₀	100:5:5:20	100:4.9:4.2:19.4	59.4	32.9	1.81
PN ₁₀₀ T ₅ H ₅ V ₃₀	100:5:5:30	100:5.0:4.8:29.6	52.5	31.0	1.69
PN ₁₀₀ T ₅ H ₅ V ₅₀	100:5:5:50	100:4.6:4.3:49.9	43.9	26.6	1.65
PN ₁₀₀ T ₅ H ₅ V ₁₀₀	100:5:5:100	100:4.7:5.0:99.0	37.2	23.2	1.60

^a Estimated by ¹H-NMR analysis. ^b Determined by GPC analysis. ^c P is short for poly, N for NIPAAm, T for TMSPM, H for HPM and V for NVP.

2.3.2 Molecular weight

The molecular weight of PNTHV copolymers was characterized by gel permeation chromatography (GPC, Waters 515) using THF as an eluent with a flow rate of 1.0 mL min⁻¹ at 35°C. Monodisperse polystyrene (Polymer Laboratories Inc., MA) was used for calibration. Sample solutions were prepared using 4 mg mL⁻¹ concentration and filtered through the Millipore filter (0.2 μm) before analysis.

2.3.3 Thermosensitivity

Dynamic light scattering (DLS) was employed to determine the sizes and distribution of PNTHV copolymers with different feeding ratios. PNTHV copolymers were dissolved at the final concentration of 1.0 mg mL⁻¹ in deionized (DI) water and then stirred at room temperature for 12 h. Before adding 1.0 mL solution into a cuvette, the copolymer solutions were purified with Millipore filter (0.2 μm) to remove any impurities. The cuvette was then placed in the bath of Malvern Zetasizer (Nano ZS, Malvern Instruments Ltd, UK) with scattering angle fixed at 173°. The measurements were performed from 20°C to 45°C with temperature fluctuation of 0.1°C. The data were collected after 10 min when the solutions had reached the setting parameters, and at least three replicates were carried out under the same conditions. The average value ± standard deviation was applied to present the average hydrodynamic diameter (D_{AH}) of PNTHV copolymers obtained by volume distribution. The DLS data were analyzed using Malvern Zetasizer Software v7.11.

2.4 Preparation of PNTHV copolymer films

PNTHV copolymers with various molar ratios were first dissolved at the final concentrations of 10 mg mL⁻¹ in

absolute ethanol and then kept under stirring at ambient temperature for above 12 h. All the copolymer solutions were filtered with Millipore filters (0.2 μm) before use. Ten microliters of different copolymer solutions were dropwise added onto the surfaces of platinum wafers. The coatings were dried in air for 30 min at room temperature and then annealed for 3 h at 125°C under vacuum to facilitate 3-trimethoxysilyl crosslinking and reacting with hydroxyl groups. Any unconnected copolymers were extracted by soaking and washing the modified platinum wafers in DI water thoroughly. The products were finally dried under vacuum at room temperature.

2.5 Characterization of PNTHV copolymer films

2.5.1 Surface wettability

For contact angle measurements, the modified platinum wafers were first dried in the fume hood and then placed onto the operating platform of Drop Shape Analyzer (DSA100, KRÜSS GmbH, Germany) successively. The static contact angles (θ) of 2 μL sessile DI water droplets were measured at room temperature with three trials for each sample. The images and values were recorded immediately after the droplet was dropped onto the surfaces and collected every 60 s thereafter until 300 s. The data were analyzed by Drop Shape Analysis Software v1.92.1.1.

2.5.2 Surface topography

The modified platinum wafers once produced were sputtered with gold using an Agar auto sputter coater (Agar Scientific Ltd, UK). In addition, the fresh modified platinum wafers were soaked in DI water of 22°C or 42°C for 3 h, then dried in a vacuum oven with the controlled temperature of

22°C or 42°C, and also covered with a thin layer of gold. The surface morphology of the specimens was observed using the scanning electron microscopy (SEM) with the Quanta 400 FEG instrument (FEI, USA) under standard vacuum conditions at an acceleration voltage of 10 kV.

3 Results and discussion

3.1 Synthesis of PNTHV copolymers

In this study, PNTHV copolymers were synthesized by free radical polymerization with NIPAAm, HPM, TMSPM, and NVP under the moderate reaction conditions (60°C, ordinary pressure). NIPAAm was applied as a main monomer, and amide linkages and isopropyl bonds located in the copolymer chains were functional groups that facilitated final products with thermosensitivity. TMSPM was a silane cross-linker that was stable during polymerization but was activated at forming covalent bonds with any materials bearing hydroxyl groups under high temperature or irradiation environments (19). HPM could provide useful hydroxyl groups for the bonding between molecular chains of copolymers (17). Both siloxane bonds of TMSPM and hydroxyl groups of HPM were employed as reactive groups of the copolymers. Free methanol was extracted on account of condensation reaction between hydroxyl and methoxyl groups, and the newly formed bonds gave rise to the integration within the film and coupling with the hydroxyl-contained surface. Although HPM was available for adjusting film hydrophilicity (20), the higher hydrophobicity of TMSPM led to the LCST of the copolymers bearing NIPAAm, HPM and TMSPM reaching 25°C (see Figure 4). Therefore NVP, a typical hydrophilic monomer, was introduced into the polynary copolymers to increase the LCST of the resultant copolymers. For the design constraint of LCST of PNTHV copolymers, the manually adjustable ratios of NIPAAm and NVP, and the fixed ratio (5%) of TMSPM/HPM to NIPAAm was applied in this study. The chemical structure of PNTHV copolymer and its bonding with the substrate and other copolymers were schematically displayed in Figure 1.

3.2 Identification of PNTHV copolymers

3.2.1 Functional groups of PNTHV copolymers

The successful synthesis of PNTHV copolymers was first illustrated by the ATR-FTIR analysis with the spectra shown in

Figure 1: Schematic diagram for molecular structure of PNTHV copolymer and three possible types of methanol removal when annealed.

Figure 2. PNTHV copolymers were characterized by the doublet absorption peaks of isopropyl groups at 1,385 and 1,365 cm^{-1} and the absorption peaks of amide II at 1,533 cm^{-1} . The mixed strong absorption peaks at 1,649 cm^{-1} belonged to amide I band of PNTHV copolymers and C=O stretching vibration of NVP, and the absorption peaks at 1,423 and 1,286 cm^{-1} manifested the characteristic stretching of C–N and bending of C–N within NVP. Having compared the characteristic peaks of the copolymers with the selected feeding ratios to those of both homopolymers (11,21), it is shown that there exist both the absorption peaks of PNIPAAm and PVP. The strong broad absorption peaks at 3,298 cm^{-1} could be attributed to hydroxyl groups in HPM. Furthermore, the absorption peaks at 2,873 and 1,082 cm^{-1} confirmed the successful incorporation of the siloxane groups. Also, the absorption peaks at 1,722, 1,269, and 1,170 cm^{-1} were assigned to ester groups arising from HPM and TMSPM. Similar findings have been reported in our previous reports (17,18). Hence, it can be confirmed that all the four reactants existed in PNTHV copolymers. Due to the difference of feeding ratios, the typical characteristic absorption peaks of different PNTHV copolymers showed a movement of 1–3 cm^{-1} . With the increase of the NVP content, the peak areas of relevant characteristic absorption peaks increased correspondingly.

3.2.2 Chemical structure of PNTHV copolymers

Figure 3 illustrates ^1H -NMR spectra (400 MHz, CDCl_3) of different PNTHV copolymers which indicated common

Figure 2: ATR-FTIR spectra of PNTHV copolymers.

traits as well as differences of the spectra. The peak appearing at 7.26 ppm was the solvent peak of CDCl_3 . As shown in Figure 3, several characteristic peaks from NIPAAm, TMSPM, HPM and NVP were overlapped. But the proton signals were clearly resolved at 1.07 ppm (e) assigned to $(\text{CH}_3)_2\text{CH}-$ (isopropyl group) in NIPAAm (13,14,21), at 3.41 (3.50) ppm (i) belonged to $-\text{OCH}_3$ in TMSPM, at 3.17 ppm (j) attributed to methylene groups next to N-atoms in NVP (13,14) and at 3.65 ppm (g) attributed to $-\text{OCH}_2-$ in both TMSPM and HPM (17,18). It could also be observed that with the rise of NVP addition, the indicative peak intensity of NVP was enhanced gradually at 3.17, 2.29 and 2.10 ppm, confirming the occurrence of copolymerization. The composition molar ratios (NIPAAm:TMSPM:HPM:NVP) of PNTHV copolymers could be estimated from the peak areas of e, i, g, and j. The actual molar ratios of PNTHV copolymers at the selected feeding ratios were also summarized in Table 1. The experimental results displayed that the outcome was highly consistent with the integrated area ratio, showing that the copolymerization had proceeded well as planned and that the final copolymers had the similar monomeric ratio to the starting feed ratio. Some studies have suggested that only a small amount of NVP participated in actual reaction, which resulted from the low reactivity ratio of NVP compared with NIPAAm in radical copolymerization (13,14,16). This may be due to different polymerization methods, reaction conditions and reactant varieties. It also demonstrates that the high participation of NVP in the polymerization can be achievable by using the synthesis strategy developed in this study.

3.2.3 Molecular weight of PNTHV copolymers

The molecular weight of PNTHV copolymers as measured by means of GPC was also concluded in Table 1. The results showed that the weight-average molecular weight (M_w , also number-average molecular weight, M_n) of PNTHV copolymers decreased significantly with the increase of the NVP content, which was consistent with other experimental results (14). This seemed partly owing to the steric hindrance of pyrrolidone ring derived from NVP. The higher the NVP proportion added, the greater the steric hindrance formed, and so the length of the molecular chains would be correspondingly reduced. The molecular weight distribution of PNTHV copolymers with M_w/M_n values ranged from 1.600 to 2.115 as estimated from GPC traces. Furthermore, the M_w/M_n values reduced progressively as the NVP content increased. This would be probably for the same reason as the trend in molecular weight. The steric hindrance of the pyrrolidone ring restricted the continuous copolymerization of four monomers. The polymerization would stop when a range of molecular chain lengths was reached.

3.2.4 Thermosensitive characters and LCST of PNTHV copolymers

The thermosensitive properties of PNTHV copolymers were characterized by variation tendency of D_{AH} with temperature, as displayed in Figure 4. It was clear that

Figure 3: ^1H -NMR spectra of PNTHV copolymers.

the D_{AH} of PNTHV copolymers synthesized from monomers in different molar ratios showed small variation first, then a sudden increase, and finally a slow increase. When the temperature was lower than their respective LCSTs, the D_{AH} of PNTHV copolymers with different feeding ratios were around 10 nm, indicating that these nanoparticles were hydratable. At this point, the hydrated hydrogen bonds between water molecules and hydrophilic groups, including amide bonds, hydroxyl groups and siloxane bonds, were considered as major forces to prevent intermolecular aggregation and intramolecular collapse of PNTHV copolymers. Favorable hydrogen bonding interactions between copolymers and water molecules resulted in good solubility (11), so the

copolymer solutions looked clear and transparent. Across LCST, the scattered nanoparticles gathered obviously and become dehydrated. As it was seen, the transparency of the solutions was changed abruptly for the copolymers of all compositions upon heating, but the opaque solutions remain being free flowing. As the temperature continued to increase, several dozen times of D_{AH} could be observed, demonstrating that the molecular chains of PNTHV copolymers aggregated dramatically due to the formation of hydrophobic interactions caused by isopropyl groups as well as hydrogen bonds between amide bonds. This process occurred cooperatively owing to destroying hydrogen bonding between polymers and water molecules and stabilization of aggregation with interchain and intrachain interactions (11,21,22).

Figure 4: Changes in average hydrodynamic diameter of PNTHV copolymers in DI water as plotted with temperature.

The LCST of thermosensitive polymers can be regulated by adjusting the relative hydrophobicity (6,12). This was achieved by copolymerizing hydrophobic NIPAAm monomers with hydrophilic NVP monomers at varying feed ratios in this study. The LCST of PNTHV copolymers went up with the increasing NVP moieties as expected. The LCST range varied from 25°C to 40°C for the zero and highest NVP content (47.62%). The LCSTs of $\text{PN}_{100}\text{T}_5\text{H}_5$, $\text{PN}_{100}\text{T}_5\text{H}_5\text{V}_5$, $\text{PN}_{100}\text{T}_5\text{H}_5\text{V}_{10}$, $\text{PN}_{100}\text{T}_5\text{H}_5\text{V}_{20}$, $\text{PN}_{100}\text{T}_5\text{H}_5\text{V}_{30}$, $\text{PN}_{100}\text{T}_5\text{H}_5\text{V}_{50}$ and $\text{PN}_{100}\text{T}_5\text{H}_5\text{V}_{100}$ copolymers were approximate to 25°C, 26°C, 27°C, 28°C, 29°C, 31°C and 40°C, respectively, showing an almost linear increase in LCST with the increasing hydrophilic component (see Figure 4). The introduction of NVP would undoubtedly enhance the hydrophilic interaction, leading to LCST elevation (11,12). Interestingly, the addition of NVP not only improved the LCST of PNTHV copolymers but also increased the intermolecular aggregation when the ambient temperature was higher than LCST, which was caused by the additional amide bonds

Figure 5: Schematic diagram for changes in the average hydrodynamic diameters of the PNTHV copolymers in DI water.

of NVP. Therefore, the D_{AH} of PNTHV copolymers with the higher NVP content was greater. When the temperature was lower than the LCST, the amide bonds of NVP combined with water to form the hydrated hydrogen bond to delay the LCST, whereas when the temperature increased to above LCST, the amide bonds of NVP could bind other amide bonds derived from PNTHV or NVP to trigger the intermolecular aggregation, as displayed schematically in Figure 5.

3.3 Fabrication of PNTHV copolymer films

Thermosensitive copolymer particles are not very useful; however, as the precursors of thermosensitive products, composition selection and proportion control of the copolymers should be conducive to the preparation of thermosensitive products and the regulation of their properties. PNTHV copolymers were made into thin films, which was convenient to check whether NVP could increase the hydrophilicity of the final products and verify the feasibility of covalent linkage between PNTHV copolymers and hydroxyl containing carriers. The synthesized copolymers were the precursors of PNTHV copolymer films. Although in the process of film preparation, the copolymers would shift from free single chain to crosslinked network, each molecular chain within the final films would not significantly change their characteristics. The thermosensitive properties of the copolymers in aqueous solutions enable PNTHV copolymer films to have clear thermosensitivity.

As mentioned earlier, the siloxane groups can react with the substrates containing hydroxyl groups under the condition of heating or irradiation (19) to facilitate the

covalent crosslinking between PNTHV copolymers and substrates; PNTHV copolymers also have hydroxyl groups, and therefore, the bonding between siloxane groups and hydroxyl groups can be formed at the same time, eventually forming a network structure of the molecular chains of PNTHV copolymers. There are two polymerization reactions involved in the fabrication of PNTHV copolymer films: first, PNTHV copolymers are generated from the double bond monomers NIPAAm, TMSPM, HPM and NVP through free radical polymerization; second, PNTHV copolymer films with the crosslinking network structure are formed by the bonding between siloxane bonds and hydroxyl groups through thermal annealing. This preparation strategy allows the addition of functional monomers in the synthesis process, which can adjust and improve the comprehensive properties of the resultant copolymers and realize the coupling of the copolymers and substrates with any shape and scale.

3.4 Characterization of PNTHV copolymer films

3.4.1 Surface wettability

Figure 6 illustrates the time-dependent changes of contact angles of modified platinum wafers with the typical contact angle images at the initial time ($t = 0$ s). The contact angles of the platinum wafers modified by PNTHV copolymer films were sensitive to the NVP content and contact time. As NVP content increased, the water contact angles decreased gradually. The uptake water ability of PNTHV copolymers increased with the increase of NVP moieties, leading to more hydrophilic surfaces. This

Figure 6: Time-dependent changes of contact angles of PNTHV copolymer films.

confirmed that siloxane bonds and hydroxyl groups within PNTHV copolymers could be bound covalently to freshly prepare the copolymer films, but the functional groups of NIPAAm and NVP, such as isopropyl groups and amide linkages remained intact, resulting in little change in

thermosensitivity and hydrophilicity of copolymer films derived from PNTHV copolymers. It is well known that a hydrophilic/hydrophobic balance stabilizes PNIPAAm in solution, and the transition of thermosensitive products is also related to a change in this balance (20). Therefore, this result is due to the more hydrophilic NVP, which was used as the component of the PNTHV copolymer films. There was also a significant decline in the contact angles of the modified platinum wafers as time went on. Because water droplets would penetrate into the PNTHV copolymer films gradually and diffused and spread on the material surfaces. This showed that the infiltration performance of PNTHV copolymer films with water was a dynamic process influenced by material composition and moisture content.

3.4.2 Surface topography

All the samples were transparent and glass like in appearance after thermal annealing. Figure 7 displays representative surface topography of PN₁₀₀T₅H₅, PN₁₀₀T₅H₅V₂₀, PN₁₀₀T₅H₅V₅₀ and PN₁₀₀T₅H₅V₁₀₀ copolymer films modified platinum wafers treated by different experimental environments. The surface morphology of the modified platinum

Figure 7: SEM images of PNTHV copolymer films including dry samples after production (A1, B1, C1 and D1) and samples after production and soaking in DI water of 22°C (A2, B2, C2 and D2) or 42°C (A3, B3, C3 and D3) for 3 h and drying in vacuum oven.

Figure 8: Schematic diagram of structure changes of PNTHV copolymer films against temperature.

wafers varied by the NVP content and the solution temperature. When comparing SEM images of the samples without immersion in DI water, the surface microstructure of $\text{PN}_{100}\text{T}_5\text{H}_5$ and $\text{PN}_{100}\text{T}_5\text{H}_5\text{V}_{20}$ copolymer films were more compact and smoother, whereas the surfaces of $\text{PN}_{100}\text{T}_5\text{H}_5\text{V}_{50}$ and $\text{PN}_{100}\text{T}_5\text{H}_5\text{V}_{100}$ copolymer films became porous and coarse.

Once immersed in water at different applied temperatures, the surface structure of the modified platinum wafers with respect to temperature in aqueous solutions also changed correspondingly. For $\text{PN}_{100}\text{T}_5\text{H}_5$ copolymer films, the surface changed from porous, rough and loose to imporous, smooth and dense as the temperature increased to above LCST, whereas the morphology of $\text{PN}_{100}\text{T}_5\text{H}_5\text{V}_{100}$ copolymer films shared similar granular structure at both working temperatures but had irregular pores with a larger size on the film surface at 42°C. The SEM images of $\text{PN}_{100}\text{T}_5\text{H}_5\text{V}_{20}$ copolymer films would seem to be a closer in comparison to $\text{PN}_{100}\text{T}_5\text{H}_5$ sample, while the microstructure changes of $\text{PN}_{100}\text{T}_5\text{H}_5\text{V}_{50}$ copolymer films were similar to that of the $\text{PN}_{100}\text{T}_5\text{H}_5\text{V}_{100}$ group. The SEM results indicated that PNTHV copolymers could be covalently linked to the surfaces of platinum wafers by droplet coating and thermal annealing, and the addition of NVP significantly changed the surface structure of PNTHV copolymer films. The surface morphology at the temperatures above LCST was obviously different from that at lower temperature, which confirmed that PNTHV copolymer films deposited on platinum wafers still showed attractive thermosensitive characters. As described in the DLS results, the increased NVP integrated more additional amide bonds into the copolymer molecular chains, which had reinforced the intermolecular aggregation above LCST (9,21). Therefore, with the increase of the NVP content, the molecular chains would have preferred to gather locally rather than holistically, leading to the formation of larger pores on the surfaces of PNIPAAm copolymer films, as schematized in Figure 8.

4 Conclusions

A series of random PNTHV copolymers bearing NIPAAm, TMSPM, HPM and NVP at different monomeric concentrations had been synthesized by free radical polymerization. The ATR-FTIR and ^1H -NMR spectra of PNTHV copolymers indicated that successful copolymerization of each of the monomers had proceeded as planned. The GPC results showed that with the increasing NVP content, a decrease in molecular weight and M_w/M_n value of PNTHV copolymers could be achieved. The DLS data showed that the LCST range of the resultant copolymers varied from 25°C to 40°C for the zero and highest NVP content (47.62%). PNTHV copolymer films were prepared on platinum wafers by drop coating and thermal annealing. The contact angle measurements demonstrated that with the increase of NVP moieties, the film surface became more hydrophilic. The SEM images indicated that the addition of NVP significantly changed the surface structure of PNTHV copolymer films. The different surface morphologies at the temperatures below and above LCST confirmed that PNTHV copolymer films deposited on platinum wafers still showed attractive thermosensitive characters. In conclusion, we have prepared temperature-sensitive PNIPAAm copolymers with high NVP participation and adjustable water uptake through a simple method. The special functional groups within the copolymers can be connected to the substrates containing hydroxyl groups by heating and generate a copolymer film with the network structure at the same time. The copolymer films formed still retain excellent temperature sensitivity and hydrophilic enhancement. This feature could be particularly beneficial in the applications of controlled drug release and nondestructive cell harvest.

Acknowledgments: This research was funded by National Natural Science Foundation of China (21604034); Key Research Plan of Liaoning Province of China (2020JH2/

10700001) and General Scientific Research Program of Department of Education of Liaoning Province of China (L2020015).

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