Fluctuation in the Phase Transition Temperature of Poly (NIPAAm-co-HEMA-co-DMAMVA)-Post-Guanine Affected by Hydrophilic/Hydrophobic Interaction: Fabrication and Characterizations

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Abstract
The phase separation and transition temperature of poly (N-isopropylacrylamide) have been developed by the terpolymerization with new pH-responsive monomer and highly hydrophilic 2-Hydroxyethyl methacrylate. The new monomer based on vanillin is called 2-((dimethylamino)methyl)-4-formyl-6-methoxyphenyl acrylate (DMAMVA) and is investigated by chemical methods (1H, 13C NMR, and FTIR). Terpolymers of dual-responsive thermo-pH with functional groups were fabricated via free radical polymerization of N-isopropylacrylamide (NIPAAm), 10 mol% 2-Hydroxyethyl methacrylate, and 5, 10, and 20 mol% DMAMVA. A selected terpolymer was used for post-polymerization with guanine via click reaction and the formation of an imine between the aldehyde group of DMAMVA and the amine group of guanine. All terpolymer and post-terpolymer are chemically evaluated. The physical properties have been implemented by GPC (molecular weight and dispersity), DSC (glass transition temperature $T_g$), TGA (steps of degradation), and SEM (morphological features). The fluctuations in phase transition temperature $T_c$ or the lower critical solution temperature LCST of the polymer solution in different pH solutions have been performed by two methods, first, the turbidity test by UV–Vis-spectroscopy, second, by micro-DSC for aqueous polymer solution. This work will be extended for more applications in bio-separation technology.

Graphical abstract

Keywords Phase transition temperature · N-isopropylacrylamide · 2-Hydroxyethyl methacrylate · Vanillin derivative · Hydrophilic/hydrophobic interaction

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Introduction

In the wake of fast speeding in industrial technology, scientists were striving toward challenging to reveal new material with unique properties that can change according to the surrounding environment. Scientists have given it many names, among them environmental, smart, stimuli-responsive, and intelligent [1–6]. They have also been discovered in nature, e.g., Venus flytrap and Mimosa pudica show responsiveness via electrical and mechanical [7]. According to their responsiveness; it has been classified as mono-responsive such as thermo-responsive [8–10], pH-responsive [11–14], ionic strength [15, 16], mechanical [17], light [18], pressure [19], however, the presence of two or more responsiveness in the same material by copolymerization of different responsive monomers is responsible for creating dual or multiple responsive polymeric materials [20–25]. One of the most popular kinds of responsive material is polymers that are environmentally changed with temperature, called thermo-responsive polymers. Recently, a researcher has revealed poly (N-isopropylacrylamide) (PNIPAAm) to be the essential thermo-responsive polymer, and this is the beginning of research in this area [26–30]. The phase separation temperature of PNIPAAm aqueous solution exhibited lower critical solution temperature LCST ($T_c$) at about ~ 32 °C as reported in many recent publications [31–33]. The transition temperature of PNIPAAm aqueous solution depends on the balance between hydrophilic groups formed via hydrogen bonds between the amide and carbonyl groups with water and the hydrophobic groups such as the isopropyl group [31]. By increasing the temperature of the polymer solution, hydrogen bonds begin breaking and decreasing the hydrophilicity and consequently increasing in hydrophobicity that improves aggregation and then separation of the polymer molecules from the solution [34]; meanwhile, this behavior is attributed to the change from the isotropic to anisotropic based on Gibbs law [34]. Another responsive material with great interest is pH-responsive; they are functional monomers and polymers that can be ionized to anionic or cationic in pH solutions producing polymer electrolytes as poly(anions) or poly(cations) [35–37]. In the last few decades, polymer and material scientists have focused on fabricating new materials with dual-responsiveness depending on thermo-pH via copolymerization of PNIPAAm with pH-responsive monomer [38–40]. Moreover, pH-responsive polymers with the tertiary amine functional group have been considered the most popular poly (cations) for their wide applications [41]. The copolymerization of poly N-(2-(dimethylaminoethyl) acrylamide) (PDMAEAm) with PNIPAAm has been recently developed for many applications, e.g., metal absorption [42], drug delivery [5], bio-separation [29]. In our recent studies, we were interested in preparing a new monomer based on vanillin as renewable and non-toxic material [43]; these thermo-pH-responsive polymers have been implemented for post-polymerization of amino acids or for improving the phase separation temperature of PNIPAAm [44]. Many recent works have studied the introduction of hydrophilic or hydrophobic monomers to PNIPAAm [39, 45]. Poly (2-Hydroxyethyl methacrylate) PHEMA is one of the highly hydrophilic polymers; it has several applications, the most important is focused on the fabrication of contact lenses [46–48]. The copolymerization of PNIPAAm with PHEMA was used to achieve hydrophilic-thermo-responsive functional and material, as discussed in many kinds of research [49–51]. This study has also been developed to study the fluctuation in the phase separation temperature, or LCST of PNIPAAm as influenced via the terpolymerization with the new pH-monomer containing a hydrophilic tertiary amino group with hydrophobic chain and hydrophilic HEMA. The functional terpolymer has been used in the post-polymerization of amino acids. In the future, the study will focus on new applications for bio-separation technology.

Experimental

Material

2-Hydroxyethyl methacrylate, 1,2-Ethanediol mono(2-methylpropenoate), Glycol methacrylate, (HEMA, 98%, Sigma-Aldrich) was extra-purified by distillation under reduced pressure, 2,2’-Azobis(2-methylpropionitrile) (AIBN, 98%, Sigma-Aldrich), anhydrous dimethylamine (DMA, 99%, Sigma-Aldrich), formaldehyde (37 wt% in water, 10–15% methanol, Sigma-Aldrich), N-isopropylacrylamide (NIPAAm, 97%, Acrös) has been purified by recrystallization from a mixture of benzene/n-hexane 60/40 v/v, Vanillin, 4-Hydroxy-3-methoxybenzaldehyde, (V, 99%, Sigma-Aldrich), acryloyl chloride or 2-Propenoyl chloride (98%, Sigma-Aldrich), guanine (98%, Sigma-Aldrich). Ethanol, dichloromethane, diethyl ether, and tetrahydrofuran (THF) have been stirred overnight in potassium hydroxide at room temperature and then distilled. Other chemicals were used as purchased.

Instrumentation

The nuclear magnetic resonance (NMR) spectroscopy model Bruker AV 500 has been used to investigate $^1$H and $^{13}$C of monomers and polymer molecules. The solid and dried material has been dissolved in deuterated CDCl₃ or
DMSO-d6, and then data has been measured at 500 MHz (1H) and 125 MHz (13C).

Compact ATR-FTIR spectroscopy with the Bruker Alpha has been used to deduce functional groups of both monomers and polymers molecules. The sample has been fixed on the surface of a ZnSe ATR crystal and then is functioning as fiber optics. By the entry of the waves of light into the sample, it was exposed to a total reflection. The total attenuated reflected beams were measured, and the final results seemed as signals that converted into an infrared spectrum.

Gel permeation chromatography (GPC) is a technique that is used to separate dissolved macromolecules according to their size and to depend on their elution through columns filled with a porous gel. It has been used for the determination of the molecular weights, including the viscosity average molecular weight (Mv), the number average molecular weight (Mn), and the weight average molecular weight (Mw); dispersity or the formal name the polydispersity index (PDI) and also known as heterogeneity index has also been measured as Mw/Mn (D). We used THF as eluent with 2 g/L 2,6-di-tert-butyl-4-methylphenol (BHT) for terpolymers; however, post-terpolymer has been measured using dimethylactamide DMA as eluent. It was compacted with Jasco 880-PU pump and Waters RI-Detector for justification of the rate of flow at 0.75 ml/min., toluene was the internal standard at 30 °C. Polymers were dissolved as 6 g/L in concentration, and then the injection process was achieved by hand. Standards gel particle PSS-SDV with high-speed polymer service columns has been filled with the porosity of 10^6 Å (guard), 10^5 Å, 10^3 Å, and 10^2 Å have been respectively used; the molecular weights were detected and recorded related to a narrow polystyrene standard. The measurements were repeated three times, and the mean of Mn, Mw, and D was added in Table 1.

Differential scanning calorimeter-DSC Analysis-Netzsch DSC 214 PolymaIt has been used to detect the glass transition temperature of solid terpolymers Tg,s. It is characterized by a temperature range of 25–600 °C, and a heating and the cooling rate at 0.001–500 K/min. The glass transition temperature was taken at the onset value of the thermogram. Data in Table 1 was calculated as the mean value of three measurements.

Thermogravimetric analysis (TGA) with the Mettler Toledo TGA/SDTA851 was used to elucidate the chemical decomposition as the change of mass with the temperature of polymer sample by heating from 25 to 600 °C at the rate of 5 °C/min. We repeated the test three times to confirm our result, and the mean value was confirmed.

Scanning Electron Microscopy (SEM) Zeiss NEON 40; the change on the surface of the polymer due to the chemical modification has been noticed as the change in the surface morphological features of polymers. It was investigated by Scanning Electron Microscopy (SEM); Zeiss NEON 40,

| Polymer | Yield (%) Composition | 1HNMR | GPC | DSC | UV–VIS |
|--------|----------------------|------|-----|-----|--------|
| VI-10-05 | 84                   | 3.25 | 8.46 | 59980  | 84.16           |
| VI-10-10 | 82                   | 6.66 | 8.58 | 58400  | 84.16           |
| VI-10-20 | 78                   | 12.63| 8.35 | 40850  | 84.16           |
| VIII    | 63.8                 | -    | -   | -    | -      |

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Table 1: Yield, composition, molecular weight, dispersity, glass temperature and transition temperature of poly(NIPAAm-co-HEMA-co-DMAMVA) and poly(NIPAAm-co-HEMA-co-DMAMVA)-post-guanine.

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| VIII    | 63.8                 | -    | -   | -    | -      |
ples have been exposed to cool and heat at a heating rate of 50 mg/ml of polymer sample dissolved in DI water; the sam-

gerat MD 3040, BECKMANN + EGLE) placed inside cooling. The manual thermostat (TEMPERATUR-MESS-

With a thermostat and the water pump for both heating and it has been connected with the water cycle of the water bath.

The suspension converted to yellow color on the edges of the flask; the stirring was continued at 0–5 °C for about 1 h until the yellowish precipitate was dominated. After this step, the reaction was left at room temperature for 6 h, it was filtered, and the solvent was removed. The purification steps were carried out by dissolving in CH2Cl2 and washing several times with deionized water, and then washing with 0.1 M Na2CO3 solution, and washing two times again with DI H2O. It was separated by the separated funnel, and the organic phase was dried overnight via MgSO4. The product was concentrated by evaporation of the solvent, and the final pure product was collected for further analysis and application. 75%, orange viscous liquid.

1H NMR (500 MHz, CDCl3): δ (ppm) = 2.19 (s, 6 H, 6-NCH3), 3.37 (s, 2 H, 5-Ar-NCH2), 3.93 (s, 3 H, 3-OCH3), 6.39 (br, 1 H, 1-OH), 7.15 (d, 1 H, 4 J = 1.8 Hz, 9-Ar–CH), 7.33 (d, 1 H, 4 J = 1.8 Hz, 7-Ar–CH), 9.76 (s, 1 H, 11-CHO).

13C-NMR (125 MHz,CDCl3): δ (ppm) = 44.32 (2 C, 6-NCH3), 56.01 (1 C, 5-NCH2), 62.21 (1 C, 3-OCH3), 109.97 (1 C, 9-Ar–CH), 123.70 (1 C, 7-Ar–CH), 125.21 (1 C, 4-Ar–C), 128.09 (1 C, 8-Ar–C), 148.68 (1 C, 2-Ar–C), 154.54 (1 C, 10-Ar–C), 190.67 (1 C, 11-CHO).

IR (KBr): ν (cm−1) = 2450–3100 (s) (CH2, CH3), 2056–2341 (s) (C–N), 1735 (s) (C = O), 1660 (s) (Ar–C–O), 1575 (s) (Ar–C=C), 1112 (s) (O–CH3), 814–847 (m) (Ar–CH).

Step 2: Synthesis of Compound (III) 2-((Dimethylamino)Methyl)-4-Formyl-6-Methoxyphenyl Acrylate (DMAMVA). The final product of the new acrylate monomer (DMAMVA)-(III) can be synthesized by the addition of 7.5 g (0.0355 mol) (DMAMV)-(II) and 7.5 g (0.187 mol) sodium hydroxide into 100 ml dry dichloromethane and transferred into 250 ml three-neck flask equipped with dropping funnel, water condenser, and a balloon of argon. The reaction mixture has been allowed to stir in an inert atmosphere. The reaction was cooled to 0–5 °C in an ice bath, and then 3.23 g (0.0355 mol) acryloyl chloride dissolved in 15 ml dichloromethane was dropped to the reaction mixture by the dropping funnel and during vigorous stirring. The suspension converted to yellow color on the edges of the flask; the stirring was continued at 0–5 °C for about 1 h until the yellowish precipitate was dominated. After this step, the reaction was left at room temperature for 6 h, it was filtered, and the solvent was removed. The purification steps were carried out by dissolving in CH2Cl2 and washing several times with deionized water, and then washing with 0.1 M Na2CO3 solution, and washing two times again with DI H2O. It was separated by the separated funnel, and the organic phase was dried overnight via MgSO4. The product was concentrated by evaporation of the solvent, and the final pure product was collected for further analysis and application. 75%, orange viscous liquid.

1H NMR (500 MHz, CDCl3): δ (ppm) = 2.19 (s, 6 H, 13-2CH3), 3.37 (s, 2 H, 12-NCH2), 3.84 (s, 3 H, 6-OCH3), 6.03 (dd, 2 J = 1.1 Hz, 3 J = 10.5 Hz, 1 H, 1-Hb = CH2), 6.34 (dd, 3 J = 10.5 Hz, 3 J = 17.3 Hz, 1 H, 2-Hc = CH), 6.64 (dd, 2 J = 1.1 Hz, 3 J = 17.3 Hz, 1-Ha = CH2), 7.37 (d, 1 H, 4 J = 1.7 Hz, 7-Ar–CH), 7.34 (d, 1 H, 4 J = 1.7 Hz, 10-Ar–CH), 9.91 (s, 1 H, 9-CHO).

13C-NMR (125 MHz,CDCl3): δ (ppm) = 45.42 (2 C, 13-2CH3), 55.72 (1 C, 12-NCH2), 62.41 (1 C, 6-OCH3), 108.75 (1 C, 7’-Ar–CH), 122.37 (1 C, 11- Ar–CH), 126.25 (1 C, 2=CH), 127.30 (1 C, 10–Ar–C), 132.22 (1 C, 1=CH2), 134.39 (1 C, 8-Ar–C), 143.50 (1 C, 4-Ar–C), 152.51 (1 C, 5-Ar–C), 162.81 (1 C, 3-COO), 191.64 (1 C, 9-CHO).
The reaction has been done three times with different molar concentrations of DMAMVA 5, 10, and 20 mol% (0.0013 mol/0.342 g), (0.00265 mol/0.697 g) and (0.0053 mol/1.697 g) respectively, and 10 mol % of HEMA (0.00265 mol/0.345 g), and (0.0265 mol/3 g) of N-isopropylacrylamide and AIBN initiator (10–3 of the total molar concentrations of monomers); they were dissolved in 60 ml absolute ethanol. The three mixtures were reacted in 100 ml round bottom flasks fitted with rubber stoppers allowed for nitrogen injection. They allowed stirring in an oil bath for 6 h at 75 °C. After the specific time has finished, the polymerization reaction has been terminated by cooling firstly at room temperature and then in the refrigerator. The terpolymers were precipitated in diethyl ether at –20 °C; they have been extra purified to remove the small molecules by dissolving in THF and again re-precipitated in Et2O. They were dried at room temperature and then in the refrigerator. The terpolymerization reaction has been terminated by cooling firstly at 6 h at 75 °C. After the specific time has finished, the polymerization reaction has been terminated by cooling firstly at room temperature and then in the refrigerator. The terpolymers were precipitated in diethyl ether at –20 °C; they have been extra purified to remove the small molecules by dissolving in THF and again re-precipitated in Et2O. They were dried at room temperature and then in the refrigerator. The terpolymerization reaction has been terminated by cooling firstly at 6 h at 75 °C. After the specific time has finished, the polymerization reaction has been terminated by cooling firstly at room temperature and then in the refrigerator.

The precipitate started appearing after 2 h; the reaction continued for a limited time and then stopped and separated. The precipitate was filtered, and then dissolved in THF, and precipitated in diethyl ether at –20 °C. The product was dark brownish crystals.

IR (KBr): ν (cm−1) = 2400–3120 (s) (CH2, CH3), 1640–1647 (s) (C = O), 1556–1560 (s) (-CH = N), 1095–1113 (s) (OCH3).

1H NMR (500 MHz, CDCl3): δ (ppm) = 0.96–1.51 (m, 12H, 9,18-2CH3), 1.53–1.66 (m, 3H, 12,1CH3), 1.65–1.95 (m, 2H, 10,14-CH repeating), 2.08–2.75 (m,6H, 11,13,15-3CH2 repeating), 3.45–3.56 (m, 3H, 7–1CH3), 3.52–3.83 (m, 2H, 20-1CH2), 3.87–3.93 (m, 2H, 19-1CH2), 4.02–4.17 (m,1H, 17-CH), 4.85–5.36 (m, 1H, 2-CH), 5.90–6.10 (m, 1H, 3-NH), 6.13–6.73 (m, 1H, 17-NH), 6.79–7.20 (m,1H, 5-Ar–H), 7.30–7.48 (m,1H, 5-Ar–H), 7.40–7.48 (m, 1H, 5-Ar–H), 8.05–8.23 (m, 1H, 4-CH=N), 12.46–12.75 (m, 1H, 1-NH).

IR (KBr): ν (cm−1): 3430–3640 (s) (NH, OH), 2988–3185(m) (CH-Aliphatic), 1640–1647 (s) (C = O), 1556–1560 (s) (-CH=N), 1095–1113 (s) (OCH3).

Results and Discussions

Synthesis of a New pH-Responsive Monomer

One of the most important applications of vanillin is the formation of vanillin-based monomers. A new strategy for the formation of a new acrylate functional monomer based on vanillin as a natural material has been achieved in this study. A new stimuli-responsive acrylate monomer for the pH-responsive has been synthesized from vanillin (4-hydroxy-3-methoxybenzaldehyde) in two steps as described in Scheme 1. The first step was used to synthesize the pre-monomer compound and form a tertiary amine group responsible for the pH-responsiveness of the whole monomer and, consequently, polymers. It has been done by reacting vanillin with formaldehyde and dimethylamine in an alkaline solution. This reaction is proceeding according to the Mannich reaction mechanism. The new compound 3-((dimethylamino)methyl)-4-hydroxy-5-methoxybenzaldehyde (DMAMV) (II) has been evaluated by 1H NMR, 13C NMR, FT IR, mass spectroscopy, and elemental analysis. Figures 1 and 2 show the 1H NMR and 13C NMR, FT IR, and elemental analysis. Figures 1 and 2 show the 1H NMR and 13C NMR, FT IR, and elemental analysis. Figures 1 and 2 show the 1H NMR and 13C NMR, FT IR, and elemental analysis. Figures 1 and 2 show the 1H NMR and 13C NMR, FT IR, and elemental analysis. Figures 1 and 2 show the 1H NMR and 13C NMR, FT IR, and elemental analysis. Figures 1 and 2 show the 1H NMR and 13C NMR, FT IR, and elemental analysis. Figures 1 and 2 show the 1H NMR and 13C NMR, FT IR, and elemental analysis. Figures 1 and 2 show the 1H NMR and 13C NMR, FT IR, and elemental analysis. Figures 1 and 2 show the 1H NMR and 13C NMR, FT IR, and elemental analysis. Figures 1 and 2 show the 1H NMR and 13C NMR, FT IR, and elemental analysis. Figures 1 and 2 show the 1H NMR and 13C NMR, FT IR, and elemental analysis.

[Please note: The above text contains a mix of chemical and textual content.]
Scheme 1 Synthesis of 2-[(dimethylamino)methyl]-4-formyl-6-methoxyphenyl acrylate, poly (NIPAAm-co-HEMA-co-DMAMVA), and poly (NIPAAm-co-HEMA-co-DMAMVA)-post-guanine

Fig. 1 $^1$H NMR spectra (CDCl$_3$) of 3-[(dimethylamino)methyl]-4-hydroxy-5-methoxy-benzaldehyde DMAV(II) (step 1)
methyl)-4-formyl-6-methoxyphenyl acrylate (DMAMVA) (III); it has been obtained by reacting compound (II) with acryloyl chloride in an alkaline solution as illustrated in Scheme 1; the first hour was done in an ice bath due to an exothermic behavior. The reaction has been performed, and the product has been purified and then investigated. The 1H, 13C NMR was successfully used to evaluate the protons and their corresponding carbons; they proved the formation of 3H of the vinyl acrylate group –CH = CH2 at δ = 6.03, 6.34, and 6.64 ppm via 2C at δ = 126.25 and 132.22 ppm; another proton 1H-CHO at δ = 9.91 ppm and 13C at δ = 191.64 ppm. Other protons and carbon atoms have also been deduced, as shown in figs. 3 and 4. The FT IR has been used for investigating the absorbance of functional groups as illustrated in Fig. 7; for compound (II) such as ν = 2450, and 1735 cm⁻¹ due to C-N [-H2C-N(CH3)2] and –C = O aldehyde. However, compound (III) recorded the absorbance at ν = 2500, 1760, 1745, and 1665 cm⁻¹ for C-N, C = O ester, C = O aldehyde, and C = C vinyl. Further, the certainty of the evaluation of compound (II) by MALDI-TOF mass spectrometry has been done, and recorded the molecular ion peak at m/z 209.11 with 100% abundance. Also, elemental analysis was performed and indicated logical results to the calculated mass percentage of each C, H, and N atom.

The new synthetic monomer has been used to form a series of functional and pH-thermo-responsive terpolymers (VI-10-05, VI-10-10, and VI-10-20), which is achieved by our first goal of that study. Random free radical polymerization has been used for the polymerization process of the new monomer (DMAMVA) as a functional pH-responsive, with N-isopropylacrylamide (NIPAAm) acting as a thermo-responsive monomer and 2-Hydroxyethyl methacrylate (HEMA) as a function with a highly hydrophilic monomer. The polymerization was established depending on the change of molar concentration of (DMAMVA) 5, 10, and 20 mol%, and 10 mol% of (HEMA) dependent of (NIPAAm), it was done in solution and using AIBN as an initiator. Polymers have been evaluated by 1H NMR and FT IR. By the 1H NMR Fig. 5, the spectra demonstrated the most specific multiple peaks of monomers, e.g., for NIPAAm, at δ = 0.95–1.22 ppm related to isopropyl –(CH3)2, and δ = 3.73–4.05 ppm to isopropyl –CH–, however, HEMA demonstrated the presence of methyl group at δ = 1.83–2.22 ppm. The third monomer DMAMVA has also been represented three specific peaks at δ = 3.42–3.47 ppm, 6.72–7.84 ppm, and 9.85–10.07 ppm for the methylene group –CH2N–, aromatic protons and aldehyde proton, respectively (Fig. 6). The FT IR investigation for the new monomer and terpolymer illustrated the absorption of the most important functional groups such as carbonyl ester and aldehyde; they have appeared at ν = 1745, and 1728 cm⁻¹ respectively, as shown in Fig. 7A and B. Eventually, the application of terpolymer by selecting VI-10-10 to achieve the click reaction and post-polymerization with guanine has been implemented. The reaction conditions were changed from acidic, neutral, and then alkaline to obtain the best conversion of terpolymer-post-guanine, as shown in Fig. 8; we observed that the alkaline solution was the best to perform the reaction in the best conversion at 78%. As we used previously, for the investigation, we used 1H NMR and FT IR; we noticed the formation of the imine

![Fig. 2 13C NMR spectra (CDCl₃) of 3-((dimethylamino)methyl)-4-hydroxy-5-methoxy-benzaldehyde DMAMV(II) (step 1)](image-url)
group at δ = 8.05–8.23 ppm corresponding to its absorption at ν = 1560 cm⁻¹ and 315 nm as shown in Fig. 7B, and fig. 8.

Miscellaneous Physical Characterizations of Poly(NIPAam-co-HEMA-co-DMAMVA) and poly(NIPAam-co-HEMA-co-DMAMVA)-Post-Guanine
GPC has been used to measure the molecular weights (number average molecular weight Mn, and weight average molecular weight Mw), further the dispersity (D) of the polymer solutions. The process was performed as described in detail previously; they dissolved in THF (6 g/L and containing 0.2 g/L of BHT) for terpolymer; however, we used dimethylacetamide DMA for post-terpolymer (VIII). Samples of terpolymers poly(NIPAAm-co-HEMA-co-DMAMVA) (VI-10-05, VI-10-10, and VI-10-20), and post-terpolymer poly(NIPAAm-co-HEMA-co-DMAMVA)-post-guanine (VIII). The GPC analysis was recorded, and the chromatograms were drawn for all polymers, as seen in Fig. 9. We recorded some observations; first, the influence of the molar concentration of DMAMVA on both of the number average molecular weights Mn, Mw and the dispersity D of terpolymers demonstrated decreasing in Mn (5.93, 5.45, and 4.85) 10^4 g/mol, and Mw (11.56, 10.79, and 10.67) 10^4 g/mol for VI-10-05, VI-10-10, and VI-10-20, respectively. However, in contrast to the dispersity D of terpolymers, they exhibited increasing by increasing the molar concentrations of DMAMVA in the terpolymer main chain; they recorded 1.95, 1.98, and 2.20, respectively. Moreover, the lowest Mn and Mw and highest dispersity D was recorded for poly(NIPAAm-co-HEMA-co-DMAMVA)-post-guanine (VIII) demonstrated (0.76, and 2.20) 10^4 for Mn and Mw, as well as 2.88 D. The decreasing in the number average molecular weight and weight average molecular weight with the high concentration of DMAMVA due to the steric hindrances of aromaticity in the terpolymer main chain; the maximum effect was noticed with the poly(NIPAAm-co-HEMA-co-DMAMVA)-post-guanine (VIII) with the high aromaticity [32]. The next observation has occurred in the formation of chromatograms with single peaks, which is interpreted by the disappearance of molecules with low molecular weights, e.g., monomers and impurities [30]; all data has been summarized in Table 1.

Two methods have distinguished the thermal characterizations of terpolymers and post-terpolymer. One of them has been used to record the glass transition temperature T_g,s of the solid polymer and performed by differential scanning calorimetry (DSC). The measurements of the glass temperature of poly(NIPAAm-co-HEMA-co-DMAMVA) (VI-10-05, VI-10-10, and VI-10-20), and post-terpolymer poly(NIPAAm-co-HEMA-co-DMAMVA)-post-guanine (VIII) have been conducted on the dry samples at 5 °C/min and in an inert atmosphere. Figure 10 exposes the diffractogram of terpolymers and post-terpolymer with guanine as the relationship between temperature and heat flow. The

![1H NMR spectrum (DMSO-d6) of poly(NIPAAm-co-HEMA-co-DMAMVA) terpolymer with 10 mol% of HEMA and 5, 10 and 20 mol% of DMAMVA](image-url)
Fig. 6 $^1$H NMR spectrum (CDCl$_3$) of poly(NIPAAm-co-HEMA-co-DMAMVA) (VI-10-10) and poly(NIPAAm-co-HEMA-co-DMAMVA)-post-guanine (VIII)

Fig. 7 FT IR spectra of monomer II and III (A), terpolymer VI-10-05, VI-10-10, VI-10-20 and post-terpolymer VIII (B)
The glass transition temperatures $T_g$ s have been taken at the onset value and declared 146.7, 142.4, and 132.5 °C for VI-10-05, VI-10-10, and VI-10-20, respectively. An opposite relation with the molar concentration of DMAMVA was observed, as the lower concentration of DMAMVA in the terpolymer main chain, the higher the glass temperature. This behavior is attributed to the balance between the hydrophilic/hydrophobic groups in the polymer main chain, which showed the domination of hydrophobicity effect at the higher concentration of DMAMVA; however, at low concentration, the terpolymer has entirely influenced by the hydrophilic groups located in NIPAAm and HEMA as well [32, 39]. By post-polymerization in poly(NIPAAm-co-HEMA-co-DMAMVA)-post-guanine (VIII), the glass transition temperature $T_g$ was recorded at 125.2 °C that exhibited the lowest $T_g$ compared to terpolymers VI-10-05, VI-10-10, and VI-10-20; it can be interpreted as discussed previously, in addition to the effect of hydrophobic groups in the guanine molecule, which directly affected on the whole polymer chain.

Another technique has been performed to investigate the thermal properties of terpolymers and post-terpolymer; we used the thermogravimetric analysis (TGA) for describing the thermal degradation steps by changing the mass percentage with temperature. The process has been conducted on terpolymers VI-10-05, VI-10-10, VI-10-20, and post-terpolymer VIII. Figure 11A and B show the thermogram of polymers $TG$ and their first derivative DTG. They demonstrated a series of thermal degradation, first at 100–120 °C for evaporation of moisture content. The onset degradation temperature $Tonset$ has been appeared as one onset by VI-10-05 at 237 °C, two for VI-10-10 238, 337, three for VI-10-20 at 238, 286, and 342 °C; while post-terpolymer exhibited multiple $Tonset$ at 233, 272, 266, and 297 °C. They demonstrated lower homogeneity of terpolymer by increasing the molar concentration of DMAMVA in the polymer main chain; further, the lowest one was observed for post-terpolymer [39, 53]. The main degradation has occurred at 273, 399, 396, and 374 °C for terpolymers and post-terpolymer. The final and complete degradation were observed for all terpolymer and post-terpolymer at 537–558 °C; it clues a decrease of fully thermal degradation by increasing the molar concentration of DMAMVA in the polymer main chain.

The morphological features of terpolymer before VI-10-10 and post-polymerization VIII were performed by scanning electron microscopy (SEM). The process was conducted on dry polymer samples pressed into small disks.
The scanning has been performed at 750× magnification. The scanning appeared in some images, as shown in Fig. 12; it exhibits waxy and coarse for terpolymers (VI-10-05, VI-10-10, and VI-10-20) before post-polymerization, while, after post-polymerization and the chemical modification (VIII); it seems as waxy and compact.

Fig. 11  A, B Thermogravimetric Analysis (TG) (A) and DTG (B) of terpolymers and post-terpolymer

Fig. 12  SEM for terpolymer VI-10-05, VI-10-10, VI-10-20, and post-terpolymer VIII at a magnification of 750×
Phase Separation Properties and Lower Critical Solution Temperature \((T_c)\) of Poly(NIPAAm-co-HEMA-co-DMAMVA) and Poly(NIPAAm-co-HEMA-co-DMAMVA)-Post-Guanine as pH-Dependent

Eventually, we are going to our main target of studying the lower critical solution temperature of terpolymers solutions and explore how the chemical structure of terpolymers and the chemical modifications by post-polymerization have affected the fluctuation of the LCST \((T_c)\). The test has been performed by two methods. First, UV-Vis-spectroscopy has been implemented three times, and the mean value has been considered. The technique depends on the turbidity of the solution by measuring the transmittance via temperature change in different pH solutions. Figure 13A showed the lower critical solution temperature \((T_c)\), and the cloud points \((C_p)\) of terpolymers VI-10-05, VI-10-10, and VI-10-20 at pH 1.68 demonstrated 36.7, 40.8, and 48.5 °C for \(T_c\), as well as the corresponding \(C_p\) at 37.5, 41.6, and 49.3 °C, respectively. The gradual rise in the transition temperature and the cloud point is due to the domination of the hydrophilic effect created by highly ionization and protonation of the tertiary amine group in DMAMVA; the slight decrease in each of \(T_c\) and \(C_p\) of VI-10-10-post-guanine VIII at 39.5, and 40.4 °C, respectively; it is attributed to an additional hydrophobic effect by guanine molecule [52]. At pH 3 as shown in Fig. 13B; it demonstrated closed results of pH 1.68; the \(T_c\) (36.5, 40.2, and 47.8 °C), and \(C_p\) (37.3, 41.4, and 48.7 °C) for VI-10-05, VI-10-10, and VI-10-20, respectively, the data proofed the similarity of conditions that the terpolymer has been exposed. Further, the post-terpolymer exhibited \(T_c\) and \(C_p\) at 39.0 and 39.8 °C for the same reason discussed previously. By increasing the pH of terpolymer solution reaching to the neutral conditions in pH 7 as shown in Fig. 13C; we observed sharp fluctuation in the \(T_c\) and \(C_p\) demonstrated (34.3, 28.7, and 21.5 °C) and (35.3, 29.5, and 26.7 °C); it exhibited sharply decreased by increasing the molar concentration of DMAMVA in the terpolymer main chain, indicating the domination of the hydrophobic groups than the hydrophilic one, rather than steric hindrances occurred in the polymer molecule [32]. Also, post-terpolymer VIII exhibited 25.2 and 26.7 °C for \(T_c\) and \(C_p\) lower than VI-10-10; the interpretation has still attributed to the hydrophobic groups in guanine and the highly steric hindrances and restricted free rotation of polymer molecule [52]. Meanwhile, the effect of the alkaline solution on the phase separation temperature has also been considered in the middle (pH 10.06) and strong (pH 12) solutions. The transition temperature and cloud point of terpolymers and post-terpolymer in pH 10.04 demonstrated lower values for each \(T_c\) and \(C_p\) than results due to pH 7; they were at 33.9, 27.8, 20.3, and 22.3 °C of \(T_c\), and \(C_p\) at 34.7, 28.9, 21.5, and 23.6 °C for all terpolymers (VI-10-05, VI-10-10, and VI-10-20), and post-terpolymer (VIII), respectively, as shown in Fig. 13 D. However, in the pH 12, as illustrated in Fig. 13 E the \(T_c\) have been observed at 32.8, 26.6, 19.7, and 22.3 °C, and \(C_p\) at 33.5, 27.8, 22.0, and 23.6 °C for terpolymers, and post-terpolymer. The dramatic decrease in the transition temperature and cloud point in the alkaline solution due to the highly intensive hydrophobic effect, which raised by increasing the molar concentration of DMAMVA in the polymer chains; moreover, the hydrophobic groups in guanine have additionally influenced in decreasing the \(T_c\) and \(C_p\). Figure 14 illustrates the statistical study of the mean transition temperature \(T_c\) of terpolymers and post-terpolymer. The ANOVA table (overall ANOVA) has reported a p-value of 0.389, despite the homogeneity of variances having indicated at 0.05 levels. The overall analysis referred to the population variances as not significantly different.

The Micro-differential scanning calorimetry (Micro-DSC) has been performed in DI water (pH 7), and at a heating rate of 5 °C/min for recording the \(T_c\) of different terpolymers VI-10-05, VI-10-10, and VI-10-20 as well as terpolymer-post-guanine VIII as shown in Fig. 15; they demonstrated 33.6, 27.5, 19.3, and 23.8 °C, respectively. By comparing these results to be obtained using turbidity, we observed a difference that interpreted the method used for recording the \(T_c\); in the turbidity, it was fixed at the point of inflection; however, the micro-DSC detected at the onset value [53]. Figure 13 F exhibited the relationship of pH vs. transition temperature with errors bars and showed the highest error bar for terpolymer VI-10-20 with the highest molar concentration of DMAMVA. Figure 13 G explained the relationship of terpolymers in various pH solutions and the \(T_c\), exhibiting two significant points at the highest and lowest \(T_c\) at pH 1.68 and pH 12 for VI-10-20. Data have also been summarized in Table 1.

Conclusion

The study presented the preparation of a new cationic monomer used to form a dual-responsive thermo-pH terpolymer with functional groups. The polymerization has been achieved with NIPAAm and HEMA as thermo-responsive and hydrophilic functional monomers. The fabrication methods were implemented in facile methods, and all compounds have been investigated and achieved good results regarding their chemical structures. Moreover, the aldehyde functional group was used for the post-polymerization with guanine. The general characterizations of polymers and post-polymer have been discussed; they demonstrated a lower value of the molecular weight, glass transition, and the degree of crystallinity with the higher molar concentration of DMAMVA and by post-guanine as well. The phase separation of polymers and post-polymer was measured in different pH solutions.
Fig. 13 A–F The change in transmittance with temperature for $T_c$ of Poly-(NIPAAm-co-HEMA-co-DMAMVA) VI-10-05, VI-10-10, and VI-10-20 and Poly-(NIPAAm-co-HEMA-co-DMAMVA)-post-guanine VIII in pH 1.68, pH 3, pH 7, pH 10.4 and pH 12 using UV–Vis Spectroscopy for 1 wt% of the polymer solution. F, the relationship of pH vs. transition temperature with errors bars. G, the transition temperatures of all polymers in pH solution.
The $T_c$ of polymers in highly acidic conditions showed the highest $T_c$ values; the value will decrease at pH7 and reach the lowest value at the basic solution. These polymers are interested in our future study in the bio-separation of more biological molecules.

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**Declarations**

**Conflicts of interest** The author declares that there are no conflicts of interest regarding the publication of this paper.
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