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Thermo-pH-Salt Environmental Terpolymers Influenced by 2-((Dimethylamino)methyl)-4-methylphenyl Acrylate: A Comparative Study for Tuning Phase Separation Temperature

Momen S. A. Abdelaty and Nidal Abu-Zahra*

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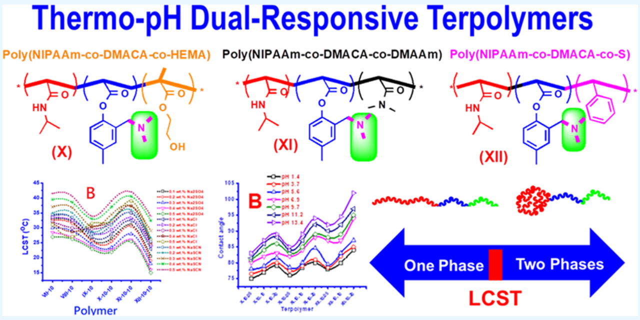
ABSTRACT: This study offers a comparison between three different types of thermoresponsive (TR) and thermo-pH-salt (TPR) multiresponsive polymers including homopoly(*N*-isopropylacrylamide) (PNIPAAm), copolymers with three different monomers, 2-hydroxyethyl methacrylate (HEMA), *N,N*-dimethylacrylamide (DMAAm), and styrene (S) at three different concentrations (5, 10, and 20 mol %), and a PNIPAAm terpolymer with 5, 10, and 20 mol % 2-((dimethylamino)methyl)-4-methylphenyl acrylate (DMAMCA) and 10 mol % HEMA, DMAAm, and S monomers. All polymers were chemically analyzed with ^{1}H NMR and Fourier transform infrared spectroscopy (FT-IR) as well as gel permeation chromatography (GPC) for the molecular weights and dispersity and differential scanning calorimeter (DSC) for the glass transition temperatures. The cloud point, also known as the phase separation temperature (C_p), was determined for all polymers by a turbidity test using a UV−vis spectrophotometer; a micro-differential scanning calorimeter was used for measuring the cloud point in deionized water. The influence of a tertiary amine cationic group of DMAMCA changed the behavior of TR copolymers into TPR by shifting the cloud point of the TPR to higher values in acidic solutions (lower pH) and to lower values in alkaline solutions. The C_p was measured at different concentrations of Hofmeister kosmotropic and chaotropic anion salt solutions in a range of pH solutions for the terpolymers. It demonstrated the same behavior as mentioned in pH solutions besides the effect of salt ions. By measuring the T_c and C_p of these polymers, we can exploit various applications of stimuli-responsive materials for sensors and biomedical technology.



1. INTRODUCTION

The importance of smart materials is increasing daily due to their multiple uses in the medical and biological fields.[1,2] Smart materials, also known as stimuli-responsive materials, are physicochemical-sensitive materials that can change their behavior according to the surrounding environment.[3−6] Scientists classified such materials according to their acting stimuli, such as temperature, pH, solvent, mechanical, ionic strength, magnetic, and light.[7−13] Moreover, researchers combined multiple stimuli for the fabrication of di- and triresponsive polymeric materials.[14−16] Poly *N*-isopropylacrylamide (PNIPAAm) is the most popular material among the thermoresponsive (TR) group. It possesses both hydrophilic and hydrophobic groups, which result in phase separation of the polymer solution by raising its temperature above a lower critical solution temperature (LCST) (32 °C) due to a change from a hydration (hydrophilic) to dehydration (hydrophobic) state.

Recent works have studied the factors that affect the hydrophilicity and hydrophobicity of PNIPAAm and hence the LCST.[17−20] *N*-Isopropylacryamide's copolymerization with another monomer is one of the effective strategies to change the LCST.[21−25] Copolymerization with 2-hydroxyethyl methacrylate (HEMA) has been widely studied due to its good mechanical properties and functionality.[26] It has been used in biosensors and actuators, drug delivery, and bioseparation.[27−29] A recent study reported a method to control the responsive temperature of the poly(NIPAM-*co*-HEMA) copolymer via ultrasonic polymerization.[30] The incorporation of *N,N*-dimethylacrylamide into the PNIPAAm chain has been used to improve the hydrophilicity of the copolymer solution and therefore raise the LCST higher than the normal of homo-PNIPAAm.[31] Copolymerization of NIPAAm and DMAAm was reported using different polymerization mechanisms, such as, free radical polymerization and control radical polymerization.[32,33] A styrene monomer was copolymerized with NIPAAm to tune the LCST of the copolymer solution.

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Poly(NIPAAm-*co*-styrene) copolymers were synthesized using styrene for controlling the hydrophilicity in PNIPAAm main chain and their biological applications.[34,35]

Another important category of smart polymers is pH-responsive (PR) polymers. These polymers are electrolyte materials with specific cationic or anionic groups which are affected by the pH of their solutions as accepting or withdrawing protons.[36−41] The pH poly(cations) include monomers with pyridine or tertiary amine, e.g., poly[(2-diethylamino)ethyl methacrylate] (PDMA), poly[(2-diisopropylamino)ethyl methacrylate] (PDEA), and poly(4-vinylpyridine) (P4VP),[42−44] whereas the pH poly(anions) include poly(acrylic acid) (PAA), poly(methacrylic acid) (PMAA), poly(4-styrenesulfonic acid), and phosphorus-containing (meth)acrylate monomers.[45,46] These smart polymers are particularly attractive in environmental and biomedical applications which involve changes in pH that take place in several specific or pathological parts.[47,48]

Combining monomers with different responsiveness is a key strategy to the formation of dual and multiresponsive polymeric materials;[49−53] the most popular category is the thermo-pH-responsive (TPR) copolymers based on combining PNIPAAm with other cationic or anionic monomers.[54−57] Many studies have been published on this category of copolymers manifesting their applications in biomedical technology.[53,−61] For example, P-cresol (3-hydroxytoluene) was used in preparing antioxidants, in addition to nonstaining surfaces.[61] Recent works described the polymerization of *p*-cresol by condensation and by using biocatalysis.[54,62−64]

Hofmeister series, introduced by Franz Hofmeister, manifested the influence of salt ions (cations and anions) on the precipitation of proteins.[65,66] A series of anions were classified, based on their strength in the chaotropic act, as a weak water interaction, e.g., (Cl^-, NO_3^-, SCN^-), and a strong water interaction, e.g., (CO_3^{2-}, SO_4^{2-}, $S_2O_3^{2-}$), which breaks the hydrogen bonds, so-called kosmotropes.[67,68] The effect of the salt concentration of these anions on the lower critical temperature of PNIPAAm copolymers has been reported in recent articles.[54,69−75]

In this study, a facile method was used to prepare a new cationic monomer. A series of hydrophilic/hydrophobic thermoresponsive copolymers were fabricated. Another new series of thermo-pH terpolymers was prepared using the same monomers with incorporation of the cationic monomer 2-((dimethylamino)methyl)-4-methylphenyl acrylate (DMAM-CA) in the polymer chain. The study focused on the changes that resulted from the addition of the new monomer, with emphasis on tuning the lower critical solution temperatures.

2. EXPERIMENTAL SECTION

2.1. Materials. The following chemicals were purchased from Sigma-Aldrich (Germany): acryloyl chloride (2-propenoyl chloride) (≥97.0%), 4-methylphenol (*p*-cresol) (99%), *N*-isopropylacrylamide (2-propenamide) (NIPAAm) (99.0%), *α*,*α*′-azoisobutyronitrile (AIBN), 2,2′-azobis(2-methylpropionitrile) (≥98.0%) (recrystallization was done in methanol), 2-hydroxyethyl methacrylate (HEMA) (99.0%), *N*,*N*-dimethylacrylamide (DMAAm) (99.0%), styrene (S) (99.9%), *N*,*N*-dimethylamine or dimethylamine (DMA) (anhydrous 99.0%), sodium bicarbonate, sodium thiocyanate (≥99%), and tetrahydrofuran (THF) anhydrous (≥99.9%, inhibitor-free). Other chemicals: 4-methylphenol, *p*-cresol (99.0%, Merck), formaldehyde solution (ACS reagent, 37 wt % in water, 10−15% methanol, Merck), magnesium sulfate (Merck), and sodium sulfate (≥99.0%, anhydrous, Merck). Chloroform and diethyl ether were used after distillation overnight with potassium hydroxide; other chemicals were used as purchased.

2.2. Instrumentation for Chemical and Physical Investigations. *2.2.1. Chemical Evaluations.* A Bruker Avance high-resolution nuclear magnetic resonance (NMR) spectrometer system, operating at 500 and 125 MHz and connected to helium recycling, was used for detecting ^{1}H and ^{13}C NMR. Samples of monomers and polymers were dissolved in deuterium chloroform-*d*, d $CDCl_3$ (99.8 atom % D, Sigma-Aldrich), or dimethyl sulfoxide-d^6 d^6 DMSO (99.9 atom % D, Merck). A Bruker VERTEX FT-IR instrument was used to conduct Fourier transform infrared spectroscopy (FT-IR) for all samples of monomers and polymers via a Vertex 70 of the high-performance, wide range instrument, from 400 and 4000 cm^{-1}.

2.2.2. Molecular Weight and Dispersity. The molecular weights, including the weight-average molecular weight M_w, the number-average molecular weight M_n, as well as the dispersity ($Đ$) of both copolymers and terpolymers samples, were measured by gel permeation chromatography (GPC); they were dissolved in THF 16 mg/mL as the eluent. The molecular weight of PS (M_w = 1300, $Đ$ 1.06) was provided as the standard of measurement.

2.2.3. Physical Characterizations. 2.2.3.1. Glass Transition Temperature. A PerkinElmer Diamond differential scanning calorimeter (DSC) was used to record the glass transition temperatures of the solid polymer (T_g) by heating the samples at 5 °C/min. The onset point on the thermograph was taken as the glass transition temperature.

2.2.3.2. Contact Angle. It is a particular method to determine the extent of the hydrophilicity and hydrophobicity of the polymer. The liquid solution was dropped on the surface of the polymer using a micropipet; meanwhile, a digital camera was used to take an image during the dropping process and falling over the polymeric surface.

2.2.3.3. Lower Critical Solution Temperature (LCST) (T_c) and Cloud Point (C_p). A PerkinElmer (Lambda 45) UV−vis spectrophotometer was used to measure the change in the UV transmittance in the polymer solution with temperature changes. This technique is also known as turbidity measurement. The temperature was varied in the range of 10−75 °C for 0.1 wt % polymer solution. A plot was drawn, and the cloud point (C_p) at 50% transmittance was measured. Additionally, we used micro-differential scanning calorimeter (SETARAM III microcalorimeter) for measuring LCSTs at the same concentration of the polymer solution (0.1%). The thermograms were used to determine the LCST at the onset value. The polymeric materials were dissolved in deionized water (pH 6.8−6.9) solutions, while they were heated/cooled at 1 °C/min.

2.3. Synthesis of 2-((Dimethylamino)methyl)-4-methylphenyl Acrylate (DMAMCA). *2.3.1. 2-((Dimethylamino)-methyl)-4-methylphenol (DMAMC) (I).* A mixture of 11.0 g (0.1 mol) of *p*-cresol, 11.0 g (0.2 mol) of dimethylamine, and 11.0 g (0.4 mol) of formaldehyde 37% was mixed in a 250 mL two-neck round-bottom flask and hung with a water condenser and water trap. 3.0 g of sodium hydroxide was dissolved in 150 mL of ethanol and added using a funnel. It was stirred and refluxed in an oil bath for 4 h at 135−140 °C. The yellowish precipitate, which appeared after 1.5 h of refluxing, was filtered off, and the crude product was recrystallized from ethanol. The product was dried under reduced pressure. The general physical properties illustrated a yellowish solid; yield of 95% mp 69 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ(ppm) = 2.37 (s, 6H, ^3J = 13.31 Hz and ^3J = 8.41 Hz, j-CH_3), 2.62 (s, 3H, f-CH_3), 3.75 (s, 2H, i-CH_2), 4.79 (br., s, 1H, a-OH), 7.14 (dd, 1H, ^3J = 15.65 Hz, c-Ar-CH), 7.33 (dd, 2H, ^3J = 9.10 Hz, d, g-Ar-H).

^{13}C NMR (125 MHz, $CDCl_3$): δ(ppm) = 25.48 (1C, f-CH_3), 44.32 (2C, j-2CH_3), 56.01 (1C, i-CH_2), 117.85 (1C, c-Ar-CH), 121.39 (1C, h-Ar-CH), 125.21 (1C, d-Ar-C), 128.09 (1C, e-Ar-CH), 131.73 (1C, g-Ar-CH), 154.54 (1C, b-Ar-C).

IR (KBr): ν (cm^{-1}): 3355−3576 (s) (OH), 2567−2875 (s) (CH-aliphatic), 2295−2170 (s) (CN), 1710−1732 (s) (−C═O), 1640−1660 (s) (C═C-Ar), 825−878 (m) (Ar-CH).

2.3.2. 2-((Dimethylamino)methyl)-4-methylphenyl Acrylate (DMAMCA). 5.00 g (0.02 mol) portion of 2-((diethylamino)methyl)-4-methylphenol compound (I) and 4 g of sodium hydroxide were suspended in 150 mL of dry dichloromethane; the mixture was carried to a three-neck flask connected with a reflux condenser and a funnel. Nitrogen gas was purged for 15 min from the nitrogen source by a needle and a balloon. The reaction vessel was allowed to stir in an ice bath at 0−5 °C. After 20 min of stirring, a solution of 1.82 g (0.02 mol) of acryloyl chloride dissolved in 20 mL of dry dichloromethane was added dropwise. The reaction was continued in the ice bath for 1 h, and then it was stirred at room temperature for 6 h. By the time, the change in the reaction appeared, i.e., the yellowish color of the precipitate changed into an orange color, it was filtered, and the solvent was removed using a rotatory evaporator. The crude product was purified by redissolving in dry CH_2Cl_2 and then washed with distilled water three times, followed by 0.1 M HCl, 0.1 M sodium bicarbonate solution, and again with distilled water. The organic phase was used and then dried overnight with $MgSO_4$. The solvent was evaporated to get the product as a yellowish viscous material; yielding 76%.

^{1}H NMR (500 MHz, $CDCl_3$): δ(ppm) = 2.44(s, 6H.a-2CH_3), 2.79 (s, 3H, g-CH_3), 3.73 (s, 2H, b-CH_2), 5.91 (dd, ^2J = 1.36 Hz, ^3J = 11.35 Hz,1H, i1-CH), 6.23 (dd, ^3J = 11.33 Hz, ^3J = 17.45 Hz, 1 H, h-CH), 6.51 (dd, ^2J = 1.42 Hz, ^3J = 17.47 Hz, i2-CH),7.11 (dd, 1H, ^3J = 7.55, f-Ar-CH), 7.36 (dd, 2H, ^3J = 7.45, ^3J = 7.32 e-Ar-H).

^{13}C NMR (125 MHz, $CDCl_3$): δ(ppm) = 25.49 (1C, h-CH_3), 46.18 (2C, a-CH_2), 56.06 (1C, b-CH_2), 114.0 (1C, e-Ar-CH), 126.05 (1C, j-CH═), 127.41 (1C, f-Ar-C), 129.34 (1C, c-Ar-CH), 131.18 (1C, g-Ar-CH), 134.30 (1C, i-Ar-C), 138.63 (1C, k = CH_2), 147.40 (1C, d-Ar-C), 163.81 (1C, l-C═O).

IR (KBr): ν (cm^{-1}): 3155 (s) (CH, CH_2, CH_3), 2310−2360 (s) (CN), 1745−1755 (s) (C═O,), 1647−1660 (s) (C═C vinyl), 835−875. (m) (Ar-CH).

2.4. Polymer Fabrication. *2.4.1. Homopoly(N-isopropylacrylamide).* Homopoly(*N*-isopropylacrylamide) was synthesized as reported in ref 73. The ^{1}H NMR and IR data are added to the Supporting Information, as shown in Figures S1 and S2.

2.4.2. Copolymers of Poly(NIPAAm-co-HEMA) (VII) Group (A), Poly(NIPAAm-co-DMAAm) (VIII) Group (B), and Poly(NIPAAm-co-co-S) (IX) Group (C). Free radical polymerization in solution was used to prepare all copolymers. In round-bottom flasks, 5, 10, and 20 mol % (0.00135 mol/0.18 g, 0.0027 mol/0.35 g, and 0.0054 mol/0.7 g) 2-hydroxyethyl methacrylate (HEMA) (VII), *N,N*-dimethylacrylamide (DMAAm) (VIII) (0.00135 mol/0.13 g, 0.0027 mol/0.27 g, and 0.0054 mol/0.54 g), and styrene (S) (IX) (0.00135 mol/0.14 g, 0.0027 mol/0.28 g, and 0.0054 mol/0.56 g) were added to 3 g (0.027 mol) of NIPAAm in 70 mL of absolute ethanol and 1,4-dioxane for (VII), (VIII), and (IX), respectively. 2,2′-Azobis(2-methylpropionitrile) (AIBN) was added at 10^{-3} mol % of the molar concentration of monomers. They were purged in nitrogen for 15 min, followed by heating in an oil bath at 70 °C for 8 h. After cooling at room temperature and then cooling in the refrigerator, the polymers were precipitated in diethyl ether at −40 °C for (VII and VIII) and −25 °C for (IX), followed by dissolving in THF and reprecipitating in diethyl ether for super purification.

2.4.3. Chemical Evaluation of Copolymers (VII, VIII, and IX) by ^{1}H NMR and FT-IR. 2.4.3.1. Poly(NIPPAm-co-HEMA) (VII-05), (VII-10), and (VII-20)-Group (A). **^{1}H NMR (500 MHz, $CDCl_3$): δ(ppm)** = 0.71−1.46 (m, 6H, k-CH_3), 1.17−1.64 (m, −CH, −CH_2 repeating unit), 1.67−1.81 (m, 3H, e-$CH_{3,}$), 3.70−3.87 (m, 2H, b-CH_2), 3.90−412 (m, 1H, l-CH), 4.25−435 (m, 2H, c-CH_2), 5.55−6.94 (br, 2H, a-OH, and l-NH).

IR (KBr): ν (cm^{-1}): 3286−3630(s) (OH, NH), 2740−3160 (CH-aliphatic), 1710, 1725 (s) (C═O, carbonyl), 1595−1610 (s) (C═O, amide).

2.4.3.2. Poly(NIPPAm-co-DMAAm) (VIII-05), (VIII-10), and (VIII-20)-Group (B). **^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm)** = 0.95−1.28 (m, 6H, h-2CH_3), 1.47−2.36 (m, CH, CH_2 repeating unit), 2.57−3.14 (m, 6H, a-2CH_3), 3.99−4.2 (m, 1H, g-CH), 6.28 (br s, 1H, f-NH).

IR (KBr): ν (cm^{-1}): 3280−3640(s) (NH), 2840−3260 (CH-aliphatic), 1695−1610 (s) (C═O, amide).

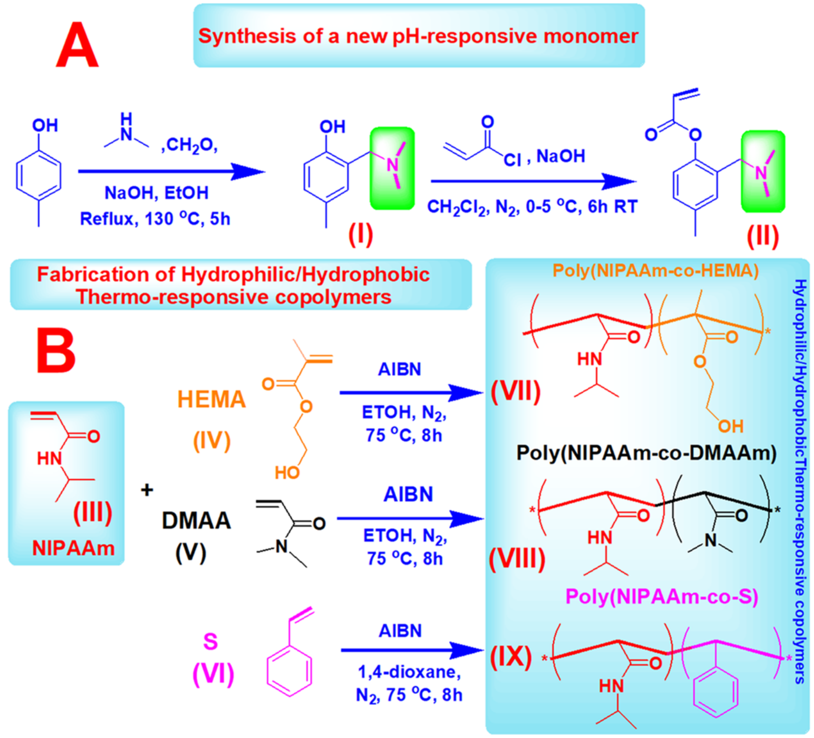
2.4.3.3. Poly(NIPPAm-co-S) (IX-05), (IX-10), and (IX-20)-Group (C). **^{1}H NMR (500 MHz, d^6-DMSO): δ (ppm)** = 0.97−1.38 (m, 6H, h-2CH_3), 1.67−2.30 (m, CH, CH_2 repeating units b, c, d, and e), 3.95−4.25 (m, 1H, g-CH), 5,96−6.38 (br s, 1H, f-NH), 6.86−7.67 (m, 5H, a-Ar-H).

IR (KBr): ν (cm^{-1}): 3245−3640 (NH), 2560−2990 (br) (CH, CH_2, and CH_3) aliphatic, 1720−1740 (CONH), 1548 (NHCH), 1300−1345 (C═C−Ar), 770−870 (CH-Ar).

2.4.4. Terpolymers of Poly(NIPAAm-co-DMIMCA-co-HEMA) Group (D) (X), Poly(NIPAAm-co-DMIMCA-co-DMAAm) Group (E) (XI), and Poly(NIPAAm-co-DMIMCA-co-S) Group (F) (XII) (10 mol % HEMA, DMAAm, and Styrene) and (5, 10, and 20 mol % DMAMCA). Free radical polymerization in solution was used to prepare all terpolymers. The mixtures of 0.0027 mol % (3 g) NIPAAm and 10 mol % (0.0027 mol % HEMA (0.33 g), DMAAm (0.27 g), and styrene (0.28 g)) were added to 5, 10, and 20 mol % (0.00135 mol/0.30 g, 0.0027 mol/0.60 g, and 0.0054 mol/1.20 g) 2-((dimethylamino)methyl)-4-methylphenyl acrylate (DMAMCA). The initiation was done by the azo initiator 2,2′-azobis(2-methylpropionitrile) (AIBN) in 60 mL absolute ethanol groups D and E of terpolymers (X, XI) and 1,4-dioxane for group F of terpolymers (XII) in round flasks. They were purged with nitrogen gas for 15 min and then heated under a nitrogen atmosphere with stirring at 75−80 °C for 6 h in an oil bath. Polymers were collected by precipitation in diethyl ether at −40 to −20 °C. The purification process was done as mentioned previously.

2.4.5. Chemical Evaluation of Terpolymers (X, XI, and XII) by ^{1}H NMR and FT-IR. 2.4.5.1. Poly(NIPAAm-co-DMIMCA-co-HEMA) (X-10-05, X-10-10, and X-10-20). **^{1}H NMR (500 MHz, d^6-DMSO): δ(ppm)** = 0.95−1.35 (m, 6H, p-2CH_3),

Scheme 1. (A) Synthesis of Premonomer (I) and Monomer (II) and (B) Synthesis of Copolymers VII, VIII, and IX (Groups A, B, and C)



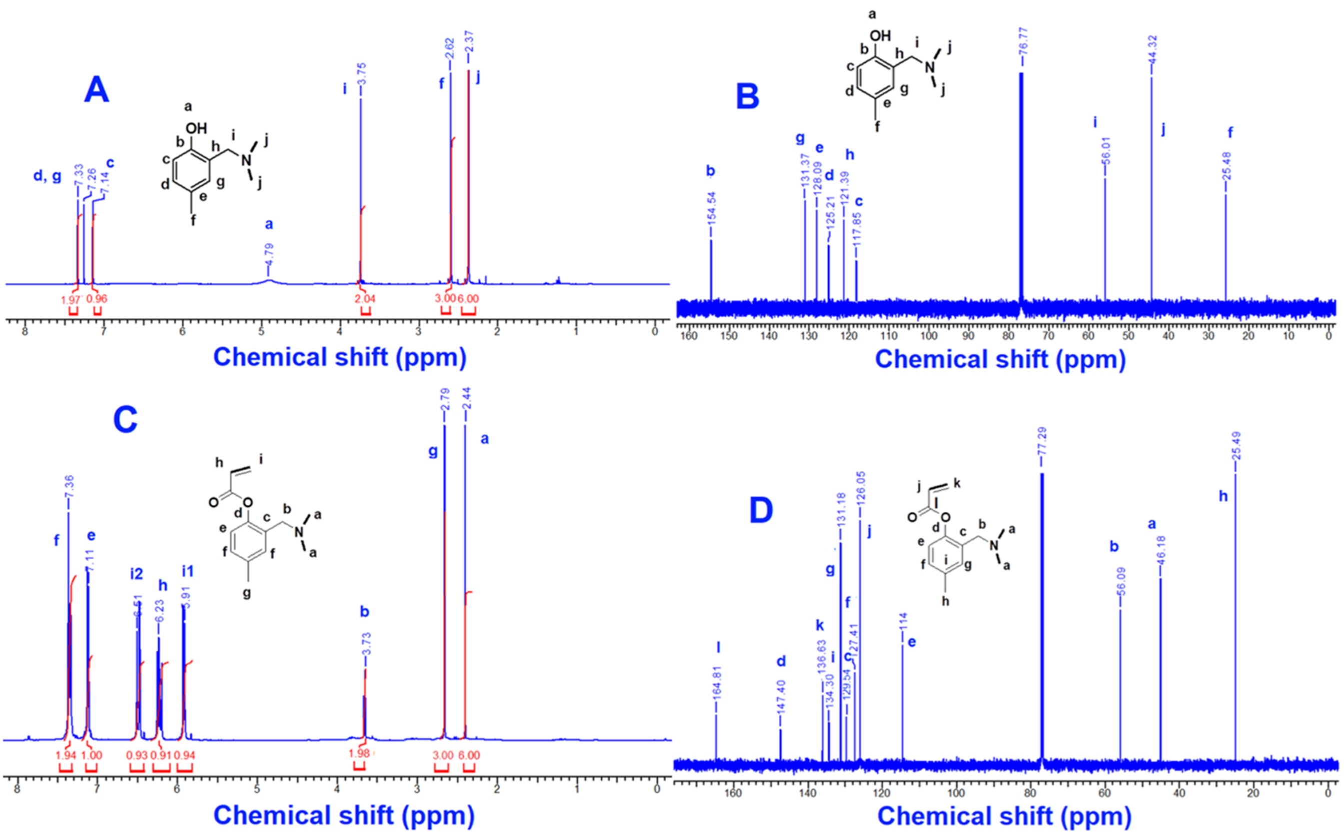


Figure 1. (A, C) ^{1}H NMR and (B, D) ^{13}C NMR spectra (CDCl$_3$) of compounds (I) and (II).

1.40–2.23 (m, repeating unit CH, CH$_2$), 2.26–2.38 (m, 6H, K-2CH$_3$), 3.73–3.87 (m, 4H, c, j-CH$_2$), 3.87–4.09 (m, 1H, o-CH-(CH$_3$)$_2$), 4.12–4.25 (m, 2H, b-CH$_2$), 5.57–6.52 (m, 1H, n-NH), 6.75–7.52 (m, 3H, h-CH-Ar),

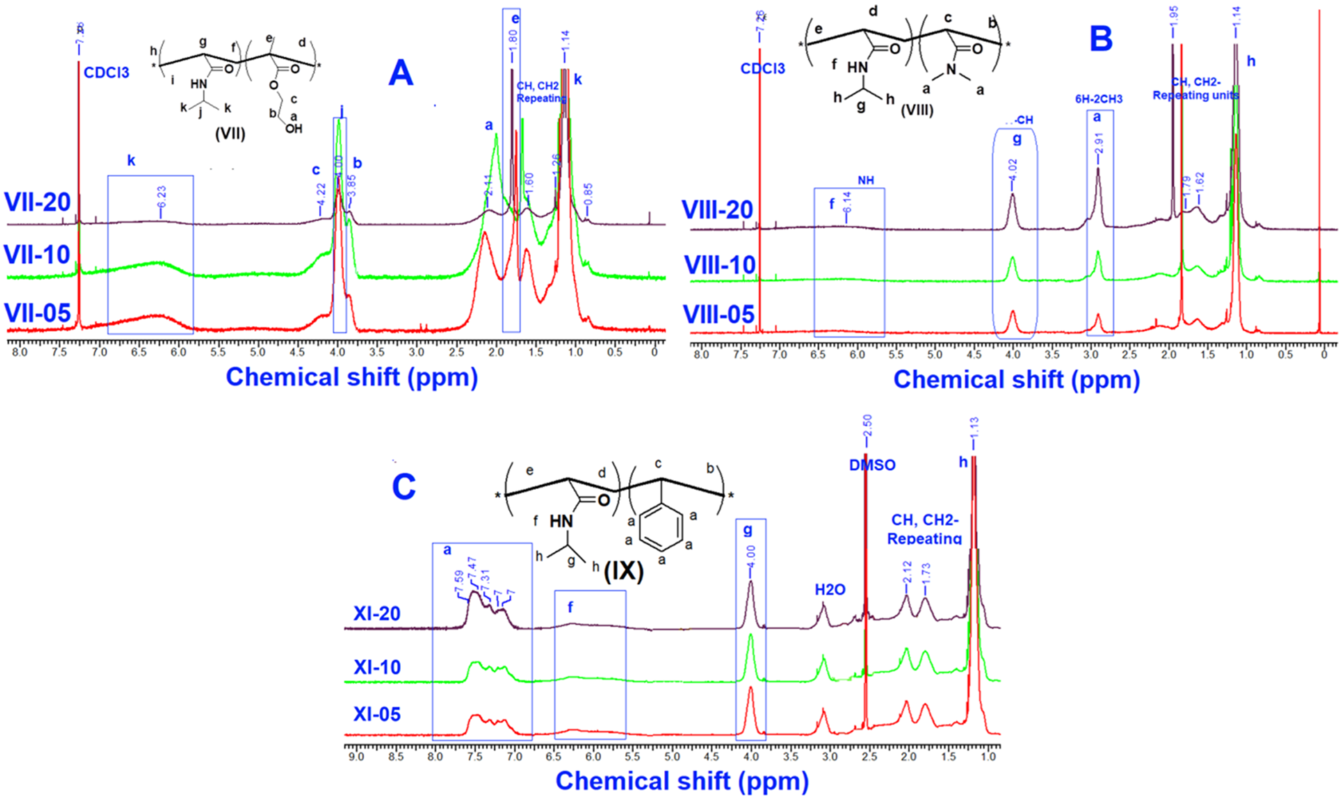


Figure 2. (A) ^{1}H NMR spectra of terpolymers of poly(NIPAAm-*co*-HEMA) in (CDCl$_3$), (B) poly(NIPAAm-*co*-DMAAm) in (CDCl$_3$), and (C) poly(NIPAAm-*co*-S) in (d^6-DMSO).

IR (KBr): ν (cm^{-1}): 3150−3630 (s) (OH), 2735−3100 (CH-aliphatic), 1744−1767 (s) (C═O, carbonyl), 1755−1765 (s) (C═O ester), 1620−1650 (s) (C═O, amide), 1500−1567 (s) (CN), 1455−1465 (s) (C═C), aromatic ring, 726−823 (s) (Ar-CH).

2.4.5.2. Poly(NIPAAm-co-DMIMCA-co-DMAAm) (XI-10-05, XI-10-10, and XI-10-20). **^{1}H NMR (500 MHz, CDCl$_3$): δ(ppm)** = 0.96−1.33 (m, 6H, m-2CH$_3$), 1.51−1.93 (m, repeating unit CH, CH$_2$), 1.95−2.33 (m, 3H, g-CH$_3$), 2.36−2.58 (m, 6H, a-2CH$_3$), 3.33−3.42 (m, 2H, h-CH$_2$), 3.89−4.19 (m, 1H, l-CH(CH$_3$)$_2$), 5.77−6.82 (m, 1H, k-NH), 7.30−7.42 (m, 2H, f-CH-Ar), 7.60−7.72 (m, 1H, e-CH-Ar).

IR (KBr): ν (cm^{-1}): 3190−3675(s) (NH), 2835−3160 (CH-aliphatic), 2370−2396 (s) (CN), 1717−1724 (s) (C═O, carbonyl ester), 1705−1711 (s) (C═O amide, NIPAAm), 1620−1650 (s) (C═O amide, DMAAm), 1520−1535 (s) (CN), 1468−1485 (s) (C═C), aromatic ring, 780−825 (s), (Ar-CH).

2.4.5.3. Poly(NIPAAm-co-DMIMCA-co-S) (XII-10-05, XII-10-10, and XII-10-20). **^{1}H NMR (500 MHz, d^6-DMSO): δ(ppm)** = 0.94−1.30 (m, 6H, m-2CH$_3$), 1.36−2.10 (m, repeating unit CH, CH$_2$), 2.05−2.23 (m, 2H, f-CH$_3$), 2.76−2.98 (m, repeating unit CH, CH), 3.27−3.44 (m, 3H, h-CH$_3$), 3.92−4.22 (m, 1H, l−CH(CH$_3$)$_2$), 6.90−7.96 (m, 2H, f-CH-Ar), 7.60−7.72 (m, a-CH-Ar), 7.80−7.92 (m, 1H, CH-Ar-styrene).

IR (KBr): ν (cm^{-1}): 3195−3665 (s) (NH), 2765−3220 (CH-aliphatic), 1713−1721 (s) (C═O, carbonyl ester), 1697−1708 (s) (C═O amide, NIPAAm), 1523−1532 (s) (CN), 1460−1475 (s) (C═C), aromatic ring, 790−825 (s), (Ar-CH).

3. RESULTS AND DISCUSSION

3.1. 2-((Dimethylamino)methyl)-4-methylphenyl Acrylate (DMAMCA) Monomer. A new pH-responsive monomer was prepared using *p*-cresol and a group of thermoresponsive copolymers based on *N*-isopropylacrylamide with different hydrophilic/hydrophobic monomers. The new monomer was incorporated into the polymer chain in the form of copolymers and terpolymers. The new pH-responsive monomer with the tertiary amine group was synthesized as described in our previous works for analogous monomers of the same family of the cationic monomers.[21,22,25,26,54,76] The new monomer was named 2-((dimethylamino)methyl)-4-methylphenyl acrylate (DMAMCA), as illustrated in Scheme 1.

At first, *p*-cresol was reacted with formaldehyde, *N*,*N*-dimethylamine to create 2-((dimethylamino)methyl)-4-methylphenol DMAMC (I) with the cationic tertiary amine group, which manages the pH-responsiveness after polymerization. The reaction was carried out in basic conditions (pH = 11.6); the reaction mechanism proceeded according to the Mannich reaction. The new compound was evaluated by ^{1}H, ^{13}C NMR, as shown in Figure 1A,B, as well as the FT-IR (shown in the Supporting Information). The protons and ^{13}C that were detected were sufficient to confirm the chemical structure; it was noticed that the presence of 6H, dimethyl groups at δ = 2.37 ppm, and 2H, methylene N-**CH$_2$** at δ = 2.62 ppm, and the corresponding ^{13}C at δ = 44.32 ppm and δ = 56.01 ppm was observed. Meanwhile, the specific methyl group and the hydroxyl group of *p*-cresol were revealed at δ = 2.62 and δ = 4.79 ppm and, consequently, ^{13}C at δ = 25.48 and 154.54 ppm. The FT-IR spectrum showed absorptions of several groups, specifically the peaks of the hydroxyl group (OH) at ν = 3355−3576 cm^{-1} and at 2170−2295 stretched (CN) of

Table 1. Yield Percentage, the Actual Composition from the ^{1}H NMR Spectra in Moles, Average Molecular Weights (the Number-Average and the Weight-Average Molecular Weight), Dispersity, Glass Transition Temperature, the Phase Transition Temperatures, and the Cloud Points in Different pH Solutions for the Groups of Copolymers A, B, and C (VII, VIII, and IX) and the Groups of Terpolymers D, E, and F (X, XI, and XII)

			composition ^{1}H NMR		$\bar{M}_n$[a] (g/mol) 10^4 (THF)	$\bar{M}_w$[b] (g/mol) 10^4 (THF)	Đ[c]		C_p[e] (°C) UV (±) 0.3 °C						T_c[f] (°C) DSC
group	polymer	%	HEMA *DMAAmS*	DMAMCA				T_g[d] (°C) DSC	pH 1.4	pH 3.7	pH 5.6	pH 6.9 (DI)	pH 9.7	pH 12.6	pH 6.9
A	**IIIa**	94	-	-	2.3		3.0	141	-	-	-	33	-	-	32.7
	VII-05	92	4.3	-	2.6	6.7	2.6	138	-	-	-	34.5	-	-	
	VII-10	91	8.8	-	2.5	5.4	2.2	133	-	-	-	37.7	-	-	38
	VII-20	90	15.7	-	2.2	4.3	2.0	126	-	-	-	41	-	-	-
B	**VIII-05**	92	4.2	-	2.0	5.0	2.5	136	-	-	-	37	-	-	-
	VIII-10	92	9.3	-	4.4	8.4	1.9	130	-	-	-	43	-	-	42.8
	VIII-20	93	16.4	-	3.0	5.0	1.6	119	-	-	-	44.5	-	-	-
C	**IX-05**	90	4.5	-	4.3	8.0	1.9	134	-	-	-	28.6	-	-	-
	IX-10	91	8.9	-	3.2	7.6	2.4	129	-	-	-	26.7	-	-	27
	IX-20	88	15.7	-	1.5	3.2	2.1	115	-	-	-	21.4	-	-	
D	**X-10-05**	89	8.7	3.4	1.8	4.6	2.5	127	36.7	36	33	31.4	29.5	29	
	X-10-10	90	9.2	7.4	1.9	4.4	2.3	121	39	38	33.5	28	27	26	28
	X-10-20	86	9.3	14.3	1.3	2.8	2.1	106	43	42.5	36	25.7	25	24	-
E	**XI-10-05**	88	9.4	3.8	1.8	4.3	2.4	126	39	38	37.5	35	34	33	-
	XI-10-10	91	9.5	7.4	1.8	3.9	2.3	122	45	44.3	42.4	33.3	31.5	31	33.5
	XI-10-20	82	8.8	13.9	1.5	3.3	2.2	108	47.6	46.3	42.5	36	33.7	33	-
F	**XII-10-05**	87	8.5	3.9	0.4	0.6	1.5	123	31	29.5	26	23.7	23	21.5	-
	XII-10-10	84	8.3	7.7	0.4	0.8	2.0	112	34	32.8	28.5	23	21.6	20	22.6
	XII-10-20	78	7.8	12.3	0.3	0.4	1.3	103	37.5	35	28.5	19	17.4	15	

[a] Number-average molecular weight. [b] Weight-average molecular weight. [c] Dispersity. [d] Glass transition temperature. [e] Cloud point (50% transmittance). [f] Lower critical solution temperature.

−NC$H_2(CH_3)_2$ tertiary amine group. Ultimately, the synthetic product 2-((dimethylamino)methyl)-4-methylphenyl acrylate (DMAMCA) was obtained by the reaction of compound (I) under the basic conditions with the acryloyl chloride, as described in Scheme 1. The reaction was carried out in an inert and cool atmosphere during the addition of acid chloride.

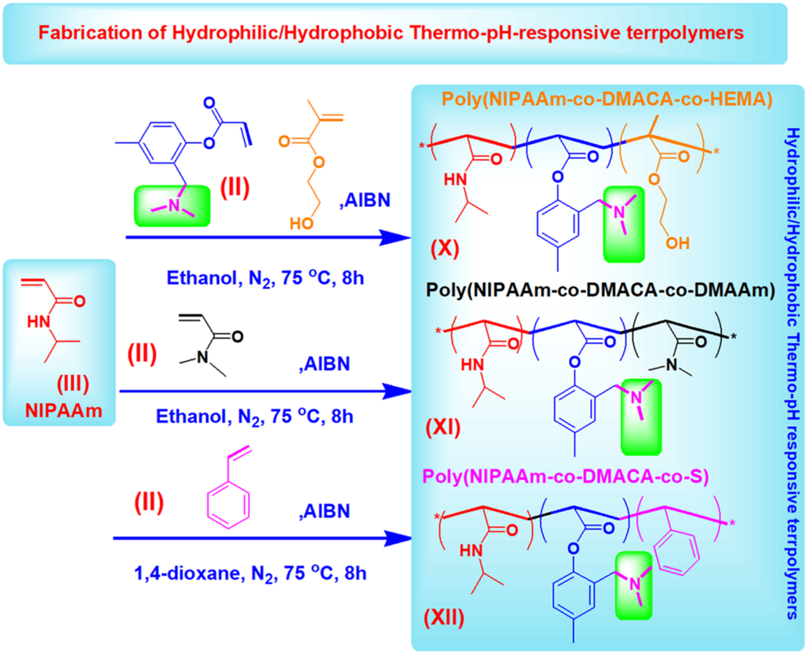
Characterization of DMAMCA was performed by ^{1}H, ^{13}C NMR, and FT-IR as previously described. We noticed that the most essential protons and ^{13}C of the chemical structure were detected; the formation of the vinyl group has been observed clearly at δ = 5.91, 6.23, and 6.51 ppm, and these also have been detected via the ^{13}C at δ = 126.05 and 138.83 ppm. Another ^{1}H and ^{13}C were recorded for the tertiary amine group in the presence of Ar-N-$\mathbf{CH_2}(CH_3)_2$ at δ = 3.73 ppm, the corresponding ^{13}C at δ = 56.09 ppm, 6H, dimethyl groups Ar-N-$CH_2(\mathbf{CH_3})_2$ at δ = 2.44 ppm, and ^{13}C δ = 58.09 and 46.18 ppm, as illustrated in Figure 1C,D. The absorptions of the functional groups were detected by the FT-IR spectrum. Peaks for the essential groups for instance, at ν = 2310−2360 cm^{-1} stretched (CN) of the −**NC**$H_2(CH_3)_2$ tertiary amine group and −C═C− vinyl group at ν = 1647−1660 cm^{-1}.

3.2. Copolymers and Terpolymers.

3.2.1. Copolymer Groups (A, B, and C) P(NIPAAm-co-HEMA), P(NIPAAm-co-DMAAm), and P(NIPAAm-co-S). In this study, we synthesized three groups of copolymers (A, B, and C), consisting of hydrophilic or hydrophobic monomers, based on NIPAAm. For group (A) P(NIPAAm-*co*-HEMA), the copolymerization was performed between NIPAAm and 5, 10, and 20 mol % HEMA in the presence of AIBN (initiator) and absolute ethanol by the free radical mechanism, as illustrated in Scheme 1. The polymers were separated in diethyl ether, and the chemical structures were evaluated by ^{1}H NMR and FT-IR. Figure 2A demonstrates the ^{1}H NMR of the copolymers of group A. All spectra exhibited protons that were expected to be seen in the polymer chain; the presence of multiple 6H of ($-CH(\mathbf{CH_3})_2$) isopropyl (NIPAAm) methyl groups at δ = 0.71−1.46 ppm and the repeating units ($\mathbf{-CH-CH_2-}$) at δ = 1.17−1.64 and at δ = 1.67−1.81 ppm, and the 3H of methyl group in HEMA at δ = 3.70−3.87 ppm attributed to the multiple methylene groups of HEMA. The distinguished protons that were used in the calculation of the existing molar concentration after the polymerization process was depending on the ^{1}H of 3H of the $\mathbf{-CH_3}$ group in HEMA and ^{1}H of the **−CH** isopropyl group of NIPAAm; they are added in Table 1. Figure 4A shows the absorption of the functional groups as was recorded by FT-IR; it exhibits the −OH group at ν = 3286−3630 cm^{-1}, stretched −C═O ester of −COO− at ν = 1710 and 1725 cm^{-1}, and the stretched −CONH− in the polymer chain at ν = 1595−1610 cm^{-1}.

For group (B), the copolymerization process of NIPAAm with 5, 10, and 20 mol % DMAAm in the PNIPAAm main chain was carried out. The copolymers are thermoresponsive polymers with additional hydrophilic/hydrophobic groups, which will influence the general characteristics of PNIPAAm. Chemical analysis using ^{1}H NMR shows the most essential multiple protons in the polymer main chain at δ = 0.95−1.28 ppm 6H of ($-CH(\mathbf{CH_3})_2$) isopropyl (NIPAAm) methyl groups, the repeating $\mathbf{-CH-CH_2-}$ has appeared at δ = 1.47−2.36 ppm, and the specific protons of DMAAm were achieved for 6H of the dimethyl groups $-N(CH_3)_2$ at δ = 2.57−3.14 ppm; they are used with the isopropyl −CH− of NIPAAm to estimate the molar percent of each monomer in the copolymer

Scheme 2. Synthesis of Terpolymers X, XI, and XII (groups D, E, and F)



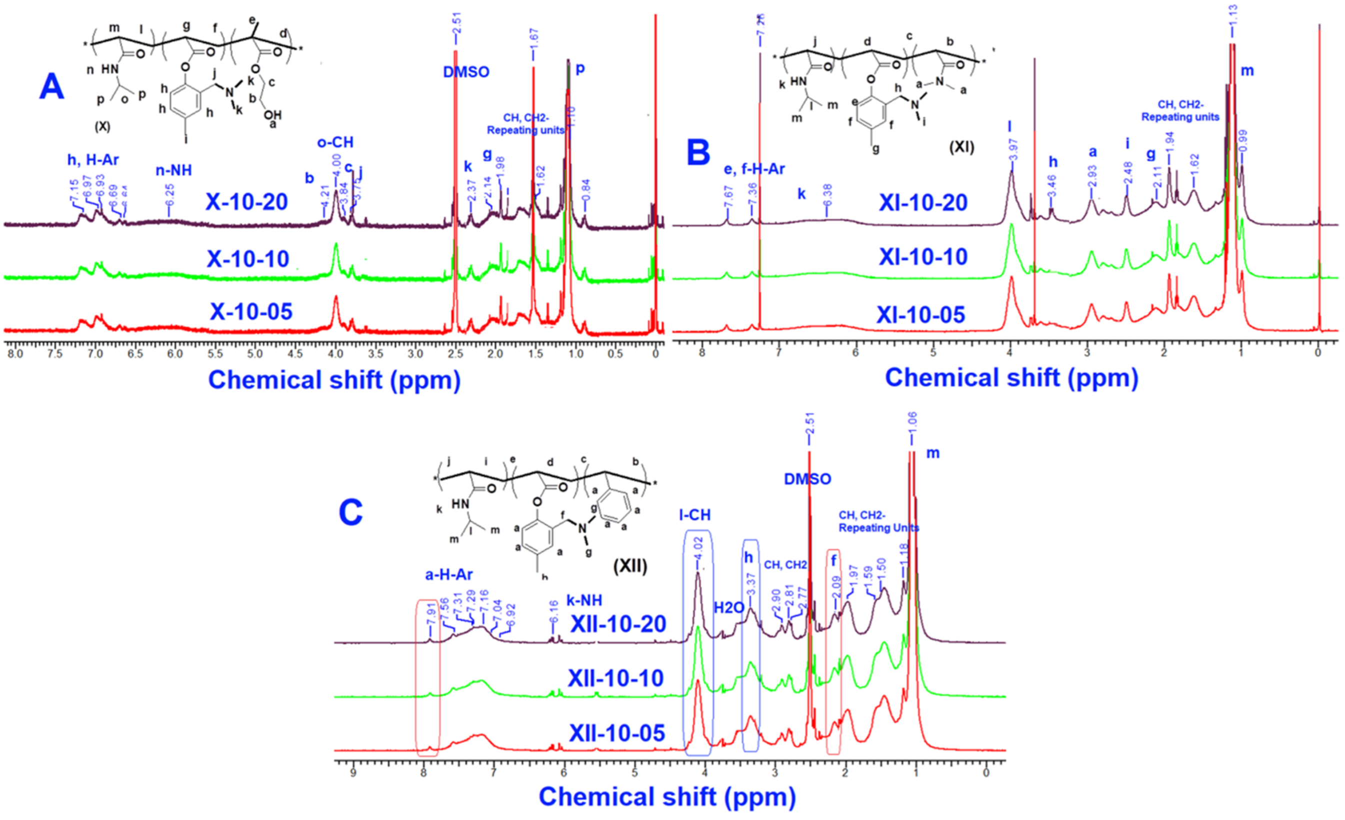


Figure 3. ^{1}H NMR spectra of terpolymers: (A) poly(NIPAAm-*co*-DMACA-*co*-HEMA) in (d^6-DMSO), (B) poly(NIPAAm-*co*-DMACA-*co*-DMAAm) in (CDCl$_3$), and (C) poly(NIPAAm-*co*-DMACA-*co*-S) in (d^6-DMSO).

chain; these are tabulated in Table 1 and Figure 2B. The FT-IR was used to determine the absorption of the functional groups, for instance, the −NH at ν = 3280−3640 cm^{-1} and at ν = 1695−1610 cm^{-1} stretched the −C═O amide of −CONH− in the polymer chain, as shown in Figure 4A.

The last copolymer group (C) is based on the copolymerization of NIPAAm with styrene in 5, 10, and 20 mol %. Figure 2C illustrates the most specific multiple protons for NIPAAm and styrene in the copolymer chain at δ = 0.97−1.38 and 3.95−4.25 ppm due to the methyl groups (−CH(CH$_3$)$_2$) isopropyl and −CH−(NIPAAm); the aromatic Ar-H protons of styrene appeared at δ = 6.86−7.67 ppm. The last issued protons were used for the determination of the chemical composition of each monomer. FT-IR was successfully used to

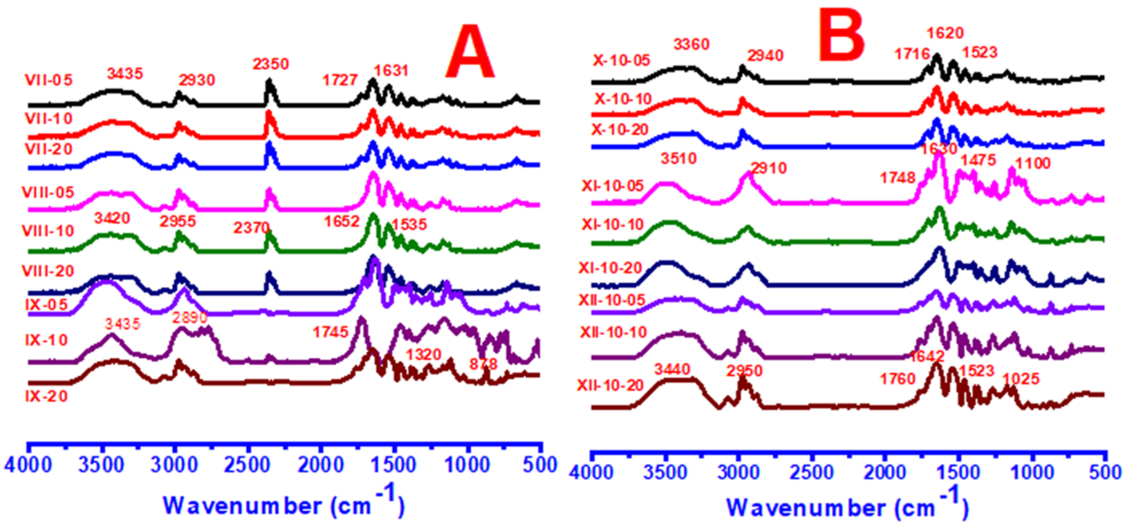


Figure 4. FT-IR spectra of (A) PNIPAAm copolymers and (B) PNIPAAm terpolymers.

record the functional groups at ν = 1720−1740 cm^{-1} (CONH) of NIPAAm; however, ν = 1300−1345 cm^{-1} (C═C-Ar) proved the presence of styrene, as shown in Figure 4A.

3.2.2. Terpolymers Groups (D, E, and F) P(NIPAAm-co-DMAMCA-co-HEMA), P(NIPAAm-co-DMAMCA-co-DMAAm), P(NIPAAm-co-DMAMCA-co-S), 10 mol % HEMA, DMAAm, and Styrene with 5, 10, and 20 mol % DMAMCA. Optimization of copolymers (groups A−C) was achieved by incorporating the new monomer (DMAMCA) with a pH-responsive cationic group into the polymer chains. The terpolymers were synthesized via a free radical polymerization technique, as illustrated in Scheme 2. The new terpolymers were characterized by their thermo-pH dual-responsive properties, in addition to the hydrophilic/hydrophobic groups present in the polymer chains, which will distinguish their characteristics from homo-PNIPAAm and their copolymers. Group (**D**) of the terpolymers consists of 5, 10, and 20 mol % DMAACA with 10 mol % HEMA. The ^{1}H NMR is shown in Figure 3A. The multiple protons in the chemical structure appeared at different positions of the chemical shift at δ = 6.86−7.67 ppm as used for the PNIPAAm chain due to the isopropyl methyl groups ($-CH(\mathbf{CH_3})_2$), and the characteristic proton of PNIPAAm was revealed at δ = 3.87−4.09 ppm. Other protons for HEMA were observed at δ = 4.12−4.25 ppm for 2H ($-CH_2-\mathbf{CH_2}-OH$); the DMAMCA has also distinguished protons, for instance, the protons 6H of Ar−$CH_2-(\mathbf{CH_3})_2$ appear at δ = 2.26−2.38 ppm and the aromatic protons 3H appear at δ = 6.75−7.52 ppm. The isopropyl H-CH (NIPAAm), H-Ar (DMAAC), and 2H-CH_2 (HEMA) are used for the actual molar composition in the main chain of terpolymer group **D**. The FT-IR has demonstrated the most particular functional groups of monomers in the terpolymer chain. One of the most important functional groups that have emerged in the spectrum, as shown in Figure 4B, is the stretched carbonyl ester and amide at ν = 1744−1767, 1755−1765, and 1620−1650 cm^{-1}; another absorption has also appeared at ν = 1500−1567 cm^{-1} (CN) and ν = 1455−1465 cm^{-1} stretched (C═C), aromatic ring.

The terpolymer group (**E**) depends on the polymerization of NIPAAm and DMAMCA (5, 10, and 20 mol %) and 10 mol % DMAAm. Figure 3B exhibits the ^{1}H NMR of terpolymers; the presence of the specific protons, such as 1H, −CH− PNIPAAm at δ = 3.89−4.19 ppm, 2H, **H**-Ar DMAAC at δ = 7.30−7.42 ppm, and 6H, $-N-(\mathbf{CH_3})_2$ DMAAm at δ = 2.36−2.58 ppm, was observed; they are used in the determination of actual composition for each monomer. Moreover, the absorption of functional groups was recorded as previously discussed by FT-IR and as illustrated in Figure 4B. The stretched carbonyl ester −COO− and amide −CONH− were revealed in addition to other functional groups as described in the Experimental Section. The terpolymerization of NIPAAm, DMAMCA, and the styrene group (F), as shown in Figures 3C and 4B, was confirmed by ^{1}H NMR and FT-IR. The protons of monomers appeared in multiplicity, indicating the terpolymerization and the disappearance of monomer units in the polymer chain. The molar concentrations of monomers were calculated from 1H, −CH− PNIPAAm at δ = 3.92−4.22 ppm, 3H, $-\mathbf{CH_3}$ DMAAC at δ = 3.27−3.44 ppm, and 1H, CH-Ar-styrene at δ = 2.36−2.58 ppm. The absorption of the functional groups was determined using FT-IR as shown in Figure 4B.

3.3. Molecular Weights (M_n and M_w) and Dispersity ($Đ$). Here, we will discuss the change in the molecular weight and the dispersity of PNIPAAm and its copolymers and terpolymers and the effect of the incorporation of the HEMA, DMAAm, and S on the growth of the copolymers' chains. Furthermore, the interaction between the new monomers and DMAMCA in the terpolymer chain is investigated. The molecular weights (weight-average molecular weight M_w and number-average molecular weight M_n) and the dispersity ($Đ$) were measured by gel permeation chromatography (GPC) with a UV spectrophotometer in tetrahydrofuran (THF), as their eluent. Figure 5A, illustrates the molecular weights of homo-PNIPAAm and PNIPAAM copolymers with 5, 10, and 20 mol % HEMA; all data are presented in Table 1. It was noticed that the chromatogram consisted of one plateau, which corroborates the vanishing of the lower molecular weight and that the polymerization has been successfully carried out. The measurement of PNIPAAm yielded M_n = 23.000 g/mol, M_w = 71.000 g/mol, and $Đ$ = 3. The copolymerization with 5, 10, and 20 mol % HEMA VII (group A) exhibited M_n = 26.000, 25.000, and 22.000 g/mol, M_w = 67.000, 64.000, and 43.000 g/mol, and $Đ$ = 2.6, 2.2, and 2.0, respectively. A gradual decrease in M_n, M_w, and $Đ$ by increasing the molar concentration of

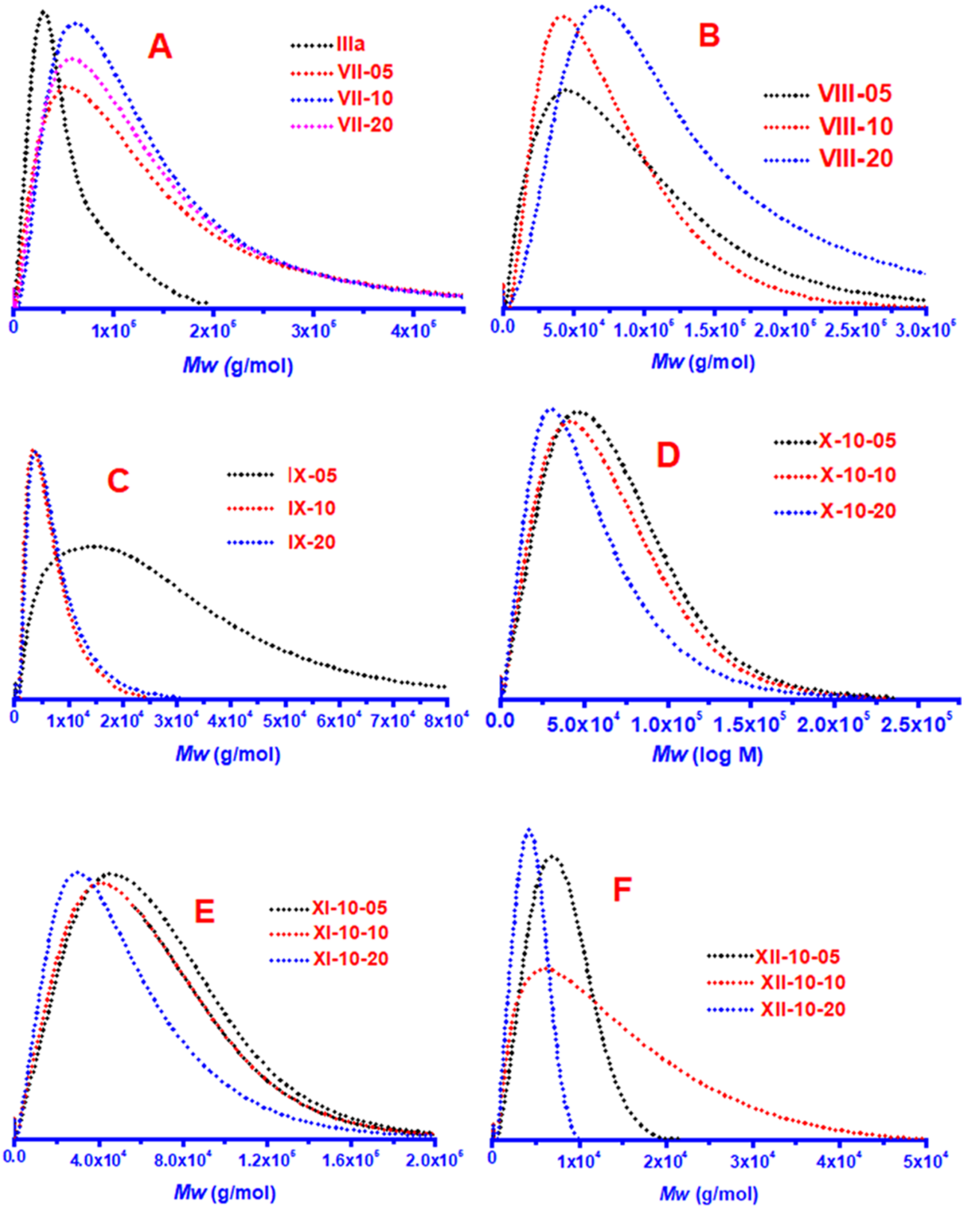


Figure 5. A−F: GPC of homo-PNIAAm, PNIPAAm copolymers, groups (A−C), and PNIPAAm terpolymers, groups (D−F).

HEMA was observed. This can be attributed to a decrease in the reactivity of the polymer chain by increasing the concentration of HEMA.[54]

The group (B) copolymerization with 5, 10, and 20 mol % DMAAm, as illustrated in Figure 5B, yielded M_n = 20.000, 44.000, and 30.000 g/mol, M_w = 50.000, 84.000, and 50.000 g/mol, and $Đ$ = 2.5, 1.9, and 1.6, respectively. These results can also be interpreted, as previously mentioned. The last group of PNPAAm copolymers was prepared with styrene, which resulted in M_n = 43.000, 32.000, and 15.000 g/mol, M_w = 80.000, 76.000, and 32.000 g/mol, and $Đ$ = 1.9, 2.4, and 2.1; respectively. A change in the dispersity value at 10 mol % styrene (IX-10) was noticed, which is higher than (IX-05), and (IX-20); the interpretation of this observation is under study.

The incorporation of 5, 10, and 20 mol % DMAMCA into the chain of the copolymers is based on the NIPAAm with 10 mol % HEMA, DMAAm, and S to produce the terpolymers groups. We noticed the influence of the molecular weights and dispersity of terpolymers by the changes in their chemical structure. The measurements of the first group (D) (X-10-05, X-10-10, and X-10-20) indicated a decrease in M_n (18.000, 19.000, and 13.000 g/mol), M_w (46.000, 44.000, and 28.000 g/mol), and $Đ$ (2.5, 2.3, and 2.1) compared with their corresponding copolymers VII (A) without DMAMCA. The steric hindrances of DMAMCA restricted the free rotation and the growth of the polymer chain.[54] This effect was dominant with all groups of terpolymers, resulting in lower M_n, M_w, and $Đ$ with higher concentrations of DMAMCA, as illustrated in Figure 5A−F and Table 1. The lowest values of M_n (4.000, 4.000, and 3.000 g/mol), M_w (6.000, 8.000, and 3.000 g/mol), and $Đ$ (1.5, 2.0, and 1.3) were observed with terpolymers XII (F) and styrene, as shown in Figure 5F. This may be attributed to a lower reactivity of the polymer chain by increasing the concentration of the HEMA.[26−28]

3.4. Glass Transition Temperature (T_g). The glass transition temperature (T_g) refers to the amorphous state of polymers in which polymers undergo a transition from a glassy state to a rubbery state. It is an essential characteristic of

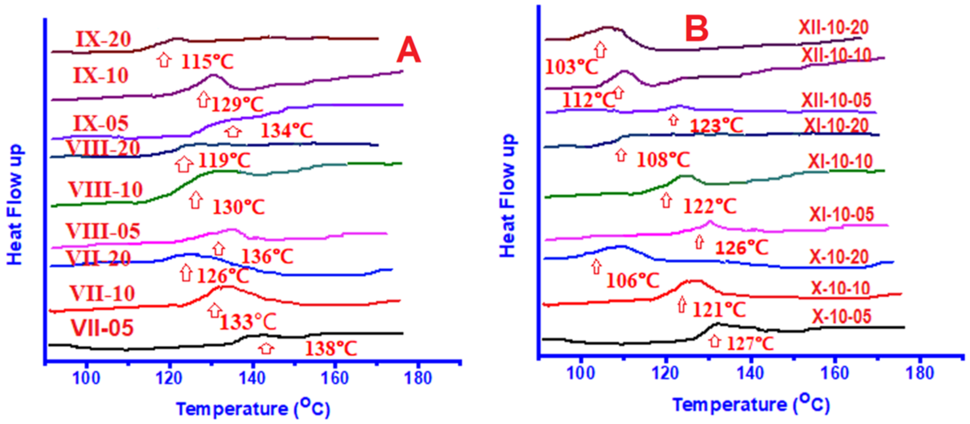


Figure 6. Glass transition temperature (T_g) of homo-PNIAAm: (A) PNIPAAm copolymers, groups (A−C) and (B) PNIPAAm terpolymers, groups (D−F).

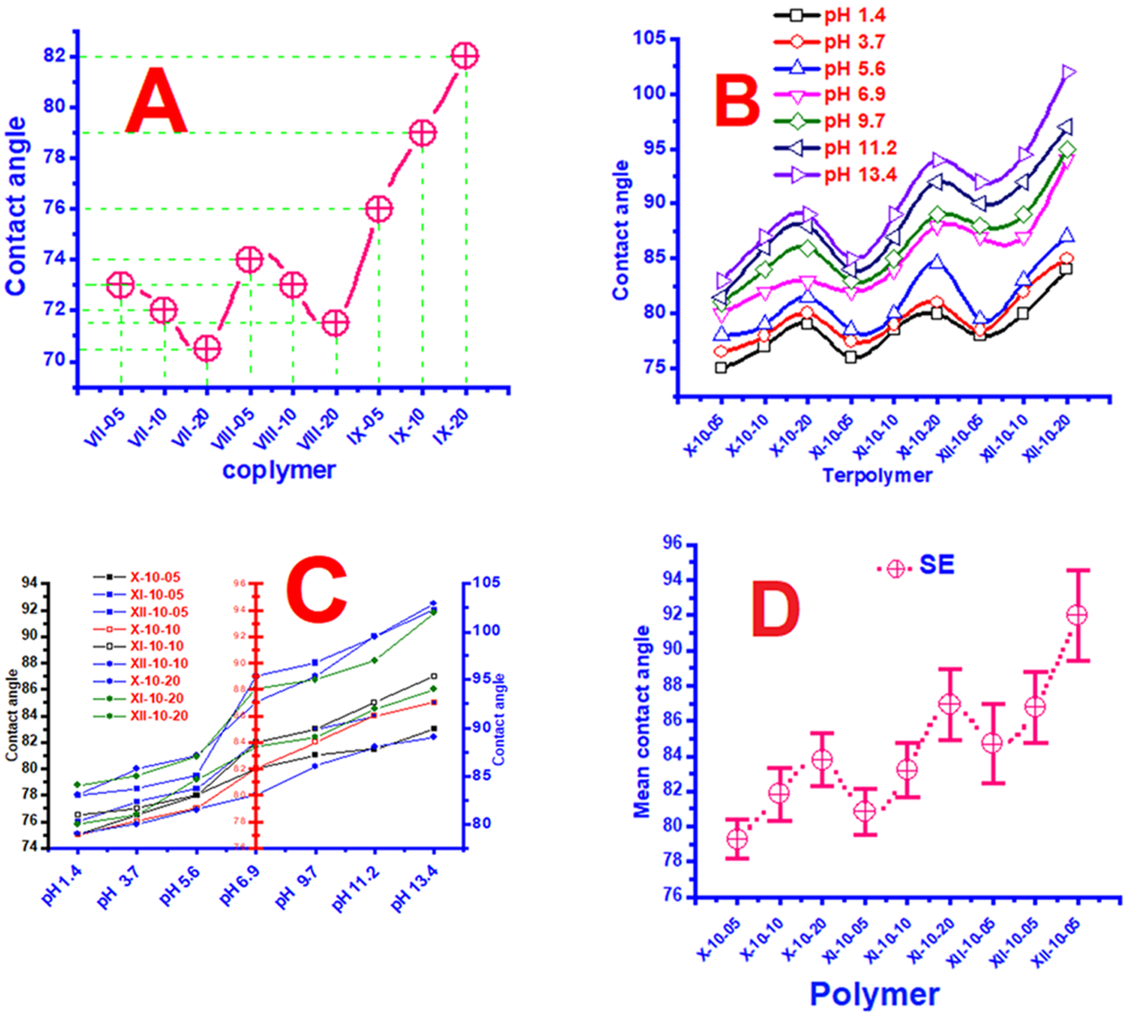


Figure 7. (A) Contact angle of copolymers (pH 6.9, DI water), (B) terpolymer in different pH solutions, (C) change of contact angles with pH for each terpolymer, and (D) analysis of variance (ANOVA) test SE of the mean contact angles of terpolymers.

polymeric material at which dramatic changes in the physical and mechanical properties occur. The glass transition temperatures of all used polymers, including homo-, co-, and terpolymers, were recorded using a differential scanning calorimeter (DSC). The onset point was recorded by the glass transition temperature of the polymer.[3] The effect of the addition of HEMA, DMAAm, and S to the PNIPAAm copolymer and DMAMCA was clearly visible in the recorded T_g's of the polymeric materials. The T_g of homo-PNIPAAm was detected at 141 °C, as shown in Figure 6A and Table 1. The group of copolymers VII (A) with HEMA in the main chain revealed T_g's at 138, 133, and 126 °C for VII-05, VII-10, and VII-20, respectively, as shown in Figure 6A; a decrease in the T_g was noticed with increasing concentration of the HEMA

Table 2. Contact Angles (Θ)° via the Wettability Test for Copolymers in DI (pH 6.9) and Terpolymers in Different pH Solutions

(Θ) (±) 0.25°								
Copolymer Groups (pH 6.9)								
A			B			C		
VII-05	**VII-10**	**VII-20**	**VIII-05**	**VIII-10**	**VIII-20**	**IX-05**	**IX-10**	**IX-20**
73°	72°	70.5°	74°	73°	71.5°	76°	79°	82°
Terpolymer Groups								
group	polymer	pH 1.4	pH 3.7	pH 5.6	pH 6.9 (DI H_2O)	pH 9.7	pH 11.2	pH 13.4
D	**X-10-05**	75°	76.5°	78°	80°	81°	81.5°	83°
	X-10-10	77°	78°	79°	82°	84°	86°	87°
	X-10-20	79°	80°	81.5°	83°	86°	88°	89°
E	**XI-10-05**	76°	77.5°	78.5°	82°	83°	84°	85°
	XI-10-10	78.5°	79°	80°	84°	85°	87°	89°
	XI-10-20	80°	81°	84.6°	88°	89°	92°	94°
F	**XII-10-05**	78°	78.5°	79.5°	87°	88°	90°	92°
	XII-10-10	80°	82°	83°	87°	89°	92°	94.5°
	XII-10-20	84°	85°	87°	94°	95°	97°	102°

in the polymer main chain. This can be attributed to the interaction between NIPAAm and HEMA in the polymer chain which increases the free volume in the polymer chain and, consequently, lowers T_g.[26] Other groups of the PNIPAAm copolymer with DMAAm and S VIII (B), XI (C) exhibited T_g's at 136, 130, and 119 °C for VIII-05, VIII-10, and VIII-20, respectively, and 134, 129, and 115 °C for XI-05, XI-10, and XI-20, respectively, as illustrated in Figure 6A.

The terpolymerization and incorporation of DMAMCA in the polymer chain have dramatically influenced the glass transition temperatures. Figure 6B exhibits the thermograms of terpolymers groups with HEMA, DMAAm, S, and 5, 10, and 20 mol % DMAMCA; X (D), XI (E), and XII (F). The T_g measurements of group D are 127, 121, and 106 °C. The lower T_g values than group (A) (NIPAAm and HEMA only) emphasized the effect of DMAMCA on the polymer chain, i.e., the increase of the free volume in the chain by increasing the concentration of DMAMCA. The next group (E) recorded T_g *values of* 126, 122, and 108 °C, whereas the last group (F) exhibited the lowest T_g's for all synthetic copolymers and terpolymers, 123, 112, and 103 °C. This is due to the effect of both styrene and DMAMCA, which spikes the free volume and gap distance in the polymer chain and consequently decreases the glass transition temperatures with increasing the molar concentration of DMAMCA, as shown in Figure 6B.

3.5. Wettability and Contact Angles of Polymers. One of the most essential measurements of surface wettability is the contact angle (Θ). This measurement is used to determine the tendency of polymeric materials to be hydrophilic or hydrophobic. The degree of hydrophilicity and hydrophobicity for polymers and their relationship with the contact angle have been discussed in detail in a recent article;[45] the contact angle for hydrophobic surfaces should be found at $\Theta > 90°$, while for hydrophilic surfaces, at $\Theta < 90°$, whereas for superhydrophobic surfaces, at $\Theta \geq 145°$. This study will show how the copolymerization of NIPAAm with different monomers will change its physical properties, and the incorporation of DMAMCA in the terpolymer chain plays a vital rule in changing the course of the polymer material. A recent study discussed the measurement of the contact angle of homo-PNIPAAm at 74.5°.[72,73] The copolymer groups with HEMA, DMAAm, and S were tested at pH 6.9 (deionized water). The first group VII (A) exhibited $\Theta = 73$, 72, and 70.5° with a gradual decline in the contact angle with increasing HEMA in the polymer chain, as shown in Figure 7A and Table 2. This is attributed to the increase in hydrogen bonds formed by the interaction between water molecules with the hydroxyl group of HEMA and the amide group of NIPAAm. This generally led to spikes in the hydrophilicity of the polymeric material.

For VIII (B) copolymers with DMAAm, the contact angles were measured at $\Theta = 74$, 73, and 71.5°, similar to the previous copolymers with a slight increase in the contact angles due to the difference in the amount of the hydrophilic groups in the polymer chain and their interaction with water on the surface. The contact angle measurements for copolymers IX (C) with styrene exhibited $\Theta = 76$, 79, and 82°, with the increase in the concentration of styrene as shown in Figure 7A.

The contact angle of terpolymers (Θ) was measured in various pH solutions (pH = 1.4, 3.7, 5.6, 6.9 (DI H_2O), 9.7, 11.2, and 13.4). The presence of DMAMCA with different molar concentrations 5, 10, and 20 mol % and different monomers HEMA (10 mol %), X (X-10-05, X-10-10, and X-10-20) (D), DMAAm (E), and S (F) revealed a significant impact on the contact angle measurements, as shown in Figure 7B and Table 2. The highest degree of hydrophilicity (lowest Θ) for terpolymers X (D) was achieved with X-10-05, the lowest molar concentration of DMAMCA, pH 1.4 (strongest acidic conditions), and $\Theta = 75°$. On the other hand, the opposite behavior was realized by increasing both the molar concentration of DMAMCA and the pH solution to reach the strongest basic condition at pH 13.4, where the polymeric material (X-10-20) changed its behavior gradually to hydrophobic. The sequence of the change in the contact angles has been added in Table 2.

For terpolymers XI (XI-10-05, XI-10-10, and XI-10-20) (E), DMAMCA, and DMAAm, the measurements exhibited values very close to those of the previous terpolymers. The lowest contact angle was observed for XI-10-05 at pH 1.4 ($\Theta = 76°$), the most hydrophilic terpolymer in this group, and the highest contact angle was observed for XI-10-20 at pH 13.4 ($\Theta = 94°$). The last case in this study for terpolymers XII (XII-10-05, XII-10-10, and XII-10-20) with DMAMCA and S was measured. The measurements revealed the highest contact angle and the lowest hydrophilicity of all of the investigated copolymers and terpolymers. The lowest contact angle ($\Theta = 75°$) was achieved at the lowest concentration of DMAMCA, XII-10-05 in pH

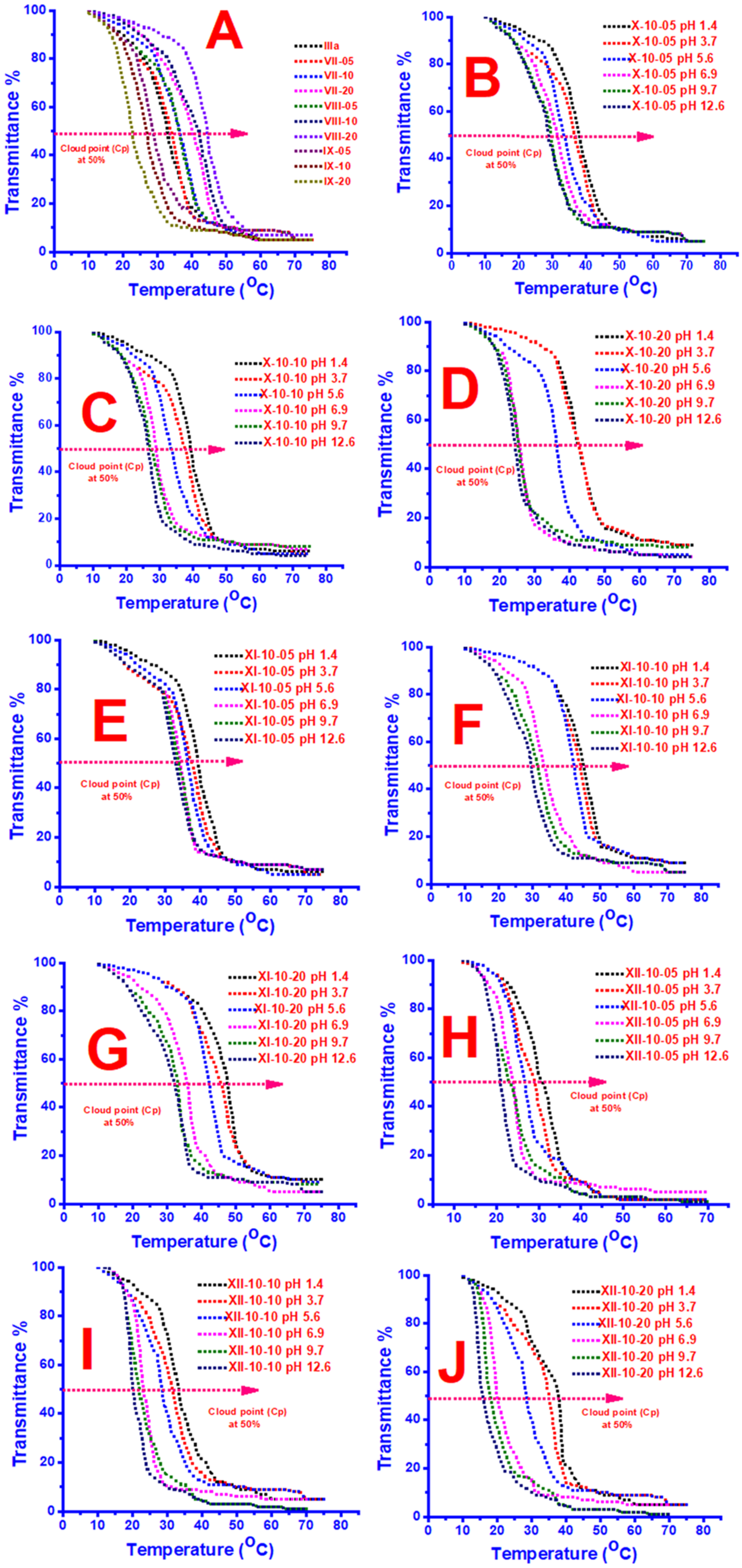


Figure 8. (A) Turbidity measurements via transmittance/temperature for the determination of C_p in PNIPAAm and PNIPAAm copolymers; (B–J) C_p for terpolymers in different pH solutions.

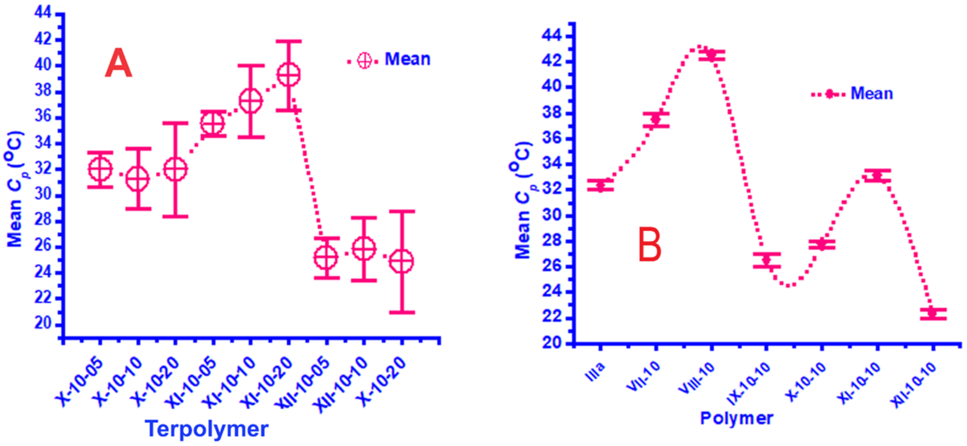


Figure 9. (A) ANOVA test (standard error SE and mean of LCST) for terpolymers with a change in pH solutions. (B) Homo-PIPAAm, copolymers, and terpolymers at pH 6.9 were recorded via a UV−vis spectrophotometer and a micro-differential scanning calorimeter.

1.4; meanwhile, the highest contact angle (Θ = 102°) was achieved for XII-10-20 in pH 13.4. This can be attributed to a couple of aromatic groups that led to an increase in the hydrophobic chains and restricted the formation of hydrogen bonding.[45,54,72] Figure 7C illustrates the change in contact angles of all terpolymers in different pH solutions.

Statistical analysis of the contact angle measurements was performed using one-way ANOVA test, which compares the means of two or more independent groups in order to determine whether there is statistical evidence that the associated population means are significantly different. The standard error of the mean values of the contact angles is shown in Figure 7D; the lowest value was recorded for X-10-05 (SE ± 1.09), while the highest value was recorded for X-10-05 (SE ± 2.56). The *p*-value was 0.459, and the homogeneity of variances is indicated at 0.06 levels. The data analysis revealed that the means were not significantly different.

3.6. Tuning of the Phase Separation Temperature of Homo-PNIPAAm, PNIPAAm Copolymers, and PNIPAAm Terpolymers. A main objective in this study is to compare the cloud point C_p, also known as the phase separation temperature, of different PNIPAAm copolymers and terpolymers. Copolymerization of homo-PNIPAAm with hydrophilic or hydrophobic groups will change the phase separation temperature by increasing or decreasing the hydrogen bonding between the polymer chain (and its groups) with the aqueous solution. C_p's was measured using a UV−vis spectrophotometer through the change of UV transmittance with temperature, also known as the turbidity test. The temperature at which the solution becomes turbid (milky) is known as the cloud point (C_p) or the separation temperature. Additionally, a micro-differential scanning calorimeter was used for LCST (T_c) measurements of both copolymers and terpolymers in deionized water.

Figure 8A illustrates the transmittance−temperature relationship for homo-PNIPAAm and PNIPAAm copolymers. Data are recorded in Table 1. The homo-PNIPAAM (IIIa) exhibited C_p temperatures at 33 °C. Copolymerization with HEMA for copolymers (VII-05, VII-10, and VII-20) resulted in C_p temperatures of 34.5, 37.7, and 41 °C, respectively, whereas copolymerization with DMAAm (VIII-05, VIII-10, and VIII-20) resulted in C_p temperatures of 37, 43, and 44.5 °C, respectively. Both copolymers demonstrated an increase in the phase separation temperature or the cloud point by increasing the molar concentration of HEMA or DMAAm in the polymer chain. This can be attributed to the domination of the hydrophilic chain by increasing the hydrogen bonds between the polymer groups acting in the amide groups in NIPAAm (or DMAAm) and the hydroxyl of HEMA and their interaction with the hydrogen bonds in the aqueous solution.

Meanwhile, copolymerization with styrene exhibited opposite behavior. For copolymers (IX-05, IX-10, and IX-20), C_p's were measured as 28.6, 26.7, and 21.4 °C, respectively. This is due to the domination of the hydrophobic chains created by the aromatic ring of styrene, which restricted the formation of hydrogen bonds. This in turn increased the consistency of turbid solution and lowered the C_p of the polymer solution.[21,26] The C_p's of thermo-pH-responsive terpolymers were recorded in a strong acidic solution (pH 1.4) as well as in neutral (pH 6.9) and strong basic (pH 12.6) solutions. The changes that appeared in the terpolymer solutions are due to the variations in the hydrophilic/hydrophobic groups and how they interact with the polar groups of the solution.

Figure 8B−D shows the C_p's of PNIPAAm terpolymers X (X-10-05, X-10-10, and X-10-20) 10 mol % HEMA and 5, 10, and 20 mol % DMAMCA. At pH 1.4, pH 3.7, pH 5.6, pH 6.9 (DI), pH 9.7, and pH 12.6, the terpolymer X-10-05 exhibited C_p temperatures of 36.7, 36, 33, 31.4, 29.5, and 29 °C, respectively; X-10-10 exhibited C_p temperatures of 39, 38, 33.5, 28, 27, and 26 °C, respectively; and X-10-20 exhibited C_p temperatures of 43, 42.5, 36, 25.7, 25, and 24 °C, respectively. The effect of the concentration of DMAMCA and the pH solution on C_p indicated that the highest C_p (43 °C) was recorded at the lowest pH (pH 1.4) with the highest concentration of DMAMCA (X-10-20). Meanwhile, the lowest C_p value (24 °C) was recorded at the highest pH (pH 12.6). The ionization of the DMAMCA in the terpolymer solution led to an increase in the solution charge, and a massive hydrogen bonding was formed; subsequently, a higher temperature was consumed to make a phase separation.[25,45,76]

Figure 8E−G illustrates the C_p's for terpolymers XI (XI-10-05, XI-10-10, and XI-10-20) 10 mol % HEMA and 5, 10, and 20 mol % DMAMCA. At pH 1.4, pH 3.7, pH 5.6, pH 6.9 (DI), pH 9.7, and pH 12.6, the terpolymer XI-10-05 exhibited C_p temperatures of 39, 38, 37.5, 35, 34, and 33 °C, respectively; XI-10-10 exhibited C_p temperatures of 45, 44.3, 42.4, 33.3, 31.5, and 31 °C, respectively; and XI-10-20 exhibited C_p temperatures of 47.6, 46.3, 42.5, 36, 30.7, and 30 °C,

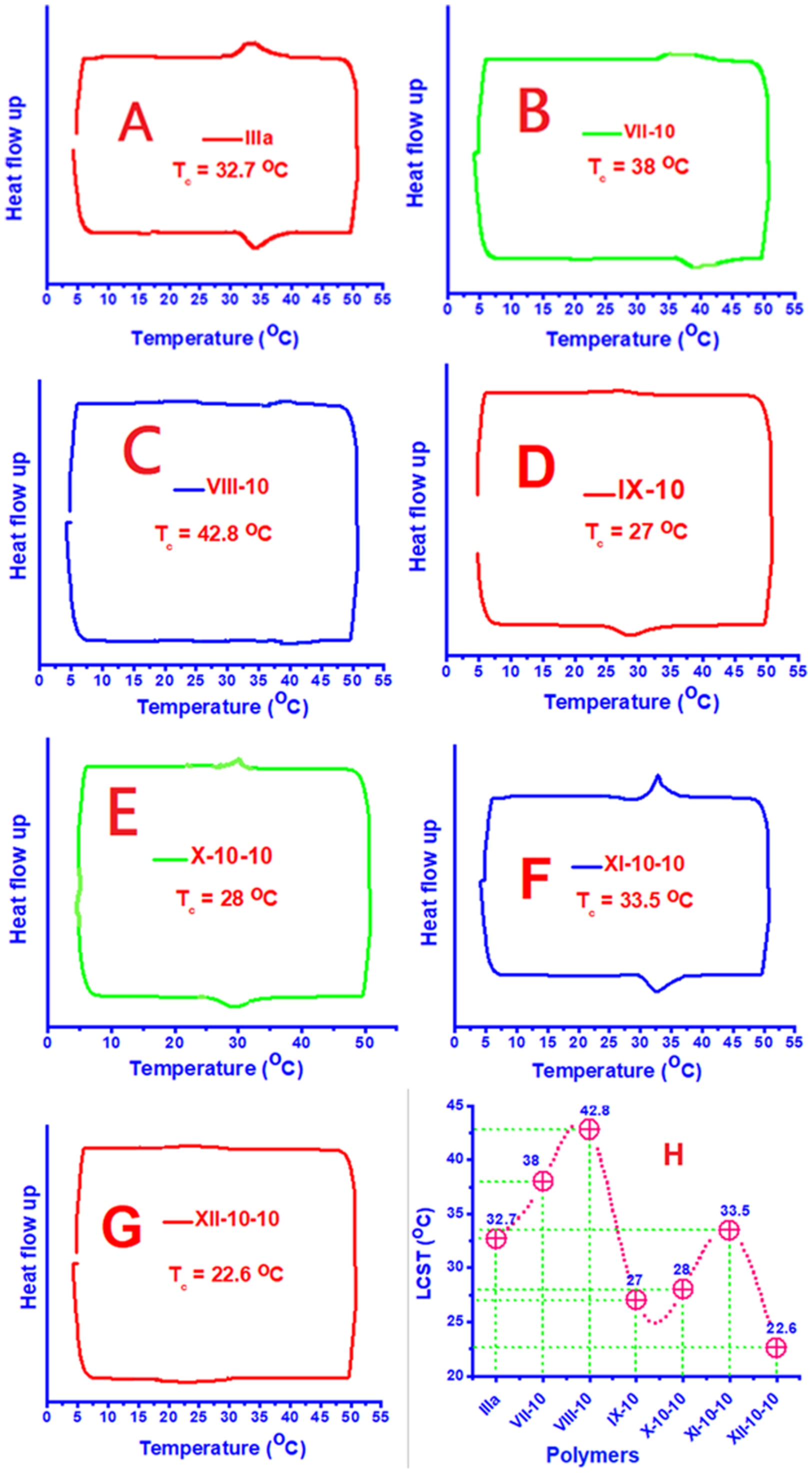


Figure 10. (A–G) Thermograms of the lower critical solution temperature (T_c) for selective polymers in DI water (pH 6.9) using the micro-differential scanning calorimeter and (H) combined measurements of all recorded T_c's.

respectively. The effect of the concentration of DMAMCA and the pH solution on C_p is consistent with the earlier results; the highest C_p (47.6 °C) was recorded at the lowest pH (pH 1.4) for XI-10-20, while the lowest C_p (30 °C) was recorded at the highest pH (pH 12.6) for XI-10-20. The notable differences between the highest C_p values of XI and X terpolymers in the acidic and basic solutions are attributed to the higher interaction of the amide groups of DMAAm with other groups to improve the formation of hydrogen bonds.[25]

Figure 8H–J illustrates the C_p's for terpolymers XII (XII-10-05, XII-10-10, and XII-10-20) 10 mol % HEMA and 5, 10, and 20 mol % DMAMCA. At pH 1.4, pH 3.7, pH 5.6, pH 6.9 (DI), pH 9.7, and pH 12.6, the terpolymer XII-10-05 exhibited C_p temperatures of 31, 29.5, 26, 23.7, 23, and 21.5 °C, respectively; XII-10-10 exhibited C_p temperatures of 34, 32.8, 28.5, 23, 21.6, and 20 °C, respectively; and XII-10-20 exhibited C_p temperatures of 37.5, 35, 28.5, 19, 17.4, and 15 °C, respectively. The C_p values for terpolymers with styrene revealed the lowest C_p within all groups of copolymers and terpolymers at the lowest pH (pH 1.4, acidic solutions) and at the highest pH (pH 12.6, basic solutions). The domination of the hydrophobic groups in the terpolymer chains extensively appeared by going from the neutral solution to the basic solution. Figure S3A shows the relationship between the pH solutions and the C_p for PNIPAAm terpolymer groups (D−F). The highest C_p was recorded for the terpolymer XI-10-20 at pH 1.4, whereas the lowest C_p was recorded for the terpolymer XII-10-20 at pH 12.6. The lower critical solution temperatures of PNIPAAm copolymers (VII, VIII, and IX), and PNIPAAm terpolymers in pH 6.9 (deionized water) are shown in Figure S3B; the highest value of T_c was observed for VIII-20 (43.9 °C), and the lowest T_c was observed for XII-10-20 (18.5 °C).

Statistical analysis of the C_p for the PNIPAAm terpolymer in different pH solutions was performed using a one-way ANOVA test, as shown in Figure 9A. The standard errors (SE±) of the mean values for X-10-05, X-10-10, X-10-20, XI-10-05, XI-10-10, XI-10-20, XII-10-05, XII-10-10, and XII-10-20 were measured as 1.33951, 2.32648, 3.63083, 0.93645, 2.7519, 2.6668, 1.50503, 2.42441, and 3.875, respectively. It exhibited the highest SE ± for XII-10-20 and the lowest SE ± for X-10-05. The p-values were calculated for SE ± of the homo-PNIPAAm, PNIPAAm copolymer, and PNIPAAm terpolymer at pH 6.9 (DI water). The highest *p*-value was found to be 0.00746 (significantly less than 0.05), which indicates that there is no significant difference in the LCST means, as illustrated in Figure 9B.

Finally, a micro-differential scanning calorimeter was used to estimate the lower critical solution temperature of the homo-PNIPAAm, PNIPAAm copolymer, and PNIPAAm terpolymer at pH 6.9 (DI water); the instrument was run by cooling/heating at 1 °C/min. The thermograms were used to record the T_c's at each onset value. Polymers (IIIa, VII-10, VIII-10, IX-10-10, X-10-10, XI-10-10, and XII-10-10) were selected for these measurements; they exhibited their T_c's at (32.7, 38, 42.8, 27, 28, 33.5, and 22.6 °C), as shown in Figure 10(A−G) and Table 1. The differences between the measurements of the C_p's obtained by the turbidity test and the T_c's obtained using the micro-differential scanning calorimeter can be attributed to the mechanisms and physical parameters measured in each method.[45,76] The highest value for T_c was measured for the PNIPAAm copolymer VIII-10, whereas the lowest value was measured for the PNIPAAm terpolymer XII-10-10, as shown in Figure 10H.

3.7. Measuring the Cloud Point (C_p) in the Hofmeister Anions.

The cloud points (C_p's) of PNIPAAm copolymers and terpolymers were measured in different kosmotropic and chaotropic anion salt solutions. Three salts were chosen (sodium sulfate Na_2SO_4, sodium chloride NaCl, and sodium thiocyanate NaSCN) and dissolved in deionized water at different concentrations (0.1 to 0.5 wt %). The turbidity test was performed via a UV−vis spectrophotometer. The following samples were used in the measurements: VII-10, VIII-10, IX-10, X-10-10, XI-10-10, and XII-10-10; the transmittance/temperature diagram was obtained for all polymers in each salt concentration as shown in Figure 11A and Table 3. The first run was performed on the PNIPAAm copolymer VII-10 with 10 mol % HEMA in 0.1, 0.2, 0.3, 0.4, and 0.5 wt %. In a stronger kosmotropic anion, Na_2SO_4 solution, C_p's were measured as 33.5, 33, 31, 29, and 27.7 °C, whereas in a weak chaotropic salt solution, NaCl, C_p's were measured as 34.7, 34, 32.5, 32, and 31.4 °C. In a strong chaotropic solution, NaSCN, C_p's were measured as 35, 36, 37.6, 40, and 42 °C.

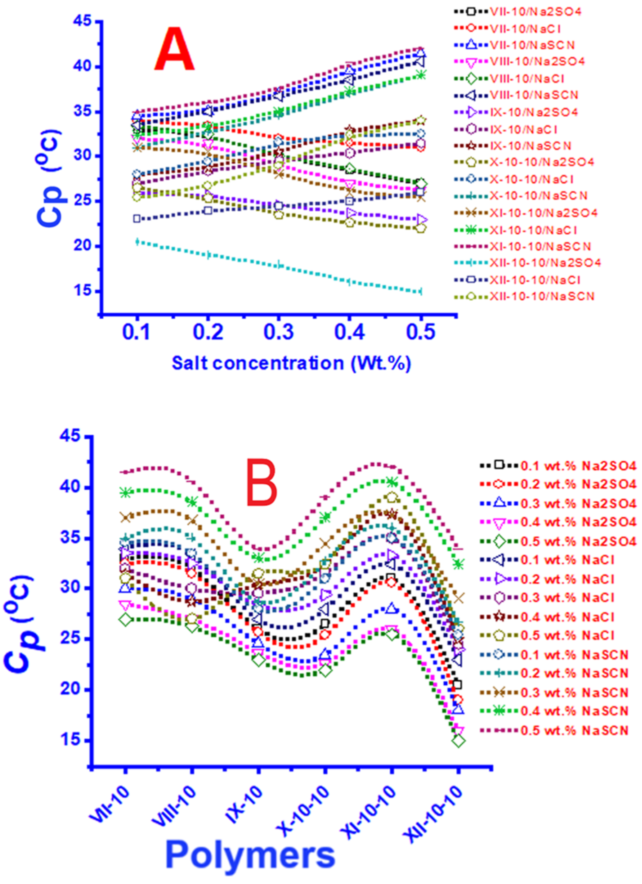


Figure 11. (A) C_p's of copolymers and terpolymers in 01, 02, 0.3, 0.4, and 0.5 wt % Na_2SO_4, NaCl, and NaSCN salt solutions. (B) C_p's of selected copolymers and terpolymers (10 mol %).

A decrease in C_p was observed with increasing Na_2SO_4 salt concentration due to the breaking in the hydrogen bonding; therefore, the domination of the hydrophobic chains restricted the hydrophilic chains and the speed of formation of the turbid solution. By using a weak chaotropic salt solution, the balance between the hydrophilic and hydrophobic chains switched to the hydrophilic side, which appeared in the C_p's. The strong chaotropic salt solution NaSCN exhibited the opposite effect to Na_2SO_4 by facilitating the formation of hydrogen bonds, increasing the hydrophilicity, slowing down the phase separation, and subsequently increasing the C_p's of the polymer solution.[45,54]

For the VIII-10 terpolymer, the C_p's were measured at 0.1, 0.2, 0.3, 0.4, and 0.5 wt % Na_2SO_4 as 32.5, 32, 30, 28, and 27 °C; in NaCl as 34, 33, 31, 29, and 28 °C; and in NaSCN as 34, 35.6, 37.3, 39.3, and 41 °C, respectively. For the IX-10 terpolymer with styrene, it exhibited C_p's in Na_2SO_4 as 26.4, 26, 25, 24, and 23.7 °C; in NaCl as 27.6, 29, 30, 31, and 32 °C; and in NaSCN as 28.6, 29, 31, 34, and 34.4 °C, respectively. The increase in C_p's is due to the hydrophobic chains caused by the aromatic ring of styrene combined with the effect of the sulfate group in Na_2SO_4 that led to the breaking of the hydrogen bonding between amide NIPAAm and water molecules, which spiked the separation of the polymer from the solution. The C_p's of PNIPAAm terpolymers in the Hofmeister salt solution exhibited a similar behavior to PNIPAAm copolymers with different values, which is due to

Table 3. Cloud Point C_p (50% Transmittance) for Selected Copolymers and Terpolymers with 10 mol % (DMAMCA) Influenced by Different Kinds and Concentrations of Salt Ions

polymer	C_p (°C) Na_2SO_4					C_p (°C) NaCl					C_p (°C) NaSCN				
	0.1 wt %	0.2 wt %	0.3 wt %	0.4 wt %	0.5 wt %	0.1 wt %	0.2 wt %	0.3 wt %	0.4 wt %	0.5 wt %	0.1 wt %	0.2 wt %	0.3 wt %	0.4 wt %	0.5 wt %
VII-10	33.5	33	31	29	27.7	34.7	34	32.5	32	31.4	35	36	37.6	40	42
VIII-10	32.5	32	30	28	27	34	33	31	29	28	34	35.6	37.3	39.3	41
IX-10	26/26.4	26	25	24	23.7	27.6	29	30	31	32	28.6	29	31	34	34.4
X-10-10	26.5/27	26	24	23	22.5	28.3	30	32	33	33.5	32	33	35	38	39.4
XI-10-10	31/31.5	31	39	26.6	26	33	34	35.5	38	39.4	35.5	3./6	38	41	43
XII-10-10	20.5/21	19.6	18.7	16.5	15.6	23.6	24.7	25	25.6	26.5	26	27	29.8	33	34.5

their influence by the incorporated monomers (HEMA, DMAAm, and S) besides DMAMCA. The interaction of all of the hydrophilic and hydrophobic groups with the polar groups and anions of the aqueous salt solution resulted in changes in C_p's in 0.1, 0.2, 0.3, 0.4, and 0.5 wt % terpolymers as the following: for X-10-10: 27, 26, 24, 23, and 22.5 °C; 28.3, 30, 32, 33, and 33.5 °C; and 32, 33, 35, 38, and 39.4 °C; for XI-10-10: 31.5, 31, 39, 26.6, and 26 °C; 33, 34, 35.5, 38, and 39.4 °C; and 35.5, 36, 38, 41, and 43 °C; and for XII-10-10: 21, 19.6, 18.7, 16.5, and 15.6 °C; 23.6, 24.7, 25, 25.6, and 26.5 °C; and 26, 27, 29.8, 33, and 34.5 °C.

The presence of DMAMCA resulted in lower C_p's in the Na_2SO_4 salt solution than copolymers with only HEMA or DMAAm (VII-10 and VIII-10) due to the effect of salt anions on the tertiary amine group and the aromaticity of DMAMCA. Both factors restricted the ionization and breaking of the hydrogen bonds, which resulted in fast phase separation with the higher salt concentrations. The opposite effect was observed in the case of the weak chaotropic salt (NaCl), in which the weak interaction of the salt resulted in C_p values being very close to those obtained in DI water (pH 6.9). The strong chaotropic salt solution (NaSCN) exhibited higher values of C_p's which increased with increasing salt concentration; these are lower than the values obtained for VII-10 and VIII-10, highlighting the effect of the hydrophobic chains produced by DMAACA. The terpolymer XII-10-10 offered lower values of C_p's than the corresponding copolymer IX-10 due to higher hydrophilicity based on the two aromatic rings (DMAMCA and S), as mentioned previously. Figure 11B illustrates the change of the C_p's for all polymers at different concentrations of salts. The statistical analysis of the mean values of C_p's of polymers in different concentrations of Na_2SO_4, NaCl, and NaSCN salts was performed by ANOVA one-way tests, as shown in Figure 12. The p-value was found to be 0.0076, well below 0.05, indicating no significant difference in the mean values of the C_p's.

4. CONCLUSIONS

This study offers a thorough comparison between homo-PNIPAAm, groups of thermoresponsive copolymers based on

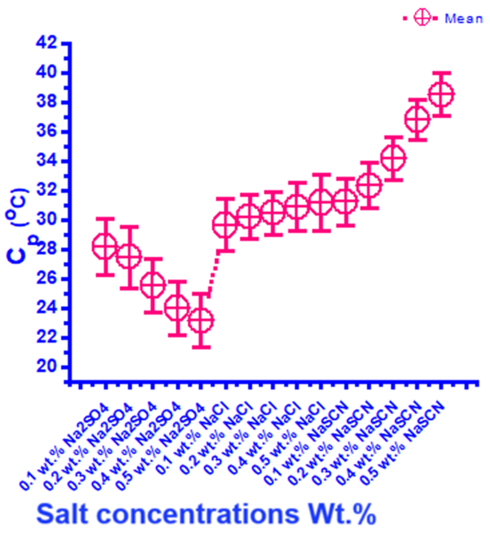


Figure 12. ANOVA test (standard error ± SE and mean C_p's) for terpolymers with different salt concentrations.

N-isopropylacrylamide with 5, 10, and 20 mol % HEMA, DMAAm, and S, and groups of thermo-pH terpolymers by incorporating 5, 10, 20 mol % of a new cationic monomer called 2-((dimethylamino)methyl)-4-methylphenyl acrylate (DMAMCA) into NIPAAm and 10 mol % HEMA, DMAAm and S. The molecular weight and dispersity of the polymers exhibited a decrease with increasing the mol % of the incorporated monomers in all groups. The glass transition temperature exhibited a similar behavior. The hydrophilicity of the copolymers, measured by the contact angle, revealed higher hydrophilic properties with lower contents of HEMA and DMAAm. An opposite behavior was observed with styrene. The cloud points of copolymers and terpolymers were influenced by the change in the hydrophilic and hydrophobic properties of the polymer chains. While PNIPAAm exhibited a C_p of 32 °C, the highest C_p in the copolymer groups was measured at 43.9 °C and the lowest LCST was measured at 21 °C. Moreover, the terpolymers manifested the greatest C_p at 47 °C and the lowest C_p at 14.6 °C. The effect of Hoffmeister anions with different salt concentrations on the C_p exhibited a variation of temperatures in different salt solutions (Na_2SO_4, NaCl, and NaSCN) and concentrations (0.1 to 0.5 wt %). The highest C_p was observed at 42 °C, whereas the lowest C_p was measured at 15 °C. The ability to vary the phase transition temperatures through different means and methods will allow us to exploit more applications of these smart polymers in sensors and biotechnology.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acsomega.3c06634.

> Synthesis of homo-PNIPAAm; ^{1}H NMR ($CDCl_3$) of poly NIPAAm (IIIa) (Figure S1); FT-IR of homo-PNIPAAm (Figure S2); T_c of all terpolymers in various pH solutions (Figure S3A); and T_c of homo-, co-, and terpolymers in DI water (pH 6.9) (Figure S3b) (PDF)

■ AUTHOR INFORMATION

Corresponding Author

Nidal Abu-Zahra − *Materials Science and Engineering Department, University of Wisconsin-Milwaukee, Milwaukee, Wisconsin 53201, United States;* orcid.org/0000-0003-3726-6219; Email: nidal@uwm.edu

Author

Momen S. A. Abdelaty − *Polymer Institute of the Slovak Academy of Sciences, 845 41 Bratislava, Slovakia; Polymer Lab, Chemistry Department, Faculty of Science, Al-Azhar University, Assiut 71524, Egypt*

Complete contact information is available at: https://pubs.acs.org/10.1021/acsomega.3c06634

Notes

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