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DEVELOPMENT OF NOVEL TEMPERATURE RESPONSIVE POLYMERIC SORBENTS AND THEIR APPLICATIONS IN WATER REMEDIATION

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DEVELOPMENT OF NOVEL TEMPERATURE RESPONSIVE POLYMERIC SORBENTS AND THEIR APPLICATIONS IN WATER REMEDIATION

DISSERTATION

A dissertation submitted in partial fulfillment of the
requirements for the degree of Doctor of Philosophy in the
College of Engineering
at the University of Kentucky

By
Shuo Tang
Lexington, Kentucky
Director: Dr. J. Zach Hilt, Professor of Chemical and Materials Engineering

Lexington, Kentucky
2018

ABSTRACT OF DISSERTATION

DEVELOPMENT OF NOVEL TEMPERATURE RESPONSIVE POLYMERIC SORBENTS AND THEIR APPLICATIONS IN WATER REMEDIATION

Water remediation utilizing sorption has found strong interest due to its inexpensiveness, universal nature and ease of operation. In particular, thermo-responsive sorbents consisting of N-isopropylacrylamide (NIPAAm) offer significant potential as "smart" and advanced materials to remove multiple aqueous pollutants. NIPAAm exhibits excellent thermo-responsiveness, which senses the external temperature variation and changes its swelling and sorption behaviors in a sharp and rapid manner. At the beginning of this work, an extensive review of literature has been compiled to provide a summary of NIPAAm-based thermo-responsive sorbents in water/wastewater remediation applications.

Initially, we developed a novel approach to synthesize and characterize NIPAAm copolymeric hydrogels. Four different polyphenolic crosslinkers including curcumin multiacrylate (CMA), quercetin multiacrylate (QMA), 4,4'-dihydroxybiphenyl diacrylate (44BDA) and chrysin multiacrylate (ChryMA) were successfully incorporated into crosslinked hydrogels. Their temperature responsiveness and lower critical solution temperature (LCST) were characterized using swelling studies and differential scanning calorimetry (DSC). Increasing the crosslinker content resulted in a significant decrease in the swelling ratio and LCST, which was due to the increased crosslinking and hydrophobicity introduced by the polyphenolic crosslinkers.

We also demonstrated the application of two sets of aforementioned crosslinked hydrogels (NIPAAm-co-CMA and NIPAAm-co-44BDA) as effective gel sorbents to capture phenol as a model contaminant. Temperature-dependent sorption was evaluated through a binding study of phenol at 10°C and 50°C. Significant enhancement in the sorption was observed at 50°C, and this can be attributed to the phase transition induced hydrophobic interactions between the copolymer gel and phenol. Moreover, the obtained hydrogels possessed facile and efficient regeneration ability in water at 10°C, without requiring harsh solvent treatment or high energy input.

Building on the sorption behavior observed with crosslinked NIPAAm hydrogels, we extended the investigation to linear copolymer systems, and these were demonstrated as a temperature responsive flocculants. Here, NIPAAm copolymers consisting of 2-phenylphenol monoacrylate (2PPMA) were successfully developed as smart flocculants to remove metal oxide nanoparticles (e.g., Fe_3O_4, CeO_2, TiO_2). The incorporation of 2PPMA enhanced the flocculation at temperatures above the LCST (e.g., 50°C), which was due to the combined hydrophobicity of 2PPMA and NIPAAm. Overall, NIPAAm-based sorbents have a variety of applications in aqueous pollutant removal and are a promising class of materials for cost-effective water remediation technology.

KEYWORDS: Temperature Responsive Hydrogel, NIPAAm, Sorption, Polymeric Sorbents, Polymeric Flocculent, Water Remediation

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DEVELOPMENT OF NOVEL TEMPERATURE RESPONSIVE POLYMERIC SORBENTS AND THEIR APPLICATIONS IN WATER REMEDIATION

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Chapter 1 Introduction

Water pollution due to toxic substances remains a serious environmental issue. The common aqueous contaminants such as heavy metals, dyes, persistent organic pollutants (POPs), and biological impurities are known to be toxic or carcinogenic (Yang, 2011; Jing et al., 2013). Therefore, their presence in the environment should be controlled. Strict legislation on the discharge of these toxic compounds makes it necessary to develop efficient technologies to remove them from wastewater (Crini, 2005). Over the past few decades, stimuli-responsive materials (SRMs) have been developed as an effective tool for aqueous pollutants removal. SRMs rapidly change their configuration, dimension or physical properties with small changes in the appropriate stimuli such as temperature, moisture, pH, electricity, light, magnetic field, and solvent (Roy et al., 2010; Hu et al., 2012). N-isopropylacrylamide (NIPAAm), as one of the most widely studied SRMs, is well known for the temperature-responsive properties. NIPAAm displays temperature controlled hydrophilic-hydrophobic phase transition or a so-called lower critical solution temperature (LCST) at around 32℃ in water. The temperature swing causes the NIPAAm polymeric network to swell or shrink at temperature below or above the LCST. Moreover, by introducing hydrophobic/hydrophilic functional groups, the LCST of NIPAAm can be tuned to a desired temperature range (Wu and Tian, 2008). Due to these unique properties, NIPAAm has demonstrated applications in many fields such as drug delivery, sensing, tissue engineering, controlled separation, etc (Qiu and Park, 2001; Schmaljohann, 2006; Klouda and Mikos, 2008; Roy et al., 2013). Recently, there has been a growing interest in the development of NIPAAm based smart materials for environmental applications, in particular, the removal and recovery of pollutants from water/wastewaters. NIPAAm has been incorporated into various forms of materials including sorbents, flocculants, membranes, etc, leading to a broad range of applications in treating different kinds of aqueous pollutants.

This dissertation provides an investigation and discussion into applications of NIPAAm based thermoresponsive smart materials for water remediation. These advanced materials represent interesting and attractive alternatives to conventional remediation tools due to their physicochemical characteristics, stimuli-responsive property, and controlled separation ability. To enhance the understanding of the application and mechanism of this particular system, an extensive review of literature was compiled in chapter 2 to provide a summary of current knowledge of NIPAAm based thermoresponsive materials in water/wastewater remediation. Chapter 3, 4, and 5 focus on the development of hydrophobically modified hydrogels that consisting of NIPAAm and four different novel crosslinkers including curcumin multiacrylate (CMA), quercetin multiacrylate (QMA), 4,4'-dihydroxybiphenyl diacrylate (44BDA), and chrysin multiacrylate (ChryMA). The goal was to study the impact of hydrophobic crosslinkers on the behaviors and properties of NIPAAm hydrogels. Chapter 6 and chapter 7 focus on the application of the smart materials. In particular, chapter 6 evaluated the application of crosslinked hydrogels as pollutant sorbents through batch binding studies to a model contaminant phenol. Two sets of the aforementioned hydrogels (NIPAAm-co-CMA and NIPAAm-co-44BDA) were tested. The effect of temperature, crosslinker density, and phase transition was studied through phenol binding studies at 10°C and 50°C. To demonstrate the recyclable use of the gel sorbents, a desorption study was conducted to release bound phenol in water at 10°C. In chapter 7, novel thermoresponsive polymeric flocculants based on NIPAAm and 2-

phenylphenol monoacrylate (2PPMA) were developed. The flocculation performance was evaluated through metal oxide nanoparticles (MONPs) removal studies. We found that the addition of hydrophobic comonomer has shown enhanced flocculation efficiency in comparison with poly(NIPAAm). Dense solid-like sediments and clear supernatant were produced due to the effective compaction of hydrophobic copolymer-MONP precipitates.

1.1 Specific Objectives

The overall objective of this research was to develop novel temperature-responsive polymeric materials (i.e., hydrogels, flocculants) for the removal of aqueous pollutants. This involved three projects, and the specific objectives are outlined below:

1. Development of thermo-responsive hydrogels based on N-isopropylacrylamide and novel hydrophobic polyphenolic crosslinkers
    a. Synthesize and characterize the novel polyphenolic crosslinkers including CMA, QMA, 44BDA, and ChryMA
    b. Development of NIPAAm polymeric hydrogel systems with the incorporation of hydrophobic crosslinkers through free radical polymerization
    c. Perform physiochemical characterizations to verify the successful synthesis of the copolymer hydrogels
    d. Evaluate the temperature responsive behaviors through swelling studies, LCST measurement, etc
2. Investigation of smart adsorption and efficient regeneration of thermo-responsive hydrogels on phenol removal from water
    a. Synthesize and characterize NIPAAm-co-CMA and NIPAAm-co-44BDA gels with improved approach

   b. Evaluation of the pollutant removal efficiency through phenol binding studies, which include: temperature dependent binding, binding isotherms, etc
   c. Demonstrate the facile desorption of bound phenol in water through temperature variation
3. The removal of metal oxide nanoparticles using N-isopropylacrylamide based copolymer flocculants
   a. Synthesize novel thermo-responsive polymeric flocculants through copolymerizing NIPAAm with 2PPMA
   b. Perform physicochemical characterization to verify successful synthesis
   c. Conduct flocculation kinetic tests with poly (NIPAAm) and NIPAAm-co-2PPMA copolymer in batch studies of removing Fe_3O_4 nanoparticles
   d. Compare the flocculation efficiency of poly (NIPAAm) and NIPAAm-co-2PPMA copolymer in three MONP suspensions including Fe_3O_4, TiO_2, CeO_2

Chapter 2 N-isopropylacrylamide (NIPAAm)-based thermoresponsive materials for water remediation

2.1 Introduction

Temperature responsive polymers are considered “smart” materials that can exhibit different properties and behaviors depending on the surrounding temperature (Aguilar and San Román, 2014a; Aguilar and San Román, 2014b; Ng et al., 2018). As one of the most widely studied temperature responsive systems, N-isopropylacrylamide (NIPAAm) polymers have demonstrated their versatile application in a variety of industries including drug delivery systems (Bae, 2002; Hoffman, 2013; James et al., 2014; Lakkadwala et al., 2015), tissue engineering (Ohya et al., 2001; Da Silva et al., 2007; Tan et al., 2009), controlled separation process (Kayaman et al., 1998; Umeno et al., 1998; Carter et al., 2006), etc. In recent years, numerous approaches have been studied for the development of NIPAAm-based thermo-responsive sorbents and their applications in wastewater remediation. These advanced materials represent attractive alternatives to conventional sorbents due to their physicochemical characteristics, stimuli-responsive properties, and controlled separation ability for selective pollutants. The adsorptive performance of these smart sorbents has been illustrated through a wide range of aquatic pollutants (Saitoh et al., 2011; Wu et al., 2011; Atta et al., 2015; Mahida and Patel, 2016d). It is necessary to enhance the understanding of how these materials are applied and the mechanisms of their adsorptive behaviors. In this chapter, an extensive list of literature has been compiled to provide a summary of current knowledge of NIPAAm-based thermo-responsive materials in water/wastewater remediation applications. The main objectives are to provide useful information about the most important features of NIPAAm-based sorbents and to give an overview of several applications. Major pollutants that have been treated with NIPAAm sorbents are listed first. Then, the synthesis and chemistry of five of the most studied NIPAAm sorbents are outlined, along with their characteristics, advantages and limitations. Applications and contaminant removal mechanisms are discussed in detail, as well as the adsorbent recovery and regeneration. This chapter will aim to serve as a summary of the work reported in the literature on NIPAAm from the respective of smart adsorbent applications.

2.2 Temperature Responsive Adsorption

A number of methods such as coagulation, membrane process, adsorption, foam flotation, photocatalytic degradation, and biological methods have been used to remove aquatic pollutants (Bhatnagar and Sillanpää, 2009). Adsorption is one of the most popular techniques due to its ease of operation and low cost of application (Gong et al., 2016a). Over the past few years, “smart” responsive sorbents have appeared in the literature with increasing frequency. In particular, the responsive sorbents based on NIPAAm have shown superior performance in the removal and recovery of various aqueous pollutants. NIPAAm has become perhaps the most popular “smart” compound due to its reversible hydrophilic/hydrophobic phase transition in an aqueous medium with respect to temperature change (Schild, 1992b). The transition occurs abruptly at what is known as the lower critical solution temperature (LCST) around 32°C (Elaissari and Bourrel, 2001; Lutz et al., 2006; Ono and Shikata, 2007; Liu et al., 2009). Since the LCST is close to physiological temperature, the phase transition of NIPAAm has been extensively studied in smart drug delivery systems (Schmaljohann, 2006; Bajpai et al., 2008; Chacko et al., 2012; Cheng et al., 2013). Recently, NIPAAm has also been demonstrated as an ideal candidate for developing controlled separation systems (Chen and Huffman, 1990; Kayaman et al., 1998; Liang et al., 1999; Hoffman, 2000; Thivaios and Bokias, 2010; Liu et al., 2011; Zhou et al., 2017). NIPAAm crosslinked gel networks exhibit temperature-dependent swelling/shrinking property, allowing for the control of adsorption and desorption of aqueous pollutants by changing the temperature. In addition, NIPAAm is capable of inducing direct or indirect binding interactions with a wide range of pollutants. The direct binding interaction is mainly attributed to the phase transition induced hydrophobicity at temperature above LCST, which provides strong binding affinity towards most hydrophobic/aromatic organic pollutants. Whereas the indirect binding comes from the copolymerized functionalities, which binds multiple pollutants through various interactions. It is well known that the properties of NIPAAm can be tailored to some extent by the incorporation of comonomers. For example, the LCST of NIPAAm, the hydrophilicity of the polymer chain, the swelling/shrinking rate of the polymeric network, and the selectivity of target pollutants can all be modified (Huffman et al., 1986). In most cases, NIPAAm copolymer gels consist of at least two functioning parts, each having a different role. Usually, the comonomer provides adsorption affinity toward specific pollutants, and NIPAAm mediates the swelling/shrinking of the polymer network as well as the hydrophilic/hydrophobic property of the sorbents. The change of NIPAAm in turns affects the adsorption performance of the pollutants, resulting in a temperature responsive binding or releasing of the sorbents. Compared to conventional sorbents such as commercial activated carbons and synthetic ion-exchange resins, the use of NIPAAm based smart sorbents offers several potential advantages: tunable binding affinity, low-cost regeneration, versatile in material design, high capacity and rate of adsorption, target adsorption through copolymerizing, etc.

2.3 Pollutants

Heavy metals are one of the largest categories of inorganic aqueous pollutants, which originate from process industries, mining and mineral processing, leather tanning, agricultural and anthropogenic activities (Salomons and Förstner, 1980; Lake et al., 1984; Vernet, 1991; Fu and Wang, 2011; Salomons et al., 2012). Many metals (e.g., Zn, Cu, Pb, Cd, etc.) have harmful effects on human physiology and other biological systems when they are found above the tolerance levels (Snowden et al., 1993; Budinova et al., 1994). Therefore, the removal of heavy metals from aqueous solution is of considerable importance. Numerous studies have investigated the application of smart NIPAAm sorbents on removing toxic metal ions from wastewater (Morris et al., 1997; Saitoh et al., 2003; Yamashita et al., 2003; Kanazawa et al., 2004; Tokuyama et al., 2006; Iyer et al., 2007; Tokuyama and Iwama, 2007; Iyer et al., 2008c; Wu and Tian, 2008; Tokuyama and Iwama, 2009; Fukuoka et al., 2010; Zhang et al., 2012; Kasgoz et al., 2013; Taşdelen et al., 2013; Yan et al., 2013; Cheng et al., 2015; Kim et al., 2015; Mahida and Patel, 2016c; Ozbas et al., 2016; Cheng et al., 2017). In most cases, the adsorption effects are not from NIPAAm but from the incorporated comonomer functional groups. NIPAAm plays a role in controlling the permeation of metal ions through the temperature-mediated swelling/shrinking. Due to the incorporation of functional comonomers, target adsorption to specific metal ions can be achieved. Since most metal ions are positively charged, anionic functional comonomers such as acrylic acid (AAc), acrylamide (AAm), and maleic acid (MA) are reported to combine with NIPAAm to provide target affinity to metal ions through complexation or chelation interactions.

Organic dyes are another large category of aqueous pollutants due to their broad applications in textile, paper production, and coloring industries (Reife et al., 1996; Martínez-Huitle and Brillas, 2009; Pereira and Alves, 2012; Chequer et al., 2013). Dyes are classified based on their structure as azo (60-70%), anthraquinones (15%), triarylmethanes (3%), phthalocyamine(2%), indigoid, oxazine, riphenylmethyl, etc (Reife et al., 1996; Tehrani-Bagha and Holmberg, 2013). Most dyes are chemically stable, and they usually contain complex aromatic structures, resulting in high toxicity to humans and persistent existence to environment (Ganesh et al., 1994; Puvaneswari et al., 2006; Padhi, 2012). The applications of thermo-responsive sorbents in dye removal have also been widely studies (Parasuraman and Serpe, 2011b; Parasuraman et al., 2012a; Parasuraman et al., 2013; Kureha et al., 2014; Yao et al., 2015; Kureha et al., 2016; Mahida and Patel, 2016d; Jiang et al., 2017; Śliwa et al., 2017). Similar to heavy metals, NIPAAm does not typically induce direct affinity to dyes, but the adsorption effects come mostly from the comonomer functionalities. Based on the anionic or cationic nature of dyes, the comonomer functionality might differ from one another, so does the binding mechanisms. However, there is an interesting example reported by Mahida et al. that the NIPAAm-co-N,N-diallyl carboxypiperidinium bromide (DACPB) nanogel system they developed could show both cationic and anionic nature in a single fragment (Mahida and Patel, 2016b). The amphoteric nature of the nanogel was capable of binding a large selection of dyes including cationic, anionic, azo and reactive.

The third class of hazardous wastes that have been frequently found in water is persistent organic pollutants (POPs), which include phenols, biphenyls, polychlorinated biphenyls (PCBs), polyaromatic hydrocarbons (PAHs), organochlorine compounds, pesticides, fertilizers, plasticizers, organic matters, etc (Wegman et al., 1986; Ali et al., 2012; Rashed, 2013). Due to their potential acute toxicities and carcinogenic nature, water pollution caused by POPs has become a severe issue to humans and animals (Organization, 2010). Many research groups have investigated the adsorptive removal of organic pollutants using NIPAAm, and these studies have mainly focused on the removal of phenolic compounds including phenol (Igarashi et al., 2004; Pan et al., 2008; Saitoh et al., 2009; Gong et al., 2016a) and its derivatives (e.g., 4-nitrophenol (4-NP), nonylphenol) (Zhen et al., 2015; Begum et al., 2017), bisphenol A (BPA) (Gong et al., 2016b), humic acid (Tokuyama et al., 2010), PCBs and trichloroethylenes (TCEs) (Xiao et al., 2013). In contrast to heavy metals and dyes, organic pollutants are usually degradable. Li et al. developed Fe/Pb nanoparticles immobilized NIPAAm hydrogel systems for the detoxification of PCBs, aimed to capture and transfer the persistent contaminants to less harmful products (Xiao et al., 2013). Similarly, silver nanoparticles embedded NIPAAm-co-AAm microgels were developed by Begum et al. for the reduction of 4-NP to 4-aminophenol (4-AP) (Begum et al., 2017). Rapid adsorption and nearly 100% degradation rate were achieved in both studies, indicating a great potential modification in scale-up applications. In general, POPs exhibit strong hydrophobicity due to the presence of aromatic groups, which allows for the direct binding to NIPAAm through hydrophobic interactions at temperature above LCST. Recent progress using NIPAAm based thermoresponsive materials to remove aqueous pollutants has been summarized in Table 2. 1. The detailed binding mechanisms of all interactions are discussed in later sessions.

Table 2. 1 Summary of water remediation applications using NIPAAm based temperature responsive materials

Pollutants	**Material form**	**Functional component**	**Binding mechanism**	**$Q_{Low\ T}/Q_{High\ T}$**	**Time**	**Low T/ High T**	**pH**	**Reference**
Removal of Heavy metals								
Cu	Micro/ nanogel	Poly(NIPAAm-MAA)	Chelation	$0.1 mmol \cdot g^{1}/0.7 mmol \cdot g^{-1}$	48h	5°C/50°C	-	(Wu and Tian, 2008)
Cu	Hydrogel	Poly(NIPAAm-AM-MA)	Chelation	$24.4 mg \cdot g^{-1}$	48h	30°C/50°C	-	(Cheng et al., 2015)
Cu	Microgel	Poly(NIPAAm-VbEDA)	Chelation	$2.5 mg \cdot g^{-1}$	100min	10°C/50°C	-	(Kanazawa et al., 2004)
Cu	Hydrogel (IPN)	Poly(NIPAAm), Poly(NaAAc)	Complexation	$0.2 mmol \cdot g^{-1}$	12h	20°C/50°C	-	(Yamashita et al., 2003)
Cu	Hydrogel Polymer	Poly(NIPAAm-MEP)	Chelation	$0.016\ mmol \cdot g^{1}/0.022 mmol \cdot g^{-1}$ $0.034\ mmol \cdot g^{1}/0.014 mmol \cdot g^{-1}$	24h	10°C/60°C	5.2	(Tokuyama et al., 2006)
Cu	Hydrogel	Poly(NIPAAm)	Hydrophobic interaction, complexation	$0.002 mmol \cdot g^{-1}/0.01\ mmol \cdot g^{-1}$	24h	10°C/50°C	-	(Tokuyama and Iwama, 2007)
Cu	Grafted polymer	Cell-g-poly(NIPAAm)	Hydrophobic interaction, complexation	$1.2 mmol \cdot g^{-1}$	48h	10°C/50°C	3.0-6.0	(Kasgoz et al., 2013)
Cu, Cr	Polymer & Grafted polymer	Poly(NIPAAm)	Complexation	-	24h	25°C/50°C	4.1-4.5	(Tokuyama et al., 2010)

Table 2. 1 (continued)

Cu Ni Cd Pb	Grafted polymer	Cell-g-Poly(NIPAAm)	Hydrophobic interaction, complexation	1.05mmol·g^{-1} 0.44mmol·g^{-1} 0.85mmol·g^{-1} 0.38mmol·g^{-1}	48h	20°C/50°C	-	(Ozbas et al., 2016)
Cu, Pb, etc	Polymer	Poly(NIPAAm-Im)	Chelation	-	-	20°C/50°C	5.0-9.0	(Saitoh et al., 2003)
Pb	Microgel	Poly(NIPAAm-AAc)	Electrostatic interaction	-	15min	20°C/60°C	3.0-8.0	(Morris et al., 1997)
Pb Hg	Nanogel	Poly(NIPAAm-DAPBD-AA)	Electrostatic interaction	1250mg·g^{-1} 1111mg·g^{-1}	16h	25°C	2.0-12.0	(Mahida and Patel, 2016c)
In	Polymer	Poly(NIPAAm)	Hydrophobic interaction, complexation	1mmol·g^{-1}	24h	20°C/50°C	0-3.3	(Tokuyama and Iwama, 2009)
Cd	Hydrogel	Poly(NIPAAm-TPEN)	Complexation	-	1h	5°C/45°C	2.1-5.3	(Fukuoka et al., 2010)
Li	Microgel	Poly(NIPAAm-M12C4)	Complexation	1.4mg·g^{-1}	20min	25°C/50°C	-	(Kim et al., 2015)
Ca	Grafted polymer	Poly(NIPAAm-VBEDA)	Chelation	0.2mg·g^{-1}/7.0mg·g^{-1}	35min	20°C/60°C	-	(Sakohara et al., 2013b)
Ni	Hydrogel	Poly(NIPAAm-HBCalix)	Chelation	4.0mg·g^{-1}	3h	10°C/50°C	-	(Yan et al., 2013)
Lanthanide	Coreshell NPs	Poly(NIPAAm-NVP)	Chelation	-	10min	20°C/40°C	2.9-5.6	(Park et al., 2014)
Removal of Dyes								
Orange II	Microgel	Poly(NIPAAm-Vim)	Electrostatic interaction	1.4 mg·g^{-1}/3.0mg·g^{-1}	20min	20°C/50°C	4.0-9.0	(Śliwa et al., 2017)
Orange II	Microgel	Poly(NIPAAm-AAc)	Hydrophobic interaction	-	5min	20°C/50°C	-	(Parasuraman et al., 2013)

Table 2. 1 (continued)

Orange II	Microgel	Poly(NIPAAm-AAc)	Hydrophobic interaction	0.12μmol·g^{-1}	12min	23°C/50°C	3.0,7.0	(Parasuraman et al., 2012a)
Orange II	Hydrogel (IPN)	Poly(NIPAAm-AAm)	Hydrophobic interaction	-	24h	25°C/40°C	-	(Guilherme et al., 2003)
Orange II	Grafted polymer	Poly(NIPAAm-DPMA)	Electrostatic interaction	Up to 20mg·g^{-1}	500min	25°C/50°C	-	(Jiang et al., 2017)
MB	Hydrogel	Poly(NIPAAm-MAA)	Electrostatic interaction	0.4mmol·g^{-1}	24h	20°C/50°C	8.4	(Huffman et al., 1986)
MB	Composite hydrogel	Poly(NIPAAm-IA)	Electrostatic interaction	Up to 22.62mg·g^{-1}	24h	25°C	6.5-6.7	(Taşdelen et al., 2017)
MB	Grafted polymer	Poly(NIPAAm)	Electrostatic interaction	10.4 mg·g^{-1}/23.8mg·g^{-1}	300min	25°C/45°C	-	(Jiang et al., 2016a)
CBB	Hydrogel	Poly(NIPAAm-MAA)	Electrostatic interaction	21.9 mg·g^{-1}/23.6mg·g^{-1}	24h	20°C/50°C	8.4	(Huffman et al., 1986)
Reactive red dye	Hydrogel (IPN)	Poly(NIPAAm-ATPMACl)	Electrostatic interaction	Up to 1428.6mg·g^{-1}	12h	0°C/80°C	3.5-9.5	(Yao et al., 2015)
Reactive red dye	Nanogel	Poly(NIPAAm-DACPB-APTAC)	Electrostatic interaction	909.1mg·g^{-1}	2h	-	2.0-12.0	(Mahida and Patel, 2016a)
R6G Erythrosine	Microgel	Poly(NIPAAm)	Hydrophobic interaction	1.0 mg·g^{-1}/2.3mg·g^{-1} 0.8 mg·g^{-1}/1.7mg·g^{-1}	5min	20°C/40°C	-	(Kureha et al., 2014)
R6G Erythrosine	Microgel	Poly(NIPAAm-AAc)	Hydrophobic interaction	41 mg·g^{-1}/55mg·g^{-1} 2.3 mg·g^{-1}/3.2mg·g^{-1}	5min	20°C/40°C	3.5-7.0	(Kureha et al., 2016)
Organic pollutants								
Phenol	Hydrogel	Poly(NIPAAm-TBP)	Hydrophobic interaction	-	60h	25°C	-	(Pan et al., 2008)

Table 2. 1 (continued)

Phenol	Hydrogel	Poly(NIPAAm-TBP)	Hydrophobic interaction	Up to 1.6mg·g^{-1}	24h	25°C	-	(Igarashi et al., 2004)
Phenols	Polymer	Poly(NIPAAm-chitosan)	Hydrophobic interaction, complexation	-	2h	30°C/60°C	-	(Saitoh et al., 2011)
Phenol	Polymer	Poly(NIPAAm-chitosan)	Hydrophobic interaction, complexation	18.9mg·g^{-1}	2h	30°C/60°C	6.8	(Saitoh et al., 2009)
Phenolic	Polymer	Poly(NIPAAm-PAA)	Hydrophobic interaction, complexation	300mg·g^{-1}	10min	30°C/40°C	6.8	(Saitoh et al., 2012)
Phenol Hydroquinone BPA	Coreshell NPs	Poly(NIPAAm)-GO	Hydrogen bonds interaction	Up to 12.74mg·g^{-1} Up to 54.2mg·g^{-1} Up to 14.6mg·g^{-1}	30h	15°C/35°C	7.0	(Saitoh et al., 2009; Saitoh et al., 2012; Gong et al., 2016a)
BPA	Composite NPs	Poly(NIPAAm)-PAC	-	247.532mg·g^{-1}	48h	25°C/40°C	7.0	(Gong et al., 2016b)
4-nonylphenol	Hybrid microgel	Poly(NIPAAm-AAm)	Catalytic reduction	-	-	-	-	(Begum et al., 2017)
Nonylphenol	Magnetic composite gel	Poly(NIPAAm)-Chitosan-Fe_3O_4	Chelation	116 mg·g^{-1}/123mg·g^{-1}	24h	20°C/40°C	5.0-9.0	(Zhen et al., 2015)
Organic	Polymer	Poly(NIPAAm)	Hydrophobic interaction	-	5min	25°C/37°C	3.5-9.0	(Saitoh et al., 1999)
Waste Solids								
Waste particles	Polymer	Poly(NIPAAm)	Hydrophobic interaction	-	2h	22°C/50°C	6.0±0.2	(Franks et al., 2009)

Table 2. 1 (continued)

Waste solids	Polymer	Poly(NIPAAm-AAc)	Hydrophobic interaction	99.2% removal	25min	25°C/40°C	<5.0	(Contreras-Andrade et al., 2015)
Surfactant	Coreshell microgel	Poly(NIPAAm-VP-DMAEM)	Hydrophobic and electrostatic interactions	Up to 1g·g^{-1}	7d	25°C	3.0-7.0	(Bradley et al., 2007)
Silica	Polymer	Poly(NIPAAm)	Hydrophobic interaction	-	24h	22°C/50°C	6.0±0.2	(Li et al., 2009)
TiO2	Polymer	Poly(NIPAAm-DMAPAA)	Hydrophobic interaction	-	40min	30°C/60°C	3.0-11.0	(Sakohara and Nishikawa, 2004)
Clay	Polymer	Poly(NIPAAm-AA-NTBA)	Hydrophobic interaction	-	24h	22°C/50°C	8.3	(Gumfekar and Soares, 2018)
TiO2	Polymer	Poly(NIPAAm-DDMACl)	Hydrophobic interaction		30min	23°C/55°C	7.3	(Deng et al., 1996)
Kaolin particles	Polymer	Poly(Naema IPAAm-BAAM-AAc)	Hydrophobic interaction	-	30min	23°C/40°C	4.3	(Sakohara et al., 2013a)
Kailin	Polymer	Poly(NIPAAm)	Hydrophobic interaction	-	50min	30°C/60°C	-	(Sakohara et al., 2002)
Kaolin	Polymer	Poly(NIPAAm-AEMA-MAAmBo)	Hydrophobic interaction	-	30min	25°C/50°C	7.0-11.0	(Lu et al., 2015)

2.4 Synthesis and Characterization of NIPAAm Based Sorbents

2.4.1 NIPAAm hydrogels

Hydrogels are crosslinked polymeric networks that can absorb large amount of water while maintaining the structure (Qiu and Park, 2001; Peppas et al., 2006). They are commonly referred as macroscopic gels, which are in "bulk" state with a size larger than one millimeter (Peppas et al., 2000). NIPAAm hydrogels are commonly reported to be prepared by free radical/redox polymerization at room temperature with the presence of ammonium persulfate (APS) and tetramethylethylenediamine (TEMED) as the initiator and accelerator, respectively. There are also cases that APS or Azobisisobutyronitrile (AIBN) is used as the thermal initiator, and the reaction then takes place at elevated temperatures (50°C-80°C) without the presence of TEMED. NIPAAm bulk gels are synthesized using homogeneous polymerization techniques, wherein NIPAAm, comonomer and/or crosslinker, and initiator are homogeneously mixed in a single medium (Khan and Lo, 2016). Water is frequently used as the solvent due to the aqueous solubility of NIPAAm. However, depending on the solubility of comonomers, organic solvents such as DMSO, THF, and benzene have been applied as well (Cole et al., 1987; Schild, 1992b; Tang et al., 2017b). One of the most widely used commercial crosslinkers is N,N'-methylenebis(acrylamide) (BIS/MBAAm); other types of crosslinker have also been developed to provide specific functionalities (Dias et al.; Tang et al., 2017a; Tang et al., 2017b). Hydrogels can be made in a variety of morphologies such as cylinder, bead, sheet, etc. After the completion of synthesis, gels are washed with excess amount of solvent and dried completely. The temperature dependent swelling study is one of the most important characterizations of NIPAAm hydrogels. The swelling ratio, which indicates the water absorption capacity, is commonly expressed by Q (mass swelling ratio). Q can be measured gravimetrically and calculated from the following equations:

$$\mathrm{Q} = M_{swollen}/M_{dry} \qquad \text{Equation 2.1}$$

$$\mathrm{Q} = (M_{swollen} - M_{dry})/M_{dry} \qquad \text{Equation 2.2}$$

Where $M_{swollen}$ is the gel equilibrium swollen mass and M_{dry} is the gel dry mass. Another important characterization is the measurement of LCST, which indicates the phase transition temperature of NIPAAm gel. LCST can be readily obtained from differential scanning calorimetry (DSC), where an endothermic peak is associated with the LCST; or from the swelling curve plotted as a function of temperature, the temperature at which Q decreases to half of the total change value is considered as the LCST (Yan et al., 2013).

The most attractive characteristics of NIPAAm hydrogels are their flexible synthesis approaches and easy separation property. NIPAAm gels have been extensively tested in a variety of pollutant treatment applications (Huffman et al., 1986; Işik, 2003; Igarashi et al., 2004; Tokuyama et al., 2006; Iyer et al., 2007; Tokuyama and Iwama, 2007; Iyer et al., 2008b, c; Pan et al., 2008; Fukuoka et al., 2010; Tokuyama and Ishihara, 2010; Taşdelen et al., 2013; Yan et al., 2013; Cheng et al., 2015; Kim et al., 2015). In 1986, Hoffman and coworkers developed a NIPAAm-co-MAA gel system for the controlled separation of methylene blue (MB), which represented a model of affinity-based thermally reversible sorbents, that can selectively remove pollutants from water (Huffman et al., 1986). More recently, Kurumada et al. synthesized a series of hydrophobically modified NIPAAm gels that contained extractant tributyl phosphate (TBP) as the functional comonomer (Igarashi et al., 2004; Pan et al., 2008). Excellent phenol removal efficiency was achieved at temperature above the LCST (50°C) due to the enhanced hydrophobic interactions between TBP and phenol. In addition, these gels can be easily separated from aqueous solution owing to their solid like property. Iwama and Tokuyama proposed a temperature-swing solid-phase extraction (TS-SPE) technique to remove heavy metals using NIPAAm gels coupled with extractant sodium n-dodecylbenzenesulfonate (SDBS) (Tokuyama et al., 2006; Tokuyama and Iwama, 2007; Tokuyama and Ishihara, 2010). Great capacity and selectivity for Cu ions were observed, and a reversible adsorption-desorption feature at a small variation of temperatures was achieved.

However, NIPAAm gels have several potential limitations, such as weak mechanical strength at low temperatures when the networks are highly swollen and loss of temperature responsiveness when high content of comonomers are incorporated. To overcome these problems, a sub-class of NIPAAm gels that have satisfactory mechanical properties and temperature responsiveness were developed by trapping poly(NIPAAm) into interpenetrating polymer networks (IPNs). A semi-IPN system consisting of poly(NIPAAm) and polyacrylamide (PAAm) were reported by Guilherme and coworkers (Guilherme et al., 2003). The IPN gels showed no change in temperature responsiveness and an enhanced mechanical durability in the process of capturing orange II and MB. Yamashita et al. developed an easy-recovery heavy metal removal IPN gel system that composed of poly(NIPAAm) and poly(sodium acrylate) (pNaAAc) (Yamashita et al., 2003). The IPN gel exhibited a sharp volume phase transition and additional functionality that can selectively bind metal ions. Yao et al. reported the NIPAAm IPN system achieved ~10 times more adsorption capacity than the single crosslinked network due to its much larger specific surface areas (Yao et al., 2015).

2.4.2 NIPAAm microgels

In order to achieve better adsorption performances such as faster kinetics and higher adsorption capacity, bulk gels were reduced to smaller size with dimensions typically of tens of nanometer to micrometers, namely, microgels (Saunders and Vincent, 1999; Oh et al., 2008). Microgels are physically different from the bulk hydrogels even though they might have similar internal structures (Garcia et al., 2007). Thus, microgels can demonstrate similar stimuli-responsive behaviors as the bulk gels. One unique feature of NIPAAm microgels is that they have expanded, “sponge-like” structure with the interstitial spaces occupied by water, hence, they are usually colloidally stable in aqueous solution (Morris et al., 1997; Bhattacharya et al., 2007).

NIPAAm microgels were first prepared and reported by Pelton and Chibante in 1986 (Pelton and Chibante, 1986). Different than hydrogels, microgels are usually synthesized by heterogeneous polymerization, through which gels are directly obtained in mesoscopic range with a uniform size and morphology (Saunders and Vincent, 1999). There are various methods to prepare NIPAAm microgels. Aqueous free radical emulsion/precipitation polymerization is the most widely reported technique (Naseem et al.; Kanazawa et al., 2004; Das et al., 2006). In a typical synthesis, NIPAAm, comonomer and/or crosslinker, surfactant (e.g., sodium dodecyl sulfate (SDS)) and initiator are mixed in a continuously stirring aqueous system at elevated temperatures (50°C-70°C). The amount of SDS plays an important role in determining the size of the microgel. In general, a lower concentration of SDS will produce larger microgels (Pelton, 2000), and higher concentration of SDS will result in smaller microgels. The synthesized microgels are usually dialyzed using membrane against DI water to remove unreacted monomers. Dynamic light scattering

(DLS) and ultraviolet-visible (UV-vis) are the most commonly used techniques to characterize the microgels, whereas DLS analyzes the hydrodynamic diameter and size distribution, and UV-vis provides information about the optical transmittance of the microgel dispersion.

NIPAAm microgels are expected to be more efficient in capturing the contaminants because of their greater surface area to volume ratio. It was reported that the adsorption equilibrium was achieved within 15 minutes of mixing in Morris's work of removing Pb ions using NIPAAm-co-AAc microgels (Morris et al., 1997). However, the same gel synthesized in bulk might take several hours or even several days to reach adsorption equilibrium. In addition, the particle size was reported to play a critical role in the adsorption process. The equilibrium pollutants adsorption capacity increases when the microgel particle size decreases (Mahida and Patel, 2016a). According to Wu et al., the NIPAAm-co-MAA microgels with smaller size (30nm) showed much higher Cu ion removal efficiency than the ones with larger size (500nm) (Wu and Tian, 2008). Since the smaller microgels possess larger effective surface area, which provides rapid rates of adsorption and rapid removal of contaminants. Although NIPAAm microgels have shown some advantages regards the adsorption performance over the bulk gels, however, the synthetic route for producing microgels is not so advantageous when compare to bulk gels. More specifically, NIPAAm microgels do not have many functional comonomer options as bulk gels due to their aqueous synthetic environment, which leads to some limitations in their application. It has been reported that NIPAAm microgels are copolymerized with hydrophilic ionic monomers, and the applications are mainly focusing on treating charged pollutants such as heavy metals (Morris et al., 1997; Kanazawa et al., 2004; Wu and Tian,

2008) and dyes (Parasuraman and Serpe, 2011b; Parasuraman et al., 2012b, 2013; Kureha et al., 2014; Kureha et al., 2016; Mahida and Patel, 2016b; Śliwa et al., 2017). However, the removal of other pollutants such as organic/aromatic compounds and biological impurities has been rarely addressed.

2.4.3 NIPAAm polymer/copolymer

In recent years, NIPAAm polymer/copolymer systems have attracted significant attention in water remediation applications due to many of their advantages such as chain mobility and high surface area. The main difference between NIPAAm polymer and hydrogel/microgel is that the polymer is not covalently crosslinked. Thus, NIPAAm polymers are developed to illustrate more for a phase change rather than a dimension change (Gil and Hudson, 2004). At temperature below LCST, NIPAAm polymer dissolves in water, and the solution is transparent; while at temperature above LCST, the aqueous polymer solution precipitates out by forming a milky suspension. During application, the pollutant adsorption occurred in the bulk polymer solution rather than at the surface of or within the gel; polymer and pollutants are homogeneously mixed resulting in maximum interaction with pollutants. The potential drawbacks of crosslinked gel system such as slow permeation are avoided in the polymer systems.

NIPAAm polymer/copolymer is usually synthesized via aqueous free radical polymerization. The synthetic route is similar to bulk gel except that no crosslinker is present in the polymerization. The resulting polymer is generally in viscous liquid form, and thus, normal washing process might not be applicable. According to the literatures [15, 27], polymer washing can be accomplished using a cellulose tubular membrane through dialyzing against water. After the polymer is dried, a cottage-like solid mass may be obtained. The polymer LCST is characterized by UV-vis through measuring the temperature-dependent transmittance, or by DSC to measure the calorimetric endothermic peak. An additional key property for NIPAAm polymers is the molecular weight (MW), since polymer with different MW can exhibit different pollutant removal efficiencies. The most widely used methods to characterize MW is through gel permeation chromatography (GPC), proton nuclear magnetic resonance (^{1}H-NMR), and viscometer.

The NIPAAm polymer/copolymer systems have been reported to remove a variety of aqueous pollutants (Saitoh et al., 1999; Saitoh et al., 2003; Tokuyama et al., 2006; Franks et al., 2009; Saitoh et al., 2009; Tokuyama et al., 2010; Saitoh et al., 2011, 2012; Cheng et al., 2017). Saitoh et al. proposed a work of using chitosan-conjugated NIPAAm polymer to remove phenols from water (Saitoh et al., 2011). Over 98% of the dissolved phenols were effectively captured by NIPAAm polymer, and the process was proven to be faster than the case of using NIPAAm-co-chitosan gel beads. In addition, the amount of pollutants adsorbed per unit mass of the NIPAAm polymer was reported to be higher than NIPAAm hydrogel in the same environment using the same technique. An interesting side-by-side study was conducted by Tokuyama et al. to compare the Cu ion adsorption behaviors of NIPAAm-co-2-methacryloyloxyethyl phosphate (MEP) crosslinked hydrogel and uncrosslinked copolymer (Tokuyama et al., 2006). The two sorbents possess completely different adsorption mechanisms, i.e., the amount of Cu adsorbed to gel increases with temperature, while that to copolymer decrease. With the same content of MEP (interactive component), the maximum amount of Cu adsorbed on the gel is smaller than that on the copolymer. The lower efficiency of the gel can be attributed to the dual role of the crosslinking points, which prevent the gel-network from deforming and function as the obstacle to adsorption.

2.4.4 NIPAAm polymer/copolymer grafted surfaces

Although NIPAAm polymers are advantageous for their high efficiency and fast kinetics, they have some shortcomings, which must be overcame in order to achieve successful applications. One of the main issues with the uncrosslinked polymer is the potential risk of introducing free polymer chains to the aqueous environment and causing secondary contamination. In addition, the polymers are highly water-soluble, thus their recovery is often not easily achievable. Therefore, a new class of sorbents is developed through grafting NIPAAm polymer/copolymer onto a solid substrate. The aim of creating this type of sorbents is to “fix” the polymers to a solid surface for an easy handling purpose of the water-soluble polymers, while the sorbents still maintain their high surface area and permeation rate. Cellulose (Kasgoz et al., 2013; Ozbas et al., 2016), mesoporous silicon (Jiang et al., 2016a; Jiang et al., 2017), porous ethylene vinyl acetate disk (Sakohara et al., 2013b) and nonwoven polypropylene film (Tokuyama et al., 2008; Tokuyama et al., 2010) have been reported as the solid base to graft NIPAAm polymer/copolymer. Their applications involve the removal of multiple heavy metal ions and organic dyes. The adsorption rate of pollutants was comparable to the polymer system and was significantly higher than crosslinked hydrogel. It is clear that the main advantage of the grafted polymer substrate is that it preserves the feature of non-corsslinked networks such as high chain mobility and surface area, while preventing the potential release of free polymer chains to the environment and making their recovery easy to accomplish. NIPAAm grafted surfaces are synthesized through graft copolymerization, which is the most widely used technique to graft polymers on the substrates (Wang et al., 2002).

2.4.5 NIPAAm incorporated composite materials

As discussed in previous sessions, poor mechanical strength is one of the shortcomings of hydrogels. IPN gels have shown certain improvements. Other than that, another approach is to incorporate NIPAAm into composite materials. Composite hydrogels can exhibit extraordinary mechanical, optical, thermal, electrical, and swelling/deswelling properties, which can potentially overcome the limitations of the neat hydrogel (Haraguchi, 2007). In addition, the composite gels possess characteristics that are not present in either of the component; the combination of these components can lead to the development of multifunctional and new materials (Sheeney-Haj-Ichia et al., 2002). Due to the scope of this work, two types of thermal responsive composite materials are discussed: composite gels and core-shell nano/microspheres.

Thermal responsive composite gels consisting of various components were synthesized and employed in various environmental applications (Pan et al., 2008; Xiao et al., 2013; Yao et al., 2015; Zhen et al., 2015; Begum et al., 2017). It was reported that improved mechanical properties and additional functionalities were found in these gels. Meanwhile, their bulk properties (e.g., LCST of NIPAAm) remained the same as neat gels. For example, Pan et al. prepared hybrid NIPAAm hydrogel with a reinforced layer of calcium alginate for phenol removal. The resulting gels were shown to adsorb phenol effectively, and the thin layer coating of calcium alginate have enhanced their mechanical durability for carrying out repeated cycles of adsorption-desorption tests (Pan et al., 2008). Yao et al. and Zhen et al. developed Fe_2O_3 and Fe_3O_4 magnetic nanoparticles embedded

NIPAAm gels, respectively (Yao et al., 2015; Zhen et al., 2015). These magnetic NIPAAm gels have been successfully used in the removal of reactive dyes and phenolic waste compounds. The uniqueness of these gels is their excellent magnetic separation properties, through which the used gels can be easily recovered using an external magnetic field. The composite gels can be readily obtained from in situ free-radical polymerization of NIPAAm in the presence of inorganic nanoparticles, or post combination of premade hydrogel and the other components through physical incorporation (penetration, immersion, etc.).

Core-shell nano/microspheres are composite particles consisting of at least two different components, with the center one as a core and outer one as a shell (Ghosh Chaudhuri and Paria, 2011). These particles are of particular interest because the properties of the core and shell can be tailored separately to suit a particular application (Bradley and Vincent, 2008). The purpose of the coating on the core particles are many folds, such as surface modification, increase particle functionality, stability, dispersibility, etc (Ghosh Chaudhuri and Paria, 2011). The synthesis of core-shell nanoparticles is a complex process and hence, there is a wide range of techniques available for producing different kinds of structures. Atom transfer radical polymerization (ATRP) and seeded emotion/free radical polymerization have been frequently reported to synthesize thermal responsive core-shell nanoparticles, and their applications include the removal of bio-wastes, organic pollutants, and heavy metals (Park et al., 2014; Gong et al., 2016a; Gong et al., 2016b; Guo et al., 2017). For example, Gong et al. developed recyclable graphene oxide (GO) core/NIPAAm shell nanoparticles for the enhancement in selective adsorption of phenols (Gong et al., 2016a). Compare to bare GO, the core-shell structured GO has larger surface area, pore volume and self-flocculation effect with rapid response to temperature. Moreover, these particles have exhibited selective adsorption to different phenols due to the different interactions and molecular structures of the shell design.

2.5 Mechanisms

Due to the complexity of comonomers and their specific characteristics, the sorption mechanism of NIPAAm-based systems is usually complicated because they implicate the presence of different interactions. In general, a given pollutant binding mechanism plays a dominant role, and other mechanisms are to varying degrees acting simultaneously (Crini, 2005). Despite the large number of papers dedicated to the removal of pollutants using NIPAAm-based smart sorbents, very few of them focused on identifying and illustrating the mechanisms of the adsorption behaviors. Some of the most widely reported mechanisms include hydrophobic interactions, complexation/chelation, and electrostatic interactions. These three mechanisms are discussed with details in the following sessions.

2.5.1 Hydrophobic interactions

Hydrophobic interactions describe the strong attraction force between hydrophobic surfaces and functional groups, such as aromatic rings, methyl, ethyl and propyl groups (Meyer et al., 2006). NIPAAm induces hydrophobic interaction at temperature above the LCST due to the aggregation of $–CH(CH_3)_2$ moieties. NIPAAm can switch from hydrophilic to hydrophobic when temperature goes across the LCST, leading to the adsorption of hydrophobic pollutants.

The effect of surface hydrophobicity of NIPAAm has been demonstrated in a large number of pollutant adsorption studies. As reported by Saitoh et al., hydrophobic organic pollutants including polycyclic aromatic hydrocarbons, alkylphenols, chlorobenzenes, and chlorophenols were effectively removed by NIPAAm polymer above LCST through hydrophobic interactions (Saitoh et al., 1999). As a comparison, the hydrophilic compounds such as polysaccharides and inorganic ions remained in the solvent system and minimum binding occurred. Generally speaking, the removal efficiency of hydrophobic pollutants will increase with increasing hydrophobic content. In addition to bind organic pollutants, Kureha and coworkers demonstrated that the hydrophobic interaction could also be employed in the separation of organic dyes (Kureha et al., 2014; Kureha et al., 2016). They investigated the temperature dependent dye uptake behavior using NIPAAm copolymer gels. Results indicated that the polymer chains were closer to each other due to the hydrophobic association of isopropyl groups, leading to the growth of hydrophobic domains, as well as the hydrophobic interactions between dyes and polymer. In addition, Parasuraman and coworkers reported that NIPAAm-co-AAc microgels could induce efficient adsorption to azo dye orange II through hydrophobic interactions (Parasuraman and Serpe, 2011b; Parasuraman et al., 2013). The amount of orange II removed from water increased from 29.5% at room temperature to 56.6% upon heating to 50°C for 120 min, and the enhanced removal efficiency was due to the phase transition induced hydrophobic interaction of NIPAAm. Similarly, Kanazawa et al. proposed N-(4-vinyl)benzyl ethylenediamine (Vb-EDA) contained NIPAAm microgel system for the removal of Cu(II) ions (Kanazawa et al., 2004). The adsorption capacity of Cu(II) ions was 0.1mg/g at 10°C, and increased dramatically to 2.5mg/g when heated to 50°C; 25 times more Cu(II) ions were captured due to the hydrophobic effect of NIPAAm at temperature above the LCST. Last but not least, Guilherme et al. studied the phase transition effect of NIPAAm-co-polyacrylamide (PAAm) gel on the removal of two aqueous dyes: a more hydrophilic one (orange II) and a less hydrophilic one (MB) (Guilherme et al., 2003). The removal efficiency was compared by measuring the partition coefficient K. MB showed higher K than orange II at temperature above the LCST, which was due to the collapsed NIPAAm chains that induced a more hydrophobic environment. Thus, the less hydrophilic MB is more likely to partition into the NIPAAm hydrogel phase.

2.5.2 Complexation/Chelation

Binding agents can attach to pollutants such as metal ions and dyes to form stable, water-soluble complexes, and this process is called complexation (Dwyer, 2012). A characteristic feature of such complex is that the pollutant molecular occupies the central position (Kanazawa et al., 2004). It is worth mentioning that NIPAAm does not directly induce complexation interactions, but the incorporated comonomers do. NIPAAm allows for the temperature-controlled molecule permeation and the reversible swelling/shrinking of the polymer network, which can either facilitate or suppress the adsorption process. These novel copolymer sorbents are advantageous over the conventional ones because they are multi-functional: one part of them forms complex with target pollutants and the other part senses the temperature change and performs the “on-off” binding. Crown ethers have remarkable properties of recognizing and binding a wide selection of metal ions by forming stable “host-guest” complexes. The copolymer of NIPAAm and crown either functionalities benzo-18-crown-6-acrylamide (B18C6Am) (Ju et al., 2009; Zhang et al., 2012), calix-4-arene (HBCalix) (Yan et al., 2013), and methacryloyloxymethyl-12-crown-4 (M12C4) (Kim et al., 2015) were reported to show strong selectivity binding towards multiple metal ions including Pb^{2+}, Hg^{2+}, Cr^{3+}, Li^{+}, Ni^{2+}. When the size of metal ion matches the cavity of the complex, the metal ions are captured into the cavity through a variety of intermolecular interactions such as coordination bonds, hydrophobic interaction, hydrogen bonds, and ionic bonds (Yan et al., 2013). The NIPAAm chains, in this case, serve as micro-environmental adjustors for the association/disassociation of the complexes, and thereby control the capture/release of the pollutant molecules. Attempts were made to combine the complexation and hydrophobic interactions to achieve a more versatile binding route for the removal of a wide selection of aqueous pollutants. For example, Tokuyama et al. proposed a temperature swing adsorption (TSA) technique and examined its feasibility for removing heavy metal ions (Tokuyama et al., 2006; Tokuyama and Iwama, 2007, 2009; Tokuyama et al., 2010). For this particular system, metal ions were first complexed with an extractant (e.g., sodium n-dodecylbenzenesulfonate (SDBS), n-octyl phosphate (OP)), and then the metal-extractant complexes were adsorbed onto the NIPAAm hydrogel through a hydrophobic interaction above the LCST. The extractant played an role of intermediator, which enhanced the selective adsorption of target metal ions onto the NIPAAm polymer network. The concept has also be employed by Yamada, Kurumada and Ozbas group (Igarashi et al., 2004; Pan et al., 2008; Ozbas et al., 2016). The removal of organic pollutants such as phenol and multiple heavy metals were evaluated in NIPAAm gel or copolymer that contained tributyl phosphate (TBP) and sodium lauryl sulfate (SLS), respectively. The proposed TSA technique is simple, environmentally friendly, and potentially applicable to a variety of separation processes.

When the binding agents are attached to the pollutants by at least two bonds and form a ring-like structure, the process is known as chelation, and the agents are called chelating agents (Dwyer, 2012). Chelation is generally considered as a special kind of complexation. Chelation is a well-known interaction in detecting and/or capturing toxic multivalent ions in waste solutions (Wu and Tian, 2008). However, it is a very pH-sensitive mechanism; a simple change of solution pH may reverse the binding activity (Bhatnagar and Sillanpää, 2009). Molecules composed of multiple nitrogen atoms are known for their chelating properties, and some of them have already been combined with NIPAAm to separate aqueous pollutants (Fukuoka et al., 2010; Guo et al., 2017). For example, N,N,N'N',-(tetrakis-2pyridylmethyl)ethylenediamine (TPEN), a hexadentate ligand with six nitrogen atoms, have been successfully incorporated into NIPAAm hydrogels to capture Cd ion (Fukuoka et al., 2010). It was reported that these gels extract Cd ion efficiently from the aqueous solution in the swelling state, while little extraction occurs in the shrinking state. In addition, ionized functionalities including hydroxyl, carboxyl, amide, and amino have been reported to chelate multivalent ions (Morris et al., 1997; Wu and Tian, 2008; Sakohara et al., 2013b; Park et al., 2014; Cheng et al., 2015, 2017; Guo et al., 2017). When ionic monomers are copolymerized into NIPAAm gels, the resulting gels may be possessing sensitivity to both temperature and pH. Cheng et al. developed NIPAAm-co-acrylamide-co-maleic acid (NIPAm-AM-MA) for the removal of Cu^{2+} (Cheng et al., 2015). The resulting comonomer gels exhibit dual-responsive adsorption phenomena over temperature and pH changes. The maximum Cu^{2+} uptake capacity happened at pH=5 and T=30°C (<LCST), and the uptake capacity increases with pH (1 to 5) and decreases with temperature. Saitoh and coworkers examined the adsorption of a wide range of heavy metals to thermoresponsive chelating copolymers consisting of NIPAAm and imidazole (Im)/iminodiacetie (IDA)/carboxylic acid (COOH) (Saitoh et al., 2003). Due to the structural difference, the three different chelating agents have exhibited different selectivity towards metal ions. The IDA copolymer showed a superior removal efficiency of >95%

recoveries of all metal ions, while the remaining two only showed high removal efficiency to certain metal ions and insufficiency to others.

2.5.3 Electrostatic interactions

Typically, the protonation of nitrogen element contained functional groups (e.g., $–NH_2$) at low pH will result in the formation of cationic (e.g., $–NH_3^+$) moiety and induce the electrostatic interaction. The pH of the aqueous solution plays an important role in electrostatic interaction since it affects the degree of ionization of the pollutants, as well as the surface properties of the sorbents. A number of studies have focused on the removal of anionic pollutants using cationic thermo-responsive NIPAAm gels (Bradley et al., 2007; Bradley and Vincent, 2008; Yao et al., 2015; Śliwa et al., 2017). For example, anionic azo dye orange II was removed through electrostatic interaction using NIPAAM-co-1-vinylimidazole (Vim) microgels (Śliwa et al., 2017). The resulting gels exhibited the ability to switch their surface charge from negative to positive as the pH changed from 9 to 4. The uptake efficiency of Orange II was significantly enhanced at low pH environment due to the protonation of Vim. Also, the removal efficiency showed a temperature dependence at low pH end: 87% at 40°C and 47% at 20°C, respectively. However, the same results was not observed at high pH end since there was no adsorption occurred. Similarly, Bradley and coworkers developed thermo-sensitive core-shell structured microgel particles to capture anionic surfactants (SDBS) (Bradley, Vincent et al. 2007, Bradley and Vincent 2008). The particles were consisting of NIPAAm-co-polyvinylpyridine (PVP) core and NIPAAm-co-2-(dimethylamino)ethyl methacrylate (DMAEM) shell. The basic pyridine group in the core become protonated at low pH, resulting in a strong positive charge and electrostatic interaction to anionic pollutants. Although electrostatic interactions were mostly reported to be effective at low pH environment, Yao et, al. developed a thermos-sensitive cationic hydrogel that induces electrostatic interaction with reactive red dye at all pH range (Yao et al., 2015). This particular gel consists of NIPAAm and 3-acrylamidopropyl trimethyl ammonium chloride (ARPMACl). The characterization of zeta potential indicated the copolymer gel remained positive charge regardless of pH change, which was mainly attributed to the $–N(CH_3)^{3+}$ moiety from ARPMACl.

2.6 Recovery and Regeneration

2.6.1 Coagulation-flocculation

Coagulation-flocculation is specifically applied to recover NIPAAm polymer/copolymer and NIPAAm polymer grafted surfaces. Numerous studies have successfully demonstrated the recovery process of NIPAAm polymers from aqueous solution through flocculation after their usage in pollutant treatment (Guillet et al., 1985; Deng et al., 1996; Saitoh et al., 2003; Sakohara and Nishikawa, 2004; Sakohara et al., 2008; Franks et al., 2009; Tokuyama et al., 2010; Forbes, 2011; Saitoh et al., 2011, 2012; Contreras-Andrade et al., 2015; Gong et al., 2016a; Gong et al., 2016b). The mechanism is explained as follows: NIPAAm polymer dissolves in the aqueous suspension that contains waste particles at temperature below LCST. Then, the surface of the particles will be sufficiently covered with polymer molecules. Upon heating (>LCST), NIPAAm polymer becomes hydrophobic, leading to the chain aggregation through hydrophobic interaction, and subsequently forming the polymer-particle precipitates/flocs (Saitoh et al., 1999). An adequate mechanical force can cause the rearrangement of the particles in the flocs, thereby discharging the water molecules and leading to the compaction of small flocs to form large ones (Gong et al., 2016b). The large flocs with the waste particles can be separated from the aqueous suspension, leaving a clear supernatant. In this technique, NIPAAm possesses the ability to modify the hydrophilicity/hydrophobicity of particle surfaces, which in turn manipulate the interparticle repulsive/attractive force between particles as a function of temperature (Li et al., 2009). The incorporation of NIPAAm allows for the rapid flocculation and compaction of the polymer flocs, which have greatly enhanced the pollutant removal efficiency compared to the conventional flocculating agents (Lee et al., 2014). One general rule of applying NIPAAm based flocculants is that the polymer should not be added at temperature higher than its LCST. Otherwise, self-aggregation would occur before pollutants flocculation. Several parameters such as the polymer molecular weight, salt concentration, temperature, pH and polymer dosage have proven to affect the flocculation efficiency significantly (Burdukova et al., 2010; Burdukova et al., 2011; Lee et al., 2014). For example, salts have a promotive effect on the condensation of the precipitated NIPAAm polymer. Aqueous p(NIPAAm) solution will become turbid instead of coagulation/flocculation in the absence of salts. However, with at low as 0.1M of salt addition, nearly 100% of polymer can be recovered through flocculation (Saitoh et al., 1999). Also, the size of the polymer-particle flocs has been found to increase with increasing polymer molecular weight (Nasser and James, 2006; Li et al., 2009; Burdukova et al., 2010). The most common explanation is that large molecular weight polymer results in the formation of large flocs via bridging attraction. In addition, increasing temperature above the LCST have also shown to increase flocs size, and this can be attributed to an increase in the attractive hydrophobic force (Kuźnik et al., 2010; Burdukova et al., 2011). Increasing polymer dosage will also result in increased flocculation efficiency since more polymer chains are covered on the particles, which enhances the polymer bridging as well as the hydrophobic interactions. Andrade et al. applied the copolymer of NIPAAm-co-AAm-co-AAc to remove solids from river water and wastewater (Contreras-Andrade et al., 2015). They found the most effective temperature of flocculation was 40°C, and further increase in temperature did not show much improvement in waste solids removal. The polymer dosage of 0.1 mg ml^{-1} was able to remove 80% of the turbidity, and the efficiency increased to 99.2% when polymer dosage increased to 1 mg ml^{-1}. However, Sakohara and Nishikawa suggested there existed a critical flocculation polymer dosage, beyond which, flocculation efficiency will be decreased (Sakohara and Nishikawa, 2004).

2.6.2 Magnetic separation

Magnetic separation has also been given a lot of attention in water remediation applications. In comparison to conventional separation techniques such as membrane filtration, centrifugation, sedimentation and etc., magnetic separation is more cost-effective, convenient, selective, fast and environmentally friendly, especially when the sorbents are within micro/nano-scale (Yavuz et al., 2006; Tang and Lo, 2013; Khan and Lo, 2016). The easy separation of magnetic sorbents from treated water can be achieved via an external magnetic field, which requires minimum energy input and power consumption. In a laboratory setting, a low-gradient magnetic separator (LGMS) or a hand-held magnet is used to provide magnetic field; for larger-scale applications, the magnetic sorbents can be separated using a high-gradient magnetic separator (HGMS) (Tang and Lo, 2013; Gómez-Pastora et al., 2014). Iron oxide nanoparticles (IONPs) such as magnetite (Fe_3O_4) and maghemite (γ-Fe_2O_3) have been extensively reported to combine with NIPAAm to synthesize thermal and magnetic dual-responsive polymer network (Ding et al., 1998; Kondo and Fukuda, 1999; Ding et al., 2000; Deng et al., 2003; Meenach et al., 2009). These two nanoparticles are characterized by their superparamagnetism feature, which means there is no magnetic moment on these materials in the absence of a magnetic field (Neuberger et al., 2005; Mahmoudi et al., 2011). The application of thermo-responsive magnetic sorbents in water treatment has been widely explored. Zhen et al. developed a pH, thermal and magnetic tri-responsive magnetic composite system which combined NIPAAm, chitosan, and Fe_3O_4 for the target removal of nonylphenol (Zhen et al., 2015). The sorbents were separated from the aqueous solution under a magnetic field in 1 min, whereas the cloudy suspension did not separate by gravity even after 30 min. The incorporated magnetic nanoparticles have greatly enhanced the separation property of the sorbents. Similarly, Jia and coworker developed a thermo-responsive magnetic microsphere for the removal of alkylphenols from real water samples including river water, spring water, pond water, and drinking water (Jia et al., 2016). Kondo et al. and Xu et al. reported the application of thermo-responsive magnetic microsphere for the purification of antibodies from wastewater (Kondo and Fukuda, 1999; Xu et al., 2012). All these mentioned materials were satisfied with both large surface area and quick magnetic separation, and hence were good candidates for magnetic affinity sorbents. However, one drawback of the magnetic NIPAAm sorbents is that the materials tend to aggregate at high temperatures. The unexpected aggregation might lead to a reduced adsorptive surface area and removal capacity of the sorbents. For future development of the magnetic sorbents, proper coatings on these materials might be an option to enhance their stability and reduce the aggregation at high temperatures.

2.6.3 Centrifugation

When separating non-magnetic sorbents, sedimentation becomes the universal solution. However, the sedimentation is a time-consuming process, and the efficiency is usually not satisfying. Centrifugation assisted sedimentation might be a more effective separation method to recovery used sorbents. Centrifugation represents one of the main groups of mechanical solid-liquid separation processes (Anlauf, 2007). The biggest advantage of centrifugation is its widespread application since the process is suitable to separate most kinds of sorbents (Anlauf, 2007). Parasuraman's group have reported a series of work that used centrifugation to separate NIPAAm-co-AAc microgels after adsorbing organic dyes from the solution (Parasuraman and Serpe, 2011b, a; Parasuraman et al., 2012a; Parasuraman et al., 2012b, 2013). The solution was allowed to settle for five minutes followed by centrifugation for 30 min at 8400 rcf to pack the microgel at the bottom of the centrifuge tube. As confirmed from differential interference contrast microscopy, 30 min is sufficient time to separate all the microgel from the solution.

2.6.4 Desorption and regeneration

Desorption and adsorbent regeneration are of crucial importance to keep the pollutant removal process sustainable and cost-effective. The fully "loaded" adsorbent may concentrate the pollutants in a thousand folds form the bulk concentration; thus, bound pollutants must be released to achieve recyclable use of the sorbents. For an effective desorption process, the sorbents should be recovered with no physical damage and undiminished adsorption performance. Therefore, maintain the mechanical stability and regain the adsorption capacity become the two key aspects for sorbents regeneration (Khan and Lo, 2016). Regardless of many studies have focused on the capture aspects of the sorbents, material regeneration has not been given enough attention. The incorporation of NIPAAm into the sorbents has brought in some uniqueness regards their regeneration. Some of the most frequently reported desorption techniques are discussed as follow.

2.6.4.1 Temperature responsive desorption

Ideally, the regeneration process should be inexpensive, non-hazardous, and easy to operate. NIPAAm based sorbents have tremendous advantages regard to achieving these goals. It is well known that NIPAAm polymer network exhibits reversible swelling/shrinkage behavior over the temperature change. This unique property has been widely applied as a switch to control the capture/release of pollutants. Jiang and coworkers have successfully employed this concept in their work of developing silica matrix supported NIPAAm copolymer for the removal of dyes (Jiang et al., 2017). The adsorption happened at low temperature (25°C), when the copolymer was in a stretching conformation, resulting in the exposure of active binding sites and the adsorption of pollutants. The desorption happened at elevated temperature (50°C) when the copolymer switched to shrinking conformation. The active binding sites are blocked and the coordination bonds are disrupted, which lead to the release of bound pollutants. Numerous studies have applied the same or similar concept to the release of bound pollutants, readers are encouraged to access these articles for more detailed experimental settings and outcomes (Tokuyama et al., 2006; Sakohara et al., 2013b; Yan et al., 2013; Jiang et al., 2016a; Jiang et al., 2016b; Song et al., 2016). In addition to capture-release through the change of polymer configuration, the change of hydrophilic/hydrophobic property on NIPAAm has also resulted in the controlled release of bound pollutants. It is known that NIPAAm exhibits hydrophobicity at temperature above the LCST; the adsorption of target pollutants through hydrophobic interactions is significantly enhanced upon heating. When temperature decreases to below LCST, NIPAAm exhibits hydrophilicity; bound pollutants are therefore released due to the diminished hydrophobic interactions. Pollutant desorption through lowering the temperature has been widely demonstrated in systems where hydrophobic interactions were applied as the dominating binding affinities (Guilherme et al., 2003; Igarashi et al., 2004; Kanazawa et al., 2004; Tokuyama et al., 2006; Tokuyama and Iwama, 2009; Tokuyama et al., 2010; Parasuraman and Serpe, 2011b; Kasgoz et al., 2013; Kureha et al., 2016; Ozbas et al., 2016). A good example was demonstrated in the work from Tokuyama et al. of applying TSA technique to remove gold (III) ions using poly(NIPAAm) gels (Tokuyama and Kanehara, 2007). NIPAAm gels were applied to bind gold (III) ions at 50°C until saturated, and then transferred to 10°C to release the bound gold (III) ions. It was reported that nearly 100% of bound gold ions were released, and the adsorption capacity decreased from 1.15mmol/g-dry gel to 0.0095 mmol/g-dry gel, respectively. A reversible adsorption-desorption process was demonstrated with up to three consecutive cycles without a loss in removal efficiency. Owing to the phase transition property of NIPAAm, pollutant desorption occurred in water through a small change of temperature, without requiring harsh elution conditions and high-energy input. The desorption of NIPAAm based sorbents through temperature variation is simple, versatile, “smart” and eco-friendly, which could greatly decrease the cost of the application and the threat of secondary contamination to the environment.

2.6.4.2 Solvent elution

The temperature mediated desorption by NIPAAm is effective in most cases, however, sometimes when strong binding interactions are present, it is difficult to achieve complete desorption solely using NIPAAm in water. Solvent elution might be used to assist the release of pollutants in order to achieve better desorption outcomes. Desorption through solvent elution/extraction is a partitioning process. When the solubility of the pollutant in a solvent is higher than that in the sorbate, desorption takes place as the pollutant is partitioning away from the sorbate (Sutikno and Himmelstein, 1983). Desorption of thermo-responsive sorbents has been achieved using several solvents including acid (e.g., HCl) (Tokuyama and Iwama, 2009; Cheng et al., 2015, 2017), alkali (e.g., NaOH) (Zhen et al., 2015), or organic solvent (e.g., methanol) (Parasuraman et al., 2013). The solvent concentration and elution time may play important roles in the desorption efficiency. Cheng et al. conducted the desorption of Cu^{2+} loaded NIPAAm-AM-MA gel in HCl solution (Cheng et al., 2015). They found the desorption efficiency increased with time; about 90% of the Cu^{2+} was desorbed within 30 min and nearly 100% Cu^{2+} desorption was attained after 2h. The same group further investigated the effect of solvent concentration on the desorption efficiency in the follow-up study (Cheng et al., 2017). It was found that the desorption efficiency increased with increasing HCl concentration; 75% of Cu^{2+} (0.03M) was desorbed in 0.1 mol L^{-1} HCl and 100% was desorbed when the HCl concentration increased to 0.5 mol L^{-1}. In most cases, the elution process was effective after several cycles of applications without losing a binding capacity of the sorbents. However, Rehman et al. reported morphological damage of the sorbents from being exposed to HCl, which caused a decreased binding capacity in later on adsorption-desorption cycles (ur Rehman et al., 2016). To avoid this potential deteriorating performance, Yao et al. proposed to use NaCl as the solvent instead of harsh acids or bases for the desorption (Yao et al., 2015). In Yao's work, NIPAAm-co-APTMACl magnetic hydrogel was washed by 1.5 mol L^{-1} NaCl after adsorbing reactive red dye (RR) from the water. No significant loss in adsorptive capacity was noticed during consecutive adsorption-desorption cycles.

2.7 Conclusion

This chapter highlights the recent developments on NIPAAm based thermoresponsive sorbents and their applications in aqueous pollutant removal. Superior sorption performance was observed in these materials in removing a variety of pollutants including heavy metals, dyes, organic pollutant, etc. In comparison to the conventional sorbents, the smart thermoresponsive sorbents possess many advantages such as the temperature moderated swelling, adsorption, recovery, and regeneration. Due to the unique thermal responsiveness, the sorption and desorption of the smart sorbent materials can be achieved in water just by a small variation of temperature change. NIPAAm sorbents are available in a variety of morphologies including bulk gels, microgels, polymer/copolymers, grafted polymer, or composite materials, allowing for the applications with multiple purposes. The morphology of NIPAAm sorbent influences its functionality, performance, efficiency, and recovery. Most of the reported NIPAAm sorbents have shown effective recovery and regeneration properties, which can further reduce the cost of the treatment process. However, the work reported so far were mainly focused on lab-scale applications, large-scale industrial applications using the thermoresponsive sorbent systems are yet to be evaluated. In addition, very limited literature that compared the smart NIPAAm sorbent systems with commercial sorbents was found. Although in recent years, tremendous progress has been accomplished in this field, there is still a great potential to design materials with enhanced properties and demonstrate their applications in industry.

Chapter 3 Synthesis and characterization of thermally responsive N-isopropylacrylamide hydrogels copolymerized with novel hydrophobic polyphenolic crosslinkers

This chapter is taken directly or adapted from work **published** in **Tang et al. (2017)** Used with permission from Shuo Tang, Rohit Bhandari, Sean P. Delaney, Eric J. Munson, Thomas D. Dziubla, and J. Zach Hilt, "*Synthesis and characterization of thermally responsive N-isopropylacrylamide hydrogels copolymerized with novel hydrophobic polyphenolic crosslinkers*"

3.0 Abstract

Two series of thermosensitive hydrogels were synthesized by copolymerizing N-isopropylacrylamide (NIPAAm) with various contents of novel hydrophobic crosslinkers, curcumin multiacrylate (CMA) and quercetin multiacrylate (QMA). The compositions of the resulting hydrogels were characterized using solid state-NMR (ss-NMR), and the temperature dependent swelling behavior and lower critical solution temperature (LCST) were characterized using swelling studies and differential scanning calorimetry (DSC). Increasing the crosslinker content resulted in a significant decrease in the LCST and swelling ratio of hydrogels, which could be attributed to the increased hydrophobicity introduced by CMA or QMA. All of the hydrogels demonstrated temperature responsive swelling with the extent of swelling decreasing with increasing crosslinker content. The lower crosslinker content gels displayed sharper phase transitions, while the high crosslinker content gels had broader phase transitions.

3.1 Introduction

Poly (N-isopropylacrylamide) (PNIPAAm) has received extensive attention as a temperature responsive polymer due to its sharp phase transition at its lower critical solution temperature (LCST) around 33°C (Hirokawa and Tanaka, 1984b; Ogata et al., 1995a; Xue and Hamley, 2002). NIPAAm based hydrogels are three-dimensional crosslinked polymeric networks, which are usually of interest for creating “smart” materials for application in biomedicine, drug delivery, tissue engineering, environmental treatment, etc (Stile and Healy, 2001; Hou et al., 2008; Klouda and Mikos, 2008; Vihola et al., 2008; Jing et al., 2013; Parasuraman et al., 2013; Kureha et al., 2014). Generally, homopolymer NIPAAm gel exhibits a reversible phase change from hydrophilic to hydrophobic state at its LCST (Yoo et al., 2000; Hou et al., 2008). When the temperature is below LCST, the polymer structure expands due to the hydration process of PNIPAAm chains, which results in hydrogel swelling. Conversely, at temperatures above LCST, the polymer network collapses (Schild, 1992b; Kim et al., 2000; Ju et al., 2001). Such phenomenon has been previously reported as a result of hydrogen bond forming/breaking between water molecules with their neighboring amide group from NIPAAm (Dimitrov et al., 2007; Lue et al., 2007; Rzaev et al., 2007; Lue et al., 2011b).

The LCST of NIPAAm can be controlled by adjusting the hydrophilic/hydrophobic balance in the polymer chain (Bae et al., 1991a). Various studies have shown that copolymerizing NIPAAm with another monomer could modify its LCST (Xue and Hamley, 2002; Choi et al., 2006; Zhao et al., 2009; Spizzirri et al., 2011). Previously, it has been reported that the LCST can either be decreased through incorporating hydrophobic co-monomers or increased by incorporating hydrophilic co-monomers (Bae et al., 1991a;

Yoshida et al., 1994; Qiu and Park, 2001; Kim and Healy, 2003). An extensive number of hydrophobic/hydrophilic molecules have been explored for modifying the LCST, including acrylic acid (AA), methacrylic acid (MAA), butyl methacrylate (BMA) and di-n-propylacrylamide (DPAM) (Galaev and Mattiasson, 1999; Qiu and Park, 2001; Xue and Hamley, 2002; Prior-Cabanillas et al., 2005; Dai et al., 2006; Rzaev et al., 2007; Lue et al., 2011b). In this study, our focus is on novel crosslinkers based on hydrophobic polyphenolic compounds for the modulation of the LCST of NIPAAm within a crosslinked matrix. Curcumin is a naturally derived hydrophobic polyphenol and is known for its numerous biological activities (e.g., demonstrated anti-cancer, anti-oxidation and anti-inflammatory properties) (Nguyen et al., 2015; Patil et al., 2015). Clinical trials suggested that curcumin was well tolerated by the human body, even at relatively high dosages (12 g/day) (Shoba et al., 1998; Cheng et al., 2001; Lao et al., 2006). As a biomedical agent, curcumin has been studied for its therapeutic use in cancer treatment through inhibiting cells proliferation and promoting apoptosis (Anand et al., 2007; Teong et al., 2015). Additionally, curcumin has shown significant impact in reducing oxidative stress induced by environmental pollutants such as metal nanoparticles, polychlorinated biphenyls (PCBs), etc. (Glauert et al., 2008; Tharappel et al., 2008). Furthermore, our recent efforts found that curcumin, and potentially other polyphenols (e.g., quercetin), have shown binding affinities to environmental contaminants (e.g., PCBs).

From our previous studies (Wattamwar et al., 2012), we have reported a method to synthesize acrylate functionalized polyphenolic molecules, including curcumin diacrylate (CDA) and quercetin multiacrylate (QMA). However, our recent studies have suggested that the polymerization reaction results in the formation of curcumin multiacrylate (CMA), which has a mixture of mono-, di-, and tri-acrylate, instead of previously reported CDA. In the current study, these designed polyphenolic acrylates were used as crosslinkers for NIPAAm to develop novel temperature responsive hydrogels. Herein, we report the influence of changes in the CMA or QMA content on the characteristics of NIPAAm-based hydrogels. The temperature dependent swelling ratios in deionized water were measured as a function of hydrogel composition. Swelling and deswelling behavior caused by a pulsing temperature change were characterized in the reversible swelling study. The goal of this study was to synthesize and characterize NIPAAm-based hydrogel systems crosslinked with novel acrylated polyphenols. These unique T-responsive hydrogels have various potential applications including use in environmental remediation.

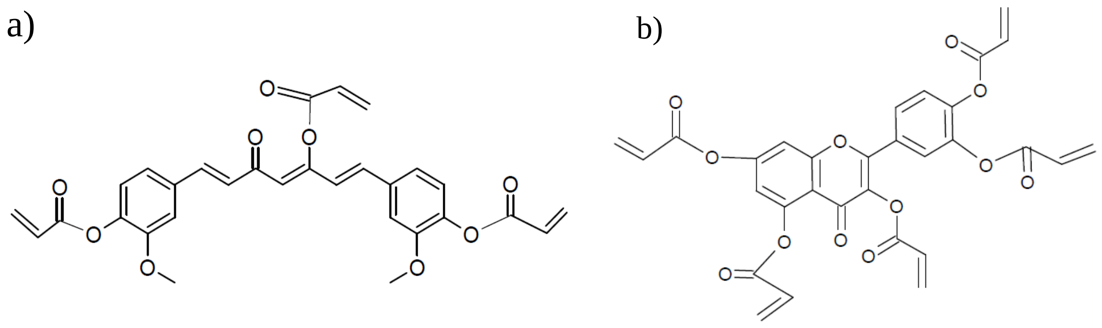
3.2 Materials and Methods

3.2.1 Materials

The monomer N-Isopropylacrylamide (NIPAAm, 97%), initiator ammonium persulfate (APS, ≥98%), quercetin, curcumin, acryloyl chloride were purchased from Sigma-Aldrich Corporation (St. Louis, USA). Poly (ethylene glycol) 400 dimethacrylate (PEG400DMA) was purchased from Polysciences, Inc (Warrington, USA). All organic solvents were obtained from Sigma-Aldrich and Fisher Scientific (Hampton, USA). Agents mentioned above were used as received without further purification. No commercial crosslinker was used in this work; the acrylated polyphenols (CMA and QMA) synthesized by our group were used as hydrophobic crosslinkers. Both CMA and QMA have multiple acrylate groups that provided enough functional moieties for creating crosslinked network with NIPAAm.

3.2.2 Synthesis of acrylated polyphenolic crosslinkers

The synthesis of hydrophobic crosslinkers, CMA and QMA, was conducted based on previously reported literature. In brief, pure curcumin and quercetin were reacted with acryloyl chloride in tetrahydrofunran (THF) and triethylamine (TEA). The reaction was allowed to proceed overnight at room temperature, followed by vacuum filtration and distillation to remove any side products, unreacted reactants and excess solvents. The resulting CMA or QMA was in powder form and stored at -20°C until use. The average molecular weight of CMA and QMA were determined by gas chromatography-mass spectrometry (GC-MS), and they were 449.5g/mol and 518.0g/mol respectively. CMA and QMA structures (full acrylated forms) are given as follow:



Curcumin multi-acrylate (CMA)

Quercetin multi-acrylate (QMA)

Figure 3. 1 Structures of acrylated polyphenols, (a) CMA, (b) QMA

3.2.3 Preparation of the copolymerized hydrogels and microparticles

Three different compositions of gels (0.9%, 1.8% and 2.7% of CMA or QMA) were synthesized through free radical polymerization. 0.9% PEG400DMA gels were prepared as the control. For a typical synthesis of 0.9% CMA gel, 0.020 g of CMA and 0.561 g of

NIPAAm were mixed with 2 mL of DMSO, vortexed for a few minutes until the monomers were well dissolved. APS was dissolved in deionized water and then added to the monomer mixture at 4.0 weight % of combined weight of NIPAAm and CMA. Then, the mixture was transferred to an aluminum pan and the reaction was carried out at 80°C preheated oven for 3 hours. The gel was washed 3 times in an excess amount of acetone followed by 3 times in an excess amount of DI water to ensure the unreacted monomers were maximally leached out. After washing, CMA gel was cut into 5 mm diameter disks and freeze-dried for at least 24 hours until no further mass change. Preliminary experiments were completed to determine the appropriate reaction conditions, which are summarized in Table 3.1. The dry gels were cryoground into microparticles through Cryo-mill SPEX6770 freezer/mill (Haan, Germany) in a set process to ensure the products in fine dried powder form. The morphology, size, and shape of the gel microparticles were characterized by scanning electron microscope (SEM) using Hitachi S4300 microscope (Tokyo, Japan). All samples for SEM were sputtered with a thin layer of gold at 20 mA for about 3 min under argon gas. Size distribution and mean size ± standard deviation of the microparticles were measured by Shimadzu SALD-7101 nanoparticle size analyzer (Kyoto, Japan).

Table 3. 1 Feed composition and reaction time of the polyphenolic gels

Sample	NIPAAm mol%	CMA mol%	QMA mol%	APS (wt %)	Time (hrs)
CMA0.9	99.1	0.9	-	4	3
CMA1.8	98.2	1.8	-	4	3.5
CMA2.7	97.3	2.7	-	4	4
QMA0.9	99.1	-	0.9	4	3
QMA1.8	98.2	-	1.8	4	3.5
QMA2.7	97.3	-	2.7	4	4

3.2.4 Solid state-NMR (ss-NMR) analysis

Room temperature solid-state NMR spectra were acquired using a Tecmag Redstone spectrometer (Tecmag, Inc., Houston, TX) operating at 75.6 MHz for ^{13}C (7.05 T static magnetic field). Samples were packed into 7.5 mm zirconia rotors and sealed with Teflon or Kel-F end caps (Revolution NMR, LLC, Fort Collins, CO). Experiments were performed using a 7.5 mm double resonance MAS probe (Varian, Palo Alto, CA). All ^{13}C spectra were acquired using magic-angle spinning (MAS) (Andrew et al., 1959) at 4 kHz, using ramped cross polarization (CP) (Pines et al., 1973), total sideband suppression (TOSS) (Dixon et al., 1982), and Spinal 64 decoupling (Fung et al., 2000) with a ^{1}H decoupling field of about 63 kHz. A 2 millisecond contact time was used in all experiments. 3-methyl glutaric acid (MGA) used for optimizing spectrometer and as an external standard, with the methyl peak referenced to 18.84 ppm (Barich et al., 2006). Spectra were acquired with a 5 second pulse delay and a 25.6 millisecond acquisition time. All spectra were processed with 30 Hz of exponential line broadening.

3.2.5 Temperature dependent swelling study

The temperature dependent swelling was carried out in an isothermal water bath with the temperature range of approximately 22°C (room temperature) to 55°C. 8mm diameter gel pieces were measured by dry mass and then immersed in deionized water for at least 24 hours at room temperature. The temperature was then increased at a 5°C increments after each measurement. The equilibrium swollen mass was measured gravimetrically in a balance after the surface water being gently wiped off. The weight swelling ratio (q) was defined as:

$$q = M_{swollen} / M_{dry} \qquad [3.1]$$

Where $M_{swollen}$ is the equilibrium swollen mass at each temperature point and M_{dry} is the dry mass of the gel after being freeze-dried. Three measurements were taken for each sample.

3.2.6 Reversible swelling study

Reversible swelling studies were conducted based upon the pulsatile temperature change. Equilibrium swelling ratios were obtained at temperatures alternated between room temperature and 55°C. The dry gels were initially swollen at room temperature until equilibrium. After mass being measured, the gels were quickly transferred to a 55°C water bath, allowed to swell for another 24 hours. After the mass was recorded, they were transferred back to room temperature bath. Exactly similar measurements were done for three cycles, where three measurements were taken for each sample.

3.2.7 LCST measurements

The LCSTs of the hydrogels were measured by differential scanning calorimetry (DSC Q200, TA Instruments Inc., New Castle, USA). In a standard procedure, the hydrogel was immersed into DI water at room temperature for 24 hours to reach an equilibrium state. Then, the gel was cut into 2 mm diameter piece and placed in a T-zero pan with mass being carefully measured. The T-zero pan was then tightly sealed with a hermetic lid and placed into the furnace along with an empty sealed reference pan. All the samples were tested under dry nitrogen atmosphere with a flow rate of 50 mL/min and heated from 10°C to 55°C at a rate of 2°C/min.

3.3 Results and Discussion

3.3.1 Copolymerized hydrogel synthesis

The crosslinking mechanisms for the copolymer hydrogels are schematically illustrated in Figure 3.2 (a) NIPAAm-co-QMA gels and (b) NIPAAm-co-CMA gels. The crosslinkers QMA or CMA were obtained by the reaction of curcumin or quercetin with acryloyl chloride. The multiple acrylate groups on QMA and CMA allow for crosslinking with the NIPAAm chain and the formation of branched network structures. Even without the presence of a normal crosslinker, CMA and QMA could still provide enough C=C to react with the vinyl group in NIPAAm. Due to this unique property, the network structures of the resulting copolymer hydrogels might be slightly different than normal hydrogel. For the reaction parameters studied, there were limited concentration ranges possible for the CMA and QMA incorporated into the hydrogel network. For CMA gels, once the crosslinker content was increased to 3.6 mol% or above, the gelation process was inhibited, resulting in a sticky product mixture instead of a hydrogel. A similar effect was observed with the QMA gels at higher crosslinker contents (i.e., greater than 3.6 mol%).

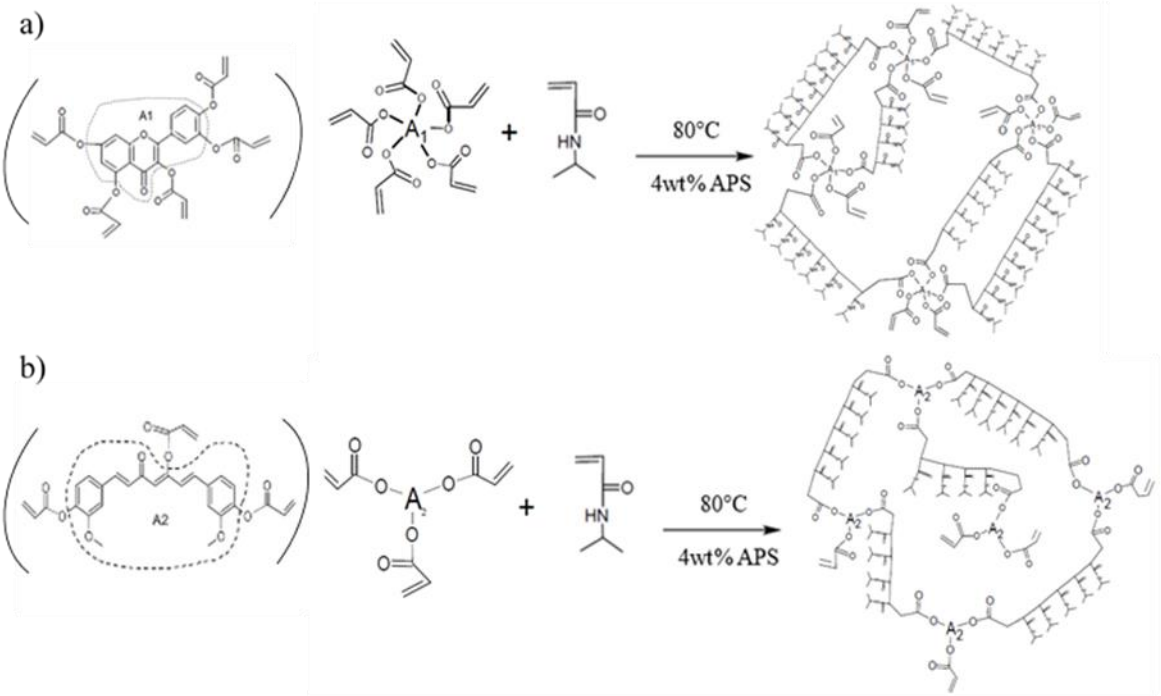


Figure 3. 2 Schematic for the polymerization of (a) NIPAAm-co-QMA gels, (b) NIPAAm-co-CMA gels

3.3.2 ss-NMR spectra

SSNMR spectra of pure NIPAAm and (a) CMA, copolymerized hydrogel with 0.9, 1.8 and 2.7 mol% of CMA content (b) QMA, copolymerized hydrogel with 0.9, 1.8 and 2.7 mol% of QMA content are given in Figure 3.3. The spectrum of CMA copolymerized hydrogel showed peaks at 23 and 42 ppm, which are attributed to the n-isopropyl group ($-CH(C_2H_6)$) from NIPAAm. The peaks at 56 and 151 ppm are characteristics of the methoxy ($-OCH_3$) and carbonyl ($-C=O$) groups from CMA, suggesting that CMA was successfully incorporated into the hydrogel matrix. Similarly, the presence of the peaks at 157 and 145 ppm in QMA copolymerized gel are the characteristics from QMA, and the peaks at 23 and 42 ppm are the characteristics from NIPAAm, which again suggests the successful crosslinking of QMA and NIPAAm monomers. Furthermore, CMA/QMA characteristic peak to NIPAAm characteristic peak ratios increased, which indicated that the content of CMA and QMA in the hydrogel increased.

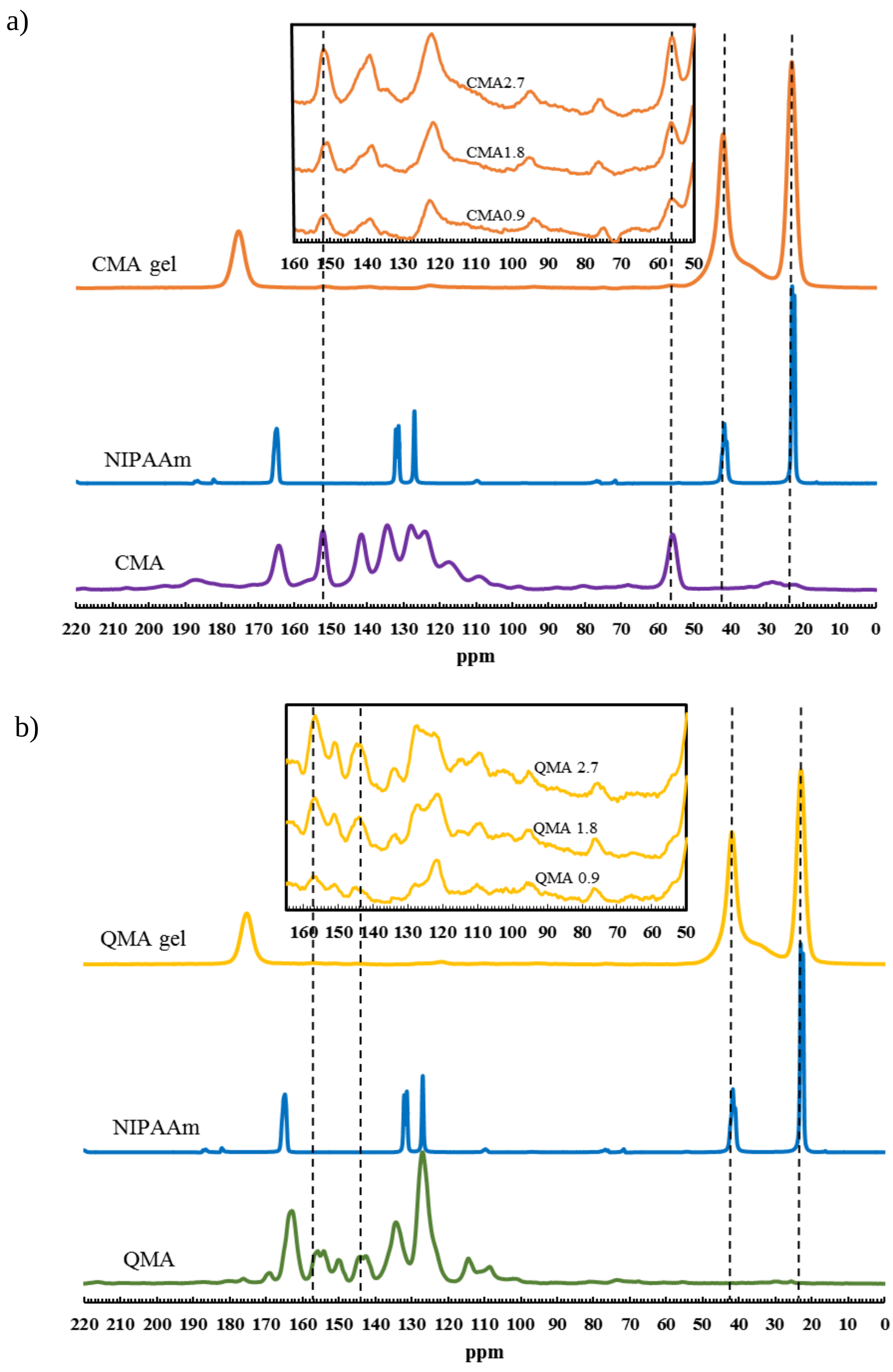


Figure 3. 3 Solid state-NMR spectra of pure monomers and hydrogels at different composition (a) CMA gel system, (b) QMA gel system

3.3.3 Characterization of the morphology

NIPAAm copolymer hydrogels were successfully synthesized using the free radical polymerization with APS as the initiator. Additionally, hydrogel microparticles were obtained through cryogrinding. Hydrogel microparticles offer several advantages over the bulk gels including enhanced solvent transport resulting in faster swelling response, increased surface area, etc. Representative images of copolymerized hydrogels and gel microparticles are shown in Figure 3.4 (a) CMA gel; (b) QMA gel; (c) CMA microparticles; (d) QMA microparticles. The designed CMA hydrogels were light orange/yellow color and the QMA hydrogels were of yellow/green color. The hydrogel color deepens and the texture became more rigid as more CMA/QMA was incorporated.

The representative SEM images are shown in Figure 3.5 (a) CMA; (b) QMA. It is observed that agglomerates were formed, suggesting the tendency of the microparticles to absorb moisture from the air very easily. From the SEM images, it is observed that the individual microparticles are approximately 5 μm in diameter. In addition, the size analyzer reported the mean diameter of the CMA and QMA microparticles as 19.8 ± 0.38 μm and 21.5 ± 0.39 μm, respectively. The size analyzer measured very small aggregates instead of separated microparticles, resulting in reported sizes larger than observed in the SEM.

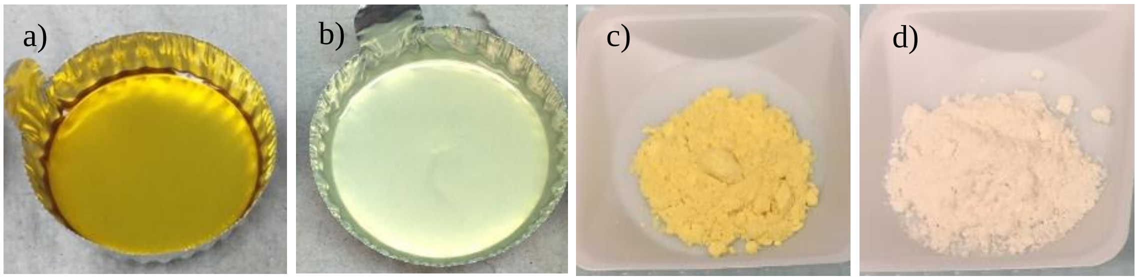


Figure 3. 4 Polyphenolic hydrogels and magnetic gels with the corresponding microparticles. (a)CMA gel; (b) QMA gel; (c) CMA gel microparticles; (d) QMA gel microparticles

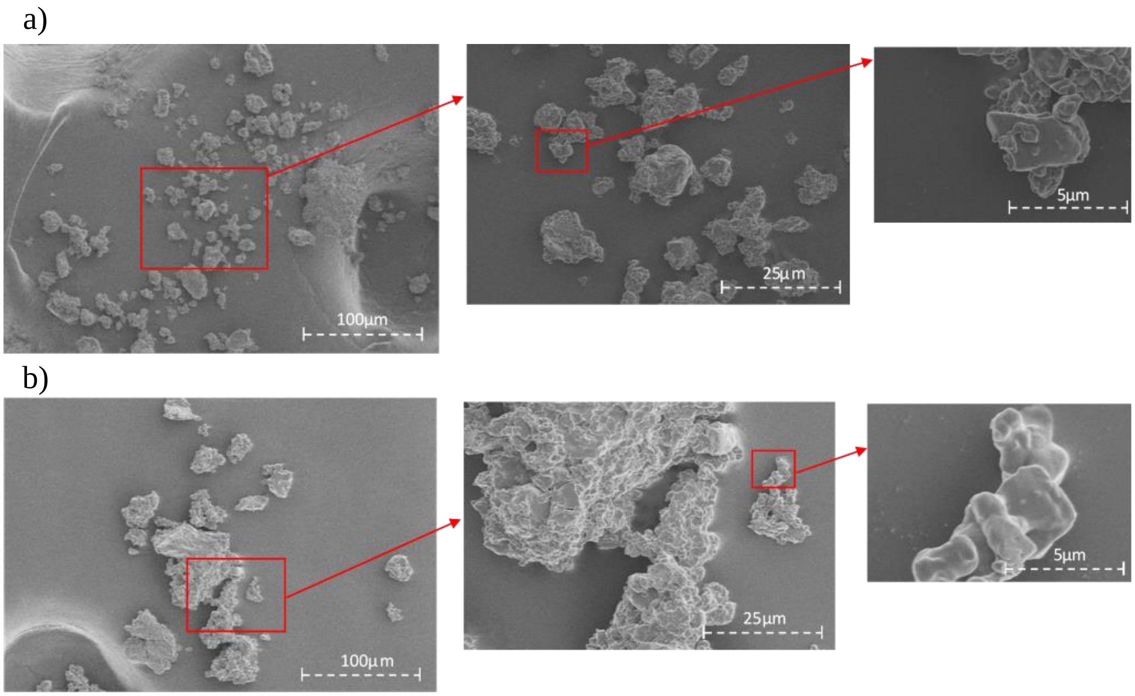


Figure 3. 5 SEM images of (a) CMA hydrogel microparticles, (b) QMA hydrogel microparticles

3.3.4 Temperature responsive equilibrium swelling

The effect of crosslinkers content on hydrogel swelling behaviors are shown in Figure 3.6. 0.9 mol% PEG400DMA gels were synthesized as the control. It can be noted that PEG 0.9 gels displayed the sharpest change in swelling ratio, and these gels showed the closest swelling behavior to homopolymer NIPAAm. Among the CMA/QMA gels, 0.9 content gels demonstrated the sharpest phase change, and the transition point occurred close to 33°C. The swelling transition became broader as more crosslinker was incorporated, which could be explained by the increased hydrophobicity introduced by CMA or QMA. The swelling ratios at room temperature decreased with increasing crosslinkers contents. As CMA or QMA content increased to 2.7 mol%, the gels had significantly reduced swelling ratios of 2.5 and 4, respectively. Zhang et al. reported this was a result of the dilution of the thermal response of NIPAAm with the incorporation of non-thermal responsive crosslinkers (Zhang et al., 2004). As expected, the swelling ratio of a hydrogel is decreased with increasing degree of crosslinking. The higher CMA or QMA content resulted in a higher degree of crosslinking. In addition, the broad phase transition noted in high CMA/QMA composition hydrogels could also be attributed to the high degrees of crosslinking.

The CMA gels showed no dependence on the content in high temperature region (40°C to 50°C), and all gels collapsed completely at 50°C. However, QMA gels displayed different degrees of swelling within the higher temperature region, and the QMA 2.7 gels showed a limited response to temperature change and did not collapse completely. This is likely due to the multifunctional nature of the QMA limiting the extent that the crosslinked network can collapse. Similar phenomenon has been observed in Atta and Elsaeed’s work (Atta et al., 2008). It is also interesting to note that QMA gels showed slightly higher swelling ratios than CMA gels. One possible explanation could be that the QMA gels did not reach the same conversion during the synthesis. As a result, QMA gels had a more loosely crosslinked network structure than CMA gels. Therefore, QMA gels were able to absorb more water at low temperature, which resulted inhigher swelling ratios.

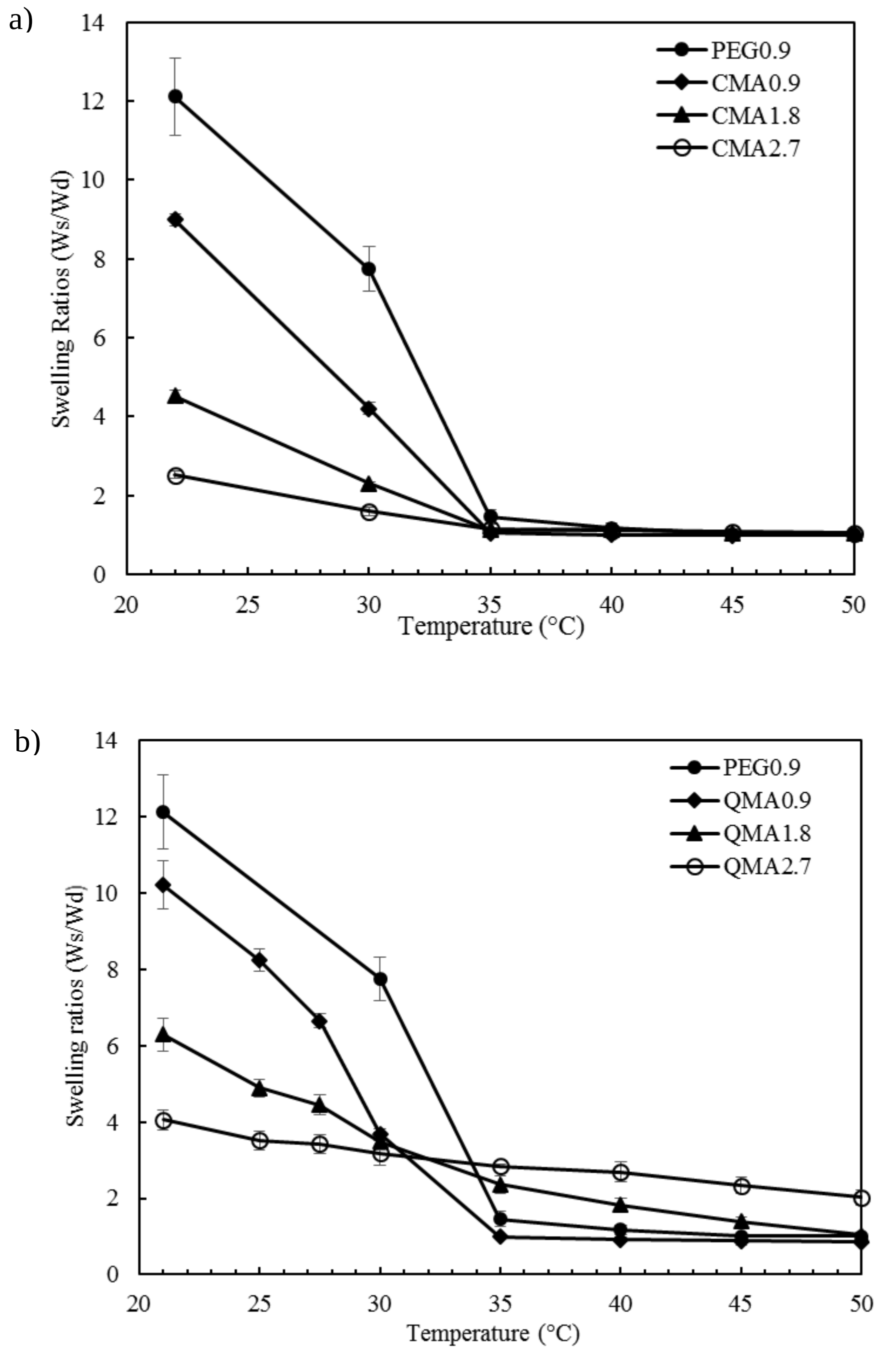


Figure 3. 6 Weight swelling ratios of NIPAAm copolymer gels in response to temperature. a) CMA gels; (b) QMA gels. Data were plotted as mean ± standard deviation and 3 measurements were finished by each sample

3.3.5 Reversible swelling study

Gels in response to pulsatile temperature change were studied in order to confirm their reversible swelling/deswelling properties, as shown in Figure 3.7. The temperature changes were designed to occur across the LCST of NIPAAm between room temperature and 55°C. The dramatic swelling ratios difference from low to high temperature could be explained by the hydrogel network collapse, followed by water being repelled from the crosslinked structure. The swelling ratio differences changed proportionally to the crosslinker composition, and the difference was getting smaller as more crosslinker being incorporated. CMA hydrogels showed completely reversible swelling properties at the chosen temperature range, and no decrease in reswelling ratios was observed, suggesting a good reversible swelling. However, QMA hydrogels showed slight decrease in reswelling ratios, and this was confirmed with a second study so that the QMA reversible swelling data shows the average of six measurements. As discussed in the previous section, we suspect that the QMA gels were not fully reacted during the synthesis, so further crosslinking happened during the reversible heating process, which resulted in a decrease in hydrogel reswelling ratio.

It is interesting to note that the PEG crosslinked NIPAAm gels did not completely collapse at 55°C in the reversible swelling study. One possible explanation could be the forming of “skin” type barrier on the hydrogel surface. Some studies (Gutowska et al., 1992; Zhang et al., 2004) reported similar phenomenon and explained it was due to the hydrogel surface forming dense and less permeable skin layer once experiencing a sudden temperature change, which resulted in a water permeation rate difference between the surface and interior hydrogel. During the experiments, we observed water bubbles formed on the surface of PEG 0.9 gel, which could be due to the poor water-permeability of the skin barrier. However, such issues were not observed with CMA or QMA hydrogels, which is probably because they had higher crosslinking degree and lower water content, so they responded slower to sudden temperature change and the retained water was being diffused out more steadily.

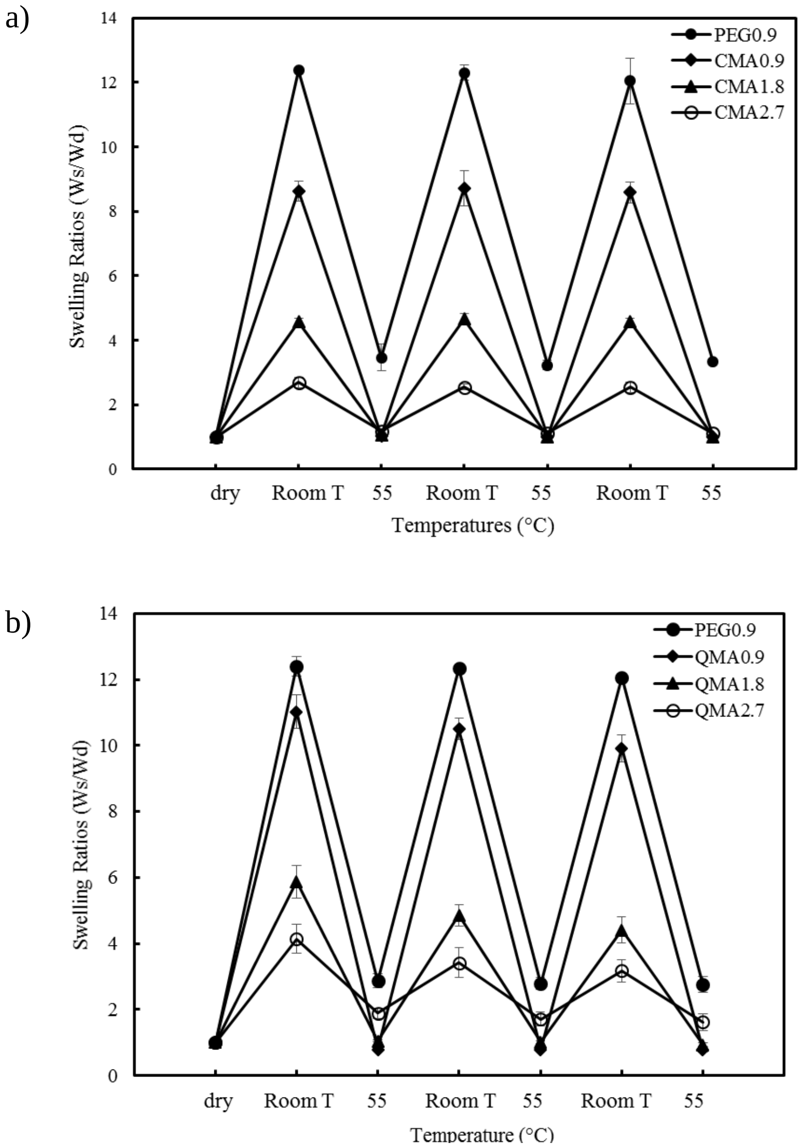


Figure 3. 7 Weight swelling ratios of NIPAAm copolymer gels in response to pulsatile temperature changes between room temperature and 55°C. (a) CMA gels; (b) QMA gels

3.3.6 LCST measurement

The LCSTs were characterized by differential scanning calorimeter (DSC). The DSC thermograms of the two NIPAAm copolymer hydrogels (0.9%-2.7%) are shown in Figure 3.8 (a) for CMA gels and (b) for QMA gels, numerical values were plotted and listed in Figure 3.8 (c). The endothermic peaks were referred to as LCSTs of the hydrogels. There appears to be distinct peaks at 32.2°C, 31.2°C, 30.4°C for CMA gels and 31.3°C, 30.4°C, 28.9°C for QMA gels, respectively. As expected, the LCSTs of the gels were shifted to lower temperatures as more CMA or QMA got incorporated. It is well known that NIPAAm has both hydrophobic isopropyl group and hydrophilic -NH-CO- group, and the hydrophilic group forms intramolecular hydrogen bonds with water at low temperature. The overall hydrophilic content was decreased, and fewer hydrogen bonds were formed thus lower temperature was needed to break the bonds. The LCST could either be decreased by incorporation of hydrophobic components or increased by the addition of hydrophilic components (Bae et al., 1991b; Huang et al., 2015).

The LCST shifting in QMA gels was more distinct than CMA gels, besides, the CMA gels showed a broader peak shape than QMA gels. An explanation for this phenomenon could be that the QMA is slightly more hydrophobic, given the molecular structures of CMA and QMA showed in Figure 3.1. Thus, the LCST was shifted more in QMA-co-NIPAAm gels due to more hydrophobic moieties being introduced into the hydrogel network.

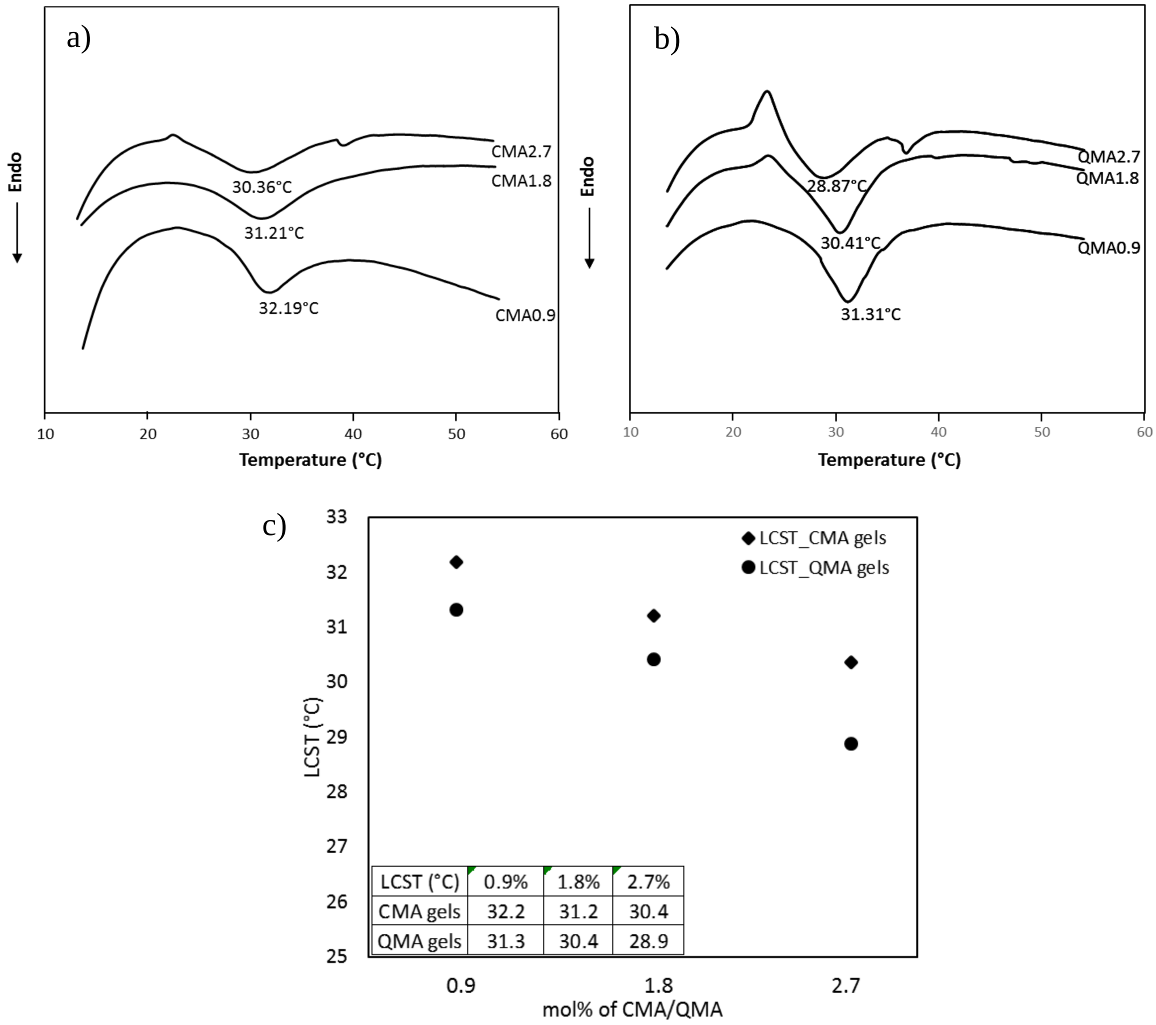


Figure 3. 8 Typical DSC thermograms of the NIPAAm copolymerized hydrogels. (a) CMA0.9-2.7%; (b) and QMA 0.9-2.7%. (c) The numerical values of the LCSTs

3.4 Conclusions

A series of temperature responsive hydrogels with various crosslinker compositions were successfully synthesized through crosslinking NIPAAm with CMA or QMA. The resulting hydrogels exhibited distinct phase transition behaviors in a narrow temperature range and good responsiveness to reversible temperature change. The addition of QMA or CMA showed significant impact in controlling the swelling behavior and LCST of the hydrogels. The swelling ratios of the gels were decreased with increasing crosslinker loading, so did their temperature responsiveness. Meanwhile, the LCSTs of the copolymer gels showed a shifting to the lower temperatures with increasing contents of crosslinkers. The discussed polyphenolic NIPAAm gels can provide an attractive platform for a variety of applications, such as an intelligent water remediation strategy to remove environmental organic pollutants (e.g., PCBs).

Chapter 4 Synthesis and characterization of thermoresponsive hydrogels based on N-isopropylacrylamide crosslinked with 4,4’-dihydroxybiphenyl diacrylate

The chapter is taken directly or adapted from work **published** in **Tang, et al. (2017)** Copyright 2017 ACS Publications. Used with permissions from Shuo Tang, Martha Floy, Rohit Bhandari, Manjula Sunkara, Andrew J.Morris, Thomas D. Dziubla, J. Zach Hilt, “*Synthesis and characterization of thermoresponsive hydrogels based on N-isopropylacrylamide crosslinked with 4,4’-dihydroxybiphenyl diacrylate*”

4.0 Abstract

A novel crosslinker [4,4’-dihydroxybiphenyl diacrylate (44BDA)] was developed, and a series of temperature responsive hydrogels were synthesized through free radical polymerization of N-isopropylacrylamide (NIPAAm) with 44BDA. The temperature responsive behavior of the resulting gels was characterized by swelling studies, and the lower critical solution temperature (LCST) of the hydrogels was characterized through differential scanning calorimetry (DSC). Increased content of 44BDA led to a decreased swelling ratio and shifted the LCST to lower temperatures. These novel hydrogels also displayed resiliency through multiple swelling-deswelling cycles, with their temperature responsiveness being reversible. The successful synthesis of NIPAAm-based hydrogels crosslinked with 44BDA has led to a new class of temperature responsive hydrogel system with a variety of potential applications.

4.1 Introduction

Hydrogels are crosslinked three dimensional polymeric networks that swell in aqueous solution but do not dissolve (Bucatariu et al., 2014; Klouda, 2015). Stimuli responsive hydrogels exhibit swelling behavior that changes in response to environmental factors such as pH, salt concentration, temperature, etc (Brazel and Peppas, 1995; Lee and Hsu, 1998; Kim et al., 2002; Lue et al., 2011a). These “smart” hydrogels have attracted a great attention due to their variety of applications in biomedical (Yoo et al., 2004; Klouda, 2015), drug delivery (Díez-Peña et al., 2004; Fu and Soboyejo, 2010; Bucatariu et al., 2014), tissue engineering (Stile et al., 1999; Ashraf et al., 2016), separation process (Freitas and Cussler, 1987) and wastewater treatment (Iyer et al., 2008a; Parasuraman et al., 2013; Ali et al., 2015), etc.

Temperature responsive hydrogels, especially the ones based on N-isopropylacrylamide (NIPAAm), are particularly appealing because of their unique properties. NIPAAm-based polymers typically exhibit a well-defined lower critical solution temperature (LCST) at 32ºC in aqueous solution at which hydrogen bonds form/break between water molecules and the NIPAAm chain, followed by the hydration/dehydration of the network (Zheng et al., 1998; Stile et al., 1999; Díez-Peña et al., 2004). The fine balance between hydrophobic-hydrophilic nature gives NIPAAm hydrogels a large change in swelling behavior over a narrow temperature range (Prange et al., 1989). This temperature modulated swelling property has been applied to develop an on-off switch for various activities such as drug delivery, controlled release, etc (Bae et al., 1991c; Parasuraman et al., 2013; Rahman et al., 2015). In addition, the LCST can be modified through incorporating a hydrophobic or hydrophilic comonomer/crosslinker to adjust the hydrophilic-hydrophobic balance within the polymer. Usually, biomedical applications require the LCST to be between ambient temperature and the body temperature (~37°C) or even above the body temperature. The incorporation of hydrophilic compounds such as methacrylic acid (MAA) (Huglin et al., 1997; Velada et al., 1998), N-hydroxyethylacrylamide (HEAM) (Fundueanu et al., 2013; Bucatariu et al., 2014) and acrylic acid (AA) (Chiu et al., 2002; Lue et al., 2011a; Rahman et al., 2015) have been demonstrated to raise the LCST. In regard to such studies, Lue et al. showed that addition of 2.7 mol% hydrophilic acrylic acid to poly-NIPAAm based gels increased the LCST from 34.82°C to 43.96°C (Lue et al., 2011a). For other research such as separation processes, it is potentially desirable to lower the LCST closer to ambient temperatures, so that large energy input is not needed to drive the transition. The incorporation of hydrophobic comonomers have been reported by several studies, for example, di-n-propylacrylamide (DPAM) (Xue and Hamley, 2002), methyl methacrylate (MMA) (Lowe et al., 1999) and butylmethacrylate (BMA) (Bae et al., 1991b). Bae et al. have reported a shift of LCST to ~17°C after the addition of 10 mol% of BMA (Bae et al., 1991b).

We synthesized, NIPPAm-based thermoresponsive hydrogels using a novel crosslinker, 4,4'-dihydroxybiphenyl diacrylate (44BDA). 44BDA is synthesized from 4,4'-dihydroxybiphenyl, which is an aromatic hydrocarbon derivative (Paramasivaganesh et al., 2013; Liang et al., 2015). 4,4'-dihydroxybiphenyl is known to work as the mesogen in combination with aliphatic dibasic acids to synthesize thermotropic liquid crystal polyesters, which were reported to exhibit unique odd-even effect (Krigbaum et al., 1983; Jannesari et al., 2005; Tokita et al., 2012). Beyond that, Chung et al. reported several studies using 4,4'-dihydroxybiphenyl as a tyrosinase inhibitor for skin whitening purpose in cosmetics field (Kim et al., 2005; No et al., 2006). This present work focuses specifically on the synthesis and characterization of 44BDA and NIPAAm-based temperature responsive hydrogels that use 44BDA as a crosslinker. In this paper, we have studied the effects of 44BDA content on the swelling behavior and LCST of NIPAAm hydrogels. The goal of incorporating 44BDA was to decrease the LCST while maintaining the temperature responsive behaviors of NIPAAm gels and to introduce the unique biphenyl functionality to the network which could potentially be useful for environmental remediation. This is the first report of the synthesis of 44BDA, as well as 44BDA crosslinked NIPAAm hydrogels.

4.2 Materials and Methods

4.2.1 Materials

4,4'-dihydroxybiphenyl, triethyl amine (TEA), acryloyl chloride (AC), N-isopryopylacrylamide (NIPAAm, 97%), and ammonium persulfate (APS, ≥98%) were purchased from Sigma-Aldrich Corporation (St. Louis, USA). Poly(ethyleneglycol) 400 dimethacrylate (PEG400DMA) was purchased from Polysciences, Inc (Warrington, USA). All solvents (dimethyl sulfoxide (DMSO), acetone, tetrahydrofuran (THF), dichloromethane (DCM), and acetonitrile (ACN)), HCl, K_2CO_3, and magnesium sulfate were purchased from VWR International (Radnor, USA). Molecular sieves (3Å) were added to the solvents to remove any moisture present and to maintain the anhydrous state of the solvents. Crosslinker 44BDA was synthesized in lab by acrylation of 4,4'-dihydroxybiphenyl.

4.2.2 Synthesis of 44BDA

44BDA was synthesized using a modification to a method reported previously (Patil et al., 2015). Briefly, 4,4'-dihydroxybiphenyl was dissolved in excess amount of THF, followed by the addition of TEA and AC with the ratio of TEA:AC:4,4'-dihydroxybiphenyl of 3:3:1. AC was added dropwise under continuous stirring on an ice bath. The acrylation process was allowed to proceed overnight under dark conditions. The mixture was then subjected to vacuum filtration to remove the precipitated triethylammonium chloride salts. Next, THF from the filtrate was evaporated under vacuum using a liquid N_2 trap. The recovered 44BDA was re-dissolved in DCM and purified by multiple washes with 0.1 M K_2CO_3 and then 0.1 M HCl to remove any unreacted AC and TEA. Then, magnesium sulfate was added to remove any remaining water from the solution, followed by the second filtration of the product. The final mixture was evaporated again under vacuum using liquid N_2 trap to obtain a dry powdered product, and it was stored at -20°C until use. A combination of mono- and di- acrylates was obtained. (See Figure 4.1 for their structures)

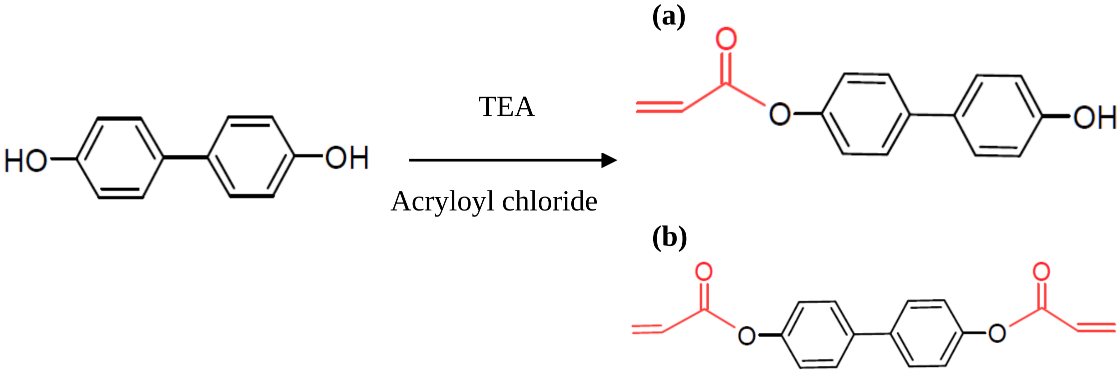


Figure 4. 1 Chemical structures of 4, 4'-dihydroxybiphenyl and the two forms of acrylates. (a) 4,4'-dihydroxybiphenyl mono-acrylate, (b) 4,4'-dihydroxybiphenyl di-acrylate

4.2.3 Confirm the acrylation through high performance liquid chromatography (HPLC)

The synthesized 44BDA was characterized using reverse-phase HPLC (Waters Phenomenex C18 column, 5 µm, 250 mm (length) X 4.6 mm (I.D.) on a Shimadzu Prominence LC-20 AB HPLC system). Samples were dissolved in ACN at 100 µg/ml. A gradient from 50/50 ACN/water to 100/0 ACN/water over 24 minutes at 1 ml/min was used with the column chamber set at 40°C. The absorbance was measured from 260 nm to 370 nm.

4.2.4 Characterizing the molecular weight of 44BDA through liquid chromatography time-of-flight (LC-TOF)

Analysis of 44BDA was carried out using a Shimadzu HPLC coupled with a Sciex TripleTOF 5600 quadrupole time of flight mass spectrometer. 44BDA was analyzed using a Zorbax Eclipse XDB C18 column, 5 µM, 4.6 X 150 mm column (Agilent). Mobile phase consisted of water with 0.1% TEA as solvent A and ACN with 0.1% TEA as solvent B. The flow rate was 0.5 ml/min with a column temperature of 30°C. The sample injection volume was 10 ul. The mass spectrometer was operated in the positive electrospray ionization mode with a curtain gas of 20 psi, ion spray voltage of 5500 V, ion source gas1/gas2 of 40 psi and temperature of 550°C.

4.2.5 Synthesis of NIPAAm-co-44BDA hydrogels

All gels were synthesized through free radical polymerization (schematic in Figure 4.2). A control system was synthesized by crosslinking NIPAAm with 0.9 mol% of PEG400DMA. The 44BDA system was crosslinked with NIPAAm at 5 different compositions (0.9, 1.8, 2.7, 3.6, and 4.5 mol%). For example, the 44BDA 0.9 gel was synthesized by dissolving 6.6 mg 44BDA with 280 mg NIPAAm in 1 ml DMSO. The initiator, APS, was dissolved in DI water (0.5g/ml) and added at 4 wt% combined weight of NIPAAm and 44BDA. The monomer and reactant solute

on was vortexed and purged with nitrogen for 5 minutes. The mixture was then equally divided into 5 shell vials with top covered by rubber stopper and allowed to react in a preheated 80°C water bath for one hour. To remove any unreacted monomers, the gel was washed with excess acetone followed by DI water (three times each for 30 minutes per wash). Then, the gels were cut into small pieces and freeze dried for 24 h until no further mass change occurred. Reaction components for all other gels have been summarized in Table 4.1.

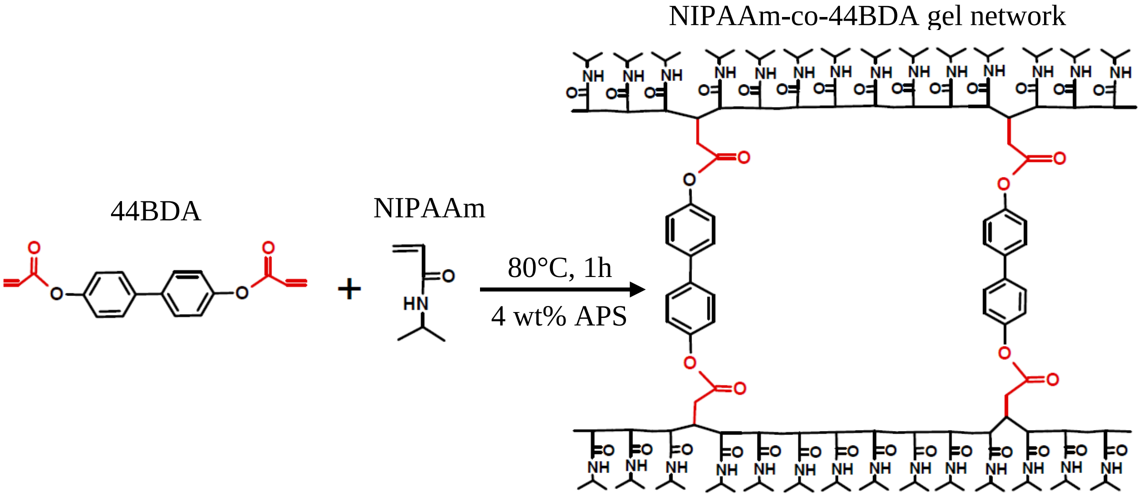
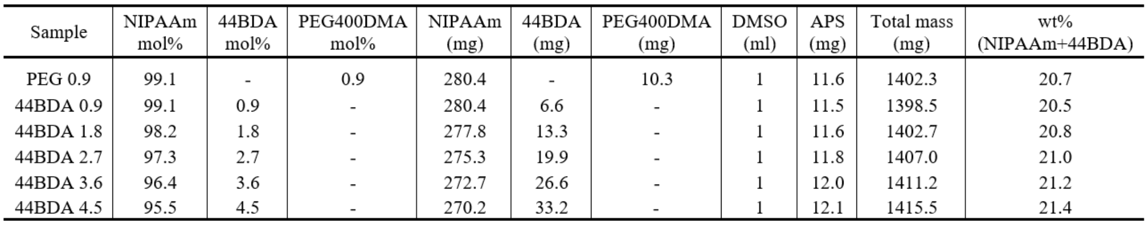


Figure 4. 2 Schematic shows the polymerization reaction and polymeric network of NIPAAm-co-44BDA gel

Table 4. 1 Feed composition of PEG control and 44BDA gels



Sample	NIPAAm mol%	44BDA mol%	PEG400DMA mol%	NIPAAm (mg)	44BDA (mg)	PEG400DMA (mg)	DMSO (ml)	APS (mg)	Total mass (mg)	wt% (NIPAAm+44BDA)
PEG 0.9	99.1	-	0.9	280.4	-	10.3	1	11.6	1402.3	20.7
44BDA 0.9	99.1	0.9	-	280.4	6.6	-	1	11.5	1398.5	20.5
44BDA 1.8	98.2	1.8	-	277.8	13.3	-	1	11.6	1402.7	20.8
44BDA 2.7	97.3	2.7	-	275.3	19.9	-	1	11.8	1407.0	21.0
44BDA 3.6	96.4	3.6	-	272.7	26.6	-	1	12.0	1411.2	21.2
44BDA 4.5	95.5	4.5	-	270.2	33.2	-	1	12.1	1415.5	21.4

4.2.6 Swelling studies

A series of swelling studies were performed to test the swelling properties of 44BDA gels. First, the gels were swelled in DI water at 25°C in an isothermal water bath to study the equilibrium swelling kinetics. Mass measurements were taken at time points of 0, 0.5, 1, 2, 4, 8, 12, 24, and 48 h. The swelling ratio was defined as swollen mass divided by dry mass as shown in Equation 4.1.

$$q=M_{swollen}/M_{dry} \qquad [4.1]$$

Once the equilibrium swellings were obtained, a temperature dependent swelling study was conducted to determine the swelling profile for each composition. In this study, gels were swelled at temperature increments of 5°C from 10°C to 50°C for 24 h to reach equilibrium swelling, mass swelling ratios at each temperature were calculated as was repeatable. In this study, gels were placed through three cycles in an isothermal water bath from swollen state at 10°C to a collapsed state at 50°C, and mass swelling ratios were recorded at each temperature after 24 h swelling.

4.2.7 LCST measurements

The LCSTs of the hydrogels were measured using differential scanning calorimetry (DSC Q200, TA instruments Inc., New Castle, USA). Hydrogels were allowed to swell completely for at least 24 h in DI water. A small piece of gel was gently dapped dry, placed in a T-zero pan, and the mass was carefully recorded. The sample was hermetically sealed in the T-zero pan and placed along with a reference pan on the heater. Samples were then heated from 10°C to 50°C at a rate of 2°C/min under dry nitrogen atmosphere at a flow rate of 50 ml/min.

4.3 Results and Discussion

4.3.1 Structural analysis of 44BDA by liquid chromatography time-of-flight (LC-TOF) mass spectrometry

Upon reaction of 4,4’-dihydroxybiphenyl (precursor) with acryloyl chloride, hydroxyl groups were replaced by acrylate groups, and depending on the number of hydroxyl groups that were replaced, two forms of acrylated product could be produced: 4,4’-dihydroxybiphenyl monoacrylate and 4,4’-dihydroxybiphenyl diacrylate. To determine the average molecular weight of the resulting product, LC-TOF was used to identify different forms of the acrylate and their corresponding percentages, with results shown in Figure 4.3. Determining the average molecular weight is critical because it is used in the following calculations for gel synthesis. The major peak presented at 12.9 minutes with molecular weight of 295 g/mol corresponds to 44BDA, and the peak intensity was reported as $4.97\text{x}10^7$ cps. According to a previous 4,4’-dihydroxybiphenyl partial acrylation study, the 4,4’-dihydroxybiphenyl monoacrylate and precursor had peaks around 9 minutes and 6 minutes, respectively (see supporting information). Referencing the partial acrylation results, the minimal peak at 9.08 minutes shown in Figure 4.3 (a) and 1 (b) corresponds to 4,4’-dihydroxybiphenyl monoacrylate. There was no measurable peak around 6 minutes in Figure 4.3 (a-c) corresponds to the precursor, which is likely due to the addition of excess amount of acryloyl chloride (3:1), and 1 mole of 4,4’-dihydroxybiphenyl only reacts with 2 moles of AC). The excess addition of acryloyl chloride resulted in approximately 100% conversion of the precursor to diacrylate product, leaving 4,4’-dihydroxybiphenyl (with molecular weight of 187 g/mol) and 4,4’-dihydroxybiphenyl monoacrylate (with molecular weight of 241 g/mol) with no measurable contribution. Two minor peaks presented at 10.26 and 17.11 minutes might be associated with impurities left in 44BDA, which could either be side products from acrylation or impurities in the precursor. Due to the approximate 100% conversion of 4,4’-dihydroxybiphenyl to 44BDA, the average molecular weight of 44BDA was considered to be 295 g/mol.

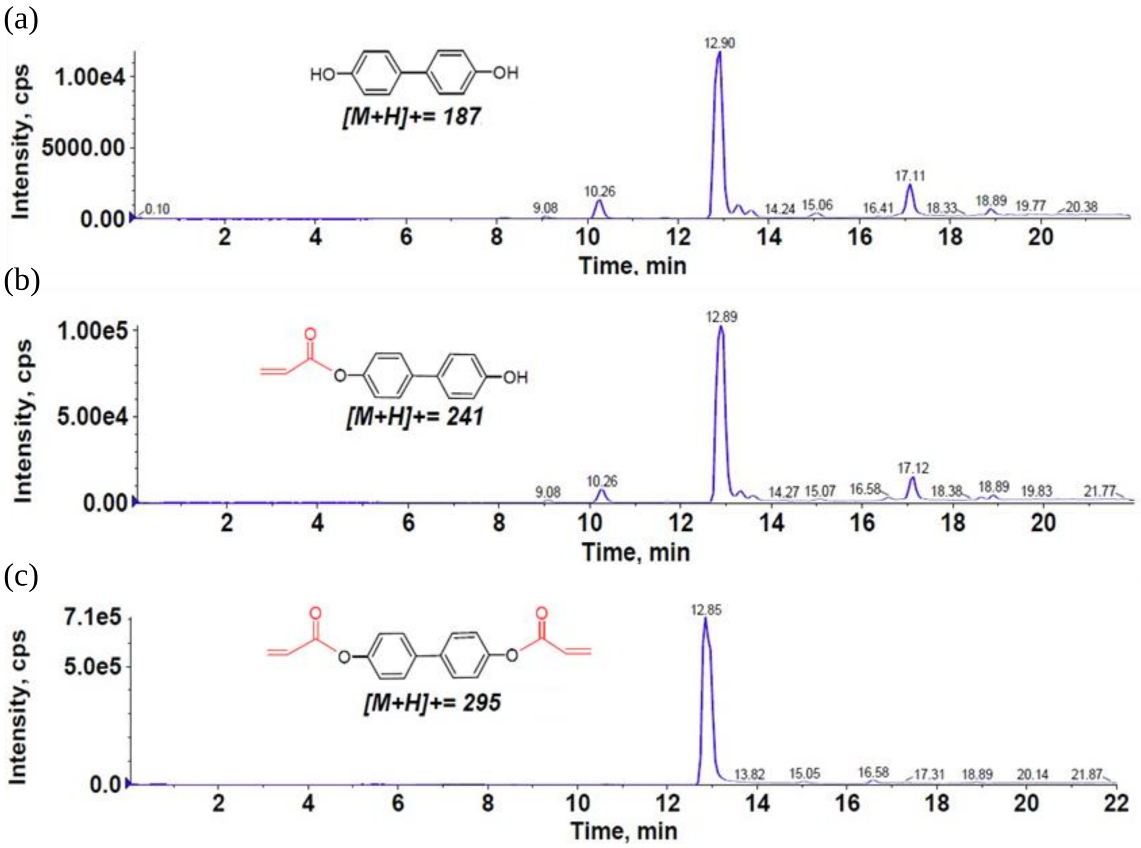


Figure 4. 3 LC-TOF spectroscopy of (a) 4,4’-dihydroxybiphenyl (b) mono-acrylate (c) di-acrylate

4.3.2 High performance liquid chromatography (HPLC)

A combined HPLC chromatogram for 4,4’-dihydroxybiphenyl and 44BDA are shown in Figure 4.4. The blue and green line represents the chromatograms for 4,4’-dihydroxybiphenyl and 44BDA respectively. The major peak observed in blue line presented at 4.5 minutes is associated with the characteristic peak of 4,4’-dihydroxybiphenyl. No peak was observed at 4.5 minutes in case of 44BDA (green line), indicating all starting material was converted to the acrylated forms. Based on an increase in hydrophobicity of the acrylated forms of 4,4’-dihydroxybiphenyl, the major peak in 44BDA presented at 11 min can be attributed to either the mono- or di-acrylate of 44BDA. Due to the excess acryloyl chloride addition during synthesis, the reaction was pushed further to produce almost 100% diacrylate. Thus, based on our analysis, the peak could be assigned to 44BDA instead of 4,4’-dihydroxybiphenyl monoacrylate, and these results were observed to be in accordance with the LC-TOF data discussed in previous section.

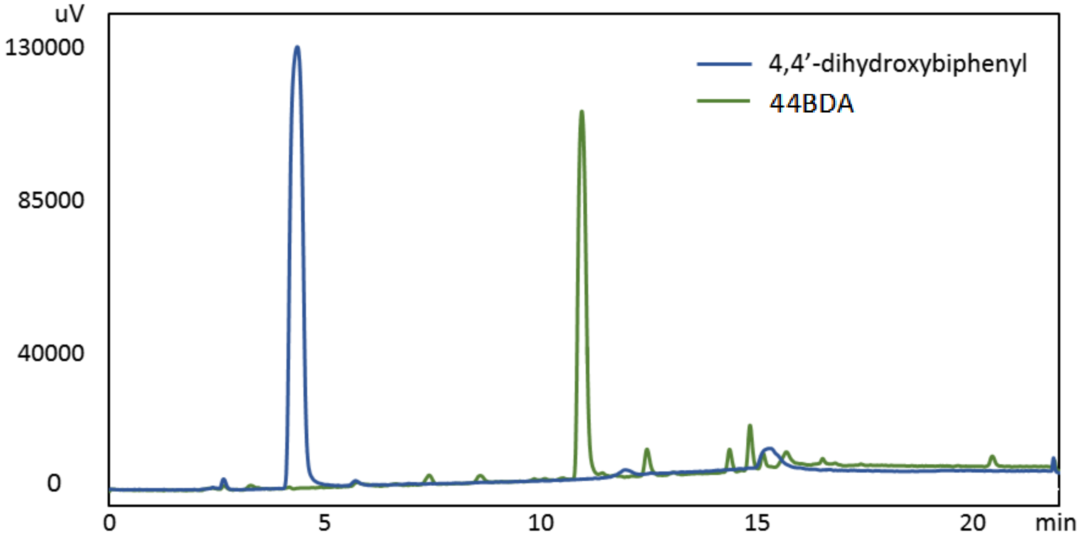


Figure 4. 4 HPLC chromatograms for 4,4’-dihydroxybiphenyl and 44BDA

4.3.3 Synthesis of NIPAAm gels crosslinked with 44BDA

Five different 44BDA crosslinked NIPAAm gels and a PEG comparison group were prepared via free radical polymerization. The acrylate groups on 44BDA allows for the crosslinking with the NIPAAm chain resulting in the network structure. Prior to gel synthesis, reaction conditions (temperature, time, N_2 purging) were optimized.

4.3.4 Swelling studies

The kinetic swelling behavior of 44BDA gels was studied at 25°C. A plot of swelling ratio versus time (Figure 4.5) shows the gels reach equilibrium swelling by 24 h. For all the swelling studies reported in this work, NIPAAm crosslinked with 0.9 mol% of PEG400DMA was chosen as a comparison group for 44BDA gels, which was labeled as PEG 0.9 control. PEG multiacrylates and multimethacrylates are commonly used crosslinkers, and it has been reported in several studies (Frimpong and Hilt, 2008; Meenach et al., 2010; Kim et al., 2014). From Figure 4.5, it was observed that the equilibrium swelling ratio decreased significantly with an increasing 44BDA content, as expected. The PEG400DMA comparison group had the highest swelling ratio, since PEG400DMA is less hydrophobic than 44BDA.

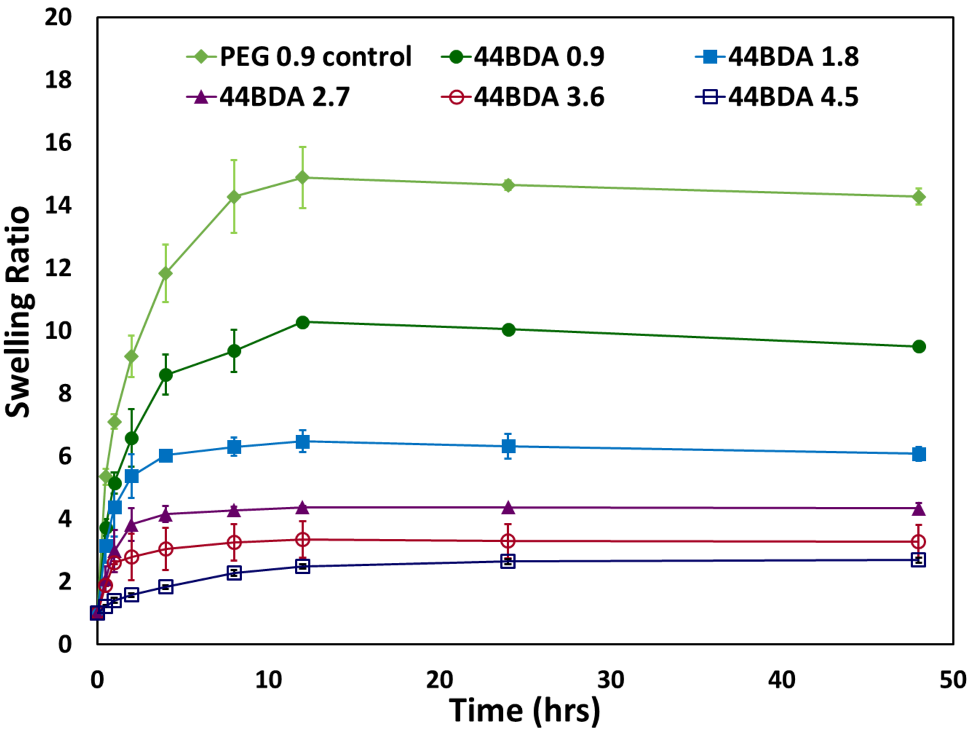


Figure 4. 5 Kinetic swelling study of PEG control gel and 44BDA gel set, error bars represent average swelling ratio ± standard deviation where n=3

A temperature dependent swelling profile of NIPAAm-based hydrogels with varying amount of 44BDA is illustrated in Figure 4.6. As temperature increased, swelling decreased until 50°C where all gels were completely collapsed. The swelling ratio decreased the sharpest between 25°C and 35°C, where the phase transitions were observed. The transition temperatures shifted away from the LCST of NIPAAm (32-33°C), which was expected as addition of a hydrophobic crosslinker should shift the transition temperature to lower temperatures. Higher 44BDA content gels showed broader phase transitions than lower content ones, which was due to their higher crosslinking degrees in gel structure. This can especially be seen in 44BDA 3.6 and 4.5 gels which require a temperature of 50°C to collapse completely, while compared to those lower crosslinked ones which collapsed completely at 35°C. Comparable investigations by Inomata et al. and Tang et al. (Inomata et al., 1995; Tang et al., 2017a) have also supported that the transition range is influence by crosslinking density.

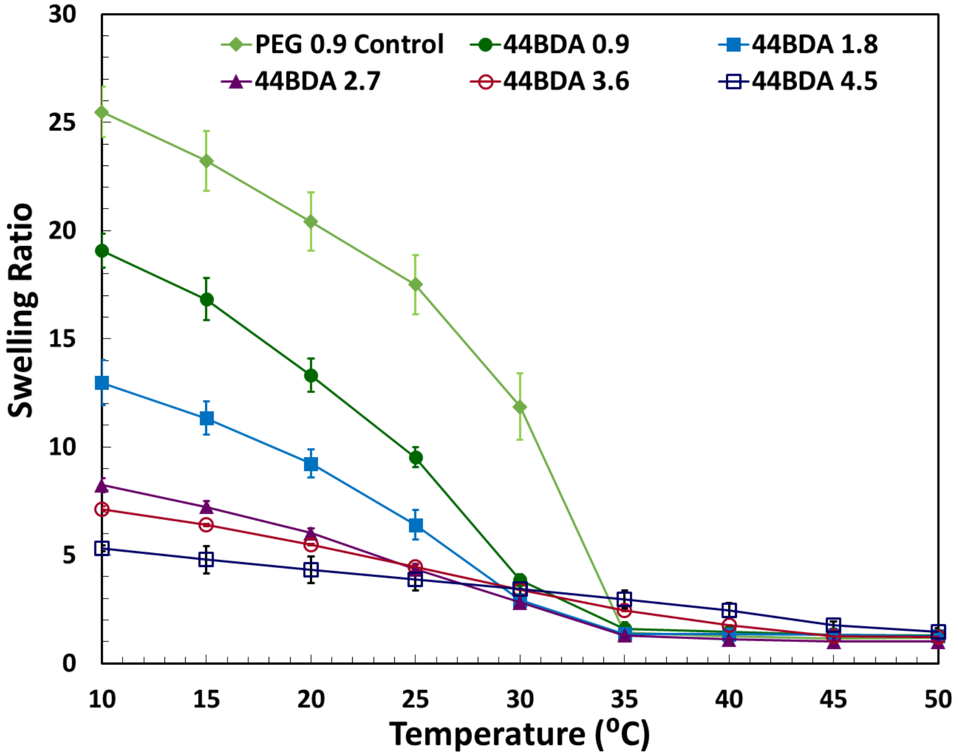


Figure 4. 6 Temperature dependent swelling profile of PEG control gel and 44BDA gel set, error bars represent average swelling ratio ± standard deviation where n=3

Reversible temperature response, which reveals the potential reusability of the gel, is important for applications of the hydrogels. In this study, reversible temperature changes were designed to span the LCST of the gels alternating between 10°C to 50°C, where gels went from being almost completely swollen to completely collapsed. A plot of swelling ratio versus temperature is shown in Figure 4.7. It can be found the gel re-swelling ratio at 10°C for the second and third cycle were very similar to the initial swelling ratio, indicating the swelling-collapse process of gels was reversible.

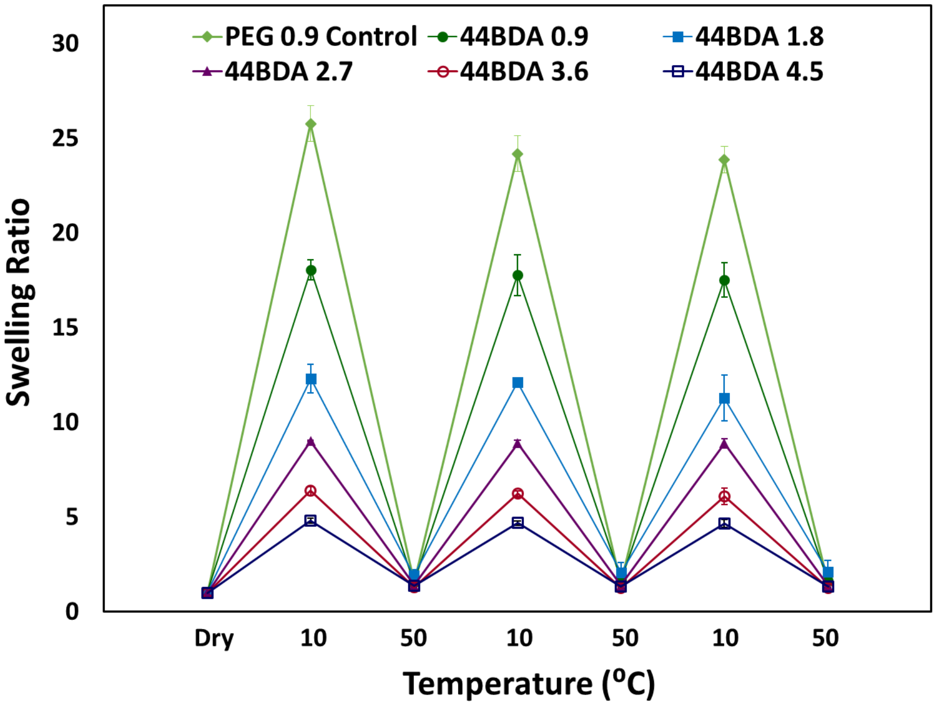


Figure 4. 7 Reversible swelling profile of PEG control gel and 44BDA gel set, error bars represent average swelling ratio ± standard deviation where n=3

4.3.5 LCST measurements

The LCSTs of PEG control and 44BDA gels were measured by DSC. Results from the analysis are shown in Figure 4.8 (a) for example thermograms and (b) for LCST values. Endothermic peaks in the thermograms represent the LCST where intramolecular hydrogen bonds are broken requiring heat (Lue et al., 2011a). PEG 0.9 control gel showed a LCST of 32.8°C, which was within the range of previously reported literature values for homopolymer NIPAAm (32-33°C) (Hirokawa and Tanaka, 1984b; Schild, 1992a; Zheng et al., 1998; Kuckling and Wohlrab, 2002). It is expected that the incorporation of hydrophobic co-monomers or crosslinkers will decrease the amount of intermolecular hydrogen bonding, resulting in less heat being required to break the hydrogen bonds and resulting in a decrease in LCST. From Figure 4.8 (b), the LCST of gels showed the expected decrease with increasing amount of 44BDA, and the LCST shifted up to 4.3°C from PEG control (32.8°C) to 44BDA 4.5 gel (28.5°C).

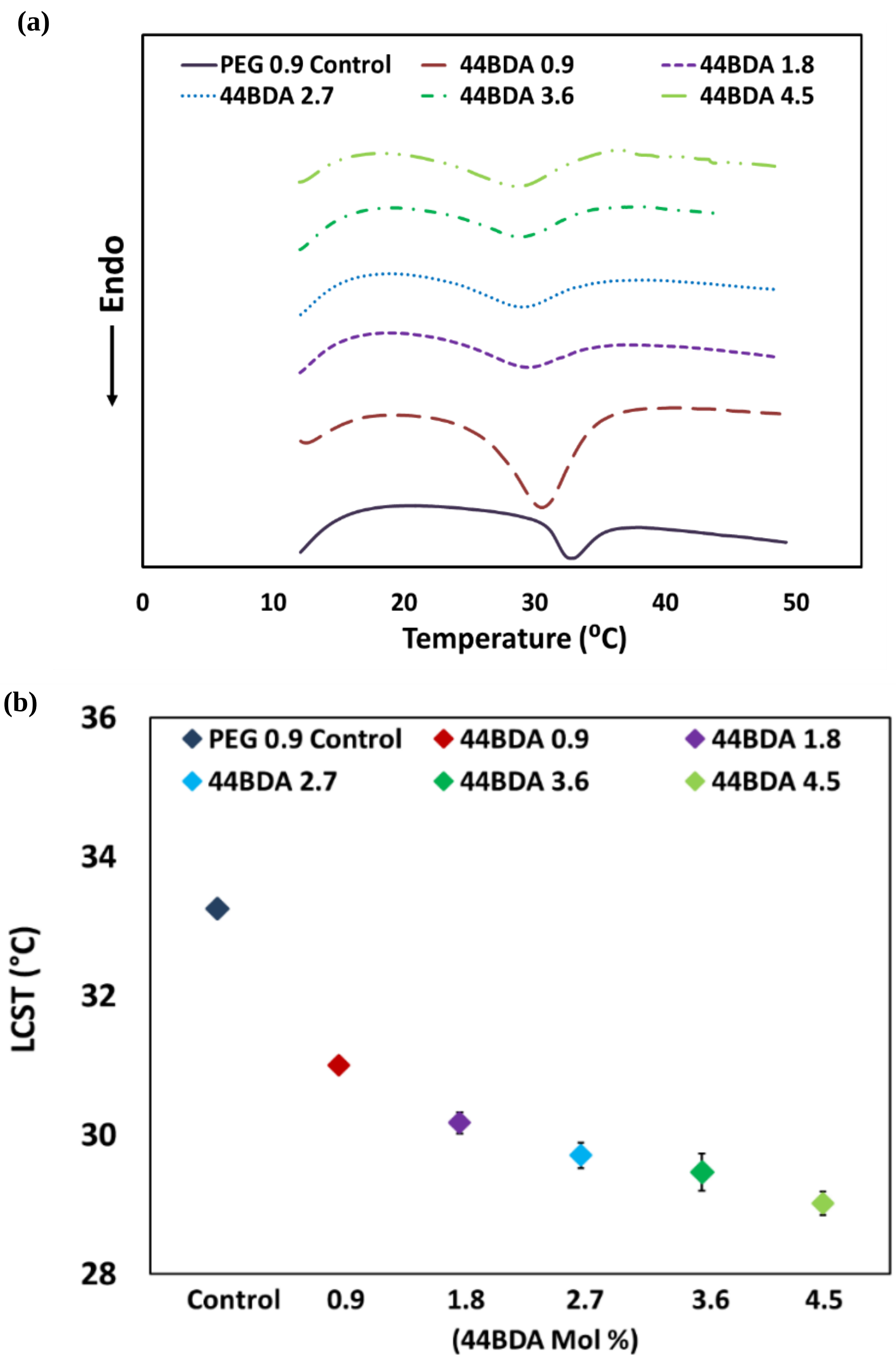


Figure 4. 8 (a) Sample DSC thermogram of PEG control gel and 44BDA gel set (b) Numerical values of PEG control gel and 44BDA gel set, error bars represent average LCST ± standard deviation where n=3

4.4 Conclusions

The hydrophobic crosslinker 44BDA was successfully synthesized, and NIPAAm was reacted with this novel crosslinker to form temperature responsive hydrogels through free radical polymerization. 44BDA content in hydrogel was varied from 0.9-4.5 mol%, and its effect on hydrogel swelling behaviros and LCST was studied. As more 44BDA was incorporated, hydrogels showed decreased swelling ratio, and the difference was especially significant in the low temperature region. Meanwhile, their LCSTs were shifted to lower temperatures with increasing 44BDA. Higher 44BDA content gels exhibited broader phase transitions due to a high degree of crosslinking. A reversible response to temperature change was seen for those hydrogels, indicating a good reusability for various applications including environmental remediation.

Chapter 5 Development of novel *N*-isopropylacrylamide (NIPAAm) based hydrogels with varying content of chrysin multiacrylate

The chapter is taken directly or adapted from work **published** in **Tang, et al. (2017)** Used with permissions from Shuo Tang, Martha Floy, Rohit Bhandari, Thomas Dziubla and Zach J. Hilt, "*Development of novel N-isopropylacrylamide (NIPAAm) based hydrogels with varying content of chrysin multiacrylate*"

5.0 Abstract

A series of novel temperature responsive hydrogels were synthesized by free radical polymerization with varying content of chrysin multiacrylate (ChryMA). The goal was to study the impact of this novel polyphenolic-based multiacrylate on the properties of *N*-isopropylacrylamide (NIPAAm) hydrogels. The temperature responsive behavior of the copolymerized gels was characterized by swelling studies and their lower critical solution temperature (LCST) was characterized through differential scanning calorimetry (DSC). It was shown that the incorporation of ChryMA decreased the swelling ratios of the hydrogels and shifted their LCSTs to a lower temperature. Gels with different ChryMA content showed different levels of response to temperature change. Higher content gels had a broader phase transition and smaller temperature response, which could be attributed to the increased hydrophobicity being introduced by the ChryMA.

5.1 Introduction

Stimuli responsive hydrogels, which are often referred to as intelligent hydrogels, are a type of hydrogel where swelling behavior changes in response to environmental factors such as pH, salt concentration, ionic strength, and temperature, or a combination therein (Brazel and Peppas, 1995; Lee and Hsu, 1998; Kim et al., 2002; Lue et al., 2011a). Among these, pH and temperature responsive gels have gained the greatest attention, and they have been shown to be easily tunable (Haq et al., 2017). *N*-isopropylacrylamide (NIPAAm)-based polymers, as one of the most widely studied temperature responsive polymers, have shown great potentials in various fields. NIPAAm-based polymers exhibit a lower critical solution temperature (LCST) at ~32–33°C in aqueous solution, which can be easily adjusted to physiological temperature through the modification of the hydrophilic/hydrophobic balance in the polymer with comonomers (Hirokawa and Tanaka, 1984a; Hoffman, 1991; Schild, 1992b; Ogata et al., 1995b; Kuckling and Wohlrab, 2002). There are numerous applications of the sharp phase transition, which can be a reversible swelling change for crosslinked systems, especially in the designing of a controlled release system e.g., drug delivery, analytical separation and detection (Díez-Peña et al., 2004; Safont et al., 2009; Ali et al., 2015; Klouda, 2015; Ashraf et al., 2016).

Chrysin (5,7-dihydroxyflavone), a naturally occurring flavonoid presents at high levels in honey and propolis, has shown potential pharmacological effects in inhibiting coronary heart disease, stroke, and cancer (Walle et al., 1999). As a flavonoid, chrysin has been widely studied both in vitro and in vivo for its anti-inflammatory, antioxidant, antiviral, and immunomodulatory effects (Comalada et al., 2006). Multiple researchers have shown that chrysin stimulates or inhibits a wide variety of enzyme systems (Wolfman et al., 1994; Nielsen et al., 1998; Zeng et al., 2003; Comalada et al., 2006). In this work, chrysin is not studied as biomedical agent, but it is acrylated and used as a hydrophobic comonomer/crosslinker that is incorporated in an NIPAAm-based temperature responsive hydrogel system.

In the present study, a series of temperature responsive hydrogels consisting of NIPAAm and varying amount of ChryMA were developed. The LCST of NIPAAm gel can be easily altered by adjusting the hydrophilic and hydrophobic balance of the network (Hoffman, 1991; Schild, 1992b). The use of comonomers to adjust the LCST of NIPAAm gels have been well studied, although such studies have focused mostly on the hydrophilic modification of the polymer network. Some of the well-known hydrophilic crosslinkers/comonomers such as acrylic acid (AA) (Chen and Hoffman, 1995; Velada et al., 1998; Jones, 1999; Yoo et al., 2000; Xue et al., 2001; Kim and Healy, 2003) and methacrylic acid (MA) (Brazel and Peppas, 1995; Brazel and Peppas, 1996; Zhang and Peppas, 2000; Qiu and Park, 2001) have been extensively reported in previous publications. However, few have reported on the hydrophobic crosslinkers/comonomers. Most recently, our group reported two sets of NIPAAm gels using hydrophobic crosslinkers curcumin multiacrylate (CMA) and quercetin multiacrylate (QMA), which have shifted the LCST of NIPAAm gel from 33°C to 30.4°C and 28.9°C, respectively (Tang et al., 2017a). Other groups, such as Gan et al., investigated the phase transition behavior of hydrophobically modified biodegradable hydrogel using poly(ε-caprolactone) dimethacrylate (PCLDMA) and bisacryloylcysatamine (BACy) as the crosslinkers. The LCST was shifted from 32.6 to 30.68°C, yet the swelling ratio remained high (~20) (Gan et al., 2016). In addition, butyl methacrylate (BMA) (Feil et al., 1993), di-n-propyl acrylamide (DPAM) (Xue and Hamley, 2002), polystyrene (Singh et al., 2017), benzo-12-crown-4-acrylamide (PNB12C4) (Wei et al., 2017), and others have been reported in recent years on the hydrophobic modification of NIPAAm hydrogel. In this work, we present novel NIPAAm hydrogels with varying content of hydrophobic comonomer/crosslinker ChryMA, which acts as a model compound for the successful synthesis of similar hydrophobic/polyphenolic materials for various fields of application.

5.2 Materials and Methods

5.2.1 Materials

N-isopropylacrylamide (NIPAAm, 97%), initiator ammonia persulfate (APS, ≥98%) triethyl amine (TEA), acryloyl chloride (AC), and chrysin were purchased from Sigma-Aldrich Corporation (St. Louis, MO, USA). Poly(ethyleneglycol) 400 dimethacrylate (PEG400DMA) was purchased from Polysciences, Inc (Warrington, FL, USA). All solvents were purchased from VWR International (Radnor, PA, USA). Molecular sieves (3 Å) were added to the solvents to remove any moisture present and to maintain their anhydrous state.

5.2.2 Synthesis of ChryMA

Comonomer chrysin multiacrylates (ChryMA) were prepared in accordance with the protocols described previously (Gupta et al., 2015; Gupta et al., 2016). Briefly, chrysin was dissolved in an excess amount of THF, followed by the addition of AC with the ratio to chrysin of 3:1. TEA was added in the same molar ratio as AC to capture the byproduct hydrogen chloride by forming a chloride salt with the progression of the reaction. AC was added dropwise under continuous stirring in an ice bath to prevent the reaction from overheating. Since Chrysin is light-sensitive, the acrylation process was conducted under dark conditions for 16 h. Then, the obtained mixture was filtered from salts and evaporated under vacuum using a liquid N_2 trap. Further purification was conducted by multiple washes with 0.1 M K_2CO_3 and then 0.1 M HCl to remove any unreacted AC and TEA. The final product was filtrated once more and vacuum dried to obtain powdered ChryMA. The product was kept in a freezer at −20°C until use.

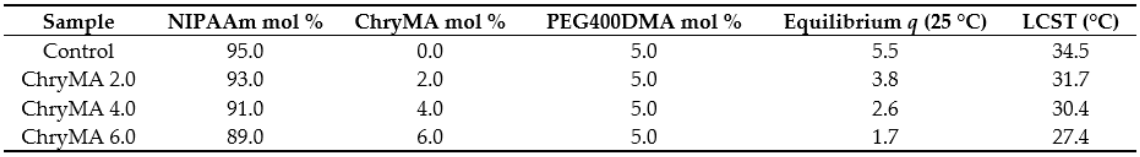
5.2.3 Characterization of ChryMA using high performance liquid chromatography (HPLC)

The obtained ChryMA was analyzed through reverse-phase HPLC (Waters Phenomenex C18 column, 5 µm, 250 mm (length) × 4.6 mm (inside diameter, I.D.) on a Shimadzu Prominence LC-20 AB HPLC system) to verify product quality. Samples were dissolved in acetonitrile (ACN) at 100 µg/mL. A gradient from 50/50 ACN/water to 100/0 ACN/water over 24 min at 1 mL/min was used with the column chamber set at 40°C. The absorbance was measured from 260 nm to 370 nm.

5.2.4 Synthesis of NIPAAm-co-ChryMA gels

NIPAAm-*co*-ChryMA hydrogels were synthesized using the free radical polymerization approach. ChryMA and NIPAAm were dissolved in DMSO with the feed ratio of 2/93, 4/91, or 6/89 mol %, and PEG400DMA (crosslinker) was kept at 5 mol %. The initiator, APS, was dissolved in deionized (DI) water to the specified concentration of 0.5 g/mL and added at 4 wt % combined weight of NIPAAm and ChryMA. To increase solubility, the reaction mixture was preheated at 80°C before adding the initiator, APS. Instant polymerization occurred, but gels were allowed to continue the reaction for 1 h to ensure high conversion. To remove any unreacted monomers, gels were washed with excess acetone and DI water three times each, for 30 min per wash. Then, gels were cut into small pieces (5 mm in diameter) and freeze-dried overnight until no further mass change occurred. Reaction components for all gels are summarized in Table 5.1.

Table 5. 1 The compositions, equilibrium swelling ratios, and LCSTs of the NIPAAm-*co*-ChryMA gels studied



Sample	NIPAAm mol %	ChryMA mol %	PEG400DMA mol %	Equilibrium q (25 °C)	LCST (°C)
Control	95.0	0.0	5.0	5.5	34.5
ChryMA 2.0	93.0	2.0	5.0	3.8	31.7
ChryMA 4.0	91.0	4.0	5.0	2.6	30.4
ChryMA 6.0	89.0	6.0	5.0	1.7	27.4

5.2.5 Kinetic swelling study

Dried gels were swelled in 5 mL of DI water at 25°C in an isothermal water bath to study equilibrium swelling kinetics. Mass measurements were taken at time points of 0, 0.5, 1, 2, 4, 8, 12, 24, and 48 h. Each sample was removed from the water bath, dabbed dry with Kimwipe to remove excess surface water, and weighed. The mass swelling ratio was defined as the swollen mass divided by the dry mass, as shown in Equation 5.1, where M_{swollen} is the wet weight measured at each time point, and M_{dry} is the dry mass after freeze-drying.

$$q = M_{swollen}/M_{dry} \qquad [5.1]$$

5.2.6 Temperature dependent swelling study

To determine the temperature responsiveness of the gels, gels discs were swelled in 5 mL of DI water at different temperatures for 24 h to reach equilibrium swelling. Swelling ratios were measured at temperature increments of 5°C from 10 to 50°C. A reversible swelling study was conducted to ensure that the swelling response of the gels was repeatable. Gels were cycled for three times in an isothermal water bath from swollen at

25°C to collapsed at 50°C. The mass of the gel was recorded after reaching the swelling equilibrium by 24 h.

5.2.7 LCST measurements

The LCSTs of the hydrogels were measured using differential scanning calorimetry (DSC Q200, TA instruments Inc., New Castle, DE, USA). Hydrogels were allowed to swell for at least 24 h in DI water for equilibrium. A small piece of gel was gently dabbed dry, and its mass was carefully measured and recorded. The sample was then hermetically sealed in the T-zero pan in order to eliminate the possibility of water evaporation, and placed along with a reference pan on heaters. Samples were heated from 10 to 50°C at a rate of 2°C/min under a dry nitrogen atmosphere at a flow rate of 50 mL/min.

5.3 Results and Discussion

5.3.1. Characterization of ChryMA

HPLC chromatograms for chrysin and ChryMA are shown in Figure 5.1. The red and blue lines represent chrysin and ChryMA, respectively. A single and distinctive peak was observed at 7.2 min in the red line, which corresponds to the chrysin with a high purity. Two peaks are shown around 10 and 11 min in blue line, which are the different acrylates of chrysin. On the basis of an increase in the inherent hydrophobicity of the acrylated chrysin, the peak at 10 min was identified as the monoacylate, and the peak at 11 min was identified as the diacrylate. No peak was observed at 7.2 min for the case of ChryMA, indicating that all of the precursor was converted to acrylated product. The composition of mono- and diacrylate was characterized in liquid chromatography time-of-flight (LC-TOF), and these two forms were determined to be present in molar amounts of 36.9% and 63.1%, respectively, which are similar to the observed ratios from HPLC absorbance peak areas. The average molecular weight of ChryMA was calculated to be 365.3 g/mol based on the composition of mono- and diacrylates in the product. The chemical structure of precursor, monoacrylate, and diacrylate are shown in Figure 5.2.

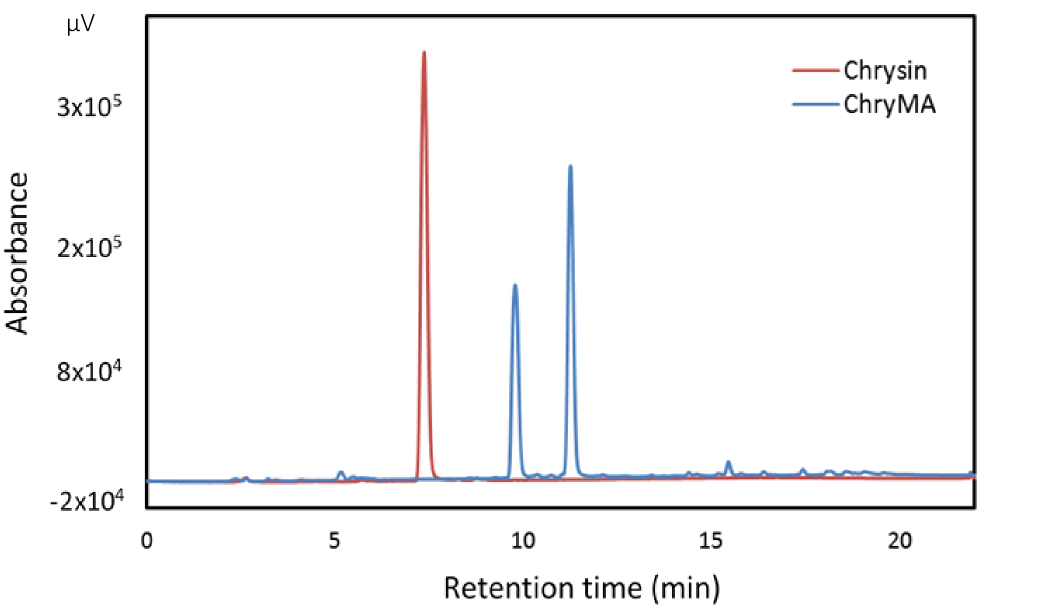
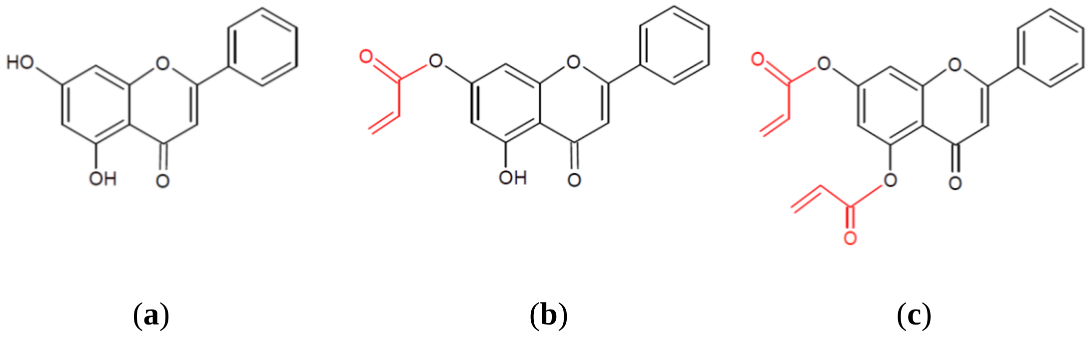


Figure 5. 1 HPLC chromatograms for Chrysin and chrysin multiacrylate (ChryMA)



(a) **(b)** **(c)**

Figure 5. 2 Chemical structure of (a) Chrysin; (b) Chrysin-monoacrylate; (c) Chrysin-diacrylate

5.3.2. Synthesis of NIPAAm-co-ChryMA gels

NIPAAm-*co*-ChryMA gels were synthesized by free radical polymerization using ammonium persulfate (APS) as a thermal initiator. The crosslinker poly(ethylene glycol) 400 dimethacrylate (PEG400DMA) was kept at 5 mol %, while the ratio of NIPAAm and ChryMA was varied to determine the influence of the hydrophobic crosslinker/comonomer in swelling behaviors and phase transition properties. The control group was synthesized using 5 mol % of PEG400DMA with the rest of NIPAAm, which is referred to as ChryMA 0.0. Three other hydrogel systems were synthesized with 2, 4, or 6 mol % of ChryMA, referred to as ChryMA 2.0, ChryMA 4.0, and ChryMA 6.0, respectively. With these reaction conditions, hydrogels could not be synthesized with more than 6 mol % of ChryMA, which is potentially due to the larger ChryMA molecule sterically hinder gel synthesis at the double bond reactive site. The texture of swollen gel became stiff and rubbery as the amount of ChryMA increased, while low ChryMA content gels were soft and flexible. The polymerization schematic of synthesizing NIPAAm-*co*-ChryMA gel is shown in Figure 5.3.

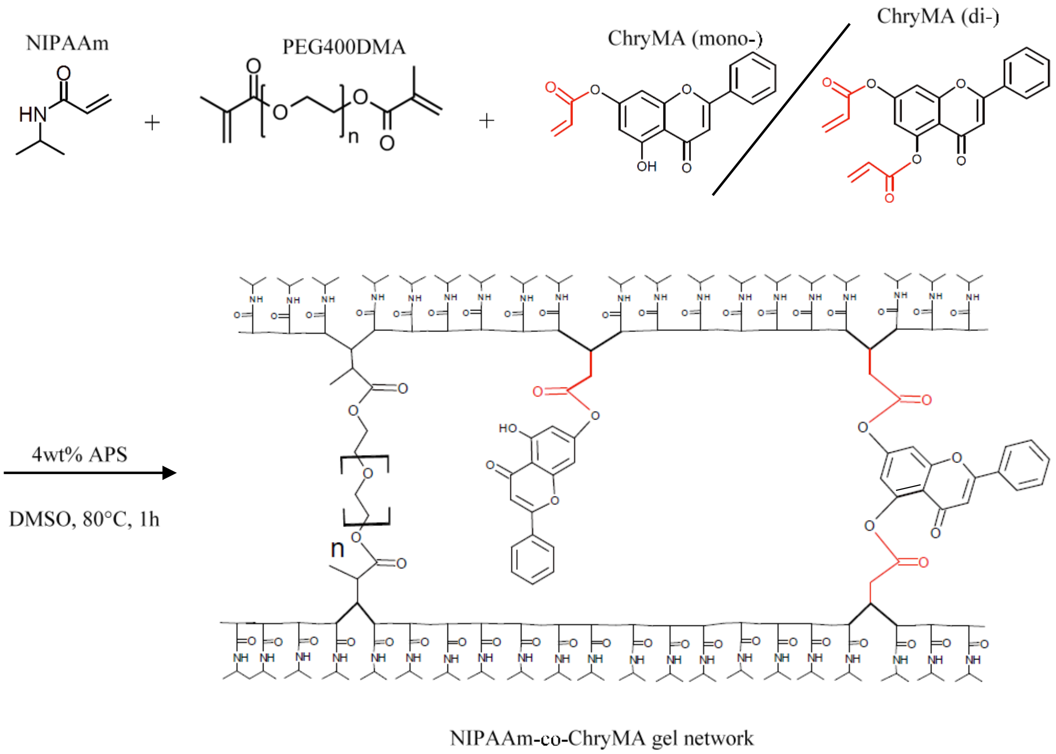


Figure 5. 3 Example polymerization scheme for synthesizing *N*-isopropylacrylamide (NIPAAm)-*co*-ChryMA gels

5.3.3. Kinetic swelling study

The kinetic swelling behavior of NIPAAm-co-ChryMA gels was studied at 25°C in a water bath for up to 48 h. The mass swelling ratio "*q*" was defined as the mass at the swollen state divided by the mass at the dry state, and the q as a function of time is shown in Figure 5.4. From the result, it can be noticed that all gels reached equilibrium swelling by 24 h, and the equilibrium swelling ratios decreased with ChryMA content. The addition of ChryMA increases the hydrophobicity of copolymer gels, and thus, the hydrogels have less affinity for water. Furthermore, the increasing ChryMA content in the gel network increases the degree of crosslinking. Both of these factors can be attributed to the lower swelling ratio of the hydrogel with a higher content of ChryMA.

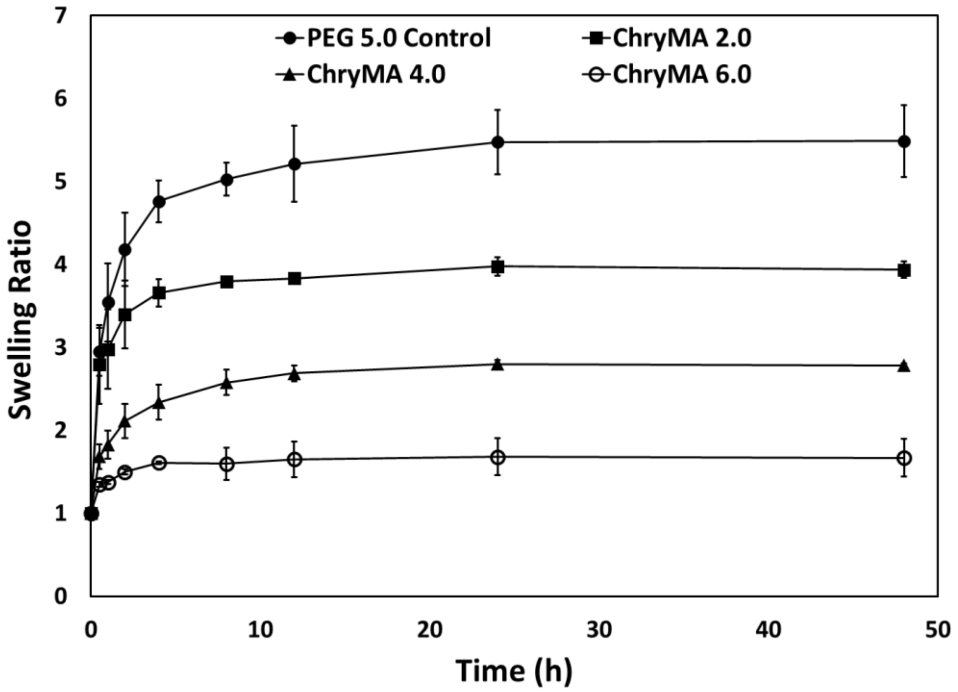


Figure 5. 4 Kinetic swelling behavior of NIPAAm-*co*-ChryMA gels

5.3.4. Temperature dependent swelling study

To study the impact of comonomer content on thermoresponsive swelling behaviors, two temperature dependent swelling studies were conducted. The first study aimed to generate a temperature swelling profile. In this study, copolymer gels were allowed to swell at different temperatures, and their mass swelling ratios were measured after 24 h. As shown in Figure 5.5, higher temperature caused a lower swelling ratio; and the higher ChryMA content led to a lower transition temperature. Meanwhile, higher ChryMA content gels showed lower swelling and broader phase transition due to more crosslinking in the structure and the addition of hydrophobic content. As temperature increased, all copolymer gels almost completely collapsed by 37.5 °C.

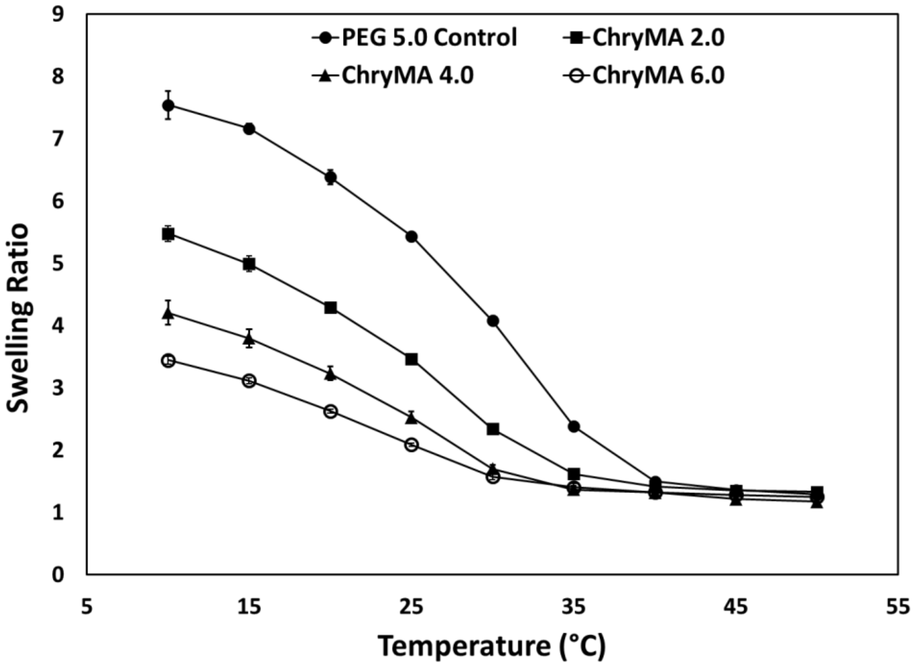


Figure 5. 5 Temperature dependent swelling profile of ChryMA hydrogels

A second reversible swelling study was also conducted, as shown in Figure 5.6. The capability of the NIPAAm-*co*-ChryMA hydrogels to swell and deswell repeatedly is important for applications. Reversible temperature changes in this study were designed to span the LCST of the gels going from 10 to 50°C for ChryMA gels. All gels showed good reversible swelling behavior, retaining swelling within 5%. One possible reason for the slight decrease in the reswelling ratio is the additional crosslink formation through repeated heating. Another reason could be that small fragments of the hydrogel samples were lost during sample handling (especially when they were swollen and fragile), as this could also contribute to the slight decrease in the swelling ratios. Additionally, bubbles formed in ChryMA 6.0 content gels during the heating cycle of the reversible swelling test, and this is likely because the outside thin "skin" barrier is more permeable to water and collapses quickly when undergoing a fast temperature transition. After this outside network collapses, trapped water inside cannot leave the hydrogel and forms a bubble. Zhang et al. (2004) reported a similar deswelling and reswelling phenomenon for higher comonomer content gels.

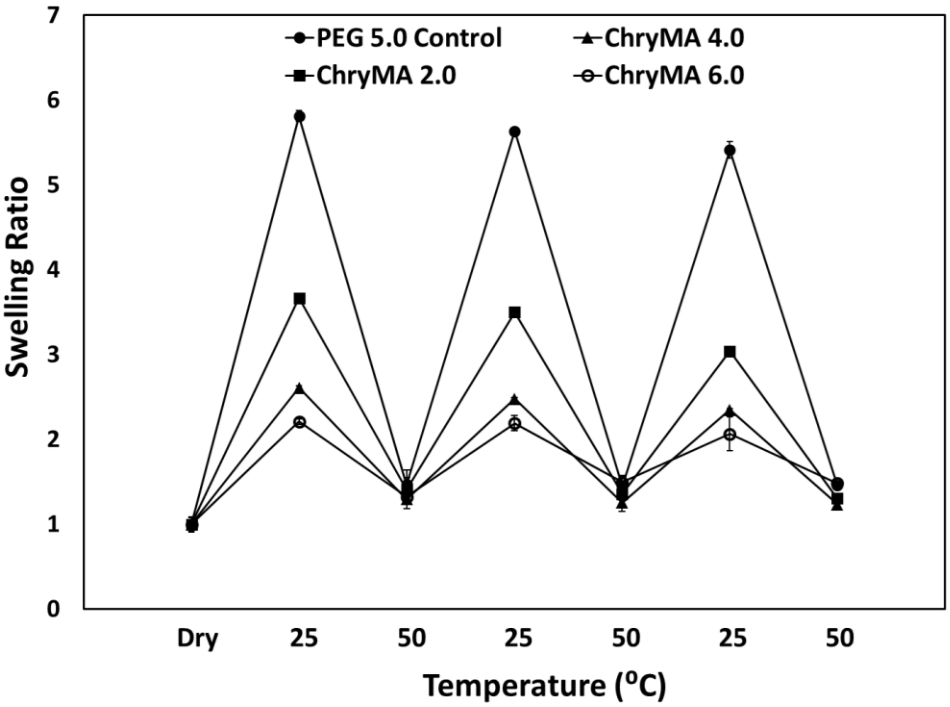


Figure 5. 6 Reversible swelling behavior of NIPAAm-*co*-ChryMA hydrogels

5.3.5. LCST measurements

Various methods are known for determining the LCST of NIPAAm hydrogels, but the most widely used methods are differential scanning calorimetry (DSC) and the equilibrium swelling ratio method. The DSC technique is often more precise since it gives information on the heat released from the cleavage of hydrogen bonds between water and the polymer chain (Boutris et al., 1997; Constantin et al., 2011). In a typical DSC thermogram, the endothermic peak is referred to as the LCST of the hydrogel, where intramolecular hydrogen bonds between water and NH-break.

Homopolymer NIPAAm is known to have an LCST around 32–33°C. PEG 5.0 control gel showed an upward shift in LCST to 34.5°C, which is likely due to the hydrophilicity of PEG400DMA. The incorporation of hydrophilic groups increases the amount of intermolecular hydrogen bonding, so that additional heat is necessary to break the hydrogen bonds, resulting in an increase in the LCST.

The NIPAAm-*co*-ChryMA gels exhibit an LCST that can be tuned from 34.5 to 27.4°C by altering the ChryMA composition, as shown in Figure 5.7. The addition of hydrophobic ChryMA shifted the LCST to lower temperatures due to the fewer hydrogen bonds, meaning that less energy was needed to beak the bonds, thus the transition temperature decreased. In addition, broader peaks were observed for high ChryMA content gels. Important characteristics of synthesized gels are summarized in Table 5.1.

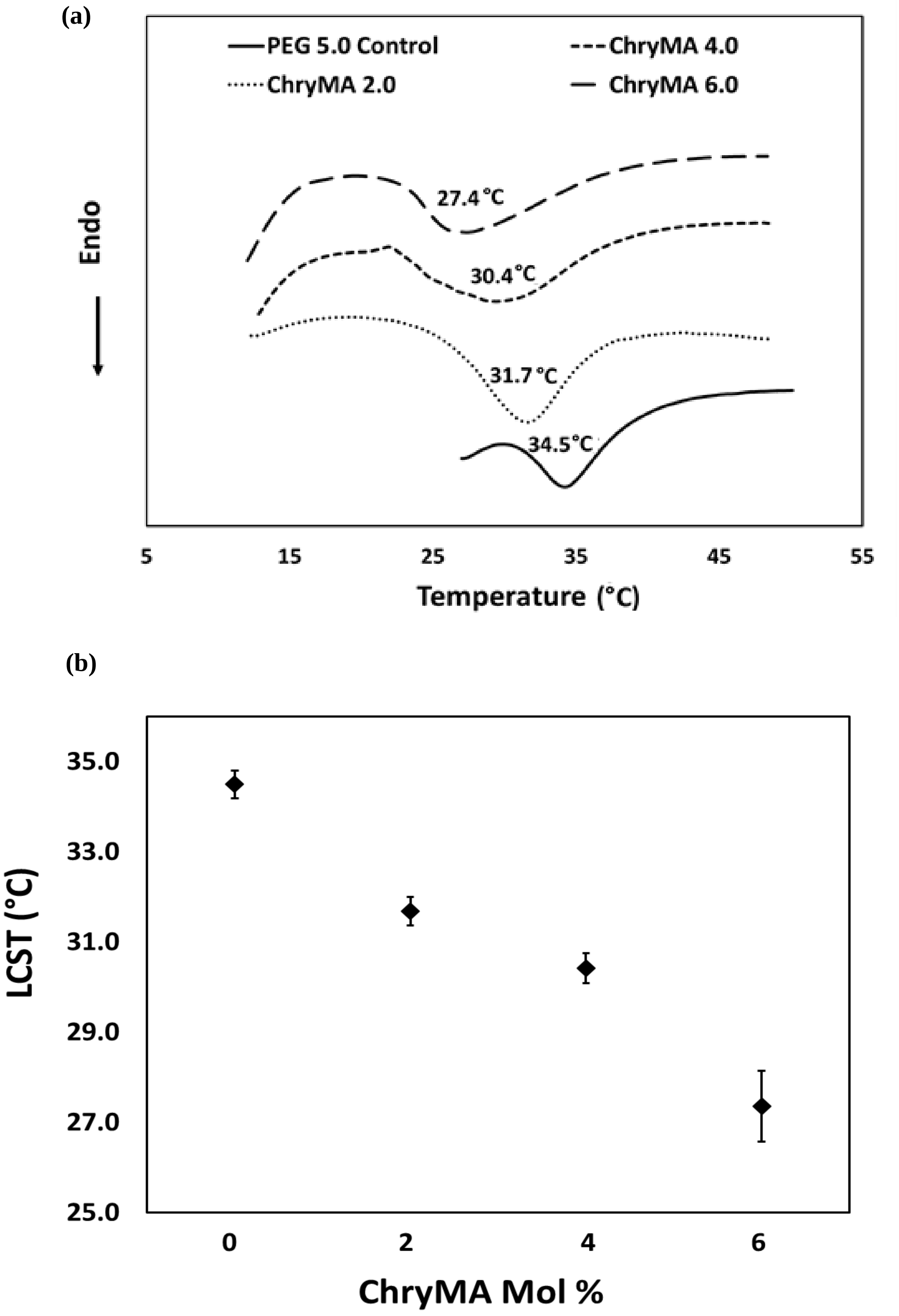


Figure 5. 7 (a) Lower critical solution temperature (LCST) measurement of NIPAAm-co-ChryMA gels; (b) LCST as a function of ChryMA content

5.4 Conclusions

Hydrophobically modified NIPAAm-*co*-ChryMA hydrogels were successfully developed through free radical polymerization. Gels with four different compositions were synthesized to study the effect of comonomer content on their swelling and phase transition behaviors. The swelling ratios of copolymeric gels decreased with an increase in ChryMA content, and the addition of ChryMA shifted the LCST to lower temperatures. As temperature increased, swelling decreased for all gels, displaying strong temperature responsive behavior, and this response was shown to be reversible. These novel hydrogels have various potential applications in biomedical, environmental, and other fields.

Chapter 6 Investigation of smart sorption and efficient regeneration of thermoresponsive hydrogels for phenol removal from water

6.0 Abstract

Two sets of smart sorbents were developed by incorporating novel hydrophobic crosslinkers into N-isopropylacrylamide (NIPAAm) hydrogels. The prepared hydrogels have shown to effectively bind phenol from aqueous solutions. The binding studies were conducted at below (10°C) and above (50°C) the lower critical solution temperature (LCST) of NIPAAm. Equilibrium binding data were fitted with Langmuir isotherm, and the results indicated that the binding capacity at T>LCST was higher than that at T<LCST. This finding was attributed to the phase transition behavior of NIPAAm around LCST, where the gels exhibit hydrophilicity below this temperature and hydrophobicity above it. The enhanced binding capacity at T>LCST was attributed to the phase transition induced hydrophobic interaction between the copolymer gel and phenol. Moreover, the obtained hydrogels possessed facile and efficient regeneration ability in water at 10°C, without requiring harsh solvent treatment or high energy input.

6.1 Introduction

Phenol has been found in the effluents of various industries, such as petrochemicals, pharmaceutical, refineries, dyes, resins, plastics, pesticides, etc (Zilli et al., 1993; Kujawski et al., 2004; Srivastava et al., 2006; Berardinelli et al., 2008). Due to its relatively high water solubility (up to 98 g L^{-1} or 98,000 ppm) (Dąbrowski et al., 2005; Srivastava et al., 2006; Berardinelli et al., 2008). Phenol can transport favorably in the natural environment. A common phenol concentration found in wastewater is 100-1000 ppm (Srivastava et al., 2006). However, the American Environmental Protection Agency (EPA) regulates its maximum concentration level of only 1 ppm (Igarashi et al., 2004; Srivastava et al., 2006).

Phenol is harmful to the organism even at low concentrations due to its protein denaturing ability (Michałowicz and Duda, 2007). The removal of phenol from effluents is essential before discharging them into water bodies. Solvent extraction (Greminger et al., 1982; Gonzalez et al., 1986), membrane pervaporation (Hoshi et al., 1997; Gupta et al., 2003; Das et al., 2008), biodegradation (Der Yang and Humphrey, 1975; Kumar et al., 2005; El-Naas et al., 2009), chemical oxidation (Comninellis and Pulgarin, 1991, 1993), and adsorption (Radovic et al., 2001; Shen, 2002; Caetano et al., 2009) are the conventional strategies for phenol treatment. Among these, adsorption is considered as one of the most effective removal technique due to its universal nature, inexpensiveness, ease of operation, and various in sorbent option (Malaviya and Singh, 2011; Ali et al., 2012; Jing et al., 2013). Currently, activated carbons (ACs) based sorbents have been widely investigated in the water purification process (Radovic et al., 2001; Dąbrowski et al., 2005). Owing to the highly porous structure and possible interactions between carbon surface and phenols, ACs have been reported to exhibit the highest adsorption capacities to phenol (200-300 mg g^{-1}) (Fierro et al., 2008). However, it is known that the adsorption of phenol on ACs is irreversible, which makes the regeneration process a challenge. Generally, the regeneration of ACs requires temperature as high as 800°C (Berardinelli et al., 2008). In addition, high expenses in manufacture and difficulties in recovery make the utilization of ACs less cost-effective for large-scale remediation.

Hydrogels have been studied as potential alternatives to ACs. Hydrogels have large water uptake ability, and they can be designed with tailored sorption affinity and capacity through incorporating comonomer functionalities. Stimuli-responsive hydrogels are an interesting category of hydrogels, which can respond to one or multiple external stimuli (e.g., temperature, pH, ionic strength, light) by changing their physical and/or chemical states (Nayak et al., 2003; Parasuraman and Serpe, 2011b). N-isopropylacrylamide (NIPAAm) is one of the most widely studied responsive compounds, with excellent thermoresponsive properties. NIPAAm exhibits an inherent lower critical solution temperature (LCST) around 32°C, and the LCST can be easily tuned up/down through copolymerizing with different monomers (Bae et al., 1991c; Yoshida et al., 1995; Qiu and Park, 2001). At temperature below 32°C, NIPAAm is hydrophilic and forms hydrogen bonding with water; at the temperature above 32°C, NIPAAm gel becomes hydrophobic due to the association of the isopropyl groups.

NIPAAm hydrogels have been studied for the removal of multiple environmental pollutants including dyes, heavy metals, etc. The main removal mechanisms can be summarized as follows: sorption through hydrophobic interactions at temperature > LCST when the isopropyl groups associate, then desorption by lowering the temperature to below the LCST (Guilherme et al., 2003; Igarashi et al., 2004; Kanazawa et al., 2004; Castellanos et al., 2007; Tokuyama and Iwama, 2007; Pan et al., 2008; Parasuraman and Serpe, 2011b; Kureha et al., 2014; Kureha et al., 2016); or sorption through chelation, complexation, or electrostatic interaction at temperature < LCST by comonomer functionalities (e.g., chelating agents, acrylic acid, chitosan and etc), then release through solvent extraction or thermo-destabilization (Yamashita et al., 2003; Fukuoka et al., 2010; Parasuraman et al., 2013; Park et al., 2014; Yao et al., 2015; Zhen et al., 2015; Cheng et al., 2017; Guo et al., 2017). In both cases, the phase transition of NIPAAm plays an important role in mediating the capture/release of the pollutants. The work discussed in this article will be focusing on the first mechanism, which has initially been reported on protein isolation (Kawaguchi et al., 1992) and later on been discovered as an effective technique for pollutants treatment. For example, Tokuyama et al. developed a novel temperature-swing hydrogel that can adsorb metal-extractant complexes through hydrophobic interaction at a temperature above the LCST, and release the complexes by lowering the temperature to below the LCST (Tokuyama and Iwama, 2007). Guilherme et al. investigated the phase transition of NIPAAm on the partition coefficient of organic dyes, the results indicated that high temperature decreased the partition coefficient and enhanced the adsorption of dyes (Guilherme et al., 2003).

Although the application of NIPAAm hydrogels as sorbents has been well studied to remove heavy metals and dyes, limited research has been reported on the removal of organic pollutants. In this work, we developed two novel NIPAAm copolymer hydrogel systems and demonstrated their effectiveness in removing phenol from aqueous solution. 4,4'-dihydroxybiphenyl diacrylate (44BDA) and curcumin multiacrylate (CMA) crosslinkers, with synthesis and characterizations details previously reported, were introduced into the hydrogel network to enhance phenol binding. The presence of aromatic/phenolic moieties in 44BDA and CMA was expected to provide binding sites for phenol through pi-pi stacking interactions. Meanwhile, the temperature triggered phase transition of NIPAAm controls the binding affinity to exhibit "on-off" status at T>LCST/T<LCST. For a better understanding of this "on-off" binding mechanism, batch binding studies to phenol were conducted at various temperatures. The effect of crosslinking density/hydrophobic content on the binding was studied. In addition, the

temperature dependent swelling and sorption were investigated to show the influence of the phase transition in the physicochemical and binding properties of the hydrogels. Equilibrium binding data at 10°C (T<LCST) and 50°C (T>LCST) were analyzed by Langmuir isotherm using non-linear regression technique. The maximum binding capacity Q_m (mg g^{-1}) and dissociate constant K_L (mg $^{-1}$) were obtained and compared. By incorporating the thermal responsive property of NIPAAm, we are able to achieve the capture and release of phenol through a small change of temperature. Moreover, the addition of hydrophobic/polyphenolic crosslinkers enhanced the phenol binding capacity.

6.2 Materials and Methods

6.2.1 Chemicals

The monomer N-Isopropylacrylamide (NIPAAm, 97%), initiator ammonium persulfate (APS, ≥98%), phenol (≥99%), 4,4’-dihydroxybiphenyl and curcumin were purchased from Sigma-Aldrich Corporation (St. Louis, USA). The crosslinkers, 44BDA and CMA, were synthesized through the acrylation of 4,4’-dihydroxybiphenyl and curcumin following an approach that has been previously developed (Tang et al., 2017a; Tang et al., 2017b). Polyethylene glycol dimethacrylate 400 (PEG400DMA) was purchased from Polysciences, Inc (Warrington, USA). Acetone and DMSO were purchased from VWR (Radnor, USA). All agents mentioned above were used as received without further purification.

6.2.2 Preparation of NIPAAm copolymerized hydrogels

The hydrogels presented in this work were prepared by free radical polymerization with NIPAAm as the monomer and 44BDA/CMA as the crosslinkers. The reaction was carried out at 80°C with APS as the thermal initiator. A control system was synthesized in the same manner by crosslinking NIPAAm with PEG400DMA. The feed composition varied from 1 to 5 mol% of the crosslinkers and the gels were denoted with following notation: 44BDA 3 represents 3 mol% of 44BDA and 97 mol% of NIPAAm. The detailed gel composition of all the systems is summarized in Table 1. In a typical synthesis, monomer and crosslinker were dissolved in DMSO, then 4 wt% of APS (pre-dissolved in DI water at 0.5g ml^{-1}) was added. The pre-gel mixture (0.5 ml) was transferred into a shell vial (45mm x 15mm; length x diameter) with the top sealed by a rubber stopper. The mixture was purged with nitrogen gas and then placed in an 80°C water bath for 1 h polymerization. To remove any unreacted monomers, gels were washed with excess acetone, 50% v/v acetone aqueous solution, and DI water three times. The washing process was conducted in an orbital shaker at 140 rpm for at least 2 h each time. Then, gels were freeze-dried overnight until no further mass change. The crosslinking process of NIPAAm copolymer gels is schematically shown in Figure 6.1.

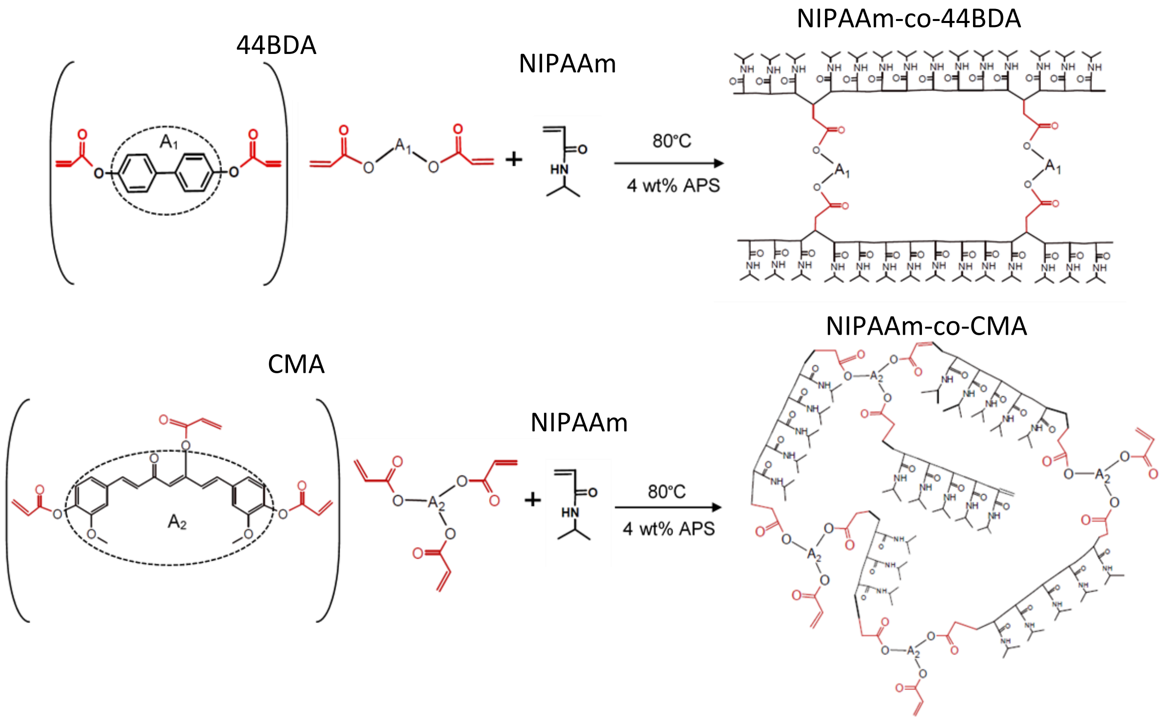


Figure 6. 1 Schematic shows the polymerization reaction and polymeric network of the copolymer hydrogels

6.2.3 Characterization of the hydrogels

The temperature responsive properties of the copolymer hydrogels were characterized through swelling studies and differential scanning calorimetry (DSC). The dry pieces were weighed first and then tested for their temperature dependent swelling behaviors in an isothermal water bath from 10°C to 50°C with a 10°C increment. The equilibrium swollen mass was measured after 24 h using gravimetric method after the surface water being gently wiped off. The mass swelling ratio (q) was defined in Equation 6.1:

$$q = \frac{M_{swollen}}{M_{dry}} \qquad [6.1]$$

Where $M_{swollen}$ is the equilibrium swollen mass at each temperature point and M_{dry} is the dry mass of the gel pieces. The LCSTs of the hydrogels were measured by differential scanning calorimetry (DSC Q2000, TA Instruments Inc., New Castle, USA). In a standard procedure, the hydrogel was immersed in DI water at room temperature for 24 h to reach an equilibrium. A small piece of gel was gently dabbed dry and then placed in a T-zero pan with mass being carefully measured. The sample was hermetically sealed and transferred onto the heater along with a reference pan. All the samples were tested under a dry nitrogen atmosphere with a flow rate of 50 mL min^{-1} and heated from 10°C to 50°C at a rate of 2°C min^{-1}.

6.2.4 Phenol sorption studies

Kinetic studies were carried out to determine the required time to reach equilibrium, and the results exhibited that the equilibrium was achieved after 24 h. To study the phenol sorption behavior as a function of temperature, dry gel pieces (~20 mg) were incubated with 1 ml of phenol solution (75 ppm) at different temperatures (10°C, 20°C, 30°C, 40°C and 50°C) for 24 h. The supernatant was then measured using a UV-vis spectrophotometer (Varian Cary50, Agilent Tech, Santa Clara, USA). Spectra of phenol in DI water was obtained, and the absorbance was measured at a wavelength of 270 nm. The effect of temperature on the visible absorption spectrum of phenol in aqueous solution was assessed in the absence of copolymer gels. It was observed that the change in temperature did not significantly impact the absorbance of phenol. The concentration of phenol in DI water was determined using a calibration curve, and the amount of bound phenol per unit mass of sorbents at equilibrium Q_e (mg g^{-1}) was calculated according to Equation 6.2:

$$Q_e = \frac{(C_0 - C_e)*V}{m} \qquad [6.2]$$

Where C_0 and C_e are the initial and equilibrium phenol concentrations (ppm/mg L^{-1}), respectively. V (L) is the volume of the solution and m (g) is the mass of the hydrogel.

The binding isotherms at temperatures below/above the LCST were determined through binding study at 10°C or 50°C. In brief, hydrogel pieces (~20 mg) were incubated in 1 ml of phenol aqueous solution at 10, 25, 50, 75, 200, 400, 800 and 2000 ppm. The phenol calibration curve of the absorbance versus concentration showed a linear correlation up to 75 ppm of phenol. Therefore, samples with higher concentrations (200-2000 ppm) were diluted with DI water. The supernatant was determined with UV-vis after 24 h and the equilibrium sorption was analyzed in the same manner as described before.

6.2.5 Releasing/desorption kinetics

The releasing kinetic study was performed after hydrogel (~20mg) equilibrium sorption in 1 ml of 75 ppm phenol solution at 50°C, followed by desorption in 1ml of 10°C or 50°C fresh DI water for up to 24 h. The phenol concentration in fresh DI water was analyzed by UV-vis spectrophotometer at different time intervals (0.5, 1, 2, 4, 8, 12, and 24 h) to determine the amount of phenol being released.

6.3 Results and discussion

6.3.1 Preparation and characterization of NIPAAm copolymer hydrogels

Images of freeze-dried 44BDA and CMA hydrogels are shown in Figure 6.2. Figure 6.3 shows the temperature dependent swelling profiles of NIPAAm hydrogels with varying amount of crosslinkers. It is well known that NIPAAm hydrogels swell at T < LCST due to the hydrogen bonding with water and collapse at T > LCST due to the hydrophobic interactions among isopropyl groups (Inomata et al., 1990; Tokuhiro et al., 1991). From Figure 6.3, it is found that both 44BDA and CMA hydrogels showed decreased swelling ratios when the temperature increased. The sharpest decrease happened between 20-30°C for 44BDA hydrogels and 20-35°C for CMA hydrogels, respectively, which is consistent with the phase transition of NIPAAm. No appreciable change happened after 40°C, indicating the hydrogels have reached complete collapsed states. Lower 44BDA/CMA content hydrogels had sharper phase transitions and higher swelling ratios. This could be due to the lower crosslinking density and higher NIPAAm incorporation. In addition, the crosslinkers are hydrophobic, resulting in 44BDA/CMA 1 hydrogels are obviously less hydrophobic than 44BDA/CMA 5 hydrogels. It is interesting to note that when comparing between 44BDA and CMA, the 44BDA hydrogels have shaper phase transitions over the LCST range. A potential explanation could be that the CMA crosslinker results in a more restricted network due to its five possible crosslinking sites.

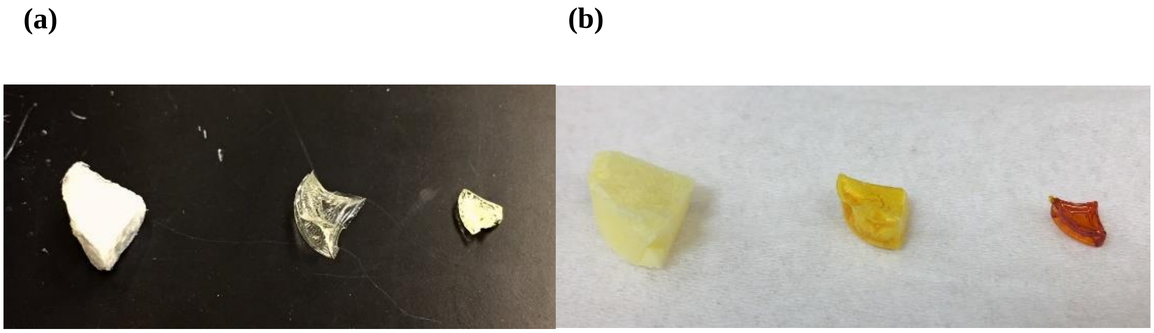


Figure 6. 2 Appearance of freeze-dried NIPAAm copolymer gels. (a) 44BDA 1, 3 and 5 gel; (b) CMA 1, 3 and 5 gel

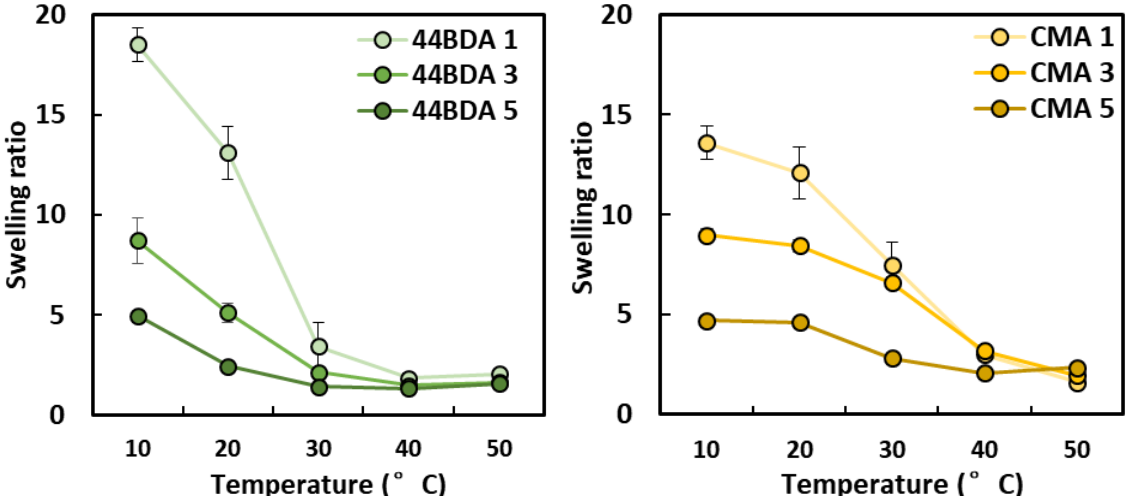


Figure 6. 3 Temperature dependent swelling of 44BDA and CMA gels. Each point represents an average of three replicates and error bars denote the standard deviation

The LCSTs of the resulting hydrogels were measured via thermal analysis using DSC, and the thermograms are shown in Figure 6.4. Clear endothermic peaks corresponding to the LCSTs were observed for all types of copolymer hydrogels. The width of the peaks indicates the phase transition range appeared between 25-35°C, which was in agreement with the swelling results above. The endothermic peak becomes broader as the crosslinker content increased because of the high crosslinking density. In general, the incorporation of hydrophobic co-monomers is known to shift the LCST to lower temperature. As can be seen from Figure 6.4, the LCST for 44BDA hydrogels (1, 3, and 5 mol%) were shifted from 32°C to 30.6°C, 28.2°C and 27.5°C, respectively. Similarly, CMA hydrogels (1, 3, and 5 mol%) were shifted to 31.3°C, 30.2°C and 28.3°C, respectively. For a comparison, the hydrophilic PEG400DMA crosslinked hydrogels were studied, and as shown in Figure

6.4, the LCSTs of PEG400DMA hydrogels (1, 3, and 5 mol%) were shifted to 32.3°C, 33.4°C and 34.1°C.

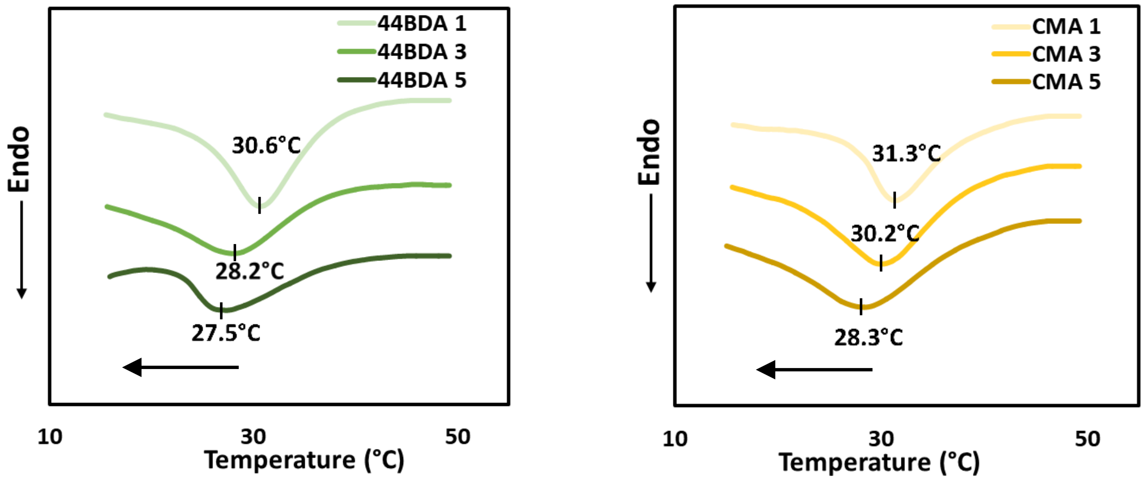


Figure 6. 4 DSC thermograms to show the LCST of 44BDA, CMA gels

6.3.2 Effect of temperature on phenol sorption

The temperature dependent phenol sorption capacity of NIPAAm hydrogels was examined by measuring the equilibrium phenol sorption from 10°C to 50°C in 10°C intervals (Figure 6.5). It can be seen that the phenol sorption increased with increasing temperature, with a sharp increase in sorption occurred around 30°C. Further increase in temperature up to 50°C did not have a significant effect on the amount of adsorbed phenol. The transition in sorption versus temperature was consistent with the transition observed in the swelling studies above. All hydrogels have shown increased phenol sorption capacity with increasing temperature. The collapsed NIPAAm chain induced a more hydrophobic environment that increased the sorption of phenol. Moreover, Figure 6.5 shows the dependence of binding capacity on the hydrophobic crosslinker content. Increasing 44BDA/CMA content in feed composition has resulted in an increased phenol sorption, which is a result of the higher the hydrophobic content leading to more the potential phenol binding sites. Thus, it can be concluded that the temperature affects not only the swelling property but also the binding capacity, and the addition of 44BDA/CMA showed an enhancement in phenol sorption.

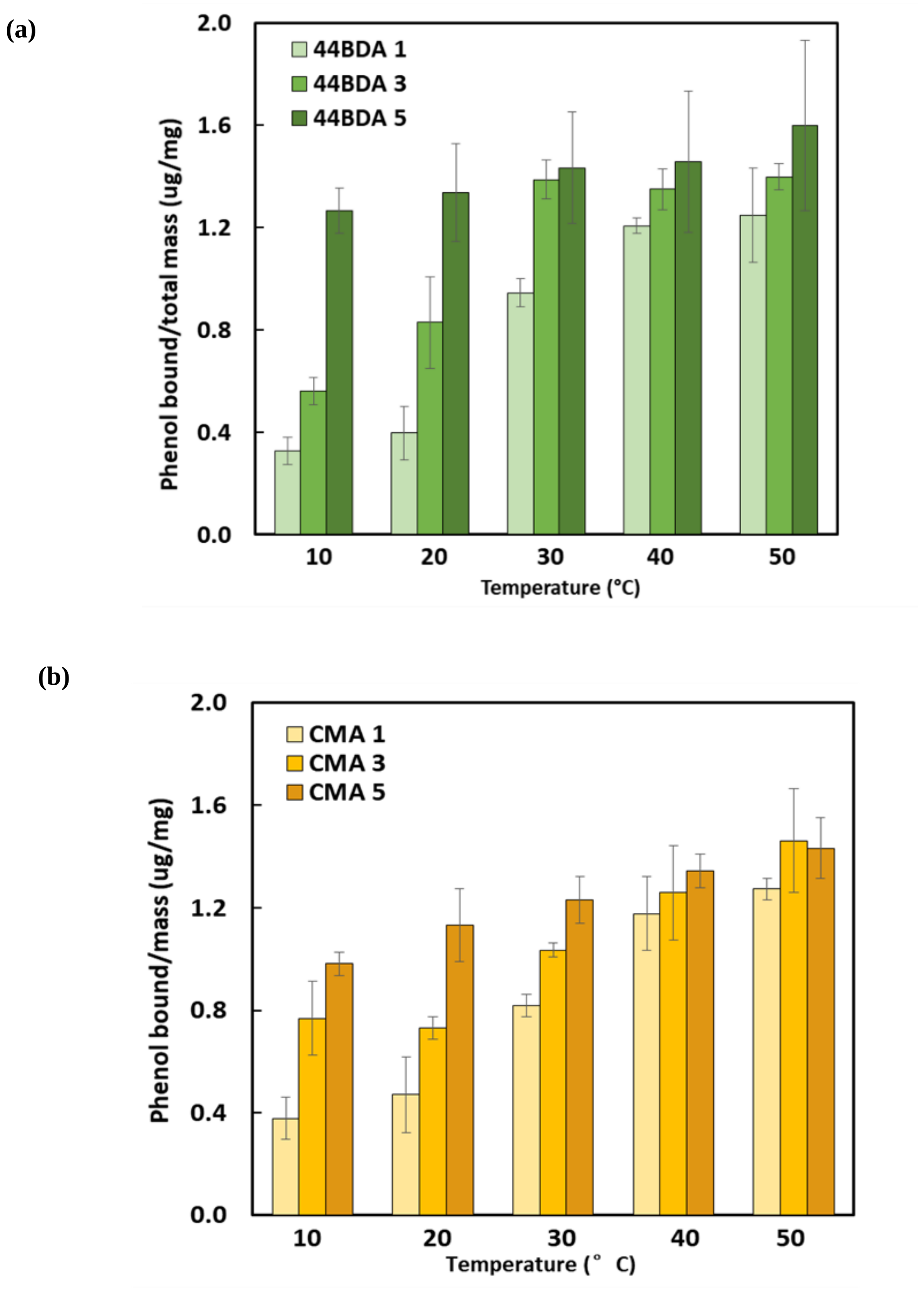


Figure 6. 5 Temperature dependent adsorption of phenol by (a) 44BDA 3 and (b)CMA 3 gels, [phenol] = 75ppm. Data represents an average of three replicates and error bars denote the standard deviation

6.3.3 Sorption isotherms at 10°C and 50°C

Figure 6.6 shows the equilibrium phenol binding isotherms of the PEG400DMA control hydrogels, and each figure represents a comparison between the binding at 10°C (<LCST) and 50°C (>LCST). The binding isotherm provides information on binding affinity and capacity of the adsorbent, which could be represented by various models. The Langmuir isotherm is one of the most widely used models because it suggests mono-layer adsorption with no strong competitive binding between sorbents and solvent (Dąbrowski et al., 2005). Data in this work were fitted with Langmuir isotherm (Equation 6.3)

$$Q_e = Q_m * \frac{K_L * C_e}{1 + K_L * C_e} \qquad [6.3]$$

Where Q_m is the maximum sorption capacity and K_L is the dissociation constant. Numerical values for Q_m and K_L were summarized in Table 6.1.

Within the investigation range, all hydrogels have shown higher binding capacities (Q_m) and smaller dissociation constants (K_L) at 50°C than those at 10°C. It is assumed that the phenol sorption at 10°C is dominated by the pi-pi stacking interactions between phenol and aromatic binding moieties from the crosslinkers, while that at 50°C is more of a combined effect of both pi-pi stacking interactions and hydrophobic interactions induced by the phase transition of NIPAAm. We have proposed a schematic to illustrate this mechanism in Figure 6.7. As a result, an enhanced sorption was observed at 50°C, with a larger value of the Q_m and a smaller value of the K_L. However, the difference in binding between 10°C and 50°C decreased as the amount of hydrophobic crosslinker increased, indicating less “on-off” binding effect in those hydrogels. Thus, the addition of the hydrophobic crosslinkers provides binding moieties but also decreases temperature responsiveness/phase transition effect, since the NIPAAm content was reduced accordingly. In this work, the maximum 44BDA/CMA content was 5 mol%, and for these systems, the sorption at 10°C and 50°C have reached a similar level, which demonstrates that there is a trade-off between enhancing the sorption and retaining the “smart” responsiveness.

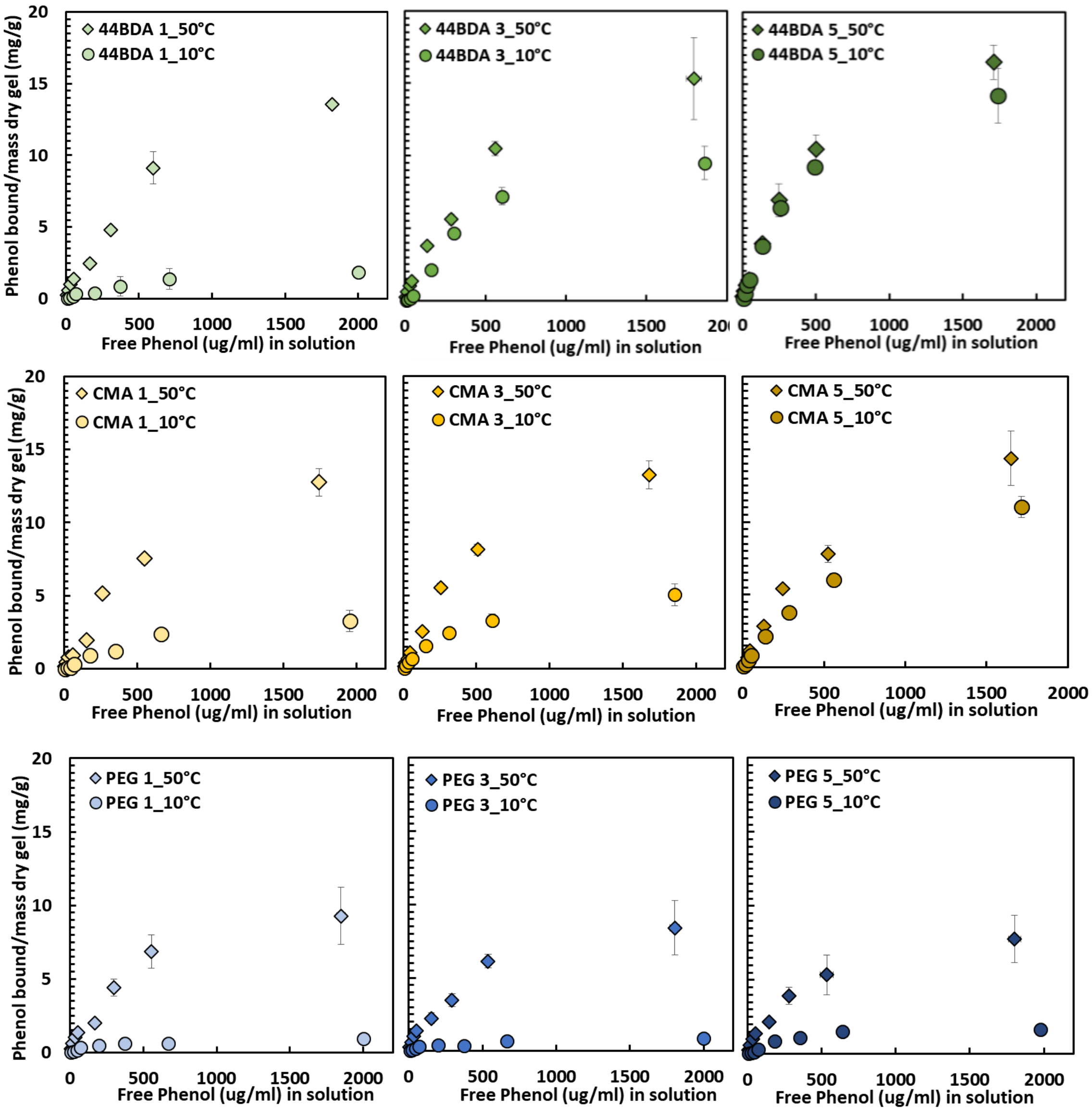


Figure 6. 6 Equilibrium binding isotherm of NIPAAm copolymer gels at 10°C and 50°C. Each point represents an average of three replicates and error bars denote the standard deviation

Table 6. 1 Numerical values for Q_m and K_L

Sample	44BDA 1	44BDA 3	44BDA 5	CMA 1	CMA 3	CMA 5	PEG 1	PEG 3	PEG 5
Q_m (mg/g)_10°C	2.51	12.56	18.43	4.68	6.19	17.54	1.02	1.01	2.01
Q_m (mg/g)_50°C	20.31	20.96	21.85	19.14	18.42	21.42	12.42	11.37	9.7
K_L (mg/L)_10°C	0.0014	0.0018	0.002	0.0013	0.0026	0.0011	0.0033	0.0025	0.0034
K_L (mg/L)_50°C	0.0011	0.0016	0.0018	0.0012	0.0015	0.0012	0.0012	0.0017	0.0022

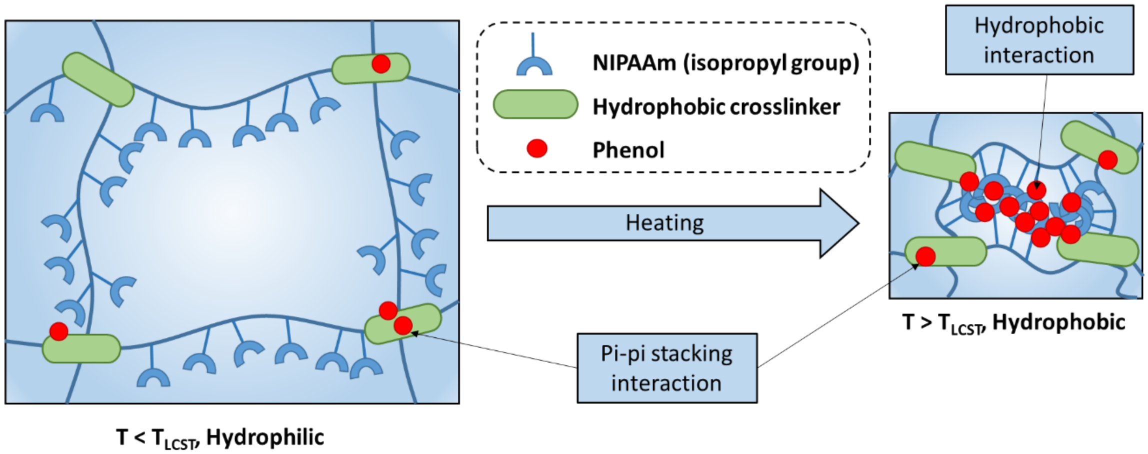


Figure 6. 7 Schematic of the temperature responsive binding mechanism of NIPAAm copolymer gel

To obtain further insights into this phenomenon, a control experiment was performed in the same manner but using PEG400DMA hydrogel, since PEG is considered to be more hydrophilic compound than NIPAAm (Gan and Lyon, 2002). As can be seen from Figure 6.6, the sorption capacities of PEG hydrogels at 10°C were lower than that at 50°C, as expected due to the phase transition of NIPAAm. The difference of binding at 10°C/50°C decreased as PEG increased, which is in agreement with the previous results and could also be explained by the loss of temperature responsiveness. However, all PEG hydrogels have shown smaller Q_m and larger K_L values when compared to 44BDA or CMA hydrogels at the same crosslinker content (both 10°C and 50°C). Furthermore, in contrast to 44BDA/CMA hydrogels, an increase in PEG from 1-5mol% have resulted in a further decrease in phenol sorption. Therefore, in this specific case of binding phenol, it can be concluded that the incorporation of hydrophilic crosslinker in NIPAAm hydrogels will decrease the sorption capacities and binding affinities, while the incorporation of hydrophobic crosslinkers will enhance the two properties.

6.3.4 Releasing kinetics

Releasing behavior was studied after the hydrogel saturated sorption of phenol at 50°C for 24 h, then desorption in 10°C/50°C fresh water. The quantity of phenol being released from the hydrogel as a function of time was plotted in Figure 6.8. 44BDA 3 and CMA 3 hydrogels were chosen as example systems for this study. In general, the high temperature is favorable for releasing bound molecules due to the thermo-destabilization effect, but the drawback of this process is its high energy input. According to the literature, a temperature of over 200°C is often needed to regenerate used sorbents through heat treatment (Jiang et al., 2017). From Figure 6.8, we find that nearly 100% of bound phenol was released at 10°C in DI water and 50% was released at 50°C in DI water (for 44BDA 3 hydrogels). Considering the aforementioned mechanism, the hydrogel exhibited hydrophilicity at 10°C, where the hydrophobic interactions were diminished and high releasing efficiency was achieved. At 50°C, the hydrogel exhibits hydrophobicity, so there was 50% of phenol remain bound due to the hydrophobic interactions, and 50% of phenol was released due to the concentration driven permeation. Similarly, CMA 3 hydrogels have also shown higher release efficiency at 10°C (95%) than 50°C (80%), but the difference was not as significant as 44BDA 3 hydrogels, indicating that 44BDA hydrogels have better regeneration ability.

The release studies have shown that 44BDA and CMA hydrogels both can achieve high-efficiency regeneration without applying a harsh solvent treatment and only using water through a small variation of temperature. The smart sorption and eco-friendly regeneration process illustrated in this work are of great significance to promote “green” remediation techniques for water treatment. Beyond that, the resulting hydrogels have provided a promising platform to further investigate other phenolic/aromatic pollutants removal methods. For example, Igarashi et al. have suggested that substituted phenols with higher hydrophobicity may be more easily to remove than phenol itself in a process that the hydrophobic interactions are involved to provide binding affinity (Igarashi et al., 2004). In the future, we will use the results generated in this work as our guide to study the removal of other pollutants, such as polychlorinated biphenyls (PCBs), etc.

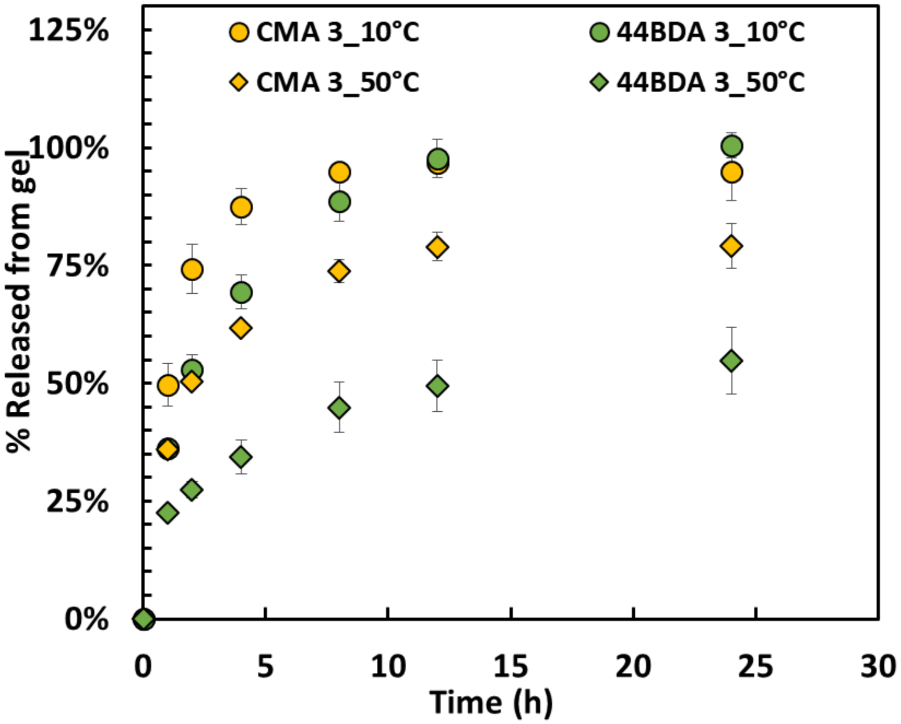


Figure 6. 8 Release curves of 44BDA 3 and CMA 3 gels at 10°C and 50°C water, respectively. Each point represents an average of three replicates and error bars denote the standard deviation

6.4 Conclusions

Two sets of thermoresponsive copolymer hydrogel sorbents were successfully developed in this work. The pollutant removal efficiency was evaluated through binding studies to phenol. The adsorption of phenol is temperature dependent. Significant enhancement in phenol binding was obtained at 50°C above the LCST, which was attributed to the hydrophobic interactions induced by the phase transition of NIPAAm. In addition, the incorporation of hydrophobic crosslinkers 44BDA and CMA has shown primitive binding effects to phenol. A facile desorption process was also achieved; nearly 100% bound phenol was released in water simply by lowing the temperature to 10°C. The prepared thermoresponsive sorbents have demonstrated an efficient temperature controlled “on-off” binding ability, which can potentially be useful for the removal of other aqueous pollutants.

Chapter 7 The removal of waste nanoparticles using a novel NIPAAm copolymer flocculant

7.0 Abstract

Temperature responsive polymeric flocculants based on N-isopropylacrylamide (NIPAAm) and a novel hydrophobic comonomer 2-phenylphenol monoacrylate (2PPMA) were synthesized through free radical polymerization. The resulting copolymer was characterized by ^{1}H-NMR and UV-vis to confirm the incorporation of 2PPMA and identify its lower critical solution temperature (LCST). The flocculation efficiency of the copolymer was examined in the solid-liquid separation of waste metal oxide nanoparticles (MONPs) in aqueous suspension. For comparison, poly(NIPAAm) was synthesized without the 2PPMA and examined in the same manner. It is known that poly(NIPAAm) can induce flocculation in particle suspension at temperature above its LCST because of the hydrophobic association of polymer chains. In this work, we found that the addition of the novel hydrophobic comonomer could increase the hydrophobic association, resulting in enhanced flocculation efficiency. Dense solid-like sediments and clear supernatant were produced due to the effective compaction of hydrophobic copolymer-MONP precipitates. Moreover, the incorporation of 2PPMA shifted the LCST of NIPAAm to a lower temperature, which is beneficial for energy conservation purposes. The novel hydrophobically modified copolymer flocculants developed in this work may lead to potential applications in industrial solid-liquid separation processes.

7.1 Introduction

The production and use of metal oxide nanoparticles (MONPs) continue to increase due to the rapid development of nanotechnology and widespread application of nanomaterials in industries (Peralta-Videa et al., 2011; Bondarenko et al., 2013). MONPs have been incorporated into various commercial products including cosmetics, sensors, catalysts, food, and biomedicine (Franklin et al., 2007; Pulicharla et al., 2014; Wang et al., 2017). As a result, considerable amount of MONPs is released into industry effluents and urban sewage streams, providing exposure routes for living organism (Liu et al., 2014). MONPs may possess adverse effects on humans and ecosystems as the released particles can make ways through the food chain (Hou et al., 2018). Multiple studies have shown that small MONPs (<30nm) can easily enter the tissues and cells of aquatic organisms, causing cytotoxicity, inflammation and cell membrane leakage (Brunner et al., 2006; Jeng and Swanson, 2006; Franklin et al., 2007; Keller et al., 2010). In addition, MONPs may generate reactive oxygen species (ROS) and induce non-ROS-mediated toxicities, leading to serious health problems (Wang et al., 2017). In comparison to the plentiful applications and toxicities explorations of MONPs, very limited research has focused on the removal of MONPs from the environment (Liu et al., 2014). Coagulation, floatation, filtration, and consolidation are the most widely used techniques to separate MONPs (Liu et al., 2014). However, due to the ultrafine size of MONPs, these conventional particle separation methods may not be sufficient, and there is a need for improved strategies for removal of MONPs.

Flocculation is a well-known solid-liquid separation process, which has been extensively applied to remove suspended and dissolved solids, colloids, and organic matter from industrial wastewater (Guillet et al., 1985; Sharma et al., 2006; Lee et al., 2014). In recent years, polymeric flocculants have attracted attention due to their high efficiency with a low dosage, broad application, and easy handling (Singh et al., 2000). However, most of the conventional polymeric flocculants are based on hydrophilic polymers. Therefore, they have common drawbacks such as high water retention in sediments, difficult to remove and recover particle flocs, etc (Sakohara et al., 2002). To improve this process, several studies have suggested using temperature responsive polymers based on N-isopropylacrylamide (NIPAAm) as an alternative, aiming to enhance the recovery of water by introducing the unique phase transition property of NIPAAm (Ng et al., 2018). NIPAAm has been widely studied for its temperature responsiveness, more specifically: the ability to undergo a temperature controlled hydrophilic/hydrophobic phase transition at lower critical solution temperature (LCST). The application of poly(NIPAAm) as flocculating agent was initially described in a patent by Guillet et al [12], and it has been extensively studied in mineral processing to remove kaolinite, clay, and silica from waste tailings (Deng et al., 1996; Sakohara et al., 2002; Franks et al., 2008; Li et al., 2009; Burdukova et al., 2010; O'Shea et al., 2010; Ghimici and Constantin, 2011; O'Shea et al., 2011; Sakohara et al., 2013a; Lu et al., 2015; Zhang et al., 2017; Gumfekar and Soares, 2018; Ng et al., 2018). In recent years, studies have reported using poly(NIPAAm) and its copolymers to remove ultrafine waste MONPs such as TiO_2 (Deng et al., 1996; Sakohara and Nishikawa, 2004; Sakohara et al., 2008). The mechanism is based on poly(NIPAAm) chains are interacting with the suspended MNOPs at temperature below the LCST through hydrogen bonding or van der Waals interactions (Besra et al., 2004; Li et al., 2009). Then, upon heating to above LCST, the adsorbed polymer molecules change to hydrophobic, which causes the polymer chains to collapse, resulting in the surface of the particles to become hydrophobic and leading to the aggregation of the polymer-MONPs flocs. Since the phase transition is reversible, the flocs disorganize and return to suspended particles after cooling the mixture down below the LCST (Sakohara et al., 2002).

In this study, we synthesized hydrophobically modified thermoresponsive flocculants based on NIPAAm and 2-phenylphenol monoacrylate (2PPMA). The goal of this study was to evaluate its flocculation efficiency in comparison to poly(NIPAAm) regarding the removal of MONPs in aqueous suspension. To the best of our knowledge, only a few groups reported the development of hydrophobic functionality modified NIPAAm flocculants (Sakohara et al., 2013a; Lu et al., 2015; Gumfekar and Soares, 2018). These materials were consisting of NIPAAm, acrylic acid (AA, ionic moiety), and N-*tert*-butylacrylamide (BAAM, hydrophobic moiety); or NIPAAm, e-aminoethyl methacrylamide hydrochloride (AEMA, ionic moiety), and 5-methacrylamido-1,2-benzoboroxole (MAAmBo, hydrophobic moiety), respectively. Enhancement in compaction and sedimentation was observed, which can be attributed to the incorporation of hydrophobic compounds. However, owing to the hydrophilicity of the ionic comonomers, the consolidation took a long time (24 hours) to complete, and the sediments still contained a significant amount of water. Through literature searching, we have not found a study that synthesized NIPAAm flocculants with only hydrophobic copolymer. The main issue might be the solubility limit of the hydrophobic compound in an aqueous solution. In this work, we developed a novel NIPAAm-co-2PPMA copolymer flocculant that retains significant solubility in water with up to 2.5 mol% of 2PPMA content. The biggest advantage of this system is that it contains only hydrophobic copolymer, which can greatly promote the polymer-particle flocs compaction by expelling water out of sediments. The sediments generated in this system are densely packed solid mass with minimum water retention. In addition, the incorporation of hydrophobic 2PPMA have shifted the LCST of NIPAAm to lower temperature; a lower LCST is preferable for conserving energy purpose. The development of hydrophobically modified smart flocculants may lead to novel strategy with enhanced efficiency in solid-liquid separation applications.

7.2 Materials and Methods

7.2.1 Materials

The monomer N-isopropylacrylamide (NIPAAm, 97%), initiator ammonium persulfate (APS, ≥98%), MONPs (TiO_2 and CeO_2), precursor 2-phenyl phenol was purchased from Sigma-Aldrich Corporation (St. Louis, USA). The comonomer 2PPMA was synthesized through the acrylation of the precursor following an approach that has been previously developed (Tang et al., 2017b). Fe_3O_4 nanoparticles were synthesized in lab following an approach that has been previously reported as well (Wydra et al., 2015). DMSO and other solvents used in monomer acrylation were purchased from VWR (Radnor, USA). All agents mentioned above were used as received without further purification.

7.2.2 Synthesis of NIPAAm polymer/copolymer

Poly(NIPAAm) and the NIPAAm copolymer with 2.5mol% of 2PPMA (2PPMA 2.5) were synthesized through free radical polymerization. In a typical synthesis of 2PPMA 2.5, 560mg of NIPAAm and 14 mg 2PPMA were dissolved in 2ml of DMSO and then added with 0.1 wt% of APS (pre-dissolved in DI water at 0.05g ml^{-1}). The solution was well mixed in a 15mm x 45mm sealed shell vial and purged with N_2 for 10 min to remove dissolved oxygen. The polymerization was carried out in 80°C water bath for one hour.

After polymerization, excess amount DI water was sprayed into the shell vial and a sticky solid mass were precipitated out of solution. The copolymer was further purified by the following method. The product was washed in DI water (200ml) to remove unreacted monomer and exchange DMSO for an easy drying process. It should be noted that the polymer/copolymer was partially dissolved in water at room temperature. Thus, the product was precipitated with addition of 10g of NaCl at elevated temperature (50°C) to collect the dissolved polymers. This washing process was repeated for three times, and the final polymer was dried in vacuum at 50°C for 24 h. The synthesis of 2PPMA and the polymerization of NIPAAm-co-2PPMA is schematically illustrated in Figure 7.1.

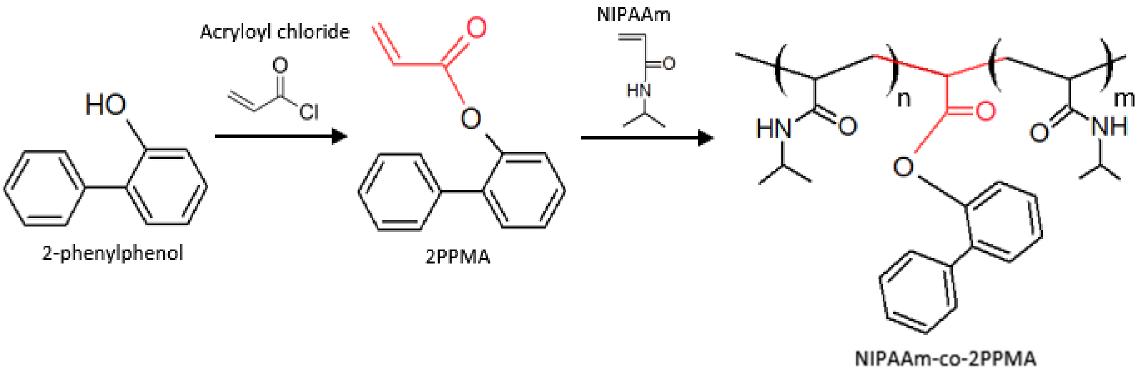


Figure 7. 1 Acrylation of 2PPMA and polymerization of NIPAAm-co-2PPMA copolymer

7.2.3 Characterization of the polymer/copolymer

^{1}H-NMR measurements were carried out on a Bruker Ascend 400 ^{1}H-NMR instrument operated at 400 MHz using deuterated DMSO as the solvent. Dry samples were dissolved in deuterated DMSO at ~10mg/ml, and 750 μl of the sample solution was measured in ^{1}H-NMR.

The LCST was determined from the changes in the transmittance as a function of temperature through NIPAAm polymer/copolymer aqueous solution at a concentration of 0.5 wt%. Around 1ml of the polymer solution was added to a quartz cuvette, and then placed in a pre-cooled/heated water bath for 5 minutes until equilibrium. The transmittance was recorded at 500nm using UV-vis spectroscopy (Varian Cary 500, Palo Alto, CA). A fall in transmittance of 50% of the initial value was noted as the LCST of the polymer (Jain et al., 2015).

7.2.4 Flocculation experiments

The flocculation test was carried out using a typical batch method described as follows. First, aqueous solution of NIPAAm polymer/copolymer and aqueous suspension of MONPs (Fe_3O_4, TiO_2, and CeO_2) were prepared at a concentration of 5mg/ml. Then, an appropriate volume of polymer/copolymer solution and MONPs suspension were mixed in a 15mm x 45mm shell vial, followed by the addition of DI water to make the final volume of 4ml. Also, NaCl was added at a concentration of 0.5M to promote the flocculation process. After the polymer solution was well mixed with MONP suspension, the shell vial was gently shaken upside down for several times before sending to a 50°C water bath. The flocculation was allowed to conduct for 10 min, and then the supernatant was removed and analyzed using iron assay (for Fe_3O_4 MONPs).

7.3 Results and Discussion

7.3.1 LCST measurement

The LCST of NIPAAm polymer/copolymer was determined from the changes in the transmittance of polymer aqueous solution as a function of temperature. The polymer exhibits hydrophilicity at temperature below the LCST. Thus, it is solubilized in low temperature water, and the solution is transparent. As the temperature increases, the solution turns to a milky white color because the polymer becomes hydrophobic and insoluble in water. The temperature dependent transmittance of poly(NIPAAm) and 2PPMA copolymer solution is shown in Figure 7.2. The light transmittance of NIPAAm polymer by UV-vis shows an LCST of 32°C, which is in good agreement with literature value (Jeong et al., 2012). It is expected that the incorporation of hydrophobic copolymer will shift the LCST of NIPAAm to lower temperature since less hydrogen bonding was formed and less thermal energy was required. As shown in Figure 7.2, with an incorporation of 2.5 mol% of 2PPMA, the LCST was lowered to 25.1°C. The decrease in LCST is beneficial in practical application since less energy is required to induce the phase transition as well as the flocculation.

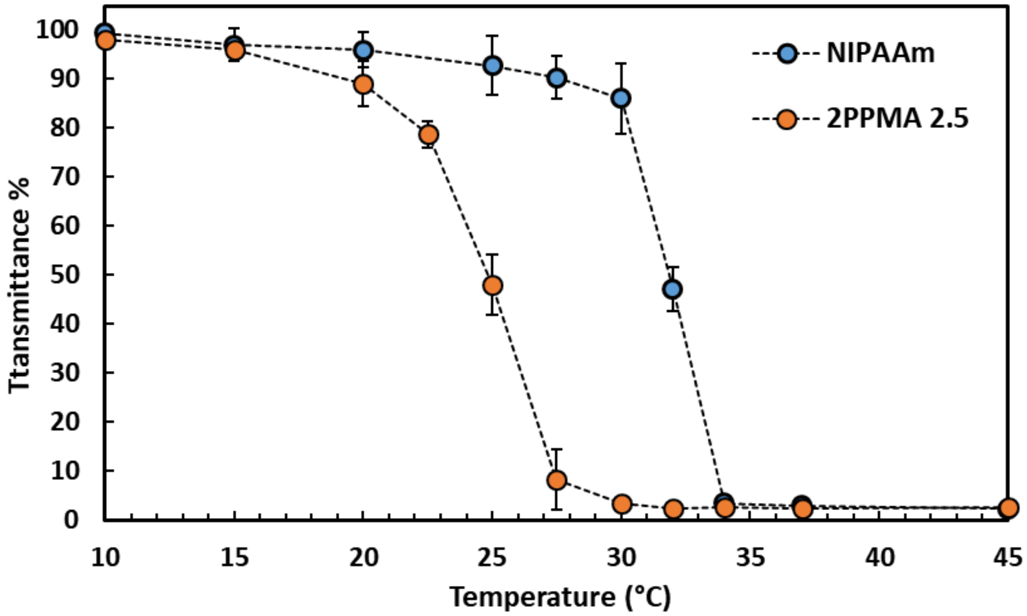


Figure 7. 2 Characterize the LCST of p(NIPAAm) and NIPAAm copolymer through UV-vis

7.3.2 ^{1}H-NMR spectra

^{1}H-NMR spectroscopy measurement was carried out to identify the polymerization of NIPAAm polymer/copolymer. As shown in Figure 7.3, the spectra of monomer NIPAAm and 2PPMA exhibit peaks at ~6.0-6.4 ppm due to the $-CH_2=CH$ functional group. These peaks are not detected in NIPAAm polymer and NIPAAm-co-2PPMA, indicating the bond break of $-CH_2=CH$ and the formation of polymer chains. The peaks at ~3.8 ppm and ~1.1 ppm correspond to –NH-CH and $–CH_3$ of NIPAAm, which are also found in poly(NIPAAm) and 2PPMA copolymers; the group of peaks at ~7.3-7.5 ppm are attributed to the $-C_{12}H_9$ of 2PPMA, which are found in 2PPMA copolymer as well. All the results above are strong evidence of the successful incorporation of 2PPMA in the NIPAAm copolymer network.

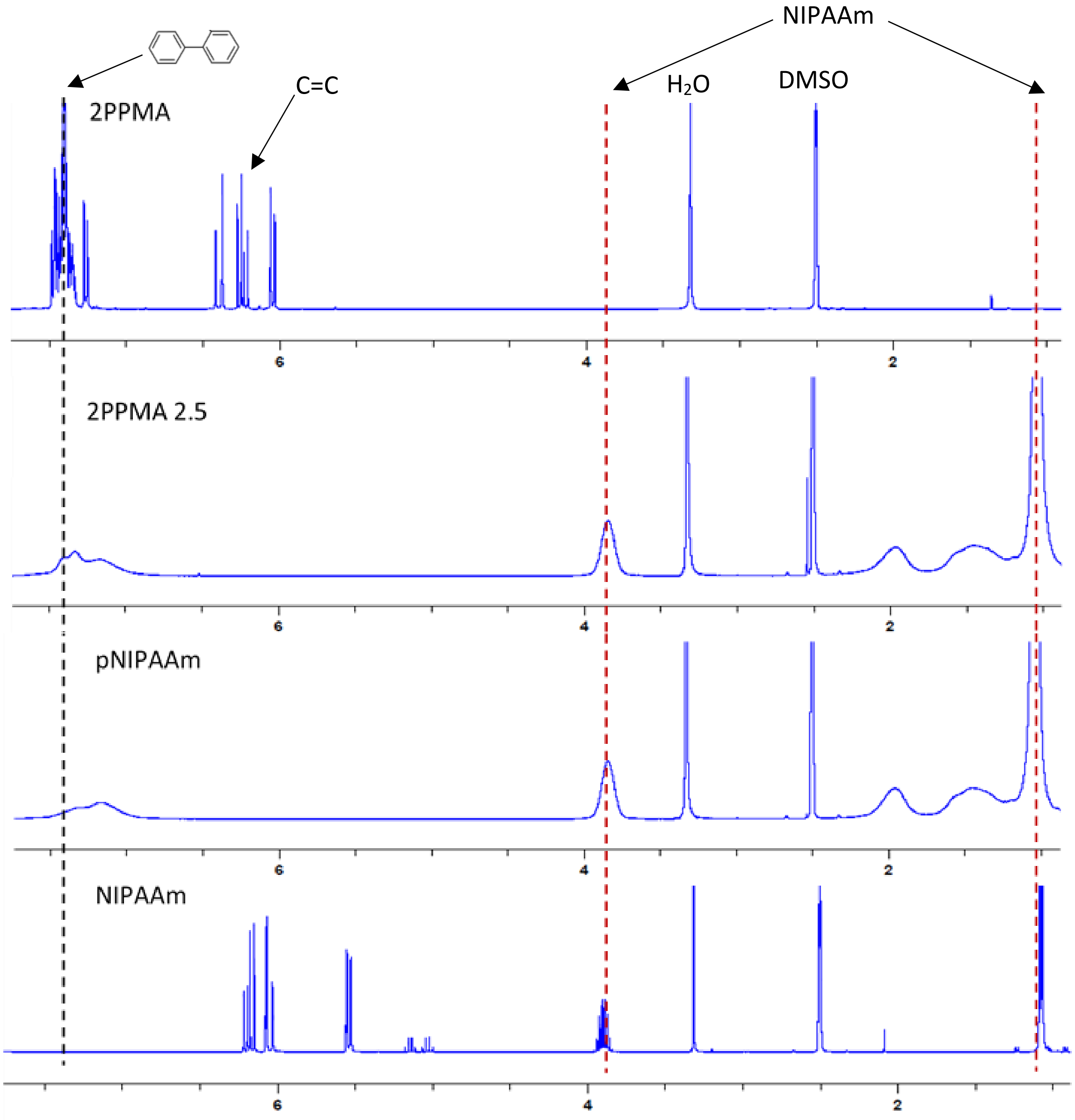


Figure 7. 3 ^{1}H-NMR spectra to illustrate the incorporation of 2PPMA in NIPAAm copolymer

7.3.3 Flocculation mechanism

Understanding the interaction between the polymers and MONPs is important in optimizing the flocculation performance. A proposed schematic that illustrates the flocculation mechanism is shown in Figure 7.4. An appropriate amount of NIPAAm polymer/copolymer is added to MONP suspension at room temperature. Then, the particle surfaces are covered with polymer molecules after a short time of gentle mixing. When temperature increases to 50°C (>LCST), the attached polymers become hydrophobic, resulting in the aggregation of polymer-MONP flocs in the suspension. However, a difference in polymer chain hydrophobicity may lead to different flocculation performances since the removal efficacy of MONPs is strongly affected by chain structure and chain hydrophobicity (Ghimici and Brunchi, 2013). It is hypothesized that the presence of additional hydrophobic 2PPMA functionality will facilitate the polymer chain aggregation at temperature above the LCST. More specifically, it is hypothesized that the biphenyl groups act as additional "crosslinkers" to connect the individual polymer chains through hydrophobic interactions, resulting in longer and more entangled polymer chains. Many studies have reported that the flocculation of fine particles using poly(NIPAAm) is mainly due to polymer bridging (Nasser and James, 2006), and longer polymer chains are beneficial to the flocculation because they create greater potential for possible attachments to other particles through extended loops/tails (Pearse and Barnett, 1980; Biggs et al., 2000). As illustrated in the schematic, the novel 2PPMA copolymer possesses better flocculation performance in comparison with poly(NIPAAm).

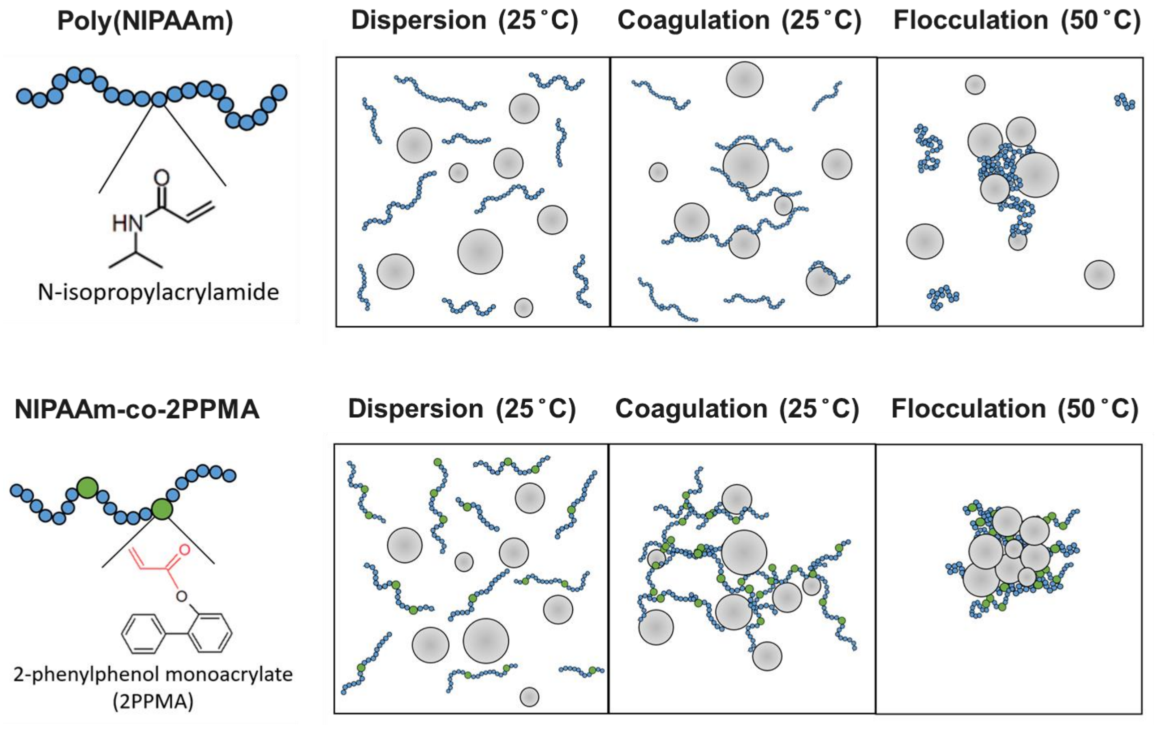


Figure 7. 4 Schematics of the flocculation with poly(NIPAAm) vs. 2PPMA copolymer

7.3.4 Kinetics

The flocculation kinetics of poly(NIPAAm) and copolymer 2PPMA 2.5 of Fe_3O_4 suspension were qualitatively measured in batch studies, and the results are shown in Figure 7.5. The pictures were taken after every 30s since the beginning of the flocculation. In this study, Fe_3O_4 was tested as an example to show the difference in flocculation efficiency between poly(NIPAAm) and 2PPMA copolymer as a function of time. Fe_3O_4 (0.5mg/ml) and NIPAAm polymer/copolymer (0.2mg/ml) were combined in a 4ml of NaCl buffer solution. It is worth mentioning that buffer components play a very important role in promoting the condensation of the precipitated polymer assemblies. In the absence of buffer components, the aqueous solution of NIPAAm polymer/copolymer become turbid instead of gathering into solid mass (Saitoh et al., 1999). The Fe_3O_4 nanoparticle suspension was prepared at room temperature and then heated to 50°C. As shown in Figure 7.5 (a), the flocculation with 2PPMA 2.5 dosage occurred within the first 30s of the process, with Fe_3O_4-polymer flocs initiated immediately after heat was applied. With time, these small flocs continued to come together eventually resulting in a large piece of solid mass. Water was repelled out of the polymer network due to the hydrophobicity of NIPAAm and 2PPMA, and the size of the solid mass kept shrinking due to the compaction of polymer-MONP sediment. The flocculation reached equilibrium after about six and half minutes when no more size change was observed. The resultant small and dense solid mass was easily removed from the water using a spatula. As a comparison, the same MONP suspension was dosed with poly(NIPAAm), as shown in Figure 7.5 (b). The flocculation occurred in a much slower manner, and unlike the 2PPMA copolymer, no immediate coagulation was observed after heating. Small flocs were formed after about 3 minutes, and they were either floating to the top or settling at the bottom. The small flocs continued to accumulate, and finally, all settled at the bottom, leaving a loosely packed sediment and turbid supernatant. The results indicated that the flocculation with 2PPMA copolymer is more efficient than poly(NIPAAm). Also, the flocculation reached to equilibrium about six and half minutes. To ensure the completion of sediment compaction, 10 minutes was used in all later tests.

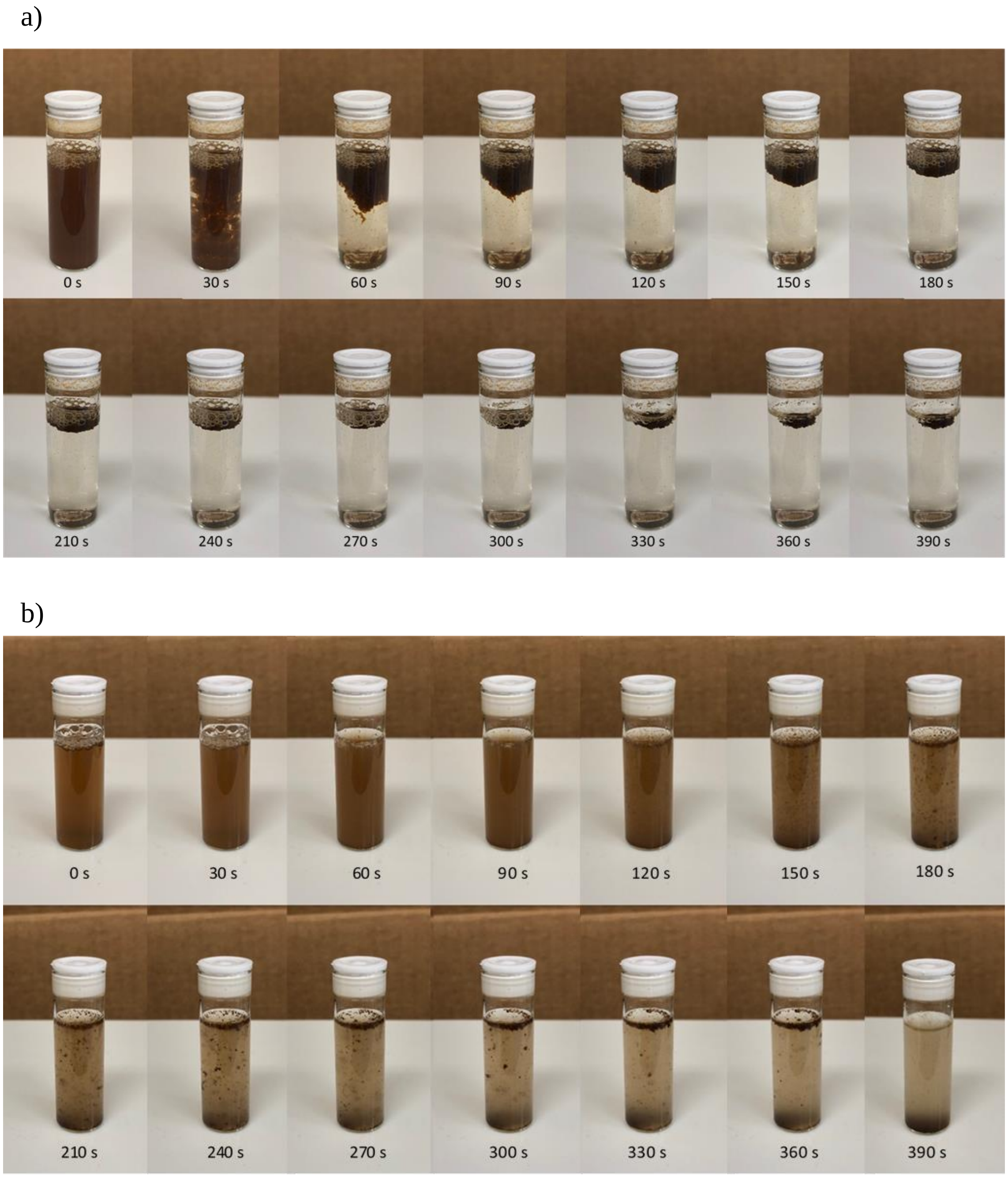


Figure 7. 5 Flocculation kinetics with Fe_3O_4 nanoparticles using (a) NIPAAm-co-2PPMA, (b) poly(NIPAAm)

7.3.5 Evaluate the flocculation efficiency as a function of MONP dosage

The flocculation efficiency of poly(NIPAAm) and 2PPMA copolymer was further evaluated in Fe_3O_4, TiO_2, and CeO_2 particle suspensions as a function of MONP dosage. MONPs at concentration of 0.01, 0.025, 0.05, 0.1, 0.2, and 0.5mg/ml were dosed with 0.2 mg/ml of NIPAAm polymer/copolymer at room temperature. The flocculation was allowed to proceed at 50°C for 10 min to reach complete equilibrium. The remaining Fe_3O_4 MONPs in the supernatant were quantitatively measured using iron assay (Figure 7.6 and Figure 7.7), and the remaining TiO_2 and CeO_2 MONPs were qualitatively evaluated (Figure 7.8 and Figure 7.9). We observed that the hydrophobic comonomer 2PPMA promoted flocculation for all three MONPs. Regardless of MONP concentration, densely packed solid mass and clear supernatant were observed in all systems. However, the same MONP suspension dosed with poly(NIPAAm) produced sediments with high water retention and turbid supernatant. The percentage bound of Fe_3O_4 was estimated through an iron assay of the supernatant, and the results are shown in Figure 7.7. 2PPMA copolymer flocculent has removed over 90% of the suspended particles at all MONP concentrations, while poly(NIPAAm) showed a decreased in removal efficiency as MONP concentration increased. It worthwhile mentioning that the results of the assay are likely artificially high for the poly(NIPAAm) system due to the suspended Fe_3O_4-polymer flocs. The highest removal efficiency (88%) occurred in 0.01 mg/ml of Fe_3O_4, and the lowest (32%) occurred in 0.5mg/ml of Fe_3O_4. A similar trend was observed in TiO_2 and CeO_2 MONP suspensions, even though the results were not quantitatively measured. It is worth to mention that the MONP suspensions dosed with poly(NIPAAm) turned more turbid at 50°C than room temperature, which was attributed to the self-aggregation of free poly(NIPAAm). These results and observations indicate that flocculants with hydrophobic 2PPMA can induce more effective polymer bridging, supporting the proposed hypothesis discussed above. The comparisons of poly(NIPAAm) and 2PPMA copolymer reveal that the hydrophobic modification can strongly affect the flocculation rate and removal efficiency of NIPAAm-based flocculants.

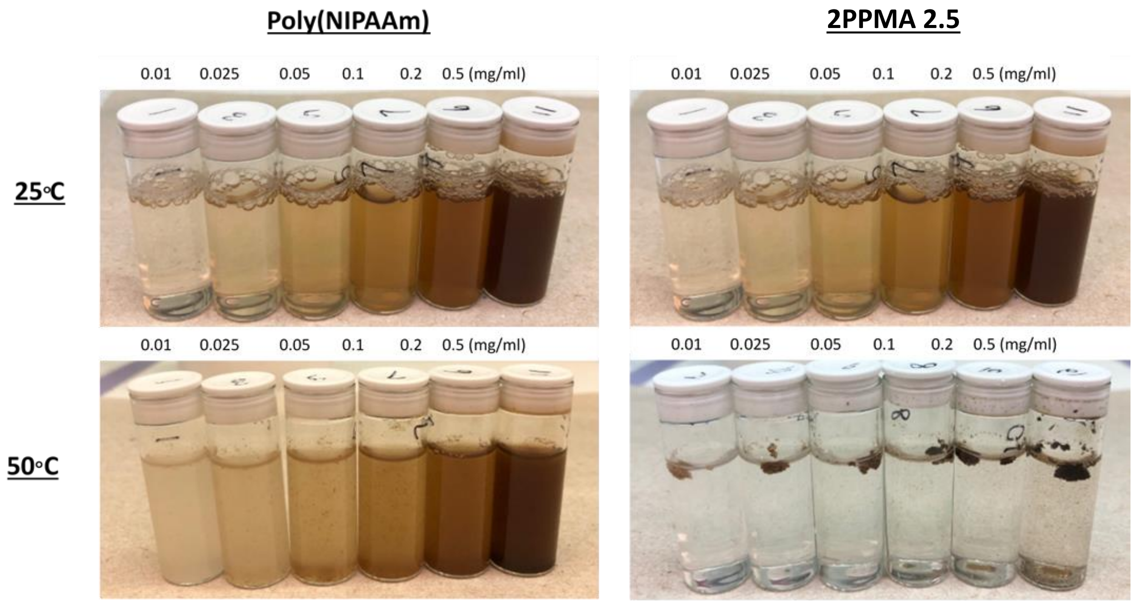


Figure 7. 6 Flocculation efficiency as a function of Fe_3O_4 nanoparticle dosage

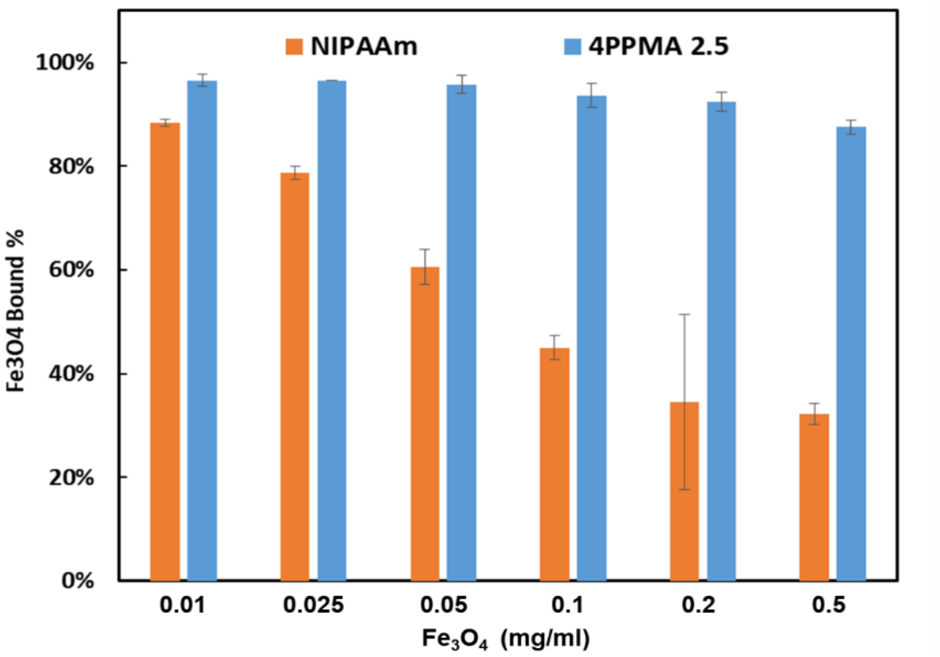


Figure 7. 7 Bound% vs Fe_3O_4 nanoparticle dosage, the supernatant was analyzed by iron assay

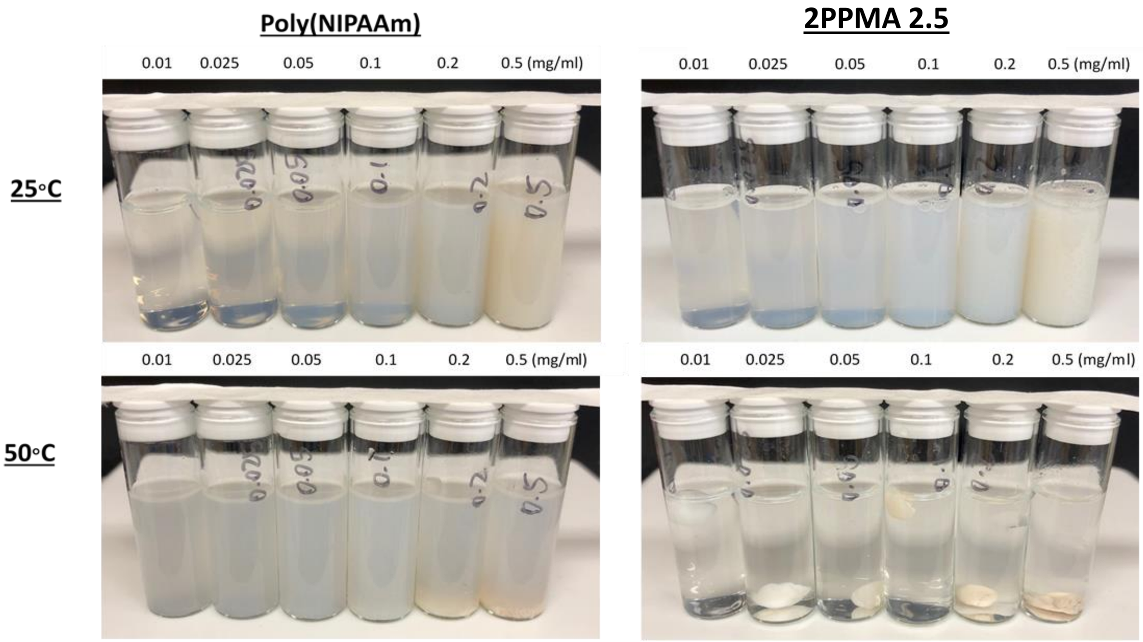


Figure 7. 8 Flocculation efficiency as a function of TiO_2 nanoparticle dosage

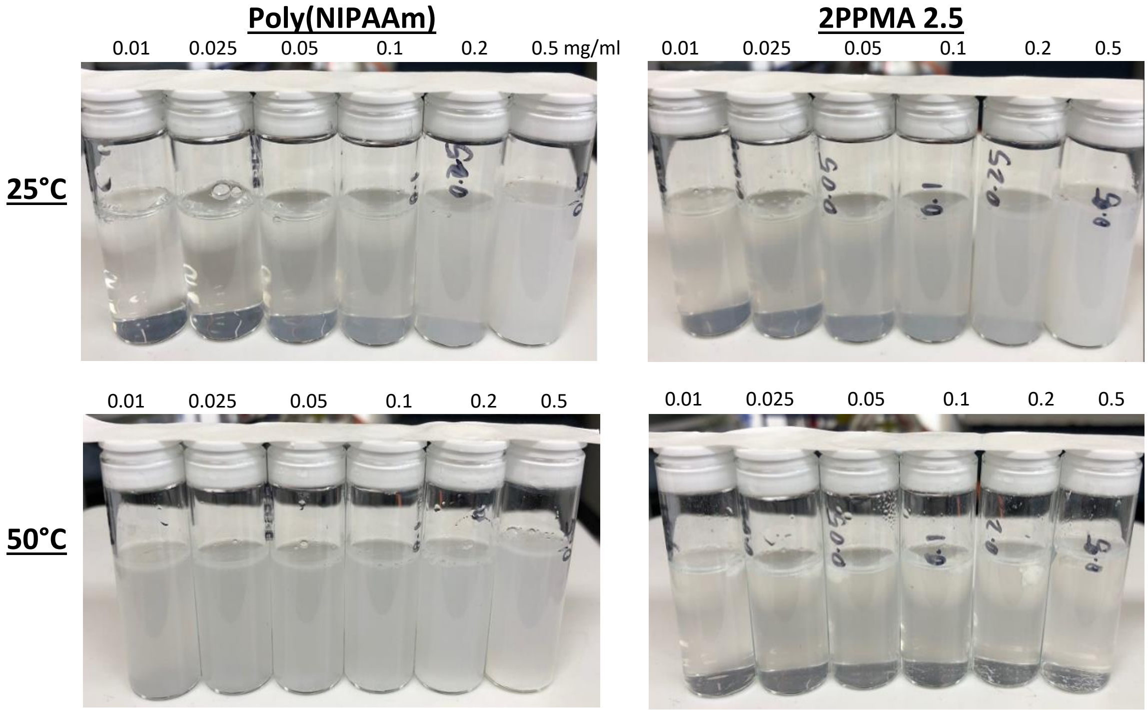


Figure 7. 9 Flocculation efficiency as a function of CeO_2 nanoparticle dosage

7.4 Conclusions

In this work, the application of smart NIPAAm polymer/copolymer flocculants in removing MONPs from aqueous suspension was investigated. Significant enhancement in flocculation performance was observed when MONPs were dosed with 2PPMA copolymer in compare with NIPAAm homopolymer. The 2PPMA copolymer has shown remarkable results in promoting sediment compaction and reducing supernatant turbidity. In addition, rapid flocculation (less than 10 minutes) was observed above the LCST with 2PPMA copolymer, whereas poly(NIPAAm) required much more time. The hydrophobically modified smart flocculants illustrated in this work produced high quality supernatant and densely packed sediments, which are regarded as promising replacements for conventional polymeric flocculants to achieve better remediation outcomes.

Chapter 8 Conclusions

In this dissertation, NIPAAm based thermo-responsive polymeric materials were synthesized, characterized, and evaluated for their applications in removing aqueous pollutants (phenol and MONPs) from water. We began by synthesizing temperature responsive hydrogels through copolymerizing NIPAAm with a variety of novel hydrophobic crosslinkers including CMA, QMA, 44BDA, and ChryMA. The resulting hydrogels exhibited distinct phase transition behaviors in a narrow temperature range and good responsiveness to reversible temperature change. In addition, the incorporation of hydrophobic crosslinkers showed significant impact in controlling the swelling and LCST of the hydrogels. The physicochemical characterization of these copolymer hydrogels revealed their potential as intelligent sorbents in water remediation applications. Therefore, as a proof-of-concept, two sets of the aforementioned NIPAAm gels, NIPAAm-co-CMA and NIPAAm-co-44BDA, were tested in batch binding studies to remove phenol as a model pollutant. The presence of aromatic/phenolic moieties in 44BDA and CMA is assumable to provide binding affinities to phenol through pi-pi stacking interactions. The effect of temperature and hydrophobic content/crosslinking density on phenol binding efficiency were evaluated. Results indicated that binding at elevated temperatures (T>LCST) was more efficient than that at lower temperatures (T<LCST), which can be attributed to the hydrophobic interaction induced by NIPAAm above LCST. In addition, the obtained hydrogels possessed facile and efficient regeneration ability in water at 10°C. These findings highlighted the potential of these novel hydrophobically modified copolymer hydrogels as cost-effective options for water remediation.

The next part of this dissertation examined the feasibility of NIPAAm polymer/copolymer as thermoresponsive flocculent for the removal of suspended nanoparticles from water. In this study, smart copolymer flocculent based on NIPAAm and hydrophobic compound 2-phenylphenol monoacrylate (2PPMA) was synthesized and characterized. Significant enhancement in flocculation performance was observed in 2PPMA copolymer compare to NIPAAm homopolymer. The 2PPMA copolymer has shown remarkable results in promoting sediment compaction and reducing supernatant turbidity. The hydrophobically modified smart flocculants illustrated in this work produced high-quality supernatant and densely packed sediments, which are regarded as promising replacements for conventional polymeric flocculants to achieve better remediation outcomes.

8.1. Significant findings

This dissertation generated significant results that contribute to the scientific community's understanding of advanced temperature responsive materials for environmental applications. Here, we have demonstrated the application of NIPAAm hydrogels and copolymer flocculants for the removal of phenol and MONPs, but the knowledge can be extended to other aqueous pollutants after appropriate modifications of the materials. In summary, the significant achievement and relevance of this work are listed below.

- Novel hydrophobic crosslinkers/comonomer including CMA, QMA, 44BDA, ChryMA, and 2PPMA were developed through acrylation of curcumin, quercetin, 4,4'-dihydroxybiphenyl, chrysin, and 2-phenylphenol
- Hydrophobically modified NIPAAm hydrogels/copolymer can be synthesized through free radical polymerization in the presence of APS as the thermal initiator

- The incorporation of hydrophobic crosslinkers decreases the LCST and swelling ability of the NIPAAm gels
- Hydrophobic crosslinkers CMA and 44BDA exhibit binding affinity to phenol presumably through pi-pi stacking interaction
- NIPAAm induces hydrophobic interaction at temperatures above its LCST, which enhances the binding interaction with phenol
- Desorption of bound phenol can be achieved in water through a small variation of temperature
- NIPAAm polymer/copolymer induces reversible flocculation of suspended particles at temperature across the LCST
- Significant enhancement in particle flocculation is observed in NIPAAm-co-2PPMA than NIPAAm homopolymer, owing to the hydrophobicity of 2PPMA
- Rapid flocculation (less than 10 minutes) can be achieved by applying the novel copolymer flocculent above the LCST; clear supernatant and compact solid flocs are collected after flocculation

Appendix 1: Supporting information for Chapter 4

Supporting information shows the LC-TOF spectrum of a 4,4’-dihydroxybiphenyl partial acrylation study, where TEA:AC:4,4’-dihydroxybiphenyl was 2:2:1 instead of 3:3:1 in the full acrylation synthesis

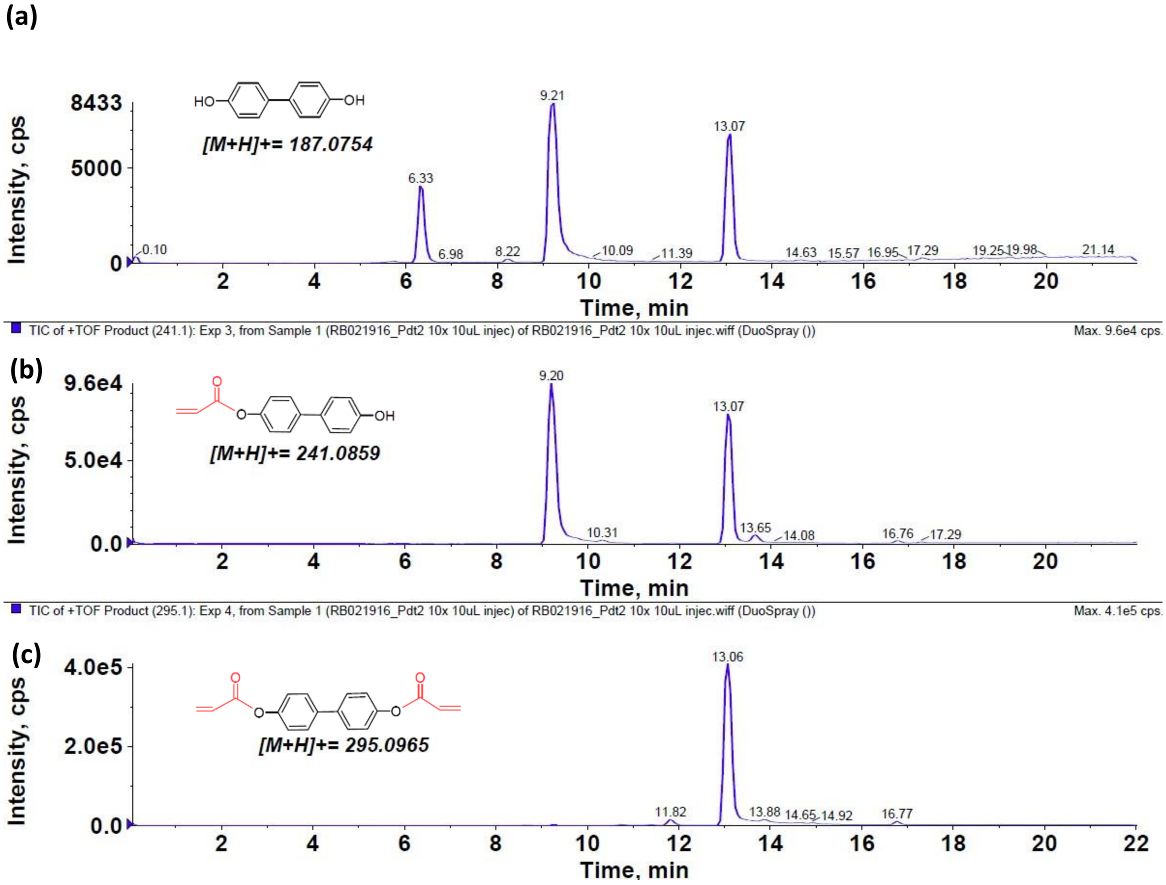


Figure A1. 1 LC-TOF spectroscopy of 44BMA partial acrylation (a) 4,4’-dihydroxybiphenyl (b) monoacrylate and (c) diacrylate

The figure shows extracted ion chromatograms for the indicated species. 4,4’-dihydroxybiphenyl and its monoacrylate and diacrylate reaction products are separable by reverse phase HPLC with retention times of ~6, 9, and 13 minutes, respectively. Detection of the lower mass species at retention times corresponding to the monoacrylate and diacrylate species is presumably due to ion source fragmentation of the parent ions.

Appendix 2: Protocol for synthesizing temperature responsive core-shell iron oxide nanoparticles via atom transfer radical polymerization

This work was done in conjunction with Rachel Boone as part of her NSF-REU research.

Uncoated or citric acid (CA) coated iron oxide magnetic nanoparticles (IONPs) synthesis

Uncoated or citric acid (CA) coated IONPs were synthesized through a co-precipitation method. Aqueous solutions of $FeCl_3 \cdot 6H_2O$ and $FeCl_2 \cdot 4H_2O$ were combined in a 2:1 molar ratio. The mixture was stirred at 300 rpm under constant nitrogen flow with a condenser. Once the solution was heated to 80°C, 30% ammonium hydroxide (NH_4OH) was added dropwise. For CA coated IONPs, citric acid monohydrate was dissolved in DI water (1.69g in 4 mL water for every 800mg nanoparticles) and injected. The system is stabilized at a temperature of 85°C. After one hour, the IONPs were separated by magnetic decanting and re-suspended in DI water for washing, and the wash process was repeated for three times. The CA coated IONPs were very stable in the solvent, so no washing was performed, only the supernatant was removed and nanoparticles suspended in DI water. The IONPs were then dialyzed against DI water for 24 hours.

Initiator coating

In the next step of the core-shell synthesis, IONPs were functionalized with an initiator for subsequent atom transfer radical polymerization (ATRP) reaction. The CA coated IONPs underwent ligand exchange with (3-Bromopropyl)trimethoxysilane (BPTS) and uncoated underwent electrostatic adsorption with 2-Bromo-2-methylpropionic acid (BMPA). For every 400 mg of either for every 400mg uncoated or CA coated IONPs, 1g of initiator was used. For both reactions, the solution was stirred at 325 rpm for 24 hours. The BMPA coated IONPs were easily separated and were magnetically decanted and washed 3 times with ethanol, one time with DI water and re-suspended in DI water. BPTS coated IONPs were magnetically decanted and washed three times with ethanol and three times with DI water and re-suspended in DI water. The washing process was modified for future batches to only removing the supernatant and suspending in DI water. BPTS coated IONPs were centrifuged at 15,000 rpm at room temperature for 20 minutes in order to achieve separation and BMPA coated IONPs were magnetically decanted.

Core-shell synthesis

For synthesis of the core-shell nanoparticles through ATRP, the ligand 4,4'-Dinonyl-2,2'-bipyridine (dNbpy) and metal complex copper(I) bromide (CuBr) were dissolved in dimethylformamide (DMF) in a 4:1 molar ratio to form the catalyst system (for 300mg nanoparticles 612mg dNbpy combined with 52.5mg CuBr). The hydrogel mixture consisted of 97.3 mol% NIPAAm and 2.7 mol% CMA dissolved in DMF (for 300mg nanoparticles, 3g NIPAAm and 330mg CMA). Chemicals are dissolved in amounts such that the total ratio of combined solvents is 75:25 DMF to DI water. The catalyst solution was mixed with the BPTS or BMPA coated IONP suspension and the resulting solution was heated and stirred at 325 rpm in the same setup as the uncoated synthesis. Once the temperature reached 60°C, the copolymer hydrogel mixture was injected and the reaction continued for 24 hours. The NIPAAm-co-CMA core-shell IONPs were magnetically decanted and washed 3 times with DMF, twice with Acetone and twice with DI water.

Characterization

The temperature sensitivity of the core-shell nanoparticles was tested using dynamic light scattering (DLS) by varying temperature and measuring the hydrodynamic diameter of the nanoparticle. First, the sample was probe-sonicated, and then a dilution was made to 0.1 mg/mL and probe sonicated. The DLS collected and averaged ten readings, repeated three times for three measurements at each temperature from 25 to 50°C in increments of 5°C.

Thermogravimetric analysis (TGA) was used to measure the extent of polymer loading and thickness of polymer coating. A dried sample of between 5 – 10 mg was loaded in a platinum pan and the weight percent was measured as temperature varied. The sample was heated at 10°C min^{-1} to 120°C, isothermed for 20 min to allow any impurities or residual water to vaporize, and then heated again at a rate of 10°C min^{-1} to 600°C.

Fourier transform infrared spectroscopy (FTIR) was used to identify functional groups and chemical functionalities of IONPs in order to confirm the presence of the polymer shell. Dried samples were placed on the diamond ATR crystal and the spectrum obtained from 700 to 4000 cm^{-1}.

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PERSONAL INFORMATION

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EDUCATION

- University of Kentucky, Lexington, Kentucky, May 2014
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RESEARCH EXPERIENCE

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PUBLICATIONS

Shuo Tang, Rohit Bhandari, Sean Delaney, Eric Munson, Thomas Dziubla, Zach Hilt. Synthesis and Characterization of Thermally Responsive N-isopropylacrylamide Hydrogels Copolymerized with Novel Hydrophobic Polyphenolic Crosslinkers. *Materials today communication* 10 (2017): 46-53.

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PATENT

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PROFESSIONAL CONFERENCE PRESENTATIONS (POSTER/ORAL)

Shuo Tang, Thomas Dziubla, Zach Hilt. Preparation of Thermally Responsive Magnetic Nanocomposites for the Removal of Environmental Pollutants, American Institute of Chemical Engineers Annual Meeting, San Francisco, CA, November 13 - 18, 2016 (oral)

Shuo Tang, Thomas Dziubla, Zach Hilt. Development of Thermally Responsive Magnetic Nanocomposites for the Capture and Release of Environmental Pollutants, Superfund Annual Meeting, Durham, NC, December 6 - 8, 2016 (poster)

Angela Gutierrez, **Shuo Tang,** Irfan Ahmad, Dustin Savage, Rishabh Shah, Thomas Dziubla, Zach Hilt. Polyphenolic Nanocomposite Materials for the Capture and Sensing of Chlorinated Organic Contaminants in water Sources, Kentucky Water Resources Research Institute Symposium, Lexington, KY, March 20, 2017 (poster)

Shuo Tang, Thomas Dziubla, Zach Hilt. Preparation of Thermally Responsive Magnetic Nanocomposites for the Removal of Environmental Pollutants, 2017 Annual Center for Clinical and Translational Science Conference, Lexington, KY, March 30, 2017 (oral and poster)

Shuo Tang, Thomas Dziubla, Zach Hilt. Development of Thermally Responsive Magnetic Nanocomposites for the Capture and Release of Environmental Pollutants, 2017 Global Grand Challenges Summit, Washington. DC, July 19 - 20, 2017 (poster)

Shuo Tang, Thomas Dziubla, Zach Hilt. Synthesis and Characterization of Thermally Responsive N-isopropylacrylamide Hydrogels Copolymerized with Novel Hydrophobic Polyphenolic Crosslinkers, 2017 American Institute of Chemical Engineers Annual Meeting, Minneapolis, MN, October 28 – November 3, 2017 (oral)

Shuo Tang, Thomas Dziubla, Zach Hilt. N-isopropylacrylamide (NIPAAm) Based Thermal Responsive Composites for Polychlorinated Biphenyls (PCBs) Removal from Water, 2017 American Institute of Chemical Engineers Annual Meeting, Minneapolis, MN, October 28 – November 3, 2017 (poster)

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UNDERGRAD PRESENTATIONS

Martha Floy, **Shuo Tang,** Thomas Dziubla, Zach Hilt. Synthesis and Characterization of Thermoresponsive Hydrogels Based on N-Isopropylacrylamide (NIPAAm) and Novel Crosslinkers, 2016 American Institute of Chemical Engineers Annual Meeting, San Francisco, CA, November 13 - 18, 2016 (poster)

Brooklyn Russell, **Shuo Tang,** Thomas Dziubla, Zach Hilt. Synthesis and Characterization of Thermoresponsive Magnetic Hydrogels with Novel Crosslinker, 2017 American Institute of Chemical Engineers Southern Student Regional Conference, Knoxville, TN, March 31- April 1, 2017 (poster)

Rachel Boone, **Shuo Tang,** Thomas Dziubla, Zach Hilt. Synthesis of Temperature Responsive Core-shell Magnetic Nanoparticles via Atom Transfer Radical Polymerization. 2017 American Institute of Chemical Engineers Annual Meeting, Minneapolis, MN, October 28 – November 3, 2017 (poster)

Rachel Boone, **Shuo Tang,** Thomas Dziubla, Zach Hilt. Investigating the Effect of Fe_3O_4 Iron Oxide Nanoparticles (IONPs) on the Thermo-responsive Swelling Properties of N-isopropylacrylamide (NIPAAm) Based Hydrogels, 2017 American Institute of Chemical Engineers Annual Meeting, Pittsburgh, PA, October 28 – November 2, 2018 (poster)

Tyler Runge, Rishabh Shah, **Shuo Tang,** Thomas Dziubla, Zach Hilt. Development of Non-covalently Crosslinked Temperature Responsive Polymeric Gels, 2018 American Institute of Chemical Engineers Annual Meeting, Pittsburgh, PA, October 28 – November 2, 2018 (poster)