Synthesis and characterization of hydrophilic polymer nanoparticles using n-isopropylacrylamide (NIPAM) via emulsion polymerization technique

Nurul Syafika Azmi[1], Nur Nasyita Kamaruddin[2], Syara Kassim[1,2] and Noor Aniza Harun[1,2]

[1]Advance NanoMaterials Research Group, School of School of Fundamental Science, Universiti Malaysia Terengganu, 21030 Kuala Nerus, Terengganu, Malaysia. [2]School of Fundamental Science, Universiti Malaysia Terengganu, 21030 Kuala Nerus, Terengganu, Malaysia.

Abstract. Poly(N-isopropylacrylamide) (PNIPAM) nanoparticles were successfully synthesized via emulsion polymerization techniques using different critical micelle concentrations (CMCs) of sodium dodecyl sulphate (SDS) surfactant, temperature and time of polymerization. The effects of surfactant concentrations on emulsion polymerization of PNIPAM nanoparticles have been discussed. Potassium persulfate (KPS) and N,N'-methylenebisacrylamide (MBAA) were used as initiator and cross-linker, respectively throughout the emulsion polymerization. The formation of PNIPAM nanoparticles was confirmed by Fourier transform infrared spectroscopy (FTIR) with absorption peaks observed at 2997 and 2930 cm^{-1} for C-H stretching of CH_3 and CH_2 groups, 1459 cm^{-1} for 2∘ amide C=O stretch , 3310 cm^{-1} and 3275 cm^{-1} for N-H stretching band. The particle size and morphology of PNIPAM nanoparticles were determined using scanning electron microscopy (SEM) where large aggregation of PNIPAM nanoparticles were observed with average diameters in the range of 20 – 50 μm and the appearance of pore structure on the hydrogel surface. Thermal stability of PNIPAM nanoparticles were obtained by thermogravimetric analysis (TGA) where it showed the percentage of mass loss at certain temperature.

1. Introduction

The studies of nanoscience and nanotechnology have advanced greatly in recent years and large amounts of research have focused in determining the properties and potential functions of nanomaterials. Nanotechnology is the study of combination of science, medical, engineering and technology at the nano-scale level ranging from 1 nm to 100 nm in size [1]. Polymeric nanoparticles (PNPs) are nanosized particulate carriers which either can entrap or encapsulate the drug substances, antigens, proteins and DNA vaccines and deliver it to the desired site of action [2]. Biodegradable polymers have received lots of attentions due to their biocompatibility, possibility for surface modifications and sustained release of the drug. Hydrophilic biodegradable polymer is a synthetic hydrolytically degradable polymer which has been remarkable developed in the application of biomedical and tissue engineering applications [3].

Amongst numerous synthetic biodegradable polymer, poly(N-isopropylacrylamide) (PNIPAM) which obtained from N-isopropylacrylamide (NIPAM) monomers offer huge interest among researcher especially in medical applications on account of their intelligent and unique stimuli-responsive properties. PNIPAM has distinctive characteristic in which its chains comprise both of hydrophobic and hydrophilic domains that can undergo rapid changes in their microstructure from a hydrophilic to a hydrophobic state cause by the alterations of the external stimuli. This external stimuli including heat, pH, ionic strength, magnetic and electric field, light, ultrasound and chemical species causes the disturbance to the environment structure of PNIPAM. PNIPAM has a thermo-sensitive effect which is related to lower critical solution temperature (LCST). Upon heated above the LCST around 32 ℃, liquid PNIPAM has turn into a gel formation structure (Dong *et al.,* 2017). The hydrogen-bonding interactions between the hydrophilic groups of PNIPAM and water are dominant below LCST, enforcing a coil-like conformation in PNIPAM resulting in water soluble PNIPAM [4, 5].

Since polymer nanoparticles have attracted the interest of many research groups and have been utilized in an increasing number of fields during the last decades, the properties of PNPs have to be optimized depending on the particular application. In order to achieve the properties of interest, the mode of preparation plays a vital role. Thus, it is highly advantageous to have preparation techniques at hand to obtain PNPs with the desired properties for a particular application [6]. In this study, PNIPAM nanoparticles were synthesized via emulsion polymerization technique, a typical emulsion polymerization formulation comprises of monomer, water, surfactant and a water soluble initiator. Previous work reported by Jagadeeshbabu *et al*. (2011) showed a thermo responsive macro porous PNIPAM hydrogel was synthesized using free radical polymerization [7]. The reaction was optimized by varying the reaction temperature, monomer, cross-linker and initiator based on the strength and swelling characteristics of the hydrogel. Synthesis of NIPAM using soap-free emulsion polymerization has been prepared by Chen *et al.* (2013) [8]. The polymerization was performed in the absence of surfactant, with the help of the initiator (KPS) and cross linker (MBA). The significance of this study was to determine the structure and physical properties of PNIPAM at lower LCST and cloud point temperature (CPT).

Surfactant has been a major role in emulsion polymerization as it become primary role to lower the interfacial tension so that the emulsification of reactive vinyl monomers and the formation of stable colloidal dispersions of nano-size polymer particles are allowed. Sodium dodecyl sulphate (SDS) is an amphiphilic molecule which is commonly anionic type surfactant that broadly utilize in the production of free radical polymers [9]. Taking into this direction, we are intrigued to explore the effects of different critical micelles concentration (CMC) of SDS in emulsion polymerization of PNIPAM nanoparticles. Hence, in this work, PNIPAM nanoparticles were synthesized via emulsion polymerization technique. The influence of different concentrations of SDS surfactant ranging from below, equivalent and above critical micelles concentrations (CMC) towards the emulsion polymerization of PNIPAM were thoroughly investigated.

2. Methodology

2.1 *Materials*
N-isopropylacrylamide (NIPAM) monomer, sodium dodecyl sulphate (SDS), N,N'-methylenebisacrylamide (MBAA) and ammonium peroxodisulfate (APS) were used as received. All the reagents and solvents used in this study are commercially available from Sigma Aldrich. Distilled water was used throughout the experiment.

2.2 *Emulsion polymerization of PNIPAM nanoparticles*
Emulsion polymerization was carried out in a 250 mL two-neck round bottom flask composed of magnetic stirrer, a reflux-condenser, nitrogen gas inlet and thermometer. A mixture of N-isopropylacrylamide (NIPAM) monomer, sodium dodecyl sulphate as surfactant, and N,N'-methylenebisacrylamide (MBAA) as cross-linker were mixed together in distilled water (3 mL). Distilled water act as dispersion medium and nitrogen gas was bubbled through the reaction mixture for 15 min and stirred at 450 rpm/min. The polymerization was occurred in the oil bath at temperature of 70 ℃ and initiated by addition of aqueous solution potassium persulfate (KPS) as initiator (0.0018 g) in 1 mL distilled water. The polymerization was completed after 2 h and the reaction was terminated by cooling to room temperature.

2.3 *Characterizations of PNIPAM nanoparticles*

2.3.1 *Fourier transmission infrared (FTIR)*
The solid sample of PNIPAM nanoparticles was prepared in the form of potassium bromide (KBr) pellet. The PNIPAM nanoparticles were mixed and crushed together with KBr powder in the ratio of 1:7. The

pellet then was placed on a plate and clamped in the right position. The FTIR spectra recorded using Perkin Elmer 100 series with sampling range from 450 to 4000 cm^{-1} and 16 times of scan number.

2.3.2 *Scanning electron microscopy (SEM)*
The hydrogel PNIPAM nanoparticles were mounted on SEM holder and coated with gold by Auto Fine Coater (JEOL) to prevent accumulation of electrostatic charge on the surface of samples. The morphology of polymer nanoparticles were observed using Oxford Instrument attached to JSM-6360 LA Analytical Scanning Microscope at acceleration voltage of 15 – 20 kV.

2.3.3 *Thermogravimetric analysis (TGA)*
The dynamic weight loss tests were conducted on TA Instruments 2050 thermogravimetric analyser (TGA). All tests were conducted in an N_2 purged (25 mL/min) using sample weights of 5 – 10 mg over a temperature range of 20 ^{o}C – 600 ^{o}C with scan rate of 10 ^{o}C/min.

3. Results and discussion

3.1   *Emulsion polymerization of Poly(N-isopropylacrylamide) PNIPAM nanoparticles*
The synthetic hydrophilic polymer nanoparticles using N-isopropylacrylamide monomer *via* emulsion polymerization were successfully performed using sodium dodecyl sulphate as anionic surfactants at different critical micelles concentration (CMC) of below, equivalent and above CMCs. The effect of surfactant concentration towards particle size and formation of polymer nanoparticles (PNPs) were studied and the parameters involved in this study were summarized in Table 1. PNIPAM nanoparticles prepared at different SDS concentration of below, equivalent and above CMC (4 mM, 8.2 mM and 10 mM, respectively). PNIPAM nanoparticles were obtained in the form of white fluffy solid right after polymerization and transformed to the solid hydrogel after dried at room temperature for 1 day. The formation of PNIPAM nanoparticles were then confirmed by FTIR spectroscopy.

Table 1. PNIPAM nanoparticles prepared *via* emulsion polymerization at different concentrations of SDS.

Polymer nanoparticles (PNPs)	Concentration of SDS (mM)
PNIPAM_1	4 (below CMC)
PNIPAM_2	8.2 (equivalent CMC)
PNIPAM_3	10 (above CMC)

3.2   *Fourier transform infrared spectroscopy (FTIR)*
Figure 1 illustrates the IR spectra of PNIPAM nanoparticles which prepared at different SDS concentration of 4 mM (PNIPAM_1), 8.2 mM (PNIPAM_2) and 10 mM (PNIPAM_3). The presence of broad peaks at 3567 cm^{-1} belongs to N-H stretching. The presence of CH stretching for CH_3 and CH_2 groups absorption peaks were observed in the range of 2930 cm^{-1} and 2997 cm^{-1}. The band at region of 1420 – 1460 cm^{-1} belongs to the characteristic of secondary amide C=O stretching. The absorption peaks for NIPAM monomer are identical to the PNIPAM nanoparticles with narrower peaks were observed [10]. It is noteworthy to mention that all PNIPAM nanoparticles that prepared at different SDS concentrations show similar pattern of FTIR spectra confirming the formation of PNIPAM nanoparticles, and this observations also proved that different concentration of SDS do not affect the structure of PNIPAM nanoparticles.
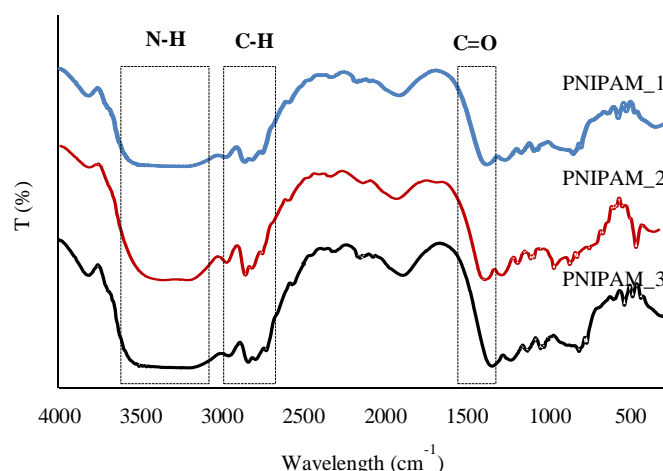
Figure 1. The FTIR spectra of PNIPAM 1, PNIPAM 2 and PNIPAM 3 prepared at below, equivalent and above CMC of SDS surfactant.

3.3   Scanning electron microscope (SEM) analysis

Scanning electron microscopy (SEM) was then performed to investigate the morphology of the PNIPAM nanoparticles. It was assumed that the morphology of pure PNIPAM hydrogels have a morphology consisting of relatively flat foils over which large craters (size around 100 nm) are visible. Even at higher magnifications, PNIPAM hydrogels exhibit a non-porous structure [11]. The SEM photographs (Figure 2) of PNIPAM nanoparticles showed most similar morphology as reported previously.

PNIPAM_1 (Figure 2a) prepared below CMC shows compact with non-porous surface structure, while, PNIPAM_2 prepared at condition of equivalent CMC showed the existence of micro and nano-pore were formed on the surface of the hydrogel (Figure 2b). In contrast, the morphology of PNIPAM 3 (Figure 2c) which prepared above CMC showed flaky nonporous structures. Therefore, it can be suggested that different concentrations of SDS can affect the morphology of PNIPAM nanoparticles.
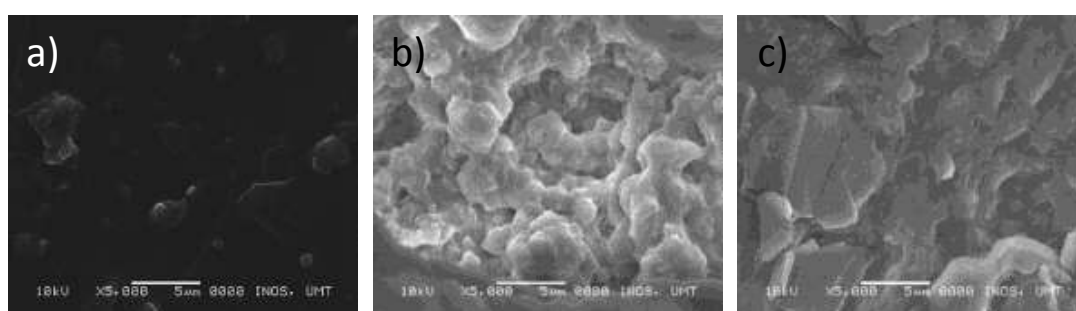
Figure 2. SEM images of (a) PNIPAM_1 (b) PNIPAM_2 and (c) PNIPAM_3

The average particle size of PNIPAM nanoparticles were determined by randomly measured the polymer particles obtained from SEM images and it was found that average particle size of PNIPAM nanoparticles in between 20 – 50 µm with large aggregations were observed. The aggregation of

polymer samples were expected to be observed under SEM on account of nature of sample preparation for SEM and during drying process of the samples.

3.4 *Thermogravimetric analysis (TGA)*

Thermal stability of polymer depends on the polymer microstructure and TGA can be utilized to determine the polymer degradation characteristics [12]. PNIPAM nanoparticles were characterized by using thermogravimetric analysis (TGA) to determine the thermal stability of nanoparticles by measuring weight loss of polymer nanoparticles as function of temperature. To confirm that the mass loss due to water lost from the hydrogel, and was not associated with decomposition of polymer itself, the effect of composition on thermal degradation of the PNIPAM nanoparticles was examined. The samples were heated from 30 ºC to 600 ºC under a nitrogen atmosphere at heating rate of 10 ºC/min. Figure 3 showed the TG curves of PNIPAM_1, PNIPAM_2 and PNIPAM_3 versus NIPAM monomer. From the graph, the first step in a range of 30 - 120 ºC is due to the water loss. At 120 - 375 ºC, it can be said that it is related to the thermal degradation of PNIPAM nanoparticles in which the degradation of the NIPAM monomer start at 120 ºC while the degradation for PNIPAM_1, PNIPAM_2 and PNIPAM_3 are found to be at 369 ºC, 372 ºC, and 369 ºC with percentage weight loss are 75 %, 63 % and 79 %, respectively. The comparison of thermal stability for PNIPAM nanoparticles samples shows that PNIPAM_2 with surfactant concentration equivalent CMC is the most stable during the thermal degradation region on account of higher thermal degradation temperature with the lowest percentage of mass loss.
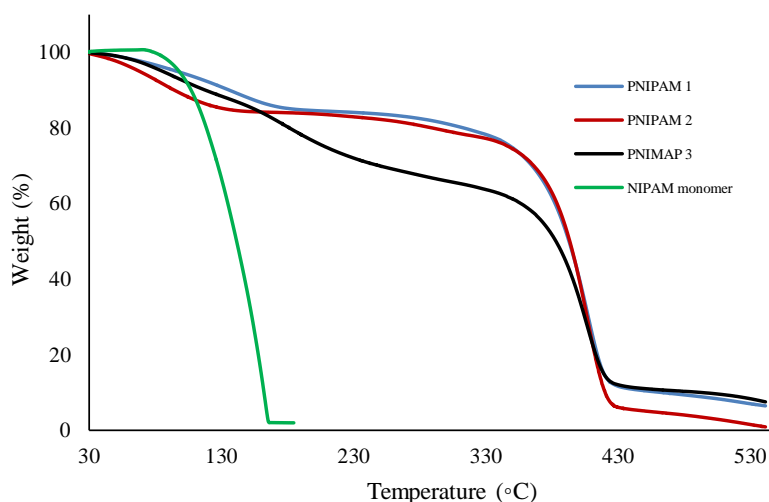

Figure 3 TG curves of PNIPAM 1, PNIPAM 2, and PNIPAM 3

4. Conclusions

Synthetic hydrophilic poly(N-isopropylacrylamide) (PNIPAM) nanoparticles were successfully produced *via* emulsion polymerization technique at different CMC of SDS surfactant. The formation of PNIPAM nanoparticles were confirmed by FTIR where the absorption spectra showed the similar peaks in all samples of nanoparticles. Scanning electron microscope (SEM) images showed different morphology of PNIPAM nanoparticles prepared at different surfactant concentrations with the existence of aggregation of PNIPAM nanoparticles. The comparison from all the TGA curves of PNIPAM nanoparticles indicates that PNIPAM_2 was more stable in terms of thermal degradation based on the highest onset temperature. It can be concluded that the different concentrations of surfactant does give significant effects towards the properties of PNIPAM nanoparticles.

5. References

[1]   Bera A and Belhaj H 2016 *J. Nat. Gas Sci. Eng.* **34** 1284 – 1309.

[2]   Sharma R, Agrawal U, Mody N and Vyas S P 2015 *Biotechnol. Adv.* **33(1**) 64 – 79.

[3]   Yin R, Zhang N, Wu W and Wang K 2016 *Mater. Sci. Eng. C Mater. Biol. Appl.* **62** 137 – 143.

[4]   Singh R, Deshmukh S A, Kamath G, Sankaranarayanan S K R S, Balasubramanian G 2017, *Comput. Mater. Sci.* **126** 191 – 203.

[5]   Pelton R 2010 *J. Colloid Interface Sci.* **348(2)** 673 – 674

[6]   Rao J P and Geckeler K E 2011 *Prog. Polym. Sci.* **36** 887 – 913

[7]   Jagadeeshbabu P E, Kumar R R S and Maheswari B 2011 Colloids Surfc *A Physicochem. Eng. Asp.* **384** 466 – 472.

[8]   Still T, Chen K, Al Sayed A M, Aptowicz K B and Yodh A G 2013 *J. Colloid Interface Sci.* **405** 96 – 102

[9]   Salager J L, Moreno N, Anton R E and Marfisi S 2002 *Langmuir* **3** 607-611

[10]   Rwei S P, Anh T H N, Chiang W Y, Way T F and Hsu Y J 2016 Materials **9(12)** 1003

[11]   Uva M and Atrei A 2016 *Gels* **2(4)** 30

[12]   Gałka P, Kowalonek J, and Kaczmarek H 2014 *J Therm Anal. Calorim* 115 1387–1394