

Swelling Properties of Crosslinked Copolymers Based on N,N-Dimethylacrylamide and Drug Loading and Release Application

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Abstract

Two crosslinked copolymeric gel systems designated as poly(sodiumacrylate-co-N,N-dimethylacrylamide-cr-N,N-methylene-bisacrylamide) ; P(SA/DMA/BIS; system-1) and poly(N,N-dimethylacrylamide-co-Acrylamide-cr-N,N-methylene-bis-acrylamide); P(DMA/AM/BIS; system-2) were prepared by radical polymerization using ammonium persulfate/N,N,N,N-tetramethylethylene diamine (APS/TEMED) as initiator. The polymerization of the two systems was carried out at room temperature with medium to high conversion. Two most important swelling properties, namely: equilibrium water content (EWC) and degree of swelling (S %) were determined gravimetrically and found high in values (EWC= 92.8-98.7 for system-1 and 88.5-83.5 for system-2 and S%= 1271-15510 and 766-545 respectively). Both swelling properties were affected by temperature and gel composition. Their values were found generally to increase with increase in temperature and the hydrophilic monomer content in the copolymer composition range chosen. Chloramphenicol was used for the drug swelling and release study. Both gel systems were studied in swelling and releasing of this drug in a proper medium. The swelling study was carried out in water/ethanol (1:1 volume ratio) and the release study was carried out in acetone using UV-Visible spectrophotometer at $\lambda_{max}=345nm$. System-1 was found to release the drug at composition 90/10 SA/DMA higher than that of the release in system-2 due to higher in hydrophilicity in system-1 than in system-2.

Key Words: Drug release, swelling properties, N,N-Dimethylacrylamide.

1. Introduction

Hydrogels are polymers having the ability to swell in water or aqueous solvent systems several hundred times ⁽¹⁻³⁾. The structure of

polymer is able to retain the solvents forming a swollen gel phase and, crosslinked, will not dissolve regardless of the solvent. These hydrogels are suitable for diverse applications as in the case of hydroxyalkylmethacrylate. The hydrogels can be a homopolymers or copolymers and crosslinking forming materials. The latter one increases the diversity of their application due to developing diverse properties of these gels for they are different in the net work chain structure.

The monomer composition of a copolymer can be manipulated to influence the permeation and diffusion characteristics of the hydrogels, and through this manipulation, hydrogels can be synthesized to accommodate a variety of drugs loaded into the matrix. These include hydrophobic and hydrophilic substances, charged or neutral small or macromolecules. This avenue of controlled drug release has been pursued in recent years (9-11), although their products are still not available in enough quantity in the market. There are several investigations on hydrogels made from sodium acrylate and comonomer such as N,N-dimethylacrylamide, or acrylamide or others regarding their swelling capacities and their applications(12,13). In our work, the study was focussed on synthesis, swelling capacities as well as drug absorption/desorption of hydrogels made from sodium acrylate (SA)/ N,N-dimethylacrylamide (DMA) and hydrogels made from DMA/acrylamide (AM).

2. Materials and Methods

The monomers used in this study, sodium acrylate(SA), was prepared in our lab, N,N-dimethylacrylamide (DMA) and acrylamide (AM) were obtained from Aldrich chemical company. The first was purified by column chromatography while the second was purified by recrystallization from hexane and ethanol. N,N-methylene-bis-acrylamide (BIS) was used as a crosslinking agent and obtained from Aldrich. Acrylic acid (AA) and standard sodium hydroxide (NaOH) were used to prepare sodium

acrylate. N,N,N,N-tetramethylethylenediamine (TEMED) and ammonium persulphate (APS) were used as a coupled initiators and used without further purification.

Preparation of hydrogels

Two systems of hydrogels were prepared in this work. Poly(SA/DMA; system1) and poly(DMA/AM; system2). In each system the amount of crosslinker(BIS) and the initiator ammonium persulfate (APS) were the same as 1% of the total weight of the monomers.

Preparation of poly (SA/DMA) gels (System 1):

The pregel solution comprising of wt % of each monomer, the initiator (APS), and the crosslinker (BIS) as shown in table 1, were degassed with nitrogen for ten minutes, the accelerator (TEMED) was then added and the solution was transferred into the test tubes of dimensions 1x10 cm, stoppered tightly and left at room temperature to polymerize. The clear gels obtained were cured by heating them in water bath at 50°C. The gel samples were removed from the test tubes, cut into discs of 0.5cm in diameter and were purified by equilibrating successively in pure distilled water. The conversion was more than 65%.

Table 1: The polymerization data for system1 and 2:

System 1 (Poly.SA/DMA) gels				System 2 (Poly.DMA gels			
S A,g	DM A,g	APS ,g	EME Dul	BIS, g *	DM A,g	AM, g	AIBN,g
10	0	0.1	240	0.1	0	10	0.0016
9	1	0.1	240	0.1	1	9	0.0016
7	3	0.1	240	0.1	3	7	0.0016
5	5	0.1	240	0.1	5	5	0.0016
3	7	0.1	240	0.1	7	3	0.0016
1	9	0.1	240	0.1	9	1	0.0016
0	10	0.1	240	0.1	10	0	0.0016

Bis concentration is the same for both systems.*

Preparation of poly (DMA/ AM) gels (System 2):

The pregel solution comprising of wt % of each monomer, the initiator (AIBN) and the crosslinker (BIS) as shown in table 1, were degassed with nitrogen for ten minutes, filled in test tubes of dimensions 1x10 cm stoppered tightly and put in water bath at 50°C for two hours, 60°C for two hours, 70°C overnight and at 80°C for two hours. The clear gels obtained removed from the test tubes, cut into discs of 0.5cm in diameter and were purified by equilibrating successively in pure distilled water. The conversion was more than 65%.

Swelling of gel samples in water:

Normal swelling procedure was performed for all gel samples in water at temperature range of 10

to 80 °C. The swelling procedure was repeated three times till equilibrium for every sample and the average weight was taken and used to determine the swelling characteristics. These characteristics were determined for all samples at the same weight for the reason of comparing these them in order to reach at reasonable conclusion.

3. Results and Discussion

Preparation and spectroscopic characterization of gel samples:

The polymeric gels from either of the two monomers in the two systems in the form of homopolymer or copolymer gels were prepared in different media and different feed composition. The first system (SA or SA/DMA) gels were prepared in aqueous media using ammonium persulphate/N,N,N',N'-tetramethyl ethylene diamine (TEMED) as a coupled initiators and N,N'-methylene-bis-acrylamide(BIS) as a crosslinker. The second system (AM or AM/DMA) gels were prepared in organic medium using 2,2'-azobisisobutyronitrile(AIBN) as initiator and BIS as a crosslinker. The gel fractions in both systems were calculated to lie in the range of (63-75%). The gel samples of the first system was prepared at room temperature (20 °C) and the second system was prepared by heating in water bath at 50, 60, 70, and 80°C for different interval of times.

The IR spectra of the copolymers shown in Figure 1 (a, b, & c) and Figure 2(a & b,) show peaks at specific regions which are in agreement with the expected peaks for these copolymer. The spectra of the SA-DMA copolymers (Fig.1 a, b, and c) show peaks at 3306cm⁻¹ corresponding to undried water and this was shown in all of the IR spectra for the gel samples; 1549 cm⁻¹ corresponding to the acrylate unit; in addition some peaks are also observed at 1322cm⁻¹, 1255cm⁻¹ and 1450 cm⁻¹ unit corresponding to C-O-C stretching coupling interaction of ester groups. The spectra of the copolymers DMA-MA (Fig.2 a and b) show peaks at 3334cm⁻¹ corresponding to NH stretching of the acrylamide unit; 1652cm⁻¹ corresponding to the dimethylacrylamide unit: and 1600cm⁻¹ corresponding to the carbonyl group to the acrylamide unit, in addition some peaks are also observed at 1457cm⁻¹ and 1407cm⁻¹ corresponding to C-O-C stretching coupling interaction of ester groups. From the above IR analysis, it was concluded that all monomeric units including acrylamide, dimethyl acrylamide, and sodium acrylate are incorporated into copolymer chain backbone.

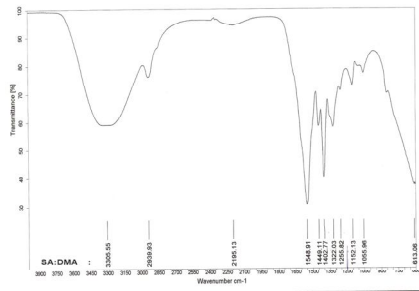


Figure 1a: IR spectra of 100% SA polymer

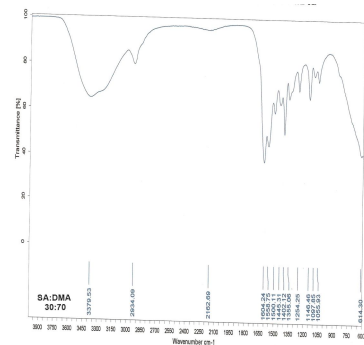


Figure 2b: IR spectra of SA-DMA 30/70 copolymer

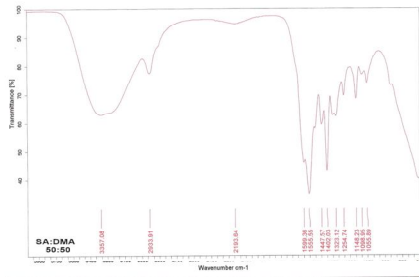


Figure 1c: IR spectra of SA-DMA 50/50 copolymer

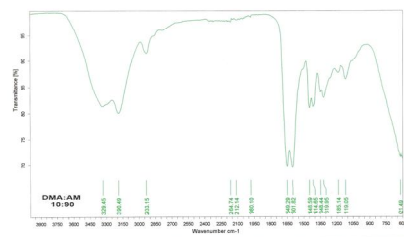


Figure 2a: IR spectra of MA/ DMA 10/90 copolymer

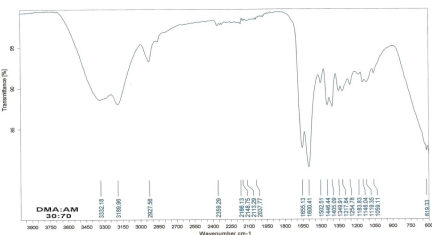


Figure 2b: IR spectra of MA/ DMA 30/70 copolymer

Effect of SA and DMA-Hydrophilic monomer contents on the swelling ratios:

One of the most important properties of superabsorbent polymers is swelling capacity and the elastic modulus of the swollen cross linked gel. Both of these properties are related to the crosslink density of the net work. Fig3-6 show the swelling ratio of the copolymers as a function of the feed composition of comonomers at different temperatures 10, 20, 30, 50, 60, and 70 °C. Tables 2a and 2b Show SA and AM contents in SA/DMA and DMA/ AM copolymeric hydrogels

Table 2a: Preparation data of (AS-DMA) copolymer hydrogels.

Samp le n ^o .	%SA	% DMA	%Conversion
1	0	100	60
2	10	90	64
3	30	70	75
4	50	50	59
5	70	30	42
6	90	10	55
7	100	0	28

Weight of accelerator =0.01 g; wt. of Cross linker = 0.1

Table 2b: Preparation data of (AM-DMA) copolymer hydrogels

Samp le n ^o .	MA %	DMA %	%Conv ersion
1	0	100	58.3
2	10	90	54.5
3	30	70	63.6
4	50	50	54.5
5	60	40	45.5
6	70	30	54.5
7	80	20	54.5
8	90	10	54.5
9	100	0	63.6

Weight of accelerator =0.01 g; wt. of Cross linker = 0.1g.

The swelling ratio of the crosslinked SA-DMA copolymer hydrogels with different contents of SA is showed in Fig. 3-6

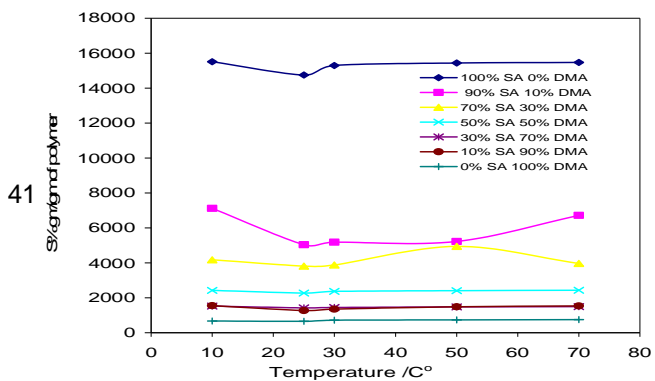


Fig.3: effect of temperature on S% for SA: DMA system

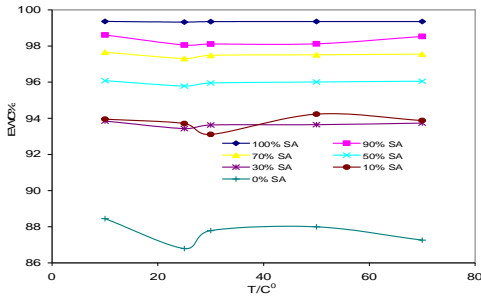


Fig.4: effect of temperature on EWC in SA: DMA system

Incorporation of SA into backbones of the hydrogel affects the swelling behavior in a positive direction. The introduction of SA dramatically increases the water uptake for (SA-DMA) hydrogels, especially at higher ratio of SA, around 92-98% ratio. The swelling ratio depends on SA content and that increases with increasing the ratio of SA in the hydrogel. The increase in swelling ratio, is due to the increase in the hydrophilic centers on the hydrogel backbone, such as $-COO^-$ which was afforded by the sodium acrylate. Swelling ratio S% starts to increase rapidly at ~90% of SA and reaches maxima at ~100% SA. This system was selected to be used for controlled-release application, because it exhibits a high water uptake. In contrast introduction of AM decreases the water uptake percent for DMA-MA copolymer hydrogels. The swelling ratio decreases with increasing the MA content in the copolymer. Swelling ratio S% decreases incontinuously, as it is shown in fig.5 .

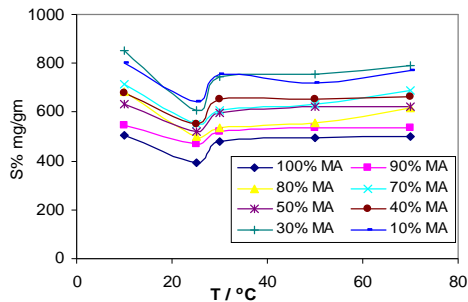


Fig.5: Effect of temperature on swelling Ratio(S%).

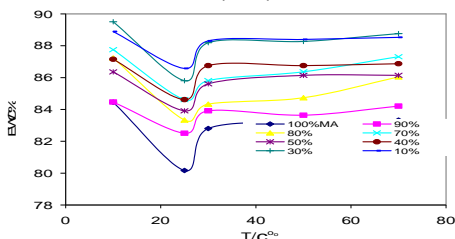


Fig.6: effect of temperature on EWC% in MA:DMA system

The decrease in swelling ratio is due to the increase in the hydrophobic centers on the hydrogel backbones. These results are in agreement with the fact that the hydrophobic groups are not favorable to the penetration of water into the bulk of the copolymer (). Therefore, the more the AM contents the lower absorbing capacity of the gel.

Effect of temperature on the swelling ratios:

The swelling capacity of both gel systems SA and MA as indicated by the equilibrium water content (EWC) and the degree of swelling (S%) were affected by temperature, this was shown by figure 7 and 8 for S% and EWC% for both systems respectively. In both systems, the swelling capacity decreased and then increased again. In system1 there is a peak at the composition 70% and S% increased sharply at temperature 50°C and increased gradually in the region where SA%=80% to almost 90% This is probably because of the interactions of the carboxylic groups , replling each other and allowing more water to inter in the hydrogel voids.

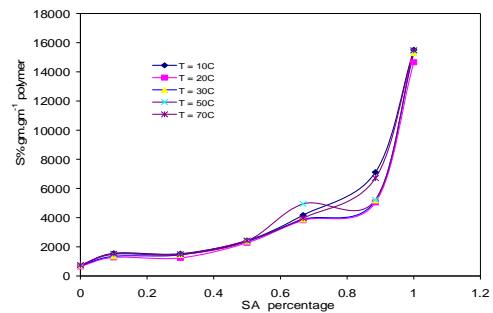


Fig.7: Effect of SA percentage on swelling ratio at different temperatures.

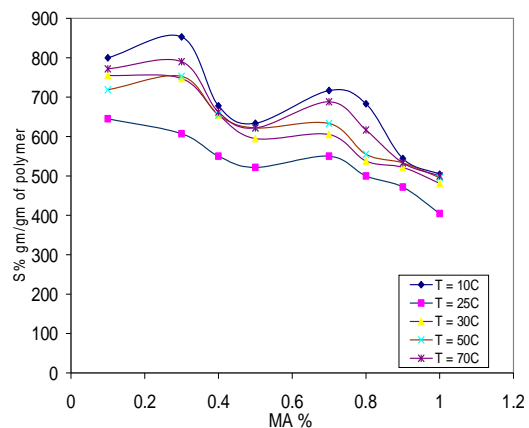


Fig.8: Effect of MA% on Swelling ratio S% for AM/DMA system at Different Temperatures

Effect of SA and AM contents on loading and release of the drug:

The drug loaded hydrogels were equilibrated in the aqueous acetone medium and chloramphenicol concentration at different time intervals were monitored at 37°C, by performing UV-VIS spectroscopy at 345 nm, with the help of calibration curve of chloramphenicol standard solutions in acetone.

Fig 8 and 9 show the effect of different contents of SA and AM comonomers on the drug concentration in the swelling medium at different interval of times in both systems SA-DMA and DMA-MA respectively. From the release profile showing in fig 9, it can be noticed that the released drug concentration profile can be divided into different segments. In the first region, the concentration of released drug increases rapidly, i.e., about 70% of the released drug took place during half of the first hour. This sharp increasing, in the curve, is attributed to the release of chloramphenicol close to or on the surface of the hydrogels. The second segment is a slower increase released drug concentration and finally, a very slow increase or constant concentration was observed, due to the release of the remaining drug that was entrapped in the bulk of the polymer. The concentration of the released drug is dependent on copolymers composition.

Like-wise the samples containing sodium acrylate (hydrophilic) component incorporated with DMA exhibit a higher drug release ratio (higher concentration) comparing to drug release ratio of 100% DMA sample, reaches a maximum at 70:30 SA:DMA ratio. Whereas; the samples containing acrylamide (hydrophobic) incorporated with DMA exhibit a lower drug release ratio (lower released drug concentration) comparing to the released drug concentration of 100% DMA. Because the DMA-AM samples were initially poorly unloaded with chloramphenicol drug swelling ratio.

4. Conclusion

A series of hydrogel copolymers of (SA-DMA) system 1 and (DMA-AM) system 2 with different ratios of SA and DMA or AM and DMA respectively, have been synthesized by radical copolymerization, the first system at room temperature using APS as initiator and TEMED as an accelerator. The gel point was observed in most compositions after 15 to 20 minutes, with a reasonable percent conversion. These copolymers were characterized by their IR spectra and other physical properties. The swelling ratio of SA-DMA system 1 was greatly improved as sodium acrylate content is increased in the

backbone of the copolymers. The water uptake was found to be maxima at 90% of sodium acrylate. whereas; the swelling ratio of DMA-AM system 2 was slightly affected as acrylamide content is increased in the backbone of the copolymers. The water uptake was found to be slightly decreased at all ratios of AM- DMA pure polymer.

Both systems were used for controlled release studies of chloramphenicol drug at different interval of times and at 37°C. (SA-DMA) copolymers show an improvement in the drug release at all ratios of SA which reached to maximum at 70% SA ratio, comparing to pure DMA copolymer .whereas; (DMA-AM) copolymers show a decreasing in the released drug concentration at all ratios of AM, comparing to pure DMA copolymer. The first system, (SA-DMA) hydrogels provided a high swelling ratio and a good drug release control, at specific ratio. It has the feasibility of control-release applications, i.e., in drug delivery systems.

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