

Poly (N-vinyl-2-pyrrolidone-co-acrylic acid): Comparing of “Traditional Heating” and “Microwave-Assisted” Free Radical Polymerization

KADRIYE KIZILBEY, SERAP DERMAN* AND ZEYNEP MUSTAFAEVA

*Yildiz Technical University, Chemical and Metallurgical Faculty, Bioengineering Department
Esenler, 34210, Istanbul, Turkey.
serapacar5@gmail.com**

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Summary: In organic chemistry microwave irradiation has become a common heat source and the use of microwave irradiation is also increasingly studied for polymerization reactions. Polymers have been synthesized at long reaction times by classical thermal methods. In contrast, microwave-assisted polymer synthesis is a well-known and most useful method, which is requiring shorter reaction times. In this study, our aims are to compare THPS and MAPS methods between themselves, and investigate the effect of temperature in MAPS method at different parameters such as reaction times, weight average molecular weight (M_w), polydispersity index (PDI), hydrodynamic radius (Rh), intrinsic viscosity ($[\eta]$) and Mark Houwink equation constant (a) of copolymers.

Firstly we synthesized N-vinyl-2-pyrrolidone-acrylic acid copolymers [P(VP-co-AA)] both with traditional heating polymer synthesis (THPS) and microwave-assisted polymer synthesis (MAPS) method comparatively in this study. Secondly, to research temperature effect on MAPS method in addition to microwave irradiation power, polymer synthesis at 40 °C, 50 °C and 80 °C were tried. For analyzing of copolymers Fourier Transform Infrared (FT-IR) spectroscopy and Gel Permeation Chromatography (GPC) system with four detectors were used.

Key Words: Microwave irradiation, radical polymerization, weight average molecular weight (M_w), polydispersity index (PDI), poly(N-vinyl-2-pyrrolidone-co-acrylic acid).

Introduction

Water-soluble macromolecules have been widely investigated and used for their applications in medicine and biotechnology [1]. Numerous water-soluble polymers, for the most acrylic derivative and vinyl type polymers such as copolymers of N-vinyl-2-pyrrolidone (VP) with unsaturated carboxylic acids have found wide applications as hydrogels, membranes, drug carriers used at drug-delivery systems in medicine and biology [2-7]. The success in application of NVP copolymers are their excellent biocompatibility and their low cytotoxicity [4, 8, 9].

Theoretically, all reactions require an energy input [10]. Heating reactions with traditional equipment, such as oil baths, sand baths and heating mantles are slow and they create hot surface on the reaction vessel where products, substrates and reagents often decompose over time [11]. On the other hand microwave-assisted method is effective and selective method [12], which involves the use of microwave radiations as an impact on chemical synthesis [13]. Microwave energy is introduced into the chemical reactor remotely, passes through the walls of the reaction vessel and heats the reactants and solvents directly [11], [14]. Better yields [15-18], rapid reaction optimization [18], shorter reaction time (usually 1/1000) [15-17, 19-22], low energy consumptions [23], reduction of by-products [15-17], no thermal decomposition of products [16, 17],

increase of product yields [19, 22, 24], reduction of required amount of solvent [10, 18], reduction the amount of waste produced by using more efficient energy transfer [10] are some advantages of microwave technique over traditional technique in organic reaction performance.

Recently, there has been growing interest in microwave heating technology which has been previously used in drug design [15, 25, 26], organic tissue engineering [15], polymer chemistry [15, 27] and etc. Microwave-assisted free radical polymerization has been widely exploited to accelerate free radical polymerization process [15, 28] and efficient than conventional heating [29].

In this study we synthesized N-vinyl-2-pyrrolidone/acrylic acid (VP:AA = 1:3) copolymers via THPS and MAPS methods. Firstly, we compared two synthesis methods each other depending reaction times, weight average molecular weight (M_w), polydispersity index (PDI), hydrodynamic radius (Rh), intrinsic viscosity ($[\eta]$) and Mark Houwink equation constant (a) of copolymers. Then we investigated the optimum temperature conditions for microwave synthesis. The effects of temperature (40 °C, 50 °C and 80 °C) in MAPS were studied by comparing the parameters mentioned before. In this study the possibility of synthesizing more

*To whom all correspondence should be addressed.

homogenous copolymers were targeted by using microwave method.

Results and Discussion

Comparing THPS and MAPS methods depending on reaction times, it was demonstrated that the microwave-assisted polymerization was significantly faster than traditional heating method. Although synthesizing copolymers by THPS method takes 4 hours, MAPS method takes only 10 minutes.

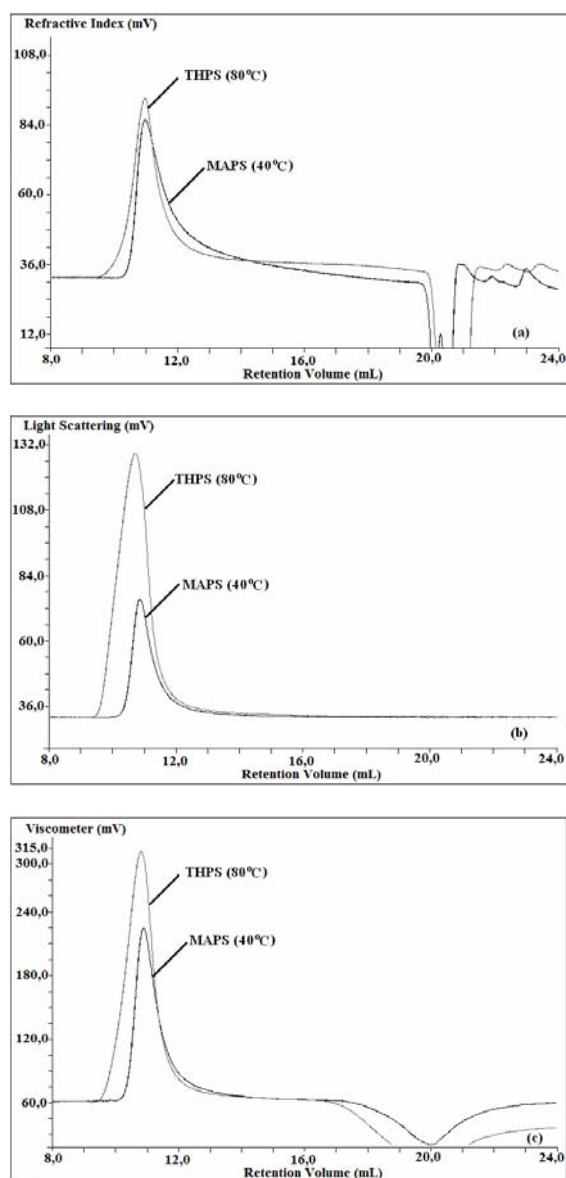


Fig. 1: GPC; RI (a), RALS (b) and VIS (c) chromatograms of N-vinyl-2-pyrrolidone/acrylic acid (VP-co-AA) copolymers (VP:AA =1:3) synthesized by MAPS and THPS methods at 80°C.

According to gel permeation chromatography (GPC) analysis, it was clearly seen from chromatograms in Fig. 1 (a,b,c) and Table 1 that the copolymer synthesized by MAPS method had lower molecular-weight than the copolymer synthesized by THPS method. Copolymers molecular weights (M_w) were 108.740 Da and 497.281 Da. Considering the circumstances like temperature, monomers, solvent and initiator amounts, all parameters were same for two synthesis methods. In MAPS method microwave irradiation energy was given to the reaction media besides heating energy. These effects cause more initiator radicals and polymer chains that synthesized copolymer had lower molecular weight.

In addition to these results polydispersity of copolymers were 2,507 and 5,282 synthesized by MAPS and THPS methods respectively. Homogeneous distribution of energy induced that copolymer which was synthesized by MAPS method, was more monodisperse than copolymer synthesized by THPS method.

While hydrodynamic radius (R_h) was 11.981 for 108.740 Da M_w copolymer synthesized with MAPS method, the copolymer with 497.281 Da molecular weight synthesized with THPS method had only two times greater R_h value. Mark Houwink equation constant (a) for copolymers calculated as 0.791 for MAPS and 0.519 for THPS methods. Intrinsic viscosity values were 1.2155 dl/g and 2.2864 dl/g for MAPS and THPS methods respectively. All R_h , $[\eta]$ and Mark Houwink a constant values supported each other and this indicated that more compact copolymer was synthesized by THPS method.

Table-1: GPC data of N-vinyl-2-pyrrolidone/acrylic acid (VP-co-AA) copolymers (VP:AA =1:3) synthesized by MAPS and THPS methods at 80°C.

P(VP-co-AA) (VP:AA=1:3), 80 °C	Microwave-assisted synthesized copolymer	Traditionally synthesized copolymer
Peak RV - (ml)	10,963	10,953
Mn - (Da)	43.374	94.139
Mw - (Da)	108.740	497.285
Mz - (Da)	194.540	3,827 e ⁷
Mp - (Da)	183.431	334.801
Mw / Mn	2,507	5,282
IV - (dl/g)	1,2155	2,2864
Rh - (nm)	11,981	21,800
Mark-Houwink a	0,791	0,519
Mark-Houwink logK	-3,866	-2,471
RI Area (mvm)	92,99	96,77
UV Area - (mvm)	0,00	0,00
RALS Area (mvm)	39,63	120,49
DP Area (mvm)	138,22	259,49
Sample conc. (mg/ml)	1	1

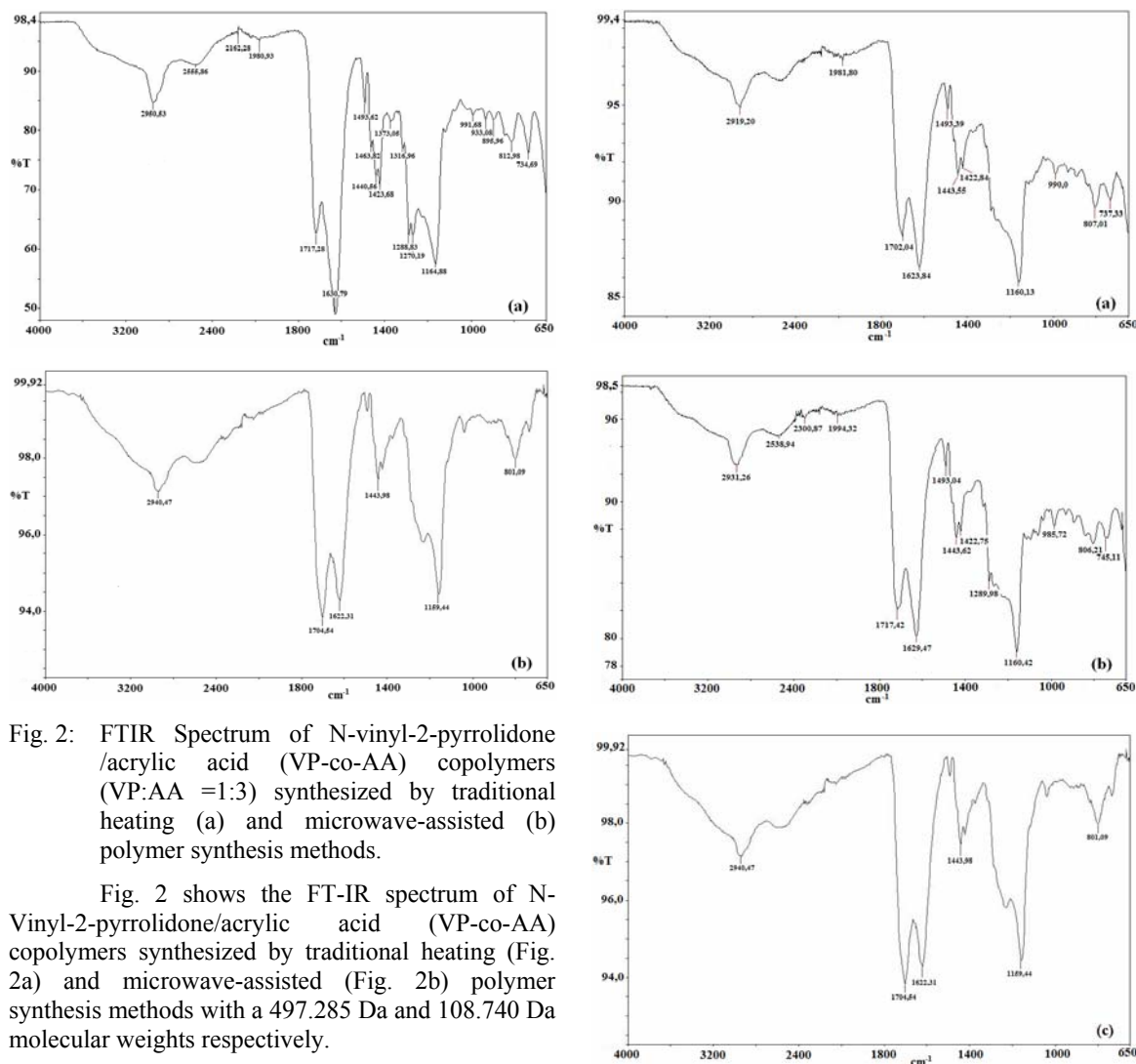


Fig. 2: FTIR Spectrum of N-vinyl-2-pyrrolidone/acrylic acid (VP-co-AA) copolymers (VP:AA =1:3) synthesized by traditional heating (a) and microwave-assisted (b) polymer synthesis methods.

Fig. 2 shows the FT-IR spectrum of N-Vinyl-2-pyrrolidone/acrylic acid (VP-co-AA) copolymers synthesized by traditional heating (Fig. 2a) and microwave-assisted (Fig. 2b) polymer synthesis methods with a 497.285 Da and 108.740 Da molecular weights respectively.

Fig. 3 shows the FT-IR spectrum of N-vinyl-2-pyrrolidone/acrylic acid (VP-co-AA) copolymers synthesized by MAPS method at 40 °C (Fig. 3a), 50 °C (Fig. 3b) and 80 °C (Fig. 3c) temperatures with a 550.744 Da, 268.209 Da and 108.740 Da molecular weights respectively.

As seen in Fig. 2 and Fig. 3, the broad absorption band around 3000-3500 cm^{-1} is ascribed to the overlapping peak of C-H group. The peaks near 2920 cm^{-1} and 2850 cm^{-1} are mainly C-H stretching vibrations of copolymers, while the peaks near 1717 cm^{-1} and 1629 cm^{-1} are C=O stretching band peak in AA and amide (CONR_2) on VP respectively. The peak appearing at 1422-1443 cm^{-1} is associated with the C-C stretching band of pyrrolidone ring [30]. There is an evident absorption peak at 1160 cm^{-1} for C-O groups and in addition to this strong narrow peak, there is a C-N stretching band at 1289 cm^{-1} .

Fig. 3: TIR Spectrum of N-vinyl-2-pyrrolidone/acrylic acid (VP-co-AA) copolymers by MAPS method at 40°C (a), 50 °C (b), 80 °C (c) temperatures.

Table-2: Characteristic peaks assigned on the FT-IR Spectrum of VP-co-AA copolymers.

2931 cm^{-1}	C-H stretching vibrations
1717 cm^{-1}	C=O stretching band peak in AA
1629 cm^{-1}	amide (CONR_2) on VP
1422-1443 cm^{-1}	(C-C) stretching band of pyrrolidone ring
1289 cm^{-1}	C-N stretching band in VP
1160 cm^{-1}	C-O stretching band in AA

The bands which belongs to both components can be seen in the FTIR spectra of P(VP-co-AA) copolymers. These results are shown in Table 2 indicates that the acrylic acid monomers copolymerized with N-vinyl-2-pyrrolidone monomers.

The effects of two different methods on reaction times, weight average molecular weight (M_w), polydispersity index (PDI), hydrodynamic radius (Rh), intrinsic viscosity ($[\eta]$) and Mark Houwink equation constant (a) of copolymers were discussed at previous results. In the second part of our experiments, we investigated the different temperature (40 °C, 50 °C and 80 °C) effects on microwave-assisted polymer synthesis at same microwave irradiation power for each synthesis.

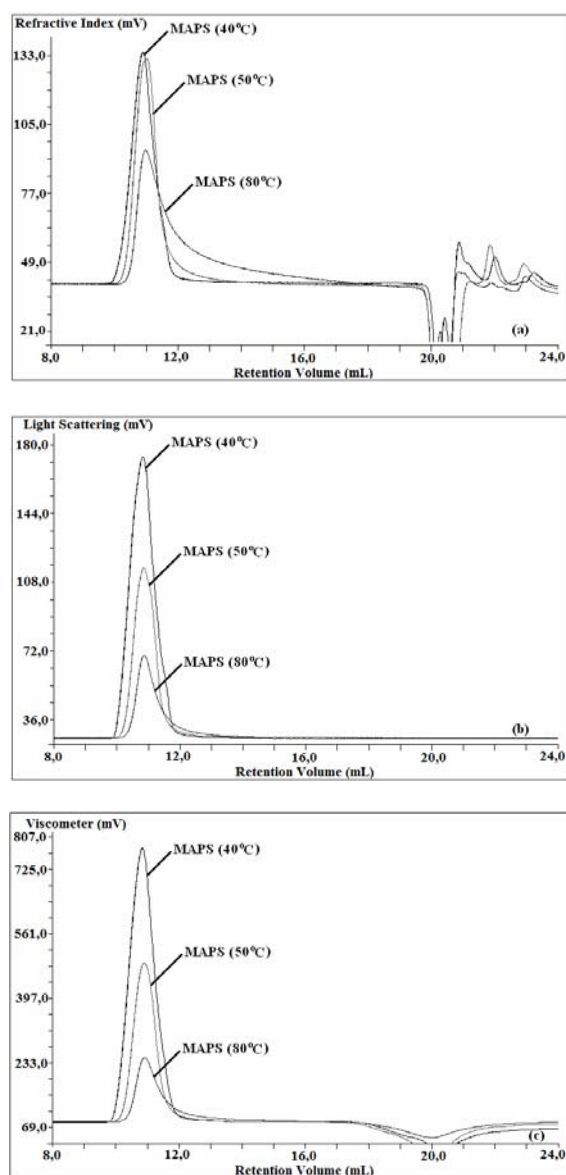


Fig. 4: PC; RI (a), RALS (b) and VIS (c) chromatograms of N-vinyl-2-pyrrolidone/acrylic acid (VP-co-AA) copolymers by MAPS method at 40 °C, 50 °C and 80 °C temperatures.

According to the gel permeation chromatography (GPC) analysis, it was clearly seen from chromatograms in Fig. 4 and Table 3 that copolymers synthesized at 40 °C, 50 °C and 80 °C by MAPS method, had molecular weights (M_w) in order of 550.744 Da, 268.209 Da and 108.740 Da. It was considered that all parameters like microwave irradiation power, monomers, solvent and initiator amounts were same for each synthesis at different temperatures.

Table-3: GPC data of N-vinyl-2-pyrrolidone/acrylic acid (VP-co-AA) copolymers by MAPS method at 40 °C, 50 °C and 80 °C temperatures.

P(VP-co-AA) (VP:AA=1:3)	Microwave-assisted synthesized copolymer		
	40 °C	50 °C	80 °C
Peak RV - (ml)	10,877	10,997	10,963
Mn - (Da)	498,970	214,576	43,374
Mw - (Da)	550,744	268,209	108,740
Mz - (Da)	635,136	333,622	194,540
Mp - (Da)	480,899	257,392	183,431
Mw / Mn	1,104	1,250	2,507
IV - (dl/g)	4,6075	2,4041	1,2155
Rh - (nm)	33,887	21,222	11,981
Mark-Houwink a	0,662	0,765	0,791
Mark-Houwink logK	-3,128	-3,760	-3,866
RI Area (mVml)	84,90	83,38	92,99
UV Area - (mVml)	0,00	0,00	0,00
RALS Area (mVml)	140,65	74,91	39,63
DP Area (mVml)	676,50	348,09	138,22
Sample conc. (mg/ml)	1	1	1

The effect of temperature on MAPS method was noticeably seen when comparing molecular weight of copolymers. Besides constant microwave irradiation power in MAPS method, variable heating energy was given to the reaction media for different temperature. Although microwave irradiation power was same at each reaction media, with the increasing temperature more initiator radicals occurred. This caused synthesis of low molecular weight copolymers.

In addition to these results, PDI of copolymers were 1.104, 1.250 and 2.507 synthesized by MAPS methods at 40 °C, 50 °C and 80 °C respectively. Increase in heating energy caused synthesis of more polydisperse copolymers. Rh values were 33.887, 21.222 and 11.981 of copolymers for reactions at 40 °C, 50 °C and 80 °C respectively. Mark Houwink equation constant a and $[\eta]$ values for copolymers were 0.662 (40 °C), 0.765 (50 °C), 0.791 (80 °C) and 4.6075 dl/g (40 °C), 2.4041 dl/g (50 °C), 1.2155 dl/g (80 °C). All Rh, $[\eta]$ and Mark Houwink a constant values supported each other and this indicated that there was a slightly increase in compactness of copolymers with the decrease in temperature.

Experimental

Chemicals

Acrylic acid (Aldrich, Germany), N-vinyl-2-pyrrolidone (Fluka), tetrahydrofuran (Riedel-de Haen), ethyl acetate (Fluka) and 4,4'-azobis(4-cyano valeric acid) (Fluka) were of analytical grade reagents.

Synthesis of poly(N-vinyl-2-pyrrolidone-co-acrylic acid) via traditional heating method

Poly(N-vinyl-2-pyrrolidone-co-acrylic acid) copolymer was synthesized by free radical copolymerization of monomers in 75:25 ($v_{\text{solvent}} : v_{\text{reactants}}$) tetrahydrofuran (THF) using 4,4'-azobis(4-cyano valeric acid) (ACVA) as the initiator. The feed composition of the monomers was kept at 25 mol % N-vinyl-2-pyrrolidone (VP) and 75 mol % acrylic acid (AA) for synthesizing of P(VP-co-AA) by free radical polymerization (Fig. 5).

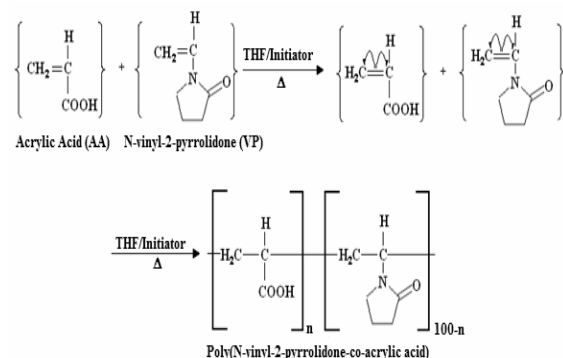


Fig. 5: Synthesis of (N-vinyl-2-pyrrolidone-acrylic acid) copolymers by traditional heating method.

The reaction mixtures were placed in polymerization reactor under nitrogen and stirred at 80 °C for 4 hours in temperature controlled water bath (Fig. 6). After filtration of white solid it was separated and purified by precipitation in ethyl acetate. Then synthesized copolymer was dried at 40 °C in vacuum.

Synthesis of poly(N-vinyl-2-pyrrolidone-co-acrylic acid) with microwave-assisted Method

Poly(N-vinyl-2-pyrrolidone-co-acrylic acid) copolymers were synthesized by free radical copolymerization of monomers in 75:25 ($v_{\text{solvent}} : v_{\text{reactants}}$) tetrahydrofuran (THF) using 4,4'-azobis(4-cyano valeric acid) (ACVA) as the initiator. The feed composition of the monomers was kept at 25 mol % VP and 75 mol % AA for synthesizing of P(VP-co-AA) by using Milestone Ethos Touch Control System (Milestone, Italy).

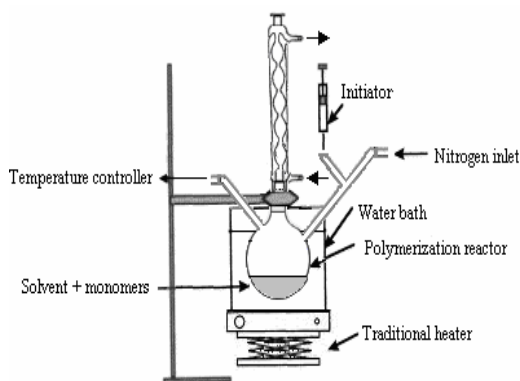


Fig. 6: Schematically drawing of the traditional heating polymerization system.

The reaction mixtures were placed in reaction tubes, freed from air oxygen and stirred at 40 °C, 50 °C and 80 °C for 10 minutes each under microwave irradiation (300 W) one after another in Milestone Ethos Touch Control System. After filtration of white solid it was separated and purified by precipitation in ethyl acetate. Then synthesized copolymers were dried at 40 °C in vacuum.

Fourier Transform Infrared Spectroscopy (FTIR) Analysis

FTIR spectra of the copolymers (ATR-FTIR) were obtained using a Spectrum One FT-IR model Perkin Elmer FTIR spectrophotometer. Samples were scanned at 650-4000 cm^{-1} with 0.5 cm^{-1} resolution. Intensity of absorption bands were calculated after baseline correction.

Gel Permeation Chromatography (GPC) Analysis

GPC analysis of the copolymers were obtained using a Viscotek TDA 302 quadruple detector system with refractive index (RI-660 nm), right angle light scattering (RALS-670 nm), four-capillary differential viscometer (VIS) and UV-Vis absorbance (UV-280 nm) detectors were used for on-line SEC signal detection. Viscotek array was calibrated using polyethylene oxide (PEO) peak in a mobile phase of Phosphate-buffered saline (PBS) at 1.0 ml/min flow rate at 25 °C. All copolymer sample concentrations were 1 mg/ml. The molecular weights were calculated on the basis of PEO standards.

Conclusion

The use of microwave irradiation in polymer chemistry is an emerging and rapidly expanding field of research [27]. The microwave synthesis requires more energy during the first few seconds only to obtain uniform and intensive initiation. The

polymerization reaction course is readily supervised by monitoring the temperature of the reaction mixture by infra-red sensors and the applied power of microwave radiation [31].

The novelty of this article is successfully synthesis of water-soluble and biocompatible P(VP-co-AA) polymer via a microwave-assisted method with shortened reaction time and this make it ideal for rapid reaction and optimization. While it takes 4 hours to synthesize copolymers in THPS method, the reaction time was 10 min in MAPS method. When THPS and MAPS methods compared on R_h , $[\eta]$ and Mark Houwink a constant values, it was clearly seen that while compact copolymer can be synthesized by THPS method, more linear copolymers can be synthesized by MAPS method. THPS and MAPS methods compared to the PDI of copolymers which is the symbol of homogeneity, the possibility of synthesizing more homogeneous copolymers by using MAPS method was shown in this study.

Differently than the literature [32], irradiation power and initiator were used at the same time at MAPS method in our study both microwave. As a result of these effects more initiator radicals and polymer chains occurred. Consequently, lower molecular weight copolymers were synthesized in MAPS method according to THPS method.

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