
CHARACTERISATION OF SYNTHESISED CROSSLINKED HYDROGELS BASED ON 1-VINYL-2-PIRROLYDINONE

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Abstract: Polymer hydrogels are three-dimensional networks formed of highly hydrophilic monomers cross-linked by hydrogen bonding, electrostatic attraction or covalent crosslinking. They may be formed of one (homo-) or multiple monomers (copolymer hydrogels). The specificity of hydrogels stems from their ability to bind large amounts of surrounding fluid, water, or biological fluids, due to their physical and / or chemical crosslinking, while remaining insoluble. Poly(1-vinyl-2-pyrrolidone) is a polar, hydrophilic, amphoteric polymer obtained from the monomer of 1-vinyl-2-pyrrolidone. The choice of synthesis conditions resulted in a large number of products of different molar masses (from several thousand to several million g/mol). It is used in many industries (in the production of adhesives, paper and detergents), especially because of its good solubility in water and in a large number of organic solvents. Poly(1-vinyl-2-pyrrolidone) are the widely used biocompatible homo polymer hydrogel carriers in drug delivery due to its water solubility and extremely low cytotoxicity. It is biocompatible and therefore safe for use in biological experiments. The aim of this work is to synthesize hydrogel based on 1-vinyl-2-pyrrolidone monomer using ethylene glycol dimethacrylate (1, 2 and 3 mol%) as crosslinker and 2,2'-azobis(2-methylpropionitrile) initiator by radical polymerization method with thermal initiation. Structural characterization of the obtained poly(1-vinyl-2-pyrrolidone) hydrogels was performed using Fourier transformation infrared spectroscopy (FTIR) methods. The synthesized hydrogels were purified from unreacted monomers, crosslinkers and initiators after extraction in methanol. The content of the residual reactants from the methanol extracts was examined using high pressure liquid chromatography (HPLC). Decanted methanolic extracts of synthesized poly(1-vinyl-2-pyrrolidone) hydrogels after 48h of residual reactant extraction were used for analysis. The extracts were filtered through a 0.45 μm cellulose membrane filter and used for HPLC analysis. After rinsing, hydrogels were dried to the constant mass in a drying oven at 40°C. In the FTIR spectra of poly(1-vinyl-2-pyrrolidone), there are no bands of valence vibrations of vinyl group 1-vinyl-2-pyrrolidone or ethylene glycol dimethacrylate, nor bands of valence C = C vibrations and deformation vibrations in the plane and out of plane of the vinyl group of monomers and crosslinkers. indicating the polymerization performed by breaking the double bonds. Residual reactant values are within acceptable limits (1.132 - 2.020% for 1-vinyl-2-pyrrolidone, 0.338 - 0.963% for ethylene glycol dimethacrylate, according to the initial amount in the reaction mixture), and also indicate a satisfactory product yield.

Keywords: hydrogel, poly(1-vinyl-2-pyrrolidone), synthesis.

1. INTRODUCTION

Poly(1-vinyl-2-pyrrolidone), p(VP), is a hydrophilic, highly polar, amphoteric polymer synthesized by free radicals chain polymerization of 1-vinyl-2-pyrrolidone monomers, in water or alcohol as a solvent, in the presence of a suitable initiator (Koetting & Peppas, 2014). By choosing polymerization conditions, a wide range of products of different molar masses can be obtained, starting from several thousand to several million $\text{g}\cdot\text{mol}^{-1}$ (Ali et al, 2014). It is biocompatible and therefore safe for use in biological experiments. p(VP) is one of the most used polymers in medicine due to its water solubility and extremely low cytotoxicity. p(VP) is a high-swelling hydrogel with values ranging from 5 to 100, sometimes up to 1000 (Maitra & Shukla, 2014). The crosslinking of 1-vinyl-2-pyrrolidone can be performed by the radiation-chemical method, which produces materials that are safe for further biomedical purposes (Đurđević, 2015). Radiation is used to crosslink and sterilize the material at the same time. The advantage of the radiation-chemical formation of a polymer network is the absence of chemical crosslinkers and auxiliary agents, such as initiators and activators. The degree of swelling of hydrogels obtained by radiation-chemical crosslinking depends on the total radiation dose applied to crosslinking (Darwis, et al, 1993). Electrochemical synthesis of 1-vinyl-2-pyrrolidone allows precise control of nanoparticle size. In aqueous solutions of argon-saturated polymers, OH • radicals generated by gamma irradiation react with PVP macromolecules by taking up hydrogen atoms, thereby forming PVP macroradicals (Benamer et al, 2006). Due to the importance of poly (1-vinyl-2-pyrrolidone) there is clearly a great interest in its functionalization, i.e. chemical inclusion of groups that may alter some properties and / or allow the incorporation of different molecules (Reinecke et al, 2010). The aim of this work

synthesis and characterisation of hydrogel based on 1-vinyl-2-pyrrolidone monomer using ethylene glycol dimethacrylate as crosslinker by radical polymerization method with thermal initiation.

2. THE EXPERIMENTAL PART

2.1. Reagents

For the synthesis of homopolymer hydrogels, the monomer 1-vinyl-2-pyrrolidone, VP, purity $\geq 99\%$ (Merck KGaA, Darmstadt, Germany) was used. Ethylene glycol dimethacrylate, EGDM, 97% purity (Fluka Chemical Corp, CH), was applied as a crosslinker of polymer chain units. 2,2'-azobis(2-methylpropionitrile), AZDN, 98% purity (Acros Organics, New Jersey, USA) were used to initiate radical polymerization. Methanol (Merck KGaA) with a purity of 99.5% was used to dissolve the reactants in the polymerization reaction.

2.2. Synthesis of hydrogels

Samples of homopolymer hydrogels poly(1-vinyl-2-pyrrolidone), with 1, 2 and 3 mol% ethylene glycol dimethacrylate crosslinkers were synthesized by radical polymerization of the 1-vinyl-2-pyrrolidone monomer. The polymerization reaction was initiated by the addition of the initiator 2,2'-azobis(2-methylpropionitrile), and the reactants were dissolved in an adequate amount of methanol. After homogenization and dissolution of the reactants, the reaction mixtures were injected into glass vials, which were subsequently warmed. All samples were subjected to a polymerization reaction initiated thermally according to the following regime: 30 min. at 70 °C, 120 min. at 80 °C and 90 min. at 85 °C. The synthesized poly(1-vinyl-2-pyrrolidone) hydrogels, after cooling, were separated from the glass ampoules in the form of long cylinders and cut into smaller cylinders. The cross-linked hydrogels p(VP) were then treated with methanol for 48 h at room temperature with occasional stirring (0.5 g of gel was overflowed with 30 cm³ of methanol each) to remove any unreacted compounds. After methanol treatment, the hydrogels were immersed in a solution of methanol/distilled water in a ratio of 75/25%, 50/50%, 25/75% and 0/100%, v/v, for 24 h, to gradually wash the hydrogels from methanol. The hydrogels p(VP) were dried at 40 °C to constant mass and further characterized.

2.3. Characterization of poly(1-vinyl-2-pyrrolidone) hydrogels

2.3.1. Infrared spectroscopy with Fourier transformation (FTIR)

Structural characterization of the obtained poly(1-vinyl-2-pyrrolidone) hydrogels was performed using Fourier transformation infrared spectroscopy (FTIR) methods. FTIR spectra of 1-vinyl-2-pyrrolidone monomer was recorded by capillary film method between two polished plates of zinc selenide (ZnSe). FTIR spectra of crosslinker ethylene glycol dimethacrylate and synthesized xerogels of poly(1-vinyl-2-pyrrolidone) are recorded by thin transparent technique tablets with potassium bromide of spectroscopic purity, vacuumed and pressed at about 200 MPa.

2.3.2. Analysis of unreacted reactants content

The residual amounts of unreacted 1-vinyl-2-pyrrolidone monomers and ethylene glycol dimethacrylate crosslinkers in the synthesized hydrogel samples after synthesis were determined by high pressure liquid chromatography. Decanted methanolic extracts of synthesized poly(1-vinyl-2-pyrrolidone) hydrogels after 48 h of residual reactant extraction were used for analysis. The extracts were filtered through a 0.45 μm cellulose membrane filter and used for HPLC analysis. The recordings were made on an HPLC Agilent 1100 Series with a diode array detector, DAD 1200 Series, the detector was set to a wavelength of 205 nm. A ZORBAX Eclipse XDB-C18 column, 4.6 \times 250 mm, 5 μm was used. The eluent were methanol 99.9% HPLC purity, 80% (A) and distilled water, 20% (B). The column was thermostated at 30 °C and the flow rate was 1 cm³·min⁻¹. The injected volumes of the analyzed samples were 10 μl each. Standard substances of 1-vinyl-2-pyrrolidone monomers and ethylene glycol dimethacrylate crosslinkers were used to construct the calibration curves. A series of standard solutions of known concentrations were made, filtered through a 0.45 μm cellulose membrane filter and analyzed by HPLC method.

3. RESULTS AND DISCUSSION

3.1. Synthesis of poly(1-vinyl-2-pyrrolidone) homopolymer hydrogel

Homopolymeric hydrogels of poly(1-vinyl-2-pyrrolidone) based on the monomer 1-vinyl-2-pyrrolidone were synthesized using an ethylene glycol dimethacrylate crosslinker and 2,2'-azobis(2-methylpropionitrile) initiator. The appearance of the synthesized homopolymers of poly(1-vinyl-2-pyrrolidone) with 1, 2 and 3 mol% EGDM after synthesis is shown in Figure 1.

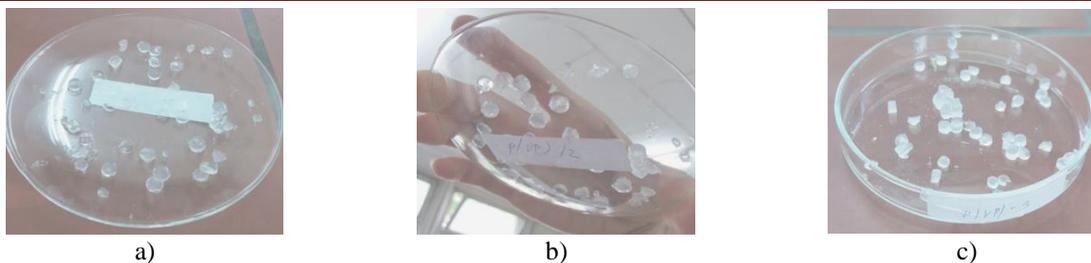


Figure 1: Synthesized poly(1-vinyl-2-pyrrolidone) homopolymers with 1, 2 and 3 mol% EGDM

3.2. Characterization of poly (1-vinyl-2-pyrrolidone) hydrogels by the FTIR method

The FTIR spectrum of the 1-vinyl-2-pyrrolidone monomer is shown in Figure 2. In the structure of the molecules of the 1-vinyl-2-pyrrolidone monomer there is a five-membered ring of cyclic amide which in the condensed state exists in the structure of the cis-cis dimer (Jimenez et al, 2019). Lactam carbonyls absorb at about 1705 cm^{-1} , and in the FTIR spectrum of the 1-vinyl-2-pyrrolidone monomer this characteristic band shows an absorption maximum at 1706 cm^{-1} . The absorption band with maximum at 3109 cm^{-1} is the result of asymmetric valence vibrations of the vinyl group, $\nu_{\text{as}}(\text{=C-H})$. Absorption bands from deformation vibrations of the in-plane of vinyl group, $\delta(\text{=C-H})$, and out of plane, $\gamma(\text{=C-H})$, occur with maxima at 1332 cm^{-1} and 981 cm^{-1} , respectively. Asymmetric C-H valence vibrations from the CH_2 group, $\nu_{\text{as}}(\text{C-H})$, give the absorption bands at 2980 cm^{-1} and 2875 cm^{-1} , respectively. A medium intensity absorption band with a maximum at 1461 cm^{-1} occurs as a result of the deformation vibrations of the C-H group, $\delta(\text{C-H})$ of the present CH_2 group in the VP molecule. The FTIR spectrum of VP monomers also exhibits a lower intensity absorption band with a maximum at 1630 cm^{-1} , which is attributed to the valence vibrations of the double C=C bond, $\nu(\text{C=C})$, present in the structure of the 1-vinyl-2-pyrrolidone molecule.

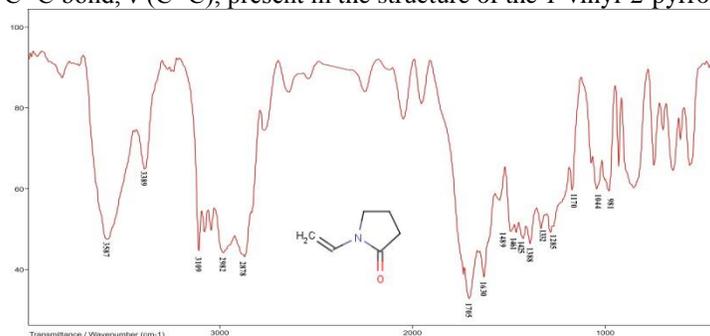


Figure 2: FTIR spectrum of 1-vinyl-2-pyrrolidone

The FTIR spectrum of the ethylene glycol dimethacrylate crosslinker is shown in Figure 3. In the FTIR spectrum of the ethylene glycol dimethacrylate crosslinker there are bands characteristic of the ester and vinyl functional groups present in the molecule. The characteristic absorption band with a maximum at 1726 cm^{-1} in the FTIR spectrum of ethylene glycol dimethacrylate is attributed to the C=O valence vibrations. The valence vibrations of the C-O bond give the band with an absorption maximum at 1152 cm^{-1} . The band with maximum at 1636 cm^{-1} comes from the absorption of the double C=C bond, and bands with maxima at 2894 cm^{-1} from $\nu_{\text{s}}(\text{CH}_3)$, at 2960 cm^{-1} from $\nu_{\text{as}}(\text{CH}_3)$, at 2930 cm^{-1} of $\nu_{\text{as}}(\text{CH}_2)$ and at 3105 cm^{-1} of the vinyl group $\nu_{\text{as}}(\text{=CH})$.

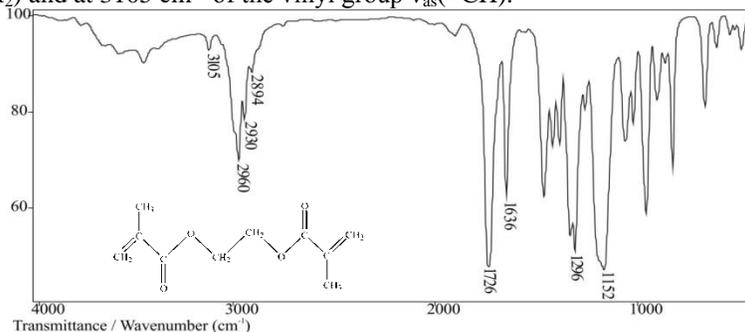


Figure 3: FTIR spectrum of ethylene glycol dimethacrylate crosslinker

The FTIR spectrum of a synthesized homopolymer of poly(1-vinyl-2-pyrrolidone) with 3 mol% EGDM crosslinker is shown in Figure 4. The FTIR spectrum of a synthesized homopolymer of poly(1-vinyl-2-pyrrolidone) with 3 mol% EGDM shows a structure different from the reactants. The absence of some characteristic absorption bands present in the FTIR spectrum of the 1-vinyl-2-pyrrolidone monomer and the EGDM crosslinker is observed, indicating the formation of a new structure. In the FTIR spectrum of the synthesized homopolymer there are no absorption bands from the valence vibrations of the vinyl group, $\nu(\text{C-H})$, and deformation vibrations in the plane, $\delta(\text{C-H})$, and outside the plane $\gamma(\text{C-H})$, present in the spectra of the reactants.

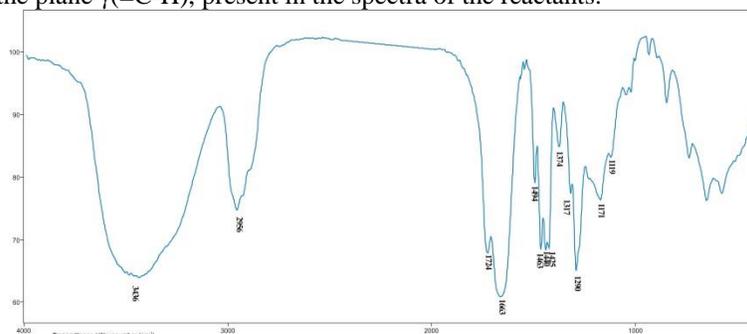


Figure 4: FTIR spectrum of poly(1-vinyl-2-pyrrolidone) homopolymer with 3 mol% of EGDM crosslinker

The absence of bands at 1630 cm^{-1} and 1636 cm^{-1} resulting from the valence vibrations of the double $\text{C}=\text{C}$ bond (present in the FTIR spectra of VP and EGDM) confirms that the polymerization process was successfully performed by breaking the double $\text{C}=\text{C}$ bond. For the FTIR spectrum of synthesized p(VP) absorption bands originating from asymmetric and symmetric valence vibrations from the CH_3 and CH_2 groups, $\nu_{\text{as}}(\text{C-H})$, give absorption maxima at 2956 and 2899 cm^{-1} , respectively. The presence of deformation CH_3 and CH_2 vibrations in the plane, $\delta(\text{C-H})$, is confirmed by the bands with absorption maxima at 1463 and 1440 cm^{-1} . The sharp bands with maxima at 1724 and 1663 cm^{-1} are derived from the valence vibrations of the $\text{C}=\text{O}$ group, $\nu(\text{C}=\text{O})$, present in the FTIR spectra of the VP and EGDM. The absorption band originating from the valence C-O vibrations occurs at 1425 cm^{-1} . In the FTIR spectrum of poly(1-vinyl-2-pyrrolidone) in the wavenumber range $3600\text{--}3300\text{ cm}^{-1}$ there is also a broad band attributable to the valence vibrations of intermolecular interactions by the type of hydrogen bond between the base $\text{C}=\text{O}$ group (acceptor) and H atoms of high acidity from the $=\text{CH-}$ group.

3.1.2. Analysis of residual monomers and crosslinkers

The solutions separated by decantation after the overflow of polymerized hydrogels with p(VP) methanol were analyzed using the HPLC method to determine the content and amount of monomers and crosslinkers which did not participate in the polymerization reactions. Samples of synthesized homopolymers of poly(1-vinyl-2-pyrrolidone) were used for analysis, which were extracted in 30 cm^3 of methanol at room temperature for 48 h, with occasional stirring. The extracts were filtered through a $0.45\text{ }\mu\text{m}$ cellulose membrane filter and used for HPLC analysis.

3.1.2.1 The calibration curve construction for 1-vinyl-2-pyrrolidone

Standard solutions of known concentrations of 1-vinyl-2-pyrrolidone, 99%, HPLC purity, filtered through a cellulose membrane filter with a pore diameter of $0.45\text{ }\mu\text{m}$ were prepared and analyzed by HPLC method. The HPLC chromatogram of standard 1-vinyl-2-pyrrolidone monomer solution has a retention time of $R_t=3.191\text{ min}$ (Fig. 5a) and the absorption maximum in the UV range is $\lambda_{\text{max}}=205\text{ nm}$. The UV spectrum of the standard VP solution (as the mean of the UV spectra from the HPLC chromatogram peak from the DAD detector) is shown in Figure 5b.

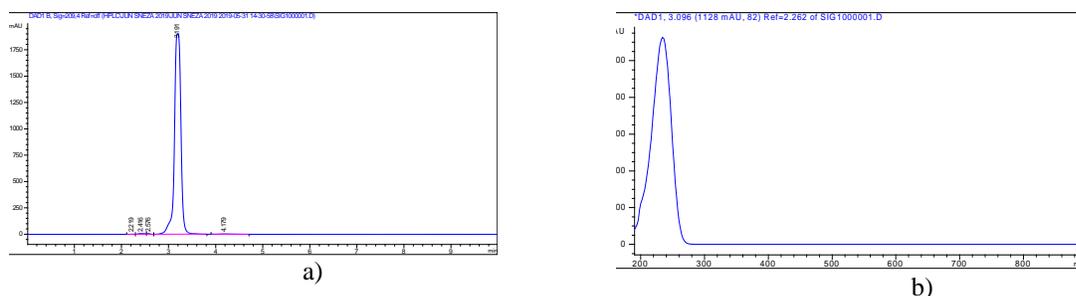


Figure 5: 1-vinyl-2-pyrrolidone standard a) HPLC chromatogram, b) UV spectrum

The constructed calibration curve for the monomer 1-vinyl-2-pyrrolidone shows linearity for concentrations in the range 0.005-0.400 mg·cm⁻³, for peak areas up to about 9000 mAU·s, and for the above area, the equation applies:

$$A_{209} = 124,2 + 16708,57 \cdot c_{VP} \quad (1)$$

where A_{209} is the peak area in mAU·s at $\lambda = 209$ nm and c_{VP} is the content of monomer 1-vinyl-2-pyrrolidone in mg·cm⁻³, the linear correlation coefficient is $R^2 = 0,998$.

3.1.2.2 The calibration curve construction for ethylene glycol dimethacrylate

Standard solutions of ethylene glycol dimethacrylate were prepared in the same way as VA. The HPLC chromatogram of ethylene glycol dimethacrylate standard solution has a retention time of $R_t = 6,137$ min (Fig. 6a) and the absorption maximum in the UV range is $\lambda_{max} = 205$ nm (Figure 6b).

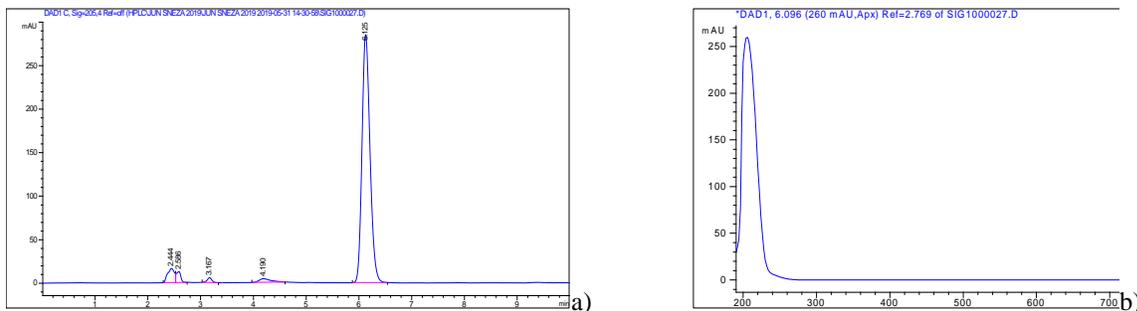


Figure 6: Ethylene glycol dimethacrylate, a) HPLC chromatogram, b) UV spectrum

The calibration curve for the ethylene glycol dimethacrylate as crosslinker shows linearity for concentrations in the range 0,001 – 0,3 mg·cm⁻³, for peak areas from 700 to 18000 mAU·s, and for the above area, the equation applies (2):

$$A = -19,3 + 76188,1 \cdot c \quad (2)$$

where A is the peak area in mAU·s at $\lambda = 205$ nm and c is the content of ethylene glycol dimethacrylate in mg·cm⁻³, the linear correlation coefficient is $R^2 = 0,998$.

3.1.2.3. Analysis of residual monomers and crosslinker

The content of monomer and crosslinker in the extracts was determined based on the calibration curves. Under chromatographic conditions, the 1-vinyl-2-pyrrolidone monomer has a retention time of $R_t = 3.191$ min, while the EGDM crosslinker has a retention time of $R_t = 6.137$ min, so that the peaks in the tested samples are well separated (Ilić-Stojanović, 2017). The detection wavelength at which the maximum absorption peak occurs in the UV range for 1-vinyl-2-pyrrolidone is 209 nm and for the EGDM λ_{max} crosslinker is 205 nm. Peak area values and obtained results of the amounts of residual 1-vinyl-2-pyrrolidone monomer and EGDM crosslinker in synthesized poly(1-vinyl-2-pyrrolidone) samples with different crosslinker content are shown in Table 1.

Table 1: Peak area values and amounts of residual 1-vinyl-2-pyrrolidone as monomer and EGDM as crosslinker in poly(1-vinyl-2-pyrrolidone) samples with different EGDM crosslinker content

mol% EGDM	xerogel mass p(VP), g	A_{VP} , mAU·s	VP in the initial reaction mixture, mg/g	VP relative to the initial amount in the reaction mixture, %	A_{EGDM} , mAU·s	EGDM in the initial reaction mixture, mg/g	EGDM relative to the initial amount in the reaction mixture, %
1	0,512	3126,6	930,013	1,132	285	69,187	0,338
2	0,524	4123,1	914,84	1,498	511,1	85,16	0,468
3	0,531	5502,2	900,15	2,020	1277	99,85	0,963

According to the calculation, the amounts of residual reactants obtained after the polymerization reaction are in the range of 10,528 to 18,184 mg·g⁻¹ for 1-vinyl-2-pyrrolidone and from 0,234 to 0,961 mg·g⁻¹ for ethylene glycol dimethacrylate relative to the amount of xerogels poly(1-vinyl-2-pyrrolidone) (Sa'adun, 2014). The content of residual reactants relative to the measured initial amounts in the reaction mixture ranges from 1.132 to 2.020% for 1-vinyl-2-pyrrolidone and for EGDM in the range from 0.338 to 0.963%. From the results obtained, it can be

concluded that the unreacted amounts of residual monomer and crosslinker during the synthesis of poly(1-vinyl-2-pyrrolidone) hydrogels are within acceptable limits and also indicate satisfactory product yield.

4. CONCLUSION

Crosslinked homopolymer poly(1-vinyl-2-pyrrolidone) hydrogels with 1, 2 and 3 mol% ethylene glycol dimethacrylate crosslinkers were synthesized using thermal-initiated radical polymerization method. In the FTIR spectra of p(VP) xerogels, there are no bands of vinyl group valence vibrations from 1-vinyl-2-pyrrolidone or ethylene glycol dimethacrylate, nor bands of valence C=C vibrations and deformation vibrations in the plane and out of plane of the vinyl group of monomers and crosslinkers, indicating the polymerization performed by breaking the double bonds. Residual reactant values are within acceptable limits (1.132- 2.020% for 1-vinyl-2-pyrrolidone, 0.338 - 0.963% for ethylene glycol dimethacrylate, according to the initial amount in the reaction mixture), and also indicate a satisfactory product yield.

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