



Hydrophilic Polyurethaneurea Containing the Copolymer of N-vinylpyrrolidone, Vinyl Acetate and Vinyl Alcohol for Possible Biomedical Use

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Abstract: The series of polyurethaneurea (PUU) containing in its structure the fragments of the copolymer of N-vinylpyrrolidone, vinyl acetate and vinyl alcohol (VP-VA) with the 1.6-hexamethylenediamine (HMDA) macrochain extender and the series of PUU with the 4.4'-diaminodiphenylmethane (DADPh) macrochain extender having different ratio of HMDA and DADPh to VP-VA (30:70; 40:60; 50:50; 60:40; 70:30) were synthesized. It has been established that PUU containing in its structure the DADPh macrochain extender is characterized by higher values of the tensile strength and relative elongation at break, glass-transition temperature and the change of the specific heat capacity and hydrophilicity compared to PUU containing in its structure the HMDA macrochain extender. It was found that the increase in amount of VP-VA copolymers in PUU structure increases hydrophilicity by 19-41% for PUU with HMDA and by 16-62% for PUU with DADPh and will contribute to a prolonged release of biologically active substances from the polymer matrix. The results obtained allowed us to determine that the PUU with VP-VA copolymer fragments in the structure synthesized with the ratio of HMDA and DADPh to VP-VA 70:30 is characterized by sufficient physical-mechanical properties ($\sigma = 3.1$ MPa, $\varepsilon = 47\%$ and $\sigma = 5.2$ MPa, $\varepsilon = 90\%$, accordingly), hydrophilicity (21.0% and 19.4%, accordingly) and can be used as a polymer matrix for medicine biologically active composite materials.

Keywords: Polyurethaneurea, N-vinylpyrrolidone Copolymer with Vinyl Acetate and Vinyl Alcohol, 1.6-Hexamethylenediamine, 4.4'-Diaminodiphenylmethane, Hydrophilicity

1. Introduction

The polyurethaneurea (PUU) are used in a variety of medical applications, such as the wound dressing [1], contact lenses [2], catheters, prostheses, blood vessels [3], antithrombogenic products [4], mechanically supporting constructions during the soft tissue reconstruction [5], metal stents coating of atherosclerotic blood vessels [6], surgical meshes [7, 8] and bone tissue engineered [9, 10], vascular tissue engineering [11].

The presence in PUU macrochain of the urethane group
$$\left(\text{—NH—}\overset{\text{O}}{\parallel}\text{C—O—} \right)$$
 similar in chemical structure to the peptide group of proteins (—CO—NH—) provides

widespread use of PUU in medical practice due to their biocompatibility.

Hydrophilicity is an important characteristic of medical polymer material matrix, because it generally ensures prolonged release of the therapeutic substance (TS) from the polymer matrix *in vivo*. Therefore, the insertion of hydrophilic chains of N-vinylpyrrolidone copolymer with vinyl alcohol (VP-VA) (Figure 1), widely used in medicine, into the polymer matrix may produce new hydrophilic polymer materials capable for more complete and prolonged release of the TS:

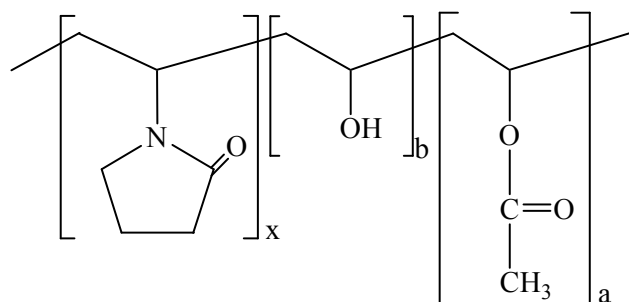


Figure 1. Copolymer of VP-VA.

The presence of copolymer is expected to increase the hydrophilicity of PUU because of availability of two types of hydrophilic groups ($-\text{OH}$ and $\text{N}-\text{C}=\text{O}$) in its structure.

Earlier, the authors [12] synthesized hydrophilic polyurethanes containing the fragments of VP-VA copolymer filled with Amizonum, which exerted a prolonged anti-inflammatory effect. The film materials with Decamethoxine based on polyurethaneurea containing the fragments of the VP-VA copolymer have been already developed. Such material with antimicrobial effect is recommended for healing wounds and burns [13]. It is known [14], that diamine-containing PUU with folic acid, which provides regenerative properties, allows the use it as burns coatings in medicine. Nevertheless, preparing film materials with improved properties based on hydrophilic PUU remains to be an important task.

The aim of our work was to synthesize the series of hydrophilic polyurethaneurea containing the fragments of VP-VA copolymer and one of two macrochain extenders: 1,6-hexamethylenediamine or 4,4'-diaminodiphenylmethane. The hydrophilic polyurethaneureas were synthesized using different ratios of the macrochain extender to the VP-VA copolymer and their structure and properties have been studied.

2. Experimental

2.1. Materials

Polyoxypropylene glycol (POPG) ("Rokopol", Poland) MM 1052 has been dried at residual pressure 1–3 mm of mercury and temperature $(80 \pm 5)^\circ\text{C}$ in the flow of dry argon for 8 hours just prior to the synthesis.

2,4-; 2,6-toluylene diisocyanate (TDI, 80/20) $\text{C}_9\text{H}_6\text{N}_2\text{O}_2$ (Merck, Germany) (MM = 174.16; $\rho = 1.22 \text{ g/cm}^3$; $T_{\text{boil}} = (133 \pm 1)^\circ\text{C}$; $n_D^{20} = 1.5678$) – mixture of isomers 2,4- and 2,6- with the ratio of 80/20, has been purified by distillation in vacuum at residual pressure 0.67 kPa, $T_{\text{boil}} = (100 \pm 1)^\circ\text{C}$. Freshly distilled TDI has been used.

1,6-hexamethylenediamine (HMDA) $\text{C}_6\text{H}_{16}\text{N}_2$ (Fluka, 99.9%) (MM = 116.21; $T_{\text{melt}} = 39\text{--}42^\circ\text{C}$) has been used without any additional purification.

4,4'-diaminodiphenylmethane (DADPh) $\text{C}_{13}\text{H}_{14}\text{N}_2$ (Fluka, 97.0%) (MM = 198.27; $T_{\text{melt}} = 88\text{--}92^\circ\text{C}$) has been used without any additional purification.

N, N'-dimethyl acetamide (DMAA) (Merck, Germany)

(MM = 87.12; $\rho = (0.940\text{--}0.942) \text{ g/cm}^3$; 99.7%) has been distilled with the mixture of benzol-water in vacuum ($T_{\text{boil}} = (52 \pm 1)^\circ\text{C}$ / 14 mm of mercury).

Triple copolymer of VP-VA-VA ($\text{OH} = 6.3$) was synthesized from the copolymer of N-vinylpyrrolidone with vinylacetate (VP-VA) (Sigma-Aldrich) (MM 50000) by alkaline alcoholysis subject to incomplete saponification [12], hereinafter will be abbreviated as VP-VA.

2.2. Study Methods

2.2.1. Mechanical Tests

The physical-mechanical properties such as tensile strength at break (σ , MPa) and relative elongation at break (ε , %) of the synthesized PUU were determined on the tension testing machine P 5 under the GOST 25.601.

The tensile strength at break was calculated using the expression:

$$\sigma = \frac{F_{\text{max}}}{b \cdot h} \quad (1)$$

where, F_{max} – maximum load at break of sample, H;

b – width of sample, mm;

h – thickness of sample, mm.

The relative elongation at break was calculated using the expression:

$$E = \frac{\Delta l}{l} \cdot 100 \quad (2)$$

where, Δl – absolute elongation of sample at break, mm;

l – initial length of sample, mm.

2.2.2. Fourier Transforms Infrared (ATR FT-IR)

Absorption spectra in the range $650\text{--}4000 \text{ cm}^{-1}$ were measured on a Tensor-37 FTIR spectrometer by the MATR method with the aid of a diamond crystal trapezoidal prism (a number of reflections of $N = 1$, an incidence angle of $\varphi = 39^\circ$). The absorption bands were assigned as described in [15].

2.2.3. Absorption Test

Hydrophilicity has been studied by determining the water absorption of PUU after its keeping in the distilled water at 37°C for 24 hours. After the required period of time, the samples were removed and gently dried using a filter paper to remove water adhering to its surface. For each sample composition, three measurements were conducted and employed in the computation of the mean and standard deviation values.

The degree of water absorption ($W, \%$) was calculated using the expression:

$$W = \frac{m_1 - m_0}{m_0} \cdot 100\% \quad (3)$$

where, m_1 – masse of the sample after keeping in water for 24 hours, g;

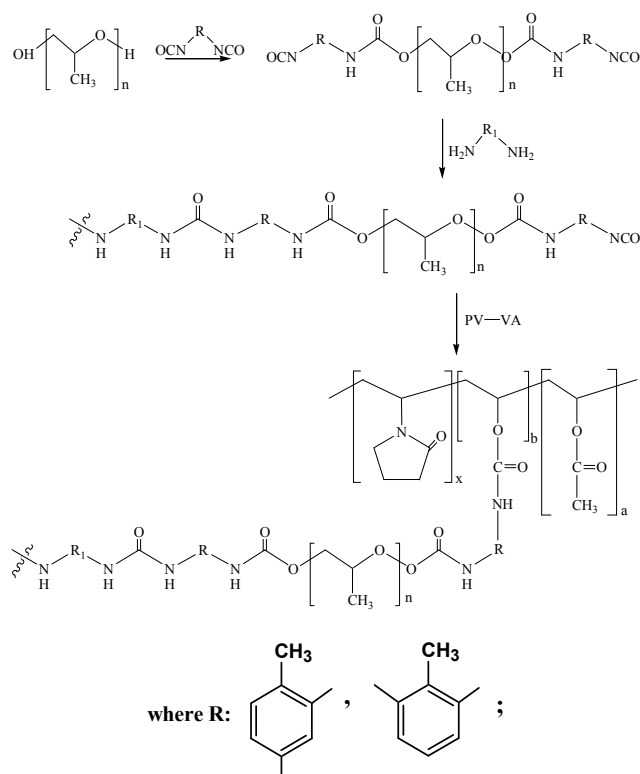
m_0 – masse of dry sample, g.

2.2.4. Thermophysical Test

Thermophysical properties (glass-transition temperature - T_g), changes in heating capacity at the glass-transition temperature (ΔC_p) have been studied by the DSC method. The study was carried out within the interval of temperature from -90 to +200°C (TA Instrument Q 2000) with the rate of heating 20 °C/min. Two heating procedures were carried out to exclude the influence of the thermal and mechanical prehistory of the material.

2.3. Preparation of PUU

Hydrophilic polyurethaneurea with fragments of the copolymer of VP-VA in the structure has been prepared in four stages by the technique described in [13]. To prepare the PUU with a different ratio of the macrochain extender to the copolymer of VP-VA, the reaction between DPP and HMDA (as well as between DPP and DADPh) has been brought to achieving a different content of free NCO groups (30, 40, 50, 60, 70% of conversion). The reaction scheme of formation of PUU containing VP-VA copolymer fragments is shown in Figure 2.



R_1 : $-(CH_2)_6-$ for PUU, wherein HMDA is a macrochain extender

for PUU, wherein DADPh is a macrochain extender

Figure 2. The reaction scheme of formation of PUU containing the VP-VA copolymer fragments.

3. Results and Discussion

3.1. Mechanical Tests

To choose the polymer material with optimal physical-mechanical properties, the series of PUU with a different ratio of HMDA:VP-VA (30:70; 40:60; 50:50; 60:40; 70:30) and DADPh:VP-VA (40:60; 50:50; 60:40; 70:30) have been prepared.

The results of physical-mechanical tests showed that the tensile strength and relative elongation at break of the prepared PUU depended on the composition and the ratio of components during the synthesis.

For polymer materials synthesized with the HMDA macrochain extender, PUU not containing VP-VA copolymer possessed the highest values of physical-mechanical properties ($\sigma = 6.6$ MPa, $\varepsilon = 544\%$) (Table 1).

Table 1. Properties of the PUU with the HMDA macrochain extender.

Samples of PUU	HMDA/VP-VA,%	σ , MPa	ε ,%
DPP+HMDA+VP-VA	30:70	0.8	21
	40:60	1.9	38
	50:50	1.6	27
	60:40	2.0	37
	70:30	2.8	46
DPP+HMDA	—	6.6	544

The insertion of the VP-VA copolymer to the PUU structure, variation of its content and the use of two different diamines during the PUU synthesis caused the changes in physical-mechanical properties of resulting material. According to Table 1, the decrease in the quantity of the VP-VA copolymer in the structure of PUU resulted in the increase of tensile strength and relative elongation at break. The highest values of physical-mechanical properties among the PUU containing the fragments of VP-VA copolymer in the structure are possessed by samples of polymer materials containing the ratio of HMDA:VP-VA = 70:30 ($\sigma = 2.8$ MPa, $\varepsilon = 46\%$).

Like in the previous case, the presence of the DADPh macrochain extender leads to the increase in physical-mechanical properties when the quantity of the copolymer decreased. The highest values of the tensile strength and relative elongation at break for the PUU with VP-VA copolymer fragments in the structure are possessed by polymer materials containing the ratio of DADPh:VP-VA = 70:30 ($\sigma = 4.3$ MPa, $\varepsilon = 91\%$) (Table 2).

Table 2. Properties of the PUU with the DADPh macrochain extender.

Samples of PUU	DADPh /VP-VA,%	σ , MPa	ε ,%
DPP+ DADPh+VP-VA	40:60	2.3	30
	50:50	3.2	38
	60:40	3.8	105
	70:30	4.3	91
DPP+DADPh	—	11.2	208

The PUU containing DADPh macrochain extender (Table 2) was characterized by higher values of the tensile and relative elongation at break in comparison with PUU containing the HMDA macrochain extender (Table 1).

Thus, the results of physical-mechanical tests allowed us to determine the optimal ratio of components during the synthesis and the influence of diamine chemical structure on the properties of the PUU with VP-VA copolymer fragments intended for further use as a polymer matrix upon medical biomaterials production.

3.2. Absorption Test

The studies of PUU water absorption demonstrated the increased hydrophilicity of resulting materials compared to original PUU. Samples of PUU containing no VP-VA

copolymer possessed the lowest values of water absorption – 3.0% for PUU synthesized with HMDA and 3.2% for PUU with DADPh (Table 3). The insertion of VP-VA copolymer into the PUU structure and the increase of the VP-VA copolymer concentration resulted in the increase of water absorption. The PUU water absorption values were 35.9% for HMDA:VP-VA 40:60 composition and 64.9% for DADPh:VP-VA 40:60 composition. Increased hydrophilicity will contribute to a prolonged release of biologically active substances from the polymer matrix.

Table 3. Water absorption of PUU synthesized with a different ratio of components.

PUU	HMDA/VP-VA,%	Water absorption,%	PUU	DADPh /VP-VA,%	Water absorption,%
DPP+HMDA	–	3.0	DPP+ DADPh	–	3.2
	70:30	21.0		70:30	19.4
	60:40	27.6		60:40	29.7
DPP+HMDA+VP-VA	50:50	34.5	DPP+ DADPh +VP-VA	50:50	48.3
	40:60	35.9		40:60	64.9
	30:70	44.4		–	–

The data presented (Table 1, Table 2) allow suggesting that PUU with VP-VA copolymer fragments in the structure synthesized with the ratio of HMDA and DADPh to VP-VA 70:30 possesses sufficient physical-mechanical properties ($\sigma = 3.1$ MPa, $\varepsilon = 47\%$ and $\sigma = 5.2$ MPa, $\varepsilon = 90\%$, accordingly) and hydrophilicity (21.0% and 19.4%, accordingly) to be used as polymer matrix for medicine biologically active composite materials with prolonged release of biologically active substances.

3.3. Atr FT-IR

The structure of synthesized PUU and urethane-formation reaction have been studied by the method of infra-red spectroscopy. The changes within the band of infra-red spectra 3000–3700 cm^{-1} and 1500–1800 cm^{-1} (Figure 3) demonstrate the process of urethane formation reaction between NCO groups of DPP and OH groups of the VP-VA copolymer.

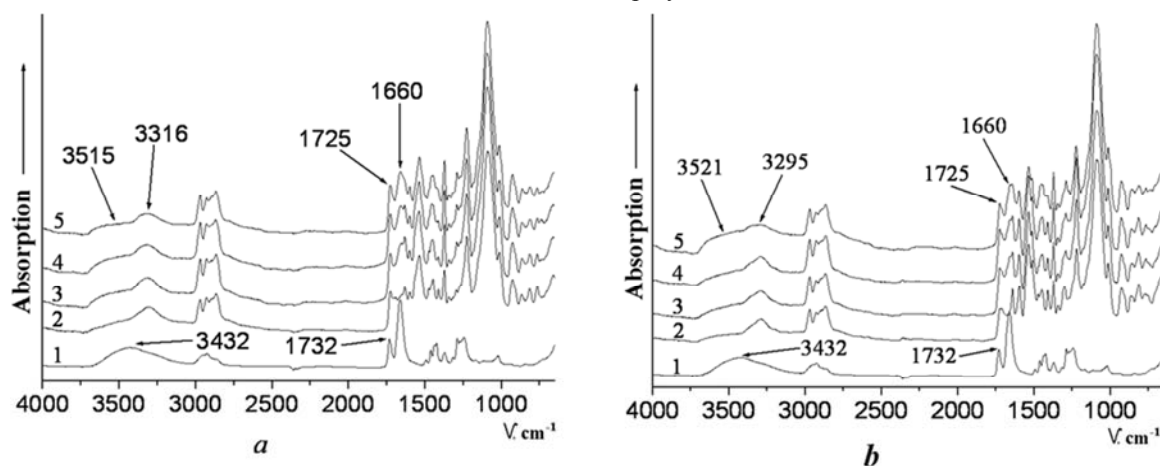


Figure 3. Infra-red spectra of the VP-VA copolymer (1a, 2b) and PUU synthesized with a different ratio of HMDA:VP-VA (a) DADPh:VP-VA (b): DPP+HMDA (2 a), DPP+ DADPh (2 b); PUU (70:30) with HMDA (3 a), with DADPh (3 b); PUU (60:40) with HMDA (4 a), with DADPh (4 b); PUU (40:60) with HMDA (5 a), with DADPh (5 b).

The absorption band ν_{OH} 3432 cm^{-1} of the VP-VA copolymer of (Fig. 3a, curve 1) is absent on the infra-red spectra of PUU synthesized with the HMDA macrochain extender within the frequency interval of the NH groups valence vibrations 3000–3700 cm^{-1} . This fact demonstrates the interaction of the OH groups of the copolymer with NCO groups of DPP with the appearance of absorption band $\nu_{\text{NH-bond}}$ – 3316 cm^{-1} and $\nu_{\text{NH-free}}$ with approximate maximum 3515 cm^{-1} (Fig. 3a, curves 3-5). The appearance of absorption band

$\nu_{\text{C=O}}$ of vinylpyrrolidone ring 1660 cm^{-1} on the spectra of PUU containing VP-VA copolymer fragments is observed within the band of spectra 1500–1800 cm^{-1} (Fig. 3a, curve 3–5).

Comparing the infra-red spectra of PUU synthesized with different ratios of components demonstrated that the presence of the VP-VA copolymer in the structure of PUU and the increase of its content results in a redistribution of the absorption band intensities of free

and bound NH groups (a minor reduction in intensity of the absorption band $\nu_{\text{NH-bond}} - 3316 \text{ cm}^{-1}$, as well as the increase in the intensity of the absorption band $\nu_{\text{NH-free}} 3515 \text{ cm}^{-1}$).

The increase in the intensity of the absorption band $\nu_{\text{C=O}} 1725 \text{ cm}^{-1}$ COO groups (Fig. 3a, curves 3–5) within the band of spectra $1500\text{--}1800 \text{ cm}^{-1}$ was observed along with the increase in the content of the copolymer in the structure of the studied polymer materials. This is due to summarization of both absorption bands: $\nu_{\text{C=O}}$ of the copolymer (Fig. 3a, curve 1) and $\nu_{\text{C=O}}$ of the polymer matrix, as well as the increase in intensity of the absorption band $\nu_{\text{C=O}}$ of vinylpyrrolidone ring 1660 cm^{-1} . In addition, the absorption band $\nu_{\text{C=O}} 1732 \text{ cm}^{-1}$ of the VP-VA copolymer shifted towards smaller frequencies (1725 cm^{-1}) demonstrating the appearance of C=O groups more bound by hydrogen bonds.

On the infra-red spectra of PUU synthesized with the DADPh macrochain extender (Fig. 3b) the changes are identical to the spectra of PUU synthesized with the HMDA macrochain extender. The infra-red spectra of PUU demonstrate the absence of the absorption band $\nu_{\text{OH}} 3432 \text{ cm}^{-1}$ of the VP-VA copolymer, appearance of the absorption band $\nu_{\text{NH-bond}} - 3295 \text{ cm}^{-1}$ and $\nu_{\text{NH-free}}$ with approximate maximum 3521 cm^{-1} and of the absorption band $\nu_{\text{C=O}}$ of vinylpyrrolidone ring 1660 cm^{-1} (Fig. 3b, curves 3–5). The redistribution of the absorption bands of free and bound NH groups (a minor reduction in intensity of the absorption band $\nu_{\text{NH-bond}} - 3295 \text{ cm}^{-1}$ and the increase in intensity of the absorption band $\nu_{\text{NH-free}} 3521 \text{ cm}^{-1}$), the increase in intensity of the absorption band $\nu_{\text{C=O}} 1725 \text{ cm}^{-1}$ of COO groups and the absorption band $\nu_{\text{C=O}}$ of vinylpyrrolidone ring 1660 cm^{-1} , as well as the shift of the absorption band $\nu_{\text{C=O}} 1732 \text{ cm}^{-1}$ of the copolymer of VP-VA towards smaller frequencies (1725 cm^{-1}) occurred due to appearance of the VP-VA copolymer in the PUU structure and with the increase of its content (Fig. 3b, curves 3–5).

3.4. Thermophysical Test

As far as the change in the composition of polymer material results in the changes in thermophysical properties of materials, the samples of polymer materials containing different ratio of macrochain extender and copolymer have been compared for their heating capacity.

The temperature dependences of the heating capacity of various PUU structures appeared to be quite similar, therefore, only curves of the PUU heating capacity of (50:50) synthesized using different macrochain extenders are shown in Figure 4. One glass transition and, accordingly, one glass-transition temperature (T_g) have been found on the thermograms of all PUUs under study indicating the single-phase systems.

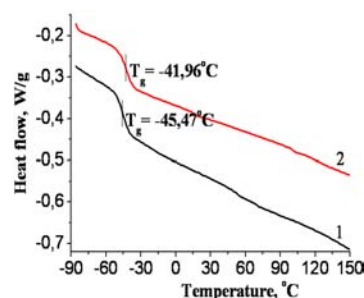


Figure 4. The typical thermograms of PUU: HMDA macrochain extender (1); DADPh macrochain extender (2) (2nd heating procedure).

The increased values of glass-transition temperature and the change of the specific heat capacity (ΔC_p) during the first and second heating procedures (Table 4) were observed in the series of PUU with increasing concentrations of VP-VA copolymer fragments synthesized with the HMDA macrochain extender. Obtained results correlate with the physical-mechanical properties described above where insertion of the increased concentrations of VP-VA copolymer to the PUU structure resulted in the decrease of the tensile strength and relative elongation at break (Table 2).

Table 4. Thermophysical properties of the PUU with the HMDA macrochain extender.

Samples of PUU	HMDA/VP-VA,%	$T_g, ^\circ\text{C}$		$\Delta C_p, \text{J/(g}^\circ\text{C)}$	
		1st heating procedure	2nd heating procedure	1st heating procedure	2nd heating procedure
DPP+HMDA+VP-VA	40:60	-42.56	-44.22	0.3427	0.3353
	50:50	-45.49	-45.47	0.3175	0.2985
	60:40	-46.0	-47.39	0.2871	0.2864
	70:30	-46.13	-47.36	0.3291	0.3172
DPP+HMDA	—	-49.84	-49.57	0.3143	0.2824

The decrease in glass-transition temperature and increased change of the specific heat capacity during the glass transition were also observed in the series of PUU with VP-VA copolymer fragments synthesized with the DADPh macrochain extender upon increased copolymer concentrations (Table 5).

Table 5. Thermophysical properties of the PUU with the DADPh macrochain extender.

Samples of PUU	DADPh /VP-VA,%	$T_g, ^\circ\text{C}$		$\Delta C_p, \text{J/(g}^\circ\text{C)}$	
		1st heating procedure	2nd heating procedure	1st heating procedure	2nd heating procedure
DPP+ DADPh +VP-VA	40:60	-40.32	-42.22	0.2534	0.2876
	50:50	-41.8	-41.96	0.2762	0.2804
	60:40	-25.63	-33.78	0.3156	0.2860
	70:30	-25.82	-33.8	0.3023	0.2695
DPP+ DADPh	—	-39.41	-40.53	0.2933	0.2593

However, the chemical structure of diamine influenced the thermophysical properties of studied polymer materials, in addition to the ratio of components during the synthesis. T_g of the 2nd heating procedure was within the band from -47.39 to -44.22°C for the PUU with the VP-VA copolymer fragments and HMDA macrochain extender and was from -42.22 to -33.78 °C for PUU with the DADPh macrochain extender. Thus, the glass-transition temperature and the value of specific heat capacity change of the PUU synthesized with the DADPh macrochain extender were higher compared to PUU synthesized with the HMDA macrochain extender. A higher T_g may be explained by a lower molecular mobility of macrochain conditioned by the presence of a hard block of DADPh in the structure of the PUU with the VP-VA copolymer fragments.

4. Conclusions

The series of PUU containing in its structure the VP-VA copolymer fragments with either the HMDA or DADPh macrochain extender and a different ratio of components have been synthesized. The urethane-formation reaction between the VP-VA copolymer and polymer matrix was confirmed by infra-red spectroscopy. The influence of diamine chemical nature on the properties of PUU has been demonstrated. According to the results obtained, PUU containing in its structure the DADPh macrochain extender is characterized by higher values of the tensile strength and relative elongation at break, glass-transition temperature and the change of the specific heat capacity and hydrophilicity compared to PUU containing in its structure the HMDA macrochain extender. The data presented allow suggesting that PUU with VP-VA copolymer fragments in the structure synthesized with the ratio of HMDA and DADPh to VP-VA 70:30 possesses sufficient physical-mechanical properties ($\sigma = 3.1$ MPa, $\epsilon = 47\%$ and $\sigma = 5.2$ MPa, $\epsilon = 90\%$, accordingly) and hydrophilicity (21.0% and 19.4%, accordingly) to be used as polymer matrix for medicine biologically active composite materials with prolonged release of biologically active substances.

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