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Characteristics of Thermoresponsive Biohydrogels †

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Abstract: The aim of this work was the synthesis of functional hydrogel materials obtained by photopolymerization. The resulting systems were characterized in terms of chemical structure using Fourier transform infrared spectroscopy. Subsequently, their sorption capacity and surface morphology were determined along with roughness analysis. The resulting materials have been modified with fluorescein dye and can be used in many branches of industry and medicine for example in innovative diagnostic systems.

Keywords: biohydrogels; hydrogels; thermoreversible materials

1. Introduction

The properties of hydrogel, like any material, depend on the stimuli acting on it. Also called superabsorbents, due to their high reversible absorption capacity of water, these materials do not react in contact with it [1,2]. Hydrogel can be formed from a variety of substances, such as poly(ethylene glycol), poly(N-vinylpyrrolidone), poly(vinyl alcohol), methacrylic acid, acrylic acid, poly(aspartic acid), maleic anhydride or polysaccharides. From what substances the material is made of, its resistance to external factors depends [3].

Oral drug in the form of hydrogel is one of the most popular ways of delivering the drug. In the digestive tract there are various environments, both acidic and alkaline. Due to the ability of free swelling in an acidic medium such as gastric juice, it is possible to release drugs, e.g. for the treatment of gastric ulcers. These are hydrogels based, among others, on N-vinylpyrrolidone, aryl acid, chitosan or polyethylene glycol diacetate. With the increase in pH, the swelling rate increases, greatly increases above pH = 7. The intestines have an alkaline environment, where the process occurs faster[4,5].

Temperature is also a factor that can affect the swelling coefficient. The higher the ambient temperature, the slower the hydrogel material swells [6]. At low temperatures, some hydrogels are liquid, the structure of the hydrogel is preserved at the temperature of the human body. Some hydrogels are cross-linked by freezing. The high incubation temperature reduces the swelling rate of the material [7,8].

Moreover, hydrogels are being tested for use as artificial muscles. This application is made possible by shrinking and stretching at a difference in the concentration of hydrogen ions in the liquid surrounding the material [9,10]. Next, based on many studies, it has been proven that the ions contained in the surrounding liquid have a major influence on the sorption capacity of hydrogel and the density of the polymer network. Studies show a high absorption capacity of distilled water, which does not contain added elements, while the smallest capacity is found in SBF liquid (simulated body fluid) where elements

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such as Na^+, K^+, Mg^{2+}, Ca^{2+}, Cl^-, HCO_3^-, HPO_4^{2-} or SO_4^{2-} are present [11,12]. Lightplays an important role because some polymers are cross-linked under UV conditions. This makes it possible to restore bonds in degraded materials, e.g. oxidation and reduction of disulfide bridges [13]. In some cases, hydrogels are used as contrast agents in magnetic resonance imaging (MRI). These special hydrogels can contain molecules that react with the magnetic field in a way that allows for a better image of a particular area of the patient's body. In electron microscopy, hydrogels are used as settling tanks to prepare biological samples for imaging. They help maintain the structure of the sample and protect it from evaporation in a vacuum.

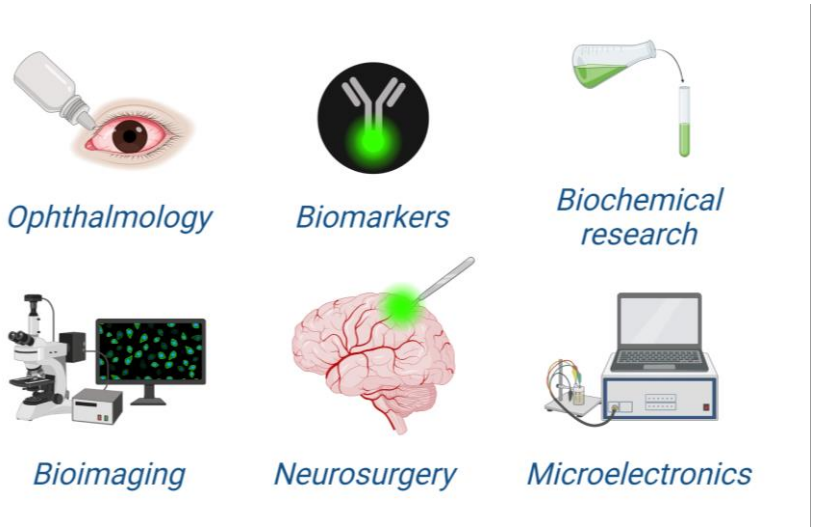


Figure 1. Uses of multisensitive hydrogel polymer systems.

Hydrogels are environmentally sensitive materials, but their application is very wide. They are used in many sectors of industry, and sensitivity to the external environment is often an advantage when used, e.g. artificial muscles or medicines. In the present work hydrogel systems exhibiting sorption capabilities in simulated body fluids were obtained. The aim of the study was to determine the influence of the amount of cross-linking agent on the properties of polymer systems.

2. Materials and Methods

2.1. Materials

The main reagents such as poly(vinyl alcohol) (PVA, crystalline powder, 87–89% hydrolyzed, Mw 13,000–23,000), poly(ethylene glycol) (PEG, powder, average mol wt. 6,000), diacrylate poly(ethylene glycol) (crosslinking agent, PEGDA, average molecular weight Mn = 700 g/mol) and 2-hydroxy-2- methylpropiophenone (photoinitiator, 97%, d = 1.077 g/mL); fluorescein (for fluorescence, free acid) were purchased from Sigma Aldrich (Saint Louis, MO, USA). All purchased reagents had purity grade: clean for analysis.

2.2. Synthesis of hydrogel materials

Hydrogel materials were obtained by photopolymerization. Appropriate amounts of the polymeric components PVA and PVP were first mixed. Fluorescein and a variable amount of cross-linking agent were then added. After thorough mixing, a photoinitiator was added to the reaction mixture and the whole was placed in polymerization form. The process was carried out at room temperature using EMITA VP-60 lamina with a power of 180 W and a wavelength of λ=320. The polymerization time for each material was 5 minutes. The composition of the hydrogel samples is presented in Table 1.

Table 1. Composition of the hydrogel materials.

10 % PEG, mL	10 % PVA, mL	Photoinitiator, mL	Fluorescein, mL	PEGDA, mL
5	5	0,05	1	2.0
				2.5
				3.0
				3.5
				4.0

2.3. FT-IR infrared spectroscopy analysis

The infrared spectroscopy analysis was performed using the Thermo Scientific Nicolet iS5 spectrophotometer equipped with an ATR attachment. Spectra were recorded in the range 3600-500 cm^{-1} (32 scans, resolution 4.0 cm^{-1}). The measurement was carried out at room temperature.

2.4. Analysis of soprtion capacity

The sorption capacity of the polymeric materials was carried out by determining the swelling coefficient. For each material, a sample of 1 cm in diameter was prepared and carefully weighed. The samples were then placed in distilled water, Ringer liquid and PBS phosphate buffer (each in 50 mL of the corresponding liquid). After 24 h and 48 h, the sample was weighed again and the swelling coefficient was determined according to the following formula (Equation 1).

$$\alpha = (m_t - m_0)/m_0 \quad (1)$$

where:
α—swelling ratio, g/g;
m_t—mass of swollen sample after time "t", g;
m_0—mass of dry sample (before the study), g.

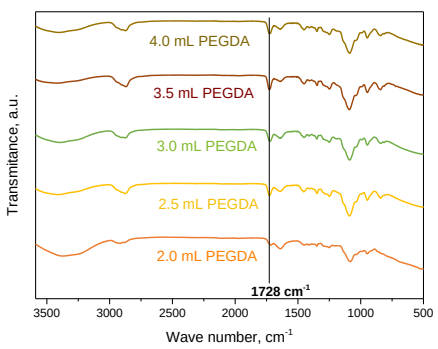
2.5. Microscopic observations and roughness profile

Then the surface morphology of the obtained materials and basic roughness parameters were determined using advanced VKX-7000 Keyence digital microscope. Observations were conducted for all received materials at room temperature.

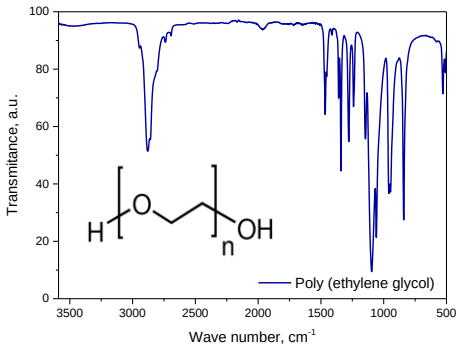
3. Result and discussion

3.1. FT-IR infrared spectroscopy analysis

Spectroscopic analysis was performed to determine the chemical structure of the resulting hydrogels. Spectroscopic spectra are presented in Figure 2.



a



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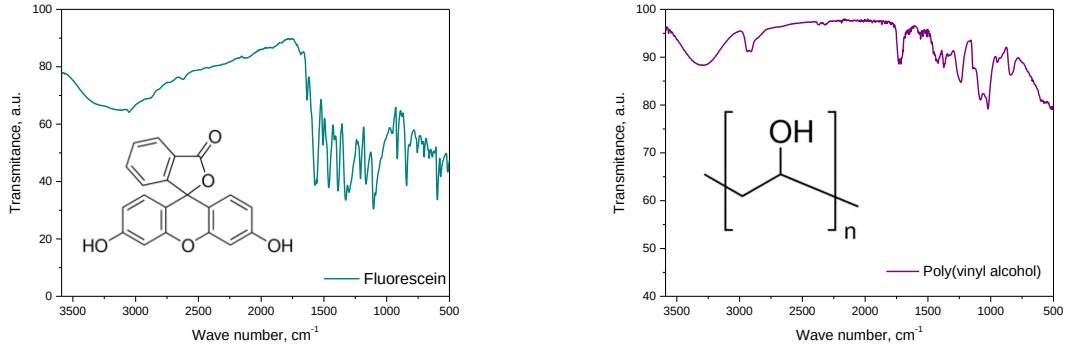


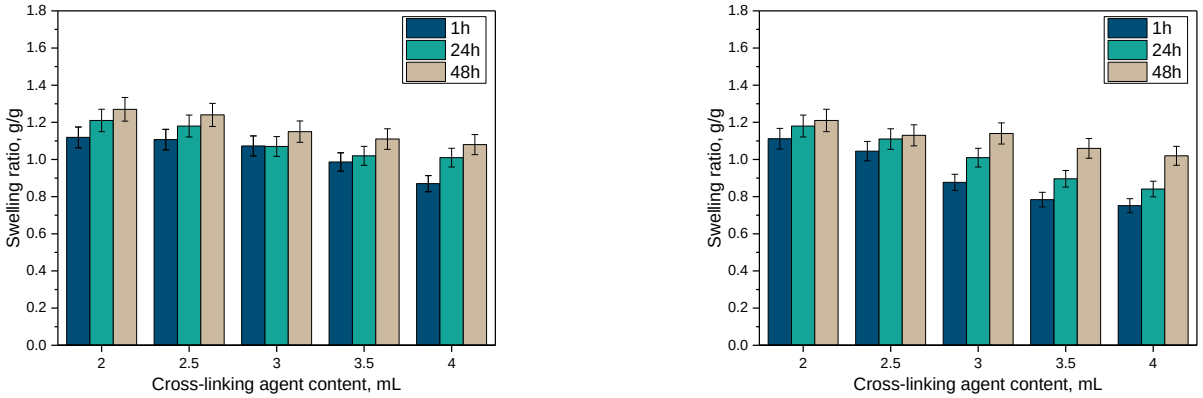
c d

Figure 2. FT-IR spectra of hydrogel materials (**a**), poli(ethylene glycol) (**b**), fluorescein (**c**) and poly(vinyl alcohol) (**d**).

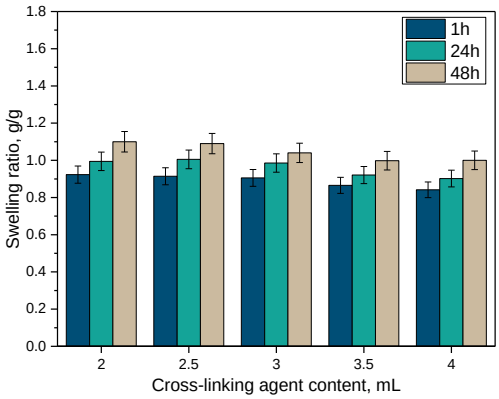
On the basis of the performed spectroscopic analysis, absorption bands characteristic of functional groups of polymer components and fluorescein were identified. No large differences were noted for samples obtained with different cross-linking agent content. However, particular attention should be paid to the absorption band at a wavelength of about 1728 cm^{-1}, which is derived from the tensile vibrations of the C=O group also present in the crosslinking agent. With the increase in PEGDA, we observe an immeasurable increase in the intensity of this band. The results obtained are consistent with the results presented by other researchers [14,15]

3.2. Analysis of sorption capacity

The results of the sorption capacity analysis in the form of swelling coefficients are presented in Figure 3.



a) b)



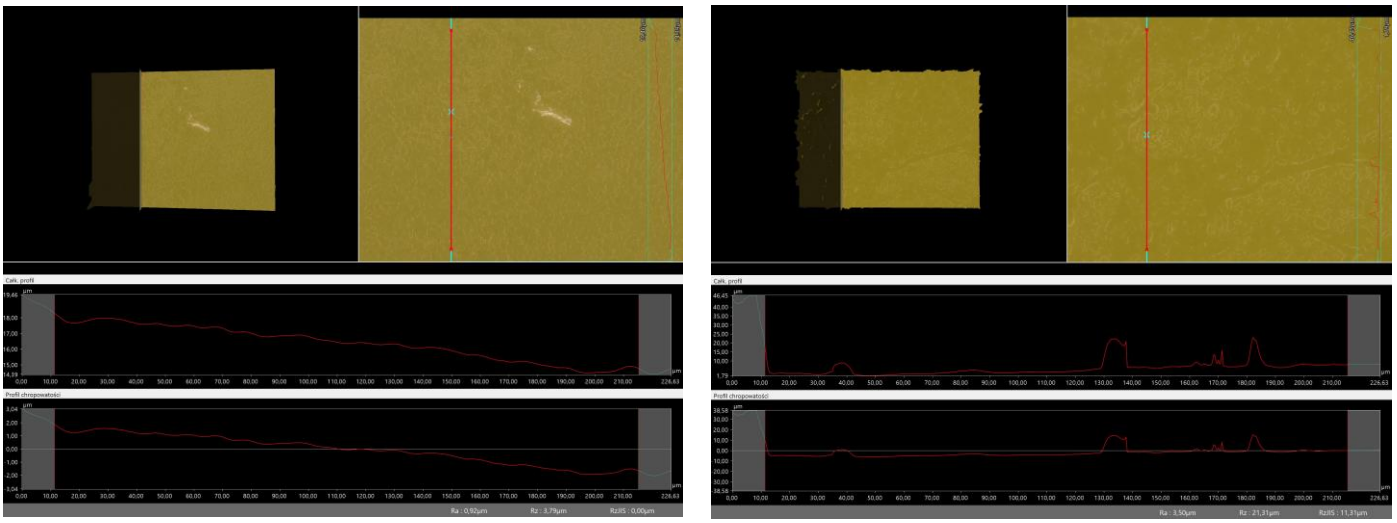
c)

Figure 3. Results of sorption capacity analysis in distilled water (**a**), Ringer solution (**b**) and PBS buffer (**c**); (n – number of repetitions, n = 3).

All materials analysed showed sorption properties. As the amount of cross-linking agent increased, decreasing values of the swelling factor were observed. The amount of cross-linking agent is one of the key parameters influencing the cross-linking process of hydrogel materials and their structure. With the amount of crosslinker, the crosslinking density of the material increases and the amount of free space for the penetrating fluid decreases. The type of incubation medium is also important. The highest values of swelling coefficients were recorded for distilled water. In the case of Ringer fluid and PBS, these factors are much lower. The presence of additional ions in these fluids may influence the formation of additional bonds and interactions, which increases the polymer density of the matrix and limits its sorption capacity. This is not the case for distilled water without additional ions.

3.3. Microscopic observations and roughness profile

Subsequently, in Figure 4 and Table 2, the results of microscopic observations and roughness parameters of the obtained hydrogel materials are presented.



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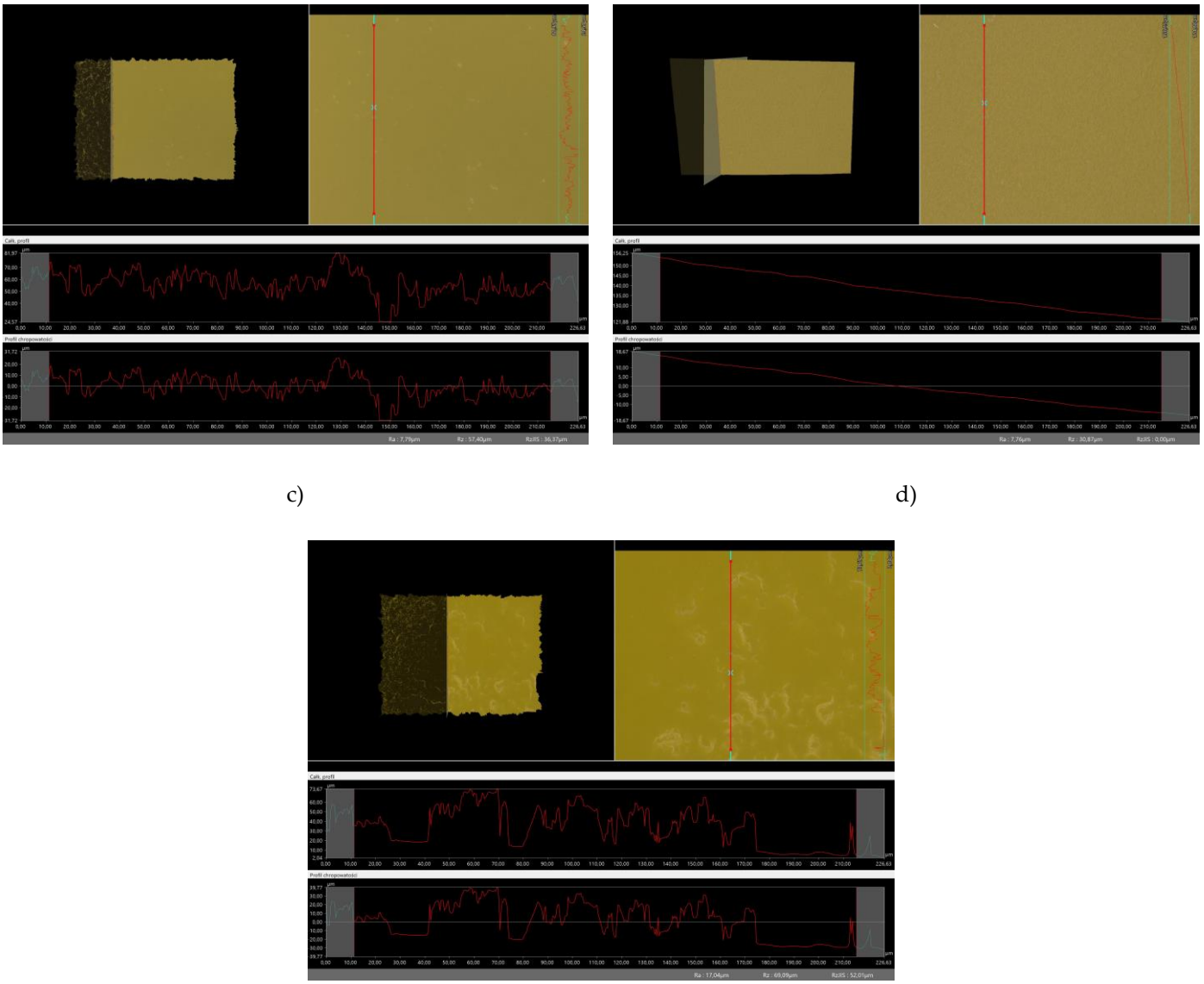

c) d)

e)

Figure 4. Digital microscope images and roughness profile of hydrogel materials with different amount of crosslinking agent: 2.0 mL (**a**); 2.5 mL (**b**); 3.0 mL (**c**); 3.5 mL (**d**); 4.0 mL (**e**).

Table 2. Parameters of roughness of hydrogel materials

Roughness parameter* [um]	2.0 mL PEGDA	2.5 mL PEGDA	3.0 mL PEGDA	3.5 mL PEGDA	4.0 mL PEGDA
Ra	0,92	3,50	7,79	7,76	17,04
Rz	3,79	21,31	57,4	30,87	69,09
Rq	1,09	4,51	10,14	8,96	19,85

*Roughness parameter: Ra - Average roughness, arithmetic mean deviation from the mean line; Rz- highest height of the roughness profile; Rq - mean square deviation of the profile on the elementary section.

Based on the analysis, it was confirmed that with an increase in the amount of cross-linking agent, the surface roughness of the obtained materials increases. The crosslinking agent is directly related to the crosslinking process of these materials and its

greater quantity changes their internal and surface structure. The effect of the amount of crosslinking agent on the physicochemical properties and surface roughness of the material is related to the crosslinking process. Increasing the amount of crosslinking agent leads to a material with a densely crosslinked structure, which also translates into a change in its surface properties such as an increase in roughness. The relationship between increasing amount of crosslinking agent and increasing roughness of these materials has been determined, which may translate into the possibility of synthesis of hydrogel with controlled and desired properties and morphology.

4. Conclusions

- The chosen photopolymerization method allows to obtain hydrogel materials modified with fluorescent dye
- As the amount of cross-linking agent increases, hydrogel materials exhibit reduced sorption properties as a result of increasing cross-linking density of the polymer matrix
- The amount of cross-linking agent also significantly affects the surface morphology and roughness of the resulting materials. With the increase in PEGDA, an increase in the value of the roughness parameters was noted.
- Determination of the correlation between the amount of crosslinking agent and the properties of hydrogel materials allows to obtain materials with desired properties due to their subsequent use.

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