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[1]al-Farabi Kazakh National University, Almaty, Kazakhstan;
[2]The National Engineering Academy of the Republic of Kazakhstan, Almaty, Kazakhstan.
E-mail: danelya.1993@gmail.com

CREATING BIODEGRADABLE DOSAGE FORMS BASED ON PENTAERYTHRITOL TETRAACRYLATE AND TETRAKIS(3-MERCAPTOPROPIONATE) PENTAERYTHRITOL

R. Shulen — Master of Engineering Science, junior researcher, al-Farabi Kazakh National University, Almaty, Kazakhstan
E-mail: shulen_ruslan@mail.ru, https://orcid.org/0000-0001-6822-3057;
D. Makhayeva — PhD, senior researcher, al-Farabi Kazakh National University, Almaty, Kazakhstan
E-mail: danelya.1993@gmail.com, https://orcid.org/0000-0003-1250-9587;
D. Kazybayeva — PhD, senior researcher, al-Farabi Kazakh National University, Almaty, Kazakhstan
E-mail: diara_92@mail.ru, https://orcid.org/0000-0001-6822-3057;
G. Irmulkametova — Candidate of Chemical Sciences, Associate Professor, al-Farabi Kazakh National University, Almaty, Kazakhstan
E-mail: galiya.irm@gmail.com, https://orcid.org/0000-0002-1264-7974;
G. Mun — Doctor of Chemical Sciences, Professor, al-Farabi Kazakh National University, academician of NEA RK, Almaty, Kazakhstan
E-mail: mungrig@yandex.ru, https://orcid.org/0000-0002-4984-7937.

Abstract. Of particular interest to scientists is creating ways to ensure continuous delivery of necessary components for treating specific diseases. Some diseases require a consistent supply of essential elements for treatment. Often, conventional forms of medication, such as tablets or capsules, might not get adequately absorbed by the body and end up being eliminated without much effect. To address this, the use of polymer-based dosage forms that degrade in the body, releasing medicinal substances gradually, extends their impact. Employing polymer carriers offers the advantage of targeting precise areas within the body, enhancing the efficient utilisation of the drug substance. Pentaerythritol tetra acrylate and pentaerythritol tetrakis (3-mercapto propionate) (PETA-PEMP) based gels form through thiol-ene click polymerisation mechanisms. The functional groups present in these gels enable the development of materials that can degrade within diverse biological and physiological settings alongside improved mucoadhesive characteristics. These attributes promise future applications in targeted delivery systems for various medical substances. This study marks the initial creation of cross-linked polymer gels using varying compositions of PETA and PEMP. The major physicochemical properties of gels were determined

through sol-gel analysis, IR and Raman spectroscopy, and optical and scanning electron microscopy. Results revealed that gels containing an excess of PETA initially showcased a porous structure, while higher proportions of PEMP monomers led to developing a denser network structure. The degradation behaviour of these gels in different environments was also investigated. Specifically, gels placed in enzyme solutions exhibited immediate degradation, whereas degradation in hydrogen peroxide solutions underwent a swelling stage before breaking down.

Keywords: biodegradable polymers, drug delivery systems, gels, thiol-ene polymerisation, biodegradation

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[1] әл-Фараби атындағы Қазақ ұлттық университеті, Алматы, Қазақстан;
[2] The National Engineering Academy of the Republic of Kazakhstan, Almaty, Kazakhstan.
E-mail: danelya.1993@gmail.com

ТЕТРААКРИЛАТ ПЕНТАЭРИТРИТОЛ ЖӘНЕ ТЕТРАКИС(3-МЕРКАПТОПРОПИОНАТ) ПЕНТАЭРИТРИТОЛНЕГІЗІНДЕ БИОДЕГРАДАЦИЯЛАНАТЫН ДӘРІЛІК ФОРМАЛАРДЫ АЛУ

Шулен Р. — техника ғылымдарының магистрі, кіші ғылыми қызметкер, әл-Фараби атындағы Қазақ ұлттық университеті, Алматы, Қазақстан
E-mail: shulen_ruslan@mail.ru, https://orcid.org/0000-0001-6822-3057;
Махаева Д.Н. — PhD, аға ғылыми қызметкер, әл-Фараби атындағы Қазақ ұлттық университеті, Алматы, Қазақстан
E-mail: danelya.1993@gmail.com, https://orcid.org/0000-0003-1250-9587;
Казыбаева Д.С. — PhD, аға ғылыми қызметкер, әл-Фараби атындағы Қазақ ұлттық университеті, Алматы, Қазақстан
E-mail: diara_92@mail.ru, https://orcid.org/0000-0001-6822-3057;
Ирмухаметова Г.С. — х. ғ. к., қауымдастырылған профессор, әл-Фараби атындағы Қазақ ұлттық университеті, Алматы, Қазақстан
E-mail: galiya.irm@gmail.com, https://orcid.org/0000-0002-1264-7974;
Мун Г.А. **—** х. ғ. д., профессор, Қазақ ұлттық университеті.әл-Фараби, ҚР ҰИА академигі, Алматы, Қазақстан
E-mail: mungrig@yandex.ru, https://orcid.org/0000-0002-4984-7937.

Аннотация. Белгілі бір ауруларды емдеуге қажетті компоненттерді үздіксіз жеткізуді қамтамасыз ету жолдарын құру зерттеушілерді ерекше қызықтырады. Кейбір аурулар емдеу үшін қажетті элементтердің тұрақты

жеткізілуін талап етеді. Көбінесе таблеткалар немесе капсулалар сияқты дәстүрлі дәрі-дәрмектер денеге дұрыс сіңбейді және көп әсер етпестен жойылады. Ағзада ыдырауы мүмкін, дәрілік заттарды шығаратын полимерлі дәрілік формаларды қолдану олардың ағзаға ұзақ әсер етуіне ықпал етеді. Полимерлі тасымалдаушыларды қолданудың артықшылығы дәрілік субстанцияны тиімді пайдалануды жеңілдететін дененің белгілі бір аймақтарына бағытталған. Пентаэритритол тетраакрилат (ПЭТА) және пентаэритритол тетракис (3-меркаптопропионат) (ПЭМП) мономерлеріне негізделген гельдердің түзілуі тиолды-басу (тиолен-клик) полимерлеу механизмдеріне негізделген. ПЭТА-ПЭМП негізіндегі гельдерде функционалдық топтардың болуына байланысты әртүрлі биологиялық және физиологиялық ортада ыдырай алатын жақсартылған шырышты жабысқақ қасиеттері бар материалдарды алуға болады. Бұл қасиеттер кейінірек медицинада кеңінен қолданылатын әртүрлі заттардың мақсатты жеткізу жүйелерінде қолданылуы мүмкін. Бұл зерттеуде әртүрлі ПЭТА-ПЭМП негізіндегі композицияларды қолдану арқылы айқаспалы полимерлі гельдер дайындалды. Гельдердің негізгі физика-химиялық қасиеттері золь-гельді талдау, ИҚ және РАМАН спектроскопиясы, сонымен қатар оптикалық және сканерлеуші электронды микроскопия арқылы анықталды. Нәтижелер құрамында артық ПЭТА бар гельдердің кеуекті құрылымы бар екенін көрсетті, ал ПЭМП құрамының жоғарылауы тығыз торлы құрылымның дамуына әкеледі. Бұл гельдердің әртүрлі орталарда ыдырауы да зерттелді. Атап айтқанда, фермент ерітінділеріне салынған гельдер бірден ыдырауды көрсетті, ал сутегі асқын тотығы ерітінділеріндегі ыдырау одан алдын ісіну сатысынан өтті.

Түйін сөздер: биологиялық ыдырайтын полимерлер, дәрілік заттарды жеткізу жүйелері, тиол-эн полимерленуі, биодеградация

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[1]Казахский национальный университет им. аль-Фараби, Алматы, Казахстан;
[2]Национальная инженерная академия наук РК, Алматы, Казахстан.
E-mail: danelya.1993@gmail.com

ПОЛУЧЕНИЕ БИОДЕГРАДИРУЕМЫХ ЛЕКАРСТВЕННЫХ ФОРМ НА ОСНОВЕ ТЕТРААКРИЛАТА ПЕНТАЭРИТРИТОЛА И ТЕТРАКИС(3-МЕРКАПТОПРОПИОНАТА) ПЕНТАЭРИТРИТОЛА

Шулен Р. — магистр технических наук, младший научный сотрудник, Казахский национальный университет им.аль-Фараби, Алматы, Казахстан
E-mail: shulen_ruslan@mail.ru, https://orcid.org/0000-0001-6822-3057;
Махаева Д.Н. — PhD, старший научный сотрудник, Казахский национальный университет им.аль-

Фараби, Алматы, Казахстан
E-mail: danelya.1993@gmail.com, https://orcid.org/0000-0003-1250-9587;
Казыбаева Д.С. — PhD, старший научный сотрудник, Казахский национальный университет им.аль-Фараби, Алматы, Казахстан
E-mail: diara_92@mail.ru, https://orcid.org/0000-0001-6822-3057;
Ирмухаметова Г.С. — к.х.н., ассоциированный профессор, Казахский национальный университет им.аль-Фараби, Алматы, Казахстан
E-mail galiya.irm@gmail.com, https://orcid.org/0000-0002-1264-7974;
Мун Г.А. — д.х.н., профессор, Казахский национальный университет им.аль-Фараби, академик НИА РК, Алматы, Казахстан
E-mail: mungrig@yandex.ru, https://orcid.org/0000-0002-4984-7937.

Аннотация. Особый интерес исследователей представляет создание способов обеспечения непрерывной доставки необходимых компонентов для лечения конкретных заболеваний. Некоторые заболевания требуют постоянного снабжения необходимыми элементами для лечения. Часто обычные формы лекарств, такие как таблетки или капсулы не усваиваются организмом должным образом и в итоге выводятся без особого эффекта. Применение полимерных лекарственных форм, способных деградировать в организме, высвобождая лекарственные вещества, способствует их пролонгированному действию на организм. Преимуществом использования полимерных носителей является нацеливание на конкретные участки организма, что способствует эффективному использованию лекарственного вещества. Образование гелей на основе мономеров пентаэритритол тетраакрилат (ПЭТА)и пентаэритритол тетракис (3-меркаптопропионат)(ПЭМП)основано на механизмах тиолен-клик полимеризации. Благодаря присутствию функциональных групп в гелях на основе ПЭТА-ПЭМП можно получать материалы с улучшенными мукоадгезивными свойствами, способные разлагаться в различных биологических и физиологических средах. Данные свойства в дальнейшем могут быть использованы в системах направленной доставки различных веществ, имеющих широкое распространение в медицине. В данном исследовании были получены сшитые полимерные гели с использованием различных композиций на основе ПЭТА-ПЭМП. Основные физико-химические свойства гелей определяли методами золь-гель анализа, ИК- и РАМАН спектроскопии, а также оптической и сканирующей электронной микроскопиями. Результаты показали, что гели, содержащие избыток ПЭТА, имеют пористую структуру, в то время как увеличение содержания ПЭМП приводит к развитию более плотной сетчатой структуры. Также была исследована деградация этих гелей в различных средах. В частности, гели, помещенные в растворы ферментов, демонстрировали немедленную деградацию, тогда как деградация в растворах перекиси водорода проходила через стадию набухания перед разрушением.

Ключевые слова: биодеградируемые полимеры, системы доставки лекарственных веществ, тиол-ен полимеризация, биодеградация

Introduction

Biodegradable materials are utilised in various industries, including packaging, agriculture, and medicine. These materials are categorised into two types: synthetic and natural biodegradable polymers. Synthetic polymers are made from petroleum-based raw materials, which are non-renewable. In contrast, natural polymers are derived from renewable biological resources. Generally, natural polymers are viewed as having fewer benefits

than synthetic polymers (Mukherjee et al., 2023: 112068).

Biodegradation is how enzymes or other living organisms break down materials. First of all, polymers undergo fragmentation via abiotic processes involving microbial breakdown. Subsequently, microorganisms assimilate these polymer fragments, leading to their mineralisation. The biodegradability of a polymer depends not only on its inherent nature but also on its chemical composition and environmental conditions. Various mechanisms and techniques exist to assess the biodegradation of polymers. Additionally, the mechanical properties of biodegradable materials are influenced by factors such as chemical composition, manufacturing methods, storage conditions, processing, ageing, and usage patterns (Samir et al., 2022: 7).

The authors (Zhang et al., 2021: 116) reviewed biodegradable polymers utilised in biomaterials. For a polymer to be effective as a biomaterial, it must exhibit three essential properties: biocompatibility, bioabsorbability, and mechanical strength. Natural polymers, such as proteins or polysaccharides, which degrade enzymatically, have been prevalent in biomedical applications for thousands of years. In contrast, synthetic biodegradable polymers have been used for about fifty years. These polymers are employed in various applications, including surgical implants for vascular or orthopedic procedures and simple membranes. Biodegradable polyesters are particularly notable for their durability and controlled degradation rates, making them extensively used as porous structures in tissue engineering, especially for constructing scaffolds. Additionally, biodegradable polymers serve as implantable matrices for controlled drug release within the body and as absorbable suture materials (Panchal et al., 2020: 4370).

Natural polymers typically degrade within biological systems through a process involving hydrolysis followed by oxidation. Therefore, when designing synthetic biodegradable materials, a primary focus is on incorporating hydrolysable linkages such as amide, ester, urea, and urethane groups. Enzymes that cleave peptides often target specific sites adjacent to these groups. Hydrophobic surfaces are less conducive to enzymatic reactions, primarily in aqueous environments. Interestingly, the fastest degradation occurs in polymers containing hydrophobic and hydrophilic segments (Kim et al., 2023: 9916).

Other considerations involve the accessibility of polymer chains to enzymes. Synthetic polymers with short repeat units and regular structures tend to pack tightly, making hydrolysable groups less accessible to enzymes. Experiments with partially crystalline materials show that amorphous regions decompose first, with decomposition rates influenced by the size, shape, and number of crystallites present. Although cross-linking reduces crystallinity, it does not improve degradation rates because the cross-links themselves restrict enzyme access. Conversely, polymers with long repeating chain stretches have a less regular structure and are more susceptible to degradation. Therefore, aliphatic chains are more prone to biodegradation than aromatic chains (Chereddy et al., 2016: 223).

The decomposition of polymers, whether in vitro or in vivo, is affected by numerous factors. These include the preparation method, the presence of low molecular weight compounds such as monomers, oligomers, or catalysts, and the polymer's size, shape, and morphology. Polymer physical and chemical properties influence the degradation process (Hermengildo et al., 2022: 111197). Studies indicate that polymers with lower molecular weight, greater hydrophilicity, and higher amorphousness degrade more rapidly. Similarly, copolymers with higher glycolide content show shorter degradation times.

Copolymers can experience either surface erosion or volumetric erosion, depend-

ing on the conditions, with volumetric erosion typically being the main degradation pathway. The biodegradation process of polymers involves the random cleavage of ester bonds within the polymer backbone, occurring uniformly across the entire material. A proposed three-phase mechanism outlines the degradation stages. Initially, there is a substantial decrease in the polymer's molecular weight without significant mass loss, which leads to the formation of soluble monomer products. These soluble monomers originate from soluble oligomeric fragments, marking the beginning of the degradation process. Ultimately, this sequence culminates in the complete breakdown and degradation of the polymer into simpler, potentially biocompatible components. (Mirjafari, 2018: 2945).

Over the past decade, thiol-ene click polymerisation has been extensively studied (Li et al., 2019: 485; Gregoritza et al., 2015: 439). This reaction offers several advantages: it occurs under mild conditions, yields high product quantities, and produces harmless by-products (Liu et al., 2017: 6182; Ki et al., 2014: 9668). Recently, thiol polymers have gained attention in biomedical applications, particularly as gels, due to their ability to tailor physical properties like biodegradability, drug release kinetics, swelling behaviour, and other crucial characteristics. (Machado et al., 2017: 201).

In thiol-ene click polymerisation, one of the reactants typically contains thiol groups, while the other contains multiple bonds (Štorha et al., 2013: 12275). The main objective of this work is to create biodegradable drug forms using PETA and PEMP through thiol-ene polymerisation and then assess their physicochemical properties and biodegradability. This method enables the rapid and straightforward production of new composite materials with enhanced properties. Due to the functional groups present in PETA-PEMP-based gels, it is possible to develop materials that decompose in various biological and physiological environments with improved mucoadhesive properties. These properties can be utilised in targeted delivery systems for various substances widely used in medicine.

Materials and methods

Materials

Pentaerythritol tetraacrylate, pentaerythritol tetrakis 3-mercaptopropionate (95 %), porcine liver esterase, N, N-Dimethylformamide (DMF) obtained from Sigma Aldrich (USA), acetone, Phosphate buffer (fixanal, pH 6.86), saults for phosphate buffer solution (NaCl, KCl, Na_2HPO_4 и KH_2PO_4) ReactiveKhimSnab (Russian Federation), hydrogen peroxide (3 % solution) from «DosFarm» (Republic of Kazakhstan). All reagents were of analytical grade and were used without additional purification.

Synthesis of PETA-PEMP gels in the presence of DMF solvent

Gels with varying compositions ([PETA-PEMP] ratios of 3:1, 2:1, 1:1, 1:2, and 1:3 wt.%) were synthesised in sealed glass vessels. PETA and PEMP monomers were mixed in a DMF solvent with constant magnetic stirring for the first hour. Depending on the composition, a cross-linked structure formed within 1–2 hours. The resulting gels were then washed in DMF for 1 hour, in acetone for 3 hours (with 3 changes of acetone), and in water for 24 hours (with about 10 water changes). The washed polymers were dried in a vacuum oven at room temperature.

Physicochemical research methods

The kinetics and extent of swelling were investigated using the gravimetric method. After measuring the mass of the washed and dried gel, each sample was immersed in a solution, and its mass was recorded using an analytical balance. Measurements were initially taken every 15 minutes and later every 30 minutes until the sample's mass stabilised.

This analysis used distilled water, isotonic solutions, and buffer solutions. The *degree of swelling* (α) of the gels was calculated using formula (1).

$$\alpha = m_x\text{-}m_0/m_0, \quad (1)$$

where m_x is the mass of the swollen gel at a certain point in time, g; m_0 is the initial mass of the gel, g.

The gels underwent sequential treatments for the sol-gel analysis: they were immersed in a DMF solution for 1 hour, followed by 3 hours in acetone, and then soaked in water for 24 hours. Subsequently, the washed gels were dried in a vacuum oven. The yield of the gel fraction (G %) was determined using formula (2).

$$G\% = m_{dryed.}*100\ \%/m_{synth.}, \quad (2)$$

where m_{dryed} – the mass of washed and dried gel, g; m_{synth}. – the mass of the synthesised and dried sample, g. The yield of the *sol fraction* (S%) was calculated using the formula (3):

$$S\ \% = 100\ \% - G\ \%, \quad (3)$$

where G % is the percentage of the gel fraction, %.

The physical and mechanical characteristics of the synthesised samples were analysed as follows:

The mass of the synthesised and washed dried gels was determined using Sartorius BP 121S analytical balances from Germany, which provide accuracy up to 0.0001 g. The samples were dried in a Binder VD 115 vacuum drying oven (Germany).

To confirm the chemical composition, IR spectroscopy was performed using a Vertex 70V Bruker IR Fourier spectrometer (USA), which covers wavelengths from 4000 to 500 cm^{-1}. Raman spectroscopy was conducted using a Solver Spectrum setup (Russia) on selected samples with a diameter of 0.5 mm.

Scanning electron microscopy (SEM) was employed with a Quanta 200i 3D system (USA) for structural analysis. Samples were freeze-dried before analysis.

Optical analysis of the gels was carried out using a Leica DM 6000M microscope from Sweden.

These methods were utilised to assess the synthesised samples' physical properties and determine mechanical behaviours using a TAXT Texture Analyzer device (UK) in a compression mode.

Study of the degradation ability of synthesised gels based on PETA-PEMP

The degradation ability of the synthesised 3:1 PETA-PEMP gels was investigated using three different environments: a buffer solution at pH 7.4, an enzyme solution, and hydrogen peroxide solutions. For hydrogen peroxide degradation studies, solutions of varying concentrations (0.1 %, 0.5 %, 1 %, 2 %, and 3 %) were employed. All experiments were conducted in sealed plastic beakers at a constant temperature of 37 ° C in a water bath, with intermittent stirring. The assessment of degradability properties involved multiple parallel experiments. The degree of degradation (DD) was evaluated using the gravimetric method until the sample mass stabilised and then calculated using for-mula (4).

$$DD = (m_0 - m_x)/m_0, \quad (4)$$

where m_x is the mass of the gel at a certain point in time, g; m_0 is the initial mass of the gel, g.

Results and discussion

Synthesis of gels based on PETA-PEMP

In this study, gels based on PETA-PEMP were synthesised using thiol-ene click polymerisation. Different ratios of components in the initial monomer mixture were used: 3:1, 2:1, 1:1, 1:2, and 1:3 weight per cent, in the presence of a DMF solvent (50 % solvent and 50 % monomers). Figure 1 illustrates the reaction scheme for forming a cross-linked PETA-PEMP structure. The interaction between monomers and the formation of covalent bonds occurs through functional groups, specifically the double bonds in PETA and the thiol groups in PEMP. When PETA is in the monomer mixture, gels with numerous double bonds are produced, whereas an excess of PEMP results in gels rich in thiol groups. The formation of these structures was confirmed through IR and Raman spectroscopy, the details of which are discussed later.

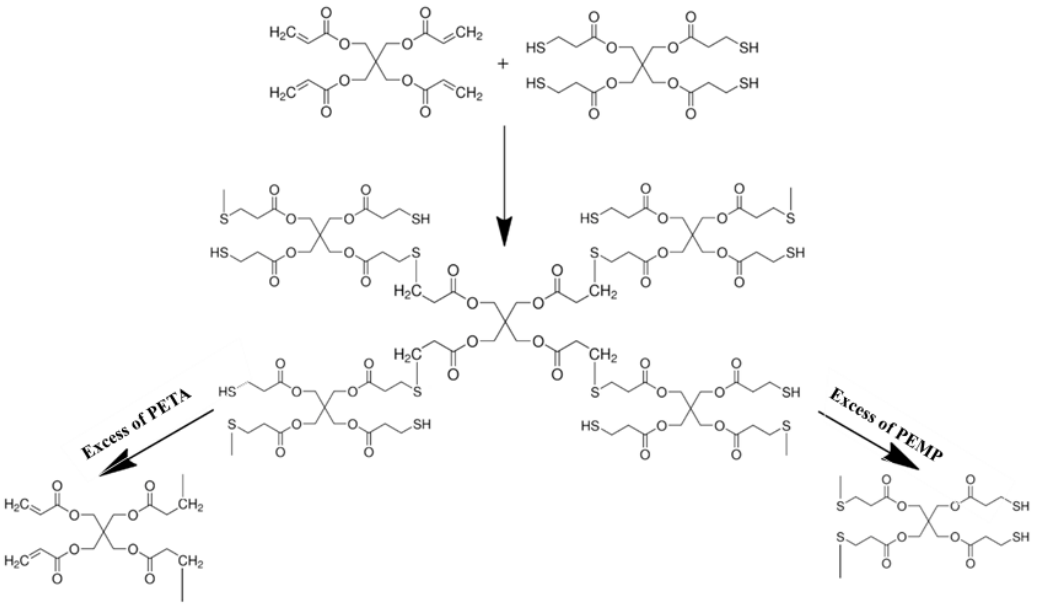


Figure 1 - Synthesis reaction scheme of gels based on PETA-PEMP.

Characteristics of gels based on PETA-PEMP

To investigate the yield of products based on the initial ratios of PETA-PEMP monomers, sol-gel analysis was conducted on the synthesised samples. Figure 2 and Table 1 depict the outcomes of this analysis.

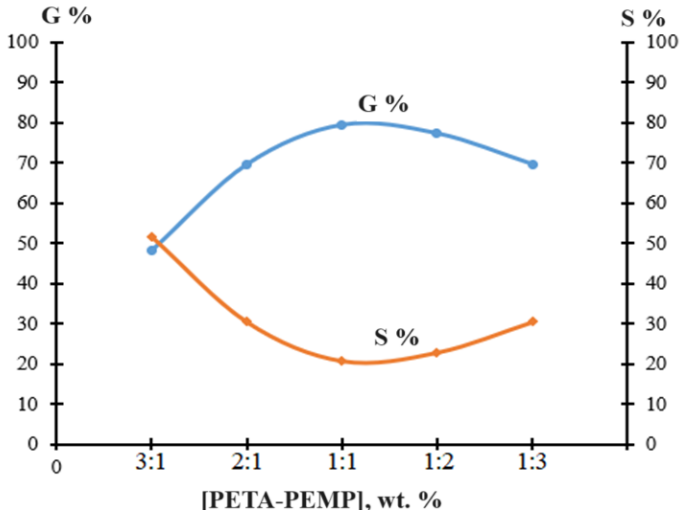


Figure 2 - Dependence of the sol and gel fraction yield of PETA-PEMP gel on the composition of the initial monomer mixture.

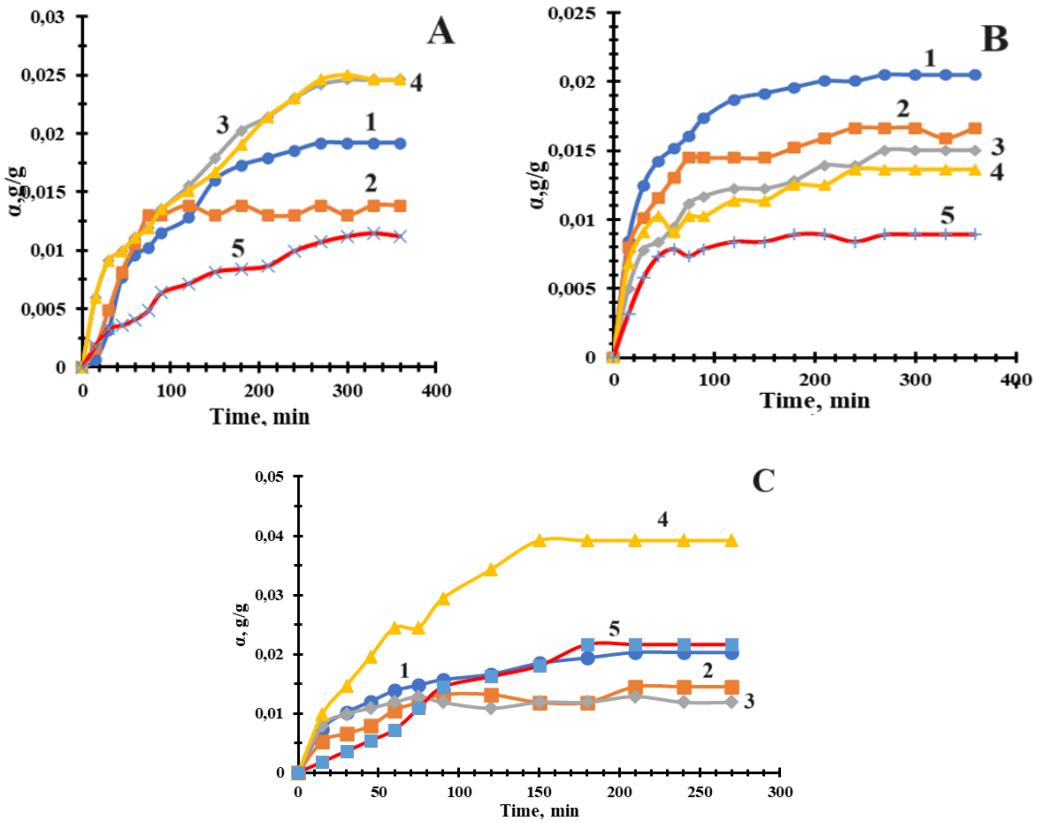
According to Table 1, the highest yield of the gel fraction occurs with the 1:1 composition, where the initial PETA and PEMP monomers are present in equal proportions. In contrast, lower yields are observed at ratios of 3:1 and 1:3 because one of the components is present in excess or deficiency. When there is an excess of PETA or PEMP, all available molecules of the other component become fully bound, leaving unreacted monomers that are subsequently washed out during the washing process. Interestingly, the yield of the gel fraction at the PETA-PEMP ratio of 1:3 is higher than that at 3:1. This difference is attributed to the denser structure of gels formed with excess PEMP.

Table 1
Results of sol-gel analysis of the obtained PETA-PEMP gels

Composition of initial monomer mixture, wt. %	№	[3:1]	[2:1]	[1:1]	[1:2]	[1:3]
Gel fraction, %	1	48,65	68,94	79,30	77,09	69,71
	2	47,32	69,71	79,58	77,04	69,91
	3	48,90	70,23	79,27	77,63	69,25
	Average	48,29	69,63	79,38	77,25	69,62
Sol fraction, %	1	51,35	31,06	20,70	22,91	30,29
	2	52,68	30,29	20,42	22,96	30,09
	3	51,10	29,77	20,73	22,37	30,75
	Average	51,71	30,37	20,62	22,75	30,38

This study examined gels synthesised from PETA-PEMP using various physicochemical methods. The swelling characteristics of these gels were evaluated in three different solutions: distilled water, isotonic solution, and a buffer solution with pH 6.86. Figure 2 (A, B, C) illustrates graphs depicting the degree of swelling over time. The gels exhibited the highest rate of swelling in the isotonic solution. The data collected determined the equi-

librium degree of swelling in these gels across different compositions (Figure 3). In an isotonic solution, the swelling capacity of the gels remained relatively consistent regardless of the composition. Conversely, in the buffer solution at pH 6.86, gels with equal proportions of PETA and PEMP in the initial monomer mixture showed the lowest degree of swelling, indicating a denser cross-linked network as supported by the gel fraction analysis. As the PEMP content increased, the swelling ability of the gels also increased, potentially influenced by the presence of -SH groups within the network. No distinct trends were observed in the influence of composition on the equilibrium degree of swelling in gels immersed in distilled water.



1 – [3:1]; 2 – [2:1]; 3 – [1:1]; 4 – [1:2]; 5 – [1:3].

Figure 3 - Dependence of the swelling rate of gels based on PETA-PEMP on the composition in distilled water (A), isotonic (B), and buffer (C) solutions.

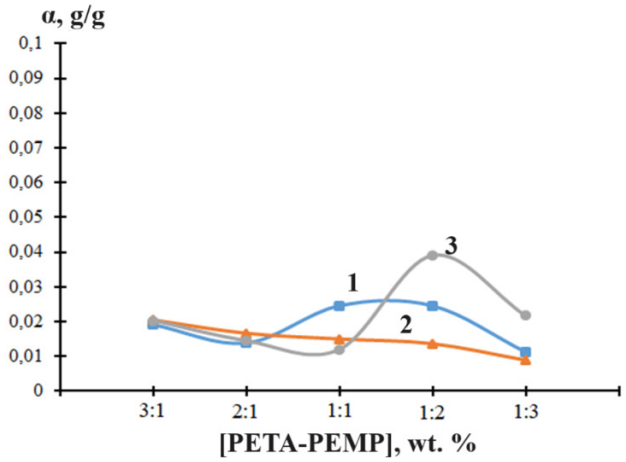


Figure 4 - Dependence of the equilibrium degree of swelling on the composition of gels based on PETA-PEMP in distilled water (1), in isotonic (2) and buffer (3) solutions.

Figure 5 displays the IR spectra of synthesised gels composed of PETA and PEMP in ratios of 3:1, 1:1, and 1:3 wt.%. A prominent peak in the 1745–1725 cm-1 range in all three spectra indicates the presence of C=O functional groups. A broader peak with lower intensity in the 1180–1140 cm^{-1} region suggests the presence of (-C-O-C-) groups within the gel composition. The absorption band observed in the 690–640 cm^{-1} region indicates the presence of (-C-S) functional groups in the polymer structure. Additionally, the peak at 1635 cm^{-1} signifies the presence of (-C=C) groups, while a small peak in the 1475–1450 cm^{-1} region indicates the presence of ($=CH_2$) groups.

It's important to note that detecting -SH groups typically require Raman spectroscopy due to their weak signal in IR spectra. This study employed Raman spectroscopy to provide a more detailed analysis of the polymer structure. The resulting Raman spectra are presented in Figure 6.

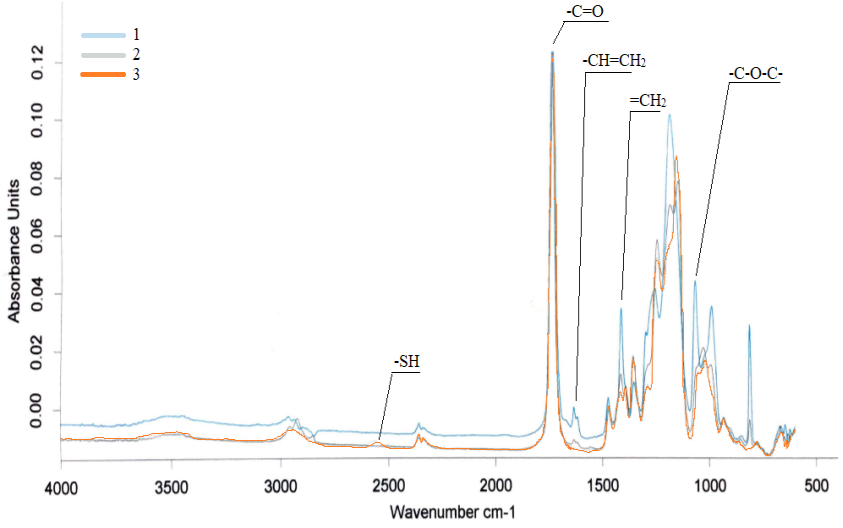


Figure 5 - IR spectra of PETA-PEMP gels of ratios [3:1] (1), [1:1] (2), and [1:3] (3).

Figure 6 illustrates the outcomes of Raman spectroscopy conducted on PETA-PEMP gels. The analysis revealed distinctive bands corresponding to specific chemical bonds within the polymer structure. The bands observed between 700–650 cm^-1 are attributed to vibrations of the C-S bond, indicating its presence in the polymer network. At 2590–2550 cm^-1, a band was identified that confirms the existence of SH groups, crucial for understanding the gel's composition and cross-linking density.

Furthermore, the band observed at 525 cm^{-1} signifies the presence of S-S bonds, suggesting an excess of PEMP in the gel composition, particularly evident in the 1:3 wt.% ratio. Bands around 1680 cm^{-1} were associated with vibrations of the -CH=CH_2 bond, confirming the presence of multiple bonds characteristic of gels with an excess of PETA (3:1 wt.%).

These findings from Raman spectroscopy provide detailed insights into the chemical structure and composition variations across different ratios of PETA-PEMP gels synthesised in this study.

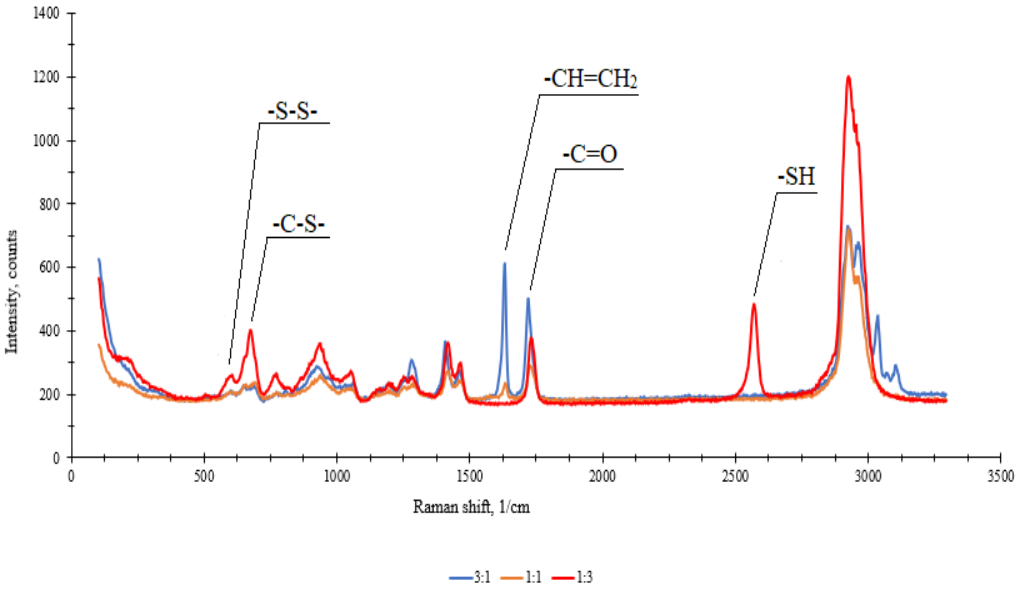


Figure 6 - Raman spectra of gels based on PETA-PEMP of ratios [3:1], [1:1], and [1:3].

Figure 7 (A, B, C) presents optical microscopy images used to study the structure and morphology of gels composed of PETA-PEMP. Samples with a diameter of 3 mm were chosen and pre-dried in a vacuum drying cabinet prior to analysis. The images indicate that gels with excess PETA exhibit a uniform structure. However, as the concentration of PETA increases in the initial monomer mixture, there is an observable emergence of crystalline supramolecular structures within the gels.

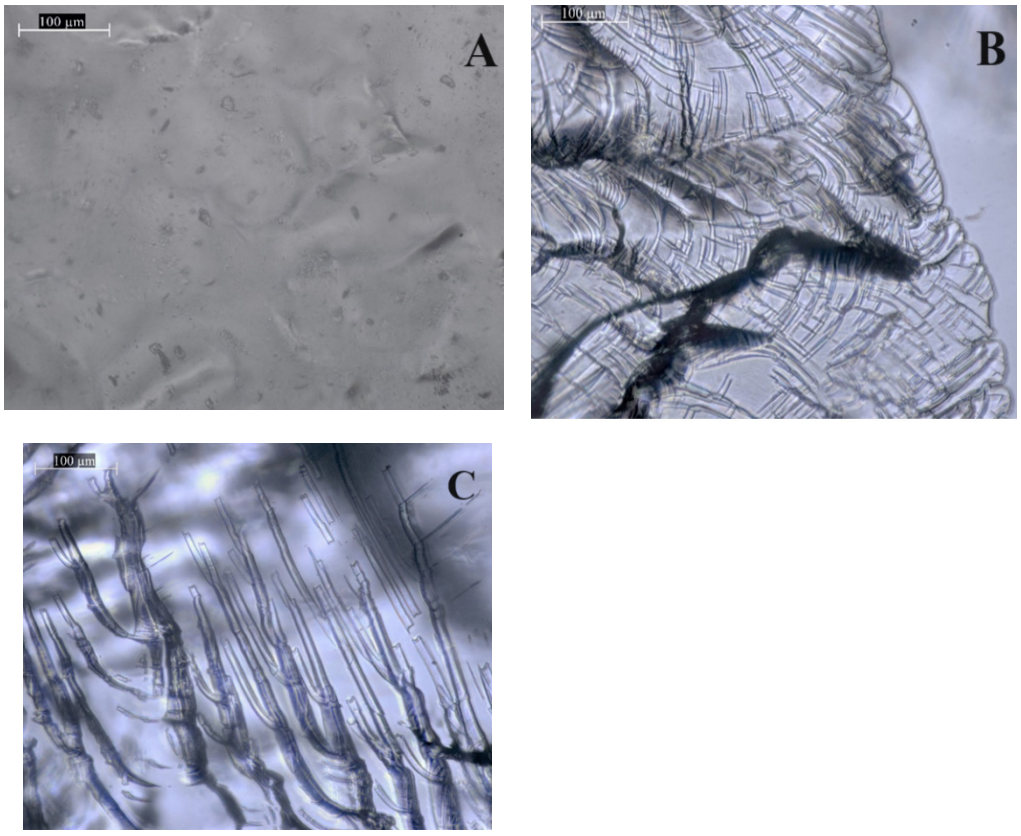


Figure 7 - Microphotographs of gels based on PETA-PEMP of ratios 3:1 (A), 1:1 (B), and 1:3 (C).

SEM was employed to conduct a detailed study of the gels' structure and morphology. The results, displayed in Figure 8 (A, B, C), reveal notable differences based on the composition of PETA-PEMP. Gels with an excess of PETA exhibit a more porous structure, as observed in the images. This porous nature correlates with the gels' swelling properties, where higher concentrations of PETA lead to increased degrees of swelling.

Conversely, as the concentration of PEMP monomers increases, a denser network structure becomes evident in the gels. This densification is reflected in the SEM images, indicating a tighter arrangement of polymer chains and reduced porosity compared to gels with excess PETA.

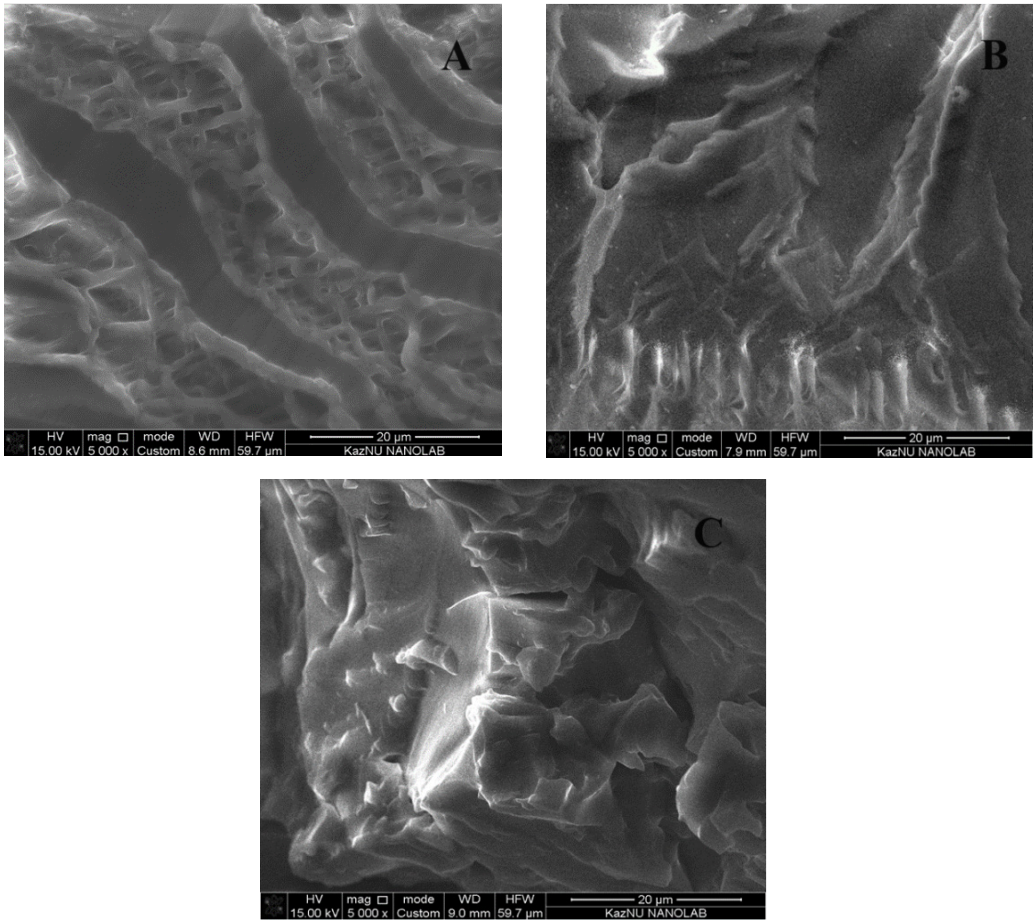


Figure 8 - SEM micrographs of gels based on PETA-PEMP of ratios 3:1 (A), 1:1 (B), and 1:3 (C).

The mechanical strength of the synthesised gels based on PETA-PEMP was evaluated through compression testing. Figure 9 illustrates that these gels exhibit significant strength and elasticity. The results evidently show the impact of varying ratios of initial monomers on the gels' strength. Gels with a higher proportion of PEMP show a slight reduction in elasticity but an increase in overall strength. This effect is likely due to the increased number of cross-links formed, which restricts the flexibility and movement of the polymer chains within the network.

On the other hand, gels with an excess of PETA in the initial mixture demonstrate higher elasticity. This elasticity can be attributed to the presence of a greater number of multiple bonds in their structure, which allows for more flexibility and resilience under compression.

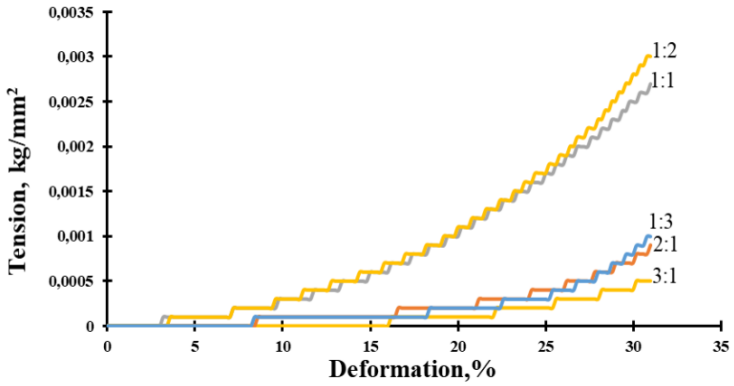


Figure 9 - Graph of stress versus strain for gels based on PETA-PEMP of different ratios.

Based on the mechanical analysis data, each sample's elastic modulus was calculated and presented in Table 2. The elastic modulus was determined by calculating the tangent of the slope of the initial linear portion of the compression curve. Increasing the concentration of PEMP in the gel composition was observed to contribute to an increase in the elastic modulus. This indicates that gels with higher proportions of PEMP exhibit greater stiffness and resistance to deformation under compression.

Table 2

Values of elastic modulus for gels of PETA-PEMP compositions at different ratios of initial monomers

Ratios of initial monomers	Modulus of elasticity, Pa
3:1 7727	
2:1	18633
1:1	29518
1:2	34519
1:3	11670

Study of the degradation ability of synthesised gels based on PETA-PEMP

An essential criterion for using polymers for drug delivery systems in medicine is their ability to biodegrade within the body. Biodegradation ensures that once the active substance in the medication is depleted, the polymer carrier can be naturally broken down and eliminated from the body, preventing any unnecessary accumulation. This process is crucial for sustained drug release and reducing the frequency of medication intake.

In this study, the biodegradation of the synthesised PETA-PEMP gels was investigated using a phosphate buffer solution containing pig liver esterase enzymes. Esterase enzymes catalyse the hydrolysis of ester bonds, which are common in organic compounds found in the human body. The experimental results, depicted in Figure 3.3.1, indicate that the gels began to degrade immediately in the presence

of enzymes.

When analysing the degradation of PETA-PEMP gels in a buffer solution simulating physiological fluid (pH = 7.4), no significant weight loss was observed. However, swelling of the gels was noted, suggesting a response to the environment similar to that of human bodily fluids. This underscores the potential biocompatibility of these gels as drug carriers in medical applications.

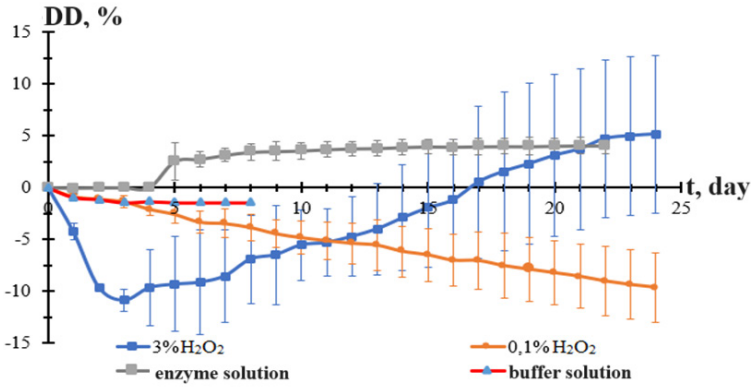


Figure 10 - Dependence of the degree of destruction of PETA-PEMP gels at a ratio of 3:1 wt.% on time in various solutions.

In areas of inflammation and oncological tumour sites, hydrogen peroxide is naturally released in small quantities. This release serves a dual role: it helps prevent infection and signals to attract immune cells, such as leukocytes, to the affected area (Shuler, Kazybayeva, 2021: 29).

This study investigated how gels based on PETA-PEMP degrade in solutions with varying concentrations of hydrogen peroxide. The experiment continued until the mass of the gels stabilised. Based on the results, a graph was generated to illustrate how the degree of degradation of the gels changes over time in these solutions (Figure 10). The graph indicates that higher concentrations of hydrogen peroxide accelerate the degradation process. The degradation primarily involved swelling of the gels before reaching a stable mass.

These findings underscore the potential of PETA-PEMP gels for applications where controlled degradation in response to hydrogen peroxide levels could be advantageous, such as in localised treatments for inflammatory conditions or in targeted drug delivery systems.

Conclusion

In this research, gels were synthesised using PETA and PEMP monomers in various ratios in the presence of DMF solvent. The synthesised gels underwent comprehensive characterisation using multiple analytical methods. Sol-gel analysis determined the yields of the sol and gel fractions, providing insights into the polymer network formation. The water absorption capacity of the gels was evaluated by assessing their degrees of swelling in different media.

Structural analysis using IR and Raman spectroscopy revealed distinctive vibrations in the spectra of gels with an excess of PEMP, indicating the presence of -SH groups. Morphological studies conducted via optical and scanning electron microscopy highlighted those gels with excess PETA exhibited a more porous structure, whereas those with excess PEMP showed a denser morphology. Mechanical testing using compression mode demonstrated that gels enriched with PETA were more elastic and resilient, whereas those with more PEMP were stronger and harder. The degradation behaviour of the synthesised gels was investigated in buffer solutions with pH=7.4, enzyme solutions, and hydrogen peroxide solutions of varying concentrations. No degradation was observed in buffer solutions, whereas enzymatic degradation with esterase and degradation in hydrogen peroxide solutions showed distinct effects. The concentration and type of H2O2 solution significantly influenced the rate and extent of degradation of the PETA-PEMP gels.

Overall, these findings contribute to understanding how the composition of PETA and PEMP monomers affects the properties and degradation behaviour of the synthesised gels, which is crucial for their potential applications in controlled drug delivery and biomedical devices.

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