

STRUCTURAL OPTIMIZATION OF BIOCOMPOSITES USING MULTIVALENT IONS AND MODIFIED MONTMORILLONITE

G.Ye. Yerlan, B.B. Tyussyupova*, S.M. Tazhibayeva, K.B. Musabekov, M.A. Murtaza

Al-Farabi Kazakh National university, Al-Farabi Ave., 71, Almaty, Kazakhstan

*Corresponding author e-mail: bakyt.tiusiupova@kaznu.edu.kz

Abstract. *Introduction.* In modern biomedicine and pharmacology, one of the central challenges is the development of highly efficient therapeutic systems with controlled drug release. *Objective.* This study investigates the influence of cation valence and concentration on the degree of crosslinking in polymer networks of alginate hydrogels prepared via ionotropic gelation. *Results and Discussion.* The structural characteristics of the synthesized materials were examined using physicochemical analysis. A detailed evaluation was conducted on the swelling kinetics and the release profiles of immobilized drugs in physiological saline. Stimuli-responsive (pH-dependent) ionotropic biocomposites capable of adapting to changes in environmental acidity were successfully synthesized. Particular attention was given to the differences in insulin release kinetics from alginate-gelatin biocomposites upon the incorporation of montmorillonite and its magnetized form. It was demonstrated that the inclusion of magnetized montmorillonite nanoparticles not only prolongs the release of the protein drug but also enables prospects for targeted transport under the influence of an external magnetic field. *Conclusion.* The findings highlight effective strategies for controlling the structure and physicochemical properties of biocomposite hydrogels. These advances represent an important step toward the development of therapeutic systems for controlled and targeted drug delivery.

Keywords: hydrogel, ionotropic biocomposites, montmorillonite, magnetosensitivity, particles, modification, swelling degree

Yerlan Gulzhan Yerlankyzy	PhD, e-mail: yerlan.gulzhan@gmail.com
Tyussyupova Bakyt Baimuratovna	Candidate of Chemical Sciences, Associate Professor, e-mail: bakyt.tiusiupova@kaznu.edu.kz
Tazhibayeva Sagdat Mederbekovna	Doctor of Chemical Sciences, Professor, e-mail: sagdat.tazhibayeva2018@gmail.com
Musabekov Kuanyshebek Bituovich	Doctor of Chemical Sciences, Professor, e-mail: musabekov40@mail.ru
Murtaza Madina Abythankyzy	Master, Junior researcher, e-mail: madinamurtaza002@gmail.com

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1. Introduction

The high density of reactive functional groups offers polysaccharides a wide range of applications. Their use in drug encapsulation preserves the biological activity and integrity of loaded drugs, regulate their distribution within the body, reduce side effects, and protects them from adverse environmental influences [1-5].

In this context, bionanocomposites are commonly formed through ionotropic crosslinking of polysaccharides with multivalent ions: cations and anions. This mechanism enhances the polymers' resistance to water and improves their mechanical properties. Comparative studies have analyzed the strength and swelling behavior of hydrogels crosslinked with different multivalent cations (Ca^{2+} , Ba^{2+} , Sr^{2+}), demonstrating that ion type significantly influences mechanical stability and structural optimization. Both equilibrium swelling and mechanical properties of hydrogels prepared with various cations have been investigated, with emphasis placed on optimizing ion concentration to achieve the desired characteristics [6-8]. A protocol for immobilizing INS1E cells in alginate hydrogels has also been reported [9], highlighting high biocompatibility and preservation of cell functionality during encapsulation. The regulation of hydrogel degradation through oxidation has been explored in another study [10]. Sodium periodate was used to oxidize alginate, varying its concentration in the range of 0%, 2.5%, 5%, and 7%. At 2.5% oxidation, the material exhibited sufficient stability to retain insulin while simultaneously degrading and integrating into tissue, underscoring the potential of alginate for injectable biodegradable drug delivery systems. Polymer hydrogels represent a promising class of biomaterials for targeted drug delivery due to their high biocompatibility and favorable physicochemical properties [11]. Their swellable and porous matrix enables absorption of large amounts of water and biological fluids, making them particularly suitable for controlled and sustained drug release [12].

The aim of this research is to optimize the matrix architecture of alginate-gelatin hydrogels via ionotropic gelation with multivalent cations, and to establish the quantitative relationship between montmorillonite (MMT) and its magnetized form, the swelling ratio in media of varying pH, and the kinetics of prolonged insulin release.

The primary novelty of this work lies in the development of a ternary biocomposite system - based on the compatibility of biopolymers and magnetized montmorillonite - designed to facilitate the delivery of protein-based drugs (specifically insulin) through a dual-factor mechanism involving pH and magnetic fields. The study elucidates how the dense layered structure of the magnetized montmorillonite acts as a physical barrier, suppressing the initial "burst" release of insulin in model medium. Moreover, the incorporation of magnetized montmorillonite imparts magnetic responsiveness to the pH-sensitive polymer matrix, thereby establishing a theoretical foundation for targeted therapeutic delivery controlled by external stimuli.

The structure of such biocomposites can be further tailored by introducing natural water-soluble polymers during ionotropic hydrogel formation. The addition of gelatin, a polyampholyte, confers pH sensitivity [13–15], while the incorporation of colloidal montmorillonite particles containing magnetic components imparts magnetosensitive properties [16, 17].

2. Experimental part

2.1 Materials

Sodium alginate (19–40 kDa, Sisco Research Laboratories, Turkey), gelatin (The Kraft Heinz Company, CHIA), calcium chloride (Sinopharm Chemical Reagent Co., Ltd, China), insulin-isophane (human genetically engineered, Novo Nordisk A/S, Denmark), iron chloride (Sigma-Aldrich Chemie GmbH Eschenstrasse 5 D-82024 Taufkirchen, Germany), buffer solutions with pH values of pH=1.0; pH=4.0; pH=7.0; pH=9.18 (Reagecon, Ireland), montmorillonite – bentonite clay powder, Eastern section 12 horizon, light gray.

2.2 Preparation of sodium alginate particles by ionotropic gelation

Alginate hydrogel particles were prepared by dropwise addition of a 1% sodium alginate solution into CaCl_2 and FeCl_3 crosslinker solutions using a syringe pump. To optimize particle formation, crosslinker solutions of varying concentrations (0.5%, 1.0%, 1.5%, and 2.0%) were tested. The particles were incubated in the crosslinker solution for 30 minutes, collected by filtration, and subsequently washed with deionized water.

2.3 Determination of particles swelling in simulated gastrointestinal media

The swelling degree of particles was determined by measuring the increase in particle mass over time. Particles were placed in model solutions simulating different sections of the gastrointestinal tract, and their mass was recorded at 30-minute intervals over a total period of 180 minutes.

Table 1 - Model solutions and their pH values used in the experiment

№	Model solution	pH value
1.	0.1 N HCl solution	1.00
2.	Potassium hydrogen phthalate, saturated at 25°C	4.00
3.	Phosphate buffer	7.00
4.	0.01 mol/kg sodium tetraborate solution	9.18

The degree of swelling was calculated using the following equation:

$$K = \frac{m_t}{m_0} \quad (1)$$

Where m_t - particle mass over time, mg; m_0 - mass of particles at the initial time, mg.

In this context, the parameter K represents the swelling rate constant. Physically, K governs the diffusion velocity of water molecules into the biocomposite network and reflects the structural resistance of the crosslinked polymer matrix during expansion.

2.4 Production of biocomposites for protein drug immobilization by ionotropic gelation

The biocomposite was prepared by mixing a 1% sodium alginate solution with an 8% gelatin solution in a 1:1 ratio ($V_1:V_2$). The resulting mixture was introduced into a crosslinking agent solution using a syringe pump. The formed alginate - gelatin biocomposites were incubated in the crosslinking solution for 30 minutes, collected by filtration, and washed with deionized water.

2.5 Preparation of Magnetically Responsive Biocomposites

Magnetic montmorillonite (MMT), synthesized using the established Elmore method, was incorporated into the sodium alginate - gelatin biocomposite at concentrations of 0.1 g, 0.25 g, and 0.5 g for different sample batches. The mixture was homogenized until a uniform dispersion was achieved and subsequently injected into a 1.5% CaCl_2 solution using a syringe pump. The biocomposites were incubated in the crosslinking solution for 30 minutes, collected by filtration, and washed with deionized water.

2.6 Study of insulin release from biocomposites

Insulin release was quantified using a UV-7504 spectrophotometer (Shanghai Hansom Technology & Sales Limited, China; wavelength range: 200–1000 nm) at the characteristic absorbance maximum of 280 nm, corresponding to aromatic amino acid residues (tyrosine) in the insulin structure. Optical density (absorbance) was measured in the UV-visible range using a spectrophotometer and a quartz cuvette with an optical path length of 1 cm. Drug-loaded biocomposites were immersed in 20 mL of buffer solution with a pH of 7.4 and incubated at 37°C with stirring (100 rpm). At predetermined intervals, aliquots of the buffer were withdrawn and analyzed for insulin concentration. Each aliquot was replaced with an equal volume of fresh buffer to maintain constant volume.

The cumulative drug release was calculated using the following equation:

$$\text{Drug released (\%)} = \frac{C_t}{C_\infty} \cdot 100 \% \quad (2)$$

where (C_t) represents the concentration of the drug released at time (t), determined via the UV-Vis calibration curve equation ($\text{Abs} = m \cdot C + b$) and (C_∞) is the theoretical concentration of insulin upon complete release from the biocomposite.

2.7 Infrared spectroscopy

IR spectra of samples (sodium alginate, gelatin, CaCl_2 , montmorillonite) were recorded using a Cary 660 Agilent FTIR spectrometer (Agilent Technologies, USA), range 7900 - 375 cm^{-1} , signal-to-noise ratio 10000:1.

3. Results and Discussion

3.1 The effect of cation valence and concentration on the network density of ionotropically formed alginate hydrogels

Alginate hydrogels were obtained via ionotropic gelation using multivalent cations (Ca^{2+} and Fe^{3+}) at varying concentrations (0.5–2.0%). Hydrogels cross-linked with calcium ions exhibited greater stability than those formed with Fe^{3+} , with stability increasing proportionally to cation concentration. The study demonstrated that the cation valence influences the structure of the hydrogels and their behavior in an aqueous environment. The swelling kinetics (K) of alginate gels, shown in Figures 1 and 2, demonstrated that Ca^{2+} -crosslinked samples continued to swell for 180 minutes across all CaCl_2 concentrations. The highest swelling rate was observed at 1.5% CaCl_2 , where K values exceeded those of 0.5%, 1.0%, and 2.0% solutions by 1.08, 0.65, and 0.79 arbitrary units, respectively. During hydrogel synthesis, the 1.5% CaCl_2 concentration was identified as optimal, producing more pronounced swelling compared to other concentrations (Figure 1).

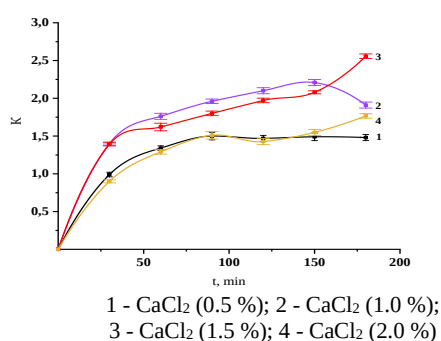


Figure 1 – Swelling kinetics of alginate hydrogels crosslinked with Ca^{2+} ions in aqueous media.

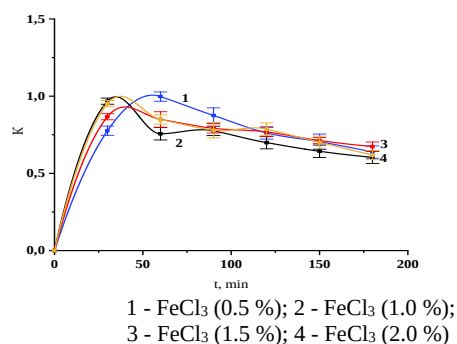


Figure 2 - Swelling kinetics of alginate hydrogels cross-linked with Fe^{3+} ions in aqueous media.

In contrast, hydrogels crosslinked with Fe^{3+} ions exhibited markedly lower swelling capacity. The maximum swelling kinetics for Ca^{2+} -based gels reached 2.55 arbitrary units, whereas Fe^{3+} -based gels did not exceed 1.0 arbitrary units (Figure 2).

3.2 Synthesis of stimuli-responsive (pH-Sensitive) and magneto-sensitive ionotropic biocomposites

To obtain pH-sensitive ionotropic biocomposite hydrogels, gelatin was introduced into sodium alginate. Specifically, gelatin was added to the sodium alginate solution at concentrations of 2%, 5%, and 8% at a 1:1 ($V_1:V_2$) ratio. The swelling kinetics of these gels in aqueous medium were subsequently investigated (Figure 3). The study demonstrated that the swelling rate of alginate - gelatin hydrogels at gelatin concentrations of 2%, 5%, and 8% exceeded that of pure alginate gels by 1.06, 1.6, 1.35, and 2.66 u.c., respectively. The highest swelling

kinetics were observed with the incorporation of 8% gelatin, identifying this concentration optimal for the synthesis of pH-sensitive biocomposite hydrogels. To impart magnetic responsiveness, magnetic montmorillonite particles were incorporated into the hydrogel matrix. In the initial step, magnetite particles were introduced into the alginate–gelatin solution prior to gelation, resulting in the formation of biocomposites containing magnetic montmorillonite.

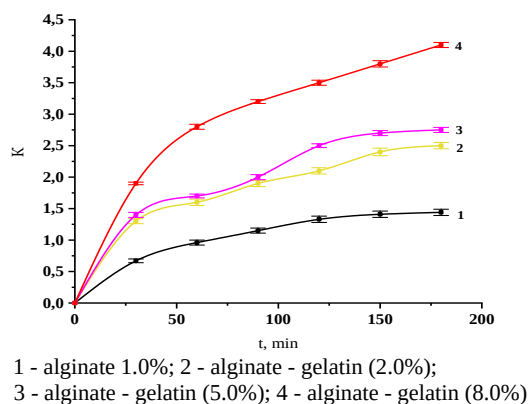


Figure 3 - Changes in the swelling kinetics of biocomposite hydrogels in aqueous medium.

Magnetic properties were confirmed using an external magnet. The resulting samples were dried at room temperature (Figure 4), after which their swelling kinetics were evaluated (Figure 5).

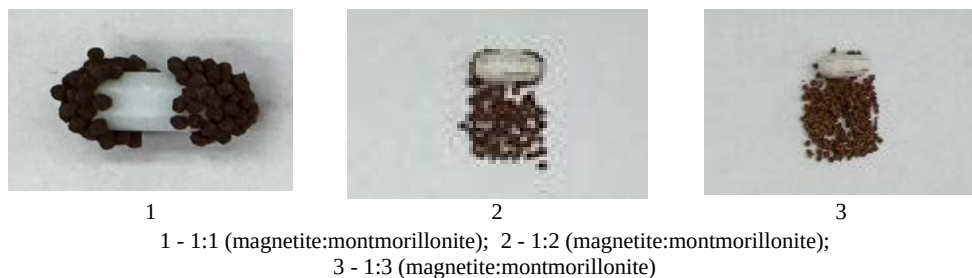


Figure 4 - Synthesized samples of biocomposite hydrogels with magnetically sensitive properties

The resonant frequency values of hydrogel-gelatin composites are given below in Table 2.

Table 2 - Resonant frequency values of biocomposites

Mass of introduced magnetite	0.1 g	0.25 g	0.5 g
Magnetite:MMT ratio			
1:1	4.314 MHz	4.312 MHz	4.310 MHz
1:2	4.348 MHz	4.346 MHz	4.345 MHz

1:3	4.335 MHz	4.345 MHz	4.354 MHz
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The magnetic properties of the synthesized biocomposites were indirectly evaluated by measuring the shift in the resonant frequency of the inductive circuit. As shown in Table 2, the resonant frequency values (expressed in MHz) vary depending on the mass of the introduced magnetite and the Magnetite:MMT ratio. The introduction of magnetic nanoparticles into the polymer matrix alters the magnetic core inductance within the measuring coil, which consequently shifts the resonant frequency. This frequency response serves as an indicator of the magnetic loading and distribution within the alginate-gelatin biocomposite network. Specifically, for the control biocomposite sample without magnetic additives, the resonant frequency was found to be 4.318 MHz. Upon the incorporation of magnetic components into the matrix, a systematic decrease in the resonant frequency was observed, signifying a pronounced increase in the magnetic sensitivity of the material. This effect is primarily attributed to the presence of structured magnetite particles capable of interacting with an external magnetic field [18-24]. Beyond the magnetic characteristics, the structural integration of the mineral phase, particularly montmorillonite (MMT), significantly influences the matrix behavior. As a result, the introduction of MMT markedly affects the swelling capacity of the biocomposites, with the overall effect being strictly dependent on the pH of the medium and the total filler content (Figure 5).

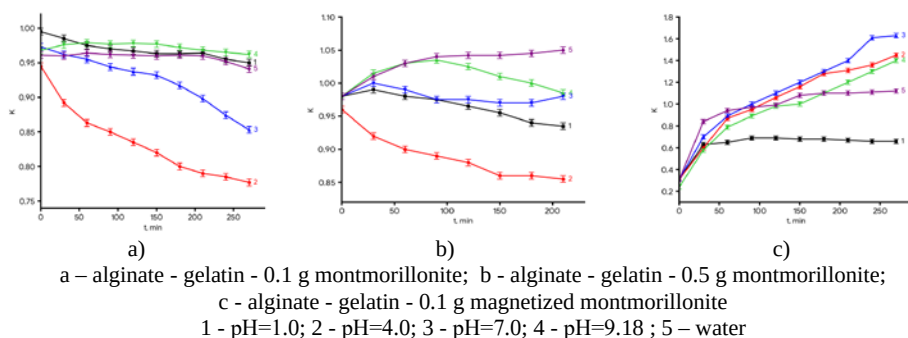
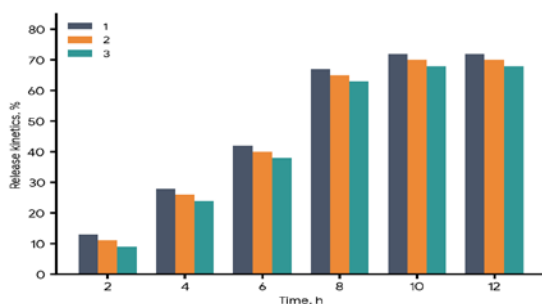


Figure 5 - Dependence of the swelling kinetics of biocomposites in the presence of montmorillonite

At low pH (1.0 - 4.0), swelling of the biocomposites is restricted due to protonation of the carboxyl groups of sodium alginate, which reduced hydrophilicity. Under neutral and slightly alkaline conditions (pH 7.0 - 9.18), dissociation of these groups enhances hydration through electrostatic repulsion between polymer chains. The addition of 0.1 g of montmorillonite increases swelling as a result of additional water sorption, however, increasing the montmorillonite mass to 0.5 g leads to structural compaction and reduced polymer chain mobility. Magnetized montmorillonite (0.1 g) exerts a more pronounced effect owing to its enhanced sorption capacity and uniform particle

distribution, while also enabling controlled manipulation under an external magnetic field. Thus, modification of biocomposites with montmorillonite provides a means of regulating swelling behavior, and the incorporation of magnetic fillers establishes a foundation for the development of biomaterials with tunable properties. Differences in the kinetics of insulin release from biocomposites were examined following the addition of montmorillonite and its magnetized form at pH 7.4 (Figure 6). The original sample exhibited a relatively high insulin diffusion rate -approximately 72% - due to the pronounced hydrophilicity and porous structure of the polysaccharide matrix. Upon incorporation of montmorillonite, the release rate decreased as a result of additional intermolecular interactions between the functional groups of the polysaccharides and the mineral layers. This modification increased gel density and restricted diffusion pathways for the insulin macromolecule.



1 – alginate - gelatin; 2 – alginate - gelatin - montmorillonite;
3 – alginate - gelatin - magnetized montmorillonite

Figure 6 - Kinetics of insulin release from biocomposites with the addition of montmorillonite in a physiological solution at pH = 7.4

Of particular interest was the system containing magnetized montmorillonite, in which insulin release was further delayed. This effect can be attributed to additional coordination and electrostatic interactions between the iron-containing centers and the polar groups of the protein, thereby enhancing the matrix's retention capacity. Consequently, the incorporation of montmorillonite-especially in its magnetized form-ensures prolonged release of the biologically active compound [21-23]. The influence of montmorillonite on the structure of alginate-gelatin polymer hydrogels was also studied using IR spectroscopy (Table 3).

Table 3 - Characteristic absorption bands in the IR spectra of the starting components and composite hydrogels

Sample/ Component	Wave number (cm ⁻¹)	Intensity	Assignment/ Functional Group
Sodium alginate	2636 1605 1100–1020	Weak/ Moderate Strong, sharp Very strong	Asymmetric C-H stretching Carboxylate (COO ⁻) stretching C-O-C carbohydrate skeleton

Gelatin	3300 1230–1245	Broad, strong Medium	Amide A stretching Amide I (C=O) & Amide III stretching
Alginate-gelatin- MMT	Shifted 1045–1030 470–520	Strong / Variable Very strong Moderate	Asymmetric COO ⁻ vibrations Si-O-Si silicate framework Si-O and M-O-Si stretching
Alginate-gelatin- mag-MMT	516 Shifted	Moderate / Sharp Strong, modified	Fe-O band appearance COO ⁻ & Amide II stretching (shifted)

The introduction of montmorillonite into the alginate-gelatin system resulted in a shift in the absorption band of carboxylate groups (COO⁻) and a change in the peaks of the carbohydrate skeletal peaks within the 1100–1020 cm⁻¹ region. These spectral changes indicate the formation of electrostatic interactions and hydrogen bonding between the polymer matrix and the silicate layers of montmorillonite. Following modification of montmorillonite with magnetite, the spectrum exhibited a distinct and intense peak at a frequency of 516 cm⁻¹, corresponding to the stretching vibrations of the Fe-O bond. This serves as direct physicochemical confirmation of the successful magnetization process [26–30].

Furthermore, coordination of iron ions with the carboxyl groups of alginate and the amide structures of gelatin resulted in a pronounced band shift and a change in peak intensity in the IR spectrum. The resulting spectral effects indicate the formation of a highly stable magnetic composite.

4. Conclusion

The principal outcome of this study is the development of an optimal technology for synthesizing a new generation of biocomposites with tunable polymer network density, achieved by varying the content of chemical, ionotropic, and physical crosslinking units. These biocomposites exhibit dual stimuli-responsiveness (pH and magnetic sensitivity) and demonstrate a more sustained release of immobilized drugs compared to conventional ionotropic polysaccharide hydrogels. The enhanced ability to prolong the physiological action of drugs underscores the practical significance of this approach and highlights its potential for advanced therapeutic applications.

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Conflict of Interest: The authors declare no conflicts of interest requiring disclosure in this article.

КӨПВАЛЕНТТІ ИОНДАР ЖӘНЕ МОДИФИКАЦИЯЛАНҒАН МОНТМОРИЛЛОНИТ НЕГІЗІНДЕ БИОКОМПОЗИТТЕРДІ ҚҰРЫЛЫМДЫҚ ОҢТАЙЛАНДЫРУ

Г.Е. Ерлан, Б.Б. Төсүпова, С.М. Тажибаева, К.Б. Мусабеков, М.А. Муртаза*

Әл-Фараби, атындағы Қазақ ұлттық университеті, Алматы, Қазақстан

Түйіндемe. *Кіріспе.* Қазіргі заманғы биомедицина мен фармакологиядағы негізгі міндеттердің бірі – дәрілік заттардың бөлінуі реттелетін жоғары тиімді терапиялық жүйелерді әзірлеу. *Мақсаты.* Бұл зерттеу ионотропты геледену әдісімен алынған альгинатты гидрогельдердегі полимерлік торлардың айқаспалы байланысу дәрежесіне катиондардың валенттілігі мен концентрациясының әсерін қарастырады. *Нәтижелер және талқылау.* Синтезделген материалдардың құрылымдық ерекшеліктері физика-химиялық талдау әдістері арқылы сипатталды. Физиологиялық тұзды ерітіндіге иммобилизделген дәрілік заттардың бөліну жылдамдығы мен ісіну кинетикасына егжей-тегжейлі талдау жасалды. Қоршаған ортаның қышқылдығының өзгеруіне жауап бере алатын, тітіркендіргіштерге сезімтал (рН-қа тәуелді) ионотропты биокөмпозиттер синтезделді. Монтмориллонит пен оның магниттелген түрін енгізу кезінде альгинат-желатин биокөмпозиттерінен инсулиннің бөліну кинетикасындағы айырмашылықтарды зерттеуге ерекше назар аударылды. Магниттелген монтмориллонит нанобөлшектерін енгізу ақуыздық препараттың бөлінуін ұзартып қана қоймай, сонымен қатар сыртқы магнит өрісінің әсерімен мақсатты тасымалдауға мүмкіндік беретіні анықталды. *Қорытынды.* Алынған нәтижелер биокөмпозиттік гидрогельдердің құрылымы мен физика-химиялық қасиеттерін мақсатты түрде реттеудің тиімді тәсілдерін көрсетеді; бұл дәрілік заттарды бақыланатын және мақсатты жеткізуге арналған терапиялық жүйелерді құру жолындағы маңызды қадам болып табылады.

Түйінді сөздер: гидрогель, ионотропты биокөмпозиттер, монтмориллонит, магнитті сезімталдық, бөлшектер, модификация, ісіну дәрежесі

Ерлан Гүлжан Ерланқызы	PhD; e-mail: erlan.gulzhan@mail.ru
Тюсюпова Бакыт Баймуратовна	Химия ғылымдарының кандидаты, қауымдастырылған профессор, e-mail: Bakyt.Tiusiupova@kaznu.edu.kz
Тажиббаева Сағдат Медербековна	химия ғылымдарының докторы, профессор, e-mail: sagdattazhibayeva2018@gmail.com
Мусабеков Куанышбек Битұвич	химия ғылымдарының докторы, профессор, e-mail: musabekov40@mail.ru
Муртаза Мадина Абытханқызы	магистр, кіші ғылыми қызметкер, e-mail: madinamurtaza002@gmail.com

СТРУКТУРНАЯ ОПТИМИЗАЦИЯ БИОКОМПОЗИТОВ С ИСПОЛЬЗОВАНИЕМ МНОГОВАЛЕНТНЫХ ИОНОВ И МОДИФИЦИРОВАННЫХ МОНТМОРИЛЛОНИТА

Г.Е. Ерлан, Б.Б. Тюсюпова*, С.М. Тажиббаева, К.Б. Мусабеков, М.А. Муртаза

Казахский национальный университет им. аль-Фараби, Алматы, Казахстан

Резюме. *Введение.* В современной биомедицине и фармакологии одной из ключевых задач является создание высокоэффективных терапевтических систем с контролируемым высвобождением лекарственных веществ. *Цель.* В работе исследовано влияние валентности катионов и их концентрации на степень сшивки полимерных сеток в альгинатных гидрогелях, полученных методом ионотропного гелеобразования. *Результаты и обсуждение.* Методами физико-химического анализа изучены структурные особенности синтезированных материалов. Проведен детальный анализ кинетики набухания и скорости высвобождения иммобилизованных лекарственных препаратов в физиологический раствор. Синтезированы стимулирующие (рН-зависимые) ионотропные биокөмпозиты, способные реагировать на изменение кислотности среды. Особое внимание уделено изучению различий в кинетике высвобождения инсулина из альгинат-желатиновых биокөмпозитов при введении монтмориллонита и его магнетизированной формы. *Заключение.* Установлено, что включение магнетизированных наночастиц монтмориллонита позволяет не только пролонгировать выход белкового препарата, но и открывает перспективы для направленного транспорта под воздействием внешнего магнитного поля. Полученные результаты демонстрируют эффективные подходы к направленному управлению

структурой и физико-механическими свойствами биокomпозитных гидрогелей, что является важным шагом для создания терапевтических систем контролируемого и адресного высвобождения лекарственных веществ.

Ключевые слова: гидрогель, ионотропные биокomпозиты, монтмориллонит, магниточувствительность, частиц, модификация, степень набухания

Ерлан Гүлжан Ерланқызы	PhD; e-mail: erlan.gulzhan@mail.ru
Тюсюпова Бакыт Баймуратовна	кандидат химических наук, ассоциированный профессор e-mail: Bakyt.Tiusiupova@kaznu.edu.kz
Тажиббаева Сагдат Медербековна	доктор химических наук, профессор, e-mail: sagdattazhibayeva2018@gmail.com
Мусабеков Куанышбек Битуович	доктор химических наук, профессор e-mail: musabekov40@mail.ru
Муртаза Мадина Абытханқызы	магистр, младший научный сотрудник e-mail: madinamurtaza002@gmail.com

References

1. Babu V.R., Patel P., Mundargi R.C., Rangaswamy V., Aminabhavi T.M. Developments in polymeric devices for oral insulin delivery. *Expert Opin Drug Deliv.* 2008, 5, 403-415. <https://doi.org/10.1517/17425247.4.4.403>
2. Li L., Wang Y. Advancements in Injectable Hydrogels for Controlled Insulin Delivery: A Comprehensive Review of the Design, Properties and Therapeutic Applications for Diabetes and Its Complications. *Polymers* 2025, 17,780. <https://doi.org/10.3390/polym17060780>
3. Liu B. Chen, K. Advances in Hydrogel-Based Drug Delivery Systems. *Gels* 2024, 10, 262. <https://doi.org/10.3390/gels10040262>
4. Ghazwani M., Hani U., Kyada A., Ballal S., Issa B.S., Abosoad M.K., Singh A., Sabarivani A. and Ray S. Advancements in insulin delivery: the potential of natural polymers for improved diabetes management. *Front. Bioeng. Biotechnol.* 2025, 13:1566743. <https://doi.org/10.3389/fbioe.2025.1566743>
5. Herrero E.P., Alonso M.J., Csaba N. Polymer-based oral peptide nanomedicines. *Ther Deliv.* 2012, 3, 657-668. DOI: 10.4155/tde.12.40
6. Malektaj H., Drozdov A.D., deClaville Christiansen J. Mechanical Properties of Alginate. Hydrogels Cross-Linked with Multivalent Cations. *Polymers* 2023, 15, 3012. <https://doi.org/10.3390/polym15143012>
7. Khvorostina M.A., Algebraistova P.Y., Nedorubova I.A. The Influence of Crosslinking Agents on the Matrix Properties of Hydrogel Structures Based on Sodium Alginate. *Inorg. Mater. Appl. Res.* 15, 2024, 388–394. <https://doi.org/10.1134/S2075113324020254>
8. Yerlan G.Y., Shen M., Tyussyupova B.B., Tazhibayeva S.M., Musabekov K., Takhistov P. Insulin Conformation Changes in Hybrid Alginate–Gelatin Hydrogel Particles. *Molecules* 2024, 29, 1254. <https://doi.org/10.3390/molecules29061254>
9. Espona-Noguera A., Ciriza J., Cañibano-Hernández A., Saenz Del Burgo L., Pedraz J.L. Immobilization of INS1E Insulin-Producing Cells Within Injectable Alginate Hydrogels. *Methods in molecular biology.* 2020, 395-405 .
10. Volpatti L.R., Bochenek M.A., Facklam A.L., Burns D.M., MacIsaac C., Morgart A., Walters B., Langer R., Anderson D.G. Partially Oxidized Alginate as a Biodegradable Carrier for Glucose-Responsive Insulin Delivery and Islet Cell Replacement Therapy. *Adv. Healthc. Mater.* 2023, 12, <https://doi.org/10.1002/adhm.202201822>
11. Kesharwani P., Bisht A., Alexander A., Dave V., and Sharma S. Biomedical applications of hydrogels in drug delivery system: an update. *J. Drug Deliv. Sci. Technol.* 2021, 66, 102914. <https://doi.org/10.1016/j.jddst.2021.102914>
12. Markand C., Vaishnav S., Khairnar V., Kale S. Advancements in Hydrogel-Based Drug Delivery Systems. *Int. J. of Pharm. Sci.*, 2024, 2, 4, 586-597. <https://doi.org/10.5281/zenodo.10968440>
13. Nichol J.W., Koshy S.T., Bae H., Hwang C.M., Yamanlar S., Khademhosseini A. Cell-laden microengineered gelatin methacrylate hydrogels. *Biomaterials.* 2010, 31, 5536-5544. <https://doi.org/10.1016/j.biomaterials.2010.03.064>

14. Duconseille A., Astruc T., Quintana N., Meersman F., Sante-Lhoutellier V. Gelatin structure and composition linked to hard capsule dissolution: A review. *Food Hydrocoll.* 2015, 43, 360 - 376. <https://doi.org/10.1016/j.foodhyd.2014.06.002>
15. Zhou Z., He S., Huang T., Peng C., Zhou H., Liu Q., Zeng W., Liu L., Huang H., Xiang L., Yan H. Preparation of gelatin/hyaluronic acid microspheres with different morphologies for drug delivery. *Polymer Bulletin.* 2015, 72, 713-723. <https://doi.org/10.1007/s00289-014-1295-z>
16. Musabekov K., Zhakyp B., Tazhibayeva S., Musabekov N., Yergaliyeva A. A research of colloidal silver immobilization in bionanocomposites of natural polymers and montmorillonite. *Eastern-European Journal of Enterprise Technologies.* 2020, 93-101. <https://doi.org/10.15587/1729-4061.2020.216995>
17. Depan D., Kumar A., Singh R. Cell proliferation and controlled drug release studies of nanohybrids based on chitosan-g-lactic acid and montmorillonite. *Acta Biomater.* 2009, 5, 93-100. <https://doi.org/10.1016/j.actbio.2008.08.007>
18. Cojocariu A., Porfire L., Cheaburu C., Vasile C. Chitosan/montmorillonite composites as matrices for prolonged delivery of some novel nitric oxide donor compounds based on theophylline and paracetamol. *Cell Chem Technol.* 2012, 46, 35-43.
19. Alboofetileh M., Rezaei M., Hosseini H., Abdollahi M. Effect of montmorillonite clay and biopolymer concentration on the physical and mechanical properties of alginate nanocomposite films. *J Food Eng.* 2013, 117, 26-33 <https://doi.org/10.1111/jfpp.12124>
20. Bello M.L., Junior A.M., Vieira B.A., Dias L.R., Sousa V.P., Castro H.C., Rodrigues C.R., Cabral L.M. Sodium montmorillonite/ amine-containing drugs complexes: new insights on intercalated drugs arrangement into layered carrier material. 2015, <https://doi.org/10.1371/journal.pone.0121110>
21. Sciascia L., Calabrese I., Cavallaro G., Merli M., Scialabba C., Liveri M.L.T. Modified Montmorillonite as Drug Delivery Agent for Enhancing Antibiotic Therapy. *Minerals.* 2021, 11, 1315. <https://doi.org/10.3390/min11121315>
22. Fatale S., Sonawane R.O., Montmorillonite: An advanced material with diverse pharmaceutical and medicinal applications. *Int. J. Biol. Macromol.* 2024, 264, 130543. <https://doi.org/10.1016/j.pharma.2024.11.001>
23. Asif A.H., Asha B.R., Prasanthi S. Montmorillonite in next-generation drug delivery: patent trends, safety insights, and industrial advancements. *J Mater Sci: Mater Med.* 2026, 75 <https://doi.org/10.1007/s10856-026-07031-4>
24. Cao J., Wu B., Yuan P., Liu Y., Hu C. Research Progress of Sodium Alginate-Based Hydrogels in Biomedical Engineering. *Gels* 2025, 11, 758. <https://doi.org/10.3390/gels11090758>
25. Guo Y.X., Liu J.H., Gates W.P., Zhou C.H. Organo-Modification of Montmorillonite. *Clays and Clay Minerals.* 2020, 68(6), 601-622. <https://doi.org/10.1007/s42860-020-00098-2>
26. Kubra A., Volkan U., Birol I., Fatih C. Adsorptive removal of crystal violet from wastewater using sodium alginate-gelatin-montmorillonite ternary composite microbeads. *International Journal of Biological Macromolecules.* 2022, 223, 543-554. <https://doi.org/10.1016/j.ijbiomac.2022.11.002>
27. Перцев Ф., Кузнецова Т., Гурский П., Перцев Н. Исследования ИК-спектров гелей желатина с добавлением составляющих компонентов продукта структурированного. *Maisto chemija ir technologija.* 2012, 46, 2, 29-37. <https://www.cabidigitallibrary.org/doi/pdf/10.5555/20133047074>
28. José M. Posada-Lotero, Maby M. Martínez-Garzón, Milton Rosero-Moreano, Francy N. Jiménez-García, Laura R. Giraldo-Torres, Daniel F. Hincapié-Rojas; Preparation and Characterization of Novel Hydroxyapatite/Montmorillonite/Gelatin-Based Composites with Bone Remineralizing Potential. *ACS Omega.* 2025, 10, 15, 15116-15128. <https://doi.org/10.1021/acsomega.4c10725>
29. Babić Radić M.M., Vukomanović M., Nikodinović-Runić J., Tomić S. Gelatin-/Alginate-Based Hydrogel Scaffolds Reinforced with TiO₂ Nanoparticles for Simultaneous Release of Allantoin, Caffeic Acid, and Quercetin as Multi-Target Wound Therapy Platform. *Pharmaceutics.* 2024, 16, 3, 372. <https://doi.org/10.3390/pharmaceutics16030372>
30. Cao J., Wu B., Yuan P., Liu Y., Hu C. Research Progress of Sodium Alginate-Based Hydrogels in Biomedical Engineering. *Gels.* 2025, 11, 758. <https://doi.org/10.3390/gels11090758>