Brief information about the project

Title	AP25795359 «Synthesis and characterization of gelatin derivatives with unsaturated anhydrides for the development of hydrogels intended for drug delivery and tissue engineering»
Relevance	Developing novel dosage forms based on gelatin with enhanced properties poses a significant challenge for the pharmaceutical industry. Gelatin, derived from collagen, is a natural polymer that has attracted considerable attention in biomedicine due to its high biocompatibility, solubility in aqueous solutions, and low immunogenic response. These attributes render gelatin particularly suitable for applications in tissue engineering and drug delivery systems. However, its mechanical strength and stability under physiological conditions are limited, which constrains its broader application. To address these limitations, various chemical modifications can enhance the functional properties of gelatin. One promising strategy involves the functionalisation of gelatin with unsaturated anhydrides, such as methacrylic, crotonic, and itaconic anhydrides. This approach not only improves the mechanical strength of gelatin derivatives but also enhances their potential for photopolymerisation, thereby facilitating the formation of three-dimensional hydrogel networks with tailored properties. Methacryloylated gelatin (gelatin-MA) has emerged as a focal point of research due to its ability to form hydrogels upon UV irradiation in the presence of photoinitiators. Additionally, gelatin inherently contains bioactive sequences, such as the arginine-glycine-aspartate (RGD) sequence, which promotes cell adhesion and migration within the matrix. The modification of gelatin with crotonic and itaconic anhydrides introduces additional functional groups, thereby opening new avenues for further enhancing its properties.
Goal	This project aims to synthesise and characterise methacryloylated, crotonoylated, and itaconoylated gelatin derivatives for developing hydrogels designed for drug delivery and tissue engineering applications.
Tasks	To achieve the project's main objective, the following tasks have been established: 1.Synthesis of methacryloylated, crotonoylated, and itaconoylated gelatin derivatives using methacrylic, crotonic, and itaconic anhydrides, respectively. 2.The structural investigation of the synthesised derivatives will employ infrared (IR) and nuclear magnetic resonance (NMR) spectroscopies. To determine the degrees of substitution, a colourimetric assay using 2,4,6-trinitrobenzenesulfonic acid (TNBS) will be utilized. Understanding these structural changes will enable predictions of the properties of modified gelatins and facilitate correlations with subsequent evaluations of their rheological characteristics. 3.The rheological properties will be investigated by determining melting and gelation points across temperature ranges of 0-40 °C (heating cycle) and 40-0 °C (cooling cycle), respectively. Isoelectric points will be assessed using dynamic light scattering (DLS) through electrophoretic mobility measurements. Additionally, the impact of pH on conformational changes will be analysed using a viscometric

	technique. These measurements are essential for understanding material behaviour in biomedical applications and will contribute to the characterisation of hydrogels. 4.Developing photocrosslinked hydrogels using methacryloylated, crotonoylated, and itaconoylated gelatin derivatives in the presence of a photoinitiator followed by UV light treatment. The physicochemical characteristics, including porosity, swelling degree, mechanical properties, and kinetics of model drug release from hydrogel matrices, will be systematically studied. These properties, influenced by earlier tasks, will inform the applicability of the hydrogels in drug delivery systems and tissue engineering. 5.The biocompatibility of methacryloylated, crotonoylated, and itaconoylated gelatin derivatives will be investigated through methodologies assessing cytotoxicity, cell migration, proliferation, and morphology. These evaluations will provide insight into the potential applications of the hydrogels in tissue engineering and will correlate directly with their physicochemical characteristics.
Expected and Achieved Results	Expected outcomes of the project implementation include the following: By 2025: Methacryloylated, crotonoylated, and itaconoylated gelatin derivatives will be synthesized using methacrylic, crotonic, and itaconic anhydrides, respectively. Structural characterization of the modified gelatin derivatives will be carried out to determine the degree of functional group substitution. For this purpose, infrared (IR) and nuclear magnetic resonance (NMR) spectroscopy, as well as quantitative analysis using 2,4,6-trinitrobenzenesulfonic acid (TNBS), will be employed. These techniques will provide a comprehensive understanding of the structural modifications occurring in gelatin molecules after chemical derivatization. By 2026: The rheological properties of the modified gelatin derivatives will be investigated, including determination of gelation and melting temperatures in the ranges of 0–40 °C and 40–0 °C, respectively. The isoelectric points will be determined by dynamic light scattering (DLS) based on electrophoretic mobility measurements. The influence of pH on the conformational structure of the modified gelatin will be studied using viscometry. Photocrosslinked hydrogels based on Gelatin-MA, Gelatin-CA, and Gelatin-IA will be developed using a photoinitiator and subsequent UV-induced crosslinking. One research article is expected to be published in a journal indexed in the Web of Science with an impact factor in the first three quartiles or in a journal indexed in Scopus with a CiteScore percentile of at least 50. By 2027: The physicochemical properties of the hydrogels will be evaluated, including porosity, swelling degree, and mechanical properties, as well as the drug release kinetics of a model compound from the hydrogel matrices. The biocompatibility of methacryloylated, crotonoylated, and itaconoylated gelatin derivatives will be assessed using standard methods for cytotoxicity, cell migration, proliferation, and morphology. One research article is expected to be published in a journal indexed in the Web of Science with an impact factor in the first three quartiles or in a journal indexed in Scopus with a CiteScore percentile of at least 50.

Names and Surnames of Research Group Members with Their Identifiers (Scopus Author ID, Researcher ID, ORCID, if available) and Links to Corresponding Profiles	1. Shatabayeva Elvira, PhD. H-index in Scopus – 2, Scopus Author ID 57188923162, https://www.scopus.com/authid/detail.uri?authorId=57188923162. H-index in the Web of Science database – 2, Researcher ID R-3120-2018, ORCID 0000-0000-1915-35198, https://orcid.org/0000-0000-1915-35198. 2. Kaldybekov Daulet, PhD – H-index in Scopus – 11, Scopus Author ID 55975396000, https://www.scopus.com/authid/detail.uri?authorId=55975396000, H-index in the Web of Science database – 11, Researcher ID F-1321-2014, ORCID 0000-0002-7191-5465, https://orcid.org/0000-0002-7191-5465

Publications list with links to them	**1. Shatabayeva E.O., Kaldybekov D.B.**, Kenessova Z.A., Tuleyeva R.N., Kudaibergenov S.E., Khutoryanskiy V.V. Development of Mucoadhesive Vaginal Films for Metronidazole Delivery Using Methacryloylated, Crotonoylated, and Itaconoylated Gelatin Blends with Poly(vinyl alcohol) // AAPS PharmSciTech, 26(2):63, 2025 (**Q2**). *https://link.springer.com/article/10.1208/s12249-025-03055-1.*
	2. **Shatabayeva E.O., Kaldybekov D.B.**, Ulmanova L., Zhaisanbayeva B.A., Mun E.A., Kenessova Z.A., Kudaibergenov S.E., Khutoryanskiy V.V. Enhancing Mucoadhesive Properties of Gelatin through Chemical Modification with Unsaturated Anhydrides // Biomacromolecules. American Chemical Society, 25(3), 1612–1628, 2024 (**Q1**). *https://doi.org/10.1021/acs.biomac.3c01183*.
	3. **Shatabayeva E.O., Kaldybekov D.B.**, Tuleyeva R.N., Irmukhametova G.S., Polatkhan A.A., Khutoryanskiy V.V. Development and Investigation of Mucoadhesive Polymers Based on Chitosan for Intravesical Therapy // Eurasian Journal of Chemistry, 29 (4 (116), 13–21, 2024. *https://doi.org/10.31489/2959-0663/4-24-2*.
	4. **Shatabayeva, E.O.,** Mun, G.A., Shaikhutdinov, Y.M., Khutoryanskiy, V.V. Gelatin: sources, preparation and application in food and biomedicine // Chemical Bulletin of Kazakh National University, 98(3), 28-46, 2020. *https://doi.org/https://doi.org/10.15328/cb1112*.
	5. Kadyrzhan K., **Kaldybekov D.,** Baipakbaeva S.; Vitulyova Y., Matrassulova D., Suleimenov I. Electronic Fourier–Galois Spectrum Analyzer for the Field GF(31) // *Applied Sciences*, 14(17), 7770 **(2024). (IF=2.5; Web of Science – Q1; Scopus CiteScore процентиль – 79)** https://doi.org/10.3390/app14177770
	6. Tatykhanova G.S., Tuleyeva R.N., Nurakhmetova Zh.A., Gizatullina N.N., Krasnoshtanov V.K., **Kaldybekov D.B.,** Aseyev V.O., Khutoryanskiy V.V., Kudaibergenov S.E. Polymer-protected gold nanoparticles for photothermal treatment of Ehrlich adenocarcinoma: *In vitro* and *in vivo* studies // *Macromolecular Chemistry and Physics,* 2400128 **(2024). (IF=2.5; Web of Science – Q3; Scopus CiteScore процентиль – 61)** https://doi.org/10.1002/macp.202400128
	7. Suleimenov I.E., Baipakbayeva S.T., Mun G.A., **Kaldybekov D.B.,** Yermukhambetova B.B., Bakirov A.S. Analysis of phase transitions of thermoresponsive polymer based on N-vinylcaprolactam and 2-hydroxyethyl acrylate in solutions from the information theory point of view // *Eurasian*

	Chemico-Technological Journal, 26(2), 67–73 **(2024). (IF=0.5; Web of Science – Q4; Scopus CiteScore процентиль – 22)** https://doi.org/10.18321/ectj1609 8. Kudaibergenov S.E., Tatykhanova G.S., Gizatullina N.N., Tuleyeva R.N., **Kaldybekov D.B.,** Gussenov I.Sh., Berzhanova R.Zh., Mukasheva T.D., Vamvakaki M., Aseyev V.O., Khutoryanskiy V.V. Anionic polysaccharide-gellan as perspective polymer for potential application in medicine and oil recovery: A mini-review // *Uzbekistan Journal of Polymers,* 2(2), 39-56 **(2023)** http://uzpolymerjournal.com/articles/article.php?id=230205 9. Moiseev R.V., **Kaldybekov D.B.,** Filippov S.K., Radulescu A., Khutoryanskiy V.V. Maleimide-decorated PEGylated mucoadhesive liposomes for ocular drug delivery // *Langmuir,* 38, 13870-13879 **(2022). (IF=3.7; Web of Science – Q2; Scopus CiteScore процентиль – 78)** https://doi.org/10.1021/acs.langmuir.2c02086 10. Brotherton E.E., Neal T.J., **Kaldybekov D.B.,** Smallridge M.J., Khutoryanskiy V.V., Armes S.P. Aldehyde-functional thermoresponsive diblock copolymer worm gels exhibit strong mucoadhesion // *Chemical Science,* 13, 6888-6898 **(2022). (IF=7.6; Web of Science – Q1; Scopus CiteScore процентиль – 91)** https://doi.org/10.1039/D2SC02074B 11. Haddow P.J., da Silva M.A., **Kaldybekov, D.B.,** Dreiss C.A., Hoffman E., Hutter V., Khutoryanskiy V.V., Kirton S.B., Mahmoudi N., McAuley W.J., Cook M.T. Polymer architecture effects on poly(*N,N*-diethyl acrylamide)-*b*-poly(ethylene glycol)-*b*-poly(*N,N*-diethyl acrylamide) thermoreversible gels and their evaluation as a healthcare material // *Macromolecular Bioscience,* 22(3), 2100432 **(2021). (IF=4.4; Web of Science – Q1; Scopus CiteScore процентиль – 80)** https://doi.org/10.1002/mabi.202100432 12. Shan X., Aspinall S., **Kaldybekov D.B.,** Buang F., Williams A.C., Khutoryanskiy V.V. Synthesis and evaluation of methacrylated poly(2-ethyl-2-oxazoline) as a mucoadhesive polymer for nasal drug delivery // *ACS Applied Polymer Materials,* 3(11), 5882-5892 **(2021). (IF=4.4; Web of Science – Q1; Scopus CiteScore процентиль – 78)** https://doi.org/10.1021/acsapm.1c01097 13. Abilova G.K., **Kaldybekov D.B.,** Irmukhametova G.S., Kazybayeva D.S., Iskakbayeva Zh.A., Kudaibergenov S.E., Khutoryanskiy V.V. Chitosan/poly(2-ethyl-2-oxazoline) films with ciprofloxacin for application in vaginal drug deliver // *Materials,* 13(7), 1709 **(2020). (IF=3.1; Web of Science – Q2; Scopus CiteScore процентиль – 73)** http://dx.doi.org/10.3390/ma13071709 14. Agibayeva L.E., **Kaldybekov D.B.,** Porfiryeva N.N., Garipova V.R., Mangazbayeva R.A., Moustafine R.I., Semina I.I., Mun G.A., Kudaibergenov S.E., Khutoryanskiy V.V. Gellan gum and its methacrylated derivatives as *in situ* gelling mucoadhesive formulations of pilocarpine: *In vitro* and *in vivo* studies // *International Journal of Pharmaceutics,* 577, 119093 **(2020). (IF=5.3; Web of Science – Q1; Scopus CiteScore процентиль – 92)** https://doi.org/10.1016/j.ijpharm.2020.119093

	15. **Kaldybekov D.B.,** Filippov S.K., Radulescu A., Khutoryanskiy V.V. Maleimide-functionalised PLGA-PEG nanoparticles as mucoadhesive carriers for intravesical drug delivery // *European Journal of Pharmaceutics and Biopharmaceutics,* 143, 24-34 **(2019). (IF=4.4; Web of Science – Q1; Scopus CiteScore процентиль – 86)** https://doi.org/10.1016/j.ejpb.2019.08.007 16. Abilova G.K., **Kaldybekov D.B.,** Ozhmukhametova E.K., Saimova A.Zh., Kazybayeva D.S., Irmukhametova G.S., Khutoryanskiy V.V. Chitosan/poly(2-ethyl-2-oxazoline) films for ocular drug delivery: formulation, miscibility, *in vitro* and *in vivo* studies // *European Polymer Journal,* 116, 311-320 **(2019). (IF=5.8; Web of Science – Q1; Scopus CiteScore процентиль – 92)** https://doi.org/10.1016/j.eurpolymj.2019.04.016
Patent information	-