Brief information about the project

Title	AP19174425 Development of the composition and technology for obtaining gels containing extracts of Limonium gmelinii plants, their pilot production, standardization, study of biological safety and activity
Relevance	The acute situation of the coronavirus pandemic, which affected the whole world and Kazakhstan in 2020, significantly influenced the domestic pharmaceutical sector. According to the international analytical company "IQVIA", from January to December 2020, the pharmaceutical market of Kazakhstan increased by 20% in value and 15% in volume, and the positive growth dynamics also remained throughout 2021. Certainly, this trend is an important sign to direct the joint efforts of pharmaceutical manufacturers, research institutions and groups in the development and production of the domestic drugs. The President Kassym-Jomart Tokayev in his state of the nation address dated September 1, 2021, instructed to increase the share of medicines and medical devices of domestic production from the existing 17% to 50% by 2025. One of the solutions to this goal could be the use of national raw material resources due to the biodiversity and rich species composition of the flora of Kazakhstan. A rational approach to this problem will be the selection of the most promising plant species, taking into account their biological activity, resource availability, harvesting conditions, the degree of complexity of technological processes for obtaining herbal medicines based on them, as well as the economic and environmental feasibility of their introduction into medicine. All these criteria are met by the plants of *Limonium Mill* genus, presented by 18 species in the flora of Kazakhstan, with *Limonium gmelinii (L. gmelinii)* and *Limonium myrianthum* having industrial reserves; their production stock exceeds 54.4 thousand tons. They grow on saline lands, are characterized by fast growth and high productivity, therefore their natural reserves will maintain at the original level subject to the rules and norms of harvesting. The roots and aerial parts of *L. gmelinii* plants were introduced into the State Pharmacopoeia of the Republic of Kazakhstan (SP RK, 2008). **Practical significance.** The results of preclinical studies will be practically significant and can serve as basis for development of Clinical Trial Protocols with the subsequent integration of the proposed drugs into practical healthcare.
Goal	The aim of the project is development of the composition and technology for obtaining new effective preparations in the form of gels based on unique substances obtained from the roots and aerial parts of Limonium gmelinii plants, their pilot production, study of their biological safety and activity.

Tasks	*Task 1*. - harvesting the aerial part, roots of *L.gmelinii*, their preparation, determination of quality indicators; - obtaining substances (LS-1) from roots of *L.gmelinii* and substance (LS-2) from aerial parts. Standardization and development of substances; - determination of the optimal proportion of substances and carbomer-940 for formation of the pilot batches of gels (G-1, G-2), considering the minimum and maximum working volumes of technological equipment, determination of critical control point; - the compatibility and critical physicochemical properties studies of substances and excipients that affect the quality of gels (G-1, G-2), the establishment of optimum concentrations of gel ingredients. *Task 2*. - development of the composition and formulations of gels and modeling of the technology for the pilot production of gels, taking into account the minimum and maximum working volumes of process equipment, determining critical control points; - study of physicochemical and pharmacotechnical properties of gels; - organization and conduction of preclinical trials to study biosafety, anti-inflammatory and immunomodulatory activity of gels; - preparation and approval of gels preclinical testing report. *Task 3*. - pilot production of three batches of gels, validation, determination of quality indicators, determination of their stability during storage and shelf life; - periodic monitoring of quality indicators of gel samples placed on stability testing; - development and compilation of regulatory documentation for registration dossier for gels;
Expected and Achieved Results	**Expected Results.** The development of safe and effective gel-based immunotherapeutic drugs using *Limonium gmelinii*, an industrially significant, wild-growing medicinal plant adapted to stressful environmental conditions, holds great promise for addressing the pressing challenges of socio-economic and scientific-technological development in the Republic of Kazakhstan. The study of the biological safety, anti-inflammatory, and immunomodulatory activities of the gels will be conducted at the National Center for Biotechnology of the SC MES RK in accordance with the positive opinion of the Local Ethics Committee of the RSE "National Center for Biotechnology" of the SC MES RK. **Achieved Results.** Plant-based gel formulations for immunotherapy have been developed using *Limonium gmelinii*, a wild-growing medicinal plant of industrial relevance adapted to stress conditions. Interim studies of the biological safety, anti-inflammatory, and immunomodulatory activities of the gels were carried out at the National Center for Biotechnology of the SC MES RK, in accordance with the positive conclusion of the Local Ethics Committee of the RSE "National Center for Biotechnology" of the SC MES RK.

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Publications list with links to them	1. Kassymova D, Zhusupova G, Ogay V, Zhussupova A, Katragunta K, Avula B, Khan IA. Phytochemical Profiles and In Vitro Immunomodulatory Activities of Extracts Obtained from *Limonium gmelinii* Using Different Extraction Methods. Plants (Basel). 2023 Nov 29;12(23):4019. doi: 10.3390/plants12234019. 2. Kassymova, D., & Zhusupova, G. (2024). РАЗРАБОТКА И ОЦЕНКА ГЕЛЕЙ ДЛЯ МЕСТНОГО ПРИМЕНЕНИЯ С РАСТИТЕЛЬНЫМИ ЭКСТРАКТАМИ ИЗ РАСТЕНИЙ ВИДА LIMONIUM GMELINII. *Известия НАН РК. Серия химии и технологии*, (4), 75–93. https://doi.org/10.32014/2024.2518-1491.252 3. **In the process of publication: Manuscript ID:** molecules-3699878 **Title:** *Exploring the chemical composition and antimicrobial activity of extracts from the roots and aboveground parts of Limonium gmelinii* **Authors:** Dariya Kassymova, Francesco Cairone, Donatella Ambroselli, Rosa Lanzetta, Bruno Casciaro, Aizhan Zhussupova, Deborah Quaglio, Angela Casillo, Galiya E. Zhusupova*, Maria Michela Corsaro, Bruno Botta, Silvia Cammarone*, Maria Luisa Mangoni, Cinzia Ingallina, Francesca Ghirga **Received:** 29 May 2025 **Section:** Natural Products Chemistry https://www.mdpi.com/journal/molecules/sections/natural_products_chemistry **Special Issue:** *Bioactive Compounds from Roots, Stems, Leaves, Flowers, Fruits, and Seeds: 2nd Edition* https://www.mdpi.com/journal/molecules/special_issues/EW64A93T9I

Patent information	-