ANNOTATION

of the dissertation submitted for the degree of Doctor of Philosophy (PhD) in the educational program “8D05301 - "Chemistry"
by Amanzholkyzy Arailym
on the topic:
"Hydrogel forms of hydroxypropylmethylcellulose and bentonite clay based on plant extract *Tamarix Hispida*"

General description of the work. The dissertation is devoted to the development of hydrogel forms based on HPMC and its compositions with extracts from the plant *Tamarix Hispida*, obtained through ultrasonic treatment of the raw material; study of the anti-inflammatory and antioxidant activity of extracts, assessment of the physicochemical characteristics of polymer forms.

The work was carried out at the Department of Chemistry and Technology of Organic Substances, Natural Compounds and Polymers and the Research Institute of New Chemical Technologies and Materials of the Al-Farabi Kazakh National University.

The relevance of the work.

Among polysaccharide-based gel matrices, cellulose ether derivatives are favored due to the ability to obtain modified forms that allow variation in solubility, duration of action, and drug release. They are also widely available and accessible due to their derivation from various raw material sources. In the production of pharmaceutical materials, hydroxypropylmethylcellulose (HPMC), also known as hypromellose, is one of the most in-demand cellulose ethers used as a carrier, filler, and coating – especially in combination with plant-derived biologically active compounds (BACs) for their antibacterial, wound-healing, antimicrobial, mucoadhesive, anti-inflammatory, and antioxidant properties. Plants of the *Tamarix* genus from the *Tamaricaceae* family are a valuable source of various biologically active compounds, extracts and isolated compounds have demonstrated antioxidant, anti-amnesic, antimicrobial, antifungal, and cytotoxic activity. One of the important compatible and structure-enhancing components for polymer compositions is the inorganic polymer bentonite clay. The presence of large deposits and reserves of bentonite clay in Kazakhstan is an additional strong incentive for the development of organo-mineral hydrogels. Using extracts of *Tamarix Hispida* as an aqueous drug component in HPMC and its clay-based compositions allows for the development of hydrogels with the required physicochemical properties, making them suitable for widespread use in medicine and pharmacology.

The aim of the dissertation is to obtain new hydrogel forms based on hydroxypropylmethylcellulose (HPMC), bentonite clay and extract from aerial part of the *Tamarix Hispida Willd*.

To achieve the stated goal, the following **tasks** were formulated:

1. Obtaining extracts based on *Tamarix Hispida* using ultrasonic treatment. Determination of the optimal extraction conditions, as well as the quantitative and qualitative composition of the obtained extracts.

2. Determination of the antioxidant and anti-inflammatory activities of the extracts from the aerial part of *Tamarix Hispida.*

3. Preparation of hydrogels based on hydroxypropylmethylcellulose, bentonite clay and their composites with *THU-10* extracts.

4. Determination of physicochemical properties and study of rheological characteristics of the obtained hydrogels based on hydroxypropylmethylcellulose, bentonite clay and their composites with *THU-10* extracts.

The object of the study: Medicinal plant material - the aerial part of the plant of the species *Tamarix Hispida* of the genus *Tamaricaceae*, its extract (THU-10) and hydrogels of HPMC, bentonite clay with THU-10

The subject of the study: Selection of optimal conditions for obtaining an extract from the aerial part of the plant species *Tamarix Hispida* of the genus *Tamaricaceae* by the method of ultrasonic extraction. Obtaining hydrogel forms based on HPMC, bentonite clay and their composites with THU-10.

Research methods: titrimetric analysis, thin-layer chromatography (TLC), HPLC, liquid chromatography–mass spectrometry (LC-MS), UV-visible spectroscopy (UV-Vis), scanning electron microscopy (SEM). The antioxidant activity of the extracts was determined using the DPPH radical scavenging assay, providing insight into free radical neutralizing capacity. In vivo anti-inflammatory activity was assessed using the carrageenan-induced paw edema model in rats, with statistical comparison to standard anti-inflammatory drugs.

The scientific novelty of the thesis

For the first time, extracts from the above-ground part of the plant species *Tamarix Hispida* of the genus *Tamaricaceae* were obtained using the ultrasonic extraction method. The method of obtaining the extract by ultrasonic extraction was optimized. The anti-inflammatory and antioxidant activity of the hydroalcoholic extract from the above-ground part of the plant species *Tamarix Hispida* was established. They exhibit pronounced anti-inflammatory and antioxidant activity. The THU-10 extract demonstrates a similar level of DPPH radical inhibition with gallic acid standards and quercetin at concentrations of 400 μg/mL and higher (% DPPH inhibition 96,08±0,48). Hydrogels based on HPMC, Bentonite clay with an extract of water-ethanol extract from the above-ground part of the plant species *Tamarix Hispida* were obtained for the first time. Composite hydrogels with HPMC and Bentonite clay with THU-10 extract were also obtained.

The main provisions for the defence:

1. The optimal conditions for obtaining a water-alcohol extract from the aerial part of the *Tamarix Hispida* by ultrasonic extraction are time of extraction 25 minutes, a raw material-to-solvent ratio of 1:6, a temperature of 20-40°C, and an

ultrasound frequency of 35 kHz, which ensure the highest yield of biological active compounds.

2. Aqueous-ethanol extract from the aerial part of the *Tamarix Hispida* (THU-10) demonstrates pronounced anti-inflammatory and antioxidant activity. The THU-10 extract demonstrates a similar level of DPPH radical inhibition with gallic acid and quercetin standards at concentrations of 400 μg/mL and higher (% DPPH inhibition 96,08±0,48)

3. Based on the analysis of rheological properties, the optimal hydrogel compositions are: a hydrogel based on bentonite clay 25%; a hydrogel based on HPMC 2-4%; a composite hydrogel based on HPMC:BC 4% (7:3) with the addition of 1% THU-10 extract.

Theoretical significance of the work:

This study expands the scientific basis for the use of hydrogels based on cellulose ethers, in particular hydroxypropylmethylcellulose (HPMC), in the development of modern drug delivery systems. The work deepens the theoretical understanding of the action of plant bioactive compounds by exploiting their potential for integration with polymer matrices for therapeutic applications. The obtained results can serve as a basis for the creation of "smart" hydrogels capable of controlled and prolonged release of medicinal substances, which contributes to the development of biomedical materials science.

Practical significance of the study:

The study offers practical solutions for the development of advanced transdermal drug delivery systems using HPMC-based hydrogels with Tamarix Hispida extracts and bentonite clay. These hydrogels eliminate the key limitations of traditional biologically active compounds by increasing their stability, prolonging the therapeutic effect, biocompatibility, and economic availability, which is especially relevant for Kazakhstan due to its rich reserves of medical plants and bentonite clay. The resulting hydrogel dressings have potential for use in wound healing, local anesthesia, and infection control, indicating high promise for their integration into pharmaceutical practice.

Relation of the thesis with research and government programs:

The dissertation work was carried out within the framework of the grant funding for young scientists under the "Zhas Galym" project for 2024–2026 by the Science Committee of the Ministry of Science and Higher Education of the Republic of Kazakhstan, project No. AP22684531, titled "Development of hydrogel forms of plant extracts based on HPMC," under the priority area "The science of life and health".

The main results of the study:

1. Alcoholic extracts based on *Tamarix Hispida* were obtained using ultrasonic treatment. The optimal conditions for the extraction method using ultrasonic extraction were determined. By using the ultrasound method, the yield of components from plant raw materials increases by 3-4 times and the extraction time is significantly reduced

(from 48 hours to 30 minutes) with an emitted ultrasound power of 20 to 35 kHz. The quantitative and qualitative compositions of the obtained extracts were determined.

2. The biological activities of THU-10 were determined. Anti-inflammatory, antioxidant activities and cytotoxicity of the extracts were investigated. The THU-10 extract demonstrated a similar level of DPPH radical inhibition with gallic acid standards and quercetin at concentrations of 400 μg/mL and higher (% DPPH inhibition 96,08±0,48).

3. Hydrogels based on hydroxypropylmethylcellulose (HPMC), bentonite clay, and its composites with THU-10 extract at various concentrations and compositions were obtained.

4. The physicochemical and rheological characteristics of hydrogels based on HPMC, bentonite clay and its composites with THU-10 extract were determined, and the optimal compositions of hydrogels were determined: based on bentonite clay 25% with the addition of 1% THU-10 extract; based on HPMC 2-4% with 1% THU-10; composites based on HPMC:BC 4% (in a ratio of 7:3) with 1% THU-10.

The personal contribution of the author was to independently planning and carrying out the experimental part of the study, interpret and process the obtained data, and work with scientific consultants to resolve issues and discuss the results of the study.

1. Ultrasonic extraction of biologically active substances *Tamarix Hispida Willd* // Chemistry of plant materials (Direct participation in the collection of experimental data, processing and interpretation of results, preparation of the article);

2. Hydrogel Delivery Systems for Biological Active Substances: Properties and the Role of HPMC as a Carrier // the review article was published in the journal Molecules (analysis of literature data, collection of empirical data, publication of the article (first author));

3. **Materials of reports at scientific conferences and symposia (collection and description of experimental data, discussion of analysis results, preparation of materials**);

4. Method for obtaining extract from plant raw materials // Utility model patent, published by the RSE "National Institute of Intellectual Property" (Direct participation in the collection of experimental data, processing, and interpretation of the results).

Approbation of the work.

The results and key findings of the scientific work were presented at the following conferences:

5th International Conference on Chemical Investigation and Utilization of Natural Resources, Ulaanbaatar, Mongolia, October 14–15, 2021: "New polymer forms of Tamarixidin and their properties". XXXI Russian Youth Scientific Conference on Problems of Theoretical and Experimental Chemistry, Yekaterinburg, April 20–23, 2021: "Synthesis and study of the properties of polymer forms of Tamarixidin". Galissultanova A., Amanzholkyzy A., Abilov Zh. A. “Preparation and rheological

properties of HPMC gels" // International Chemistry and Chemical Technology Congress "XI International Congress of Birimzhanov" – Almaty, 2021. – P.142.

Publications.

Article in the journal "Chemistry of Plant Raw Material": "Ultrasonic Extraction of Biologically Active Substances from *Tamarix Hispida* Willd," 2021, No. 3, pp. 283–289. percentile – 23 (in the Scopus database), https://doi.org/10.14258/jcprm.2021038695.

Utility model patent, published by RSE "National Institute of Intellectual Property", 2022, No. 28: "Method for obtaining extract from plant raw material".

Article in the journal ***Molecules*** (Switzerland), which in 2024 was ranked in Q1 in the field of "Chemistry (miscellaneous)" with an SJR of 0.865 and a percentile of 80 (according to the Scopus database): "Hydrogel Delivery Systems for Biologically Active Substances: Properties and the Role of HPMC as a Carrier" *Molecules* **2025**, *30*(6), 1354, **https://doi.org/10.3390/molecules30061354**.

Volume and the structure of the thesis. The dissertation is presented in 121 pages of text and consists of an introduction, 3 chapters, a conclusion, 21 tables, 68 figures, and a list of references comprising 193 sources.

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