ANNOTATION

The dissertation work of Aishabibi Duisenbekkyzy Karzhaubayeva entitled «**Comparative pharmacognostic study of plants of the genus Saussurea L. and prospects for their application**», submitted for the degree of Doctor of Philosophy (PhD) in the educational program 8D10140 – Pharmacy

Relevance of the topic. The pharmaceutical industry of the Republic of Kazakhstan is developing; however, the majority of medicines and their substances are imported from foreign suppliers. According to 2021 data, about 86.9% of registered medicines in Kazakhstan are imported, while only 13.1% are produced domestically. Such significant dependence on imports represents a serious obstacle to ensuring pharmaceutical security and the stable supply of the population with high-quality medicines.Enhancing the production potential of domestic products, the effective use of local plant raw material resources, and the intensification of scientific research have become urgent tasks. The flora of Kazakhstan comprises more than 6,000 plant species, among which hundreds possess medicinal properties. However, many of them have not yet undergone comprehensive phytochemical and pharmacological analysis, which indicates the necessity of improving research efforts.

In this regard, the "Comprehensive plan for the development of the pharmaceutical and medical industry for 2020–2025" was adopted, in which import substitution and the increase of domestic production volumes were defined as strategic priorities.

In the flora of Kazakhstan, 41 species of plants of the genus Saussurea L. are found, of which 9 species are widely distributed in the high-mountain areas of the southern regions, in particular in the Tolebi, Kazygurt, and Baydibek districts of Turkistan region. Although some of these species have been traditionally used in folk medicine, their morphological-anatomical, phytochemical, and pharmacological characteristics are still insufficiently studied from a scientific perspective.

In-depth scientific research of Saussurea species growing in our country is an important and relevant task for assessing the potential of domestic medicinal plant raw materials and developing new phytopreparations of natural origin. Such studies can make a significant contribution to replacing imported substances in pharmaceutical production, increasing the availability of domestic products, and improving public health.

Research aim: A comparative pharmacognostic study of plants of the genus Saussurea L. and the scientific substantiation of their potential use in medicine.

Research objectives:

1. Identification of the authenticity of *Saussurea sordida* Kar. & Kir. and *Saussurea alpina* (L.) DC. herbs (macroscopic and microscopic analysis).

2. Determination of quantitative indicators of *Saussurea sordida* Kar. & Kir. and *Saussurea alpina* (L.) DC. herbs (determination of moisture content, total ash, ash insoluble in 10% hydrochloric acid, particle size distribution, and content of impurities).

3. Extraction of *Saussurea sordida* Kar. & Kir. and *Saussurea alpina* (L.) DC. herbs using various solvents, followed by qualitative analysis of biologically active substances and determination of their quantitative content.

4. Determination of acute and chronic toxicity of the total complexes isolated from *Saussurea sordida Kar. & Kir.* and *Saussurea alpina* (L.) DC. herbs, as well as evaluation of their biological activity.

Research objects: The aerial parts of Saussurea sordida and Saussurea alpina were used as research objects. The herb of Saussurea sordida was collected in august 2022 during the flowering period in the foothills near the village of Keregetas, Kaskasu rural district, Turkestan region (geographical coordinates: N 42°12’10”, E 70°12’30”). The herb of Saussurea alpina was collected in august 2022 during the flowering period in the territory of the Sayram-Ugam National Nature Park, Turkestan region (geographical coordinates: N 42°30’19”, E 69°77’03”).

Research methods: Morphological and anatomical studies of Saussurea sordida and Saussurea alpina were carried out in accordance with the standard methodology of the State Pharmacopoeia of the Republic of Kazakhstan. Examination of sections and microphotography were performed using a MEIJI Techno “MT300L” microscope (Japan) equipped with a digital camera (magnification ×40, ×100, ×400, ×1000).

The qualitative composition of biologically active compounds in the plant material was determined using modern phytochemical analysis methods.

For the isolation and determination of biologically active compounds, the following methods were applied: extraction, chromatography (TLC, HPLC, GC-MS), and spectral methods of analysis (spectrophotometry, IR spectroscopy, atomic absorption spectroscopy).

Pharmacological activity, as well as acute and chronic toxicity, were evaluated through preclinical studies (in vivo methods).

Statistical data processing was carried out using the STATISTICA software (Version 6–10, StatSoft Inc., USA) and the StatPlus 7.0 application software package.

Scientific novelty of the study. This research focused on promising species of the genus Saussurea L. growing in southern Kazakhstan with the aim of their potential utilization and substitution of imported medicinal plant raw materials in the Republic of Kazakhstan. The plants *Saussurea sordida* and *Saussurea alpina* had not been previously studied in the territory of the Republic of Kazakhstan; the research was conducted for the first time. The medicinal plant raw materials were processed to meet standard conditions, and a draft temporary analytical regulatory document for the plant raw material was developed.

Practical significance. As a result of scientific research, the main groups of biologically active substances were identified. The phytochemical composition of Saussurea species growing in the southern part of Kazakhstan was studied, and the prospects for their use in medicine were scientifically substantiated. The acute and chronic toxicity of the obtained extracts was determined, and their low toxic effects were confirmed. Based on these data, the pharmacological activity of the plant material was evaluated, particularly its antioxidant and anti-inflammatory properties.

In order to enable further use of the raw material for medicinal purposes and to standardize quality indicators, a draft temporary analytical regulatory document was developed. The temporary analytical regulatory document for the promising medicinal plant material — the herb of Saussurea sordida — was implemented at the testing center of «BioEtica» LLP and at the production facility of «Zerde-Phyto» LLP.

The results of pharmacognostic and toxico-pharmacological studies of the plant material from Saussurea sordida and Saussurea alpina were integrated into the production process of «Zerde-Phyto» LLP. The research findings were also incorporated into the educational process and scientific research activities of the Department of Pharmacognosy at «South Kazakhstan medical academy» JSC as practical training material. The obtained results are protected by copyright, and two utility model patents (issued in July and December 2023) as well as a notification of invention based on a positive formal examination report (No. 2025/0150.1 dated 24.02.2025) have been obtained.

Key provisions submitted for defense:

- results of anatomical and morphological studies of *Saussurea sordida* and *Saussurea alpina* herbs;
- results of the determination of quantitative parameters of *Saussurea sordida* and *Saussurea alpina* herbs;
- results of the study of biologically active compounds in *Saussurea sordida* and *Saussurea alpina* herbs (qualitative and quantitative analysis);
- evaluation of *Saussurea sordida* herb as a promising medicinal plant raw material and development of a draft temporary analytical regulatory document for its implementation in pharmaceutical production;
- results of the determination of acute and chronic toxicity of the total complexes isolated from *Saussurea sordid*a and *Saussurea alpina* herbs (toxicological analysis);
- results of the evaluation of biological activity of the total complexes isolated from *Saussurea sordida* and *Saussurea alpina* herbs (pharmacological analysis).

Publications on the dissertation topic: Based on the results of the research, 18 scientific papers have been published, including: 1 article in an international peer-reviewed journal indexed in the Scopus database, 3 articles in journals recommended by the Committee for Quality Assurance in the Sphere of Science and Higher Education of the Ministry of Science and Higher Education of the Republic of Kazakhstan, 9 theses and articles in the proceedings of international scientific and practical conferences (Russia, Uzbekistan, Tajikistan), 2 patents for utility models, 3 certificates of registration in the State Register of Rights to Copyright-Protected Objects, and 1 patent application for an invention, which has received a positive decision on formal examination and is currently undergoing substantive examination.

Conclusion

Comprehensive studies have shown that the aerial parts of *Saussurea sordida* Kar. & Kir. and *Saussurea alpina* (L.) DC. represent biologically active and pharmacologically promising plant raw materials.

Morphological and anatomical studies made it possible to identify diagnostic features that ensure the authenticity and qualitative conformity of the plant raw material. The obtained data serve as a basis for distinguishing the two species and for carrying out pharmacognostic standardization.

During the determination of numerical indicators, it was established that the moisture content, total ash, amount of ash insoluble in 10% hydrochloric acid, degree of fragmentation, and proportion of foreign impurities in both species fully comply with the requirements of the State Pharmacopoeia of the Republic of Kazakhstan. The maximum yield of extractive substances was obtained using 70% ethyl alcohol.

Phytochemical analysis showed that both plants are rich in biologically active compounds. Qualitative and quantitative methods confirmed the presence of flavonoids, phenolic compounds, polysaccharides, amino acids, essential oils, and ascorbic acid. According to UV spectrophotometry, TLC, and HPLC data, the main flavonoids are rutin, quercetin, and naringin, while the phenolic compounds are represented mainly by gallic acid. It was found that *Saussurea alpina* contains more quercetin, whereas *Saussurea sordida* is richer in rutin and naringin.

According to gravimetric analysis, the polysaccharide content was 3.02% in *Saussurea sordida* and 2.462% in *Saussurea alpina*. The content of essential oils was 1.9% and 1.6%, respectively.

Gas chromatographic and mass spectrometric analyses revealed a wide spectrum of biologically active compounds, among which mono- and sesquiterpenes, as well as phenolic and fatty acid derivatives, predominated.

As a result of the study of the elemental composition of Saussurea sordida and Saussurea alpina it was found that these plants are rich in macro- and microelements, while the content of heavy metals does not exceed the permissible levels. The measurement results obtained in the radiological laboratory were within the natural background range. These plants are environmentally safe and biologically valuable medicinal raw materials.

Toxicological studies showed the absence of acute and chronic toxicity of the extracts of both plants. Histological analysis revealed no pathological changes in the organs of experimental animals, which indicates the biological safety of the studied samples.

The results of *in vitro* tests of antioxidant activity showed that the extract of *Saussurea sordida* exhibits higher activity compared to the extract of *Saussurea alpina*. The study of anti-inflammatory activity showed a weak effect in both plants; however, the absence of toxicity allows their consideration as auxiliary components of phytopreparations.

In general, the conducted research for the first time provided a comprehensive scientific characterization of the morphological, anatomical, and phytochemical features of *Saussurea sordida* and *Saussurea alpina*, substantiated their chemical composition, safety, and antioxidant activity. The obtained data make it possible to consider these species as promising raw materials for the production of pharmaceutical preparations and biologically active additives.

Comparative conclusion and prospective evaluation. As a result of morphological, anatomical, phytochemical, and pharmacological studies, both

similarities and differences between the herbs of *Saussurea sordida* and *Saussurea alpina* were identified. Morphologically and anatomically, both plants possess characteristic diagnostic features: *Saussurea alpina* is distinguished by pronounced glandular hairs, whereas *Saussurea sordida* has well-developed epidermal cells and conducting elements. According to numerical indicators, both species fully comply with the requirements of the State Pharmacopoeia of the Republic of Kazakhstan.

Phytochemical analysis confirmed the presence in both herbs of polysaccharides, flavonoids, phenolic compounds, alkaloids, sesquiterpene lactones, essential oils, and ascorbic acid.

The results of antioxidant activity assessment demonstrated the advantage of *Saussurea sordida*: the antioxidant content, recalculated to quercetin and gallic acid equivalents, was significantly higher than in *Saussurea alpina*. This indicates more pronounced anti-inflammatory and biologically active properties of this species.

Toxicological studies confirmed the absence of acute and chronic toxic effects in both plants, confirming their safety. At the same time, the anti-inflammatory activity of both species was found to be weak.

Thus, the comparative analysis showed that *Saussurea sordida* surpasses *Saussurea alpina* in terms of flavonoid and phenolic compound content, antioxidant activity, chromatographic and spectroscopic characteristics, as well as the absence of toxicity.

Consequently, *Saussurea sordida* is the more promising species in terms of the concentration of biologically active substances, the intensity of antioxidant action, and biological safety. The extracts of this plant can serve as a basis for the development of new phytopreparations with enhanced pharmacological efficacy.