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Түйін: «Глюконил®, қабықпен қапталған таблеткалар, 1000 мг» препаратының технологиялық процесінің валидациясы өткізілді. Процестің әрбір маңызды кезеңі үшін технологиялық процестің оңтайлы параметрлері анықталады, дәрілік препараттың қауіпсіздігі мен тиімділігіне әсер ететін бақыланатын сапа көрсеткіштерінің тізбесі және оларды қабылдау критерийлері белгіленеді, сынамалардың көрнекілігін қамтамасыз ететін іріктеудің ұтымды схемасы әзірленеді. Үш өнеркәсіптік валидациялық сериялардың өндіру кезінде алынған нәтижелер дәрілік препаратты сериядан сарияға дейін және дозаланған дәрілік нысанның әрбір бірлігі үшін өндіру процесінің тұрақтылығы мен сенімділігін дәлелдейді.
Түйінді сөздер: технологиялық процесінің валидациясы, қабылдау критерийлері, сынамалар алу, сапа көрсеткіштері, қабықпен қапталған таблеткаларды өндіру технологиясы.

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Resume. The technological process of the preparation «Gluconil®, coated tablets, 1000 mg» was validated. For each critical stage of the process, the optimal parameters of the technological process are determined, a list of controlled quality indicators affecting the safety and efficacy of the medicinal product, and the criteria for their acceptability are established, a rational scheme for sampling is developed, ensuring their representativeness. The results obtained in the production of three industrial validation batches prove the consistency and reliability of the production process of the medicinal product from batch to batch and for each unit of the dosage form.
Key words: process validation, acceptance criteria, sampling, quality indicators, technology for producing coated tablets.

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DEVELOPMENT OF TECHNOLOGY FOR COLLECTION, DRYING AND STORAGE OF MEDICINAL PLANT RAW MATERIALS OF FERULA ZAILIYSKAYA (FERULA TRANSILIENSIS)

Резюме: *The article presents the proper technology for the collection, processing, drying and storage of medicinal plant raw materials of the roots of the Ferula transiliensis. The optimal period for collecting roots - in early spring and late autumn, at the end of the growing season, was established by the research results. During this period, the maximum accumulation of essential oils in the organs of the plant occurs. It is recommended to dry the raw materials in the open air in the shade, without exposure to direct sunlight, or in dryers at a temperature not exceeding 40° C, and periodically turn them over.*
Storage conditions are established: temperature not higher than 25 ° C, humidity 50 ± 5%, in well-ventilated premises.
Key words: *medicinal plant raw materials, collection, drying, Ferula transiliensis, essential oils, gum, GACP (good agricultural and collection practices).*

Relevance. Medicinal plant materials are whole or coarsely crushed roots of Ferula transiliensis, harvested in early spring and late autumn, at the end of the growing season. [1].

Ferula transiliensis belongs to the species of perennial plants of the Ferula genus of the Apiaceae family. Taproot, thickened, the neck is woody, branched, the branches are short, shrouded in fibers and stalks of dead leaves. Stems, being several, 40-70 cm tall, round, smooth, like the leaves, glaucous and glabrous, slightly branching at the top. Basal leaves are collected in several petioles. Petioles are round, articulated near the plate, the latter is broadly rhombic in outline, repeatedly pinnately dissected into small lanceolate or lanceolate-ovate, thick, 3-10 mm long lobules, sometimes incised into several lobules. Stem leaves with a reduced plate are on lanceolate sheaths, the upper leaves without plates. Umbrellas are 10-18-rayed, without envelopes and with envelopes, unequal rayed, up to 8 cm long, spread apart, 0-20 flowered. The petals are 1mm long. Fruits

Table 1 - Dynamics of the accumulation of essential oil in the roots of Ferula transiliensis, depending on the phase of development, % Ferula transiliensis, depending on the development phase

No.	Series	Collection time	Plant development phase	Essential oil content, %
1	01 ES	10.04.2020	Early spring	0,60±2
	02 ES	11.04.2020		
	03 ES	12.04.2020		
2	01 BP	25.06.2020	Blooming period	0,50±2
	02 BP	26.06.2020		
	03 BP	27.06.2020		
3	01 LA	05.10.2020	Late autumn, at the end of the growing season	0,56±2
	02 LA	06.10.2020		
	03 LA	07.10.2020		

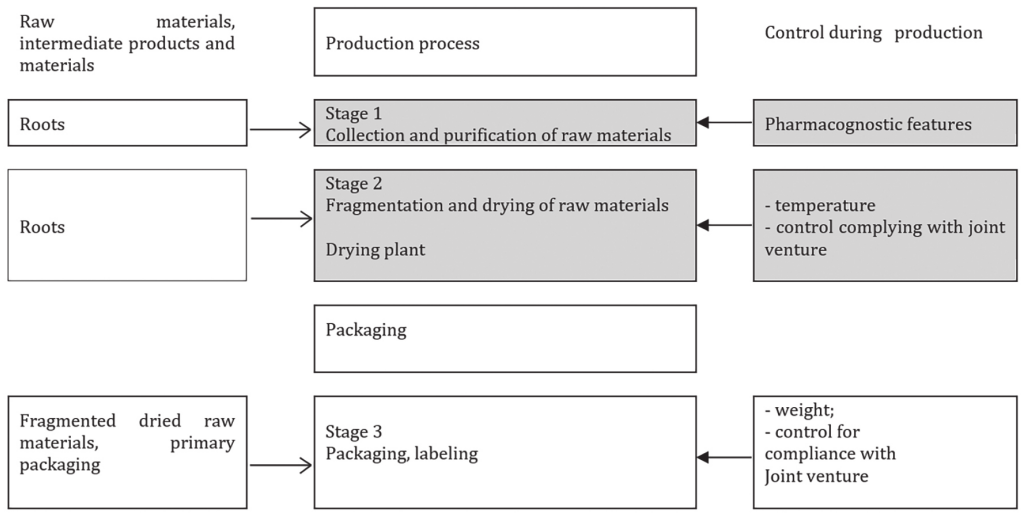
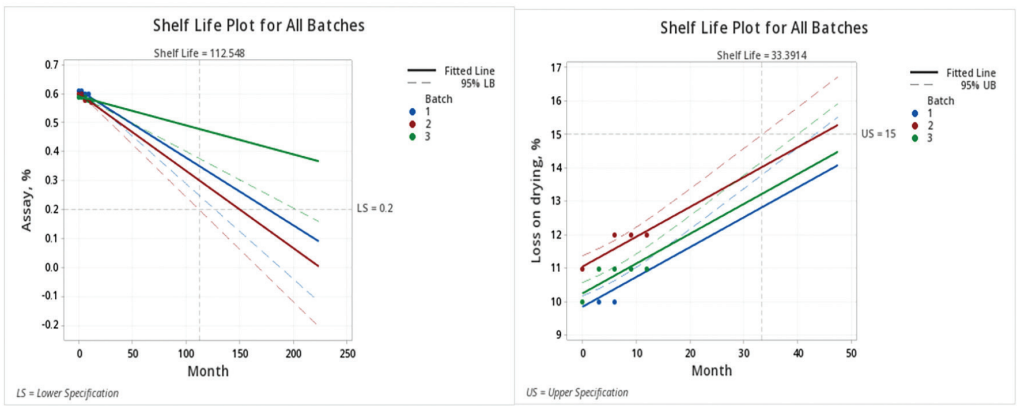


Figure 1 - Flow chart of collection, drying and storage of Ferula transiliensis roots



A B

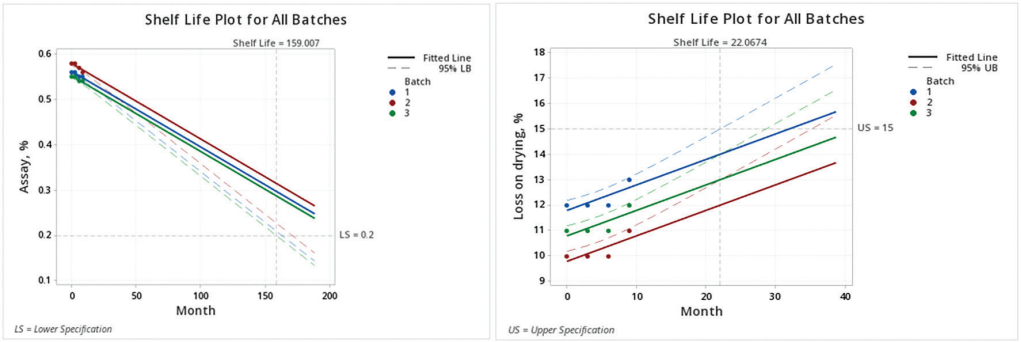
Figure 2 - Regression graphs of the stability of series 01ES, 02ES, 03ES: A) for the data of quantitative determination of essential oils and B) weight on drying

are elliptical, glaucous, 6-7 mm long, their dorsal ribs are filiform, barely protruding. The budding phase occurs from May to July, flowering - in July, fruiting - in August [2-5].

The plant contains essential oil (2.54–19.6%), flavonoids (2.44–2.88%), phenol carboxylic acids [6]. The massive roots contain aromatic resins, most of which are esters of ferulic acid and gum. The essential oil contains sulfur compounds, some terpenes, sesquiterpenes, coumarins, carboxylic acids (acetic and undecylic) and sulfanilic acid [7]. The pungent odor is due to the content of 2-butyl-1-propenyl disulfide and some other disulfides, which are destroyed during heat treatment [8, 9].

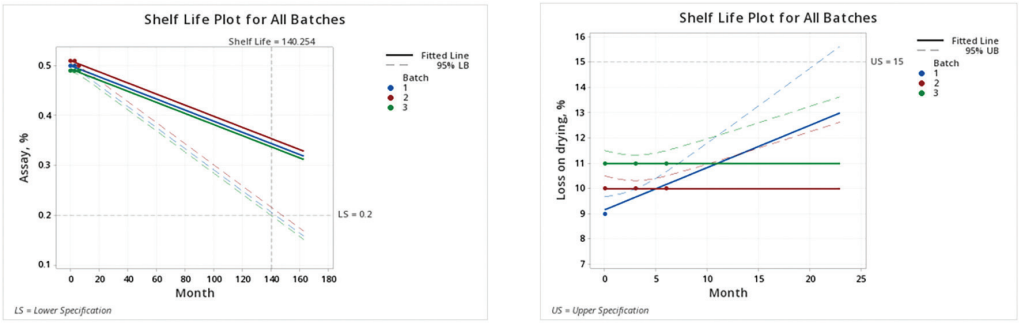
The distribution area is in Central Asia, Pamir-Alai. It grows mainly on rocks in the subalpine and alpine belts. In the Republic of Kazakhstan, it occurs in the Zailiyskiy, Dzhungarskiy Alatau, Tarbagatai, as well as in Kungei Alatau and the Western Tien Shan [2-5].

To ensure the quality of medicinal plant materials, the appropriate collection, post-harvest processing, drying and storage conditions are required.



A B

Figure 3 - Regression graphs of the stability of the 01LA, 02LA, 03LA series: A) for the data of the quantitative determination of essential oils and B) the mass upon drying



A B

Figure 4 - Regression graphs of the stability of series 01BP, 02BP, 03BP:
A) for the data of the quantitative determination of essential oils and B) mass upon drying

The study aims to develop a technology for collecting, processing after harvesting, drying and establishing the storage conditions for the roots of ferula Zailiyskaya of pharmacopoeial quality.

Materials and methods

The collection and procurement of medicinal plant materials for the roots of the Zailiyskiy ferula (Ferula transiliensis) were carried out following the Good Practice for the Collection of Medicinal Plants (GACP) in early spring and late autumn, at the end of the growing season on the mountain slopes of the Zailiyskiy Alatau tract, Almaty region. The organization of the collection of laboratory batch of medicinal plant products was carried out under the established standards for the collection of wild-growing medicinal species following Article 42 of the Forest Code of the Republic of Kazakhstan. The collection of raw materials was carried out in dry weather from 7:00 to 10:00. The plant was identified in the RSE at the Institute of Botany and Phytoniring of the Republic of Kazakhstan. The base of the experiment was "Fitoleum" LLP, Esik, the Republic of Kazakhstan.

Results and discussion

It is well known that the highest content of essential oils in a plant is in the morning, so the collection of roots was carried out in the morning from 7.00 to 10.00 h [10]. Table 1 shows the study of the content of essential oil in the roots of Ferula transiliensis, depending on the phase of plant development. It has been experimentally established that the maximum content of essential oil is observed in the raw material in early spring (0.60%) and late autumn, at the end of the growing season (0.56%). The optimal time for harvesting LRS on the mountain slopes of the Zailiyskiy Alatau tract has been determined.

Optimal technology for obtaining fragmented roots of Ferula transiliensis (Figure 1) has been developed. It consists of the following technological stages: collection, cleaning and fragmentation, drying and packaging (Figure 1). In dry weather, the roots were dug up with shovels from 7.00 to 10.00 in the morning. The dried aerial part was separated from the roots, the ground shook off and the remaining stems and leaves were cut off. Cleaning and further processing of materials were carried out in "FitOleum" LLP. The roots were washed with running water; if necessary, they were fragmented. Then they were dried in dryers at a temperature not higher than 40 ° C or in special conditions in the open air in the shade, without being exposed to direct sunlight. In the process of drying, the roots were periodically turned over. The collected raw materials were controlled by the following quality indicators: description (macro and microscopy); loss in mass on drying; total ash; ash, insoluble in 10% hydrochloric acid; heavy metals; foreign matters such as solid soil particles, dirt, dust, insects; residual moisture; essential oil content; Microbiological purity; radionuclides. The raw materials were packed in dark glass jars of 100 g each, a label was attached indicating the name of the raw material, the place of preparation, the time of collection and the net weight. Based on the presented technology, the following documents were developed: laboratory regulations, a draft analytical regulatory document, a quality specification for finished raw materials. Methods used in standardization have successfully passed validation tests.

The above series are put to long-term stability studies in primary packaging. The stability tests and the establishment of the shelf life of the dried fragmented roots of Ferula transiliensis were carried out

following national standards [link] for 6 months (01BP, 02BP, 03BP), 9 months (01LA, 02LA, 03LA), 12 months (series 01ES, 02ES, 03ES) under conditions of long-term tests.As part of the stability study, a stability specification for the medicinal product was developed using validated pharmacopoeial methods. It includes the following parameters: "Description", "Identification", "Impurities", "Weight loss on drying", "Quantitative determination" and "Microbiological purity" under test conditions: 25 ± 2 ° C and 50 ± 5% RH. The frequency of quality parameters control is 0, 3, 6, 9, 12 months depending on the start of the experiment.

Evaluation of stability and determination of shelf life was carried out with the Minitab program using regression analysis of dependence on storage time. The study used the data from nine series collected at different stages of plant development (three series each).

Figure 2 shows the regression graphs of the stability of the 01ES, 02ES, 03ES series for the data of the quantitative determination of essential oils and mass upon drying, Figure 3 - for the 01LA, 02LA, 03LA series, Figure 4 - for the 01BP, 02BP, 03BP series.

Intermediate results of long-term stability tests of medicinal plant raw materials showed that during the study period, the qualitative and quantitative composition of biologically active substances was within the regulatory limits. In addition, a preliminary storage period of 42 months was established using regression analysis of the data.

Conclusions. Technology has been developed for the collection, processing, drying and storage of plant materials of Ferula transiliensis roots complying with the principles of GACP. A technological scheme, laboratory regulations, a draft analytical normative document, and a stability report have been developed. Based on the studies carried out, technological and pharmacopoeial criteria for the quality of raw materials have been established. The obtained laboratory batches of medicinal plant materials in dark glass packaging were used to study the stability in real-time. Interim results of the study allow us to predict the conditional shelf life at a temperature of 25 ± 2 ° C and relative humidity of 50 ± 5% for 2 years.

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РАЗРАБОТКА ТЕХНОЛОГИИ СБОРА, СУШКИ И ХРАНЕНИЯ ЛЕКАРСТВЕННОГО РАСТИТЕЛЬНОГО СЫРЬЯ ФЕРУЛЫ ЗАИЛИЙСКОЙ (Ferula transiliensis)

Резюме: В статье представлена надлежащая технология сбора, обработки, сушки и хранения лекарственного растительного сырья корней ферулы заилийской (Ferula transiliensis). В соответствии с результатами исследований установлен оптимальный период сбора корней – ранней весной и поздней осенью, по окончании вегетационного периода. В данный период происходит максимальное накопление эфирных масел в органах растении. Рекомендовано производить сушку на открытом воздухе в тени, без воздействия прямых солнечных лучей или в сушилках при температуре не выше 40°С и периодически их переворачивая.

Установлены условия хранения: температура не выше 25°С, влажность 50±5%, в хорошо проветриваемом помещении.

Ключевые слова: Лекарственное растительное сырье, сбор, сушка, Ferula transiliensis, эфирные масла, камедь, GACP (good agricultural and collection practices).

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ІЛЕ ФЕРУЛАСЫНЫҢ (FERULA TRANSILIENSIS) ДӘРІЛІК ӨСІМДІК ШИКІЗАТЫН ЖИНАУ, КЕПТІРУ ЖӘНЕ САҚТАУ ТЕХНОЛОГИЯСЫН ӘЗІРЛЕУ

Түйін: Мақалада Іле ферула (Ferula transiliensis) тамырларының дәрілік өсімдік шикізатын жинау, өңдеу, кептіру және сақтаудың тиісті технологиясы келтірілген. Зерттеу нәтижелеріне сәйкес тамыр жинаудың оңтайлы кезеңі белгіленді – ерте көктемде және кеш күзде, вегетациялық кезеңнің соңында. Осы кезеңде өсімдік ағзаларында эфир майларының максималды жинақталуы байқалады. Ашық ауада көлеңкеде, күн сәулесінің тікелей әсерінсіз немесе кептіргіштерде 40 °С-тан аспайтын температурада кептіру және оларды мезгіл-мезгіл айналдыру ұсынылады. Сақтау шарттары анықталған: 25°С-тан аспайтын температурада, ылғалдылық 50±5%, жақсы желдетілетін бөлмеде.

Түйінді сөздер: Дәрілік өсімдік шикізаты, жинау, кептіру, Ferula transiliensis, эфир майлары, камедь, GACP (good agricultural and collection practices).