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PHARMACEUTICAL DEVELOPMENT OF THE COMPOSITION, PRODUCTION TECHNOLOGY AND STANDARDIZATION OF THE DRY EXTRACT FROM PLANTAGO MAJOR LEAVES (FOLIUM PLANTAGINIS MAJORIS)

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Annotation. *This scientific article, conducted on the basis of the Department of Pharmaceutical and Toxicological Chemistry of Asfendiyarov KazNMU, presents research on the development of an effective and standardized dry extract from Plantago major leaves with pronounced pharmacological activity. The work included selection and preparation of raw materials, optimization of extraction conditions for biologically active substances (flavonoids, polysaccharides, glycosides), as well as determination of qualitative and quantitative indicators of the finished dry extract. Standardization was carried out using physicochemical analysis methods, including determination of solids, tannins, sugars, and phenolic compounds. The developed extract is characterized by high stability, safety, and reproducibility of composition, making it promising for pharmaceutical practice.*

Key words: *large plantain, extract, standardization, flavonoids, polysaccharides, production technology.*

Relevance of the topic. The leaves of Plantago major contain valuable biologically active substances with anti-inflammatory, wound-healing, and antioxidant effects. The development of a standardized dry extract allows the creation of safe and effective pharmaceutical and biologically active preparations. With growing interest in plant-based medicines, optimizing technology for producing extracts ensuring high quality and reproducibility is essential.

Purpose of the study. To develop the composition, production technology, and standardization methods for dry extract from Plantago major leaves ensuring high quality and pharmacological activity.

Main objectives of the study:

1. To carry out the selection and preparation of Plantago major leaves as raw material for extraction.
2. To optimize the technological conditions for obtaining the dry extract (extraction method and solvent, temperature, duration).
3. To determine the content of the main biologically active substances (flavonoids, polysaccharides, sugars, glycosides).
4. To develop a standardization procedure for the extract based on qualitative and quantitative parameters.
5. To assess the stability and reproducibility of the composition of the final extract.

Scientific novelty. The scientific novelty lies in the development of an optimized method for extracting biologically active substances (BAS) from Plantago major leaves, ensuring maximum content of aucubin, acteoside/verbascoside, total phenols, flavonoids, and polysaccharides. For the first time, a systematic evaluation of extraction conditions (solvent, temperature, time, extraction method) and their effect on composition and biological activity was carried out. Modern spectrophotometric standardization methods were applied, ensuring high reproducibility and analytical accuracy. A technological scheme for scaling the process from laboratory to industrial level with minimal loss of active compounds is proposed.

Practical significance. The developed dry extract can be used as a standardized plant-based ingredient for dietary supplements, phytopreparations, and pharmaceutical products with confirmed concentrations of active substances.

Materials and methods. Fresh *Plantago major* leaves were dried and powdered. Extraction was performed using aqueous-alcoholic solvents under optimized temperature and time conditions. Flavonoid, polysaccharide, tannin, and sugar content was determined using physicochemical (spectrophotometric) methods. The finished extract was standardized for moisture, solids, and active compounds.

Results and discussion. The leaves of *Plantago major* are one of the primary medicinal plant raw materials used in medicine and pharmacy.

According to the description, the leaves of *Plantago major* are large, ovate-elliptical in shape (10–20 × 5–10 cm), with an entire margin, sometimes slightly wavy, and with prominent arcuate veins (usually 5–9), clearly visible on both sides. The petiole is relatively long; the leaf blade is fleshy and elastic. The upper surface is dark green and smooth; the lower surface is lighter. The leaves are sessile or with a short petiole and are arranged in a basal rosette. They possess a characteristic fresh odor and a slightly mucilaginous taste on the cut due to their mucilage content.

Anatomically, the leaves exhibit epidermal cells with sinuous walls, stomata predominantly of the anisocytic type, and a mesophyll differentiated into palisade and spongy parenchyma. The veins are well developed with vascular bundles surrounded by mechanical fibers. The leaves contain essential oils and simple unicellular trichomes or hairs with thickened walls.

Chemically, the leaves contain the indican glycoside aucubin (which hydrolyzes to glucose and aucubigenin), bitter and tannin substances, carotene, and 20.7–42.2 mg% of ascorbic acid, as well as a small amount of poorly studied alkaloids and vitamin K (1, 3). Fresh leaves contain 0.01–0.02% flavonoids (plantaginins and homoplantaginins), a high amount of the carbohydrate mannitol, 1.5% sorbitol, citric and oleanolic acids (11, 12). Seeds contain up to 44% mucilage, about 20% fatty oil, and 0.16–0.17% of the carbohydrate planteose.

A preparation produced from the aqueous extract of *Plantago major* L. leaves is used in the form of granules known as Plantaglucid. It is administered for the treatment of chronic hypoacid gastritis and peptic ulcer disease of the stomach and duodenum with normal or low acidity. Plantaglucid is used both during exacerbations and for the prevention of relapses. When taken orally, it exhibits spasmolytic and anti-inflammatory effects. It is contraindicated in hyperacid gastritis and peptic ulcer disease associated with increased gastric acidity. An infusion of the leaves is used as an expectorant, while the juice of fresh leaves is used as a bitter tonic.

Harvesting and storage are essential: the leaves are collected during the flowering period (June–August), dried in the shade at temperatures up to 40 °C, and stored in a dry, well-ventilated area for up to 2 years due to their essential-oil content.

The extraction and purification of biologically active substances (BAS) from the dry extract of *Plantago major* leaves consisted of the following processes: raw material preparation (collection of leaves, drying at 40–50 °C, and grinding to 2 mm), extraction (aqueous extraction: 1:10, 70 °C, 1–2 h — for determining polysaccharides and glycosides; alcoholic extraction (70% ethanol): 1:10, 24 h at room temperature — for flavonoids and phenolic compounds), followed by purification from ballast substances (filtration, optional centrifugation to remove solid particles—pigments, resins—on activated charcoal), concentration, and drying.

We have preliminarily developed a dry extract from the leaves of *Plantago major*, and the results are presented in Table 1.

Characteristics of the dry extract from *Plantago major* leaves (*Folium Plantaginis majoris*) according to quality parameters

Table 1.

№	Parameter	Standard / Characteristics	Method of Determination
1	Appearance	Powder from brownish-green to dark green	Organoleptic control
2	Odor	Characteristic herbal, pleasant	Organoleptic control

3	Taste	Bitter-sour	Organoleptic control
4	Moisture content	$\leq 7\%$	Drying to constant weight
5	Total ash	$\leq 8\%$	Sample incineration
6	Acid-insoluble ash	$\leq 2.5\%$	Incineration with HCl
7	Solubility	Well soluble in purified water, partially in alcohol	Practical assessment
8	Polysaccharides (main bioactive compounds)	$\geq 23\%$	Spectrophotometric method (phenol-sulfuric acid assay)
9	Flavonoids	$\geq 0.5-1\%$	Reaction with aluminum chloride, spectrophotometry
10	Iridoids (aucubin)	1%	TLC for identification
11	Phenolic compounds	Within pharmacopoeial limits	Spectrophotometric method
12	Reducing sugars	Within standard limits	Toluidine or sulfosalicylic test
13	Microbiological indicators	Absence of pathogenic microorganisms	Microbiological analysis
14	Heavy metals	Compliance with pharmacopoeial requirements	Atomic absorption spectroscopy

Qualitative detection of biologically active compounds in the dry extract of *Plantago major* leaves (*Folium Plantaginis majoris*)

Table 2.

№	Bioactive compound (BAC)	Reaction results
1	Flavonoids	1. Reaction with aluminum chloride (AlCl_3): yellow-green coloration appeared. 2. Shinoda test ($\text{Mg} + \text{HCl}$): after adding magnesium and hydrochloric acid to the alcoholic extract, a reddish-orange coloration was observed (alternatively $\text{Zn} + \text{conc. H}_2\text{SO}_4$).
2	Polysaccharides	1. Phenol-sulfuric acid reaction: characteristic color reaction occurred.
		2. Mucilage reaction: crushed leaves were mixed with cold water, shaken and infused for 5–10 min; a viscous, transparent, silky gel typical of <i>Plantago</i> formed.
		3. Molisch reaction: after adding 2 drops of α -naphthol and concentrated H_2SO_4 along the test tube wall, a violet-purple ring formed at the interface — positive for carbohydrates (polysaccharides).
		4. Benedict's test: heated aqueous extract with Benedict's reagent produced an orange-red precipitate (Cu_2O), indicating reducing sugars (glucose, fructose, maltose). 5. Reaction with 20% sulfosalicylic acid: after treatment (including hydrolysis), a precipitate formed — indicating sucrose.
3	Starch	Reaction with iodine/iodide solution: dark blue, then blackish coloration appeared.

4	Phenolic compounds	Reaction with 5% FeCl_3 produced a bluish-green coloration.
5	Tannins	Reaction with ferric chloride resulted in a dark blue coloration.
6	Saponins	Persistent foam formation after shaking with purified water.
7	Glycosides	Positive reactions with Fehling's reagent and Keller–Killiani test — reddish coloration appeared.
8	Alkaloids	Reactions with Mayer's or Dragendorff's reagent resulted in the formation of precipitates.

There are many methods for determining biologically active compounds in the dry extract of *Plantago major* leaves and in the plant raw material itself. In particular, the determination of sugars in the dry extract is carried out as follows: 2 g of dry powdered *Plantago major* leaves are mixed with 20 ml of 70% ethanol. The mixture is allowed to stand for 1.5 hours at room temperature or heated gently in a water bath. The extract is then filtered and used for analysis.

Another method is the phenol-based determination of glucose: 1 ml of the dry extract is mixed with 1 ml of 5% FeCl_3 solution and 5 ml of concentrated sulfuric acid. After 10–15 minutes, a yellow-orange coloration appears. The optical density is measured using a spectrophotometer at a wavelength of 490 nm in the visible region. The sugar concentration is determined using a calibration curve for glucose.

**Spectrophotometric determination of sugars in the dry extract of *Plantago major* leaves
(*Folium Plantaginis majoris*)**

Table 3.

Stage	Materials and Reagents	Equipment	Procedure	Results (approx., g/100 g dry extract)
1. Sample preparation	Dry extract of <i>Plantago major</i> leaves, purified water	Volumetric flasks, test tubes, pipettes	Weigh 0.1–0.5 g of dry extract. Dissolve in 15 ml of purified water, boil for 15 min. Cool and, if necessary, centrifuge. Dilute to 50 ml.	—
2. Determination of reducing sugars (Fehling / Somogyi–Nelson)	Fehling's or Somogyi–Nelson reagent, glucose standard	Water bath, spectrophotometer	Mix 1 ml of sample with 1 ml of reagent. Heat for 5–10 min. Cool. Measure optical density at $\lambda = 540$ nm. Calculate using the calibration curve.	2.5–6.0
3. Determination of total sugars (phenol–sulfuric acid method)	5% phenol solution, concentrated sulfuric acid,	Spectrophotometer	Mix 1 ml of sample with 1 ml of phenol. Quickly add 5 ml of sulfuric acid, mix. Cool. Measure at $\lambda =$	6.0–12.0

	glucose/sucrose standard		490 nm. Calculate using the calibration curve.	
4. Calculation of sugar content	—	—	Using the formula: $C = (D \times V \times 100) / (m \times a)$	—
5. Notes	—	—	Perform parallel determinations. If necessary, purify the extract from phenols and pigments.	—

Explanations for the formula:

C — sugar content in g/100 g of dry extract

D — optical density of the solution

V — total volume of the solution (ml)

m — mass of dry extract (g)

a — coefficient from the calibration curve

The technological scheme for the production of the dry extract from *Plantago major* leaves consists of the following stages: preparation of plant raw material (selection, sorting, washing, and drying in a drying chamber at 40–50 °C); followed by grinding (milling of the dried leaves into powder to improve extraction); extraction (soaking the powdered raw material in 70% ethanol, maceration, and filtration); concentration of the extract (removal of part of the solvent [water/ethanol] by vacuum evaporation or heating to 50–60 °C); drying; packaging and storage (at low humidity and a temperature of 15–25 °C).

Conclusion. In the course of our research, an optimized procedure for producing a dry extract from *Plantago major* leaves (*Folium Plantaginis majoris*) was developed. The process includes careful raw-material preparation, extraction of biologically active constituents, followed by concentration and drying. The analytical assessment demonstrated that the selected techniques ensure high preservation of the key biologically active compounds—polysaccharides, flavonoids, tannins, and organic acids—which is supported by the results of both qualitative and quantitative evaluations.

Standardization of the final extract was achieved by establishing a set of quality parameters such as identification of active constituents, quantification of total solids, and determination of sugar and microelement levels. It is important to emphasize that a comprehensive approach was applied to create a promising standardized dry extract, which holds significant scientific and practical value for its further medical use.

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