# DEVELOPMENT OF TECHNOLOGY OF PLANT SPECIES FOR COMPLEX MASTOPATHY THERAPY

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**Introduction.** Many years of experience of domestic phytochemical production does not diminish the urgency and importance of the problem of standardization and quality control of both phytopreparations and medicinal plant raw materials, which is the source of their production. The composition of biologically active substances (BAAs) contained in medicinal plant raw materials may vary during the process of plant growth, harvesting, drying and storage, transportation, method and apparatus to obtain them, so control of critical parameters at each stage is important and requires the use of new approaches.

Based on the concept of harmonization of the national legislative framework for quality control of medicinal products with the European Pharmacopoeia (EP), the relevant articles of the EP are used as a basic document in the development of the articles of the State Pharmacopoeia of Ukraine. The following general articles are listed in the General Monographs section of the EP: "Medicinal Herbal Products", "Medicinal Herbal Raw Materials" and "Medicinal Herbal Teas" [1].

Currently, in Ukraine, the quality of herbal remedies and raw materials is governed by the following general monographs of SPhU: "Medicinal Herbal Raw Materials", "Medicinal Herbal Remedies", "Medicinal Herbal Species$^{N}$", "Medicinal Herbal Teas", and "Medicinal Herbal Teas, Soluble" [2].

Manufacture of medicines in the European Union is carried out in accordance with the requirements of Good Manufacturing Practice (GMP). The quality of herbal medicinal products and their differences with medicinal products containing active substances with a defined chemical structure are set out in Directive 75/318 / EEC as amended.

At present, the range of medicines for the treatment of mastopathy is represented, for the most part, by foreign manufacturers, which are currently not economically available to the general population of Ukraine. The structure of the range of drugs used in mastopathy therapy by country of origin is shown in Fig. 1.

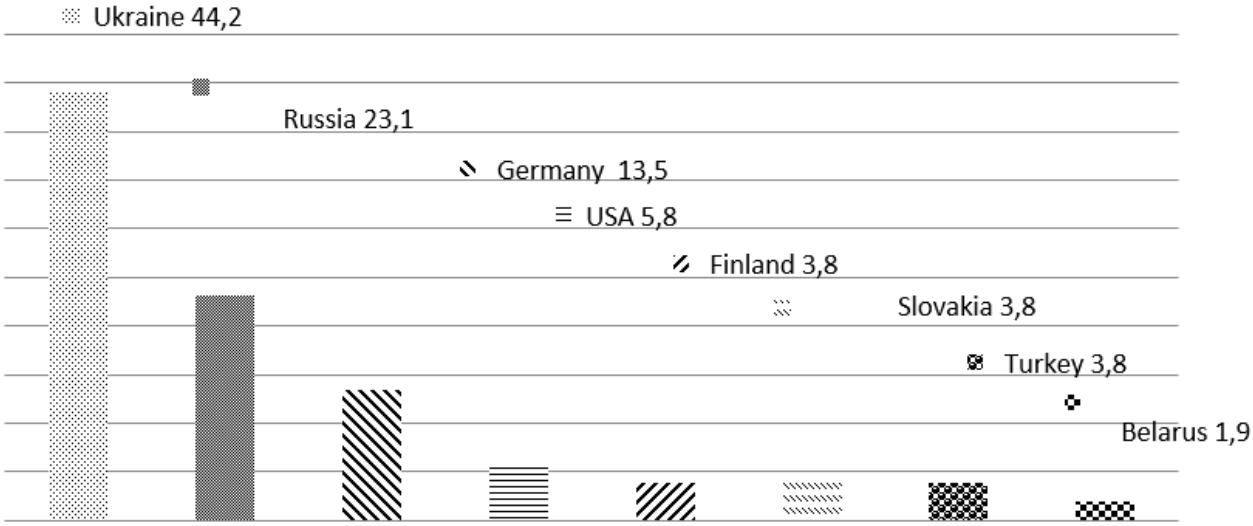


**Fig. 1. Market structure of medicines used in mastopathy therapy by country of origin**

Almost 44% of the assortment is domestic products. That is, drugs that provide both physical (availability at the place of sale of the drug) and economic affordability (the price of the drug suits the consumer) [3, 4].

Given the need to implement the principles of import substitution, the development of original domestic preparations based on medicinal herbs for the treatment of mastopathy is relevant.

The use of standardized drugs based on medicinal plant raw material (MPRM) will allow more comprehensive coverage of all links in the pathogenetic picture of mastopathy, reduce the dose of synthetic chemotherapy and pay more attention to quality rehabilitation of women, while maintaining their health and reproductive function [5, 6].

The importance of the above has led to the development of a new drug in the form of species for use in gynecology. Based on the results of pharmaco-technological, physicochemical, biopharmaceutical studies, the composition of the medicinal herbal product was selected. The development used medicinal plant raw materials, approved for medical use by the Ministry of Health of Ukraine and containing phytohormones - biologically active substances, capable of correcting the hormonal level - hop cones, parsley sowing leaves, stevia honey grass. Due to the multisymptomatic course of mastopathy, vitamins and raw materials were added to the collection, which strengthens the immune status of the organism: nettle leaves, common cranberries and dog rose hips. Excess of sex hormones has a negative impact, therefore, patients are usually prescribed hepatoprotectors, the purpose of which is to stimulate the function of hepatocytes and normalize intracellular

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metabolism of phospholipids. To improve the metabolism of hormones in the liver and excretion of products of their metabolism we used MPRM, which has a choleretic and diuretic effect: corn columns with receptacles, field horsetail grass [7, 8].

The pharmaceutical market of Ukraine has no analogues of standardized medicinal herbal species for complex treatment of mastopathy, but the available components have long been used in folk medicine [9].

**Material & methods.** According to the results of pharmacotechnological studies, a technological scheme for obtaining non-dosed and dosed species was developed (Figs. 2 – 3).

**Results & discussion. "**Mastonorm" species technology includes the following stages of the production process:
• Preparation of medicinal plant raw materials.
• Production of "Mastonorm" species.
• Filling, packing and marking of "Mastonorm" species.
• Filling, packing and labelling of "Mastonorm" species in filter bags

Only raw materials, packaging materials and printed matter that have been subjected to incoming quality control in accordance with the specifications of the input control and are allowed to use for the production of "Mastonorm". Stage 1 is carried out in the premises of weighing plant raw materials, which according to the technical regulations refer to unclassified with controlled parameters.

**Stage 1**
**Preparation of medicinal plant raw materials**

Plant raw materials used for the preparation of the drug must be subject to input control for compliance with regulatory requirements. After passing the input control, raw materials are given the status of "Permitted for use" and labelled with appropriate labels. Raw materials in bags or boxes are transported by means of transport carts from the stock of vegetable raw materials No. 1 to the premises of weighing of raw materials. Raw materials are viewed on the table. They reject mouldy raw materials, foreign objects, minerals (stones, earth, etc.) and organic (parts of plants of other species, pieces of rope, etc.) impurities. Discarded raw materials and impurities are collected in bags or plastic boxes (containers) for waste. The revised raw material is collected in bags or plastic boxes (containers) for raw material and weighed by weights according to the material balance of the batch in the following quantity:

On the bags / containers with weighed raw materials they affix identification labels, which indicate: the name of the preparation, batch, date, name of the raw material, quantity of raw material, shelf life, name and signature of the executor. With the transport trolleys, bags / containers of raw material are transferred for mixing to the Manufacturing room.

**Stage 2**
**Production of "Mastonorm" species**

Stage 2 is carried out in a room that is classified as unclassified one with controlled parameters. Before the start of stage 2, check the proper preparation of the premises, technological equipment, auxiliaries and materials (the presence of identification labels, preparation protocols) with an appropriate mark in the production protocol of the preparation.

Transportation of raw materials within the site is carried out by means of transport carts. The waste generated during Stage 2 is collected, accounted, stored and disposed.

Medicinal plant raw material is manually loaded into the mixer. After loading on the mixer attach the label "In Work" (on the label indicate: the name of the drug, batch, date, total amount of raw material, position, name and signature of the performer) and stir the raw material for 50 ± 5 min. The rotation speed of the mixer drum is 15 – 20 $min^{-1}$. Prepared unpacked "Mastonorm" species (a mixture of pieces of various shapes with inclusions of dark red in different shades, the smell is slightly aromatic) is unloaded by gravity into mobile collectors.

In weighing scales consistently, collectors weighed and verified the total weight of unpackaged species "Mastonorm". An identification label is affixed to each collector.

Collectors with the "Mastonorm" collection are handed over to the premises for packing the species for Stage 3 - the filling, packaging and marking of the "Mastonorm" species. The finished product series is formed from a single mixer load.

**Stage 3.**
**Filling, packing and marking of "Mastonorm" species**
*100.0 g species in plastic bags enclosed in cardboard packs;*
*100.0 g species per pack based on aluminum foil;*
*100.0 g species in "Doy-packs"*

Stage 3 is spent indoors species packing facilities that are classified as unclassified room with controlled parameters.

Before the start of stage 3, check the proper preparation of the premises, technological equipment, auxiliaries and materials (the presence of identification labels, preparation protocols) with a corresponding mark in the production protocol of the preparation.

Transportation of materials within the site is carried out by means of transport carts. Waste arising from the operations of Stage 3 is collected, accounted for, stored and disposed of in accordance with the enterprise standard.

**100.0 g species in plastic bags enclosed in cardboard packs**

*Species packing*

Medicinal plant raw materials used for the preparation of the drug must be subject to input control for compliance with regulatory requirements. After passing the input control, the materials are given a "Permitted to Use" status and labelled with appropriate labels. The primary packaging materials are delivered to the site from a stock of consumables.

Non-dosed species "Mastonorm" is manually packed into plastic bags of 100.0 g by weight. The collecting packs are sealed on the table with a pulse sealer. During the packing and sealing process, they visually check the appearance of the package and reject the packages with defects. The collection of discarded packages is returned for

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re-packaging into new plastic bags, and the damaged packages are placed in plastic waste bins (containers).

The sealed packets with "Mastonorm" species are transmitted through the transfer window to the table for the collection packing operation.

Remains of unused plastic bags are returned to the consumable warehouse and form the act of transfer. Discarded packets are transferred for further disposal and constitute an act of transfer.

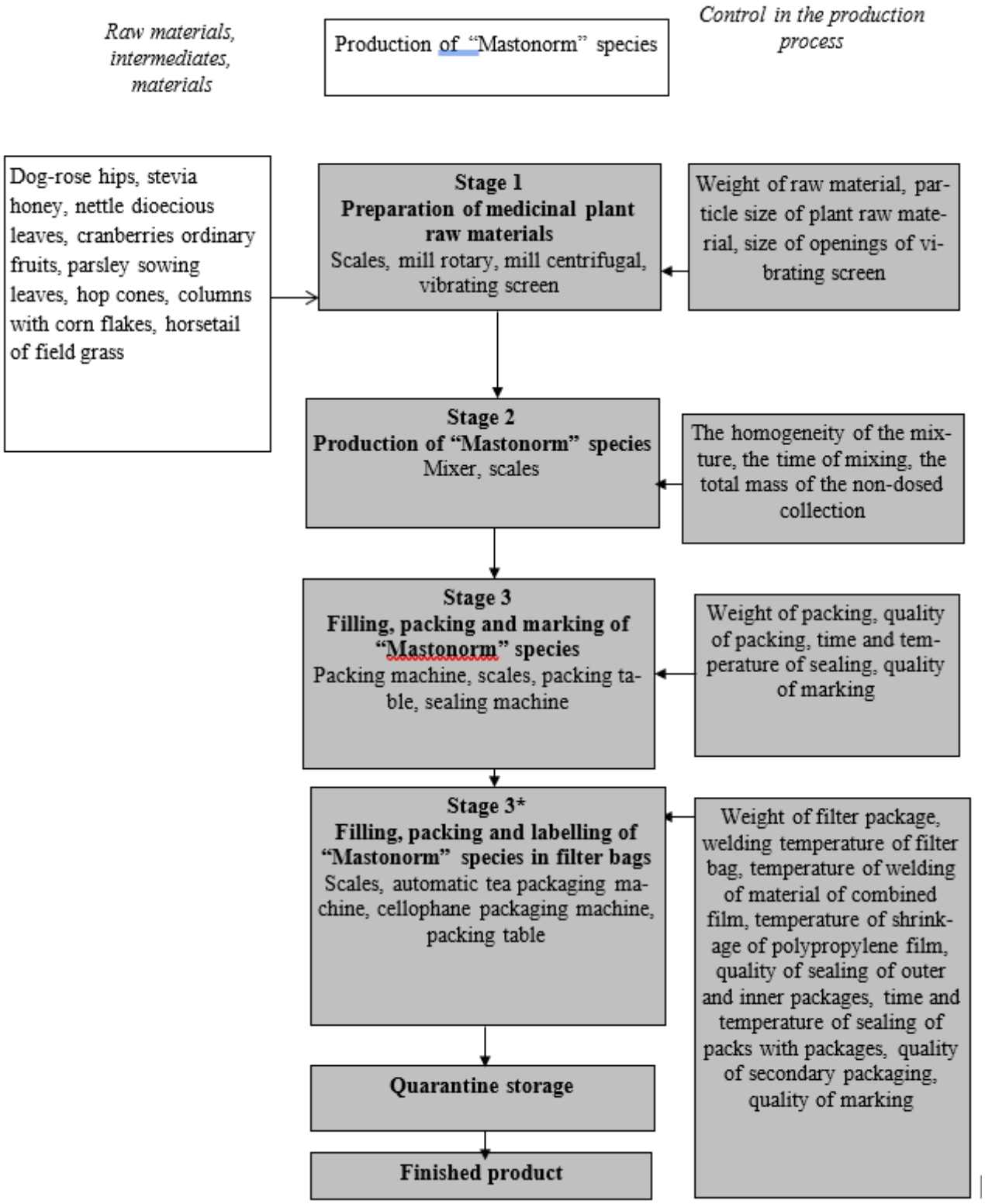


**Fig. 2. Technological schemes of receiving the «Mastonorm» species in aluminium foil packs, polyethylene and "Doypacks" and 1.5 g filter packs**

*Species packing and labelling* Materials for primary packaging (plastic bags),

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secondary packaging (packs of cardboard), group packaging (boxes of corrugated cardboard), sticker (logo) must be subject to input control for compliance with regulatory requirements. After passing the input control, the materials are given a "Permitted to Use" status and labelled with appropriate labels.

The secondary packaging material (packs of cardboard) is labelled with a batch number and a shelf life and sent to the site. Bulk packing materials (corrugated cardboard boxes and group labels), sticker (logo) are delivered to the site from a stock of consumables.

Before packing, the cardboard boxes and packs are inspected and manually collected on the table. Non-glued bundles, deformed bundles / boxes with defective prints are rejected. The discarded bundles are placed in plastic waste bins (containers) and the discarded bins are placed on pallets in the waste area. The collected packs are placed in plastic boxes (containers) for the collected packs, which together with the collected boxes are stored until the beginning of the packaging process in the area for prepared materials.

On the table, packaged species is manually loaded into packs of cardboard and on the upper valve of the pack in the centre, paste a sticker and logo of the enterprise. The upper and lower valves in the centre are glued with a narrow adhesive tape. The packs with species are stacked 48 pieces in boxes of corrugated cardboard and glued with a wide adhesive tape. Apply a group label of approved sample to the boxes. Boxes with finished product with the help of transport trolleys are transferred to the material gateway.

"Mastonorm" species is transferred from the material gateway to the warehouse of finished goods in the quarantine area. The drug series gives the status "Quarantine".

An average finished product sample is selected for analysis on compliance with the requirements of the QCP for "Mastonorm" species. After receiving positive results of the analysis of the batch of the drug are given the status of "Approved for sale" and transferred to the area of primary storage.

Finished products are stored in accordance with the enterprise standard. Remains of unmarked printed products are returned to the consumables warehouse and form the act of transfer. Discarded printed products and remnants of the labelled printed products are transferred for further disposal and constitute an act of transfer.

The following are only the features of species in other types of packaging.

**100.0 g species per pack based on aluminium foil**

*Species packing*

Un-dosed species "Mastonorm" is packed up to 100.0 g in a material combined film on the basis of aluminium foil by means of a packing machine. Before packing, and periodically during the shift, check the mass of the collection in the package by weighing 100 ± 4 g.

During the packing process, they visually check the appearance of the package: reject packages with defects and packages with fuzzy marking on the batch and shelf life. The sealed packets with "Mastonorm" species are transmitted through the transfer window to the table for operation - packing and marking species.

***100.0 g species in "Doy-packs"***

*Species packing*

Non-dosed species "Mastonorm" is packed up to 100.0 g in packages "Do-pack" by means of packing installation. Before packing, and periodically during the shift, check the mass of the species in the package by weighing 100 ± 4 g.

It is allowed to store the prepared raw material for not more than 48 hours in a special zone in the warehouse of medicinal plant raw materials No. 1, designated as the "Prepared Raw Material Zone", with an air humidity of not more than 60% and a temperature not exceeding 25 ° C.

**Stage 3***

**Filling, packing and labelling of "Mastonorm" species in filter bags**

The technology of manufacturing the "Mastonorm" species up to the stage of filling, packing and marking of the "Mastonorm" species in filter packages is carried out similarly to the production of a 100.0 dosage.

Preparation of process equipment for operation (scales, automatic packing machine, cellophane packing machine) and its operation are carried out in accordance with the requirements and provisions of the technical regulations and operating instructions.

Before the start of stage 4, check the proper preparation of the premises (absence of pre-production, documents and materials not required for the process), technological equipment, auxiliaries and materials, the presence of identification labels with a corresponding mark in the production protocol of the preparation.

*Species packing*

Primary packaging material (heat-sealing filter paper and aluminium foil film-based material) must be subject to input controls for compliance with regulatory requirements. After passing the input control, the material is given a "Permitted Use" status and labelled with appropriate labels.

The primary packaging material is delivered to the site from the consumable warehouse via a material gateway.

On the automatic tea packaging machine affix the label "In work" (the label indicates: the name of the drug, series, date, position, name and signature). The batch number and shelf life of the automatic tea packaging machine shall be determined in accordance with the instruction manual of the automatic tea packaging machine.

Non-dosed species "Mastonorm" is packed up to 1.5 g into filter bags from filter thermal welding paper, which is sealed into the material by a combined film based on aluminium foil on an automatic packaging machine. Before packing, and periodically during the change, check the mass of the collection in the package by weighing 1.5 ± 0.2 g.

During the packing process, the welding temperature of the filter paper (120 - 125 ° C) and the temperature of the welding of the combined film material (100 - 105 ° C) are monitored at least once per hour.

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At least once an hour visually check the quality of seam welding of the outer and inner packages, the presence of a cut on the outer package, the quality of the marking of the series and expiration date. Poor packages are rejected.

The collection of all discarded packages is collected in plastic boxes (containers) for collection unpacked and returned for re-packaging in new packages, and the damaged packages are placed in plastic boxes (containers) for waste. The discarded packets, after completion of the packing process, are transferred for further disposal and constitute an act of transfer. The remnants of the packaging material (filter paper, combined film material) are returned to the consumable warehouse and form the act of transfer.

The sealed packets with the "Mastonorm" species are transmitted through the transfer window to the table for operation - packing and marking the species.

*Species packing and labelling*

Secondary materials (cardboard packs and polypropylene film) and group packaging (corrugated cardboard boxes) must be subject to input controls for compliance with regulatory requirements. After passing the input control, the materials are given a "Permitted to use" status and labelled with appropriate labels.

The secondary packaging material (packs of cardboard) is labelled with a batch number and a shelf life and transmitted to the site via the material gateway.

Bulk packing materials (corrugated cardboard boxes and group labels) are delivered to the site from the consumables warehouse via a material gateway.

Before packing, cardboard boxes and boxes are examined and manually collected on the table. Badly glued bundles, deformed bundles / boxes, and bundles / boxes with defective prints are rejected. The discarded bundles are placed in plastic waste bins (containers) and the discarded bins are placed on pallets in the waste area. The collected packs are placed in plastic boxes (containers) for the collected packs, which together with the collected boxes are stored until the beginning of the process of packing in the area for prepared materials.

On the table, packaged species in packages, manually put in packs of cardboard for 20 pieces. Packs of packets are sealed in a polypropylene film using a cellophane packing machine. During the sealing process, the welding temperature (125 - 130 ° C) and the heat shrinkage temperature of the polypropylene film (120 - 125 ° C) are monitored, and the quality of the bundle sealing is visually checked.

On the table, packs wrapped in film are packed with 36 pieces in boxes of corrugated cardboard and glued with a wide adhesive tape. Apply a group label of the approved sample to the boxes. In Ukrainian, the country of origin, the city and name of the enterprise, its trademark and address, the name of the preparation in Latin and Ukrainian, the surname or number of the packer, the batch number, the number of packages shall be indicated. Boxes of finished product with the help of transport trolleys are transferred to the material gateway.

**Conclusions**

1. The technology of "Mastonorm" species was developed.
2. The technological scheme of obtaining "Mastonorm" species in industrial conditions was developed.
3. The technological industrial regulation of production of the "Mastonorm" species in different types of packing has been developed: plastic bag enclosed in cardboard packs; aluminium foil packs; "Doy-packs" and filter packages of 1.5 g № 20.

**Development of technology of plant species for complex mastopathy therapy**

**Zuikina S. S., Vyshnevska L. I.**

**Introduction.** At present, the range of medicines for the treatment of mastopathy is represented, for the most part, by foreign manufacturers, which are currently not economically available to the general population of Ukraine. Structure of the range of medicines used in mastopathy therapy, by country of origin. Almost 44% of the assortment is domestic products. That is, these drugs provide both physical (availability at the place of sale of the drug) and economic affordability (the price of the drug suits the consumer). Given the need to implement the principles of import substitution, the development of original domestic preparations based on medicinal herbs for the treatment of mastopathy is relevant. The use of standardized drugs based on medicinal plant raw materials (MPRM) will allow more comprehensive coverage of all pathogenetic mastopathy pathways, reduce the dosage of synthetic chemotherapy drugs, and pay more attention to the quality of women's rehabilitation while maintaining their health and reproductive function. The importance of the above has led to the development of a new drug in the form of collection for use in gynaecology, which includes various types of MPRM, capable of effectively acting on all the etiological and pathogenic links of mastopathy. The pharmaceutical market of Ukraine has no analogues of a standardized herbal remedy for complex treatment of mastopathy, but the available ingredients have long been used in folk medicine. **Material & methods.** Based on the results of pharmaco-technological studies, a technological scheme of obtaining non-dosed and dosed species for use in the complex treatment of mastopathy was developed. **Results & discussion.** The main stages of the process of collecting and the critical parameters that are monitored at each stage are identified. The technology of collecting in different types of packing is described: in aluminium foil packs, plastic bags and "Doy-packs" and filter bags.Vegetable raw materials used for the preparation of the drug must be subject to input control for compliance with regulatory requirements. "Mastonorm" species technology includes the following stages of the production process: preparation of medicinal plant raw materials, production of "Mastonorm" species, weighting, packaging and marking of the "Mastonorm" species. For dispensing, there is a step of filling, packing and labelling "Mastormorm" species into filter bags.

**Conclusion.** The technology of "Mastonorm" species was developed. The technological scheme of obtaining "Mastonorm" species in industrial conditions was developed. The technological industrial regulation of production of the "Mastonorm" species in different types of packing has been developed: plastic bag enclosed in cardboard packs; aluminium foil packs; "Doy-packs" and filter packages of 1.5 g № 20.

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**Key words:** technology, medicinal plant species, mastopathy.

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