Modern requirements for standardization breast fees, their components and medicines based on them

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Current requirements to the pectoral species, their components and medicinal preparation standardization

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SUMMARY

The growing demand for pharmaceutical substances of herbal origin and herbal medicinal preparations, as well as modern high requirements for the quality of medicines, necessitate improving approaches to their standardization. The purpose of this study was to study the state of regulatory documentation and methods for analyzing the authenticity, good quality and safety of the use of medicinal plant materials, collections and extracts based on them within the framework of end-to-end standardization. The paper considers the issues of the validity of the medical use of phytopreparations for the treatment of diseases of the upper respiratory tract (breast collection), in particular for breast collection No. 4, discusses the general principles of their use.

Key words: phytopreparations, breast collection No. 4, dry extract, standardization, pharmacological activity.

RESUME

A growing demand for herbal substances and preparations as well as high standards of quality in the development, manufacture and control of medicinal products requires a need to improve approaches of medicines standardization. The aim of the present study was to examine the requirements of the regulatory documentation and to analyze the methods of identification, safety, purity, and quality of herbal substances, species and their extracts. This paper investigate the medical use of herbal formulations (pectoral species, in particular pectoral species No. 4) for the treatment of upper respiratory tract infections from the perspective of evidence-based medicine, and the general principles of their use were discussed.

Keywords: herbal formulations, pectoral species No. 4, dry extract, standardization, pharmacological activity.

INTRODUCTION

According to the World Health Organization, the annual incidence of upper respiratory tract infections (URT) in the population is about 44%. Their etiological factors include: infectious agents (most often pneumococci, influenza bacillus, respiratory viruses), technogenic loads, allergens, comorbid conditions, especially in conditions of reduced immunity. Incorrectly selected antimicrobial therapy can contribute to the protracted nature of the disease, the development of complications and the chronicity of the process.

Along with antibiotic therapy, which often leads to a number of side effects (allergy, selection of resistance, dysbiosis, etc.), in medical practice, plant-based medicines are increasingly used as part of the complex therapy of infectious and inflammatory diseases of the bronchi or as an alternative drug. Phytopreparations are distinguished by low toxicity, the possibility of long-term use and relative affordability [1, 2].

According to the research company IMS Health, on the Russian pharmaceutical market there is a tendency to increase the volume of sales of phytopreparations [23]. Currently, about 7.8% of all registered medicinal products are herbal preparations and pharmaceutical substances of herbal origin (over 1.5 thousand names). The state register of medicines contains 410 trade names of herbal medicines. Of these, 46.8% are monopreparations (contain only one type of raw material) and 53.2% are combined forms (fees, finished herbal medicinal products), of which 1.0% are breast fees [5, 16].

Medicinal charges are mixtures of two or more types of medicinal plant raw materials (MPR) of various processing methods, possibly with the addition of substances of mineral, synthetic, plant and animal origin. They can be dosed or under-dosed and are available in single-dose or multi-dose packages [6]. When compiling multicomponent mixtures of plant origin, it is important: information about the etiology and pathogenesis of the disease, contraindications to the use of medicinal products, their composition of biologically active substances, use in traditional and folk medicine, as well as the optimal combination of collection components, taking into account the potentiation, synergism and antagonism of the pharmacological action [14] ...

The therapeutic effect of the charges is due to the complex action of individual components in the composition of mixtures of various medicinal plant materials (MPR), the mildness of the action and, as a rule, the absence of side effects with prolonged use.

The most popular medicinal fees for the prevention and treatment of infectious diseases of the upper respiratory tract are breast fees No. 1–4. They include well-known species of medicinal plant materials (coltsfoot leaves, oregano herb, licorice roots, etc.) (Table 1).

Table 1

Nomenclature and content of medicinal product included in the breast collection [15]

Chest fee number 1	Breast fee No. 2	Breast fee number 3	Chest fee number 4
- Marshmallow roots - 40%; - coltsfoot leaves - 40%; - oregano herb - 20%.	- coltsfoot leaves - 40%; - plantain big leaves - 30%; - licorice roots - 30%.	- licorice roots - 28%; - Marshmallow roots - 28.8%; - sage leaves - 14.4%; - anise ordinary fruit - 14.4%; - pine buds - 14.4%.	- chamomile flowers - 20%; - marsh wild rosemary shoots - 20%; - marigold flowers - 20%; - violets grass - 20%; - licorice roots - 15%; - peppermint leaves - 5 %.

The charges have anti-inflammatory, expectorant, antimicrobial effects, etc. due to the complex contained in them of various groups of biologically active substances (polysaccharides, saponins, essential oils, etc.) (Table 2). In particular, it is known that glycyrrhizin of licorice roots stimulates the activity of the ciliated epithelium in the trachea and bronchi, and also enhances the secretory function of the mucous membranes of the upper respiratory tract. In addition, licorice root has an antispasmodic effect on smooth muscles due to the content of flavone compounds, the most active of which is liquiditoside, and anti-inflammatory properties are provided to a greater extent by glycyrrhizic acid, which is released during the hydrolysis of glycyrrhizin. Undergoing metabolic transformations in the body, glycyrrhizic acid has a corticosteroid-like effect [19]. When choosing a collection, the individual characteristics of the patient and the presence of concomitant diseases, as well as the medications he takes, are taken into account. For example, calendula flowers are not recommended for use during pregnancy due to their stimulating effect on the muscles of the uterus, licorice roots -

simultaneously with antihypertensive, antiarrhythmic and hypolipdemic drugs (in the experiment, inhibition of CYP3A4 was observed, which can cause an increase in the concentration of calcium antagonists, statins, antihistamines, immunosuppressants) [4].

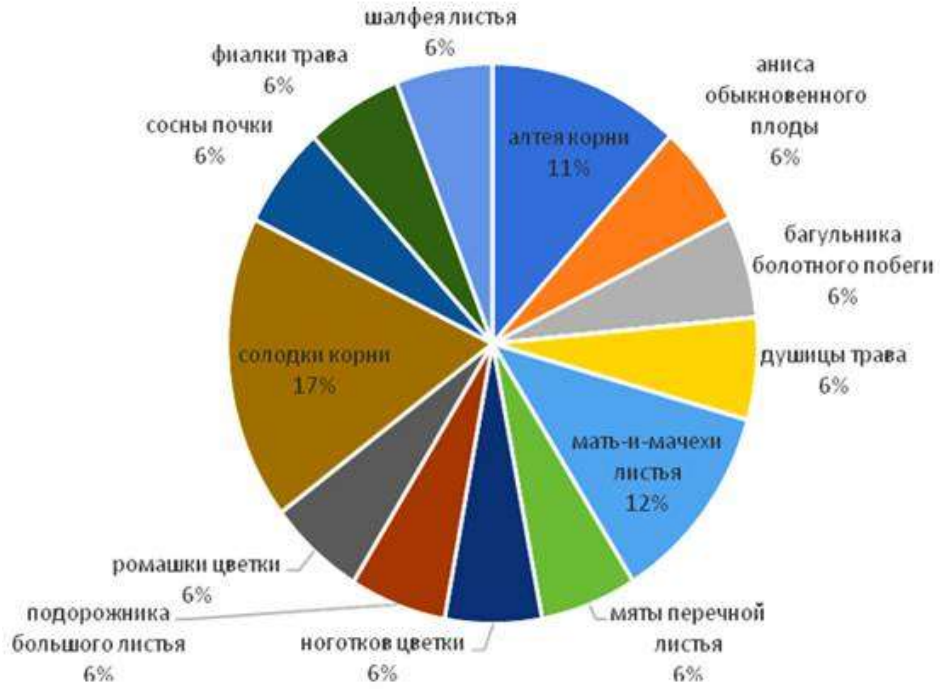

Fig 1. Relative occurrence of individual components in the composition of pharmacopoeial breast feeds.

The relative frequency of certain species of medicinal plant raw materials in collections varies in the range of 6–17% (Fig. 1). Most often, licorice roots are included in the composition of prescriptions for the treatment of URT diseases (occurrence - 17%). The most rational, from the point of view of the pharmacological effect, is the combination of types of medicinal plant raw materials in breast collection No. 4 (HS). In addition to expectorant and anti-inflammatory, the collection also has an antispasmodic effect due to the shoots of wild rosemary that are part of it [1]. In addition to its own pharmacological action, mint leaves are often added to the composition of many collections as a flavoring agent.

table 2

Chemical composition of components of breast collection No. 4 [1, 17, 24]

No. p / p	Name component	Biologically active substances	Pharmacological activity
1	Chamomile flowers	Essential oil (chamazulene, farnisene, myrcene); flavonoids (derivatives of apigenin, luteolin and quercetin); coumarins; sesquiterpene lactones; phenol carboxylic acids; organic acids; vitamin C; carotene, gums; polysaccharides.	Antispasmodic, anti-inflammatory, antiseptic, wound healing, diaphoretic, choleretic and mild analgesic effect
2	Marigold flowers	Carotenoids (β- and γ-carotenes, lycopene, flavoxanthin, etc.); saponins; flavonoids (isoquercetin, narcissin, rutin); essential oils; resin; coumarins; tannins.	Anti-inflammatory, antiseptic and choleretic action. Stimulates reparative processes in diseases of the gastrointestinal tract.
3	Rosemary shoots	Essential oil (iceol, palustrol, etc.); flavonoids; phenologlycosides (arbutin); tannins; coumarins; organic acids; resin.	Expectorant, anti-inflammatory, bactericidal, antitussive, antispasmodic
4	Violet herb	Flavonoids (rutin, vitexin, orientin); anthocyanins; salicylic acid; essential oil.	Expectorant anti-inflammatory action
5	Licorice roots	Saponins (glycyrrhizin), 27 flavonoids (liquiditin, isoliquiritin, lacrizide, etc.); polysaccharides; vitamin C; a small amount of essential oil; gums; resin.	Expectorant anti-inflammatory
6	Mint leaves	Essential oil (menthol); oleanolic and ursolic acids; flavonoids; carotenoids.	Antispasmodic

Among the herbal preparations presented on the domestic pharmaceutical market, breast collection No. 4 is the most popular and ranks second in the ranking in terms of the share of sales among other herbal remedies of Krasnogorskleksredstva JSC [22]. The collection was developed at the Department of Pharmacognosy of the Moscow Medical Academy. THEM. Sechenov (now Sechenov University) and introduced into the production of Krasnogorskleksredstva JSC. The experience of clinical practice is more than 20 years [1]. The collection includes 6 components: chamomile flowers, wild rosemary shoots, marigold flowers, violets grass 20% each, licorice roots 15% and mint leaves 5% [15].

The therapeutic effect of GS No. 4 is due to the antibacterial effect of chamomile and calendula flowers, wild rosemary shoots, the expectorant and enveloping effect of licorice roots, violet herb and wild rosemary shoots, anti-inflammatory and antispasmodic effects of chamomile and calendula flowers, licorice roots, and 18 mint leaves.

The efficacy and safety of individual components of the collection has been studied in several works, which, of course, is important in accordance with the principles of evidence-based medicine. Since the criteria for the effectiveness of herbal and synthetic drugs are the same, the best way to prove the validity of the use of herbal remedies is randomized controlled or observational clinical trials. Among such works is a randomized, double-blind, placebo-controlled study of licorice roots, during which their anti-inflammatory activity was proved. At the moment, only a small

some of the thousands of medicinal plants used have been studied from the point of view of evidence-based medicine, therefore, research in this area should be continued in order to expand the indications for the use of existing drugs and accumulate material for inclusion in the national formulary of herbal remedies [20, 21].

However, the disadvantages of fees include the incompleteness of the dosage form and inaccurate dosing [1, 12, 18]. In this regard, there are problems in the standardization and quality control of plant collections, since the quantitative assessment of phytopreparations by the amount of substances does not give an accurate idea of the percentage of each of the components that make up the medicinal plant mixture. Therefore, at the present stage of the development of medicine and pharmacy, it is important to improve the methods of standardization of multicomponent herbal mixtures using unified techniques. The dosage form that the patient takes is, in most cases, an infusion and decoction. The production of aqueous extracts of charges does not fundamentally differ from their production from individual medicinal plants (the method of application and doses are indicated on the packaging, in the description of the collection, as a rule, the ratio of raw material and extractant is: 1-2 tablespoons of the mixture per 200 ml of water). The resulting extracts are stored in the refrigerator for no more than two days to avoid microbial contamination. During storage, the charges can stratify, which leads to instability of the content of biologically active substances in the drug dose. The lack of precise clear criteria for quality control, instability during storage, and inaccurate dosing create the need to transfer plant fees to a more rational DF to obtain standardized aqueous extracts, which are dry extracts [1, 18]. Dry extracts are concentrated extracts from medicinal plant raw materials. Their undoubted advantages are: ease of use, storage stability, the possibility of more accurate dosing. 1-2 tablespoons of the mixture per 200 ml of water). The resulting extracts are stored in the refrigerator for no more than two days to avoid microbial contamination. During storage, the charges can stratify, which leads to instability of the content of biologically active substances in the drug dose. The lack of precise clear criteria for quality control, instability during storage, and inaccurate dosing create the need to transfer plant fees to a more rational DF to obtain standardized aqueous extracts, which are dry extracts [1, 18]. Dry extracts are concentrated extracts from medicinal plant raw materials. Their undoubted advantages are: ease of use, storage stability, the possibility of more accurate dosing. 1-2 tablespoons of the mixture per 200 ml of water). The resulting extracts are stored in the refrigerator for no more than two days to avoid microbial contamination. During storage, the charges can stratify, which leads to instability of the content of biologically active substances in the drug dose. The lack of precise clear criteria for quality control, instability during storage, and inaccurate dosing create the need to transfer plant fees to a more rational DF to obtain standardized aqueous extracts, which are dry extracts [1, 18]. Dry extracts are concentrated extracts from medicinal plant raw materials. Their undoubted advantages are: ease of use, storage stability, the possibility of more accurate dosing. During storage, the charges can stratify, which leads to instability of the content of biologically active substances in the drug dose. The lack of precise clear criteria for quality control, instability during storage, and inaccurate dosing create the need to transfer plant fees to a more rational DF to obtain standardized aqueous extracts, which are dry extracts [1, 18]. Dry extracts are concentrated extracts from medicinal plant raw materials. Their undoubted advantages are: ease of use, storage stability, the possibility of more accurate dosing. During storage, the charges can stratify, which leads to instability of the content of biologically active substances in the drug dose. The lack of precise clear criteria for quality control, instability during storage, and inaccurate dosing create the need to transfer plant fees to a more rational DF to obtain standardized aqueous extracts, which are dry extracts [1, 18]. Dry extracts are concentrated extracts from medicinal plant raw materials. Their undoubted advantages are: ease of use, storage stability, the possibility of more accurate dosing. the inaccuracy o

In the regulatory documentation (ND) of the State Pharmacopoeias (GF) XI, XIII and XIV editions, there have been some changes in the requirements for the standardization of fees and their components. Unfortunately, modern regulatory documents for fees and pharmaceutical forms based on them are predominantly the property of enterprises and information on quality indicators is not available.

Within the framework of the end-to-end standardization of pharmaceutical substances of origin and herbal vegetable medicinal products, it is important to have a unified approach to the analysis of certain types of medicinal products, their mixtures (collections), as well as extracts based on them. Therefore, a comparative analysis of ND was carried out on the segment "medicinal plant preparation - collection - pharmaceutical substance (extract)".

The results of information and analytical studies showed that the General Fund of the XIII edition first introduced OFS.1.5.1.0001.15 "MEDICINAL HERBAL RAW MATERIALS", which includes the following sections: "BASIC TERMS AND DEFINITIONS", "QUALITY INDICATORS AND TEST METHODS OF HERBAL VEGETABLES" "PRODUCTION". Since this article was compiled taking into account modern approaches to assessing the quality of medicinal plant raw materials, it was included in the GF XIV edition without changes.

The indicators of the collection quality are standardized in accordance with the OFS.1.4.1.0020.15 "CHARGES" of the GF XIV edition in comparison with the GF XI there were a number of changes in the sections: "Cooking" (now - "FEATURES OF TECHNOLOGY"), "External signs", "Authenticity" (now - "Microscopic signs"); the section "TESTS" includes such indicators as: "Content of active substances", "Moisture", "Total ash content", "Ash content insoluble in hydrochloric acid", "Grinding and impurity content". New indicators have appeared: "Qualitative microchemical and histochemical reactions", "Qualitative reactions", "Chromatography", "Spectrum (UV spectrum)", "Mass uniformity for dosed and non-dosed collection", "Pest infestation of stocks", "Radionuclides", Heavy Metals, Pesticide Residues, Microbiological Purity, Quantification, PACKAGING, LABELING, TRANSPORTATION, STORAGE and SHELF LIFE.

The quality of extracts is regulated by OFS.1.4.1.0021.15 "EXTRACTS". The article was introduced instead

articles of the GF XI edition and is a revised ND based on the modern requirements of domestic and foreign pharmacopoeias. A number of changes were made to the monograph. In particular, the following sections have been added: "FEATURES OF THE TECHNOLOGY", "TESTING", "PACKING" and "LABELING". In the section "TESTS" the following indicators are normalized: "Description", "Loss in mass on drying", "Bulk volume and particle size distribution", "Acid number, peroxide number, iodine number, saponification number", "Solubility", "Refractive index" , "Residual organic solvents", "Weight (volume) of the contents of the package." The rest of the indicators of the "TESTS" section ("Ethyl alcohol", "Heavy metals", "Solids", "Density") and the "STORAGE" section are retained from the ND of the previous edition [6, 9–11, 13].

As part of the end-to-end standardization of individual components and fees, uniform quality criteria are needed, therefore, at the next stage of the study, a comparative analysis of the requirements of individual components of the collection was carried out (Tables 3, 4). The analysis of tests for the authenticity of the FS (Table 3) showed that the description of external signs (compared with the requirements of the General Pharmacopoeia Monograph on the medicinal product of the GF XIV edition) of whole raw materials is present in all FS GF X, XI and XIV editions, the characteristics of crushed and powdered raw materials of chamomile flowers and marigolds , mint leaves were absent, powder characteristics were not given in the Violet Grass FS. In SP XIV, the external signs of powder of wild rosemary shoots are not considered. The description of the anatomical and diagnostic signs in the modern ND is given in sufficient detail; additions are required for chamomile flowers and mint leaves; for all types of raw materials, there is no quantity, as well as the size of some anatomical features that have diagnostic value (stomata, hairs, crystalline inclusions, etc.); the characteristic of rosemary shoots powder is not presented.

The section "DEFINITION OF BASIC BAS GROUPS" (previously - "Qualitative reactions") is present in all FS. The authenticity of the raw materials is confirmed by thin layer chromatography (TLC), while this section was absent in the private PS GF XI.

To determine the quality of medicinal plant raw materials, numerical indicators (NP) (now - "TESTS") are of great importance, in particular the content of active substances and methods for their determination. The GF XIV edition provides quality indicators for whole, crushed and powdered raw materials. When comparing the sections of the pharmacopoeias, it was revealed that the standardization of medicinal products must be carried out simultaneously for several groups of biologically active substances - for an individual compound, for the sum of substances in terms of an individual substance, for the content of extractive substances, which is the correct approach due to the complex chemical composition of medicinal plants and repels from subsequent standardization of manufactured medicinal products based on them (Table 4). In FS for wild rosemary shoots, standardization is required for the amount of flavonoids, as one of the dominant groups of biologically active substances in this type of raw material.

Quantification is predominantly carried out using spectral analysis methods. The method is characterized by selectivity, accuracy, availability for implementation in industrial production [3]. Impurities in private pharmaceuticals are regulated in approximately the same way. For all types of raw materials in GF XIV, safety indicators are standardized (in the GF XIII editions appeared for the first time), characterizing the contamination of raw materials with ecotoxicants. These include: "heavy metals", "radionuclides", "pesticide residues" and "microbiological purity".

Table 3

Determination of the authenticity of components of breast collection No. 4
in domestic pharmacopoeias of the latest editions [7]

Component collecting	ND	Pharmacopoeia section		
		External signs	Microscopy	Definition major groups BAS / Qualitative reactions
Chamomile flowers	GF XI Art. 7	Submitted by detailed description	Not full enough described	Section is missing

		whole raw materials. Absent availability information pubescence of all parts of the inflorescence and peduncles; and no characteristics crushed raw materials and powder.	diagnostic signs anatomical structure of individual parts inflorescences, absent a description of the pollen. Absent powder characteristic. Dimensions not specified anatomical diagnostic signs (stomata, hairs, glands, crystalline inclusions). Description not accompanied illustrative material.	
	GF XIV FS.2.5.0037.15	In detail characterized by signs of a whole, shredded and powder-forged raw materials. In the description of the whole additionally given characteristic surface peduncle, the rest description not has changed.	Described in detail diagnostic signs anatomical structure whole, crushed and powdered raw materials. Characteristic anatomical sizes diagnostic signs requires additions. Pollen microscopy is not illustrated.	TLC ethanol (96%) recoveries from LRS to silica gel, by compared with standard sample routine and quercetin.
Marigold flowers	GF XI Art. 5	No information about pubescence all parts of the inflorescence, nature of the surface peduncle. Description missing crushed raw materials and powder.	Described in detail signs anatomical structure of raw materials. Absent powder characteristic. Dimensions not specified anatomical diagnostic signs (stomata, hairs crystalline inclusions). Description not accompanied illustrative material.	Section is missing
	GF XIV FS.2.5.0030.15	Characteristic signs of a whole raw materials were left without changes. Added analysis of crushed and powdered raw materials. For	Described in detail diagnostic signs anatomical structure whole, crushed and powdered raw materials. Characteristic	TLC ethanol (70%) recovery from LRS to silica gel, by compared with stan- free sample routine,

		powdered raw materials required shape characteristic particles.	anatomical sizes diagnostic signs requires additions.	chlorogenic and caffeic acid. TLC chloroform extract from calendula flowers on silica gel substrate, on compared with stan- free sample β-carotene and quality reaction to triterpene connections
Ledum swamp escapes	GF XI Art. 1	Detailed description of the whole raw materials. Characteristic crushed raw materials not given in full. Powder analysis absent.	Analysis missing microscopic stem signs. Not indicated dimensions anatomical diagnostic signs (stomata, hairs, glands, crystalline inclusions). The stated material is not illustrated. Powder description not presented.	Section is missing
	GF XIV FS.2.5.0059.18	Characteristic whole raw materials are not has changed. Description crushed raw materials supplemented. Analysis missing powdered raw materials.	Described in detail diagnostic signs the anatomical structure of the sheet from the surface, squashed drugs stem and fruit for whole and crushed raw materials. Characteristic microscopic signs of powder, and also the sizes of the anatomical diagnostic signs requires absent.	TLC of the subject solution (to essential oil derived from Medicinal product with a quantity venous definition, add toluene) on plate with a layer silica gel, by compared to standard thymol samples and menthol; two qualitative reactions to flavonoids and tanning substances.
Violets grass	GF XI Art. 62	Description of the whole raw material outlined in detail. Characteristic	Anatomical description diagnostic signs of a stem, no fruit presented.	Section is missing

		crushed raw materials not given in full. Description of external powder signs absent.	Characteristic anatomy flower structure insufficiently stated in detail. Powder characteristic not shown. Dimensions missing anatomical diagnostic signs (stomata, hairs crystalline inclusions). Description not accompanied illustrative material.	
	GF XIV FS.2.5.0044.15	For whole raw materials more precise view dissection of the sheet records (lyre pinnate); additionally indicated distinctive features of two types of producing plants (Violatri color L. and Viola arvensis Murr.). Added by color description fruits. Described outward signs powder, but required additions (form particles, pubescence and surface character pieces). Shredded raw materials characterized not in detail.	Described in detail diagnostic signs of all parts of the herb whole, crushed raw materials and powder. Dimensions missing anatomical and diagnostic signs (stomata, hairs, crystalline inclusions; cells idioblasts - for fetuses).	TLC ethanol (96%) recoveries from LRS to silica gel, by compared with standard a sample routine; quality NS reaction to polysaccharides.
Licorice roots	GF X Art. 573	Signs of the whole raw materials characterized in detail. Shredded raw materials not fully described.	Described in detail diagnostic signs anatomical structure of whole raw materials and powder. Outlined material not illustrated.	Section is missing
	GF XIV	Description of the whole raw materials have not changed, with the exception of	Described in detail diagnostic signs	TLC of the subject solution (extract from

		absence information about location conducting elements. In detail characterized signs shredded and powdered raw materials.	anatomical structure of whole, crushed raw materials and powder.	Medicinal products carry out with a mixture of alcohol 96% - water (1: 1)) on silica-gel plate on compared with stan- free samples 18β-glycyrrhizin acid and quercetin.
Mint peppery leaves	GF XI Art. eighteen	Description not given the nature of the foundation, no information about the presence of a petiole and its size, character surfaces and pubescence, not venation is indicated, and also missing availability information essential oil glands. No description crushed raw materials and powder.	Not detailed enough described diagnostic signs the anatomical structure of the leaves. The characteristics of the powder are not shown. Dimensions missing anatomical diagnostic signs (stomata, hairs, glands). Description not accompanied by illustrative material.	Section is missing
	GF XIV FS.2.5.0059.18	Provided information about the presence of a petiole and essential oil glands. Given characteristic shredded and powdered raw materials. Description particle shape requires supplements (powder).	Added description anatomical structure of flowers and stems. Submitted by characteristic powdered raw materials. Description diagnostic signs the anatomical structure of the petiole, as well as anatomical dimensions diagnostic signs (stomata, hairs, glands) require additions.	For TLC use extraction from medicinal product dichloromethane, spend on silica gel plate, results compare with standard samples of menthol and thymol.

Table 4

Numerical indicators and methods for the quantitative determination of active substances components of breast collection No. 4 [7]

Component collecting	ND	Pharmacopoeia section	
		Numerical Indicators / Testing	quantitation
Chamomile flowers	GF XI Art. 7	Whole raw materials. No essential oilless than 0.3%; humidity not more than 14%; total ash no more than 12%; ash,	Determined content essential oil (steam distillation according to method 1

		insoluble in 10% hydrochloric acid solution, not more than 4%; leaves, stems, baskets with the remains of peduncles longer than 3 cm, no more than 9%; baskets blackened and brownish no more than 5%; organic impurities (parts of other non-poisonous plants and baskets of other types of chamomile) not more than 3%; mineral impurity no more than 0.5%.	or 2).
	GF XIV FS.2.5.0037.15	Compared to the GF XI edition in raw materials additionally the content of active substances is regulated by the amount of flavonoids in terms of rutin - not less than 1.2% and extractive substances extracted by water - not less than 18%; for whole, crushed raw materials and powder, the indicator is given fineness: particles passing through a sieve with holes of 0.18 mm, no more than 5% (whole raw materials), particles that do not pass through a sieve with holes of 5 mm, no more than 5%, particles passing through a sieve with holes of 0 , 18 mm, - no more than 5% (crushed raw materials), particles that do not pass through a sieve with holes of 2 mm, - no more than 5% (powder); Indicators characterizing the safety of the use of raw materials are normalized1...	The content of the sum of flavonoids in conversion to rutin (SFM after reaction with aluminum chloride with a solution of 5% and diluted acetic acid) and extractive substances, recoverable by water (gravimetry). Analysis the content of essential oil is carried out according to method 1 or 2 similarly to SP XI.
Marigold flowers	GF XI Art. 5	Whole raw materials. Extractivesubstances recoverable with 70% alcohol, not less than 35%; humidity not more than 14%; total ash no more than 11%; the remains of peduncles, including those separated from the baskets during analysis, no more than 6%; baskets with completely crumbling reed and tubular flowers (receptacle with wrappers) no more than 20%; brownish baskets no more than 3%; other parts of the plant (pieces of stems and leaves) no more than 3%; organic impurity no more than 0.5%; mineral impurity no more than 0.5%.	The content of extractives is determined, recoverable with 70% alcohol (gravimetry).
	GF XIV FS.2.5.0030.15	Added metrics for whole,crushed raw materials and powder:the sum of flavonoids in terms of rutin - not less than 1%; extractives recoverable with water - not less than 35%; ash insoluble in	The content of the sum of flavonoids in conversion to rutin (SFM after reaction with aluminum chloride with a solution of 5% and diluted acetic acid) and

		hydrochloric acid not more than 5%; crushing of raw materials: particles passing through a sieve with holes with a size of 0.5 mm, no more than 5% (whole raw materials), particles that do not pass through a sieve with holes 5 mm in size - no more than 5%; particles passing through a sieve with holes of 0.5 mm - no more than 5% (crushed raw materials), particles that do not pass through a sieve with holes of 0.18 mm - no more than 5% (powder) 1...	extractive substances extracted with water and 70% alcohol (gravimetry).
Ledum swamp escapes	GF XI Art. 1	Whole raw materials. No essential oil less than 0.1%2; humidity not more than 14%; total ash no more than 4%; ash insoluble in 10% hydrochloric acid solution, no more than 1%; grayish-brown stems no more than 10%; organic impurity no more than 1 %; mineral impurity no more than 0.5%. Shredded raw materials. Comparedwith whole raw materials, the indicators "Particles that do not pass through a sieve with holes with a diameter of 5 mm" (no more than 5%) are additionally regulated; "Particles passing through a sieve with apertures of 0.5 mm" (no more than 10%).	The content of essential oil is determined (steam distillation according to method 2). The content of ice in the essential oil is determined by the GLC method.
	GF XIV FS.2.5.0059.18	The PE section entered the private FS for raw materials unchanged1...	Without changes
Violets grass	GF XI Art. 62	Whole raw materials. Extractivesubstances recoverable by water, not less than 30%; humidity not more than 14%; total ash no more than 13%; ash, insoluble in 10% hydrochloric acid solution, no more than 3%; yellowed leaves and stems no more than 7%; other parts of the plant (fruits, fruit valves, roots, including those separated by analysis) no more than 3%; organic impurity no more than 3%; mineral impurity no more than 1%. Shredded raw materials. Comparedwith intact raw materials, the indicators "Particles that do not pass through a sieve with holes with a diameter of 7 mm" are additionally standardized (no more than 10%); "Particles passing through a sieve with apertures of 0.5 mm" (not	The content of extractives is determined, recoverable by water (gravimetry).

		more than 10%).	
	GF XIV FS.2.5.0044.15	Changes have been made to the section: the sum of flavonoids in terms of rutin - not less than 1%; the amount of polysaccharides - at least 8%; crushing of raw materials: particles passing through a sieve with holes of 0.5 mm, no more than 5% (whole raw materials), particles that do not pass through a sieve with with holes of 2 mm, - no more than 5%, of particles passing through a sieve with holes of 0.18 mm, - no more than 5% (powder)1...	The content of the sum of flavonoids in conversion to rutin (SFM after reaction with aluminum chloride with a solution of 5% and diluted acetic acid), the sum of polysaccharides and extractive substances, recoverable by water (gravimetry).
Licorice roots	GF X Art. 573 (In GF XI - absent)	Extractive substances extracted with 0.25% ammonia solution, not less than 25%; moisture in whole and cut raw materials is not more than 14%. For the wholecrude raw materials: total ash is notmore than 8%; ash insoluble in 10% hydrochloric acid, not more than 2.5%; roots, flabby in the fracture, yellow-brown and the remains of stems not more than 4%; organic impurity no more than 1%; mineral impurity no more than 1%. For whole refined raw materials: total ash no more than 6%; ash, insoluble in 10% hydrochloric acid acid, no more than 1%; roots poorly cleaned of cork, no more than 15% (roots with remnants of more than three areas of dark brown cork on one piece or if the diameter of the remains of cork is more than 10 mm are considered to be poorly cleaned); roots, darkened and brownish from the surface, but light yellow in the fracture, no more than 20%; organic impurity no more than 0.5%; mineral impurity no more than 0.5%. For cut unrefined raw materials: dark brown particles in the fracture no more than 4%; particles larger than 10 mm, no more than 5%; particles passing through a sieve with a hole size of 0.5 mm, no more than 0.5%; organic impurity no more than 1%; mineral impurity no more than 0.5%. For chopped clean-baked raw materials: root particles,darkened from the surface, no more than 15%; particles poorly cleaned from cork, no more than 3%; particles larger than 6 mm no more than 10%; particles passing through a sieve with a hole size of 1 mm, no more than 2%. For powder:	The content of extractives is determined, recoverable by water (gravimetry). Content of glycyrrhizic acid (not less than 6%) identified by one of following methods: alkalimetry or SPM after acid hydrolysis and reactions with ammonia solution.

		moisture no more than 10%; total ash no more than 7%; ash insoluble in 10% hydrochloric acid, no more than 1.5%; particles that do not pass through a sieve with a hole size of 0.125 mm, no more than 3%.	
	GF XIV	The indicator "Extractive substances recoverable 0.25% ammonia solution "(at least 25%); for whole, choppedrefined, unrefined raw materials and powder summarized the indicator "ash general "(no more than 8%); forof crushed raw materials and powder, the indicator is given: "ash,insoluble in hydrochloric acid "(no more than 2.5%); for chopped peeled licorice roots changed the indicator "Crushing of raw materials" on the lower sieve: particles passing through a sieve with holes of 0.18 mm - no more than 5%; powder grinding: particles that do not pass through a sieve with holes of 2 mm - no more than 5%; particles passing through a sieve with holes of 0.18 mm, no more than 5%; indicated indicator "organic impurity": (no more than 0.5%); mineral admixture (crushed unrefined raw materials and powder) - no more 1 %;crushed refined raw materials -no more than 0.5%1...	The content of glycyrrhizic acid (SFM after acidic hydrolysis and reaction with ammonia solution).
Mint peppery leaves	GF XI Art. eighteen	Whole raw materials. No essential oil less than 1%; humidity not more than 14%; total ash no more than 14%; ash insoluble in 10% hydrochloric acid solution, no more than 6%; blackened leaves no more than 5%; stems no more than 10%; particles passing through a sieve with holes of 0.5 mm, no more than 8%; organic impurity no more than 3%; mineral impurity no more than 1%.	The essential oil content is determined (steam distillation according to method 1 or 2).
	GF XIV FS.2.5.0059.18	Compared with the article of the GF XIV ed. Indicators are regulated: the sum of flavonoids in terms of luteolin - not less than 0.6% (whole raw materials); essential oil - not less than 0.8%; the sum of flavonoids in terms of luteolin - not less than 0.6%	The content of the sum of flavonoids in converted to luteolin (SFM after reaction with aluminum chloride with a solution of 5% and acetic acid divorced). Analysis

		(shredded raw materials); ethericoils - not less than 0.8%; sum of flavonoids in terms of luteolin - not less than 0.6% (powder); crushing of raw materials: particles passing through a sieve with holes of 0.5 mm, no more than 5% (whole raw materials), particles that do not pass through a sieve with holes 5 mm in size - no more than 5%; particles passing through a sieve with holes of 0.18 mm, - no more than 5% (crushed raw materials), particles that do not pass through a sieve with holes of 2 mm, - no more than 5%, particles that pass through a sieve with holes of 0.18 mm, - no more than 5% (powder) 1...	the essential oil content is carried out according to method 2.

Note:
1For all types of raw materials, the GF XIV edition regulates safety indicators: "heavy metals", "radionuclides", "residual quantities of pesticides", "microbiological purity". They are standardized in accordance with the requirements of the General Pharmacopoeia Monograph "Determination of the content of heavy metals and arsenic in medicinal plant raw materials and medicinal plant preparations", the General Pharmacopoeia Monograph "Determination of the content of radionuclides in medicinal plant raw materials and herbal medicinal products" herbal medicinal products ", the General Pharmacopoeia Monograph" Microbiological Purity ".
2 The content of essential oil in raw materials intended for producing ice must be at least 0.7% and ice in it must be at least 17%. The determination of the ice content in the essential oil is carried out by the manufacturer of the ice preparation.

Thus, the analysis of the regulatory documentation showed that most of the articles on individual components generally meet modern requirements and require small additions.

Components of HS No. 4 contain a varied composition of biologically active substances, such as: essential oils, flavonoids and phenol carboxylic acids, polysaccharides, saponins, mucus, tannins, vitamins, which determine the pharmacological effect of infusion and collection [1, 24]. Phenolic compounds and polysaccharides predominate among them and, given that essential oils practically do not pass into water extraction during the preparation of an infusion, it is advisable to propose as a method of standardizing collection by the content of flavonoids, polysaccharides, tannins, the content of glycyrrhizic acid (as one of the important marker compounds) in accordance with modern pharmacopoeial requirements.

CONCLUSION

The carried out information and analytical research showed perspective obtaining and using pharmaceutical substances of plant origin and medicines based on them (extracts, etc.). This allows not only to rationally use the resources of medicinal plant raw materials, but also provides the patient with a modern dosage, easy-to-use DF for the treatment and prevention of URT diseases. A scientifically grounded choice of quality indicators was made for standardization of the extract obtained on the basis of breast collection No. 4.

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