Ф А 2.2.1-32-367

MINISTRY OF HEALTH OF UKRAINE

NATIONAL UNIVERSITY OF PHARMACY

faculty for foreign citizens' education

department of pharmaceutical preparations technologies

QUALIFICATION WORK

on the topic: **« DEVELOPMENT OF COMPOSITION OF CAPSULES FOR THE TREATMENT OF RESPIRATORY DISEASES »**

Prepared by: higher education graduate of
group Фм18 (5,0д) англ. – 7
specialty 226 Pharmacy, industrial pharmacy
educational program Pharmacy
Saidi Said

Supervisor: associate professor of higher education institution of department of pharmaceutical preparations technologies, PhD, associate professor Denys PULIAIEV

Reviewer: professor of higher education institution of Department of Industrial Technology of Drugs, Dr. of Pharmacy, professor Inna KOVALEVSKA

Kharkiv — 2023 year

ANNOTATION

The qualification work is devoted to the development of the composition of capsules for the treatment of respiratory diseases. A literature review was conducted regarding the development potential of hard capsules. The nomenclature of drugs for the treatment of respiratory diseases was studied. The effect of auxiliary substances on the technological characteristics of encapsulation masses and their quality indicators was studied. A technology for the production of hard capsules containing a mixture of plant extracts has been developed.

The work has 47 pages and includes an introduction, three chapters, general conclusions, a list of used sources and appendices. The work contains 30 references to scientific literature and is illustrated with 8 figures and 8 tables.

Key words: mixture of plant extracts, capsules, pharmaceutical technology, treatment of respiratory diseases.

АНОТАЦІЯ

Кваліфікаційна робота присвячена розробці складу капсул для лікування для лікування захворювань органів дихання. Було проведено дослідження літератури щодо потенціалу розробки твердих капсул. Було вивчено номенклатуру препаратів для лікування захворювань органів дихання. Досліджено вплив допоміжних речовин на технологічні характеристики мас для капсулювання та їх показники якості. Розроблено технологію виготовлення твердих капсул, що містять суміш рослинних екстрактів.

Робота має 47 сторінки і включає вступ, три розділи, загальні висновки, список використаних джерел і додатки. Робота містить 30 посилань на наукову літературу та ілюстрована 8 рисунками та 8 таблицями.

Ключові слова: суміш рослинних екстрактів, капсули, фармацевтична технологія, лікування захворювань органів дихання.

TABLE OF CONTENTS

INTRODUCTION

Relevance of the research topic. Respiratory diseases are one of the most important health problems due to their high prevalence, often severe with frequent complications. Treatment of these diseases to date remains a difficult problem due to the fact those respiratory diseases with different etiologies similar to clinical manifestations. Therefore, it is important in the arsenal of medicines have the effect of which will be aimed at the reduction and elimination of the main manifestations of the disease, regardless of etiology, and at the same time be safe for treatment.

In recent years, more and more recognition has herbal medicinal products. The advantage of plant-based drugs is that biologically active substances of plants more natural included in the metabolic processes of the human body, unlike synthetic drugs.

The purpose the development of science-rationale of technology and composition capsules for the treatment of respiratory diseases.

The object of research a mixture of linden flower and licorice root extracts.

The following research **methods** were used in the work: complex physico-chemical and technological research and to create the optimal composition of the solid dosage form.

The practical significance of the results. In the course of the work, the rational composition of the capsules was substantiated. The technology of capsules has been developed.

Approbation of research and publication results. The qualification work was tested at the «Current issues of creating new medicines: materials of the XXIX international scientific and practical conference of young scientists and students» (April 19-21, 2023, Kharkiv). - Kharkiv: NUPh, 2023. Published abstracts: Puliaiev D.S., Saidi Said. Development of composition of capsules for the treatment of respiratory diseases. Modern achievements of pharmaceutical business: collection of scientific works, issue 1. – Kharkiv, NUPh publishing house, 2022. P.181.

Structure and scope of qualification work Qualification work is made at 47 pages, consists of the introduction, three chapters, conclusions, list of sources used, which contains 30 items. The work is illustrated at 5 tables and 7 figures.

CHAPTER 1
PROSPECTS OF CREATION OF SOLID DRUGS FOR TREATMENT OF RESPIRATORY DISEASES

1.1. The etiology and pathogenesis of respiratory diseases.

Diseases of the respiratory tract can carry acute and chronic character. Acute respiratory infections (ARI) have diverse etiological structure. Most of them is viral nature (SARS). These are influenza, parainfluenza, adenovirus, respiratory syncytial, rhinovirus, rotavirus, enterovirus, coronavirus disease, less often - reovirus and picornavirus infection. SARS often occur during the cold season, can take the character epidemics [5, 29].

Other causes development of acute respiratory disease is viral-bacterial associations, bacteria, fungi, protozoa.

Species etiological structure of respiratory diseases undergoes changes with time. If in 80 years in the etiology of respiratory diseases observed absolute predominance of streptococci (especially pneumococcus) and staphylococci, then last decade of their importance is declining, there is a significant expand the range of pathogens. Increased the role of intracellular microorganisms: chlamydia and mycoplasma. The essential role belongs to hemophilic stick. Together, these pathogens cause constitute to 40-50% of all cases of diseases. A role in the development of respiratory disease belongs to fungi, gram-negative organisms of enteric family and anaerobes [5, 15].

Acute bacterial respiratory disease may arise as an independent pathology. However, 60% of ARI cases is a complication of viral infections in 20% - so-called childhood infections, bacterial and viral (measles, scarlet fever). The development of these complications often contributes to activation of endogenous flora or superinfection. Unfavorable background is the presence in the patient of chronic tonsillitis, sinusitis, otitis, developmental abnormalities of the respiratory tract, respiratory allergies.

Furthermore, repeated respiratory infections contribute to the formation of chronic diseases of the respiratory tract, changing reactivity of the organism, sensitized of it, reduce or modify the general or local immunity.

At chronic diseases of respiratory tract as opposed to acute increases etiological role of anaerobes (particularly Bacteroides), fungi (usually genus Candida and Aspergillus), gram-negative microorganisms of family of enteric gramnegative bacteria that are not fermented, and associations of aerobic and anaerobic bacteria.

The etiology of infections of the upper and lower respiratory tract also has its own peculiarities [7, 28].

In the etiology of upper respiratory tract infections leading role played by respiratory viruses. In addition to viruses predominant role are play streptococci (eg, b- hemolytic streptococcus group A), staphylococci (Staphylococcus, epidermal). Less - other types of streptococcus and staphylococcus, intracellular pathogens (mycoplasma, chlamydia), frequency of detection which can, however, exceed 20%, fungi (most often family Candida), rarely - Gram-negative pathogens of enteric family.

In the etiology of diseases of the lower respiratory tract are the most important viral and bacterial associations. In second place are bacteria, followed by pure viral nature of disease finally - fungi and protozoa. Moreover, at the etiological structure of acute bronchitis and pneumonia affects community-acquired (domestic) or nosocomial character of infection. Thus, in the etiology of community-acquired pneumonia and bronchitis prevail gram-positive cocci (45-55%) pneumococci (30-40%), other streptococci (5-10%), rarely - Staphylococcus (5%). Hemophilic rod is up to 12% of all cases; intracellular pathogens - Chlamydia (10-12%), mycoplasma (10-20%) and Legionella (2-4%) - can cause one third or a quarter of all diseases. These pathogens can continued exist in the epithelial cells of the respiratory tract and reticulohistiocytic system and promote the protracted and chronic flow of inflammation [28, 30].

Pathogens of respiratory diseases that is penetration into tissue, that are lining the respiratory tract, causing irritation of the mucous membranes, the development of inflammation and other changes.

Parainfluenza viruses, rhinoviruses and cytomegalovirus cause epithelial dystrophy with rejection of entire layers. RS virus causes epithelial hyperplasia with infringement of bronchial conductivity and development of obstructive syndrome. Adenovirus infection accompanied by a pronounced exudative component of inflammation, loosening and rejection of epithelial, formation of cell infiltrates that contributes to airway obstruction and atelectasis. At bacterial and fungal lesion of mucosa observed sero-purulent or purulent exudation, infiltration of the mucosa by neutrophils and macrophages. Haemophilus influenzae and pseudomonas aeruginosa, streptococcus pneumoniae are producing substances that disrupt the mucociliary clearance, destruction and rejection of epithelium. Many microorganisms produce enzymes that destroy elastin that helps reduce the functional activity of the bronchioles and bronchi, the formation of their strain and ectasia, development of bronchial obstruction [4, 7].

At the heart development of bronchial obstruction is hyperplasia of mucosal swelling and increased secretion of viscous mucus with high adhesive properties. These factors disrupt the mucociliary transport (evacuation of sputum) slow motility ciliated epithelial of bronchi and bronchioles, causing of their obstruction, which may be accompanied by bronchial dyskinesia, breach of external respiration and hemodynamic change in bronchopulmonary system. In patients with bronchial hyperactivity and / or allergic of the bronchi obstruction can be amplified and supported the development of bronchospasm.

Respiratory disease is heterogeneous in etiology, but similar in epidemiology and clinical manifestations group of diseases. However, each separate form of respiratory disease has features of flow caused by the pathogen kind of influence on the character of lesions of the mucous membranes. The same factor is determined by the presence or absence of bronchial obstruction phenomena.

Depending on the localization of the pathological process distinguish between disease of upper and lower respiratory tract.

To infections of the upper respiratory tract (nadhortanniy area) include rhinitis, sinusitis, adenoiditis, angina, chronic tonsillitis, pharyngitis, laryngitis, otitis media or a combination thereof [5, 28].

To infections of the lower respiratory tract include laryngotracheitis, tracheitis, bronchitis and pneumonia.

The most common manifestations of acute respiratory disease upper respiratory tract infections (colds), are known to be nasal congestion, runny nose, watery eyes, sore and scratchy throat, cough, often accompanied by violation of health, moodiness, decreased appetite, fever.

With the development of respiratory diseases of the lower respiratory tract is the most common symptom of their defeat is a cough caused by infectious inflammation, bronchospasm, violation of mucus secretion, increased viscosity of secretions that disrupt the evacuation of sputum. Other manifestations of respiratory pathologies of the lower respiratory tract can be pain, deterioration of general condition, sleep disturbance, appetite, rapid breathing, fever.

Infections of the upper and lower respiratory tract can be characterized as acute and chronic flow.

Chronic respiratory diseases contribute to frequent acute respiratory diseases, their late and poor treatment, presence of chronic foci of infection, respiratory allergies, immunodeficiency, and hereditary and congenital diseases of the respiratory system and adverse effect of etiological factors of the environment. [5, 27]

Thus, overall clinical picture of respiratory disease depends on the etiology, localization of inflammation, defeats of mucous membrane character, form and severity of the disease, age of the patient.

1.2. Phytotherapy of respiratory diseases.

Whereas that respiratory diseases accompanied by development of inflammation, cough, thick sputum and complexity of its allocation, allergic reactions, treatment of these diseases requires combination therapy that allows a positive impact on all parts of the pathological process.

Treatment of these diseases is aimed at the relief of inflammation, activation of the immune system, including increasing of local immunity of the mucous membranes of the respiratory tract, restoring patency, mucociliary transport and elimination of bronchial obstruction. The choice of drugs is determined by the nature and localization of lesions, clinical manifestations, course of the disease and pharmacological action of drugs [16, 22].

Higher efficiency, optimal healing properties and good tolerability have a combination of drugs, which include herbal substances. Today is the actual creation of multicomponent drugs that combine extracts of several plants. It provides comprehensive effect of the drug on respiratory tract. Such drugs must have bronchodilator, mucolytic, expectorant and anti-inflammatory action.

An important part of therapy is the treatment of respiratory diseases of cough that is primed for eliminating the causes that its cause. Choice coughed against drugs must pass, considering the mechanism of action of drugs against cough [17, 29].

At infectious and inflammatory diseases of the upper and lower respiratory tract, accompanied by cough with difficult separable sputum and where **is** no effective herbal peripheral of afferent action (that moisturize, envelop), used in the treatment methods of efferent action - expectorant herbal medicines.

Expectorant drugs increase the activity of ciliated epithelium and peristalsis bronchioles, thereby contributing to the promotion of sputum and its removal. At the same time, they increase the secretion of bronchial glands, increase the amount of secretions and reduce its viscosity, contributing to the removal of mucus from the respiratory tract [15, 17, 30].

With insufficient effects of herbal expectorants drugs for treatment should be connected synthetic mucolytic drugs that thinning sputum by breaking disulfide bonds of mucopolysaccharides or peptide bonds of protein molecules, thereby altering the chemical and physical properties of sputum, leaving unchanged its volume.

In severe, protracted and complicated course infections of the respiratory tract, feverish conditions more than 2-3 days destination of herbal medicine may be considered as a supplementary method of treatment in combination with other drugs [16, 28]

Thus, changing of the etiological disease structure in environmental conditions requires the search for new approaches to the most adequate selecting of therapy. Great importance has the inclusion of herbal drugs into treatment complex. With their help is possible to provide a safe and effective treatment and prevention of diseases of the respiratory tract. The final result of treatment depends on proper selection of drugs. Necessary to remember that monotherapy may not always provide sufficient clinical effect, while an integrated treatment leads to greater success. At severe forms or complicated currents of both acute and chronic diseases of herbal and homeopathic series can be used as components of an adequate combined therapy.

Among the main advantages of herbal medicine are the following:

• biological relationship between plant active substances and physiologically active substances the body;

• the possibility of long-term and safe application;

• multivalency action that allows for treatment of the underlying and related diseases;

• simplicity and ease of preparation and application;

• the possibility of using as prophylactic measure;

• compatibility with synthetic drugs;

• efficacy at functional disorders of the body, less severe diseases, enhancing the therapeutic effect of specific therapy and, when used as a maintenance treatment [16, 34].

The pharmacological effect of the drug that is developing determined by the content of biologically active substances: saponins and flavonoids.

Licorice extract contains glycyrrhizic acid, flavonoids, sitosteryn, pectin, sugar, starch, slime and other biologically active substances. Hlitsyryzynova acid detects anti-inflammatory properties. Liquiritoside (flavonoid glycoside) and 2,4,4-trioksyhalkon act as antispasmodics. Pentacyclic triterpene - carbenoxolone - accelerates healing of gastric ulcers.

Extract of linden due to substances (fatty acid, farnesol, carotenoids, flavonoids, tannins, glycosides, vitamin C, phytosterols, essential oil, saponins, tannins) that part of it has antimicrobial, anti-inflammatory action, are used as a diaphoretic and antipyretic at quinsy, bronchitis, colds.

The developed by us drug recommended in the complex therapy of acute and chronic respiratory diseases, ODS, and pneumonia [5,16,17].

Thus, the therapeutic effect depends on the ratio of herbal medicines of biologically active components. Important to note that herbal combined that comprised of several herbal ingredients have diverse effects, combining expectorant, bronchodilators, anti-inflammatory and other effects. From this perspective, many herbal preparations dosage forms can be used as the drug of choice for treatment of ARI in patients of different age groups.

1.3 Analysis the domestic market of drugs for the treatment of respiratory diseases.

Considering the factor of economic availability of drugs, the study of drugs for the producing countries and determine the fate of drugs import manufacture indicating that drugs for the treatment of respiratory diseases represented by 131 company, of which 28.24% are Ukrainian manufacturers 63.80% of foreign and 2.28% multinational companies. Leading positions occupied Western Europe

(33.57% in the number of manufacturers and 35.83% in the number of drugs) (Fig. 1) [29].

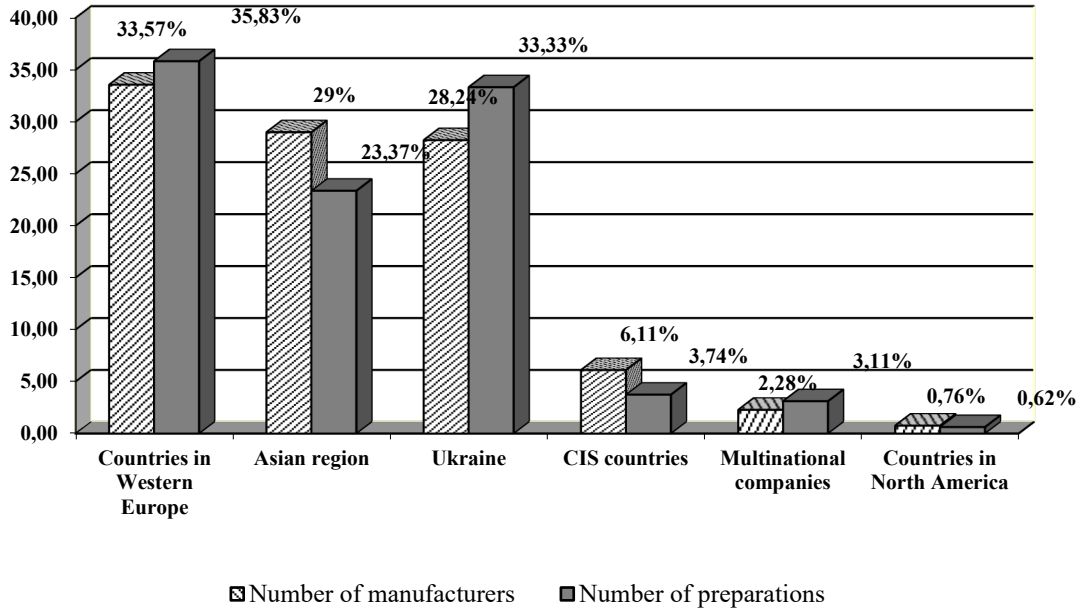


Fig. 1.1. The structure domestic market of drugs for the treatment of respiratory diseases by region

Analysis of the range drugs for the treatment of respiratory diseases indicate that the population of Ukraine is provided by drugs 23 countries, as well as production of three multinational companies. Leading position among the countries of Western Europe occupied by Germany, Czech Republic and Switzerland that supply Ukrainian market by 50, 16 and 11 of drugs, the total share of which is almost a quarter of all drugs represented group (24%).Of the countries in the Asian region first in the number of manufacturers and represented drugs takes India, 28 pharmaceutical enterprises of which produce 58 drugs of studied group. It should be noted that India is a leader not only among Asian countries, but also among foreign producers. Among the neighboring countries importing medicines is Russia, Belarus and Latvia, but their contribution is insignificant and not more than 2% for each. North American region represented only by United States, whose contribution to the overall structure of a select group of drugs is no more than 1% (Table 1.1).

Considering that one of the important factors that guides consumers when choosing drug is primarily price, the role of domestic drugs increased. But

attention is drawn to the fact that, despite the relatively high figures concerning Ukrainian production (the share of which among drugs in the study group is 33.33%), the proposal drugs for the treatment of respiratory diseases, unfortunately, is not updated with new drugs, but they are expanded by duplicating of existing traditional preparations for a long time being in circulation on Ukraine pharmaceutical market [16, 22, 26].

Table 1.1

Total number of manufacturers that offer drugs for the treatment of respiratory diseases in Ukraine pharmaceutical market

Country	Number of manufacturing firms	The share of manufacturing firms, (%)	Number of drugs	The share of registered drugs, (%)
1. Ukraine	37	28,24	107	33,33
Countries of Western Europe				
1. Germany	17	12,98	50	15,58
2. France	5	3,82	7	2,18
3. Switzerland	4	3,05	11	3,43
4. Czech Republic	4	3,05	16	4,98
5. UK	3	2,29	3	0,93
6. Poland	3	2,29	7	2,18
7. Bulgaria	2	1,53	5	1,56
8. Belgium	1	0,76	1	0,31
9. Slovenia	1	0,76	4	1,25
10. Austria	1	0,76	1	0,31
11. Netherlands	1	0,76	1	0,31
12. Italy	1	0,76	4	1,25
13. Slovakia	1	0,76	5	1,56

Continuation of the table 1.1

The Asian region				
1. India	28	21,37	58	18,07
2. Vietnam	4	3,05	6	1,87
3. Pakistan	2	1,53	4	1,25
4. Israel	2	1,53	5	1,56
5. Jordan	1	0,76	1	0,31
6. Turkey	1	0,76	1	0,31
Neighboring countries				
1. Russia	5	3,82	5	1,56
2. Belarus	2	1,53	4	1,25
3. Latvia	1	0,76	3	0,93
North American region				
1. USA	1	0,76	2	0,62
Multinational companies				
1. India / United Kingdom	1	0,76	3	0,93
2. Switzerland / Germany	1	0,76	2	0,62
3. Ukraine / Belgium	1	0,76	5	1,56
Total:	131	100	321	100

Respiratory disease involving inflammation of the mucous membrane of the respiratory tract, hypersecretion of bronchial glands, formation viscous sputum, violation of bronchial passability and bronchospasm, so the most optimal in pharmacotherapy of this disease is the impact on all parts of the pathological chain can be achieved by the appointment of combined drugs. Furthermore, the combined drugs to allow to reduce their doses, leading to a reduction of side effects. View of the above, it is appropriate explore the domestic market of drugs for treatment of respiratory diseases in part of contribution of combined drugs to the overall structure of the assortment. Obtained data indicate that the depth of

range of single-component and combined preparations actually the same, but attention is drawn to the fact that the combined drugs, which include in most cases the medicinal herbs are offered mostly by foreign manufacturers. Thus, the analyzed data indicate about the expediency of creation of more affordable by price domestic combined drugs that have multi-vector action and increase the effectiveness of pharmacotherapy of respiratory diseases [7, 17, 28].

Given the above it can be concluded that the range of drugs for the treatment of respiratory diseases represented mainly import manufacture drugs, there is a variety of trade names and dosage forms of production, but it should be noted that not all patients can buy necessary drugs, given their high cost. That is why in conditions of unstable economic situation in the country is particularly important is expand the range of new domestic combined drugs in order to enhance provision of population effective, safe and affordable drugs.

1.4. The current state of production technology of capsules

1.4.1. Advantages of application of capsulated drugs

In the nomenclature of finished drugs are of great importance have capsules and granules. But recently more and more attention pays to encapsulated drugs.

Gelatin capsules, while still young dosage form, thanks to a number of advantages and technical progress (production of high-performance and high-precision automated equipment for manufacturing and filling capsules) since the 50s of XX century, becoming more popular for doctors, consumers and manufacturers. Development of modern technological methods that allow encapsulate medicinal substances with different physicochemical characteristics, contributes to a significant expansion of the range of drugs in this dosage form. For today preparations in the form of gelatin capsules intended as for oral as well as for local application, make up to 9-12% range of drugs in countries with developed pharmaceutical industry. Preparations in the form of gelatin capsules are represented in range of almost all pharmacological groups [8, 27].

From more than 4,100 trade names of drugs presented at the Ukrainian and Russian pharmaceutical markets, 425 (10.4%) - in the form of capsules.

Such popularity of this form of drug for producers, consumers and doctors is explained by a number of advantages and positive characteristics, including:

- the accuracy of dosing, modern equipment provides high precision of filling capsules by filler (with a tolerance that does not exceed ± 3%) and minimum losses;

- high performance: the type of used equipment, method of filling, characteristics of filler and its dosage, modern automatic machines allow you to obtain 120,000 capsules per hour;

- high bioavailability: studies conducted by many scientists (Eckert, Lindvald and others.) showed that the capsules break down faster than capsules or pills, and their liquid or non-compacted solid content quickly and easily absorbed in the human body;

- expansion of indications for application in some cases as capsule dosage form as help identify new kind of pharmacological activity that is not detected for the same dose in other dosage forms (for example, a group of scientists of scientific laboratory of the Italian firm «Pharmagel» was found that the capsules temazepam in dose of 20 mg showed tranquilizing properties, while the same dose capsules gives a hypnotic effect and can be used as a sleeping pill);

- high stability: capsule coating provides a sufficiently high tightness and insulation labile components contents from various adverse environmental factors (air oxygen, direct sunlight, humidity fluctuations etc.), due to this often possible to avoid the use of antioxidants or stabilizers or reduce their number;

- correcting ability - shell capsules also helps hide the unpleasant taste that have most of drugs.

- this is particularly important in pediatrics because application of such popular in this field of medicine dosage forms, such as syrups,

- not always rational (for example malfunctioning due to dosage, insufficient stability of some drugs and i.e.);

- minimize the possibility of production errors - the possibility of using different dyes and marking allows to reduce the danger of mistakes and change of drugs in the production process;

- high aesthetics is achieved through the use of various dyes when receiving shell capsules. Although color is not objective factor in the choice of medications, but it is an important psychological factor in the choice of drug. At this use is based application of additional therapeutic effects of color. Today's leading pharmaceutical companies V 1000 different colors and shades for coloring the shells of capsules;

- ability to specify certain properties of medicines; This can be most clearly demonstrated by the creation of so-called enteric soluble capsules (resistant to gastric juice, but those that break down readily in the environment of the small intestine) and capsule retard (prolonged release of drug) that can be achieved by various technological methods;

- sparing technological modes - technological methods of encapsulation allow to avoid unwanted for many labile substances effect of moisture, pressure [8, 26].

A variety of drugs in capsule form, the difference between physical and chemical properties of encapsulated substances requires quite diverse approaches to the creation of drugs in this dosage form. Development of optimal composition and technology of capsulated drugs is determined by physicochemical, crystallographic and technological properties of medicinal powders that are included to their composition. These properties are closely interrelated and affect the process of obtaining capsules [6, 27].

Granular dosage forms by compactness and convenience of application are somewhat inferior tablet, but they should give priority to the development of new dosage forms, which include plant extracts. Latest in the tableting stick to press tool which could lead to obtaining low-quality products.

1.4.2. Factors that influence the technological and biopharmaceutical mass values for encapsulation.

The choice of optimal technological scheme of production capsules depends on the physico-chemical and technological properties of substances, their number as part of a medicinal product mixture fractional composition and other factors. At impossibility immediately fill the capsule powder granulation method is used.

Granulation - is the process converting powdered material to particles (grains) of certain value. Absolute uniformity of granules may be achieved by varying the ratio of granulate fractions.

Granulation improves fluidity, provides a uniform flow velocity in a capsule strictly certain amount of weight.

To widely applied technological processes belongs wet granulation, since most drug substances have a poor fluidity and Requires entry of binders and lubricants. In pharmaceutical manufacturing wet granulation is used to produce the finished dosage form "granules" intermediate product for dosage form "capsules" and "capsules". To granulate nominated such technological requirements as turnover, volume and bulk density, solubility, and others. The traditional method of obtaining granules is mixed with components of weight moisturizer and pushing wet mass through a sieve with holes of appropriate size. Grain size as the dosage form, limited by technical documentation: 0,2 - 3,0 mm [9, 25].

Changing the properties of granules may lead to changes in the properties of the drug. Thus, conducting of wet granulation on the mixer with followed drying in a dryer shelf and the pellet company Glatt, Ball or Zankety with different technologies can provide medications completely different physicochemical properties and effect on its bioavailability. For example, through the multilayer coating particles of active ingredient appropriate auxiliary substances for appropriate technology can be obtained granulated, which will provide slow release of the active ingredient from the dosage form. This will ensure continued presence of the active ingredient in small concentrations in the blood and a

relatively weak loading on the liver or kidneys, which deduce drug from the blood. In simple mixture of these same components will be obtained dosage forms of active ingredients that are released quickly (loading dose of the active substance in the blood, their rapid output and high loading on the liver or kidneys). Thus, varying technologies can vary the properties of the drug. A similar situation with the replacement of auxiliary substances. Therefore, the approach to the choice of technology of granulation is very complex stage drug development technology [8, 19].

Auxiliary substances that apply when using wet granulation.

Medicine as a complex physical-chemical system as a whole is not only active substance responsible for the therapeutic effect. All parameters of quality of the product to some extent depend from used auxiliary substances, so on their optimal selection is paid more attention. Composition of used auxiliary substances significantly effect on the conditions of the process, structural and mechanical parameters and consumer properties of the finished product, and therefore - on its value.

Today presented an extensive range of auxiliary substances which are used in the manufacture of solid dosage forms. Depending on the physical and chemical properties of active substances, methods of their recommended dosages and some other factors are used auxiliary substances with different functions, fillers (solvents), raising agents (disintegrants), anti-friction (sliding, lubricating) agents, taste correctors, regulators dynamics of release of active substances, dyes. However, there is no any clear separation of auxiliary substances by their function in the dosage form. The same substance, according to the way of it applications can be used for different purposes.

The bulk of medicinal powders require special training before encapsulation. With this purpose, use a wet granulation method. The purpose of granulation is the formation of particles of a certain size, shape, structure, certain physicochemical and pharmacological technological properties. Granulation allows to correct the technological properties of powders, provides a more uniform distribution of the

active ingredient, more accurate dose of the active substance reduces the effect of temperature and humidity on the quality of the dosage form.

Now is used several ways granulation. The most common method of wet granulation - a multistage process that usually is around eight stages. The use of new binding materials reduces the number of stages. Thus, the use of modified starch as binding agent and filler reduces the stage soaking and cooking starch paste, and thus - reduce costs. Therefore, this manufacturing process is widely used because most of drugs have a bad turnover and pressing and therefore requires entry of binding and plasticizing agents [8, 26].

At using method of wet granulation are used fillers, disintegrants, binders, lubricating substance.

Fillers provide mass for filling of capsules of required optimum volume. For this purpose, in the manufacture of drugs in the form of hard capsules used milk sugar, microcrystalline cellulose (MCC), calcium phosphate dibasic, sodium chloride, polyhydric alcohols (eg, mannitol, sorbitol, xylitol and isomalt, which are formed by oxidation of monosaccharides) and talc, sucrose, lactose, starch, cereals, corn or potato starch and other substances that let you adjust density volume and provide fillers the necessary fluidity and MCC also allows slow down the absorption, which is essential for the prolongation action of the drug. It goes well combined with natural extracts, fortified additives and enzymes.

When using fillers their number ranges from 0.02 to 50% relative to the total weight of the mixture.

In order to improve strength, improve the accuracy of dosing powdered material, providing the necessary technological properties of the granulate using binders, humidifiers.

To achieve the necessary adhesive force between the particles of complex powders to prevent stratification of mixture with different content and complex ingredients of granulate necessary to introduce binders. Qualitative and quantitative composition of the binders depends on the physicochemical properties of substances subject to wet granulation. As binders used water, ethyl alcohol,

sugar syrup, 5-10% starch paste, modified starch solutions, 1-10% gelatin solutions, 5-20% solutions PVP, polyvinyl alcohol, kolidonu, plazdonu, 1-2% solutions of methylcellulose, crystalline methylcellulose, carboxymethylcellulose, sodium carboxymethylcellulose, and others. Their composition and quantitative ratio are chosen individually in each case.

If simple moisturizing provides normal granulating powders substances using water. Alcohol is used for granulation hygroscopic powders often when to composition of the mixture included dry extracts. They form the water sticky, resinous mass which cannot granulate [8, 19, 26].

For a mixture of substances with alcohol and water do not form a granulating mass, using solutions of macromolecular substances whose effectiveness depends on the molecular weight. For example, preference is given to polyvinylpyrrolidone trade name Kollidon®, having a molecular weight of from 2,000 to 1,5 x 106, Klucel® EF molecular weight from 45000 to 70000-80000 and others.

In evaluating effectiveness of binder's parameters that determine the strength of granules are wetting powders, film formation of binder substances and its deformation. Wetting ability increases in sequence: PVP - gelatin - hydrolyzed of starch paste - PVS -OPMTS. Binding capacity of macromolecular compounds also determined by molecular mass of substances. The most efficient and fast binders are cellulose derivatives used for highly springiness and elastic low substances less effective - starch derivatives.

Disintegrating substance introduced into granulate to improve their disintegration in the gastrointestinal tract, which is necessary for the release and subsequent absorption of active ingredients. As disintegrants are used substances of different chemical nature: starch, methylcellulose, sodium carboxymethylcellulose, alginic acid and its sodium salt, amylopectin, Carbopol (improve disintegration due to swelling), twin (improve wetting particles) [19, 25].

Antifrictional substances increases the fluidity of granulate. They are divided into three groups: 1 - slidings (starch, talc, kaolin, aerosil, low-fat milk powder,

polyethylene 4000); 2 - lubricating (stearic acid and its salts, vaseline oil, tween, polyethylene 400, silicon-containing); 3 - substances which prevent sticking (talc, starch, stearic acid, its salts).

Lubricants - substances that provide to the material slippery and prevent the adhesion of its particles, namely magnesium stearate, aluminum and calcium, talcum, silicones. When using auxiliary means their total number relative to total weight of the mixture is from 0.1 to 10%, preferably from 0.1 to 1%. Lubricants are also used as hydrophobic agents with a large specific surface, which is very important when using hygroscopic materials. Medications that improve fluidity, for example, silicas, in particular, silicas of high purity, produced under the trade name Aerosil®, may be added in an amount of 0.1 to 5% relative to the total weight of the mixture.

When selecting auxiliary substances important their indifference. Many drugs under certain auxiliary substances become unstable and in them occur chemical changes [6, 8, 25].

Thus, for the granulation mixtures which structure includes dry extracts can be used auxiliary substances that are moistened active ingredients and do not cause the formation of adhesive, resinous mass.

Conducted analysis of the literature concerning pharmacotherapy proved the relevance of creating new herbal medicines for the treatment of respiratory diseases.

CONCLUSIONS TO CHAPTER 1

1. On the basis of the analysis of data of literature the major factors influencing emergence and the course of acute respiratory diseases are defined.

2. On the basis of analysis findings of the market of medicines for treatment of acute respiratory diseases expediency of creation of firm dosage form with phytocomponents is established.

3. The analysis of current state of production of firm dosage forms is carried out.

CHAPTER 2
OBJECTS AND METHODS OF RESEARCH

The aim of our work is the development of composition and technology of the drug in capsule form for treatment respiratory diseases based on a combination of plant compounds.

With the aim of substantiation of theoretical structure, optimization of technological production parameters of capsules to the research subject were dry extracts of linden flowers and licorice root which provide basic pharmacological effect and their mixes with auxiliary substances.

2.1. Characteristics of active and auxiliary substances as objects of research

Characteristics of active substances

Linden flower extract. Amorphous powder from light brown to brown color, forms lumps, bitter taste, specific odor. Soluble in water, sparingly in glycerol. Containing flavonoids, tannins, volatile oil and mucilage components, are used due to their antibactericidal, anti-inflammatory and astringent effects.

Licorice root extract. Brown fine powder with characteristic odor and taste is easily soluble in water. The polysaccharide fraction of licorice has hown remarkable immunomodulatory activity, especially by strengthening phagocytosis in the endothelial reticular system and stimulating interferon production. Glycyrrhizin has long demonstrated its strengthening action on hydrocortisone anti-inflammatory activity. Other flavonoid components of licorice root, such as liquiritoside, have also shown in vitro anti-inflammatory activity. In the respiratory system it has a similarly soothing and healing action, reducing irritation and inflammation and has an expectorant effect, useful in irritating coughs, asthma and chest infections.

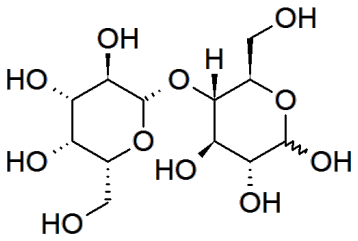
Characteristics of the auxiliary substances.

Potato starch dry (CAS Registry Number 9005-25-8).

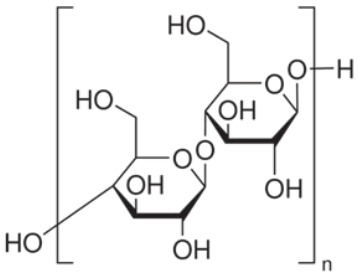
$(C_6H_{10}O_5)$ n

White with crystal, odorless, with a mass fraction of humidity 17 - 20%, without mechanical impurities. Normalized humidity, acidity, ash content, the number of specks (unseparated pulp particles), the content of sulfur dioxide.

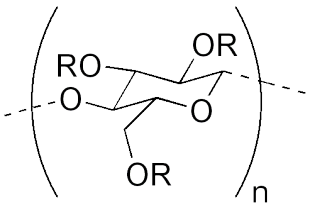
Lactose Granulac 140 (CAS Registry Number 63-42-3) - white or almost white crystalline powder, odorless, weakly sweet taste, easily soluble in water, very slightly soluble in ethanol, practically insoluble in ether and chloroform.



Microcrystalline cellulose 101 and 102 (MCC) (CAS Registry Number 9004-34-6) - snow-white powder, odorless and taste. The substance is not soluble. It can serve as filling, gluing and disintegrant the substance.



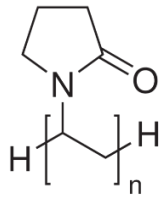
Methylcellulose (CAS Registry Number 9004-67-5).



R = H or CH_3

Fiber powder is practically odorless and tasteless. Soluble in cold water, forms a gel when heated, at prolonged heating and boiling occurs coagulation.

Polyvinylpyrrolidone (PVP)(CAS Registry Number 9003-39-8).



PVP results from the polymerization of vinylpyrrolidone. Different chain lengths yield in different viscosities. Traditionally, the degree of polymerization is characterized by the K-value, which is essentially a function of the viscosity in aqueous solution. We offer two grades of major importance, PVP K-25, K-30 and PVP K-90.

Ethanol (CAS Registry Number 64-17-5)

CH_3CH_2OH

A colorless, clear, volatile, flammable liquid. Hygroscopic. Mixed with water and methylene chloride. Lights smokeless blue flame. Boils at a temperature of about 78 ° C. The relative density of 0.805 to 0.812. It is used in the pharmaceutical field as a solvent.

Purified Water (SPhU, 1st ed., P. 307) - liquid without color, odorless. Used as an auxiliary substance in various stages of the process.

2.2. Methods of research

In the study of properties of the capsules being developed have used common methods of organoleptic, technological and physico-chemical studies that allow objectively evaluate their quality based on obtained results.

Physical and chemical properties

Shape and size of particles. The particle size of powders is determined by their length and width, which is measured using a microscope equipped with a micrometer grid at a magnification of 400 or 600 times.

Particle shape is established against to the average length of the particles to the average width. At this method the particles are conditionally divided into three main types: elongated - the ratio of length to width - more than 3: 1; lamellar -

length exceeds the width and thickness of not more than 3 times; equiaxed - have a spherical, polyhedral shape close to izodiathermic.

Specific surface area - total surface occupied by a powdery substance, and the contact surface - the surface, which is formed at a contact between the powder particles.

True density of the powder is determined by the ratio of mass to volume of the drug, at zero porosity of powder. As a comparison, use any liquid, wetting, but does not dissolve the powder. Determination is carried out using a pycnometer. True density (ρ kg / m^3) of powder is determined by the formula:

$$\rho = \frac{m \cdot \rho_l}{m + m_1 + m_2}$$

where m - mass of substance, g;

ρl - liquid density, g/cm^3;

m1 - mass of the pycnometer with the substance, g;

m2 - mass of the pycnometer with a liquid and substance, g.

Hygroscopicity. If vapor pressure in the air more than the elasticity of solids on the surface, whereas the powder mass prepared for tableting starts absorb vapor from the air and blur in absorbed water. Moisture absorption kinetics determined by weight method in (normal) ordinary conditions, under extreme (desiccator over water - 100% relative humidity), or in a climate chamber.

$$X = \frac{m_k - m}{m_k} \cdot 100$$

where m - mass of substance, g;

mk - mass of substance after the experiment, g

X - water absorption, %.

If substance is highly hygroscopic, it determines use of auxiliary substances - moisture stimulants.

Technological properties

Technological properties of powdered medicinal substances depend on their physico-chemical properties.

Fraction (granulometry) composition or allocation of powder particles by size, have some influence not its flowability, and hence of rhythmical work of tableting machine, stability of the obtained tablet mass accuracy of dosage of the drug as well as the qualitative characteristics of tablet (appearance, disintegration, strength, etc.).

Fastest and most convenient method for determining the of dispersion is sieve analysis. Technics of this analysis is that 100,0 g of analysed powder sieved through a sieve set (hole diameter 2.0; 1.0; 0.5; 0.25 and 0.1 mm). A weighed sample of material is placed on the largest (upper) mesh sieve and shaken entire set of sieves (manually or vibration installations) for 5 minutes, and then find the mass of each fraction and its percentage content.

Tapped (volume) density - is mass per unit volume of freely bulk powdered material. The tapped density depends on the shape, size, density of the powder particles (granules), and their moisture. According to the bulk density is possible to predict the volume of the matrix channel. Determination of bulk density of powder is carried out on the device of bulk density control.

Is weighed 5.0 g of the powder to the nearest 0.001 g and filled up it into measuring cylinder. Sets the amplitude of oscillations (35-40 mm) through the adjusting screw and after the mark on a scale fix the position by lock nut. Frequency of oscillation is set by means of a transformer within 100 - 120 osc / min counter. Further, turned on device by toggle switch and watching at benchmark of powder in the cylinder. When the powder becomes permanent (typically 10 minutes) device is switched off.

Bulk density was calculated using the formula:

$$\rho_{н} = \frac{m}{V} = \frac{5 \times 10^{3}}{V}$$

where ρн - bulk density, kg / m^3;

m - mass of the bulk material, kg;

V - volume of the powder after compacting in cylinder, m^3.

Depending on the bulk density powders are distinguished as follows:

ρн > 2000 kg / m^3 - a very heavy;

2000> ρн > 1100 kg / m^3 - heavy;

1100> ρн > 600 kg / m^3 - average;

ρн <600 kg / m^3 - lungs.

Fluidity (flowability) - is ability of the powdered system to fall out of the funnel capacitance or "flow" under gravity and to ensure uniform filling of the channel matrix. Material having poor flowability in the hopper adheres to the walls, which gives rhythm of it enters to the matrix. This leads to the fact that a given mass and density of the capsules will fluctuate.

Flowability is determined on the vibration device for removing characteristics of bulk materials.

In the device is provided vibration of cone funnel by its rigid connection with an electromagnetic device that uses on AC power. Weighed portion of powder (granules) weighing 50.0 g (to the nearest 0.01 g) was poured into the funnel when the valve is closed, turned on device and stopwatch. After 20 second of jolting that is needed to obtain stable reading, open flap and fixed expiry time of the material from the hopper. Accuracy of flow time - up to 0.2.

Flowability is calculated by the formula:

$$V_c = \frac{m}{t \pm 20},$$

where: Vc - Flowability kg / s;

m - mass of sample, kg;

t - full-time of experiment, s;

20 - time of jolting, s.

In determining the flowability of powders with low bulk density is allowed to use sample weighing of 30.0 g with the aid of the VP-12A is defined as the angle of repose - the angle between the cone the bulk material and the horizontal plane. The angle of repose varies widely - from 25 to 30°C for the free-flowing material and 60-70 ° C for coupled materials.

Flowability of powders is complex characteristic that is determined by the dispersion and particle shape, wet mass and by granulometric composition. This technological characteristic can be used when choosing a tableting technology.

Quality control of capsules

One of the main conditions for the industrial production of capsules is conformity of finished products to the requirements of regulatory and technical documentation. Quality of capsules is determined by various parameters, which are divided into the following groups:

1. organoleptic;
2. physical;
3. chemical;
4. bacteriological;
5. biological.

CONCLUSIONS TO CHAPTER 2

1. On the basis of the analysis of data of literature concerning phytotherapy of SARS active components of dosage form – dry extracts of linden and licorice root extract are defined

2. The complex of physical and chemical, farmako-technology and biopharmaceutical methods of capsules of appropriate quality, necessary for receiving, is established

CHAPTER 3
DEVELOPMENT OF COMPOSITION AND TECHNOLOGY OF CAPSULES FOR TREATMENT OF RESPIRATORY DISEASES

3.1. Study of the physico-chemical and technological properties of dry linden and licorice extracts.

Study of the physico-chemical and technological properties of powdery substances is an important stage in the development of technology of solid dosage forms because of these properties is largely dependent the choice of technology and the quality of the final product. It is known that plant extracts due to complex multicomponent composition, have unsatisfactory physicochemical and technological properties. This is an obstacle to the creation of finished dosage forms directly from dried extracts without using auxiliary substances and pre-granulation.

Studied physico-chemical and technological properties of dry extracts that has most important value when choosing technology of solid dosage forms. The research results are presented in Fig. 3.1-3.3 in the table. 3.1.

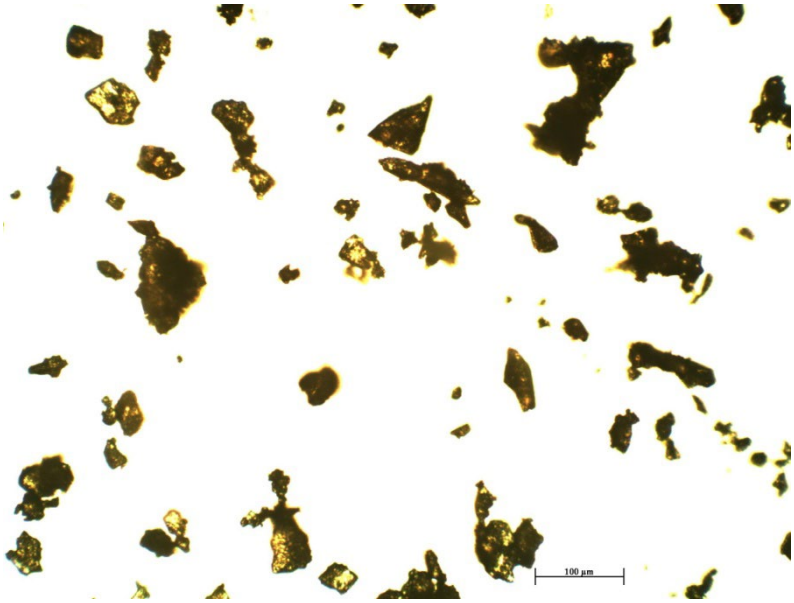


Fig. 3.1. The form of particles of dry linden extract.

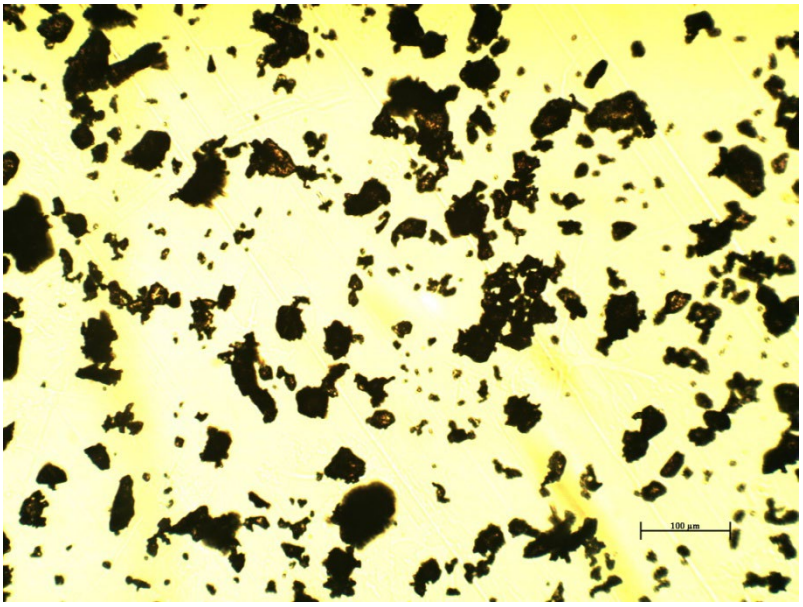


Fig. 3.2. The form of particles of dry licorice extract.

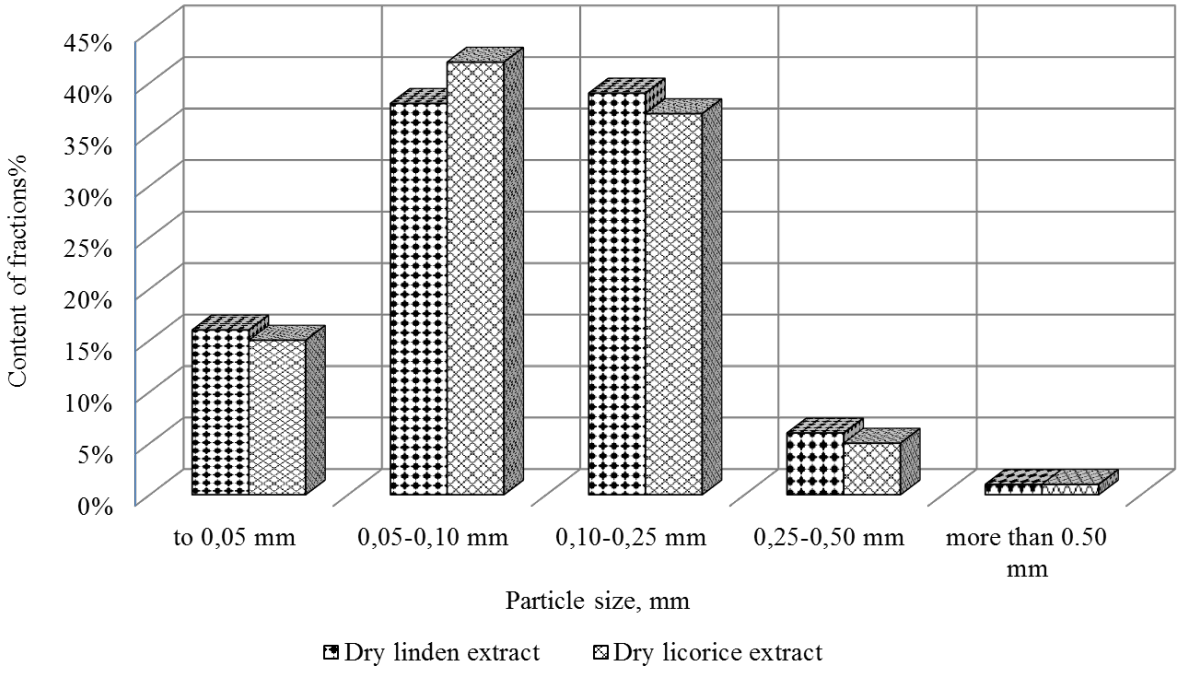


Fig. 3.3. Fractional composition of linden and licorice extracts.

The shape and size of particles cause technological characteristics of substances, such as fluidity, compressibility, bulk weight, surface area, and others. Determined, that the dried studied extracts are amorphous powders with particles of anizodiametric form whose size is in the range from 0.01 mm to 0.1 mm (Fig.

3.1, 3.2). Form factor approaching 0.25 - 0.45. As a result, they do not have fluidity and have high compactness, as evidenced by the data given in the table 3.1.

Analysis of fractional composition showed that both substances are polydisperse with lots of dust-like fractions, which are capable of forming conglomerates (Fig. 3.3).

In the table 3.1. presented data of study technological characteristics of active substances.

Table 3.1

Technological properties of dry linden and licorice extracts

Name	Residual moisture, %	Bulk density, g / cm^3 ρ_0	Bulk density, g / cm^3 ρ_{1250}	Fluidity, g / s	Compactedness
Linden extract	4,4 ±0,2	0,45±0,01	0,62±0,01	∞	0,28±0,1
Licorice extract	4,5 ±0,3	0,33±0,01	0,58±0,01	∞	0,43±0,1

Obtained data suggest that an extract of licorice is a substance with a large power of adhesion between particles that causes their poor fluidity (index of compacting 0.44). Extract of linden have index of compacting 0.28, which can be attributed to powders that have good fluidity. But polydispersity of composition of this substance causes low index of fluidity.

The next stage was study of the hygroscopicity of active components of dosage form that is developed (Fig.3.4, 3.5).

Obtained results show that studied dry extracts are highly hygroscopic substances. The equilibrium humidity of environment at which there is no change of weight of dry extract, is in the area of 23%. At humidity of environment of 75% increase in weight is 8,0-9,0% at 5 hours. At the same time residual moisture in the initial moment of research was quite high and amounted to 4.0-4.5% (Table 3.1.).

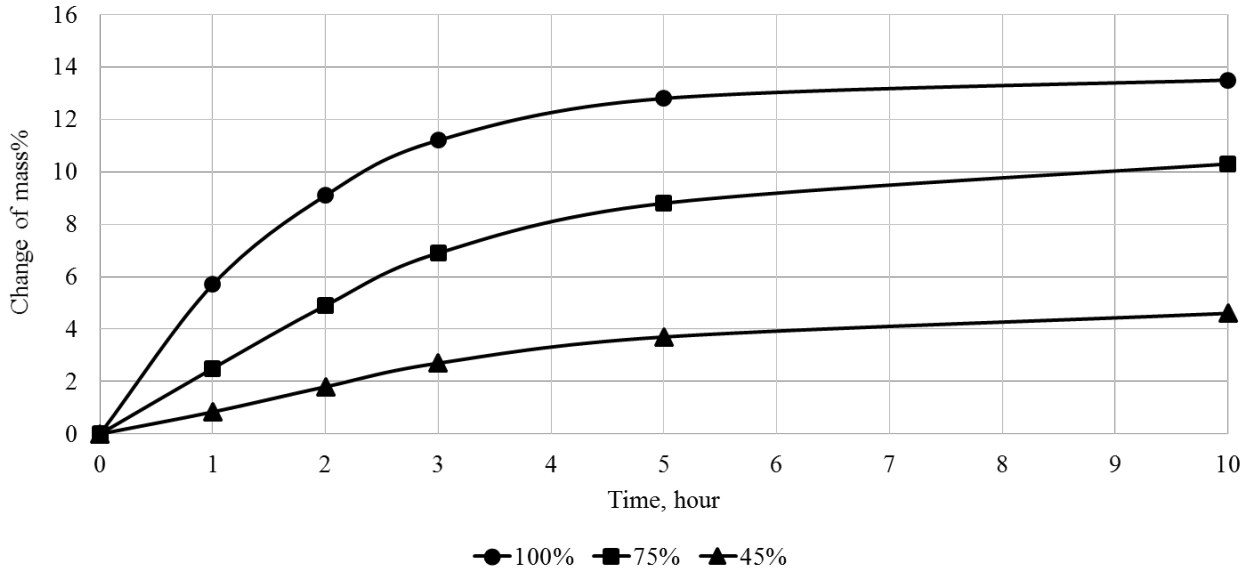


Fig. 3.4. Hygroscopicity of linden dry extract.

At 100% relative humidity of air granules absorb moisture very quickly, while their structure is destroyed.

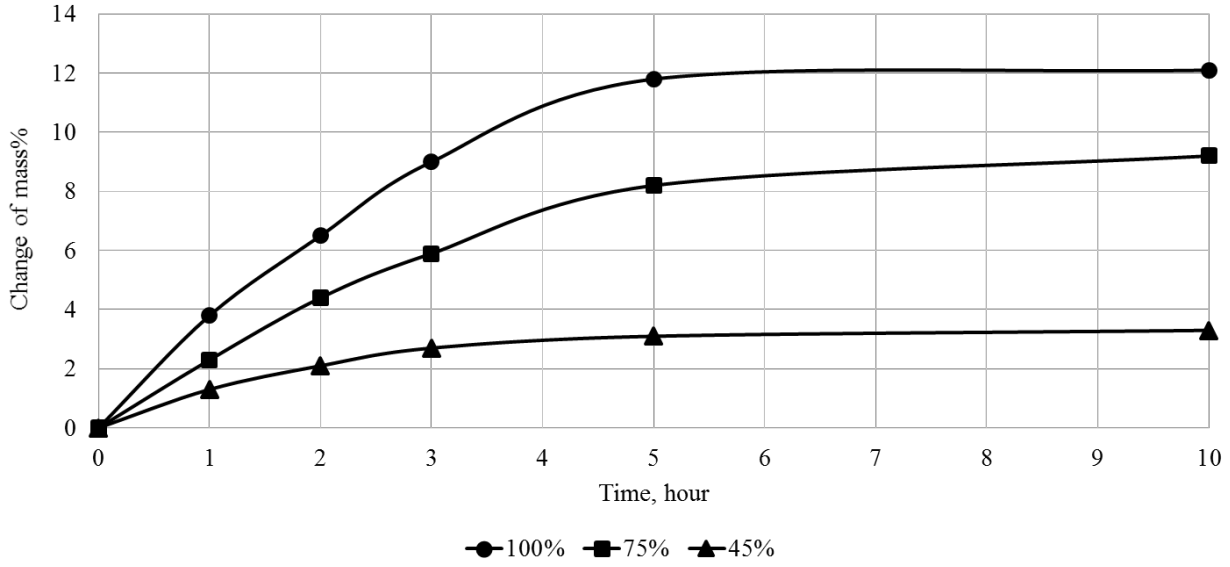


Fig. 3.5. Hygroscopicity of licorice dry extract.

Thus, conducted studies have shown necessity of using efficient auxiliary substances that reduce water absorption and improve technological characteristics of dry extracts, as well as preliminary granulation.

3.2. Choice and substantiation of composition of auxiliary substances for granules with dry extracts of linden and licorice.

Introduction into granular mass of filler is necessary for improvement flowability, compression and reduce water absorption of plant material. For select filler were studied technological properties traditionally used in the pharmaceutical industry substances such as potato starch, microcrystalline cellulose (MCC), milk sugar (lactose) (Table. 3.2).

Table 3.2

Technological properties of fillers

Filler	Bulk weight g/ cm ^{3}	Fluidity, g / s	Compressibility, H	Fraction less than 0.05 mm% (wt)
1	2	3	4	5
Potato starch	0,65±0,02	∞	35±0,2	54,4±0,4
MCC 101	0,29±0,02	2,5±0,2	92±0,5	-
MCC 102	0,32±0,02	2,9±0,2	93±0,5	5,3±0,4
Lactose Granulac 140 (MEGGLE)	0,61±0,02	6,0±0,2	78±0,3	3,8±0,4

Analysis of the data presented in the Table 3.2 shows that the largest fluidity have lactose probably because of the spherical shape of particles and relatively high value of bulk weight. MCC have the largest compressibility, but its fluidity is within 2.5-3.0 g / s. Worst technological indicators has starch.

Thus, the study of technological properties of fillers showed prospects of using for the studied lactose extracts because of content of the small dust-like fraction (<0.05 mm), very high values of fluidity. In addition, fractional composition and bulk weight of lactose and studied extracts close to the value that is necessary to achieve homogeneity of mixing at granulation.

For establishing the influence of filler at hygroscopic and technological properties of extracts they were mixed with various fillers and obtained granules in a laboratory apparatus for wet granulation. As a humidifier was used 5% solution

of polyvinylpyrrolidone (PVP), 3% solution of methylcellulose, their mixture and ethyl alcohol 96%. The content of the extracts in the mixture - 34%.

Dried obtained granules at temperature 50 C to a residual moisture of 1.5%. Then conducted a comparative analysis of the granules by technological properties, which presented in tables 3.3, 3.4, 3.5, 3.6.

Table 3.3

The main technological properties of granules with dry extracts of obtained by the method of wet granulation with PVP solution of 5%.

Composition of granulate (Content of extracts - 34%, filler - 66%)		Bulk density, g / cm^3 ρ_0	Bulk density, g / cm^3 ρ_{1250}	Fluidity, g / s	Compactedness	Abrasion resistance, %
Potato starch	A mixture of dry extracts	0,43±0,02	0,52±0,02	5,2±0,3	0,17±0,3	0,95±0,3
MCC 102		0,52±0,02	0,58±0,02	6,3±0,3	0,10±0,3	0,56±0,2
Lactose Granulac 140		0,55±0,02	0,62±0,02	6,0±0,3	0,11±0,3	0,75±0,1

Analysis of the data presented in the table. 3.3 showed that the introduction of auxiliary substances considerably improved technological properties of active components. Index of compression is within the 0.05 - 0.15, indicating about good rheological properties. Also, the low value of this index leads to the conclusion about slight effort, which should be applied when filling capsules. Granules produced using starch as filler, had the lowest technological properties. The obtained granules had heterogeneous composition and unstable structure. This can be explained by the fact that at moistened of granular mass by humidifier happens partial swelling of the starch grains. As a result, happens decrease in bulk weight of granules, it becomes looser.

Granules with MCC and lactose have a fairly low coefficient of compression and high index of abrasion resistance. However, granules with MCC have a lower fluidity than granules of lactose, so in the case of used as a filler MCC necessary application of highly efficient lubricants.

Table 3.4

The main technological properties of granules with dry extracts of obtained by the method of wet granulation with solution of MC 3%

Composition of granulate (Content of extracts - 34%, filler - 66%)		Bulk density, g / cm^3 ρ_0	Bulk density, g / cm3 ρ_{1250}	Fluidity, g / s	Compactedness	Abrasion resistance, %
Potato starch	A mixture of dry extracts	0,72±0,02	0,78±0,02	7,2±0,3	0,07±0,03	0,45±0,3
MCC 102		0,70±0,02	0,76±0,02	8,3±0,3	0,05±0,03	0,36±0,2
Lactose Granulac 140		0,75±0,02	0,80±0,02	8,0±0,3	0,06±0,03	0,35±0,1

Application of 3% MC solution significantly improved fluidity, reduced grip strength of granules to a minimum (0.05) and significantly increased the strength of granules that can lead to increased disintegration time. Compression of granules does not depend of the type of filler and has minimal indexes.

Table 3.5

The main technological properties of granules with dry extracts of obtained by the method of wet granulation with solution of MC 0.5% and PVP 5%

Composition of granulate (Content of extracts - 34%, filler - 66%)		Bulk density, g / cm^3 ρ_0	Bulk density, g / cm^3 ρ_{1250}	Fluidity, g / s	Compactedness	Abrasion resistance, %
Potato starch	A mixture of dry extracts	0,58±0,02	0,65±0,02	8,3±0,3	0,11±0,03	0,63±0,3
MCC 102		0,62±0,02	0,67±0,02	8,5±0,3	0,07±0,03	0,43±0,2
Lactose Granulac 140		0,67±0,02	0,72±0,02	9,4±0,3	0,07±0,03	0,45±0,1

Application as humidifier mixture of macromolecular substances in concentrations 0.5% and 5% of MC and VFR respectively is allowed to obtain granules with minimum effort cohesion with good fluidity. Indicators of bulk density can be attributed of obtaining granules to the average by the severity of the flowing material that does not needs additional introduction of auxiliary substances to improve compression.

Table 3.6

The main technological properties of granules with dry extracts of obtained by the method of wet granulation with solution with ethanol

Composition of granulate (Content of extracts - 34%, filler - 66%)		Bulk density, g / cm^3 ρ^0	Bulk density, g / cm^3 ρ_{1250}	Fluidity, g / s	Compactedness	Abrasion resistance, %
Potato starch	A mixture of dry extracts	0,53±0,02	0,61±0,02	8,7±0,3	0,13±0,3	1,1±0,3
MCC 102		0,57±0,02	0,64±0,02	9,5±0,3	0,11±0,3	0,97±0,2
Lactose Granulac 140		0,59±0,02	0,67±0,02	10,0±0,3	0,12±0,3	0,95±0,1

Obtained granulate using ethyl alcohol at a sufficient fluidity irrespective of filler has poor strength indicators and needs at encapsulation additional sealing.

For the final determination of type of humidifier, we conducted researches of disintegration of obtained granules (Figure 3.6).

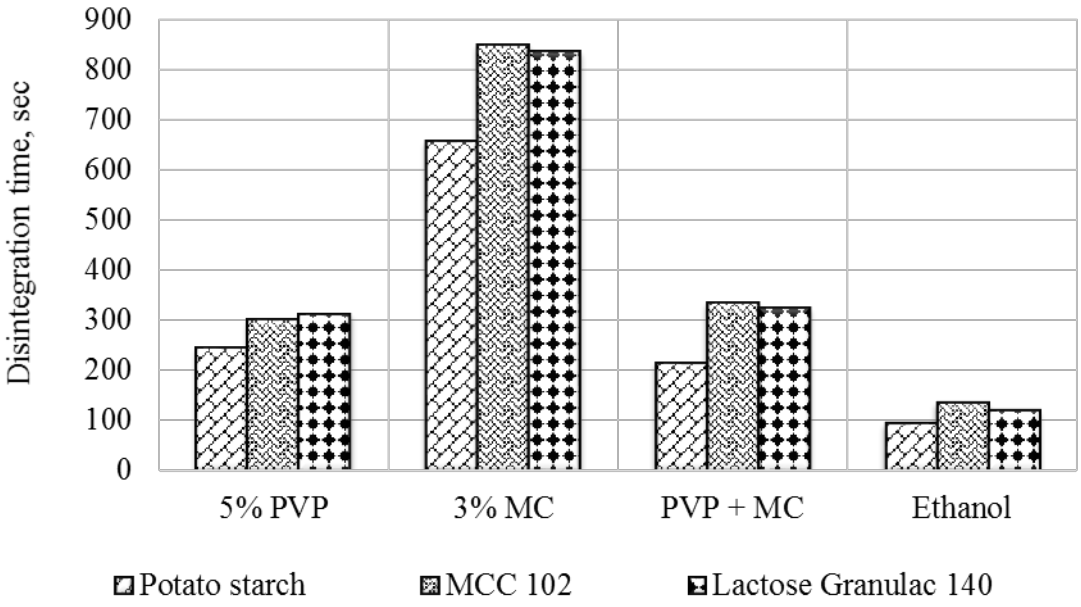


Fig. 3.6. Disintegration time of granulates samples

Obtained data of determination disintegration of samples that were studied indicate about reducing the time of disintegration occurs in series of 3% MC→PVP + MC → 5% PVP → ethanol. When comparing the indicators of strength, which vary in series MC→ MC + PVP → 5% PVP → ethanol can conclude that the best moisturizer is a mixture of solution and 5% PVP 0.5% MC. Indicators of disintegration, sealing, strength correlate with the value of fluidity.

Because dry extracts of linden and licoriceare highly hygroscopic substances, we had the task to reduce their hygroscopic by introduction of filler moisture regulating properties. It is known that among these fillers lactose largely reduces the hygroscopic of extract. Obtained research confirmed that data for our facilities (Fig. 3.7).

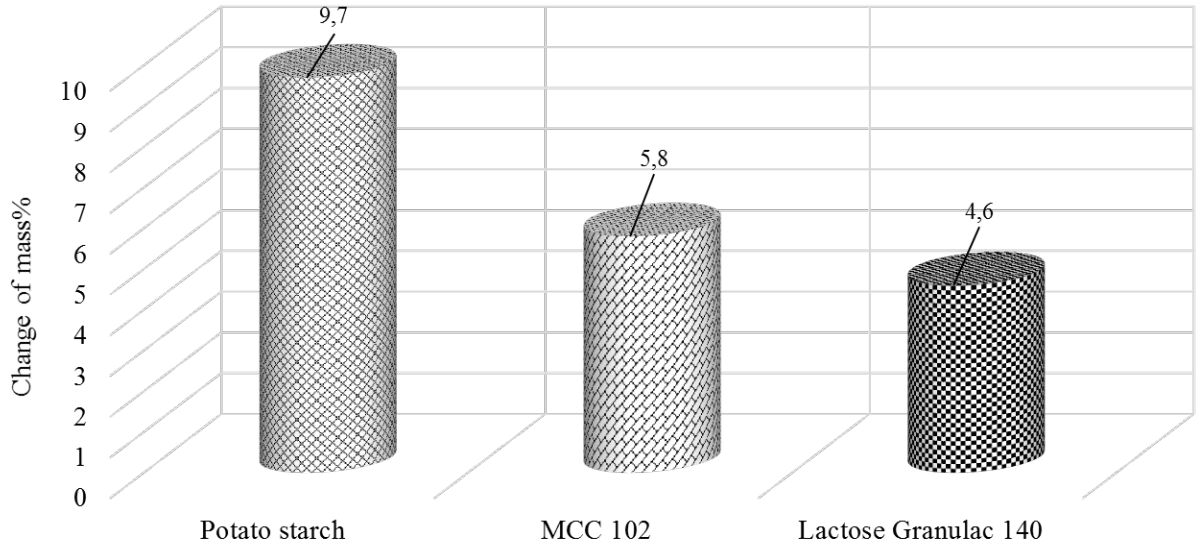


Fig. 3.7. Change of mass of granules sample with dry extracts by 3 hour of observation at a relative humidity of air 100%.

In order to improve moisture resistance and fluidity of the capsule mass we have introduced into its structure aerosil in the amount of 1%.

Conducted studies allow to conclude that the optimal filler in the development of solid dosage forms with dry extracts of linden and licorice is lactose. Putting it into the capsules can significantly improve the technological properties of active substances and reduce their ability to absorb moisture.

Study of moisture content, moisture absorption kinetics of extracts showed that the plant components have significant high percentage of humidity and moisture absorption, that is indicating that the feasibility of establishing of a drug in capsule form.

Thus, as a result of conducted researches we proposed composition of the solid dosage form in the form of capsules:

	g
Dry linden flower extract (in terms of dry matter)	0,20
The dry extract of licorice root (in terms of dry matter)	0,10

Lactose Granulac 140	0,55
Aerosil	0,009
Polyvinylpyrrolidone (PVP)	0,015
Methyl cellulose (MC)	0,0015
Average weight	0,876

The resulting mass for encapsulation has bulk density of 0.670 g / ml, which corresponds capsule number 000 - the average content of the capsule - 1.37 ml.

3.3. Description of technological process of capsules production for the treatment of respiratory diseases.

By obtained results of the research we have developed technology of capsules for the treatment of respiratory diseases. The process consists of the following stages:

Stage 1. Preparation of the raw material. Each batch of raw material (main and auxiliary) and packaging material before using in production is subject to control for compliance to normative documents. First, active and auxiliary substances are weighed at series in calibrated marked storage tank. Components of mass for encapsulation are weighed on the scales and sieving through the sieve with appropriate holes diameter in calibrated storage tanks.

Stage 2. Preparation of a humidifier. Measure out the water in the measuring tank and fed to the reactor, in which is loaded sifted and weighed PVP and MC. Mixed for 20 minutes. Obtained humidifier transmitted to the stage of granulation.

Stage 3. Mixing, humidification and granulation. Mixing and moisture of mass is carrying out in granulator-mixer at running extract and input ventilation. In the granulator-mixer loaded sifted and weighted mass of active and auxiliary substances. Carry out mixing during (10 ± 1) min. Then to the dry ingredients is added humidifier - 5% solution of PVP and 0.5% MC and conduct mixing during (10 ± 1) min to uniform moisture distribution throughout the mass, the latter

should be uniform, well-hydrated and should ball up at squeezing in the hand. Wet granulation is carried out through the granulator with holes diameter of 1.0 mm. The wet granulated shipped in the tank.

Stage 4. Drying of granules. Wet granulate from the tank is fed in drying cabinet polychkovoho type and dried at (60 ± 1) °C during 1.50 hours to a residual humidity of (2,0 ± 1,5) %. Control and regulation of temperature of drying is carried out by automatic devices. Humidity of granulate determined by moisture meter. Dry mass is shipped in the tank.

Stage 5. Dry granulation and sieving. From the tank dry granulate is passed through a calibrator with holes diameter of 1.0 mm, collecting granules in the container.

Stage 6. Dusting of granules. The obtained granules and aerosil are fed into the mixer and carrying out powdering (5 ± 1) min. The mass is unloaded in the tank.

Stage 7. Encapsulation. Granules from collection loaded into the automatic capsule filling machine. Encapsulated by capsules №000, average weight 0,90 ± 0,02g.

The required weight of capsule is set by the depth of filling the matrix. Regulation of filling matrices is carried out using of the filling regulator. Selectively every 30 minutes check capsule weight by electronic scales. In the process of encapsulation is taking samples for chemical analysis. The container with capsules after positive test result with a passport of OCC, is transported to the packing stage.

Stage 8. Packaging capsules in blister packs. Stage 9. Packaging in packs. Packing packs in boxes. Capsules packed by 10 pieces in blister with aluminum foil on the machine. Contoured packages of 5 pieces with leaflet put in carton packs. At this stage provide control of drug at microbiological purity.

The general scheme of technological process in Figure 3.8.

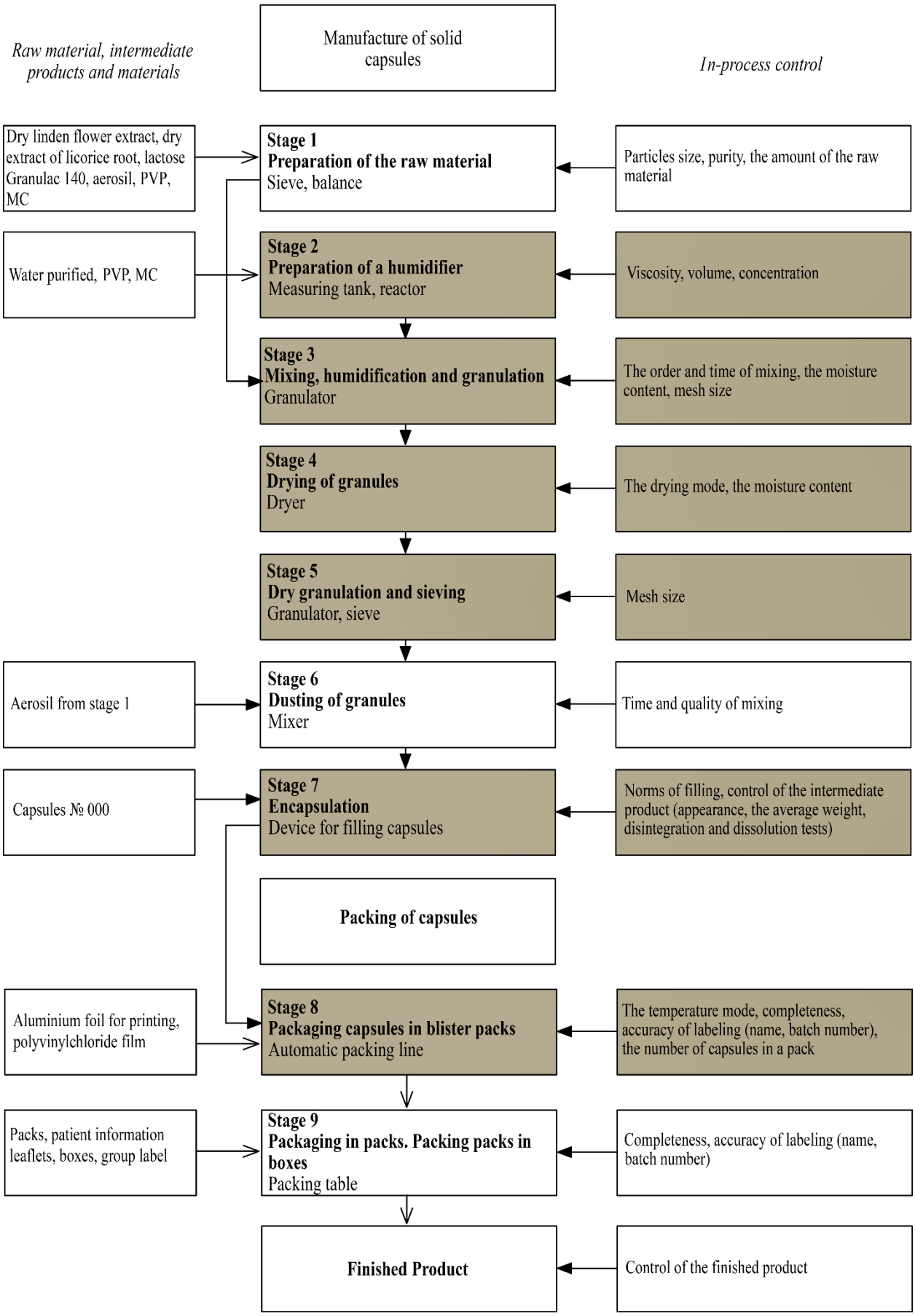


Fig. 3.8. The technological scheme of manufacturing capsules

CONCLUSIONS TO CHAPTER 3

1. During physico-chemical and farmako-technology researches it is established that dry extracts possess the low flowability, high absorbing capacity and unsatisfactory indicators of compactibility.

2. For the purpose of rational choice of excipients properties of potato starch, microcrystallic cellulose and lactose are studied. Technical characteristics on mixes for granulation with different humidifiers are established (MC of 3%, PVP of 5%, PVP of 5% of MC 0.5%i ethanol). On the basis of the conducted researches the rational structure of capsules the technology scheme of their production is offered.

GENERAL CONCLUSIONS

1. Literature review presented characteristics and evaluation of drugs that are used for treatment of respiratory diseases. Grounded expediency of developing new combined drugs in capsule form based on substances of natural origin.

2. The conducted analysis of the current state of production of solid dosage forms in the form of capsules.

3. Were studied physical and chemical and technological parameters linden flower extract and licorice root. The results showed that they do not meet the technological requirements for creating the drug.

4. Were studied influence of auxiliary substances on pharmaco-technological of obtained granules. It was established that the best humidifier for mixture that is encapsulated are solutions of MC 0.5% and 5% PVP and optimum filler is lactose.

REFERENCES

1. Abbasi IN, Ahsan A, Nafees AA. Correlation of respiratory symptoms and spirometric lung patterns in a rural community setting, Sindh, Pakistan: a cross sectional survey. BMC Pulm Med. 2014; 12:81.

2. Ahn JH. An update on the role of bronchoscopy in the diagnosis of pulmonary disease. Yeungnam Univ J Med. 2020; 37(4):253–61.

3. Bhattacharyya O, Delu Y, Wong ST, et al. Evolution of primary care in China 1997–2009. Health Policy. 2021; 100(2–3):174–80.

4. Chen Z. Launch of the health-care reform plan in China. Lancet. 2009;373(9672):1322–4.

5. CPC Central Committee. State Council. The outline of the Healthy China 2030 strategy. 2019. http://www.gov.cn/zhengce/2019-07/15/content_5409694.htm. Accessed 1 May 2021.

6. Donaldson MS, Vanselow NA, Yordy KD, editors. Institute of Medicine Committee on the Future of Primary Care. Defining primary care: an interim report. Washington, DC: National Academies Press; 2014.

7. Doyle C, Lennox L, Bell D. A systematic review of evidence on the links between patient experience and clinical safety and effectiveness. BMJ Open. 2013; 3(1):e001570.

8. Duvall K, Frank GW. Identifying chronic obstructive pulmonary disease in primary care of urban underserved patients: tools, applications, and challenges. J Natl Med Assoc. 2020; 102(7):570–8.

9. GBD 2015 Chronic Respiratory Disease Collaborators. Global, regional, and national deaths, prevalence, disability-adjusted life years, and years lived with disability for chronic obstructive pulmonary disease and asthma, 1990–2015: a systematic analysis for the Global Burden of Disease Study 2015. Lancet Respir Med. 2017; 5:691–706.

10. Hu S, Tang S, Liu Y, et al. Reform of how health care is paid for in China: challenges and opportunities. Lancet. 2018; 372:1846–53.

11. Huang K, Yang T, Xu J, et al. Prevalence, risk factors, and management of asthma in China: a national cross-sectional study. Lancet. 2019; 394(10196):407–18.

12. Jang JG, Chung JH. Diagnosis and treatment of multidrug-resistant tuberculosis. Yeungnam Univ J Med. 2020; 37(4):277–85.

13. Jin HJ. Biological treatments for severe asthma. Yeungnam Univ J Med. 2020; 37(4):262–8.

14. Kim S, Lim JH, Woo CH. Therapeutic potential of targeting kinase inhibition in patients with idiopathic pulmonary fibrosis. Yeungnam Univ J Med. 2020; 37(4):269–76.

15. Krinke KS, Tangermann U, Amelung VE, et al. Public preferences for primary care provision in Germany—a discrete choice experiment. BMC Fam Pract. 2019; 20(1):80.

16. Kuang L, Liang Y, Mei J, et al. Family practice and the quality of primary care: a study of Chinese patients in Guangdong Province. Fam Pract. 2015; 32(5):557–63.

17. Kuo YF, Chen NW, Baillargeon J, et al. Potentially preventable hospitalizations in medicare patients with diabetes: a comparison of primary care provided by nurse practitioners versus physicians. Med Care. 2015; 53(9):776–83.

18. Li X, Krumholz HM, Yip W, et al. Quality of primary health care in China: challenges and recommendations. Lancet. 2020; 395(10239):1802–12.

19. Li X, Lu J, Hu S, et al. The primary health-care system in China. Lancet. 2017; 390(10112):2584–94.

20. Mafi JN, Wee CC, Davis RB, et al. Comparing use of low-value health care services among U.S. advanced practice clinicians and physicians. Ann Intern Med. 2016; 165:237–44.

21. Ministry of Health of the People’s Republic of China. China health statistical yearbook 2009. Beijing: Peking Union Medical College Publishing House; 2015.

22. National Health Commission of the People's Republic of China. China health statistical yearbook 2019. Beijing: Peking Union Medical College Publishing House; 2019.

23. National Health Commission of the People's Republic of China. China health statistical yearbook 2020. Beijing: Peking Union Medical College Publishing House; 2020.

24. Peng B, Zhang PJ, Wu SN, et al. Chronic respiratory disease management in grassroots medical institutions of China. Chin Gen Pract. 2018; 21(13):1513–20.

25. Santos AFD, Rocha HAD, Lima A, et al. Contribution of community health workers to primary health care performance in Brazil. Rev Saude Publica. 2020; 54:143.

26. Wang C, Xu J, Yang L, et al. Prevalence and risk factors of chronic obstructive pulmonary disease in China (the China Pulmonary Health [CPH] study): a national cross-sectional study. Lancet. 2018; 391(10131):1706–17.

27. Wang J, Wang P, Wang X, et al. Use and prescription of antibiotics in primary health care settings in China. JAMA Intern Med. 2014; 174(12):1914–20.

28. Wang W, Haggerty J, Loban EK, et al. Evaluating primary health care performance from user perspective in China: review of survey instruments and implementation issues. Int J Environ Res Public Health. 2019; 16(6):926.

29. WHO. Global status report on noncommunicable diseases 2014[R]. https://www.who.int/publications/i/item/9789241564854. Accessed 1 May 2021.

30. Wong WCW, Jiang S, Ong JJ, et al. Bridging the gaps between patients and primary care in China: a nationwide representative survey. Ann Fam Med. 2017;15(3):237–45.

APPLICATIONS

Appendix A

МІНІСТЕРСТВО ОХОРОНИ ЗДОРОВ'Я УКРАЇНИ
НАЦІОНАЛЬНИЙ ФАРМАЦЕВТИЧНИЙ УНІВЕРСИТЕТ

АКТУАЛЬНІ ПИТАННЯ СТВОРЕННЯ НОВИХ ЛІКАРСЬКИХ ЗАСОБІВ

МАТЕРІАЛИ
XXIX МІЖНАРОДНОЇ НАУКОВО-ПРАКТИЧНОЇ
КОНФЕРЕНЦІЇ МОЛОДИХ ВЧЕНИХ ТА СТУДЕНТІВ

19-21 квітня 2023 року
м. Харків

Харків
НФаУ
2023

DEVELOPMENT OF COMPOSITION OF CAPSULES FOR THE TREATMENT OF RESPIRATORY DISEASES

Saidi Said
Scientific supervisor: Puliaiev D.S.
National University of Pharmacy, Kharkiv, Ukraine
d.s.puliaiev@nuph.edu.ua

Introduction. Respiratory diseases are one of the most important health problems due to their high prevalence, often severe with frequent complications. Treatment of these diseases to date remains a difficult problem due to the fact those respiratory diseases with different etiologies similar to clinical manifestations. Therefore, it is important in the arsenal of medicines have the effect of which will be aimed at the reduction and elimination of the main manifestations of the disease, regardless of etiology, and at the same time be safe for treatment.

In recent years, more and more recognition have herbal medicinal products. The advantage of plant-based drugs is that biologically active substances of plants more natural included in the metabolic processes of the human body, unlike synthetic drugs.

Aim. Development of composition capsules for the treatment of respiratory disease.

Materials and methods. The physicochemical, technological and biopharmaceutical methods have been used in study.

Results and discussion. The characterization and evaluation of medications used to treat respiratory diseases in literary sources has been explored. It has been demonstrated how quickly novel combination medications in capsules form based on medicinal plant materials may be developed. The research of medicinal raw materials is important for producing novel medications, according to the literature.

As active substances, a dry extracts of linden flower and licorice root is proposed, which is characterized by inflammatory, antimicrobial, diaphoretic, antipyretic antiallergic, expectorant, spasmolytic actions.

During physicochemical and technology researches it is established that dry extracts possess the low flowability, high absorbing capacity and unsatisfactory indicators of compactibility. For the purpose of rational choice of excipients properties of potato starch, microcrystallic cellulose and lactose are studied. Technical characteristics on mixes for granulation with different humidifiers are established (MC of 3%, PVP of 5%, PVP of 5% of MC 0.5%i ethanol). Based on the studies carried out, a rational composition of capsules and a technological scheme for their production are proposed.

Conclusions. Development of composition of the capsules for the treatment of the respiratory disease was conducted.

RATIONALE OF THE CREAM COMPOSITION FOR THE URTICARIA TREATMENT

Ziati Ibtissam[1], Kovalov V.M.[2]
Scientific supervisor: Kovalov V.V[1]
[1]National University of Pharmacy, Kharkiv, Ukraine
[2]Kharkiv National Medical University, Kharkiv, Ukraine
volodyakw@gmail.com

Introduction. Significant prevalence, variety of clinical forms, chronic relapsing course, a large number of complications put allergic diseases in a number of priority interdisciplinary problems

Ф А 2.2.1–32-366

National University of Pharmacy

Faculty for foreign citizens' education
Department of pharmaceutical preparations technologies

Level of higher education master

Specialty 226 Pharmacy, industrial pharmacy
Educational program Pharmacy

APPROVED
The Head of department
of pharmaceutical preparations
technologies
Oleksandr KUKHTENKO
"01" September 2022

ASSIGNMENT
FOR QUALIFICATION WORK
OF AN APPLICANT FOR HIGHER EDUCATION

Saidi Said

1. Topic of qualification work: «Development of composition of capsules for the treatment of respiratory diseases », supervisor of qualification work: Denys PULIAIEV, PhD, assoc. prof.

approved by order of NUPh from "06 st" of February 2023 №35

2. Deadline for submission of qualification work by the applicant for higher education: April 2023.

3. Outgoing data for qualification work: capsules, active ingredients: mixture of plant extracts.

4. Contents of the settlement and explanatory note: literature review on the topic, objects and methods of research, experimental part, conclusions.

5. The work should contain tables, graphs, figures in a volume sufficient to cover the topic.

6. Consultants of chapters of qualification work

Chapters	Name, SURNAME, position of consultant	Signature, date	
		assignment was issued	assignment was received
1	Denys PULIAIEV, associate professor of higher education institution of department of pharmaceutical preparations technologies	17.11.2022	17.11.2022
2	Denys PULIAIEV, associate professor of higher education institution of department of pharmaceutical preparations technologies	09.03.2023	09.03.2023
3	Denys PULIAIEV, associate professor of higher education institution of department of pharmaceutical preparations technologies	21.04.2023	21.04.2023

7. Date of issue of the assignment: «01» September 2022.

CALENDAR PLAN

№	Name of stages of qualification work	Deadline for the stages of qualification work	Notes
1	The study of literary sources in the main directions of the treatment of respiratory diseases. Writing a literature review.	September 2022	**done**
2	Definition of objects and methods of research. Formation of the second chapter.	October 2022	**done**
3	Study of physico-chemical and pharmaco-technological properties of research objects.	January 2023	**done**
4	Substantiation of the composition and technology of capsules with mixture of plant extracts for the treatment of respiratory diseases. Formation of chapter 3.	April 2023	**done**

An applicant of higher education _____ Saidi Said

Supervisor of qualification work _____ Denys PULIAIEV

ВИТЯГ З НАКАЗУ № 35
По Національному фармацевтичному університету
від 06 лютого 2023 року

нижченаведеним студентам 5-го курсу 2022-2023 навчального року, навчання за освітнім ступенем «магістр», галузь знань 22 охорона здоров'я, спеціальності 226 – фармація, промислова фармація, освітня програма – фармація, денна форма здобуття освіти (термін навчання 4 роки 10 місяців та 3 роки 10 місяців), які навчаються за контрактом, затвердити теми кваліфікаційних робіт:

Прізвище студента	Тема кваліфікаційної роботи		Посада, прізвище та ініціали керівника	Рецензент кваліфікаційної роботи
• **по кафедрі технологій фармацевтичних препаратів**				
Саіді Саід	Розробка складу капсул для лікування захворювань органів дихання	Development of composition of capsules for the treatment of respiratory diseases	доцент Пуляєв Д.С.	доцент Ковалевська І.В.

Підстава: подання деканата, н/п ректора

Ректор

Вірно. Секретар

Національний фармацевтичний університет
Факультет з підготовки іноземних громадян

Ф А2.8-47-110

ВИСНОВОК

Комісії з академічної доброчесності про проведену експертизу щодо академічного плагіату у кваліфікаційній роботі здобувача вищої освіти

№ 113192 від « 10 » травня 2023 р.

Проаналізувавши випускну кваліфікаційну роботу за магістерським рівнем здобувача вищої освіти денної форми навчання Саіді Саід, 5 курсу, _____ групи, спеціальності 226 Фармація, промислова фармація, на тему: «Розробка складу капсул для лікування захворювань органів дихання / Development of composition of capsules for the treatment of respiratory diseases», Комісія з академічної доброчесності дійшла висновку, що робота, представлена до Екзаменаційної комісії для захисту, виконана самостійно і не містить елементів академічного плагіату (компіляції).

Голова комісії,
професор **Інна ВЛАДИМИРОВА**

4%

24%

REVIEW

of scientific supervisor for the qualification work of the master's level of higher education of the specialty 226 Pharmacy, industrial pharmacy

Saidi Said

on the topic: **«Development of composition of capsules for the treatment of respiratory diseases »**

Relevance of the topic. The problem of creating solid dosage forms of combined action with the substantiation of the composition, the rational choice of excipients and the optimal technology is quite relevant and opens up new opportunities in the complex therapy of treatment of respiratory diseases.

Practical value of conclusions, recommendations and their validity. The analysis of literature sources on rational pharmacotherapy of treatment of respiratory diseases, considering their etiology and pathogenesis, was carried out, the range of drugs for the treatment of these pathologies available on the pharmaceutical market of Ukraine was studied, and the relevance of developing a new drug in the form of capsules with mixture of plant extracts was proved. A technology for the manufacture of a medicinal product is proposed, according to which a technological scheme for its production is drawn up.

Assessment of work. The results of the experiments were statistically processed and presented in the work in the form of tables and graphs. The conclusions are the logical conclusion of theoretical and experimental studies.

General conclusion and recommendations on admission to defend. The master's work of Saidi Said meets all the requirements for qualification work and can be submitted for defense at the State Examination Commission of the National University of Pharmacy.

Scientific supervisor Denys PULIAIEV

«13» of April 2023

Ф А 2.2.1-32-356

REVIEW

for qualification work of the master's level of higher education, specialty 226 Pharmacy, industrial pharmacy

Saidi Said

on the topic: **«Development of composition of capsules for the treatment of respiratory diseases »**

Relevance of the topic. One of the urgent problems of our time is the increase in the growth of respiratory diseases treatment. The range of medicines for the treatment of these pathologies of Ukrainian production is limited, most of the drugs have a unidirectional effect. Therefore, the development of domestic complex preparations for the treatment of respiratory diseases is an urgent task.

Theoretical level of work. Based on the literature data, the author substantiates the need to create capsules for treatment of respiratory diseases. Saidi Said conducted a search for the most appropriate active substances and auxiliary components.

Author's suggestions on the research topic. As active ingredients, the author proposed mixture of plant extracts. The expediency of using and experimentally confirmed number of excipients in the composition of the proposed preparation is substantiated.

Practical value of conclusions, recommendations and their validity. In the course of the work, the rational composition of the capsules was substantiated. The technology of capsules has been developed, according to which a technological scheme has been drawn up.

General conclusion and assessment of the work. The conclusions formulated in the work are based on experimental data and follow logically from the results obtained. The qualification work of Saidi Said meets all the requirements for qualification works and can be submitted for defense at the State Examination Commission of the National University of Pharmacy.

Reviewer _____ professor Inna KOVALEVSKA

«18» of April 2023

Ф А2.2.1-91-287

МІНІСТЕРСТВО ОХОРОНИ ЗДОРОВ'Я УКРАЇНИ
НАЦІОНАЛЬНИЙ ФАРМАЦЕВТИЧНИЙ УНІВЕРСИТЕТ

Витяг з протоколу
засідання кафедри технологій фармацевтичних препаратів НФаУ
№ 3 від 20 жовтня 2022 року

Голова: завідувач кафедри, доктор фарм. наук, проф. Кухтенко О. С.

Секретар: к. фарм. н., доц. Січкар А. А.

ПРИСУТНІ: зав. каф., проф. Кухтенко О. С., доц. Безрукавий Є. А., доц. Кутова О. В., доц. Ляпунова О. О., доц. Манський О. А., доц. Ніколайчук Н. О., доц. Сайко І. В., доц. Січкар А. А., доц. Солдатов Д. П., доц. Степаненко С. В., доц. Трутаєв С. І., ас. Сердюк Є.В.

ПОРЯДОК ДЕННИЙ:
1. Про представлення до захисту в Екзаменаційну комісію кваліфікаційних робіт здобувачів вищої освіти випускного курсу НФаУ 2022 року випуску

СЛУХАЛИ: про представлення до захисту в Екзаменаційній комісії кваліфікаційної роботи на тему: «Розробка складу капсул для лікування захворювань органів дихання» здобувача вищої освіти випускного курсу Фм18 (5,0д) англ. – 7 групи НФаУ 2023 року випуску Саіді Саід
Науковий (-ві) керівник (-ки) _к.фарм.н., доц. Денис ПУЛЯЄВ_____
Рецензент_____д.фарм.н., проф. Інна КОВАЛЕВСЬКА_____

УХВАЛИЛИ: Рекомендувати до захисту кваліфікаційну роботу здобувача вищої освіти _5_ курсу Фм18 (5,0д) англ. – 7 групи Саіді Саід
на тему: «Розробка складу капсул для лікування захворювань органів дихання»

Голова
завідувач кафедри,
доктор фарм. наук, проф. _____ Олександр КУХТЕНКО
(підпис)

Секретар
к. фарм. н., доцент _____ Антоніна СІЧКАР
(підпис)

Ф А2.2.1-32-042

НАЦІОНАЛЬНИЙ ФАРМАЦЕВТИЧНИЙ УНІВЕРСИТЕТ

ПОДАННЯ
ГОЛОВІ ЕКЗАМЕНАЦІЙНОЇ КОМІСІЇ
ЩОДО ЗАХИСТУ КВАЛІФІКАЦІЙНОЇ РОБОТИ

Направляється здобувач вищої освіти Саіді Саід до захисту кваліфікаційної роботи
за галуззю знань 22 Охорона здоров'я
спеціальністю 226 Фармація, промислова фармація
освітньою програмою Фармація
на тему: «Розробка складу капсул для лікування захворювань органів дихання»

Кваліфікаційна робота і рецензія додаються.

Декан факультету _____ / Світлана КАЛАЙЧЕВА /

Висновок керівника кваліфікаційної роботи

Здобувач вищої освіти Саіді Саід виконав на кафедрі технологій фармацевтичних препаратів НФаУ кваліфікаційну роботу, яка присвячена створенню складу капсул для лікування захворювань органів дихання.

В процесі роботи Саіді Саід дослідив загальні напрями етіопатогенезу та терапії захворювань органів дихання, обґрунтував доцільність створення та застосування капсул із сумішшю рослинних екстрактів. Автором було обґрунтовано оптимальний склад капсул та розроблено промислову технологію їх отримання.

У цілому подана до захисту кваліфікаційна робота Саіді Саід на тему «Розробка складу капсул для лікування захворювань органів дихання» відповідає вимогам, що висуваються до кваліфікаційних робіт, оцінюється позитивно і може бути рекомендована для захисту в Екзаменаційну комісію НФаУ.

Керівник кваліфікаційної роботи Денис ПУЛЯЄВ

«13» квітня 2023 р.

Висновок кафедри про кваліфікаційну роботу

Кваліфікаційну роботу розглянуто. Здобувач вищої освіти Саіді Саід допускається до захисту даної кваліфікаційної роботи в Екзаменаційній комісії.

Завідувач кафедри технологій
фармацевтичних препаратів Олександр КУХТЕНКО

«21» квітня 2023 р.

Qualification work was defended
of Examination commission on
« ____ » _____2023
With the grade _____
Head of the State Examination commission,
D.Pharm.Sc., Professor
_____ / Oleh SHPYCHAK /