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QUALIFICATION WORK

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

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ANNOTATION

The development of capsule formulation for the treatment of respiratory disorders is the focus of the qualifying work. A review of the literature on the development potential of hard capsules was done. A study was conducted on the names of medications used to treat respiratory conditions. It was investigated how supplementary materials affected the technological properties of encapsulating masses and their quality indicators. A method has been devised to produce hard capsules that contain a combination of plant extracts.

An introduction, three chapters, general conclusions, a list of cited sources, and appendices are all included in the 40-page work. The text is illustrated with 8 figures and 6 tables and includes thirty references to scholarly literature.

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

АНОТАЦІЯ

Кваліфікаційна робота присвячена розробці рецептури капсул для лікування респіраторних захворювань. Проведено огляд літературних джерел щодо актуальності розробки твердих капсул. Проведено дослідження назв лікарських засобів, що використовуються для лікування респіраторних захворювань. Досліджено вплив допоміжних матеріалів на технологічні властивості капсульованих мас та їх якісні показники. Розроблено спосіб отримання твердих капсул, що містять комбінацію рослинних екстрактів.

Робота складається зі вступу, трьох розділів, загальних висновків, списку використаних джерел та додатків на 40 сторінках. Текст проілюстрований 8 рисунками та 6 таблицями і містить тридцять посилань на наукову літературу.

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

CONTENT

INTRODUCTION

Relevance of the research topic. Respiratory disorders are one of the most serious health issues because of their great incidence, which is typically harsh and often complicated. The management of these illnesses has been problematic to date due to the fact that they are respiratory diseases with diverse etiologies and clinical presentations. As a result, it is critical to have an arsenal of drugs that have the effect of reducing and eliminating the main signs of the disease, regardless of origin, while also being safe for treatment.

Herbal therapeutic treatments have gained increased prominence in recent years. The advantage of plant-based medications is that, unlike synthetic drugs, physiologically active chemicals from plants are more naturally incorporated into the metabolic processes of the human body.

The purpose the creation of science-based technologies and composition capsules for the treatment of respiratory disorders.

The object of research a combination of anise and black elderberry extracts.

The work employed the following research methods: complicated physicochemical and technological investigation, as well as the development of the ideal solid dosage form composition.

The practical significance of the results. Throughout the work, the reasonable composition of the capsules was supported. Capsule technology 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 XXXI international scientific and practical conference of young scientists and students» (April 23-25, 2025, Kharkiv). - Kharkiv: NUPh, 2025. Published abstracts: Alidrissi Torabi Firdraousse. Development of capsule composition for the treatment of respiratory diseases. Modern achievements of pharmaceutical

business: collection of scientific works, issue 1. – Kharkiv, NUPh publishing house, 2025. P.142.

Structure and scope of qualification work the 40-page qualification work includes an introduction, three chapters, conclusions, and a list of the 30 references that were used. Six tables and eight figures are used to show the work.

CHAPTER 1
PROSPECTS OF CREATING SOLID DRUGS FOR TREATING RESPIRATORY DISEASES

1.1. The cause and development of respiratory illnesses.

Respiratory tract diseases can be either acute or chronic. The majority of them are viral in nature (SARS). These include of respiratory syncytial, adenovirus, influenza, and parainfluenza, virus, rhinovirus, rotavirus, enterovirus, coronavirus illness, and, less commonly, reovirus and picornavirus infections. SARS frequently occurs during the winter season, and it has the potential to cause outbreaks.

Acute respiratory disease can also be caused by viral-bacterial interactions, bacteria, fungi, or protozoa.

The etiology of respiratory illnesses varies by species across time. If streptococci (particularly pneumococcus) and staphylococci were the absolute predominance in the etiology of respiratory disorders for 80 years, their relevance has declined in the recent decade, indicating a significant expansion of the range of pathogens. Chlamydia and mycoplasma have been given a larger role within cells. Hemophilic sticks play a crucial role. Together, these pathogens account for 40-50% of all infections. Fungi, gram-negative enteric bacteria, and anaerobes all have a role in the development of respiratory disease [5, 15].

Acute bacterial respiratory illness can manifest as a separate pathology. But 60% of cases of ARI are a result of viral infections, with 20% caused by so-called childhood diseases, both bacterial and viral. The development of these problems frequently adds to the activation of endogenous flora or superinfection. Chronic tonsillitis, sinusitis, otitis, respiratory tract developmental anomalies, and respiratory allergies are all signs of an unfavorable background.

Additionally, by altering the organism's reactivity, sensitizing it, and lowering or altering general or local immunity, recurrent respiratory infections aid in the development of chronic respiratory tract illnesses.

The etiological involvement of anaerobes, fungi, gram-negative microorganisms from the family of enteric gram-negative bacteria that are not fermented, and associations of aerobic and anaerobic bacteria is increased in chronic respiratory tract disorders compared to acute diseases.

Upper and lower respiratory tract infections have distinct causes [7, 28]. Respiratory viruses play the most important role in the etiology of upper respiratory tract infections. In addition to viruses, streptococci play important roles. Other forms of streptococcus and staphylococcus are less common, as are intracellular infections (mycoplasma and chlamydia), which can be detected at a frequency of more than 20%, fungi (most commonly from the Candida family), and, infrequently, Gram-negative enteric pathogens.

The most significant viral and bacterial correlations are found in the pathogenesis of lower respiratory tract illnesses. Bacteria come in second, followed by the pure viral character of the disease, and finally fungi and protozoa. Furthermore, the etiology of acute bronchitis and pneumonia influences whether the infection is acquired in the community (domestic) or in a hospital setting. Gram-positive cocci predominate in the etiology of community-acquired pneumonia and bronchitis, followed by pneumococci (30-40%), various streptococci (5-10%), and, infrequently, Staphylococcus (5%).

Hemophilic rods account for up to 12% of all cases, whereas intracellular infections such as Mycoplasma, Chlamydia, and Legionella can account for one-third or one-quarter of all disorders. These infections can persist in the respiratory tract's epithelial cells and the reticulohistiocytic system, promoting the long-term flow of inflammation [28, 30].

Illness of the respiratory system Pathogens infiltrate the tissue lining the respiratory tract, resulting in inflammation, irritation, and other changes to the mucous membranes.

Epithelial dystrophy is caused by parainfluenza viruses, rhinoviruses, and cytomegalovirus, which reject whole layers. The RS virus produces epithelial hyperplasia, which inhibits bronchial conductivity and leads to the development of

obstructive syndrome. Infection of adenovirus is accompanied with a strong exudative component of inflammation, epithelial loosening and rejection, and the production of cell infiltrates, which lead to airway blockage and atelectasis. Sero-purulent or purulent exudation was found at bacterial and fungal mucosal lesions, as well as neutrophil and macrophage infiltration.

Chemicals produced by Streptococcus pneumoniae, Haemophilus influenzae, and pseudomonas aeruginosa disrupt rejection, epithelial damage, and mucociliary clearance. Many microbes produce enzymes that degrade elastin, which reduces the functional activity of the bronchioles and bronchi, causes strain and ectasia, and contributes to bronchial blockage [4, 7].

Increased secretion of viscous mucus with high sticking properties and hyperplasia of mucosal edema are caused by bronchial blockage. These variables impair mucociliary transport, slow motility ciliated epithelium of bronchi and bronchioles, creating obstruction, it could be followed by a rupture in external breathing or bronchial dyskinesia, and hemodynamic changes in the bronchopulmonary system. Bronchial hyperactivity and/or allergies can exacerbate and assist the development of bronchospasm in individuals.

The cause of respiratory disease varies, but the epidemiology and clinical signs are comparable. However, each type of respiratory disease has distinct aspects of flow induced by the pathogen's influence on the character of mucous membrane lesions. The presence or absence of bronchial obstruction determines the same factor.

Differentiate between upper and lower respiratory tract diseases based on where the diseased process is located.

Examples of upper respiratory tract infections include otitis media, laryngitis, pharyngitis, chronic tonsillitis, angina, adenoiditis, sinusitis, rhinitis, or a combination of these conditions [5, 28].

Lower respiratory tract infections include pneumonia, bronchitis, tracheitis, and laryngitis.

The most common symptoms of acute respiratory conditions, like upper respiratory tract infections (colds), include congestion of the nose, cough, runny nose, sore and scratchy throat, and watery eyes. These symptoms are sometimes accompanied by fever, moodiness, decreased appetite, and a loss of health.

A cough brought on by viral inflammation, bronchospasm, a violation of mucus secretion, and increased secretion viscosity that impedes sputum evacuation is the most common sign of a lower respiratory tract disease. Pain, a decline in general health, difficulty sleeping, hunger, fast breathing, and fever are further signs of lower respiratory tract disorders.

There are two types of respiratory tract infections: acute and chronic. The presence of chronic tonsillitis, respiratory allergies, and immunodeficiency congenital and hereditary respiratory system diseases, the incidence of acute respiratory diseases, their inadequate and delayed treatment, and the detrimental effects of environmental etiological factors are all caused by chronic respiratory diseases. [5, 27]

Therefore, the etiology, location of inflammation, breakdown of mucous membranes, type and severity of the disease, and age of the patient all influence the respiratory disease's overall clinical appearance.

1.2. Plant-based treatment for respiratory disorders.

The development of inflammation, coughing, thick sputum and its complex distribution, and allergic reactions are the hallmarks of respiratory illnesses; nonetheless, they require combined therapy that addresses all facets of the pathological process.

Decreasing inflammation, boosting the immune system, which includes boosting the respiratory tract's mucous membranes' local immunity, and reestablishing patency, facilitating mucociliary transport, and clearing bronchial obstruction are the objectives of treatment for these disorders. The choice of treatment is influenced by the kind and location of lesions, clinical symptoms, the course of the disease, and the pharmacological effects of drugs [16, 22].

Combining drugs, including herbal ones, improves tolerance, improves therapeutic properties, and increases effectiveness. Nowadays, extracts from several plants are combined to create multicomponent drugs. It shows how the drug affects the respiratory system in its entirety. These drugs must have expectorant, bronchodilator, mucolytic, and anti-inflammatory qualities.

A key part of therapy for coughing respiratory problems is treatment, which attempts to eliminate the underlying causes. The decision to cough against drugs must be recognized because of the manner they prevent coughing [17, 29].

Herbal expectorant medications are utilized as efferent action treatments for upper and lower respiratory tract inflammatory and viral illnesses, which are characterized by coughing up difficult-to-separate sputum and the absence of effective herbal afferent action peripherals that moisturize and envelop.

Anticipatory medications make ciliated epithelium and peristalsis bronchioles more active, which helps to promote and eliminate sputum. Simultaneously, they stimulate bronchial gland secretion, producing more secretions and lowering their viscosity, which helps clear the respiratory tract of mucus [15, 17, 30].

Herbal expectorants should be used in combination with synthetic mucolytic drugs that thin sputum by breaking the peptide bonds of protein molecules or the disulfide bonds of mucopolysaccharides. This will change the sputum's chemical and physical characteristics while maintaining its volume.

Herbal medicine may be used as an additional therapy option in conjunction with conventional medications for severe, prolonged, and complex respiratory tract infections and feverish situations lasting more than two to three days. [16, 28]

Because environmental factors might change the etiological illness structure, it is necessary to find new ways to choose the best course of treatment. The use of herbal medications in treatment complexes has gained significant importance. Diseases of the respiratory system can be prevented and treated safely and effectively with their assistance. Choosing the right medications is essential to the outcome of treatment. It is important to keep in mind that integrated treatment

yields better results than monotherapy, which may not always produce enough therapeutic effect. Herbal and homeopathic remedies can be utilized as parts of an effective combined therapy for severe forms or complex currents of both acute and chronic disorders.

Herbal medicine offers several key advantages. It is known for its potential to be used safely over the long term, its capacity to address underlying and related conditions through multifaceted mechanisms, and its straightforward preparation and application methods. Additionally, herbal remedies are often compatible with synthetic medications, making them a versatile option. They are particularly effective in managing functional disorders, milder health issues, and in enhancing the therapeutic outcomes of targeted treatments, as well as serving as a supportive option in maintenance therapy. [16, 34].

The amount of physiologically active compounds, such as flavonoids and saponins, in the medicine determines its pharmacological action.

Anise extract contains essential oil rich in anethole, along with flavonoids, coumarins, organic acids, and small amounts of fatty acids. Anethole exhibits pronounced expectorant, antispasmodic, and mild antimicrobial properties. Flavonoids and coumarins contribute to the anti-inflammatory and antioxidant effects, supporting respiratory health and facilitating mucus clearance from the airways.

Black elderberry extract is rich in anthocyanins, flavonoids, organic acids (such as malic and citric), vitamin C, tannins, and essential oils. The anthocyanins are known for their antiviral and immunomodulatory activity, especially against respiratory viruses. Flavonoids and vitamin C enhance antioxidant protection, while tannins provide astringent and anti-inflammatory effects. The extract is commonly used in the prevention and supportive treatment of colds, flu, and bronchitis. [5,16,17].

Therefore, the proportion of biologically active ingredients in herbal medications determines their therapeutic impact. It is important to remember that herbal mixtures made up of multiple herbal constituents have a variety of effects,

including bronchodilators, expectorants, and anti-inflammatory properties. According to this viewpoint, patients of various ages can be treated with ARI using a variety of herbal preparation dose forms as the preferred medication.

1.3. The current level of capsule production technologies

1.3.1. Benefits of using medications in capsule form

Capsules and granules are very important in the naming of finished pharmaceuticals. However, encapsulated medications have received increasing interest lately.

Despite being a relatively new dosage form, gelatin capsules have gained popularity among physicians, consumers, and manufacturers since the 1950s due to a number of benefits and technological advancements. The spectrum of medications in this dosage form has significantly expanded due to the development of contemporary technological techniques that enable the encapsulation of medicinal compounds with various physicochemical properties.

Nowadays, in nations with developed pharmaceutical industries, 9–12% of the drug range consists of preparations in the form of gelatin capsules meant for oral and local application. Gelatin capsule-based preparations are found in practically every pharmacological area [8, 27].

This drug's popularity among manufacturers, consumers, and healthcare professionals is driven by a range of advantages and favorable characteristics. The precision of dosage is ensured by modern equipment, which allows capsules to be filled with remarkable accuracy, maintaining a tolerance of no more than ±3% and minimizing losses. High-performance capabilities are also notable, as advanced automatic machinery can produce up to 130,000 capsules per hour, depending on the filler properties and dosage techniques. Studies by scientists such as Eckert and Lindvald have shown that capsules offer superior bioavailability, decomposing faster than tablets and allowing the body to easily absorb their liquid or non-compacted solid contents. Furthermore, capsules may expand the scope of use in certain cases, revealing new pharmacological properties not observed in other

dosage forms. For instance, research by scientists from the Italian company "Pharmagel" demonstrated that 20 mg temazepam capsules exhibit tranquilizing effects, while the same dose in capsules can also serve as a hypnotic, functioning effectively as a sleeping aid.

High stability: Since capsule coating offers a high enough degree of tightness and insulation to protect labile components from a variety of harmful environmental factors (such as air oxygen, direct sunlight, humidity fluctuations, etc.), it is frequently possible to avoid using antioxidants or stabilizers altogether or to use them less frequently;

Ability to correct: Shell capsules also help mask the taste of most drugs.

This is especially crucial in pediatrics because the use of common dose forms in this field of medicine, like syrups, is not always logical (for instance, some medications may malfunction due to dosage or lack of stability); it also reduces the likelihood of production errors. The potential to use various dyes and markings lowers the risk of errors and drug substitutions throughout the manufacturing process;

When receiving shell capsules, a variety of dyes are used to produce great aesthetics. Color is a significant psychological factor when choosing a drug, even though it is not an impartial consideration. The use of extra color-related therapeutic benefits is the basis for this utilization. The top pharmaceutical corporations of today may color capsule shells with a thousand distinct hues and tones; they can even define certain qualities of medications [4, 28].

The development of so-called enteric soluble capsules, which are resistant to gastric juice but decompose easily in the small intestine's environment, and capsule retard, which allows for a delayed release of medication, are the best examples of this.

Preserving technical modes: Encapsulation techniques enable the avoidance of undesirable effects of moisture and pressure on a variety of labile substances [8, 26].

Numerous medications are available in capsule form, and the physical and chemical characteristics of encapsulated substances necessitate a wide range of approaches for developing medications in this dosage form. The physicochemical, crystallographic, and technological characteristics of the medicinal powders that are added to the composition of capsulated pharmaceuticals determine the development of the best possible composition and technology. The method of obtaining capsules is impacted by these closely linked features [6, 27].

Forms of granular dosage are a little less effective than tablets due to their compactness and ease of use, but they should prioritize the creation of new dosage forms that incorporate plant extracts. Recent developments in tableting stick to press tools may result in subpar output.

1.3.2. Determinants of the biopharmaceutical and technological mass values for encapsulation.

The physico-chemical and technological characteristics of the substances, their quantity in a medicinal product mixture, their fractional composition, and other aspects all influence the choice of the best technological scheme for producing capsules. When filling a capsule is impossible, the granulation method of powder is employed.

The process of turning powdered material into particles (grains) with a certain value is called granulation. By altering the ratio of granulate fractions, granules can be made completely uniform.

Granulation increases fluidity and ensures a consistent flow rate in a capsule with a specific weight.

Wet granulation is a widely used technological method since most medicinal compounds are not very fluid and require the addition of binders and lubricants. Wet granulation is used in pharmaceutical manufacturing to create the final granules and the intermediate product for dosage forms "capsules" and "capsules." Technological requirements like turnover, volume and bulk density, solubility, and others were designated in order to granulate. Granules are traditionally made by

combining weight moisturizer ingredients and forcing wet material through a sieve with the right size holes. According to technical documentation, the grain size as the dose form is up to 3.0 mm [9, 25].

Modifying the granules' characteristics could alter the drug's characteristics as well. Wet granulation on a mixer, followed by drying on a dryer shelf, and pellets from Glatt, Ball, or Zankety, which have different processes, can therefore produce drugs with entirely different physicochemical characteristics and effects on their bioavailability. Granulating active ingredient particles using a multilayer coating that employs the appropriate auxiliary chemicals and technologies, for example, can result in a progressive release of the active ingredient from the dosage form.

This will guarantee that the active ingredient remains in the blood in trace amounts and that the liver and kidneys, which remove drugs from the blood, experience very little loading. Dosage forms of rapidly released active ingredients will be obtained in a simple mixture of these identical components. As a result, different technologies can change the drug's characteristics. The substitution of supplementary compounds presents a comparable circumstance. As a result, granulation technology selection is a very complicated step of drug development [8, 19].

Additional materials that are useful when wet granulation is used.

In its whole, medicine is a complicated physical-chemical system that includes more than just the active ingredient that produces the therapeutic effect. The best choice of auxiliary components is given more consideration because all aspects of the product's quality are somewhat dependent on them. Utilized auxiliary materials' composition has a major impact on the process's circumstances, the final product's mechanical and structural characteristics, and, consequently, its value.

Today, a diverse range of auxiliary materials is employed in the production of solid dosage forms. These substances serve various purposes, including acting as fillers (solvents), disintegrants to aid in breakdown, anti-friction agents for

improved sliding and lubrication, taste modifiers, release dynamics regulators, and coloring agents. Their selection depends on the physical and chemical properties of the active ingredients, the recommended dosage methods, and several other relevant factors. However, the auxiliary compounds in the dosage form are not clearly separated based on their function. Depending on how it is used, the same material can serve a variety of functions.

Before encapsulation, most medicinal powders require specialized preparation, often achieved through the wet granulation process. This method helps produce particles with defined size, shape, and structure, along with specific physicochemical, pharmacological, and technical properties essential for the intended application. Granulation makes it possible to improve the technical characteristics of powders, distribute the active ingredient more evenly, and provide a more precise dosage of the active ingredient, which lessens the impact of humidity and temperature on the dosage form's quality.

Granulation is being used in a variety of ways. The most popular technique for wet granulation is a multi-step procedure that typically consists of eight steps. There are fewer steps when new binding materials are used. As a result, using modified starch as a filler and binding agent lowers the amount of time spent soaking and heating starch paste, which lowers expenses. Because most medications have poor turnover and pressing, binding and plasticizing agents must be added, which is why this production procedure is so popular [8, 26].

Fillers, disintegrants, binders, and lubricants are employed in the wet granulation process.

Fillers are essential for providing capsules with the necessary mass to achieve the ideal volume. In the production of hard capsules, various materials are utilized, including talc, sucrose, lactose, starches, cereals, microcrystalline cellulose (MCC), dibasic calcium phosphate, sodium chloride, and polyhydric alcohols like mannitol, sorbitol, xylitol, and isomalt. These substances help adjust density and volume while ensuring the desired fluidity of the fillers. Additionally, MCC plays a crucial role in slowing absorption, which supports the prolonged

activity of the drug. It is particularly effective when combined with enzymes, fortified supplements, and natural extracts. When fillers are used, their percentage of the mixture's total weight varies from 0.02 to 50%.

Strength can be increased by increasing the precision of powdered material dosing and by utilizing humidifiers and binders to provide the granulate with the required technological qualities.

In order to prevent stratification of mixtures with varied contents and complex granulate materials, binders must be used in order to create the required adhesive force between the particles of complex powders. The physicochemical characteristics of the materials undergoing wet granulation determine the binders' qualitative and quantitative makeup.

Normal granulating powders can be produced with water by simple moisturizing. Granulation hygroscopic powders are frequently made with alcohol when dry extracts are a part of the mixture's makeup. They create a resinous, water-sticky material that is incapable of granulating [8, 19, 26].

By employing solutions of macromolecular chemicals whose efficacy is dependent on the molecular weight, a mixture of substances containing alcohol and water does not produce a granulating mass. For instance, polyvinylpyrrolidone under the trade name Kollidon®, which has a molecular weight between 2,000 and 1,5 x 106, Klucel® EF, which has a molecular weight between 45000 and 70000-80000, and others, are preferred.

Wetting powders, binder substance film development, and deformation are factors that affect the strength of granules when assessing the effectiveness of binder. The order of increasing wetting capacity is PVP, gelatin and hydrolyzed starch paste. The molecular mass of substances also determines the binding capacity of macromolecular compounds. Cellulose derivatives are the fastest and most effective binders; they are utilized for very elastic and springy materials, while starch derivatives are less effective.

A dissolving agent is added to granulates to enhance their breakdown in the digestive system, which is essential for the release and subsequent absorption of

active substances. Starches, methylcellulose, alginic acid, amylopectin, carbopols (which improves disintegration by swelling), and twin (which improves wetting particles) are among the several chemical substances employed as disintegrants [19, 25].

Antifriction agents are used to enhance the fluidity of granulates and are categorized into three groups. The first group includes sliding agents, such as starch, talc, aerosil, and polyethylene 4000. The second category comprises lubricants, including stearic acid and its salts, tween, and silicon-based substances. The third group consists of anti-adhesion materials, such as talc, stearic acid and its salts, which prevent sticking and improve processing efficiency.

Lubricants are compounds, such as magnesium stearate, aluminum, calcium, talc, and silicones, that make a material slick and stop its particles from sticking to it. When employing auxiliary methods, their total number in relation to the mixture's total weight falls between 0.1 and 10%, ideally between 0.1 and 1%. Additionally, lubricants have a large specific surface area and are hydrophobic, which is crucial when working with hygroscopic materials. Drugs that increase fluidity, such as silicas-specifically, high-purity silicas sold under the brand name Aerosil®-can be added in amounts ranging from 0.1 to 5% of the mixture's total weight.

Their apathy is crucial while choosing additional substances. Numerous medications undergo molecular changes and become unstable under specific auxiliary chemicals [6, 8, 25].

Therefore, auxiliary substances that are wet active components and do not result in the development of sticky, resinous mass can be employed for granulation combinations that contain dry extracts.

An examination of the literature on pharmacotherapy demonstrated the value of developing novel herbal remedies for the management of respiratory conditions.

Conclusions to chapter 1

1. The main factors impacting the onset and progression of acute respiratory illnesses are identified based on the literature study.

2. The market's analysis of medications for treating acute respiratory conditions is used to determine how quickly a solid dosage form including phytocomponents can be created.

3. The production status of firm dosage forms is now being analyzed.

CHAPTER 2
OBJECTS AND METHODS OF RESEARCH

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

Characteristics of active substances

Anise Extract. Anise extract is typically a light to medium brown powder with a mild aroma and slightly sweet flavor, showing good water solubility. It is rich in polysaccharides, particularly those noted for their immunomodulatory capabilities. These compounds support the immune system by enhancing phagocytic activity in the reticuloendothelial system and stimulating the natural production of interferons. Anise flavonoids also contribute anti-inflammatory benefits, complementing its use in respiratory disorders by alleviating inflammation, soothing mucosal irritation, and assisting in mucus clearance.

Black Elderberry Extract. Obtained from the dark berries of Sambucus nigra, this extract is usually a deep violet to purplish-brown powder with a tart-sweet flavor and fruity aroma. It is water-soluble and packed with anthocyanins, flavonoids, and organic acids. These constituents offer antioxidant, antiviral, and anti-inflammatory properties. In respiratory applications, elderberry extract helps reduce the severity and duration of cold and flu symptoms by supporting immune defense, lowering inflammation in the airways, and aiding in mucosal recovery.

Characteristics of the auxiliary substances.

Potato starch dry. It is odorless, white with crystal, has a mass fraction of 17–20% humidity, and is free of mechanical contaminants. Sulfur dioxide content, ash content, normalized humidity, acidity, and the quantity of specks (unseparated pulp particles).

Lactose Granulac 140 - crystalline powder that is white or almost white, odorless, has a somewhat sweet flavor, dissolves readily in water, dissolves very slightly in ethanol, and is nearly insoluble in ether and chloroform.

Microcrystalline cellulose (MCC) - tasteless, odorless, snow-white powder. The material is insoluble. It can be used as a disintegrant, glue, and filler.

Methylcellulose. Fiber powder has almost little flavor or smell. It is soluble in cold water, gels when heated, and coagulates when heated and boiled for an extended period of time.

Polyvinylpyrrolidone (PVP). Vinylpyrrolidone is polymerized to produce PVP. Various chain lengths result in varying viscosities. The K-value, which is basically a function of the viscosity in aqueous solution, is traditionally used to describe the degree of polymerization. PVP K-25, K-30, and K-90 are the two grades of primary importance that we offer.

Ethanol. A transparent, colorless liquid that is combustible and volatile. humid. combined with methylene chloride and water. lights a blue flame without smoke. reaches a boiling point of roughly 78 °C. between 0.805 to 0.812 in terms of relative density. It is employed as a solvent in the pharmaceutical industry.

Purified Water - odorless, colorless liquid. utilized as a supporting material at different phases of the procedure.

2.2. Methods of research

Common organoleptic, technical, and physico-chemical study techniques have been employed in the investigation of the capsules' qualities, enabling an objective assessment of their quality based on the results obtained.

Physical and chemical properties

Particle size and shape. A microscope fitted with a micrometer grid at 400 or 600 times magnification is used to measure the length and width of powder particles in order to determine their size.

The form of the particles is determined by comparing their average length and breadth. The particles are conditionally separated into three primary categories using this method: Lamellar means that the length is at least three times greater than the breadth and thickness; elongated means that the length to width ratio is

greater than three to one; and equiaxed means that the shape is spherical and polyhedral, almost izodiathermic.

Specific surface area - entire surface area that a powdered material occupies, as well as the contact surface-the surface created when the powder particles come into contact with one another.

The mass to volume ratio of the medicine with zero powder porosity indicates the true density of the powder. Use any liquid as a comparison that wets but does not dissolve the powder. A pycnometer is used for determination.

Hygroscopicity. In contrast, the powder mass prepared for tableting begins to collect vapor from the air and blur in absorbed water if the air's vapor pressure is greater than the surface elasticity of solids. Weight-based measurements of the kinetics of moisture absorption under (normal) everyday conditions, extreme conditions (desiccator over water, 100% relative humidity), or climatic chambers. The employment of auxiliary compounds, or moisture stimulants, is determined by a substance's degree of hygroscopicity.

Technological properties

The physico-chemical characteristics of powdered medications determine their technological attributes.

Fraction (granulometry) composition or distribution of powder particles according to size, have some effect on the tableting machine's rhythmic operation, the stability of the mass of the resulting tablet, the precision of the drug's dosage, and the qualitative aspects of the tablet (appearance, disintegration, strength, etc.).

Sieve analysis is the quickest and most practical way to find the dispersion. The analysis's methodology involved passing 100,0 g of the powder under study through a set of sieves with holes up to 0.1 mm in diameter. After placing a weighed sample of material on the largest (upper) mesh sieve and shaking the complete set of sieves for five minutes (either manually or with vibration equipment), the mass of each fraction and its percentage content are determined.

Tapped density - is the mass of freely powdered material per unit volume. The size, shape, density, and moisture content of the powder particles (granules) all

affect the tapped density. The volume of the matrix channel can be predicted based on the bulk density. The bulk density control device is used to determine the powder's bulk density.

Five grams of the powder were weighed to the closest 0.001 grams and then put into a measuring cylinder. Using an adjustable screw, set the oscillation amplitude (35–40 mm), and then use a lock nut to secure the setting once the scale mark has been reached. A transformer is used to set the oscillation frequency between up to 120 osc/min counter. Additionally, the gadget was activated via a toggle switch, and the powder benchmark in the cylinder was seen. The device is turned off after the powder is permanent, which usually takes ten minutes.

Fluidity (flowability) - is the powdered system's capacity to "flow" or fall out of the funnel capacitance under gravity and guarantee consistent channel matrix filling. Poorly flowing material in the hopper sticks to the walls, giving the matrix a rhythmic entry. This results in the fact that the capsules' specific mass and density will vary.

The vibration device used to remove bulk material features determines flowability.

The device's stiff connection to an electromagnetic device that runs on AC power allows the cone funnel to vibrate. After closing the valve and turning on the device and timer, a weighed portion of powder (granules) measuring 50.0 g was poured into the funnel. The flap will open and the material's expiration time will be fixed after 20 seconds of jolting, which is required to get a stable measurement. Flow time accuracy: up to 0.2.

The angle of repose, or the angle between the bulk material's cone and the horizontal plane, can be used to determine the flowability of powders with low bulk densities. A sample weighing 30.0 g can be used with the VP-12A. For free-flowing materials, the angle of repose ranges from 25 to 30°C, while for coupled materials, it ranges from 60 to 70°C.

Powder flowability is a complicated property that depends on the granulometric composition, wet mass, and particle shape and dispersion. When selecting a tableting technology, this technological feature can be exploited.

Conclusions to chapter 2

1. Dry extracts of black elderberry and anise extract are defined based on the data analysis of literature regarding phytotherapy of SARS active components of dose form.

2. It is demonstrated that the complex of physical and chemical, technological, and biopharmaceutical ways of producing capsules of suitable quality, required for receiving

CHAPTER 3
COMPOSITION AND TECHNIQUE DEVELOPMENT OF CAPSULES FOR RESPIRATORY DISEASE TREATMENT

3.1. Examination of the dry anise and black elderberry extracts, as well as their technological and physicochemical aspects.

Researching the physicochemical and technological characteristics of powdered materials is a crucial step in the development of solid dosage form technology since these characteristics have a significant impact on the technology selection and end product quality. It is well known that plant extracts have inadequate physicochemical and technical qualities because of their complicated multicomponent composition. This makes it difficult to produce completed dosage forms straight from dry extracts without the need for pre-granulation and other ingredients.

Examined the technological and physicochemical characteristics of dry extracts, which are crucial when selecting a solid dosage form technology. The research findings are shown in the table in Figs. 3.1–3.3. 3.1.

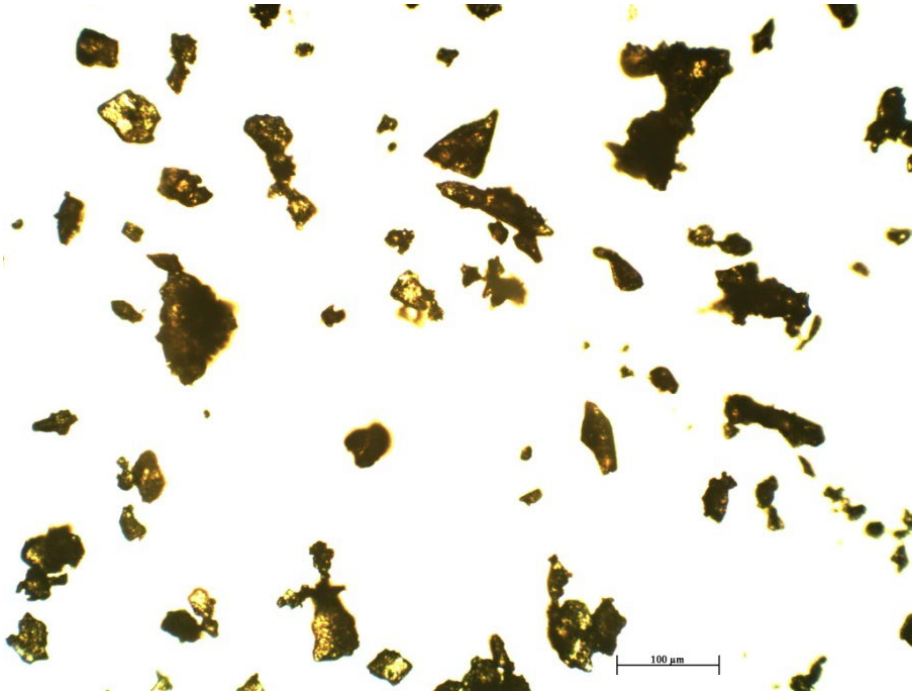

Fig. 3.1. The shape of dry black elderberry extract particles

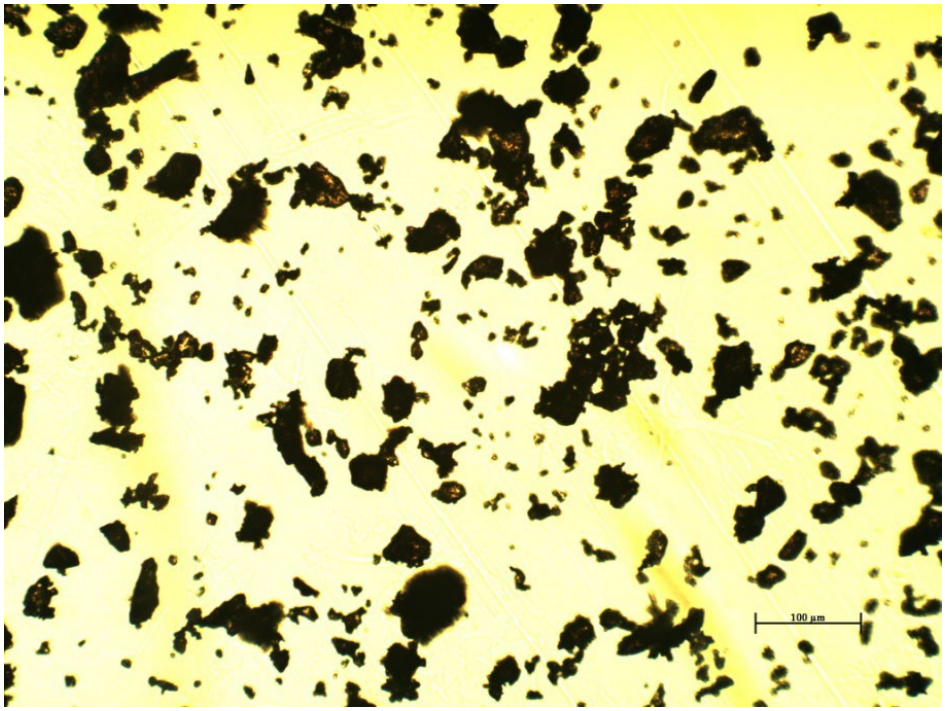

Fig. 3.2. The shape of dry anise extract granules

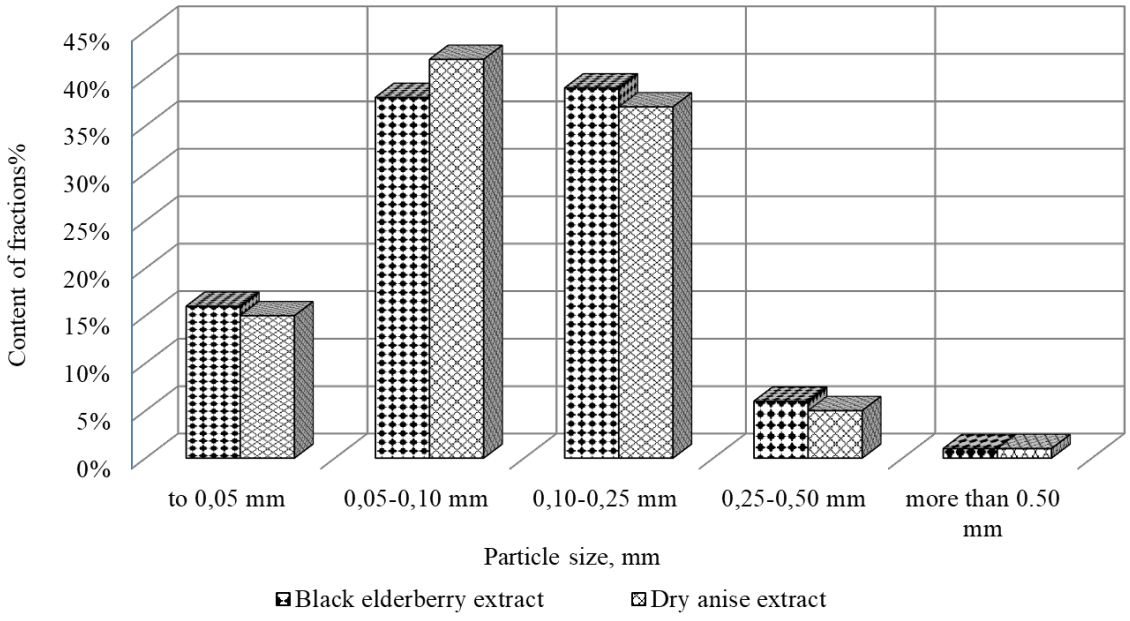

Fig. 3.3. The fractional makeup of anise and black elderberry extracts

Particle size and shape affect a substance's bulk weight, surface area, compressibility, fluidity, and other technical properties. With anizodiametric

particles ranging in size up to 0.1 mm, the dried extracts under investigation were discovered to be amorphous powders (Fig. 3.1, 3.2). In the range of 0.25 to 0.45 is the form factor. As a result, Table 3.1's data indicates that they are extremely compacted and lack mobility. Both substances are polydisperse, with several dust-like fractions that can form conglomerates, according to fractional composition analysis (Fig. 3.3).

Data on the study's technological properties of active ingredients are shown in table 3.1.

Table 3.1

Technical characteristics of anise and dry black elderberry extracts

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

According to the data collected, anise extract exhibits a significant degree of particle adherence, leading to low fluidity. The high fluidity of the black elderberry extract accounts for the 0.28 index of compacting. However, this substance's low index of fluidity is caused by its polydispersity of composition.

The next step was examining the hygroscopicity of the active ingredients in the established dosage form (Fig. 3.4, 3.5).

The findings indicate that the dry extracts under study are extremely hygroscopic. The environment's equilibrium humidity, where the dry extract's weight remains constant, is around 23%. Weight increases by 8.0 to 9.0% after 5 hours in an atmosphere with a 75% humidity level. In addition, residual moisture was relatively high at the start of the study, ranging up to 4.50% (Table 3.1).

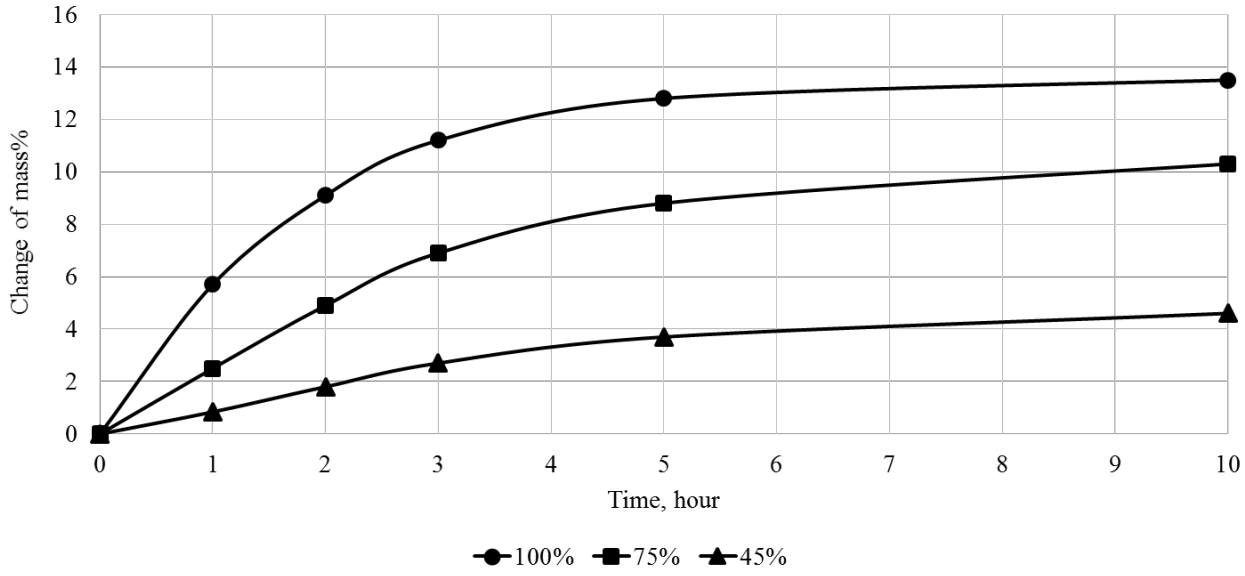

Fig. 3.4. Hygroscopicity of black elderberry dry extract

Granules easily absorb moisture at 100% relative humidity of air, but their structure is damaged.

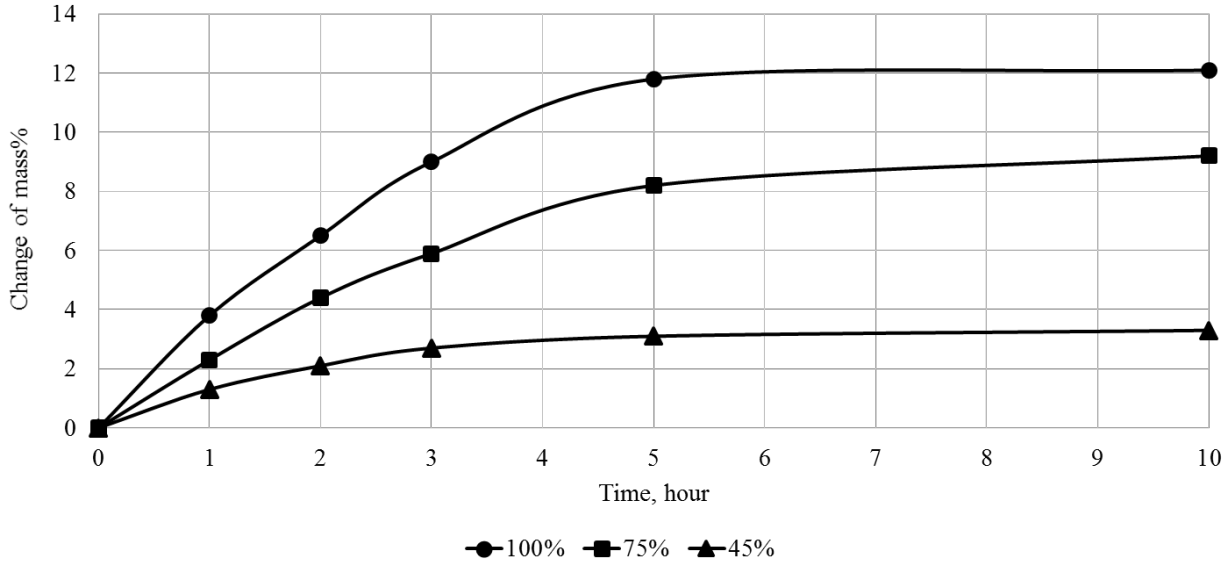

Fig. 3.5. Anise dry extract hygroscopicity

Accordingly, research has demonstrated the need for effective supplementary materials that decrease water absorption and enhance the technological properties of dry extracts, as well as initial granulation.

3.2. Selection and validation of the auxiliary material composition for granules containing anise and black elderberry dry extracts.

For plant material to increase flowability, compress, and absorb less water, filler must be introduced into the granular mass. Technological features of some fillers, including lactose, microcrystalline cellulose (MCC), and potato starch, which are commonly employed in the pharmaceutical business, were examined (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

Lactose has the highest fluidity, according to an analysis of the data in Table 3.2. This is most likely due to the spherical form of the particles and the comparatively high bulk weight value. Although MCC has the highest compressibility, its fluidity is between 2.50 and 3.0 g/s. Starch is one of the worst technological indicators.

Because of the small dust-like percentage (<0.05 mm) and extremely high fluidity values, the technological qualities of fillers were evaluated, and the results indicated potential for application in the lactose extracts under research. Furthermore, the bulk weight and fractional content of lactose and the extracts under study are near the values required to achieve homogeneity of mixing during granulation.

They were combined with different fillers to create granules in a lab apparatus for wet granulation in order to determine the impact of filler on the hygroscopic and technical properties of extracts. As a humidifier, 96% ethyl alcohol, a 3% methylcellulose solution, and a 5% polyvinylpyrrolidone (PVP) solution were used. Extracts comprise 34% of the mixture.

Dried the resulting granules to a 1.5% residual moisture content at 50 ^{0}C. The granules were then compared according to their technological characteristics (tables 3.3 - 3.6).

Table 3.3

The primary technological characteristics of granules with dry extracts are produced by wet granulation using a 5% PVP solution

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

Examination of the information shown in the table. 3.3 demonstrated how the use of auxiliary chemicals significantly enhanced the active components' technological qualities. A compression index between 0.05 and 0.15 indicates good rheological characteristics. Additionally, the low index value suggests that a small amount of effort should be used when filling capsules. The granules with the lowest technological qualities were those made with starch as a filler. The granules that were produced had an unstable structure and a varied content. This can be explained by the fact that partial swelling of the starch grains occurs when the granular material is moistened by a humidifier. As a result, the granules' bulk weight decreases and they become looser.

Granules containing lactose and MCC have a high index of abrasion resistance and a relatively low coefficient of compression. However, MCC granules are less fluid than lactose granules, so when using MCC as a filler, highly effective lubricants must be applied.

Table 3.4

The primary technical characteristics of the granules with dry extracts produced using the wet granulation process with a 3% MC solution

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

The use of 3% MC solution greatly enhanced fluidity, decreased granule grip strength to a minimum of 0.05, and greatly increased granule strength, which may result in a longer disintegration time. Granule compression has low indices and is independent of filler type.

Table 3.5

The primary technical characteristics of the dry extract-containing granules produced by wet granulation using a 0.5% MC and 5% PVP solution

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

Granules with good fluidity and low cohesiveness can be produced by combining macromolecular components in a humidifier at concentrations of 0.5% and 5% of methylcellulose and VFR, respectively. The severity of the flowing material that does not require the addition of auxiliary substances to assist compression can be used to determine the average bulk density indicators.

Table 3.6

The primary technological characteristics of granules containing dry extracts produced using the wet granulation process in an ethanol solution

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

Regardless of filler, the obtained granulate made with ethyl alcohol at a sufficient fluidity has weak strength indications and requires extra sealing during encapsulation.

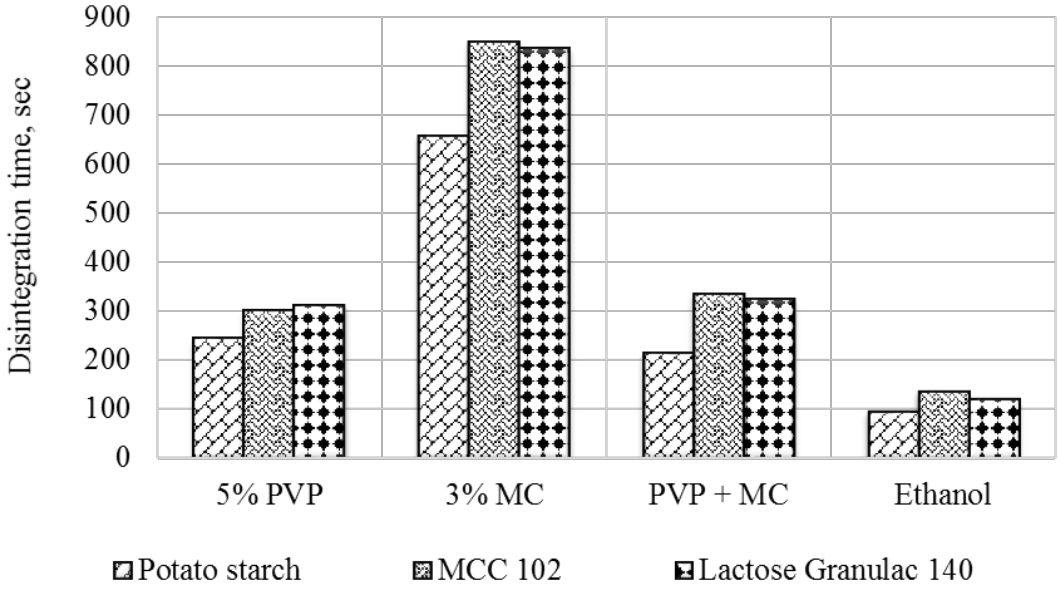

Fig. 3.6. Granulate sample disintegration time

We investigated the disintegration of the produced granules in order to determine the type of humidifier at the end (Figure 3.6).

The analysis of the disintegration data for the tested samples reveals a reduction in disintegration time as the composition transitions from using 3% MC, then a combination of PVP and MC, followed by 5% PVP, and finally ethanol. Based on a comparison of strength indicators, which vary across compositions starting with MC, then combining MC with PVP, followed by 5% PVP, and ending with ethanol, the optimal moisturizer is identified as a solution containing 5% PVP and 0.5% MC. Additionally, the fluidity value demonstrates a correlation with disintegration, sealing, and strength properties, indicating its importance in determining the overall performance of the formulation.

It was our responsibility to lessen the hygroscopicity of the dry extracts of aniseand black elderberry by adding filler qualities that regulate moisture. Lactose is recognized to significantly lessen the extract's hygroscopicity among these fillers. The data for our facilities was validated by obtained study (Fig. 3.7).

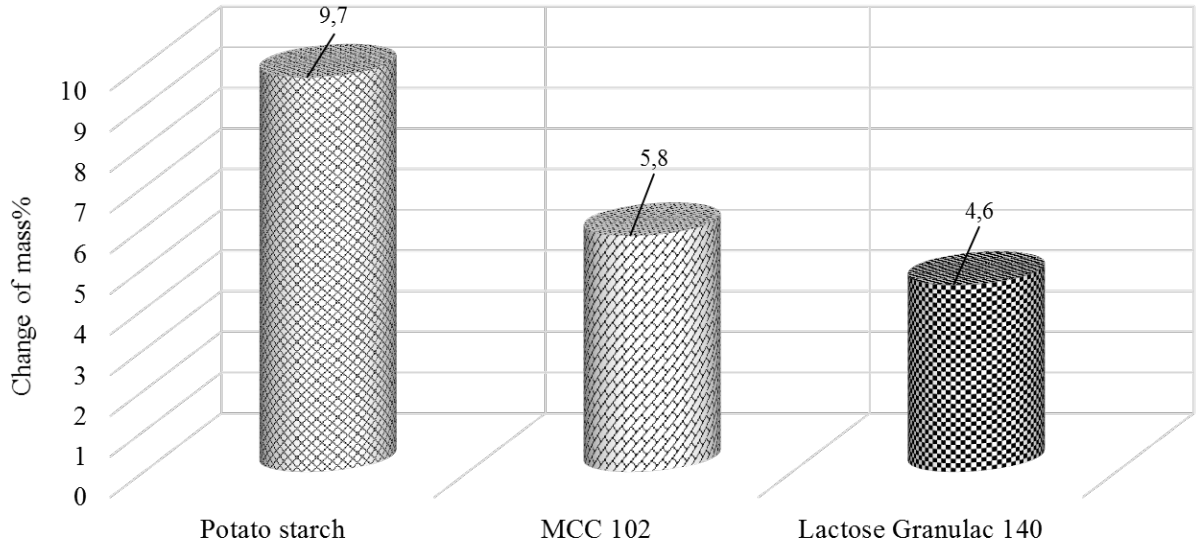

Fig. 3.7. Change of mass of the sample of granules with dry extracts after three hours of observation at 100% relative humidity in the air

We have added 1% of aerosil to the capsule mass's structure to increase its fluidity and resistance to moisture.

Studies have shown that lactose is the best filler to use when creating solid dosage forms with dry anise and black elderberry extracts. By adding it to the capsules, the active ingredients' technical qualities can be greatly enhanced and their moisture-absorbing capacity decreased.

A study of the extracts' moisture absorption kinetics revealed that the plant components had a notably high percentage of both humidity and moisture absorption, suggesting that a medication in capsule form would be feasible.

Consequently, we recommended the following formulation of capsules based on our analysis:

	g
Dry black elderberry flower extract	0,20
The dry extract of anise	0,10
Lactose	0,55
Aerosil	0,009
PVP	0,015
MC	0,0015
Average weight	0,876

The bulk density of the prepared mass for encapsulation is measured at 0.670 g/ml, corresponding to an average volume of 1.37 ml for a capsule of size 000.

3.3. An explanation of the technical procedure used to produce capsules for the treatment of respiratory conditions.

Based on the research findings, we have created a capsule technology to treat respiratory conditions. The following steps make up the process:

Stage 1: Raw material preparation. Before being used in production, every batch of packing materials and raw materials (primary and auxiliary) must be

checked for compliance with regulatory requirements. First, a calibrated, marked storage tank is used to weigh the active and auxiliary compounds in series. In calibrated storage tanks, mass components for encapsulation are weighed on scales and sieved through a sieve with the proper hole diameter.

Stage 2: Get a humidifier ready. PVP and MC are loaded, sorted, and weighed in the reactor after the water has been measured out in the measuring tank. For 20 minutes, mix. The humidifier was transferred to the granulation step.

Stage 3: Granulation, humidification, and mixing. In a granulator-mixer, mass is mixed and moisture is added while extract and input ventilation are operating. The bulk of active and auxiliary chemicals was sorted and weighed before being placed into the granulator-mixer. Continue mixing for 10 ± 1 minutes. The humidifier, which consists of a 5% PVP solution and 0.5% MC, is then added to the dry ingredients. Mixing is done for 10 ± 1 minutes to ensure that the mass is evenly moist and that it will ball up when squeezed in the palm. The granulator with 1.0 mm-diameter holes is used for wet granulation. The tank contained the wet granulated.

Stage 4 involves drying the granules. The wet granulate is transferred to a drying cabinet, where it is dried for 1.5 hours at a temperature of 60 ± 1 °C until the residual humidity reaches 2.0 ± 1.5%. Automatic systems monitor and regulate the drying temperature throughout the process. The humidity of the granulate is measured using a moisture meter, and once dried, the mass is shipped in a designated tank.

Stage 5: Sieving and dry granulation. Dry granulate from the tank is collected in a container by passing it through a calibrator with 1.0 mm-diameter holes.

Stage 6: Granule dusting. The resulting granules and aerosil are added to the mixer and powdered for five to one minute. In the tank, the bulk is unloaded.

Stage 7: Encapsulation. The automatic capsule filling machine was filled with granules from the collection. Capsules №000, with an average weight of around 0.90 ± 0.02 grams.

The depth at which the matrix is filled determines the necessary weight of the capsule. The filling regulator is used to regulate the filling matrices. Use electronic scales to check the weight of the capsules selectively every 30 minutes. Samples are taken for chemical analysis during the encapsulation process. Following a positive test result and an OCC passport, the capsule container is moved to the packing stage.

Step 8: Blister-packaging the capsules. Step 9: Packing. Packs are packed in boxes. The machine packs the capsules in blisters of ten pieces with aluminum foil. Five-piece touring bundles with leaflets were placed in carton shipments. Provide drug control at this point while maintaining microbiological purity.

Figure 3.8 shows the overall layout of the technological process.

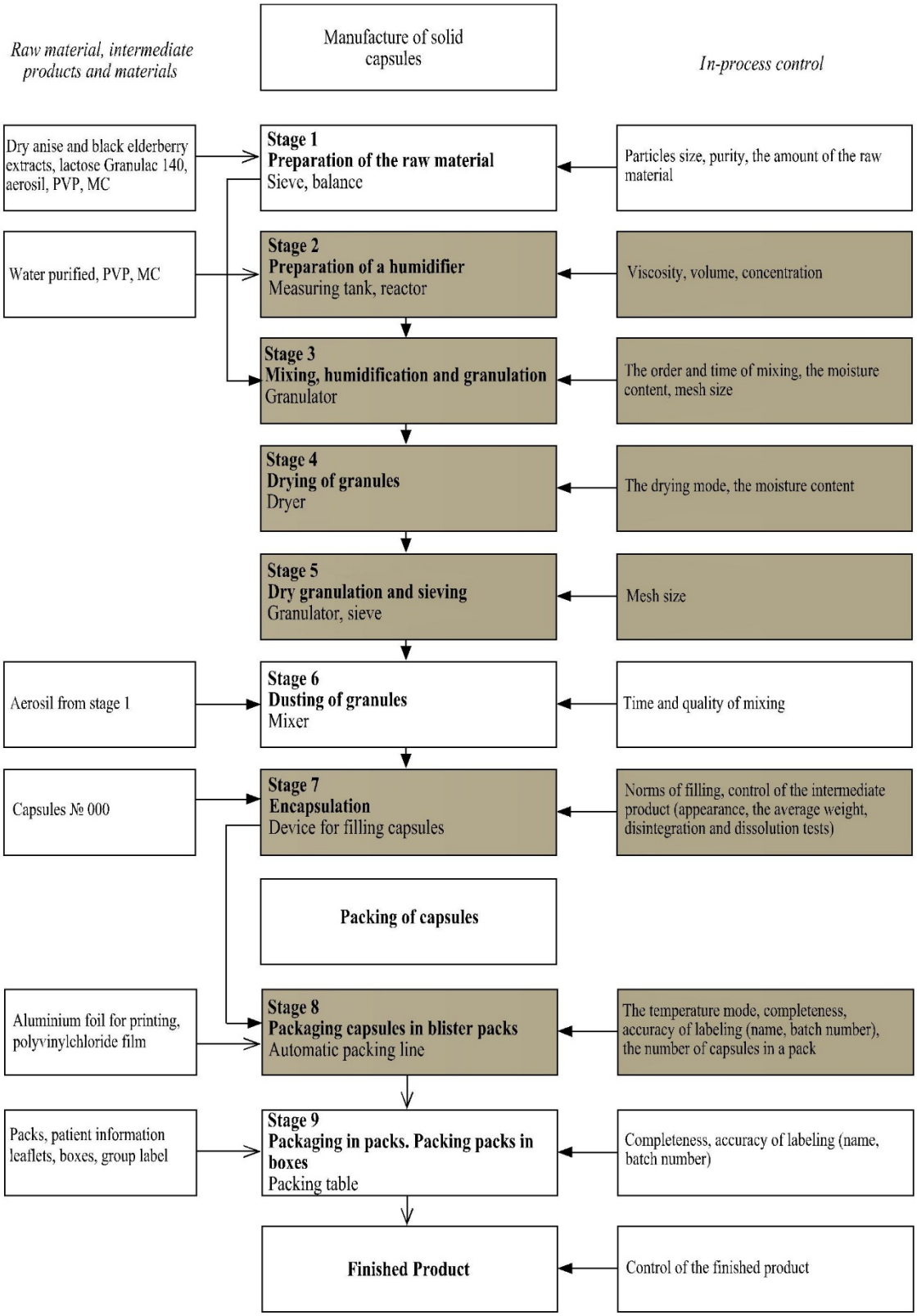

Fig. 3.8. The technology used in capsule production

Conclusions to chapter 3

1. It has been determined through physico-chemical and farmako-technological study that dried extracts have a high absorption capacity, low flowability, and inadequate compactibility indicators.

2. Properties of lactose, microcrystallic cellulose, and potato starch are investigated in order to make an informed choice of excipients. Mixtures for granulation with various humidifiers have technical parameters that are established. The technical scheme for producing capsules is provided based on the rational structure of the capsules as determined by the completed research.

CONCLUSIONS

1. The physicochemical and technological properties of dry anise and black elderberry extracts were extensively studied. The results revealed significant challenges related to their high hygroscopicity, poor flowability, and inadequate compactibility. These characteristics necessitate the use of auxiliary materials and a pre-granulation process to improve their handling and suitability for encapsulation.

2. An in-depth evaluation of fillers, including lactose, microcrystalline cellulose (MCC), and potato starch, highlighted lactose as the most effective option. The spherical particle shape and high bulk density of lactose significantly enhance the flowability and homogeneity of the granulated mixture. Additionally, lactose was found to reduce the hygroscopicity of the extracts, a critical factor for ensuring the stability and shelf life of the capsules.

3. The study identified the optimal combination of humidifiers for wet granulation. A solution containing 5% polyvinylpyrrolidone (PVP) and 0.5% methylcellulose (MC) demonstrated superior performance. This combination improved granule fluidity and cohesiveness while maintaining appropriate disintegration times, ensuring consistent drug release and efficacy.

4. Aerosil was incorporated into the capsule formulation at a concentration of 1% to address the high moisture absorption of the plant extracts. This addition significantly improved the granules' resistance to moisture and enhanced their fluidity, enabling efficient handling during the encapsulation process.

5. The finalized capsule formulation, comprising dry black elderberry extract, dry anise extract, lactose, aerosil, PVP, and MC, was shown to yield a robust product with desirable physical and chemical properties. The average capsule weight was optimized to ensure accurate dosing and uniformity, with a bulk density that aligns with the requirements for size 000 capsules.

6. A comprehensive technical process for capsule production was developed, comprising eight key stages: raw material preparation, humidifier preparation, granulation, drying, sieving, dusting, encapsulation, and packaging. Each stage was meticulously designed to optimize quality, minimize material waste, and comply with regulatory standards. The encapsulation process, in particular, was fine-tuned to ensure precise filling and weight consistency of the capsules.

7. The granulation studies demonstrated that lactose, in combination with the identified humidifiers, produced granules with high abrasion resistance and optimal rheological properties. MCC granules, although strong, required additional lubricants due to lower fluidity. Starch granules were found to have the weakest structure, making them unsuitable for this application.

8. The technological process also addressed the challenges of granule disintegration and capsule sealing. Granules produced with PVP and MC exhibited balanced disintegration times, ensuring effective release of the active ingredients. Ethanol-based granulation methods, while yielding granules with sufficient fluidity, produced weaker structures requiring additional reinforcement during encapsulation.

9. The moisture absorption kinetics of the plant extracts were thoroughly analyzed, revealing a high affinity for atmospheric humidity. By incorporating lactose and aerosil into the formulation, the moisture stability of the capsules was significantly improved, enhancing their storage stability under various environmental conditions.

10. The study established a rational capsule composition and production methodology, demonstrating the feasibility of producing high-quality capsules for the treatment of respiratory diseases. The proposed formulation and process effectively mitigate the technological challenges associated with the complex properties of plant-based extracts, providing a reliable solution for pharmaceutical applications.

REFERENCES

1. Phytotherapeutic potential of *Pimpinella anisum* (anise) in respiratory diseases / N. Ali et al. *Journal of Herbal Medicine*. 2021. Vol. 28. P. 1–8.

2. The effect of *Sambucus nigra* (elderberry) on cytokine production / V. Barak et al. *European Cytokine Network*. 2020. Vol. 31, № 2. P. 66–71.

3. Bensky D., Gamble A. *Chinese Herbal Medicine: Materia Medica*. 2020. 3rd ed. Eastland Press. P. 354–358.

4. Benzi G., Ceci A. Herbal medicines as supportive treatment in respiratory tract infections. *Phytotherapy Research*. 2019. Vol. 33, № 12. P. 3104–3112.

5. Respiratory benefits of herbal extracts in clinical practice / M. M. Berger et al. *Journal of Integrative Medicine*. 2021. Vol. 19, № 1. P. 45–52.

6. Block K. I., Mead M. N. Immune system effects of *Sambucus nigra* extracts. *Alternative Medicine Review*. 2020. Vol. 25. P. 47–52.

7. Chandrasekaran C. Phytochemical standardization of dry extracts for capsule formulations. *Pharmacognosy Research*. 2021. Vol. 13, № 3. P. 150–158.

8. Anti-inflammatory effects of anise oil in animal models of asthma / A. Chatterjee et al. *Pulmonary Pharmacology & Therapeutics*. 2020. Vol. 63. P. 9–16.

9. Elderberry for prevention and treatment of viral respiratory illness: a review / R. Christensen et al. *Advances in Integrative Medicine*. 2021. Vol. 8. P. 85–93.

10. Capsule formulations of herbal extracts for bronchitis therapy / H. Dold et al. *Pharmaceutical Development and Technology*. 2019. Vol. 24. P. 832–839.

11. Dunning T. Respiratory herbal medicine: efficacy and mechanisms. *Australian Journal of Herbal Medicine*. 2020. Vol. 32, № 4. P. 130–138.

12. Biological activities of *Pimpinella anisum* essential oil / F. K. El-Baz et al. *Journal of Applied Pharmaceutical Science*. 2021. Vol. 11, № 2. P. 42–48.

13. Capsule development from dry herbal extracts / S. Finlay et al. *Pharmaceutical Sciences and Research*. 2022. Vol. 17, № 3. P. 201–209.

14. Elderberry extract and its role in treating influenza and colds / E. Ghasemi et al. *Journal of Medicinal Plants Research*. 2021. Vol. 15, № 1. P. 19–24.

15. Habtemariam S. *Sambucus nigra* L. (Black Elderberry) as an antiviral agent: a review. *Frontiers in Pharmacology*. 2020. Vol. 11. P. 17–26.

16. Pharmacological properties of anise seed extract / T. Hasanloo et al. *Iranian Journal of Basic Medical Sciences*. 2021. Vol. 24, № 5. P. 630–636.

17. Huang L. Development of herbal capsule dosage forms for respiratory conditions. *Journal of Pharmaceutical Innovation*. 2022. Vol. 17. P. 182–190.

18. Iwu M. M. *Handbook of African Medicinal Plants*. 2019. 2nd ed. CRC Press. P. 240–243.

19. Effects of anise and elderberry on oxidative stress in lung tissues / S. Jahan et al. *Biomedicine & Pharmacotherapy*. 2021. Vol. 139. P. 9–15.

20. Immunostimulatory effects of *Sambucus nigra* extract / H. Y. Kim et al. *International Journal of Molecular Sciences*. 2020. Vol. 21, № 3. P. 1124–1132.

21. Development of phytocapsules with mucolytic action / Kumar R. et al. *Drug Development and Industrial Pharmacy*. 2021. Vol. 47. P. 1045–1052.

22. Antiviral properties of natural compounds in respiratory infections / A. Lichota, et al. *Pathogens*. 2020. Vol. 9, № 9. P. 737–744.

23. Mahendra P., Bisht S. Anise and its pharmacological potentials. *Asian Pacific Journal of Tropical Biomedicine*. 2019. Vol. 9, № 1. P. 1–9.

24. Miller A. L. The role of herbal medicine in the treatment of respiratory diseases. *Alternative Medicine Review*. 2020. Vol. 25. P. 18–25.

25. Herbal dry extracts: technological aspects of capsule design / A.Mohammadi et al. *Journal of Drug Delivery Science and Technology*. 2022. Vol. 69. P. 1–8.

26. Antitussive effects of anise and elderberry combination / M. Moradi et al. *Journal of Ethnopharmacology*. 2021. Vol. 267. P. 11–20.

27. Orhan I. E. An overview on the pharmacology of *Pimpinella anisum*. *Phytotherapy Research*. 2019. Vol. 33, № 11. P. 2870–2880.

28. Synergistic effects of plant extracts in respiratory formulations / L. R. Perez et al. *Journal of Herbal Pharmacotherapy*. 2020. Vol. 19, № 3. P. 290–298.

29. Development of herbal capsule formulations for COPD patients / M. Shokrzadeh et al. *Iranian Journal of Pharmaceutical Research*. 2021. Vol. 20, № 2. P. 78–84.

30. Natural product-based inhibitors of respiratory viruses / J. R. Weng et al. *Molecules*. 2020. Vol. 25, № 21. P. 5120–5130.

APPLICATIONS

Appendix A

МІНІСТЕРСТВО ОХОРОНИ ЗДОРОВ'Я УКРАЇНИ
НАЦІОНАЛЬНИЙ ФАРМАЦЕВТИЧНИЙ УНІВЕРСИТЕТ

АКТУАЛЬНІ ПИТАННЯ СТВОРЕННЯ НОВИХ ЛІКАРСЬКИХ ЗАСОБІВ

МАТЕРІАЛИ
XXXI МІЖНАРОДНОЇ НАУКОВО-ПРАКТИЧНОЇ
КОНФЕРЕНЦІЇ МОЛОДИХ ВЧЕНИХ ТА СТУДЕНТІВ

23–25 квітня 2025 року
м. Харків

Харків
НФаУ
2025

продемонстрували покращення зволоження шкіри при використанні косметичних гелів з вмістом хітозану та ектеїну.

Висновки. Оцінка біофармацевтичних властивостей косметологічних гелів є невід'ємною частиною сучасного підходу до розробки ефективних дерматокосметичних засобів. Технологічні аспекти, такі як вибір гелеутворювача, оптимізація складу та методики дослідження *in vitro/ex vivo/in vivo,* дозволяють створювати науково обґрунтовані продукти з прогнозованими властивостями.

Подальші дослідження в цьому напрямку є перспективними для підвищення ефективності, переносимості та споживчого сприйняття косметичних засобів.

DEVELOPMENT OF CAPSULE COMPOSITION FOR THE TREATMENT OF RESPIRATORY DISEASES

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

Introduction. Since respiratory disorders are so common and can cause serious consequences, they rank among the most significant health issues. Since the etiology of these respiratory disorders is similar to their clinical presentations, treating them has proven to be a challenging task thus far. Therefore, regardless of the cause, it is crucial to have medications in the arsenal that will both be safe to use and have an impact that will reduce and eliminate the disease's primary signs.

Herbal therapeutic treatments have gained increasing popularity in recent years. The benefit of plant-based medications is that, in contrast to manufactured pharmaceuticals, the physiologically active components of plants are more naturally incorporated into the body's metabolic processes.

Aim. is 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. It has been investigated how drugs used to treat respiratory conditions are described and assessed in literary works. It has been shown how fast new combination drugs made from medicinal plant ingredients may be created in the form of capsules. According to the literature, research on medicinal raw materials is crucial for creating new drugs.

Dry extracts of anise and black elderberry are suggested as active ingredients; these extracts have antibacterial, diaphoretic, antipyretic, expectorant, antiallergic, inflammatory, and spasmolytic properties.

It has been determined through physicochemical and technological study that dry extracts have a high absorption capacity, limited flowability, and inadequate compactibility indicators. Lactose, microcrystallic cellulose, and potato starch characteristics are investigated in order to make an informed excipient selection. There are specified technical criteria for mixtures used in granulation with various humidifiers. A technological plan for producing the capsules and a logical composition for them are suggested based on the research that have been conducted.

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

Ф А 2.2.1–32-366

National University of Pharmacy

Faculty pharmaceutical
Department of industrial technology of medicines and cosmetics

Level of higher education master

Specialty 226 Pharmacy, industrial pharmacy
Educational and professional program Pharmacy

APPROVED
The Head of department
of industrial technology of medicines
and cosmetics
Olena RUBAN
"02" September 2024

ASSIGNMENT
FOR QUALIFICATION WORK
OF AN APPLICANT FOR HIGHER EDUCATION

Torabi Firdraousse ALIDRISSI

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

approved by order of NUPh from "27" of September 2024 № 237

2. Deadline for submission of qualification work by the applicant for higher education: May 2025.

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 industrial technology of medicines and cosmetics	09.09.2024	09.09.2024
2	Denys PULIAIEV, associate professor of higher education institution of industrial technology of medicines and cosmetics	18.11.2024	18.11.2024
3	Denys PULIAIEV, associate professor of higher education institution of industrial technology of medicines and cosmetics	03.02.2025	03.02.2025

7. Date of issue of the assignment: «02» September 2024.

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 2024	**done**
2	Definition of objects and methods of research. Formation of the second chapter.	October 2024	**done**
3	Study of physico-chemical and pharmaco-technological properties of research objects.	January 2024	**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 2024	**done**

An applicant of higher education _____ Torabi Firdraousse ALIDRISSI

Supervisor of qualification work _____ Denys PULIAIEV

ВИТЯГ З НАКАЗУ № 237

По Національному фармацевтичному університету

від 27 вересня 2024 року

Затвердити теми кваліфікаційних робіт здобувачам вищої освіти 5-го курсу Фм20(4,10д) 2024-2025 навчального року, освітньо-професійної програми – Фармація, другого (магістерського) рівня вищої освіти, спеціальності 226 – Фармація, промислова фармація, галузь знань 22 Охорона здоров'я, денна форма здобуття освіти (термін навчання 4 роки 10 місяців), які навчаються за контрактом (мова навчання англійська та українська) згідно з додатком № 1.

Прізвище, ім'я здобувача вищої освіти	Тема кваліфікаційної роботи		Посада, прізвище та ініціали керівника	Рецензент кваліфікаційної роботи
по кафедрі промислової технології ліків та косметичних засобів				
Алідріссі Торабі Фідраусі	Розробка складу капсул для лікування респіраторних захворювань	Development of capsule composition for the treatment of respiratory diseases	доц. Пуляєв Д.С.	доц. Ковальов В.В.

Ректор

Вірно. Секретар

ФА2.8-03-317

ВИСНОВОК

експертної комісії про проведену експертизу
щодо академічного плагіату у кваліфікаційній роботі

здобувача вищої освіти

«02» травня 2025 р. № 331104333

Проаналізувавши кваліфікаційну роботу здобувача вищої освіти Алідріссі Торабі Фідрауссі, групи Фм20(4.10) англ-01, спеціальності 226 Фармація, промислова фармація, освітньої програми «Фармація» навчання на тему: «Розробка складу капсул для лікування респіраторних захворювань / Development of capsule composition for the treatment of respiratory diseases», експертна комісія дійшла висновку, що робота, представлена до Екзаменаційної комісії для захисту, виконана самостійно і не містить елементів академічного плагіату (компіляції).

Голова комісії,
проректор ЗВО з НПР,
професор **Інна ВЛАДИМИРОВА**

Ф А 2.2.1-32-353

REVIEW

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

Torabi Firdraousse ALIDRISSI

on the topic: **«Development of capsule composition 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 Torabi Fidraussi ALIDRISSI 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 assoc. prof. Denys PULIAIEV

«13» of May 2025

Ф А 2.2.1-32-356

REVIEW

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

Torabi Firdraousse ALIDRISSI

on the topic: **«Development of capsule composition 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. Torabi Fidraussi ALIDRISSI 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 Torabi Fidraussi ALIDRISSI 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 assoc. prof. Volodymyr KOVALOV

«15» of May 2025

Ф А2.2.1-91-287

МІНІСТЕРСТВО ОХОРОНИ ЗДОРОВ'Я УКРАЇНИ
НАЦІОНАЛЬНИЙ ФАРМАЦЕВТИЧНИЙ УНІВЕРСИТЕТ

Витяг з протоколу
засідання кафедри промислової технології ліків та косметичних засобів НФаУ
№ 12 від 16 травня 2025 року

Голова: завідувач кафедри, доктор фарм. наук, проф. Рубан О. А.

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

ПРИСУТНІ: зав. каф., проф. Рубан О.А., проф. Ковалевська І.В., проф. Бобрицька Л.О., проф. Гриценко В.І., проф. Сліпченко Г.Д., проф. Кухтенко О. С., доц. Безрукавий Є. А., доц. Кутова О. В., доц. Манський О. А., доц. Ніколайчук Н. О., доц. Пуляєв Д.С., доц. Січкар А. А., доц. Солдатов Д. П., доц. Трутаєв С. І., ас. Пономаренко Т.О.

ПОРЯДОК ДЕННИЙ:
1. Про представлення до захисту в Екзаменаційну комісію кваліфікаційних робіт здобувачів вищої освіти випускного курсу НФаУ 2025 року випуску

СЛУХАЛИ: про представлення до захисту в Екзаменаційній комісії кваліфікаційної роботи на тему: «Розробка складу капсул для лікування респіраторних захворювань» здобувача вищої освіти випускного курсу Фм20 (4,10) eng - 01 НФаУ 2025 року випуску Торабі Фідрауссі АЛІДРІССІ
Науковий (-ві) керівник (-ки) _к.фарм.н., доц. Денис ПУЛЯЄВ_____
Рецензент_____к.фарм.н., доц. Володимир КОВАЛЬОВ_____

УХВАЛИЛИ: Рекомендувати до захисту кваліфікаційну роботу здобувача вищої освіти _5_ курсу Фм20 (4,10) eng - 01 Торабі Фідрауссі АЛІДРІССІ на тему: «Розробка складу капсул для лікування респіраторних захворювань»

Голова
завідувач кафедри,
доктор фарм. наук, проф. _____ Олена РУБАН
(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 Торабі Фідрауссі АЛІДРІССІ 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 респіраторних захворювань»

Кваліфікаційна робота і рецензія додаються.

Декан факультету _____ / Микола ГОЛІК /

Висновок керівника кваліфікаційної роботи

Здобувач вищої освіти Торабі Фідрауссі АЛІДРІССІ виконала на кафедрі промислової технології ліків та косметичних засобів НФаУ кваліфікаційну роботу, яка присвячена створенню складу капсул для лікування захворювань органів дихання.

В процесі роботи Торабі Фідрауссі АЛІДРІССІ дослідила 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 Торабі Фідрауссі АЛІДРІССІ на тему «Розробка складу капсул для лікування респіраторних захворювань» 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» травня 2025 р.

Висновок кафедри про кваліфікаційну роботу

Кваліфікаційну роботу розглянуто. Здобувач вищої освіти Торабі Фідрауссі АЛІДРІССІ допускається до захисту даної кваліфікаційної роботи в Екзаменаційній комісії.

Завідувач кафедри промислової технології
ліків та косметичних засобів Олена РУБАН

«16» травня 2025 р.

Qualification work was defended

of Examination commission on

« » of June 2025

With the grade _____

Head of the State Examination commission,

D.Pharm.Sc, Professor

_____ / Volodymyr YAKOVENKO/