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QUALIFICATION WORK

on the topic: **«DEVELOPMENT OF THE COMPOSITION AND TECHNOLOGY OF ANTIALLERGIC SYRUP»**

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ANNOTATION

Qualification work contains 43 pages, 6 figures, 5 tables, a list of references of 43 titles.

In order to develop the composition of the medicinal syrup with anti-allergic effect, substances of natural origin were selected as active pharmaceutical ingredients - dry extracts of Knautia arvensis and Urtica urens. Glucose and fructose were chosen as the base of the syrup, flavor corrector - citric acid and pear essence, preservative - sodium benzoate. The manufacturing technology of the medicinal syrup for the treatment of allergies has been substantiated.

Key words: allergy, syrup, dry extracts of Knautia arvensis and Urtica urens, glucose and fructose, composition, technology.

АНОТАЦІЯ

Кваліфікаційна робота містить 43 сторінки, 6 рисунків, 5 таблиць, список літератури з 43 найменуваннь.

З метою розробки складу лікарського сиропу протиалергічної дії в якості активних фармацевтичних інгредієнтів було обрано субстанції природного походження – сухі екстракти свербіжниці польової та кропиви жалкої. В якості основи сиропу були обрані – глюкоза та фруктоза, коригент смаку –лимона кислота та грушева есенція, консервант – натрію бензоат. Обґрунтовано технологію одержання лікарського сиропу для лікування алергії.

Ключові слова: алергія, сироп, сухі екстракти свербіжниці польової та кропиви жалкої, глюкоза та фруктоза, склад, технологія.

CONTENTS

LIST OF ABREVIATIONS

API – active pharmaceutical ingredients

AD - allergic diseases

g– gram

SPU– State Pharmacopoeia of Ukraine

INTRODUCTION

The relevance of the topic.

The frequency of allergic diseases in the 21st century, has reached epidemic proportions, increasing by 2-3 times every decade. Today, allergic pathology is one of the six most common human diseases. According to statistics, every fifth inhabitant of our planet suffers from allergies. The study of the prevalence of allergic diseases is carried out both according to official statistics and with the help of targeted epidemiological studies, which are more reliable [1, 32].

These data show that the problem of allergic diseases in Ukraine is not only of medical, but also of social importance [3].

In the aspect of the above, it should be noted that the use of pharmaceuticals for the treatment of allergy symptoms must be considered and justified [5].

Active pharmaceutical ingredients that are part of antihistamine drugs have a large number of side effects and are not always safe for the patient's body. Therefore, especially in our time, the use of medicinal products of plant origin is extremely relevant [33].

The advantages of medicinal plants include:

- low toxicity;

- the possibility of long-term use without significant side effects and the risk of the development of resistant strains of microorganisms;

- are better tolerated by the body than synthetic ones;

-give less unwanted side effects [27,33].

Thus, the development of medicinal products based on APIs of plant origin was and remains an urgent task of modern pharmacy and medicine.

The purpose and research tasks. The purpose of our work is the theoretical substantiation of the rational composition and technology of a new anti-allergic action drug in the form of syrup with dry extracts of Knautia arvensis and Urtica urens.

To achieve the purpose it was necessary to solve the following tasks:

- Analyze and summarize literary data on classification, etiopathogenesis, symptoms and modern methods of treatment and prevention of allergic diseases;
- To study the pharmaceutical market of drugs for the treatment of allergic diseases;
- To theoretically substantiate and develop in laboratory conditions the composition and technology of anti-allergic syrup with dry extracts of Knautia arvensis and Urtica urens;
- Develop a technological scheme for the manufacture of syrup for the production of syrup according to the proposed technology.

Research objects. Dry extracts of Knautia arvensis and Urtica urens.

The subject of research is the composition and technology of medicinal syrup for the treatment of allergies.

Research methods. Physico-chemical, pharmaco-technological studies are applied during the qualification work, which allow to control the incoming substances and the developed dosage form.

Approbation of research results and publication. In the collection of scientific papers "Problems and achievements of modern biotechology", a work on the topic "Relevance of the creation of medicinal syrup of anti-allergic action" was published, where the feasibility of developing medicinal syrup for the treatment of allergies was proven.

Structure of work. Qualification master degree work consists from introduction, three chapters, general conclusions, a list of used sources (43), and appendix. The content of work is presented on 43 pages of basic text and contains 5 tables and 6 figures.

CHAPTER 1
REVIEW OF THE LITERATURE

1.1. Allergy is a "disease of civilization"

Allergy is an increased sensitivity ("hypersensitivity"), a changed reaction of the human body to the influence of certain factors (allergens). Hypersensitivity (allergy) means that the body's immune system, which protects against infections, diseases and foreign bodies, reacts to the allergen with a violent reaction and excessive protection against completely harmless substances. Immunoglobulins, blood cells, circulating immune complexes, and biologically active substances are involved in the development of allergies [33].

There are allergic reactions caused by immune pathochemical reactions mechanisms, and pseudoallergic, which occur without an immune stage. The term "allergy" was introduced by the Austrian pediatrician K. Pirke in 1906 and comes from two Greek words: allos - other and ergon – action [3].

Allergy is a global medical problem, because about 25% of the population suffers from some kind of allergic disease. The number of allergy cases is steadily

increasing all over the world, the number of not only allergic reactions has increased, a large number of severe conditions with damage to the respiratory organs, skin and mucous membranes, joints, lymphatic system, etc. have appeared [4,5].

Causes of allergies

Everything that surrounds us can cause allergies: household chemicals, animal hair, food products, plant pollen, mold, insects, latex, medicines, domestic dust, cosmetics, alcohol, seafood, even cold and sunlight. The development of allergies begins with the release of histamine into the blood. This causes irritation of the mucous membrane of the nasopharynx, runny nose and sneezing begin, swelling appears. The nature of allergies remains largely a mystery. Allergies can suddenly appear and disappear just as suddenly. But basically, the nature of allergy is immunological, and it hides in a violation of the regulation of the immune response. In addition, predisposition to one or another type of allergy is inherited (atopy), so if one parent suffers from allergies, there is a 25% chance that his child will develop allergies. The chance of having an allergy increases to 80% if both parents suffer from allergies [6].

Currently, there is a tendency to self-intake large quantities medicines from different pharmaco-therapeutic groups at the same time, which leads to the development of allergies. This caused the development of many new diseases and complications (allergy, dysbacteriosis, toxic reactions, nephritis, hepatitis, etc.). This also includes diseases that develop on an immunological basis (anaphylactic shock, urticaria, bronchial asthma, atopic dermatitis, eczema, and others) [4,18,31,35,37].

Food allergens. They can be food products or substances formed during cooking and long-term storage. It is believed that food products of protein origin (animal and vegetable proteins) have the most pronounced allergenic activity. Fats, carbohydrates, trace elements often cause false allergic reactions. The most common food allergens include: coffee, cocoa, chocolate, citrus fruits, strawberries, raspberries, eggs, meat of animals and birds, honey, fish, caviar,

crabs, crayfish, milk, carrots, beets, tomatoes, buckwheat, cereals (rye, wheat, millet, rice, corn), legumes, nuts. 51 names of food allergens are produced in Ukraine [26].

Household allergens. These include, mainly, allergens of domestic dust, pillow feathers, and book dust. The leading household allergen is domestic dust allergen. There is evidence that dust collected from different regions and even from different homes can differ significantly in its antigenic properties. As pointed out by B. Guerun (1994), the composition of domestic dust with regard to the occurrence of household sensitization includes the following distribution: house dust mites, epidermis of domestic animals, molds and insects. The main role in the allergenic activity of domestic dust belongs to micromites of the genus Dermatophagoides pteronyssinus. They got the name of "bed" mites. It is also known that the composition of domestic dust often includes hair and dander of pets, as well as rodents. The important role of cockroaches in the development of allergic reactions has been proven. Ukraine produces 8 series of domestic dust allergens, 3 types of mite allergens, daphnia allergens, and pillow feathers [33].

Epidermal allergens. They can be part of household dust and have an independent significance in the development of the clinical picture of AD. These include: human, horse, pig dandruff; hair of a dog, cat, rabbit, guinea pig, mouse, sheep, goat, etc. The frequency of pet dander allergy ranges from 1 to 4% in adults and up to 11% in children. Hypersensitivity to the hair of dogs and cats is most common. The fur of sheep, goats, wool fabrics - all this makes the question of allergy to them important. Mice and rats are important in homes where these animals live freely [6].

Insect allergens – are found in their saliva, poison and body. An allergic reaction occurs with hymenoptera bites, dipterans and bedbugs, as well as contact with secretions and particles of the body of insects or inhalation of these particles. Sensitization to the venom of hymenoptera insects occurs in 0.3–5% of the population, allergy to bee venom is noted in 22–43% of beekeepers. Mortality

from insect bites in England is 4-5 cases per year. In the USA, more than 50 people die every year from the same reason [3].

Among the millions of cases of spider bites, scorpion stings (mostly toxic reactions) and bee stings (mostly allergic reactions) every year, deaths from insect bites occur 3 times more often than from rattlesnake bites. We produce 5 types of insect allergens, which meets the requests of allergists. Unfortunately, not all patients and general practitioners know that only SIT with bee and wasp allergens can save patients with insect allergies from a fatal prospect [6].

Chemical allergens. They include the vast majority of chemicals that people come into contact with at work and in everyday life. Among chemicals, allergens include metals and their salts, pesticides, and synthetic polymers. They cause professional AD. Salts of metals (chromium, nickel, platinum), rosin, etc., can also cause AD. It should be remembered that about 4 million chemicals are obtained from natural products or synthesized artificially, and up to 60 thousand of them are used daily. About 1,500 active substances are part of pesticides, 4,000 are part of medicines, and 2,000 are used as excipients. More than 5,000 substances are used as food additives. Almost all of them can act as potential allergens. Testing of latex allergens (6-8% of medical workers suffer from latex allergy), cosmetics and detergents has now begun [3,33].

Medicinal allergens are a type of chemical allergens. These include chemical, enzyme preparations and synthesis products of fungi and bacteria. Medicines are mainly haptens, which become direct allergens only when conjugated with a carrier protein. Ukraine produces standard kits for diagnosing drug allergies. But, despite the order of the Ministry of Health No. 127/18 dated 04/02/2002, the diagnosis of drug allergy in almost all institutions is still carried out with the help of routine skin tests, which are both dangerous and not very informative [6,33].

Infectious allergens. Infectious allergens include allergens of bacteria, fungi, viruses, protozoa and helminths. Allergic reactions mainly occur in contact with opportunistic and non-pathogenic microorganisms and less often - with

pathogenic ones. Fungi attract special attention as allergens. There are data that they are the cause of 20-30% of AD. Fungal spores can be found everywhere - in the ground, water, air, and rooms. In reality, a person comes into contact with 100 types of fungi [3,6].

Allergy symptoms

Allergies are associated with the following symptoms:

• runny nose and tearing;

• dry night cough that recurs regularly;

• wheezing in the lungs and suffocation;

• itching, throat irritation;

• rash and other skin reactions [22].

Allergy is characterized by pronounced clinical polymorphism. Any tissues and organs can be involved in the allergy process. With the development of allergies, the skin, gastrointestinal tract, and respiratory system are more often affected. Allergic reactions of the immediate and delayed type are distinguished, but this distribution of allergies is largely conditional [24].

Thus, urticaria is considered one of the forms of immediate-type allergy, however, urticaria can be accompanied by serum sickness, as a classic form of delayed-type allergy. The following clinical variants of allergies are distinguished: hay fever (pollinosis), rhinitis, allergic toxicoderma, conjunctivitis, urticaria, Quincke's edema, serum sickness, hemolytic crisis, thrombocytopenia, allergic dermatoses, enteropathies, bronchial asthma, anaphylactic shock. Any single allergen can cause a number of symptoms. For example, birch pollen allergen in a pollinosis patient can cause not only rhinoconjunctivitis, but also provoke bronchospasm and cause urticaria. Most allergic patients sufferer from a whole range of allergens, for example, to pollen, household and epidermal allergens at the same time. Substances, for example, metals, latex allergen, medicinal and cosmetic products, household chemicals, food products, aeroallergens and other allergens

can affect the skin or directly enter the body through the mucous membrane of the gastrointestinal tract or by injection [32,37].

Allergies can also occur in response to insect bites or emotional disorders. Allergic skin lesions are called allergodermatoses. Common signs of allergic dermatoses are itching and reddening of the skin, rashes on the skin like urticaria (swelling, blisters) or eczema (flaking, dry skin). The most common allergic dermatoses are atopic dermatitis (exudative diathesis, neurodermatitis), urticaria, contact dermatitis [9].

Hay fever. Itching in the nasopharynx, runny nose, watery eyes, sneezing and throat irritation are sometimes called allergic rhinitis and usually caused by allergens that are present in the air, such as pollen, dust and animal hair. This reaction of the body is called "hay fever", it is seasonal and occurs during the flowering period of various plants. Classic manifestations of allergic conjunctivitis are "hail tears", "feeling of sand" in the eyes, burning and photophobia. Food allergy in children is most often manifested in the form of diathesis. Symptoms from the respiratory tract can be caused not only by aeroallergens, but also by infections (acute respiratory infections, SARS, pneumocystosis, chlamydia, neisseria, etc.), which can cause the development of bronchial asthma of infectious-allergic origin. To prevent the development of such serious complications, it is necessary to be regularly examined for the presence of hidden infections that are transmitted sexually [10,11].

Quincke's edema – one of the manifestations of drug allergy. This is a severe reaction that differs from urticaria in that it affects the deeper layers of the skin. The worst option for the development of an allergic reaction is anaphylactic shock (from the Greek *ana* - reverse and *philaxis* - protection). This sharp and severe form of allergic reaction most often occurs in response to medication or insect bites, usually bees or wasps. With anaphylactic shock, a sudden state of itching occurs, which is immediately followed by difficulty breathing and shock (caused by a sharp drop in blood pressure), weak pulse, pallor and profuse sweating (sometimes reddening of the skin is observed) [10].

Treatment of allergies

The best way to treat an allergy is to find out its cause and, if possible, avoid contact with this allergen. To determine the cause of the allergy, a person needs to consult a dermatologist or an allergist. If it is not possible to identify the cause of the allergy, a symptomatic treatment can be chosen [9].

Allergy symptoms are caused by the release of a chemical called histamine (one of the mediators of inflammation), and antihistamine drugs are an effective method of allergy treatment. Until now, there is no single method of treatment that completely cures allergies, so the fight against allergic diseases consists either in suppressing the immune response itself, or in neutralizing substances that are formed during allergies and cause inflammation. However, with proper allergy treatment, its manifestations can be minimized. The most promising method of allergy treatment is specific immunotherapy with allergens. Currently, there are many terms that denote this method of treatment - specific immunotherapy (SIT), allergen-specific immunotherapy (ASIT), specific desensitization, specific hyposensitization, immunotherapy with allergens, allergy vaccination therapy, allergy vaccination. Patients often refer to SIT as "allergy shots" or "allergen treatment." For this, a person is injected with more concentrated solutions of the allergen for several weeks. Such a gradual introduction forces the body to produce something like an antidote. Do not try to self-diagnose or treat any allergy. In the case of skin manifestations of allergies, asthma, chronic bronchitis and emphysema, the diagnosis and treatment should be made and prescribed by a doctor [1,4].

1.2. Dosage forms for children and features of their technology

Dosage forms for children (DFC) include medicinal products in the age-appropriate dosage, which have a corrected taste, the necessary effectiveness of action and convenient use of the package. The production of DFC in the developed countries of the world is carried out by dozens of companies, and their nomenclature in the pharmaceutical practice of individual countries reaches hundreds of items. France (55 companies produce 102 drugs), the USA, England, and Germany take the leading places in the production of DFC in the world. In France, there is a specialized department that produces medicines for infants [13].

The problem of creating a DFC, put forward by the World Health Organization (WHO), is relevant and timely, because the peculiarities of the physiological and biochemical processes of a child's body indicate that half the dose of drugs prescribed for an adult cannot be adequate for a child. Thus, it is unacceptable to recommend taking medicines with teaspoons or 1/4 of a tablet [9].

A human embryo contains 94.5% water, an infant – 74.7%, and an adult – 61.5% on average. A newborn makes 40-60 respiratory movements per minute, an adult - 15-18; pulse in a newborn is 140, in an adult 70–80; the complete circulation of blood in a newborn is 12 s, and in an adult - 22 s. Differences in tissue hydration, breathing rate, heartbeat, and others give reason to assume unequal distribution of medicinal substances, especially water-soluble ones, in the body of an adult and a child. In addition, the child's body is characterized by incomplete development or even the absence of a number of enzyme systems that play an important role in the biotransformation of medicinal substances, a different level of their adsorption, metabolism and excretion [19].

Children are very sensitive to sulfonamides, prone to allergic reactions, convulsions, very poorly tolerate pain, very bright light and bitter. Pain for a child is a severe neuropsychological injury that minimizes the pharmacotherapeutic effect of drugs [20].

Requirements for dosage forms developed for children:

- the medical form for children is selected taking into account the age of the child;

- most drugs are developed for internal use;

- mainly liquid forms are recommended for preschool children (syrups, solutions, suspensions, elixirs, rinses, emulsions, soluble tablets, granules for further dissolution) [13,20].

For school-aged children, in addition to the above-mentioned dosage forms, tablets, dragees, capsules, granules, rectal dosage forms in age-appropriate dosages are also being developed.Medicines in the form of tablets or dragees should not be given to children under 3 years of age, especially tasty and brightly colored, attractive ones that resemble confectionery. All dosage forms for newborns and children of the first year of life are produced sterile. Limits of the quantitative content of microorganisms are set by the Ministry of Health. They have their own features and special designations that distinguish them from similar forms for adults in terms of the quantitative content of biologically active substances, the form of release, color, packaging and other parameters [9].

When creating DFC, only harmless auxiliary substances are used, mainly natural products. Their number should be justified, which optimally ensures the necessary therapeutic effect and stability of the medicine. For coloring, harmless dyes approved for medical practice should be used. Corrective substances should give the medicine a pleasant taste and smell and do not reduce its activity and stability, but it should contain as few different chemicals as possible [19].

The volume of the liquid containing the medicine in the package should not be too large - 2.5–10 ml is sufficient, i.e. the amount of the drug for the minimum course of treatment. It is also necessary to create a DFC of prolonged action [20].

In case of incompatibility or unsatisfactory compatibility of ingredients, so-called "mix" packages are created. Medicinal substances in them are stored separately from the corrigent solution and are mixed immediately before use. In

addition, concentrates are created from powders and granules to which water is added before use [9,19].

For accurate dosing of medicinal products, special dosing devices should be used (dosing spoons, beakers, droppers, pipettes, etc.). The medication package must have a protective device that allows it to be opened only by adults. For solutions containing potent substances, it is recommended to add drops that are added in a package with a special dosing device [19,20].

When developing tablets and dragees for children, one should strive for their smallest size (from 3-4 mm in diameter and below) and a biconvex shape [9].

Among medicines for children, oral dosage forms with an improved taste are most widely represented (syrups, suspensions, emulsions, drops, granules, powders and briquettes for dissolution); no less important are rectal dosage forms (suppositories, micro-enemas, rectal ointments and capsules), as well as solid dosage forms: tablets (including enteric-dissolving, chewable and effervescent), dragees, capsules, lozenges, powders in starch capsules, etc.); the rest, approximately 2–3, are injection forms and products for external use (ointments, creams, pastes, powders, ear drops) [20].

The creation of oral medicines for children requires, in comparison with others, a higher content of fillers, taste and smell correctors, preservatives, stabilizers, solubilizers, coagulants, etc. Therefore, children's drugs intended for internal use should be considered as a complex therapeutic system, the components of which determine the rate and completeness of absorption of medicinal substances, potentiation and synergism of action, retention time in the blood, their transport to target organs and cells, as well as the way of elimination from body [9].

Faster absorption of medicinal substances from the stomach and intestines of children is due to greater permeability of cell membranes, intensive blood circulation, less influence of hydrochloric acid and enzymes [9,19].

Absorption of drugs from the stomach in children occurs by passive diffusion and depends on the acidity of gastric juice, which changes depending on

age. In children under one month, the pH of gastric juice is about 5.8; in children under one year - 4.5; in more older children - 3.0-2.5; in adults - 1.5-1.8. Therefore, the main efforts of researchers are directed to the development of special oral preparations with improved taste and to the creation of dosage forms - substitutes for injections [19,20].

Depending on the aggregate state, dosage forms for children can be divided into 3 main groups: liquid, solid and gaseous. Liquid dosage forms make up 70% of the total amount of DFC produced. They provide a high speed of absorption, the possibility of varying the dose, convenience and ease of use. However, in liquid medicines intended for oral administration, the taste and smell of medicines are more pronounced, which are the cause of some serious complications during treatment. The pleasant smell, taste and appearance of medicines have a beneficial effect on the child's nervous system and the body as a whole. The creation of so-called "tasty" medicines in pediatrics is achieved by correction [13,20].

Adjustment is a change in the mixture of sensations of taste, smell, touch, appearance, which in combination is called the perception of a substance. Adjustments can be made in several directions, the most recognized and promising of which is the use of corrective substances [19].

Corrigents should give medicines a pleasant taste, smell and color; mix well with medicines, do not reduce their activity, and stability; to be indifferent or useful substances for the body; be stable in a certain pH range, resistant to light [13].

Taste is a complex set of sensations determined by the physical and chemical properties of substances, the conditions of its reception and the general state of the body. Medicines with a sweet taste are preferred by 73% of children, slightly sweet by 38% and sweetish by 31% [9].

The most favorable temperature for the manifestation of taste sensations is in the range of 30-35 °C. More cold and hotter worsens the occurrence and perception of taste sensations [9].

The four main groups of taste - sour, sweet, salty and bitter are complemented by the influence of temperature and tactile receptors [20].

By increasing the viscosity, it is possible to improve the taste, due to which the macromolecules of the medium prevent direct contact of the medicinal substance with the taste receptors [19].

Sucrose, which in some cases also acts as a preservative and solubilizer, has often been used as a corrective drug until now. However, having a low sweetness potential, it is added to dosage forms in large quantities. So, in order to mask the bitter taste of diphenhydramine, it is necessary to use 50-100 times more sucrose in relation to it [20].

Currently, domestic pharmacy uses fructose, maltose, lactose, invert sugar, citric acid, glycerin, and saccharol (developed at the National Agricultural Research and Development Institute) as correctives; abroad are widely used dulcin, saccharin, sorbitol, natural and artificial honey, carboxymethyl cellulose, mannitol, as well as artificial sweeteners cyclomates (sodium and calcium salts of cyclohexylsulfamic acid), with a sweetness index 30 times higher than sugar [13,19].

Various fruit syrups have the widest spectrum of action: cherry, raspberry, black currant, orange, cocoa syrup, etc. To adjust the salty and intensely sweet taste, various fruit essences, essential oils, citrus extracts, vanillin, etc. are often added to syrups. Syrups, mucus, aromatic substances are added to oily medicines to mask an unpleasant sensation. In addition to the above-mentioned corrigents, DFC also include thickeners - sodium alginate, agar, agaroid, pectins; preservatives - ethyl alcohol, benzoic acid and sodium benzoate, benzalkonium chloride, etc.; Among the dyes, amaranth, tartrazine, carmine, saffron, indigo, carotene, pigments of resinous substances are used [9].

Many researchers call various shades of yellow and red the optimal color of DFC. Excipients used for DFC should be harmless, mostly natural products. The number of them, including carbohydrates [19,20].

CONCLUSIONS TO CHAPTER 1

1. Based on the analysis of the literature, it was found that today allergic pathology is one of the six most common human diseases, and there is every reason to believe that the problem of allergic diseases in Ukraine is important not only medically, but also socially.

2. Dosage forms for children and features of their technology have been characterized .

CHAPTER 2
RESEARCH OBJECTS AND METHODS

2.1. Characteristics of research objects

KNAUTIA ARVENSIS, synonym – SCABIOSA ARVENSIS

A perennial herbaceous plant of the Caprifoliaceae family. It has a multi-headed rhizome that develops a wintering rosette of leaves in autumn. The stem is grooved, erect, 20-70 cm tall, simple or branched in the upper part, whitish from short pubescence and, in addition, with longer rough hairs. The leaves are opposite, lanceolate, rough-haired; basal and lower stem leaves are petiolate, oblong-lanceolate or pinnately incised, with a larger upper lobe, toothed at the edges, upper stem leaves are oddly pinnate, with whole or toothed lobes, short-petiolate or sessile, rarely entire leaves [34,36].

The flowers are bisexual, irregular, in flattened hemispherical heads, surrounded by a wrapper of lanceolate pointed, ciliated leaves on the edge; the calyx consists of small sepals of unequal size, arranged in two rings (at the base and at the top of the ovary); corolla is funnel-shaped, 4-lobed (blades are elongated egg-shaped, slightly narrowed to the tip), larger and more irregular in the head of the outer flowers. The fruit is an achene. Blooms from June to September [34,36].

Prevalence

Knautia arvensis grows throughout Ukraine, except for the southern regions of the Kherson region and the northern regions of the Crimean region, in fields, meadows and among shrubs [34,36].

Procurement and storage

For the manufacture of medicines, the grass of field scabious is used, which is harvested during the flowering of the plant. Dry under shelter in the open air [34,36].

Chemical composition

Contains iridoids, saponins, tannins and bitter substances, carotene (up to 140 mg% in fresh leaves) and sugars [34,36].

Pharmacological properties and use

The infusion promotes the removal of toxic metabolic products from the body (both those formed during normal metabolic processes and those formed during painful changes in various organs), has an expectorant, antiseptic, anti-inflammatory and dermotonic effect. It is taken internally for cough, bronchitis, inflammation of the bladder, in the case of chronic, protracted allergic dermatitis, fissures of the anus, and as a remedy for itching. When used externally, a strong infusion of field scabious is considered an effective remedy for various skin diseases, in particular, scabies [34,36].

URTICA URENS

A monoecious annual herb, covered with stinging hairs, a plant of the Urticaceae family. The stem is erect, four-sided, 15-60 cm tall. The leaves are opposite, whole, elliptic or ovate, sharp, sharp-toothed along the edge, 4-5 cm long. The flowers are light green, small, unisexual, collected in interrupted axillary panicles (inflorescences are no longer than the petioles of the leaves in the axils of which they are contained); perianth is four-parted, fruit is an achene. Blooms in May – September [34,36].

Prevalence

Urtica urens grows throughout the territory of Ukraine on the banks of rivers, as a weed in gardens, in gardens, near homes, among bushes [34,36].

Procurement and storage

Nettle leaves (Folia Urticae urensis) used for treatment, are collected during the flowering of the plant, separating it from the stem, and dried necessarily in the

shade, as quickly as possible. Drying is stopped when the central veins become brittle. 22-23% of dry raw material is obtained. Shelf life - 2 years [34,36].

Chemical composition

Contains vitamins: phylloquinone (vitamin K1) - 0.2%, carotenoids - up to 50 mg%: β-carotene - up to 60%, hydroxy-α-carotene, luteoxanthin, lutein-epoxide, violaxanthin, xanthophyll, xanthophyll-epoxide; ascorbic acid (vitamin C) - 0.6%, thiamine (vitamin B1), riboflavin (vitamin B2), pantothenic acid (vitamin B3), tocopherols (vitamin E), nicotinic acid (vitamin PP); chlorophyll - 5%, carbohydrates: starch - 10%, gums; organic acids: oxalic, succinic, fumaric, lactic, citric, henna, formic, silicic, butyric, glycolic, glycerol; phenolic acids: gallic, n-coumaric, caffeic, ferulic in the hydrolyzate; coumarins: ellagic acid; flavonoids: quercetin in the hydrolyzate; tannins - 3.1%; nitrogen-containing compounds: alkaloids - 0.019–0.29%, acetylcholine, histamine, 5-hydroxytryptamine; glycoside urticin, essential oil: methylheptenol, acetophenone; steroids: sitosterol, porphyrins; macro- and microelements: Si, Fe, Cu, Mn, B, Ti, Ni [34,36].

Pharmacological properties and use

Leaf infusion is used as a hemostatic (for pulmonary, intestinal, uterine, hemorrhoidal and other bleeding), diuretic (for edema) and tonic. The use of infusion is also indicated for nervous disorders, rheumatism, allergies and anemia, for habitual constipation, dyspepsia and gastric colic. The plant is widely used in dermatology and cosmetics: internally - for eczema, itching, urticaria; locally - with seborrhea of the head, circular or nested baldness, hair loss. Nettle is also valued as a food product [34,36].

Apple pectin

Natural polysaccharide, the main structural component of which is methoxylated D-galacturonic acid, which is a finely ground powder without extraneous impurities from light gray to cream in color with a slightly sour taste of apple. The presence of a fibrous fraction of pectin in the form of flakes is allowed. The degree of grinding is below 0.35 mm. Mass fraction of moisture not more than

10%, pH of 1% solution is 3, degree of esterification not less than 70%, mass fraction of nitrates in terms of NO_3^- ion not more than 0.18%, mass fraction of fibrous fraction particles larger than 0.5 mm in size. no more than 20%, density – 1.24 g/cm3, thermal conductivity at 50°C – W/m·k, compacted layer – 0.13, loose layer – 0.06, ignition temperature – 257ºC; electrified to humidity – 8% [38,39,40].

Xylitol

Hygroscopic crystals with a sweet taste, soluble in water, alcohol, glycols, acetic acid and pyridine [38,39,40].

Sucrose

Crushed crystals of white refined sugar, no larger than 0.1 mm. Soluble in water and ethanol, slightly soluble in methanol, insoluble in diethyl ether [38,39,40].

Fructose

In aqueous solutions, fructose exists as a mixture of tautomers, in which β, - D- fructopyranose predominates and contains, at 20 °C, about 20% β - D- fructofuranose and about 5%- D- fructofuranose: From aqueous solutions of D- fructose crystallizes in the pyranose form (D - fructopyranose) - in colorless crystals, well soluble in water, at low temperatures - in the form of mono- and hemihydrates, above 21.4 °C - in the anhydrous form. Fructose is unstable in both alkaline and acidic solutions; decomposes under the conditions of acid hydrolysis of polysaccharides or glycosides [38,39,40].

Glucose

White crystalline powder with a sweet taste. Easily soluble in water R, slightly soluble in 96% ethanol R [38,39,40].

Citric acid

White crystalline substance, melting point 153°C, well soluble in water, soluble in ethanol, slightly soluble in diethyl ether [38,39,40].

Sodium benzoate

White crystalline powder without odor or with a faint odor, sweet-salty taste, easily soluble in water (1 : 2) and glycerol (1 : 9), relatively soluble in ethanol (1: 45)[38,39,40].

2.2. Characteristics of research methods

The appearance of the objects of research and syrup was determined by organoleptic indicators: color, transparency of the solution, smell, taste [38,39,40].

Transparency of the solution. A test tube made of colorless transparent neutral glass with a flat bottom, having an inner diameter of 15 to 25 mm, was used. The determination was made in diffused daylight, viewing along the vertical axis on a black background (SPU, ed. 1, 2.2.1, p. 15) [38,39,40].

Color. It was determined visually by comparing the color of the studied samples with purified water. The comparison was carried out in the same test tubes made of colorless transparent glass in diffused daylight, viewing the samples horizontally on a white background (SPU, ed. 1, 2.2.2, pp. 15-17) [38,39,40].

The pH value was determined by the potentiometric method using a pH-meter of the pH-340 type (SPU, ed. 1, 2.2.3, p. 17) [38,39,40].

The corrective potential of the sweetening substances in the studied syrup was studied using the method of O.I. Tentsova. Two groups of tasters (selected as experts), observing all the rules of tasting, evaluated the taste of dosage forms with and without a corrector. The first group of tasters evaluated the taste according to the emotional feeling on a 5-point scale: very pleasant - 5; pleasant - 4; good – 3; bad – 2; very bad - 1. The second group of tasters conducted an organoleptic evaluation of the main taste of the same samples also according to a 5-point system: not bitter - 5; not very bitter - 4; slightly bitter - 3; bitter - 2; very bitter - 1. The evaluation data of both groups are compiled in a general table and a numerical index of the main taste is derived. Indices are derived as the arithmetic mean value of all indicators. The higher the taste index, the higher is the corrective potential of sweetening agents. Double assessment of the correcting potentials of masking

substances ensures the objectivity and reliability of the method. The bitter, burning taste of the aqueous extract was masked with the help of sweeteners, which were chosen by determining the corrective potential of the main taste and taste sensations in relation to the taste of the aqueous extract, taken as a standard of bitter taste [7,8].

The method of taste assessing using letter and number indices (by I. A. Yegorov). In order to express the data of the organoleptic evaluation of the drug in more objective and comparable indicators, the so-called "taste formula" was proposed. Its essence is that the most important qualitative characteristics of the drug are evaluated by letter and numerical indexes that make up the "taste panel", which later makes it possible to write down the general formula of the taste of these drugs. The oral cavity is rinsed with purified water, the test substance is applied to the appropriate area of the tongue with a glass stick, and taste sensations are recorded (no more than 30 seconds). At the same time, the substance should not fall on other areas of the tongue, and the number of tasting samples and the order of their analysis should not cause fatigue. The researcher must rinse his mouth before and after the test. The taste of the dosage form is determined at a temperature of 20-30°C. The sample dosage form should not be swallowed [7,8].

The table presents a taste map of shades of taste, in which "not bitter", "not sour", not salty", and "not sweet" are indicated by index 1 and correspond to the taste of water. Index 2 indicates slightly bitter, slightly sour, slightly salty and slightly sweet taste. This shade indicates a barely perceptible taste and corresponds to the threshold concentration: G2 - 0.0002% aqueous solution of quinine hydrochloride; K2 - 0.02% aqueous solution of citric acid; C2 - 0.1% aqueous solution of sodium chloride and O2 - 0.38% sucrose solution. The bitter, sour, salty and sweet taste is marked by index 3, which corresponds to the normal taste that a person is used to in everyday life. It is well felt, does not cause negative emotions, and is pronounced. It is marked by index 4 strong taste effect:

very bitter, very sour, very salty, very sweet (sweet). The specified taste exceeds our concepts of taste, for example, in relation to food - it is oversalted, sweet - mawkish, burning, disgusting. Such a taste causes unpleasant sensations in the mouth [7,8].

Statistical processing of research results

Statistical processing of research results was carried out according to the methodology given in the section "Statistical analysis"[38,39,40].

CONCLUSIONS TO CHAPTER 2

1. A brief description of the dry extracts of Knautia arvensis and Urticae urens and auxiliary substances that were used in the development and research of the antiallergic syrup is given.

2. Methods of physico-chemical, pharmaco-technological and microbiological research have been determinated, which made it possible to develop the composition and technology of the syrup and standardize this dosage form.

CHAPTER 3
EXPERIMENTAL PART
DEVELOPMENT OF COMPOSITION AND TECHNOLOGY OF ANTI-ALLERGIC SYRUP

3.1. Market analysis of drugs for the treatment of allergies

In the treatment of allergic diseases, an important place is occupied by antihistamine drugs (AHD) [41,42,43].

The information base of the research was the data of the SE "State Expert Center of the Ministry of Health of Ukraine", data of the audit of the retail segment of the pharmaceutical market of the "Pharmstandard" system of the "Morion" company [41].

As of October 10, 2023, 128 medicinal products of group R06A "Antihistamines for systemic use" were registered in Ukraine. During the year, the number of registered antiallergic antihistamine drugs constantly fluctuates, while registered drugs are not always presented on the market [42].

Therefore, the analysis of the market of offers was carried out taking into account the data of the marketing research company "Morion", regarding the actual volumes of consumption. During 2022, 157 MPs with anti-allergic action were presented on the pharmaceutical market of Ukraine (taking into account different dosage forms, dosages, number of doses in a package and types of packaging) [41,43].

All three generations of antihistamines are available on the market. The data are given in table 3.1

Table 3.1

Classification of antihistamine drugs

Antihistamines of the I generation	Antihistamines of the II generation	Antihistamines of the III generation
Azelastine Alimemazin	Akrivastin Astemizole	Desloratadine Levocetirizine

Antihistamines of the I generation	Antihistamines of the II generation	Antihistamines of the III generation
Antazolin Dexchlorpheniramine Dimenhydrinate Dimetinden Diphenhydramine Diphenylpyraline Quifenadine Clemastine Mebhydrolin Meclozin Mepyramine Oxomemazine Pyrilamine Promethazine Trimerazine Pheniramine Chloropyramine Chlorpheniramine Cyclizine Cyproheptadine	Ebastine Epinastine Levocabastin Loratadine Mizolastine Oxatomid Terfenadine Cetirizine	Fexofenadine

I generation drugs are also called sedative (by the dominant side effect), in contrast to non-sedative drugs of the II generation. The III generation includes fundamentally new drugs - active metabolites of drugs of the II generation and therapeutically active enantiomers (chirally pure molecules), which exhibit the highest antihistamine activity and at the same time are devoid of the sedative effect and cardiotoxic effect inherent in drugs of the II generation [42,43].

The modern pharmaceutical market of Ukraine for drugs for the treatment of allergic diseases is mainly represented by foreign manufacturers - 66% and only 34% of the entire assortment consists of drugs of domestic production. The data are shown in the figure 3.1.

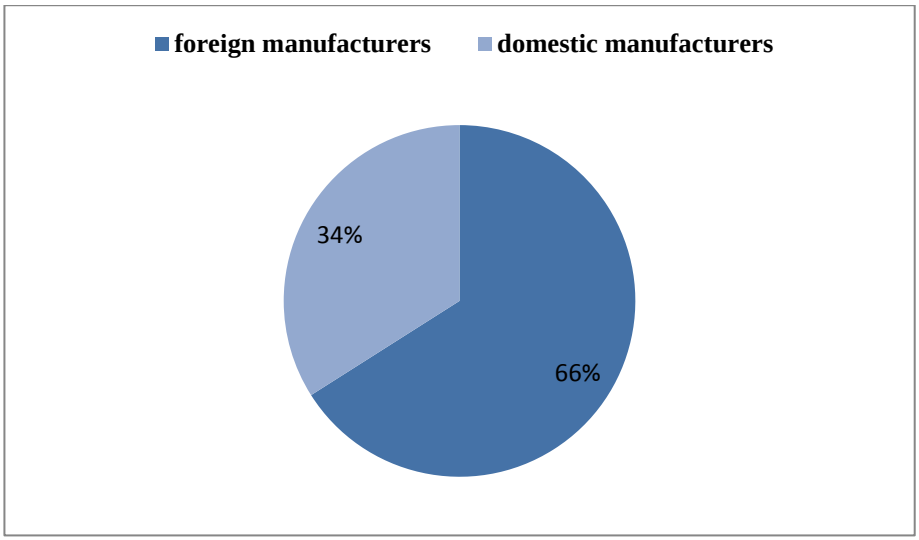

Figure 3.1. Diagram of the ratio of anti-allergic drugs depending on the manufacturer

Therefore, the first task of modern medicine and pharmacy is to increase the assortment of domestic drugs for the treatment of a given pathology. The range of allergy products is made up of 24 foreign and 22 domestic manufacturers. The supply leaders are companies from Germany, Belgium, India and Poland (Figure 3.2) [42,43].

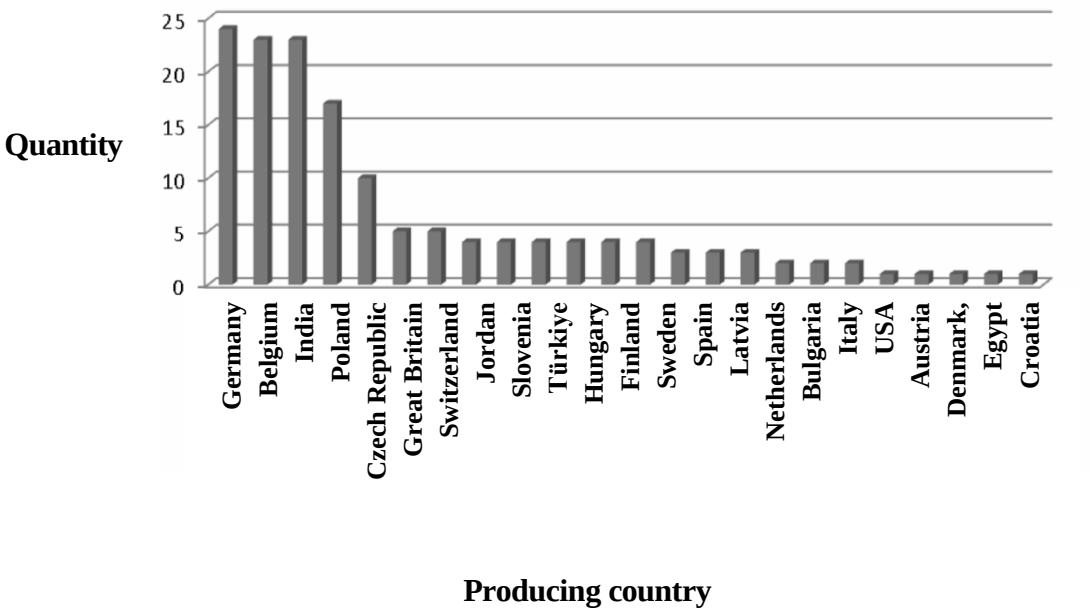

Figure 3.2 Foreign countries producing anti-allergic drugs

Thus, on the domestic market of pharmaceuticals used for the treatment of allergic diseases, there is a high negative dependence on imports [41].

Pharmaceutical forms of antihistamines can be divided into three groups: solid, liquid and semisolid. Solid medicinal forms include tablets, capsules, dragees and rectal suppositories, and liquid forms include solutions for injections, syrups, suspensions, drops, as well as eye drops. The largest number of drugs is produced in a solid dosage form. Semisolid dosage forms are represented by ointments, gels, creams. Liquid dosage forms are mainly represented by solutions for injections and syrups. Syrups are used in pediatrics, which is related to the possibility of their use in younger children. The results of the marketing analysis showed that the market is dominated by solid medicinal forms, which occupy 38.67%, semisolid– 24.67%, liquid – 15.33%, and pressurized drugs – 21.33%. The data are presented in Figure 3.3[41,42,43].

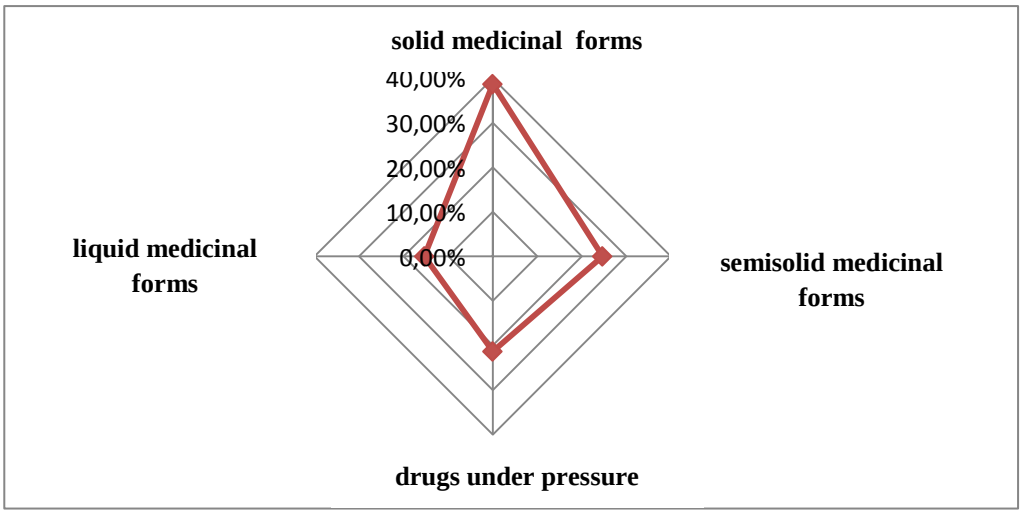

Figure 3.3. Distribution of antihistamine drugs by dosage form.

Among antiallergic drugs, herbal drugs account for 8.2%, and synthetic drugs account for 91.8%, respectively (Figure 3.4) [42,43].

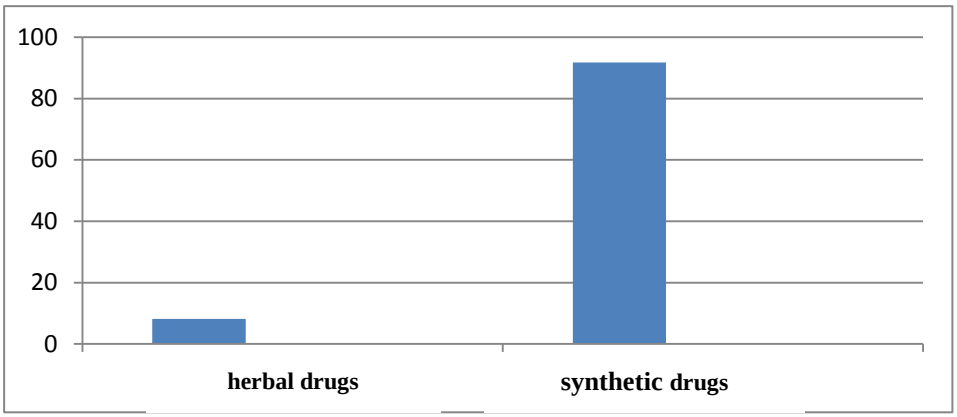

Figure 3.4. Distribution of antiallergic agents by origin

The majority of drugs that are approved for allergy treatment are monocomponent (75%), and multicomponent - 25% among registered drugs. Data are indicated in Figure 3.5 [41,43].

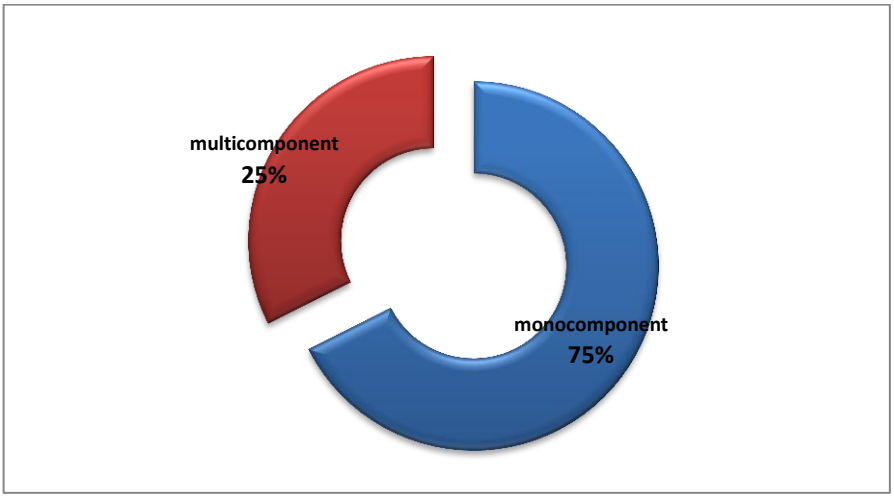

Figure 3.5. Distribution of drugs for the treatment of allergies according to their components

It was established that the drugs of the studied group are represented mainly by synthetic drugs of imported production, therefore the development of domestic drugs in the form of syrup with components of natural origin is currently an urgent problem of both medicine and pharmacy [41,42,43].

3.2. Justification of the amount of active and auxiliary substances in the composition of the syrup

Taking into account the fact that the dosage of the proposed medicinal syrup is assumed to be teaspoons (5 ml) or table spoons (15 ml) three times a day (depending on the age of the patient), it is advisable to use dry extracts of Knautia arvensis and Urtica urens in the amount of 1%.The selected concentrations of active substances are within permissible therapeutic limits and should be used for therapeutic and preventive purposes [21,23,25].

When creating medicinal forms for children, only harmless excipients should be used. Their number should be justified to ensure the optimal therapeutic effect and stability of drugs. Corrective substances should give the medicine a pleasant taste and smell and not reduce its activity and stability [7].

Currently, domestic pharmacy uses: fructose, glucose, sucrose, xylitol, sorbitol, natural and artificial honey as correctives. The composition of children's dosage forms, in addition to the above-mentioned corrigents, also includes thickeners - sodium alginate, agar, agaroid, pectins [8].

Corrigents and thickeners provide the necessary viscosity and are able to mask unpleasant organoleptic characteristics of active pharmaceutical ingredients (API) [7,8].

At the first stage, we produced samples of syrups in which fructose, glucose, sucrose and their combinations, as well as xylitol, were used as correctors. Apple pectin in a concentration of -1% was chosen as a thickener.

The test samples were examined according to the following indicators:

- appearance;
- transparency;
- viscosity;
- relative density;
- fluidity [16,28,29].

The results of the research are given in table 3.2

Thus, summarizing the above, it can be concluded that only one sample obtained using xylitol at a concentration of 54% does not withstand the test. Therefore, this sample was not used in further research [7,29].

Table 3.2

Physical and physicochemical studies of syrup samples

The content of auxiliary substances in 100 g of syrup	**Appearance**	**Transparency**	**Viscosity,Pa·s**	**Fluidity**	**Relative density, g /cm^3**
Sucrose 54.0 Apple pectin 1.0	Viscous brown liquid	Transparent	1.44±0.03	+	1.3±0.02
Glucose 54.0 Apple pectin 1.0	-//-	-//-	1.40±0.03	+	1.30±0.04
Fructose 54.0 Apple pectin 1.0	-//-	-//-	1.32±0.02	+	1.27±0.03
Sucrose Glucose at 27.0 Apple pectin 1.0	-//-	-//-	1.36±0.02	+	1.30±0.03
Glucose Fructose at 27.0 Apple pectin 1.0	-//-	-//-	1.48±0.03	+	1.38±0.02
Xylitol 54.0 Apple pectin 1.0	Gel-like brown mass	-//-	1.60±0.03	-	1.28±0.04

3.3. Study of the masking potential of individual taste corrigents in the drug being developed

Taste is a complex set of sensations determined by the physical and chemical properties of a substance, the conditions of its reception and the general state of the body. Any aftertaste arises as a total perception based on taste, touch, temperature and smell sensations. Organoleptic evaluation of drug samples was carried out using the methods of A.I. Tentsova and I.A. Egorov. The results of the research are given in the table 3.3.

To improve the taste properties of the processed product, citric acid monohydrate was added [7,8].

The selection of its required amount was carried out by evaluating the main taste of the obtained samples (table 3.4).

The data in Table 3.3 show that the anti-allergic syrup with dry extracts of Knautia arvensis and Urtica urens based on glucose and fructose 27.0 each, apple pectin 1% and citric acid 0,15% has the taste formula - K1 O3 (non-sour, sweet).

Table 3.3

Study of the organoleptic characteristics of the developed syrup

Corrigent content in 100 g of syrup	Main taste	Taste (evaluation of emotional sensations)	The flavor formula
Sucrose 54.0 Apple pectin 1.0	2.32±0.11	2.20±0.22	K2 O2(slightly sour, slightly sweet)
Glucose 54.0 Apple pectin 1,0	2.82±0.24	2.33±0.14	K2O3 (slightly acidic sweet)
Fructose 54.0 Apple pectin 1.0	4.30±0.06	4.20±0.21	K2O3 (slightly acidic sweet)
Sucrose Glucose at 27.0 Apple pectin 1.0	3.53±0.15	4.11±0.17	K2O2 (slightly sour, slightly sweet)
Glucose Fructose at 27.0 Apple pectin 1.0	4.64±0.12	4.520±0.23	K1O3 (non-acidic, sweet)

Table 3.4

The influence of different concentrations of citric acid on taste sensations

Concentration of citric acid, %	The value of the numerical index, points	
	sense of taste	sense of basic taste
0	4.5	4.6
0.1	4.6	4.7
0.15	4.8	4.9
0.2	4.7	4.7
0.25	4.7	4.7

As can be seen from the data in table 3.4, syrups with 0.15% citric acid content had the highest taste index, further increasing its concentration (0.2-0.25%) is impractical.

To give the syrups a pleasant smell, which has a positive effect on the general perception of patients, a fruit food flavoring was selected (table 3.5).

Table 3.5

Results of evaluating the influence of fruit essences on the taste of syrups

Name and amount of flavorings in the composition of the syrup, 0.1 %	The average score of the objective sensations of the syrup
Apricot essence	4.3
Barberry essence	4.5
Pear essence	4.8

The syrup with pear essence was found to have the highest score (4.8), so this particular flavoring was selected for taste adjustment [7,8].

Based on the results of the conducted experiments, the following composition of the antiallergic syrup was chosen for further research.

Syrup composition:

Dry extract of Knautia arvensis –1.0 g

Dry extract of Urtica urens –1.0 g

Glucose –27.0 g

Fructose – 27.0 g

Apple pectin – 1.0 g

Citric acid –0.15 g

Sodium benzoate –0.2 g

Pear essence –0.1 g

Water purified up to 100 ml

3.4. Development of syrup manufacturing technology

The process of obtaining the developed syrup consists of a set of sequentially implemented stages. The main stages of syrup manufacture include: production preparation (sanitary preparation of premises, equipment, personnel), preparation of raw materials, materials, solvents, packaging, labeling, packing and unloading.

Stage 1. Preparation of substances

All active and auxiliary substances are weighed on scales and measured using measuring devices.

Stage 2. Preparation of glucose and fructose solution

In the reactor (P-1), glucose and fructose are dissolved in heated purified water, apple pectin until completely dissolved, after cooling, citric acid is added.

Stage 3. Preparation of syrup

The contents of reactor (P-1) are transferred to reactor (P-2), dry extracts of Knautia arvensis and Urtica urens, sodium benzoate are added while stirring until complete dissolution, then pear essence is added and brought to the mark with water.

Stage 4. Packing syrup into bottles

Filling, packing, labeling operations are carried out on an automatic line, which consists of the following equipment :

- filling and packaging machine;
- automatic visual control;
- labeling machine;
- packing table;
- conveyor for vials testing ;
- conveyor for moving finished products.

Stage 5. Packing vials with syrup into bundles

Each vial, together with instructions and a spoon with a dispenser, is packed in a cardboard pack.

Stage 6. Packing of bundles in boxes

Bundles with vials are placed in boxes by hand on the packing table. 50 packs of vials are placed in each box. The boxes are turned and pasted with adhesive tape on a paper base. Next, the products are sent to the quarantine warehouse, where the controller of the quality control department selects an average sample for analysis from the finished batch of products. Product quality control is carried out, and based on the result, the batch is sent to the finished product warehouse.

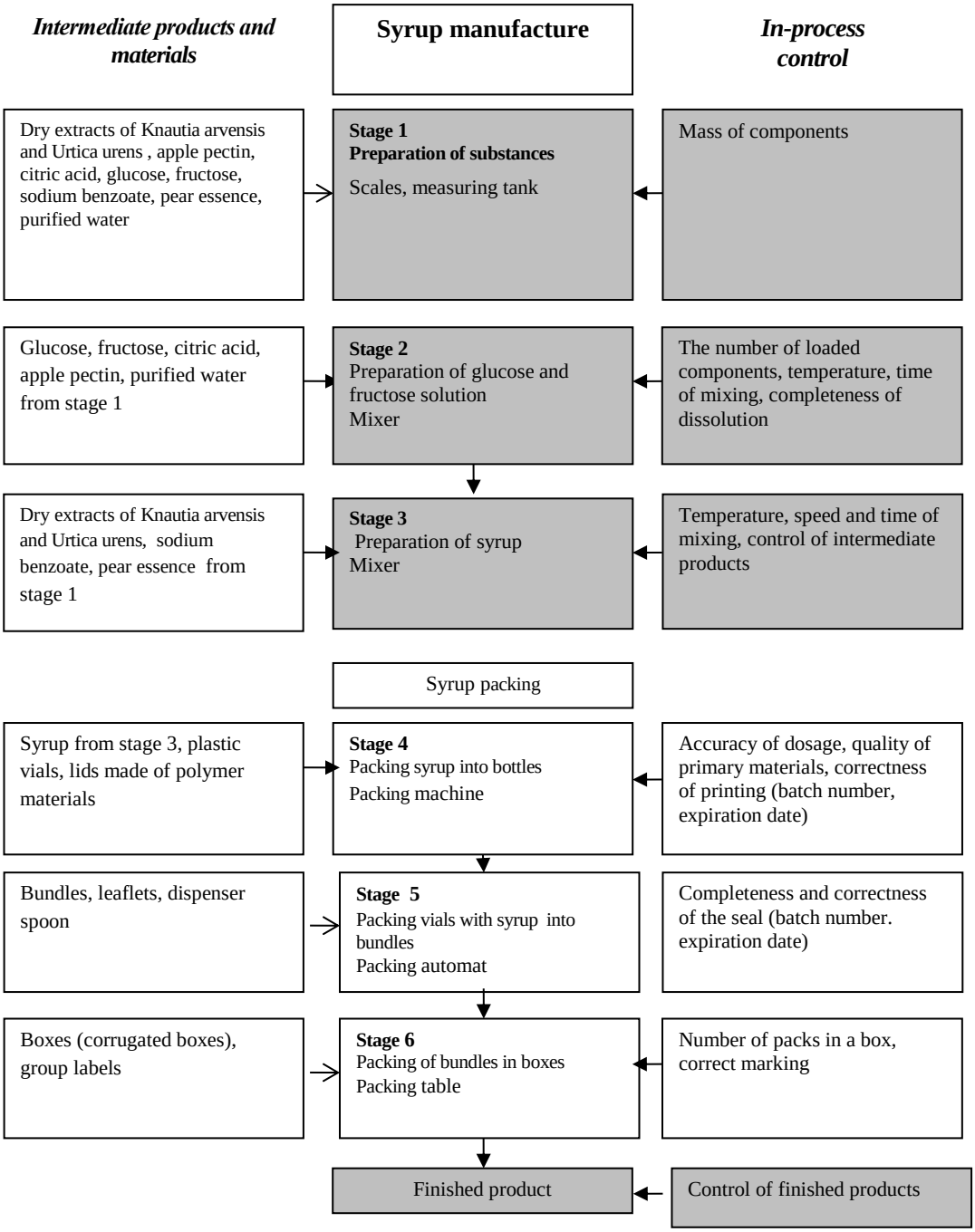

Figure 3.6. Technological scheme for the manufacture of syrup

CONCLUSIONS TO CHAPTER 3

1. Based on the analysis of the literature, it was found that allergic pathology is one of the six most common human diseases today, and there is every reason to believe that the problem of allergic diseases in Ukraine has not only medical, but also social significance.

2. Studies of the domestic pharmaceutical market of antiallergic drugs showed that 66% of registered drugs are foreign-made and only 34% are domestic. These medicinal products are represented by 24 foreign and 22 domestic manufacturers. It was determined that the leaders of supply are the firms of Germany, Belgium, India and Poland.

3. Organoleptic studies have established that syrup based on glucose and fructose has the best taste index.

4. The technological scheme of the industrial production of anti-allergic syrup has been developed.

CONCLUSIONS

1. The conducted studies have proved the feasibility of developing a combined medicinal product in the form of a corrected syrup based on plant raw materials- dry extracts of Knautia arvensis and Urtica urens.

2. On the basis of the conducted research, the composition and technology of an antiallergic syrup based on medicinal plant raw materials for use in pediatrics were substantiated.

3. On the basis of physico-chemical and organoleptic research methods, it was determined that syrup based on glucose and fructose has the best taste index and the optimal amount of each ingredient was determined.

4. On the basis of a complex of physicochemical, technological, and microbiological studies, the optimal composition of the syrup was scientifically substantiated: dry extract of Knautia arvensis – 1.0 g, dry extract of Urtica urens – 1.0 g, glucose – 27.0 g, fructose – 27.0, apple pectin – 1.0 g, citric acid – 0.15 g, sodium benzoate – 0.2 g, pear essence – 0.1 g, purified water up to 100 ml.

5. The technological scheme for the production of syrup, which allows for the production of standardized medicinal products with controlled properties, is substantiated.

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Appendix

Appendix A

МІНІСТЕРСТВО ОХОРОНИ ЗДОРОВ'Я УКРАЇНИ
НАЦІОНАЛЬНИЙ ФАРМАЦЕВТИЧНИЙ УНІВЕРСИТЕТ
КАФЕДРА БІОТЕХНОЛОГІЇ

MINISTRY OF HEALTH OF UKRAINE
NATIONAL UNIVERSITY OF PHARMACY
DEPARTMENT OF BIOTECHNOLOGY

ПРОБЛЕМИ ТА ДОСЯГНЕННЯ СУЧАСНОЇ БІОТЕХНОЛОГІЇ

PROBLEMS AND ACHIEVEMENTS OF MODERN BIOTECHNOLOGY

Матеріали
ІІІ міжнародної науково-практичної
Інтернет-конференції

Materials
of the III International Scientific and Practical
Internet Conference

ХАРКІВ
KHARKIV
2023

УДК 615.1: 615.3: 615.012.6: 57

Електронне видання мережне

С 89 Проблеми та досягнення сучасної біотехнології: матеріали III міжнародної науч.-практ. інтернет-конф. (24 березня 2023 р., м. Харків). – Електрон. дані. – Х. : НФаУ, 2023. – 443 с. – Назва з тит. екрана.

Збірка містить матеріали науково-практичної конференції, тематика якої охоплює такі напрями: фармацевтична та медична біотехнологія, перспективні біологічно активні речовини, харчова біотехнологія, продукти здорового харчування, екологічна біотехнологія, природоохоронні технології, біотехнологія у рослинництві, тваринництві та ветеринарії, сучасні біотехнології для народного господарства, розробка, виробництво, забезпечення та контроль якості лікарських засобів, мікробіологічні дослідження на етапах розробки, виробництва та контролі якості харчових продуктів, ветеринарних та лікарських препаратів, організаційно-економічні аспекти діяльності біотехнологічних та фармацевтичних підприємств у сучасних умовах, маркетингові дослідження у біотехнології та фармації, теорія та практика підготовки здобувачів вищої освіти спеціальності «Біотехнології та біоінженерія».

Для широкого кола науковців, магістрантів, аспірантів, докторантів, співробітників біотехнологічних та фармацевтичних підприємств та фірм, викладачів вищих навчальних закладів наукових і практичних працівників фармації та медицини.

Автори опублікованих матеріалів несуть повну відповідальність за підбір, точність наведених фактів, цитат, економіко-статистичних даних, власних імен та інших відомостей. Матеріали подаються мовою оригіналу.

УДК 615.1: 615.3: 615.012.6: 57

Relevance of the creation of medicinal syrup of anti-allergic action

Hasdo Walid, Kryklyva I.O.
National University of Pharmacy, Kharkov, Ukraine
irinakrikliva@ukr.net

The incidence of allergic diseases in the 21st century has reached epidemic proportions, increasing every 10 years by 2–3 times. Today, allergic pathology is one of the six most common human diseases.

These data indicate that the problem of allergic diseases in Ukraine is not only of medical, but also social importance

It should be noted that the use of pharmaceuticals for the treatment of allergy symptoms should be considered and justified. Active pharmaceutical ingredients that are part of antihistamines have a large number of side effects and are not always safe for the patient's body.

Therefore, especially in our time, extremely relevant is the use of herbal medicines. The variety of conditions that can affect the health of the population determines the relevance of research aimed at creating safer pharmaceuticals for allergies, which will include plant substances.

Therefore, the work aimed to develop the composition and technology of a complex medicinal syrup with antihistamine action based on plant components.

The advantage of it will be the presence of a wide range of pharmacological activities, low toxicity, and the absence of adverse reactions with its prolonged use.

As active pharmaceutical ingredients, we have chosen dry extract of *Knautia arvensis*, which is characteristic of detoxification, antiseptic, anti-inflammatory and dermotonic effects and *Urtica urens*, which cleanses the blood and normalizes the immune system.

Ф А 2.2.1-32-366

National University of Pharmacy

Faculty for foreign citizens' education
Department of Industrial Technology of Drugs
Level of higher education master
Specialty 226 Pharmacy, industrial pharmacy
Educational program Pharmacy

APPROVED
The Head of Department
of Technologies of
Pharmaceutical
Preparations

_____
Olena RUBAN
"_15_" __of May__ 2022

ASSIGNMENT
FOR QUALIFICATION WORK
OF AN APPLICANT FOR HIGHER EDUCATION

Walid HASDO

1. Topic of qualification work: «Development of the composition and technology of antiallergic syrup», supervisor of qualification work: Iryna KRYKLYVA, PhD, assoc. prof.

approved by order of NUPh from "6th" 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: dry extracts of Knautia arvensis and Urtica urens, glucose and fructose, citric acid, pear essence, sodium benzoate.

4. Contents of the settlement and explanatory note (list of questions that need to be developed): literature review, objects and methods, experimental part, references

5. List of graphic material (with exact indication of the required drawings):

tables – 5, pictures – 6

6. Consultants of chapters of qualification work

Chapters	Name, SURNAME, position of consultant	Signature, date	
		assignment was issued	**assignment was received**
1	Iryna KRYKLYVA, professor of higher education institution of department Industrial Technology of Drugs	20.05.2022	20.05.2022
2	Iryna KRYKLYVA, professor of higher education institution of department Industrial Technology of Drugs	15.12.22 - 21.01.2023	15.12.22 - 21.01.2023
3	Iryna KRYKLYVA, professor of higher education institution of department Industrial Technology of Drugs	18.02.2023	18.02.2023

7. Date of issue of the assignment: «15» __May _____2022.

CALENDAR PLAN

№ з/п	**Name of stages of qualification work**	**Deadline for the stages of qualification work**	**Notes**
1.	Literature review	September	**Done**
2.	Experiment planning	October	**Done**
3.	Experiment execution	November-February	**Done**
4.	Processing of results	March- April	**Done**
5.	Submission to EC	April	**Done**

An applicant of higher education _____ Walid HASDO

Supervisor of qualification work _____ Iryna KRYKLYVA

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 5 років 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 заводської технології ліків**				
Хасло Валіа	Розробка складу та технології сиропа протиалергічної дії	Development of the composition and technology of antiallergic syrup	доц. Крикуна І.О.	доцент Маньский О.А.

Підстава: подання в.о. ректора

Ректор

Підп. Секретар

Ф А2.8-47-110

ВИСНОВОК

Комісії з академічної доброчесності про проведену експертизу

щодо академічного плагіату у кваліфікаційній роботі

здобувача вищої освіти

№ 112415 від « 20» квітня 2023 р.

Проаналізувавши випускну кваліфікаційну роботу за магістерським рівнем здобувача вищої освіти денної форми навчання Хасдо Валід, 5 курсу, _____ групи, спеціальності 226 Фармація, промислова фармація, на тему: «Розробка складу та технології сиропа протиалергічної дії / Development of the composition and technology of antiallergic syrup», 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**

1%

29%

Ф А 2.2.1-32-353

REVIEW

for qualification work of the master`s level of higher educftion, specialty 226 Pharmacy, industrial pharmacy

Walid HASDO

on the topic: «Development of the composition and technology of antiallergic syrup».

Relevance of the topic. The frequency of allergic diseases in the 21st century, has reached epidemic proportions, increasing by 2-3 times every decade. Today, allergic pathology is one of the six most common human diseases. According to statistics, every fifth inhabitant of our planet suffers from allergies. The study of the prevalence of allergic diseases is carried out both according to official statistics and with the help of targeted epidemiological studies, which are more reliable. Walid HASDO's qualification work is devoted to the development of a medicinal syrup for the treatment of allergies.

Practical value of conclusions, recommendations and their validity.

Based on the analysis of literature data, the author chose APIs of natural origin and their concentration. By conducting technological research, excipients and the optimal base in the composition of the medicinal syrup were selected. A rational technology for obtaining syrup has been developed, on the basis of which a technological scheme for its production has been drawn up.

Assessment of work. The successful solution of tasks enabled the author of the qualification work to achieve the goal and obtain practical and theoretical results. The work was done at a sufficient scientific level, which indicates the author's ability to work with literary sources, analyze, systematize and generalize the experimental data obtained.

General conclusion and recommendations on admission to defend. The qualification work of Valid HASDO meets all the requirements for qualification works and can be presented for defense at the Examination Commission of the National University of Pharmacy.

Scientific supervisor _____ Iryna KRYKLYVA

«05» April 2023.

Ф А 2.2.1-32-356

REVIEW

for qualification work of the master`s level of higher educftion, specialty 226 Pharmacy, industrial pharmacy

Walida HASDO

on the topic: «Development of the composition and technology of antiallergic syrup».

Relevance of the topic. The author of the work proved the high prevalence of allergic diseases, which are one of the most common diseases in clinical practice. Every fifth inhabitant of the planet suffers from allergies. The data show that the problem of allergic diseases in Ukraine is of great not only medical, but also social significance. The author of the qualifying work proposed the development of a new domestic drug in the form of a medicinal syrup for the treatment of allergic pathology.

Theoretical level of work. The author analyzed the range of drugs for the treatment of allergies. The choice and concentration of active pharmaceutical ingredients in the composition of the medicinal product is theoretically substantiated. The composition of the necessary excipients and the optimal basis for creating a medicinal syrup have been selected.

The author's suggestions on the topic of research. The author proved the need to create a new domestic drug with components of origin in the form of a syrup. Taking into account the properties of the API, excipients were selected and their rational concentrations were established, and the optimal base for the syrup was chosen.

Practical value of conclusions, recommendations and their validity. Based on the results of pharmaco-technological studies, the author of the work substantiated the composition and developed the technology for producing the syrup; a technological scheme is drawn up. The material of experimental studies is presented logically, consistently, and the results are structured. The reliability of the results is confirmed by a significant volume of conducted studies and statistical methods of their processing.

Disadvantages of work. There are incorrect expressions and grammatical errors in the work.

General conclusion and evaluation of the work. The qualification work of Walid HASDO based on the results of research and the volume of the experiment performed can be presented for defense at the Examination Commission of the National University of Pharmacy.

Reviewer _____ assoc. prof. Oleksandr MANSKY

«11» April 2023

МІНІСТЕРСТВО ОХОРОНИ ЗДОРОВ'ЯУКРАЇНИ
НАЦІОНАЛЬНИЙ ФАРМАЦЕВТИЧНИЙ УНІВЕРСИТЕТ

ВИТЯГ З ПРОТОКОЛУ № 9

« 21 » квітня 2023 року

м. Харків

засідання кафедри

заводської технології ліків

ПРИСУТНІ: проф. Рубан О.А., проф. Бобрицька Л.О., проф. Гриценко В.І., доц. Хохлова Л.М., доц. Сліпченко Г.Д., доц. Ковалевська І.В., доц. Криклива І.О, ас. Пономаренко Т.О., лаборанти та аспіранти.

ПОРЯДОК ДЕННИЙ:

1. Обговорення кваліфікаційних робіт щодо їх представлення до захисту в Екзаменаційній комісії НФаУ.

СЛУХАЛИ: здобувача вищої освіти5 курсу групи Фм18(4,10)англ-1 Валида ХАСДО про представлення до захисту в Екзаменаційній комісії НФаУ кваліфікаційної роботи на тему: «Розробка складу та технології сиропу протиалергійної дії». (Керівник: к.фарм.н., доцент Ірина КРИКЛИВА).

В обговоренні кваліфікаційної роботи брали участь проф.Бобрицька Л.О., доц. Хохлова Л.М., доц. СліпченкоГ.Д.

УХВАЛИЛИ: рекомендувати до захисту в Екзаменаційній комісії НФаУ кваліфікаційну роботу здобувача вищої освітифакультету з підготовки іноземних громадянгрупи Фм18(4,10д)англ-1 Валіда ХАСДО тему: «Розробка складу та технології сиропу протиалергійної дії».

Голова
Завідувачка кафедри ЗТЛ **Олена РУБАН**

Секретар **Тетяна ПОНОМАРЕНКО**

Ф А2.2.1-32-042

НАЦІОНАЛЬНИЙ ФАРМАЦЕВТИЧНИЙ УНІВЕРСИТЕТ

ПОДАННЯ

ГОЛОВІ ЕКЗАМЕНАЦІЙНОЇ КОМІСІЇ
ЩОДО ЗАХИСТУ КВАЛІФІКАЦІЙНОЇ РОБОТИ

Направляється здобувач вищої освіти Валид ХАСДО до захисту кваліфікаційної роботи за галуззю знань 22 Охорона здоров'я

спеціальністю226 Фармація, промислова фармація

освітньою програмоюФармація

на тему:«Розробка складу та технології сиропу протиалергічної дії».

Кваліфікаційна робота і рецензія додаються.

Декан факультету _____ /Світлана КАЛАЙЧЕВА /

Висновок керівника кваліфікаційної роботи

Здобувач вищої освіти Валид ХАСДО у процесі роботи розглянув сучасні підходи до лікування алергії, провів аналіз асортименту засобів для терапії даного захворювання та обґрунтував доцільність створення нового вітчизняного лікарського засобу у формі сиропу для лікування алергії. Автором обґрунтовано оптимальний склад і розроблено технологію одержання лікарського сиропу. Валид ХАСДО допускається до захисту даної кваліфікаційної роботи у Екзаменаційній комісії Національного фармацевтичного університету.

Керівник кваліфікаційної роботи

_____ Ірина КРИКЛИВА

«05» квітня 2023 року

Висновок кафедри про кваліфікаційну роботу

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

Завідувачка кафедри

заводської технології ліків

_____ Олена РУБАН

« 21» квітня 2023 року

Qualification work was defended

of в Examination commission on

« __ __ » _____2023 г.

With the grade_____

Head of the State Examination commission,

DPharm Sc. Professor

_____ / Oleg SHPYCHAK /