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MINISTRY OF HEALTH OF UKRAINE

NATIONAL UNIVERSITY OF PHARMACY

faculty for foreign citizens' education

Department of Industrial Technology of Drugs

QUALIFICATION WORK

on the topic: **SELECTION OF EXCIPIENTS AND STUDY OF THEIR INFLUENCE ON QUALITY INDICATORS OF TABLETS WITH DRY EXTRACT OF CLOVER AND CALENDULA**

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ANOTATION

The qualification work contains 48 pages, 10 tables, 14 figures, and a list of references.

The article considers the range of existing drugs on the Ukrainian market and proves the relevance of creating tablets with plant materials (dry clover and calendula extracts) for the treatment of cardiovascular diseases.

The author has studied the physicochemical and pharmacotechnological properties of the extracts, selected excipients and substantiated the introduction of each. The influence of excipients on the quality of the obtained tablets was studied.

Key words: tablets, extracts, supplementary speech.

АНОТАЦІЯ

Кваліфікаційна робота містить 48 сторінки, 8 таблиць, 14 рисунків, список літератури.

Розглянуто асортимент існуючих препаратів на ринку України та доведено актуальність створення таблеток з рослинною сировиною (сухим екстрактом конюшини та календули) для лікування сердцево-судинних захворювань.

Автором проведено вивчення фізико-хімічні та фармакотехнологічних властивостей екстрактів, проведено вибір допоміжних речовин та обгрунтовано введення кожного. Вивчено вплив допоміжних речовин на показники якості отриманих таблеток.

Ключові слова: таблетки, екстракти, допоміжні речовини.

CONTENTS

LIST OF CONDITIONAL ABBREVIATIONS

API – active pharmaceutical ingredient

BP - blood pressure

CPS - a natural chopper

MCC - microcrystalline cellulose

MP– Medicinal product

NTD - normative and technical documentation

SPU – State Pharmacopoeia of Ukraine

INTRODUCTION

The relevance of the research problem. Cardiovascular diseases, coronary heart disease and stroke, are the leading causes of death and one of the main factors of disability worldwide. In Ukraine, cardiovascular disease is the leading cause of mortality. Our country remains one of the world leaders in this indicator.

Cardiovascular diseases most often occur against the background of poor circulation. Too early in a modern person's life, due to impaired blood flow, performance, memory, intelligence, vision, hearing, stress tolerance, etc. decrease.

The occurrence and course of cardiovascular and cerebrovascular diseases are closely related to the presence of risk factors, the main ones being high blood pressure, impaired lipid metabolism, overweight, unhealthy lifestyle (smoking, unhealthy diet, alcohol abuse, lack of physical activity), and environmental factors (psycho-emotional stress, harmful environment at work and at home). Some studies show that the risk of heart disease is higher among groups of people who have more than one of these risk factors (e.g., sedentary smokers).

Wheel choosing preventive herbal medicines, patients are guided by their own preferences, experience, pharmacists' advice, advertising, etc.

We chose dry clover and calendula extract as the active ingredient.

Purpose and objectives of the study. The primary objective of the master's thesis is to study the physicochemical and pharmacotechnological properties of dry clover and calendula extract, substantiate the composition and technology of tablets, and determine the effect of excipients on the quality of tablets.

To achieve this goal, it was necessary to solve the following tasks:

- to review the literature on the prevalence of cardiovascular diseases and treatment approaches;

- to analyze the range of drugs for the treatment of cardiovascular diseases and the development of drugs based on plant materials;

- to study the physicochemical and pharmacotechnological properties of dry

clover extract;

- to experimentally substantiate excipients for the creation of tablets and to study the effect of excipients on the quality of the resulting tablets.

Objects of study. Dry extract of clover and calendula, physicochemical and pharmacotechnological properties. Excipients, mass for tableting, intermediates and finished dosage form - tablets.

Subject of the study. Development of tablets based on dry clover extract. Study of the technological properties of the extract, selection of excipients and the effect of excipients on the quality of tablets.

Research methods. In order to solve the tasks, physical, chemical and pharmacotechnological studies were used, namely:

- methods for determining fluidity, bulk density, angle of natural slope, pressability of powders and pressing force, resistance of tablets to crushing, disintegration;

- methods for determining the average weight and abrasion resistance.

Approval of research results and publications. Fragments of the master's thesis are covered in the publication: X International Scientific and Practical Conference "Modern Achievements in Pharmaceutical Technology" dedicated to the 60th anniversary of Doctor of Pharmaceutical Sciences, Professor Yevhen Gladukh.

Scope and structure of the work. The qualifying thesis is presented on fifty-one pages of printed text and consists of the following structural elements: introduction, literature review (Chapter 1), experimental part (Chapters 2-3), general conclusions, references, which includes thirty sources. The paper is illustrated with 8 tables and 13 figures.

SECTION 1
DISEASES OF THE CARDIOVASCULAR SYSTEM AND THE PRODUCTION OF NEW DRUGS WITH PLANT MATERIALS

1.1. Prevalence of cardiovascular diseases and their causes

The severity cardiovascular disease has continued to rise for decades in almost all middle- and low-income countries. It is also alarming that the age-standardized rate of cardiovascular disease has begun to rise in some high-income countries where it had previously been declining [3, 6, 33].

The number of cases of cardiovascular disease has almost doubled from 271 million in 1990 to 523 million in 2019, and the number of deaths from cardiovascular disease has steadily increased from 12.1 million in 1990 to 18.6 million in 2021 [8, 9].

According to a ranking based on the number of deaths in Ukraine, the most common causes are:

1. cardiovascular diseases (64.3 %)
2. Neoplasm (14.1 %)
3. Diseases of the digestive system (4.3 %)
4. Neurological disorders (3.1 %)
5. Self-harm and interpersonal violence (2.7 %)

Ischemic heart disease is the most generic form of cardiovascular disease and the leading cause of health loss in Ukraine [10, 14].

It is possible to reduce the severity of cardiovascular disease in Ukraine by reducing the main risk factors among the population that lead to premature death:

High blood pressure. High blood pressure (BP) without proper treatment can lead to heart attack, stroke, kidney or heart failure, impaired vision, and other complications. Even a moderate increase in blood pressure is associated

with a decrease in life expectancy [21].

Poor nutrition. The main enemies of the heart are overeating, insufficient consumption of vegetables and fruits, and uncontrolled consumption of high-calorie foods, drinks, and salt. According to experts, the cause of most diseases is unhealthy diet and related disorders of the digestive system. Proteins, fats and carbohydrates should be present in the daily diet.

Cholesterol. Eating too much food high in saturated fat can increase blood cholesterol levels. Therefore, reduce the amount of saturated fat in your diet. Give preference to lean meat (poultry, rabbit) and low-fat foods.

High body mass index. Being overweight increases the risk of cardiovascular disease.

Tobacco smoke. Every tenth death from heart disease is caused by smoking. Smoking is one of the key risk factors for coronary heart disease, stroke, and peripheral vascular disease.

High glucose levels. Excessive amounts of sugar in the diet not only lead to excess weight, but also contribute to the development of serious diseases such as diabetes. Adults with diabetes have a 2-3 times higher risk of heart attack and stroke than others. The overall risk of death among people with diabetes is at least twice as high as among people of the same age who do not have diabetes. 6.2% of deaths in the world are related to diabetes.

Polluted air. Long-term exposure to air pollution is a risk factor for cardiovascular disease. This "invisible killer" claims the lives of 800 people every hour and can cause or exacerbate long-term painful diseases such as cancer, respiratory or heart disease.

Impaired renal function. Impaired renal function is an important risk factor for cardiovascular complications. Heart disease is the most common cause of death among hemodialysis patients. When the kidneys are not working properly, the hormonal system that regulates blood pressure must work harder to increase blood supply to the kidneys. When this happens, your heart must work

harder, which can lead to heart disease.

Alcohol consumption. There is no safe dose of alcohol. Alcohol consumption is harmful to the cardiovascular system, causes hypertension and increases the risk of strokes and cancer.

Low physical activity. Regular physical activity reduces the risk of cardiovascular disease. According to the WHO, to prevent heart disease, you need to engage in physical activity for at least 150 minutes a week.

1.2. Modern approaches to the treatment of heart failure

The main goals of heart failure treatment are:

1. - the possibility of eliminating or correcting the etiologic factor of HF.

2. - elimination or reduction of clinical symptoms of HF.

3. - prevention of hospitalizations due to HF decompensation and other cardiovascular causes;

- improving the quality of life.
- increased life expectancy.

Medication treatment.

All medications for the treatment of HF can be divided into two main categories according to the degree of evidence of their effectiveness. Essential medicines include drugs whose effect is proven, not in doubt, and which are recommended specifically for the treatment of HF [21, 24].

Medicines used to treat HF:

- angiotensin-converting enzyme inhibitors (enalapril, captopril, lisinopril, ramipril, trandolapril, fosinopril, perindopril, etc.);

- beta-blockers (bisoprolol, carvedilol, metoprolol succinate CR/XL, nebivalol);

- diuretics (furosemide, torasemide, hydrochlorothiazide, metolazone,

spironolactone, etc.);

- cardiac glucoside drugs (digoxin);

- If-channel inhibitor in the sinus node (ivabradine);

- angiotensin II receptor blockers (candesartan, valsartan, losartan).

Additional and auxiliary medicines:

- antiplatelet agents (acetylsalicylic acid, clopidogrel, etc.);

- anticoagulants (rivaroxaban, dabigatran template, warfarin, heparin, low-molecular-weight heparins, hirudin, hiluron);

- antiarrhythmic drugs (amiodarone, sotalol);

-metabolic drugs (L-carnitine, prednisone, thiotriazoline, glutamate, coenzyme Q10, taurine);

- hypolipidemic drugs (statins - atorvastatin, simvastatin, rosuvastatin, etc.) [26].

Herbal remedies for the treatment of cardiovascular diseases

The medicinal value of medicinal plants depends on the content of different classes of biologically active substances (BAS): glucosides, alkaloids, flavonoids, vitamins, essential oils, tannins, carbohydrates, coumarins, chromones, etc. They all have different mechanisms of action on the human body. The peculiarity of phytotherapy is that medicinal plants always contain substances belonging to several groups of BASES, providing a complex effect on the human body. The natural combination of dietary supplements helps to normalize metabolic disorders, has a beneficial effect on many vital functions of organs and body systems normalizes the nervous system, improves blood supply to the brain and blood circulation in the heart, enhances the excretion of toxic metabolic products from the body, helps to protect cell membranes and restore tissues [29-31].

Let's consider the existing groups of drugs based on plant materials. The list is given in Table 1.

Table 1

Groups of herbal medicines in the treatment of cardiovascular diseases

№ n/a	Group of medicines	Actions	Name of the medicinal plant raw materials
1	Cardiotonic drugs	Increase myocardial contraction, regardless of changes in pre- and post-load on the heart, can increase the strength of heart contractions	Cardiac glycosides are contained in such plants as purple and woolly foxglove, hellebore, jaundice, mountaineer, May lily of the valley, strophanthus, sea onion, oleander. Cardiotonic agents also include blood-red hawthorn, astragalus, and lemongrass, which have a nootropic effect (lowering blood pressure by reducing the frequency and strength of heart contractions).
2	Vasodilators, antiarrhythmic, antihypertensive and antispasmodic agents	Reduce systemic blood pressure (hypotensive effect) in case of arterial hypertension. Normalize the rate (frequency) of heart contractions and restore disturbed heart rhythm	Hypotensive effect is inherent in mother wort, marsh shrub, sweet clover, geranium meadow, hawthorn, blue cyanosis, choke berry, and woolly straggles. Flavonoids, Coumadin, alkaloids contained in peppermint, anise, hops, hawthorn, parsnip, lemon balm, fennel, periwinkle, oregano have antispasmodic effect.
3	Antisclerotic agents	Substances that can lower blood cholesterol levels and increase the excretion of precursors of its synthesis in the liver with bile have an anti-sclerotic effect. An important aspect of the anti-sclerotic effect is strengthening the strength of the vascular wall due to flavonoids, vitamin P and tocopherol (vitamin E)	Garlic, onions, wild garlic, wild garlic, mistletoe, dandelion, burdock, yarrow, fragrant rue, hawthorn, seaweed, Japanese diascorea, clover, nettle, calendula, flax seeds have these properties.

Continuation of Table 1

1	2	3	4
4	Diuretics Sedatives, psychotropic drugs	Sedatives are necessary for cardioneurosis, for the relief of spasms of nervous effects on the vessels of the heart, for the relief of spasms of regional arteries of the heart, brain and extremities, as well as for the normalization of sleep (psychosedative effect)	Diuretic medicinal plants: horsetail, knotweed, kidney tea, lingonberry, birch, bearberry, blueberry, juniper, dill, fennel. Chamomile, marsh dried flower, cyanosis, thyme.

Herbal medicines are divided into the following groups:

1. Medicinal plant materials: dried, freshly harvested parts of medicinal plants (to produce medicinal products). Minipreparations from medicinal plant material are one type of crushed, rarely whole medicinal plant. Herbal mixtures - mixtures of several types: crushed, whole medicinal plant material, sometimes with the addition of salts, essential oils.

2. Total crude herbal products contain biologically active and related substances (infusions and decoctions, tinctures, extracts, elixirs).

3. The total purified herbal products contain biologically active substances and are maximally purified from concomitant and ballast substances.

4. Phyto preparations of individual maximally purified compounds (biologically active substances of targeted action isolated from plants).

5. Complex herbal products contain compounds isolated from plants and substances of non-plant origin (synthetic, endocrine, etc.).

The structural analysis of the pharmaceutical market segment under study (Fig. 1) showed that the largest share of the assortment (44.9%) is occupied by homeopathic remedies, which have become widespread in recent years.

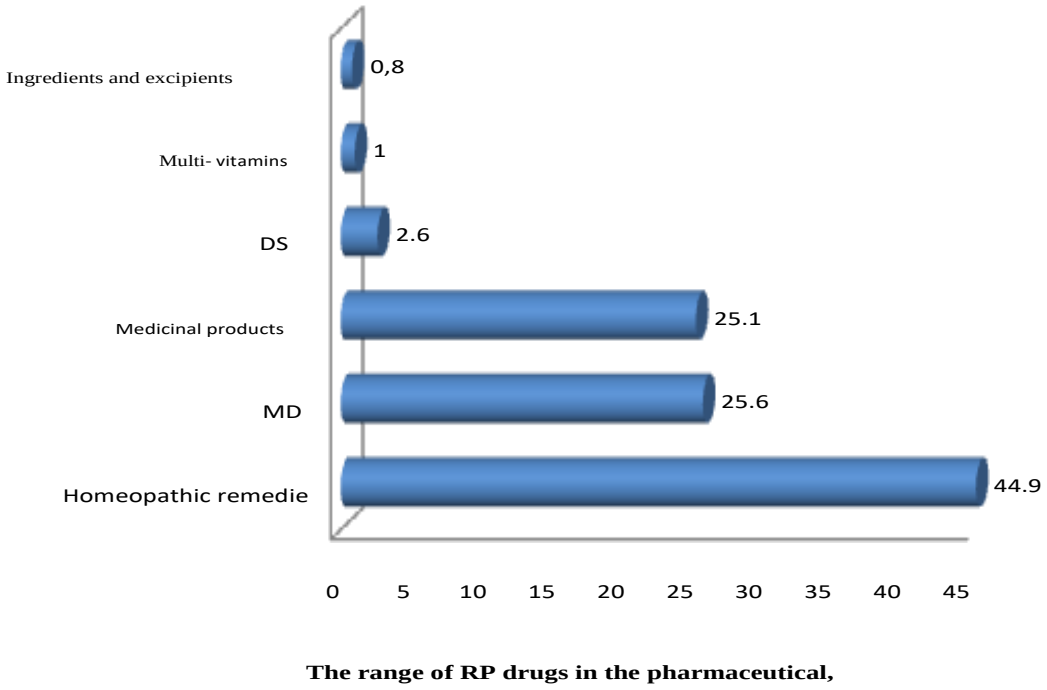


Figure 1. Structural analysis of the pharmaceutical market

The following groups: "Medicinal plants, raw materials and preparations from them" are represented by 25.6%; "Medicinal products" - 25.1%. Other groups have insignificant shares in the structure 0,8–2,6 % [4].

The analysis of the above groups by manufacturers shows that one third of the assortment (36.6%) is Rx drugs from domestic manufacturers (Fig. 2). [12, 17].

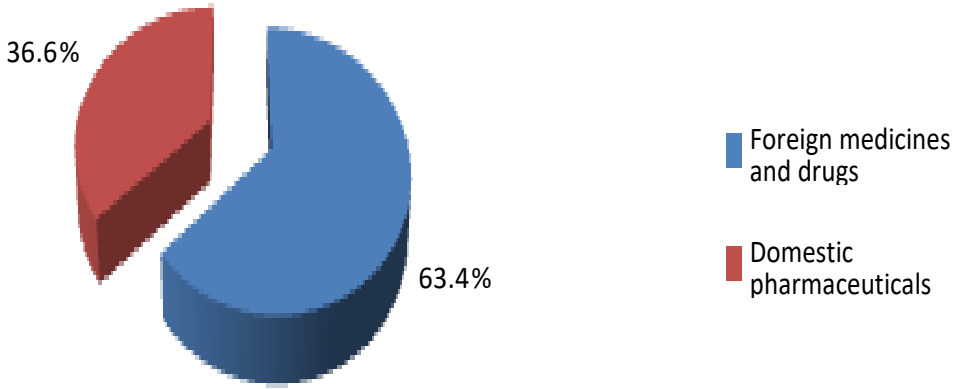


Figure 2. Market analysis by manufacturer

The next stage of the analysis is devoted to the study of medicinal products by composition (single-component and multicomponent), Fig. 3. For the study, we selected two groups: "Medicinal plants, raw materials and preparations from them" and "Medicinal products". In the group "Medicinal plants, raw materials and preparations from them", 92% (537 items) were single component, the remaining 8% (47 items) included several medicinal plants. The picture is different for OTC drugs: 31.8% are single-component drugs, and the remaining 68.2% are multicomponent drugs. Among multicomponent herbal medicines, there are various herbs used in medicine with cardiological, expectorant, vitamin, gastrointestinal, and other effects [15, 23].

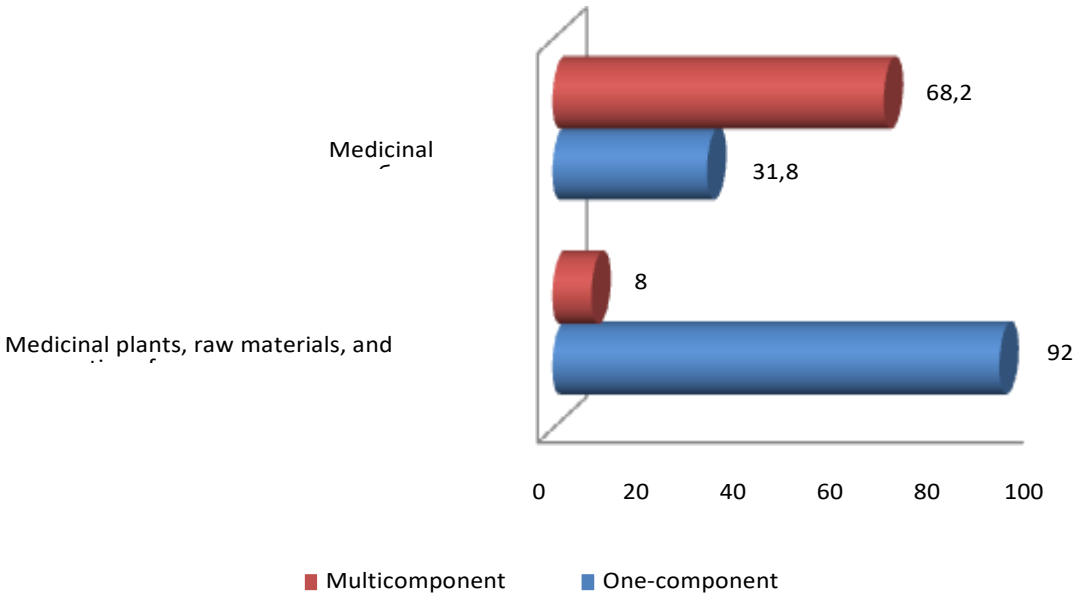


Figure 3. Classification of drugs by composition

In total, the list of medicinal plants in the State Register of Medicinal Products included 242 items. The top rankings are as follows: mint (22), valerian and yarrow (18), licorice (17), chamomile (16), plantain (15), etc. (Fig. 4)

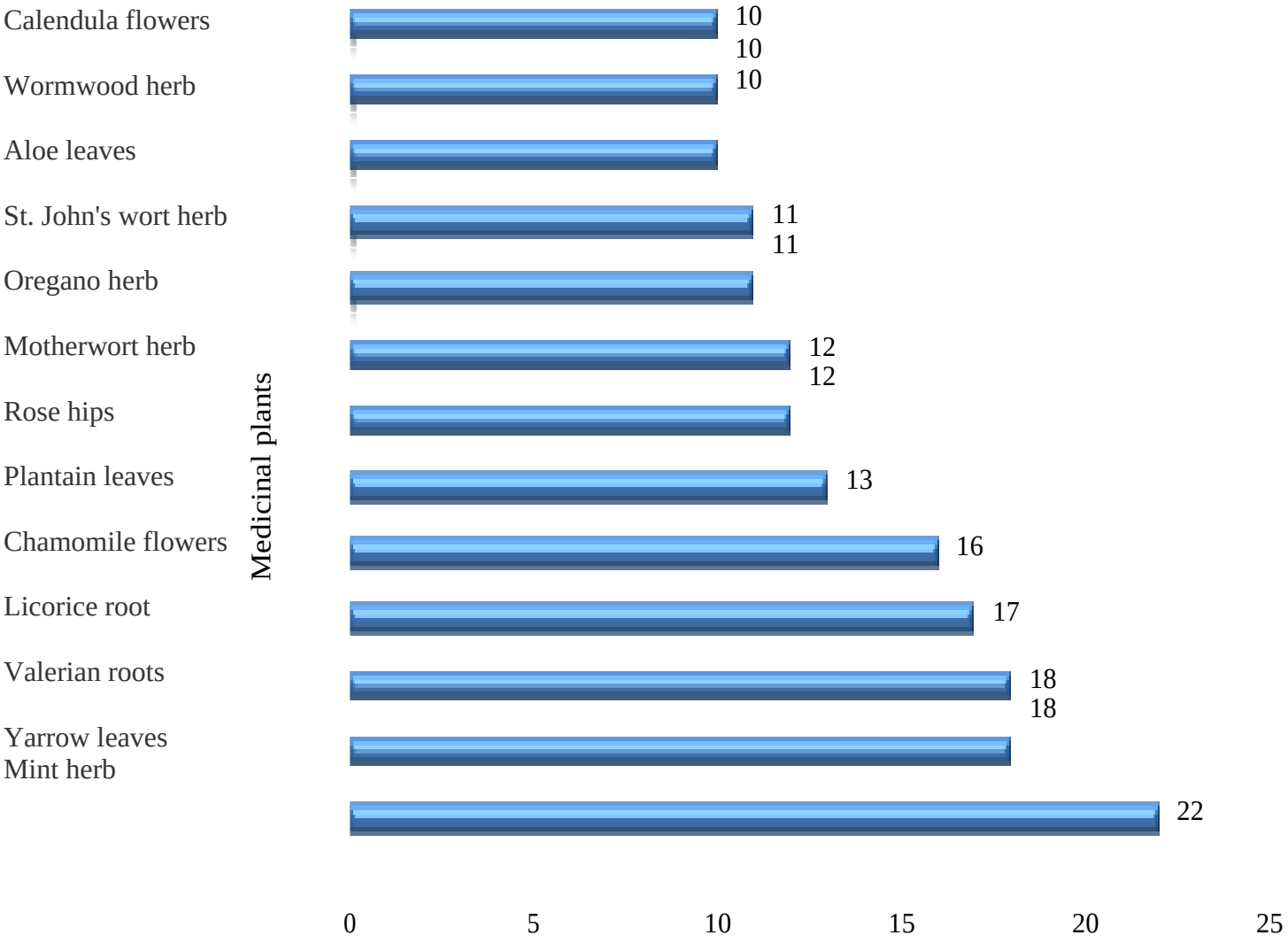


Figure 4. Distribution of medicinal plants in the State Register

Most often, domestic preparations are made from valerian, hawthorn, rose hips, ginseng, eucalyptus, chamomile, licorice, lily of the valley, etc. Plants [18-20].

When studying the structure of the assortment [25] by types of dosage forms, it was found (Fig. 5) that a significant share is represented by plant materials (65.4%), liquid forms are in second place, and solid dosage forms are only 12.2%.

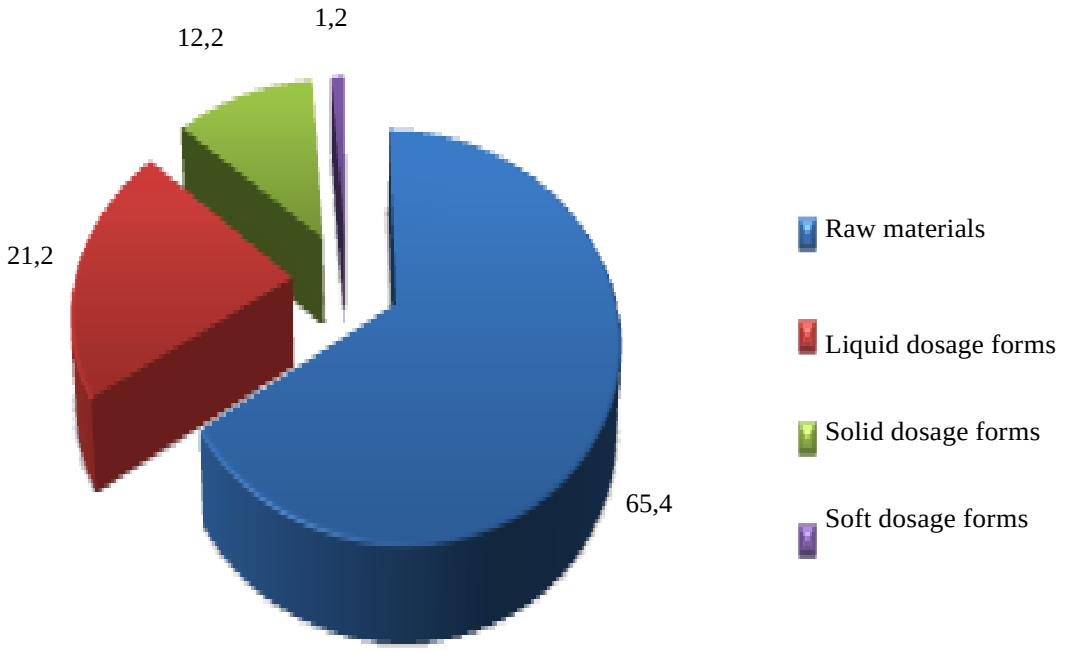


Figure 5. Distribution by dosage form

The studies have proved the relevance of creating new effective solid medicines for the treatment of cardiovascular diseases with plant materials.

1.3. Direct pressing method for the manufacture of tablets

Tablets (Tabulettae) are a solid dosage form obtained by pressing medicinal substances or a mixture of medicinal and excipients and intended for internal, external, sublingual, or parenteral use. An important point in of tablet technology is pressing. Tablets were first produced in 1895. Nowadays, tablets are widely used as a dosage form of many drugs.

The tablets are flat and biconvex round, oval disks, or other shaped plates, and may also be cylindrical. The diameter of the tablets can range from 3 to 25 mm. The pharmaceutical approach to a drug considers the type of dosage form

as one of the leading factors in the bioavailability of a drug substance. Recently, considerable attention has been paid to the creation of a rational form of drugs [22].

Tablets produced by the pharmaceutical industry account for approximately 87% of finished drug production. The production of tablets worldwide is growing by 10-15% annually [23].

The development of the optimal composition and technology of tablets is determined by the physicochemical, crystallographic and technological properties of the medicinal powders that make up their composition [5]. These parameters are closely interrelated and affect the technological process. The volumetric and technological properties of the substances to be pressed and the physical and mechanical characteristics of the resulting tablets are largely determined by the crystal structure of the particles. Therefore, the study of these issues can be useful in predicting the most efficient way to produce tablets. When manufacturing dosage forms from powdered material, grinding, mixing, granulation and tableting operations are performed.

The tablet manufacturing technology is selected according to the physicochemical and technological properties of the active ingredient: fractional composition, bulk and relative density, and fluidity, which make it possible to determine the optimal process parameters: the nature and amount of humectant, the pressing method, the volume of the matrix space, the pressing capacity required for particle adhesion in the tablet, and the shape, size, and strength of the crystals.

Depending on the amount of active ingredient in the future tablet, the amount of excipients in the tablet is determined [23]. Currently, pharmaceutical plants manufacture tablets in three main ways:

1. Direct pressing of substances.
2. Briquetting.
3. Pressing with preliminary wet granulation

The development of tablet technology is a complex process that requires full knowledge of the properties of the main and excipients used in the production of tablets. To facilitate this work, technological maps are used, which contain the results of studies and tests conducted with medicinal substances under identical conditions. The use of control charts is recommended to control tablet quality indicators [32]. When assessing the factors that have impact on the production of tablets by various methods, it is recommended to use a simulation model [34]. The modeling method makes it possible to better assess the suitability of new substances for tableting, the prospects for the use of equipment, excipients, and production methods.

The most convenient method for production is direct pressing. The direct pressing method has several advantages [28]. It allows achieving high labor productivity, significantly reduce the time of the technological cycle by eliminating several operations and stages, eliminate the use of several items of equipment, reduce production space, and reduce energy and labor costs. To date, this method is used to produce a few tablet types, as most medicinal substances do not have properties that allow for direct pressing.

These properties include the isodiameter shape of the crystals, sufficient fluidity and compressibility, and low adhesion to the press tool. The angle of natural slope is of great importance, which for well-flowing materials is between 25° and 3°. The value of the slope angle is significantly influenced by the roughness of the particles, moisture content and dispersion of the powder.

Particle size also has a major impact on the ability to press - the less crystalline the component, the smaller the particles should be. A system consisting of two fine powders produces more homogeneous mixtures. In direct pressing, the particle size usually does not exceed 50–100 microns, and the mixing process is highly homogeneous. The properties required for direct

pressing can be achieved by targeted crystallization, by using forced feeding of the tablet mass into the matrix, or by optimal input/output of excipients [5].

The effectiveness of excipients in direct pressing depends on their density, moisture content, particle size, etc. The best results are obtained when using excipients whose density is close to that of the drug substance, and whose particle size and fluidity allow for uniform retention of the drug substance particles.

One of the most important aspects of the tablet manufacturing process is the selection of the optimal pressing pressure, which affects not only the quality of the tablets (strength, solubility, etc.) but also the wear of the press tool [5].

There is a linear relationship between the strength, pressing pressure, and relative density of a material. Substances with a pronounced plastic deformation have a positive value of the material compaction parameter, and in brittle substances, this parameter approaches zero [7].

The pressing pressure and plasticity of the material affect the uniformity of the density distribution of the substance in the tablets. To improve the plastic properties of medicinal substances, it is proposed to introduce plasticizers into the composition of tablet masses. Coating drug particles with silicons or Tween-80 reduces the formation of bonds during plastic deformation of the particles.

Dosage accuracy is the dosing of the tablet mass during the tableting process, which is a complex process. Dosing accuracy depends on many conditions. Dosing will be accurate if the same amount of tablet mass is always fed into the die slot during the entire tableting process. In addition, the dosing accuracy depends on the rate of trouble-free filling of the die slot and the homogeneity of the tablet mass.

CONCLUSIONS TO SECTION I

1. The article analyzes the literature on the prevalence of cardiovascular diseases, considers the causes of their occurrence and methods of treatment.
2. The assortment of existing drugs on the Ukrainian market and drugs based on plant materials of this direction of action is considered. It was found that these are foreign-made drugs, the share of drugs in the form of solid dosage forms is not large, which justifies the creation of new drugs with plant materials.
3. The method of direct pressing is discussed as a promising method for the manufacture of tablets.

SECTION II.
OBJECTS AND METHODS OF RESEARCH

2.1. Characteristics of active substances and excipients

Dry clover extract is a green powder, moderately soluble in water. It has a specific odor and taste.

Clover roots, leaves and flowers are saturated with essential oils and contain a considerable number of organic acids (coumaric, salicylic, ketoglutaric), vitamins (groups A, B, B1, C, K and E), tannins, fiber, protein, macro- and microelements (chromium, selenium, iron, phosphorus, magnesium, calcium, etc.). The green mass and flowers of clover include proteins, tannins, many flavonoids, carotenoids, as well as furfural, xanthine, tyrosine, asparagine, and other useful substances. Clover increases the level of healthy HDL cholesterol, thins the blood, and has a protective and strengthening effect on the cardiovascular system [27, 28].

Clover is rich in flavonoids of various groups: isoflavans, isoflavones, isoflavanones, flavonols, pterocarpans and their glycosides.

It has been shown that aqueous and ethyl acetate extracts of meadow clover leaves exhibit strong antioxidant activity in comparison with standards (butylated hydroxyanisole and butylated hydroxytoluene, known synthetic antioxidants). Therefore, it seems promising to consider these extracts as a new valuable source for pharmaceuticals [32].

It was found that meadow clover and/or ginkgo biloba showed strong antioxidant activity and protective effects against sodium arsenite-induced neurotoxicity. In addition, it is noted that the presence of a combination of ginkgo biloba and meadow clover showed better protective effects against its neurotoxicity compared to each of them alone.

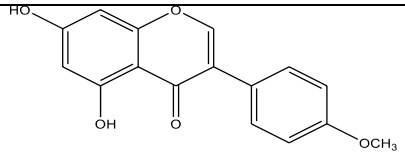
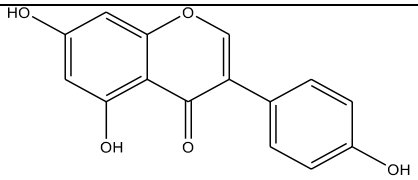
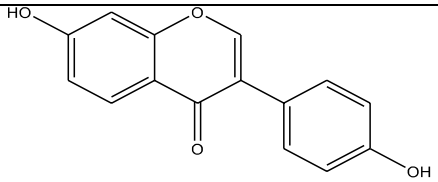
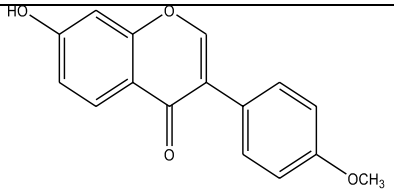
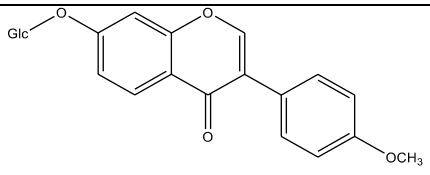
Water-soluble polysaccharides from meadow clover exhibit pronounced

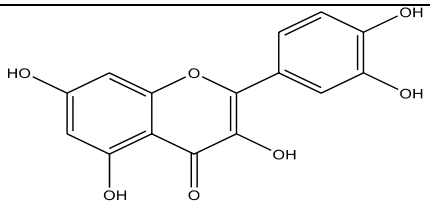
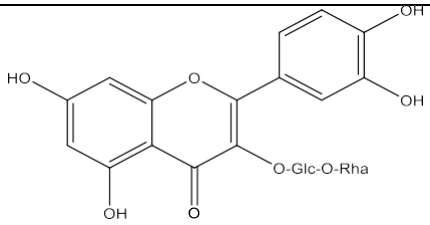
immunotropic properties and are promising for the treatment of Ige-dependent diseases (bronchial asthma, urticaria, atopic rhinitis, atopic dermatitis, food allergies, etc.

It has been established that the sum of flavonoids from meadow clover grass has antihypertensive activity and low toxicity. It has been proven that the sum of flavonoids isolated from meadow clover stimulates intestinal motility, its effect is comparable to that of acetylcholine [1, 11]. Table 3 shows the flavonoids contained in clover.

Table 3

Structural formulas of clover flavonoids

Name	Structural formula
Biochanin A	
Genistein	
Daijin	
Formononetin	
Ononin	

Quercetin	
Rutin	

The list of existing products in the form of dietary supplements with clover is given in Table 4.

Table 4

Medicinal products based on clover

Name of the drug and manufacturer	Substance	Dosage form	Action
Red Clover / Nature's Way Inc., USA	Red clover	Capsules	Estrogenic effect
Red Clover Cleanser / Planetary Herbals	Honeysuckle flowers, echinacea purpurea root extract, sorrel root, red clover aerial part, American ginseng root, ginger root and liquorice root	Tablets	Estrogenic effect, for the prevention and treatment of diseases of the cardiovascular system
Promensil / Pharma Care (Europe) Ltd	Clover extract	Tablets	Estrogenic effect, for the prevention and treatment of diseases of the cardiovascular system
Rimostil / Gall Pharma Austria	Clover extract	Capsules	Estrogenic effect
Menoflavon/ Melbrosin International, Vienna, Austria	Clover extract	Capsules	Estrogenic effect

Calendula dry extract is one of the most active and versatile plant extracts, which is used in all kinds of cosmetic preparations. There are many forms of release of calendula components - powders, tinctures, oils, extracts, calendula ointments, essences and their use as cosmetic components is quite extensive, but any preparation of calendula perfectly preserves its healing effects. Easily soluble in hot water, polysorbate-80, a barely noticeable precipitate is possible.

Calendula flowers contain carotenoids, resins, mucilage, bitterness (calendene), flavonoids, salicylic and malic acids, triterpene glycosides, saponin, and phytoncides. Concentrates zinc, copper, molybdenum and selenium.

Dry extract is obtained from the flowers of calendula, petals of which have a powerful anti-inflammatory, antibacterial and antiseptic effect. The extract contains a lot of vitamins, minerals and useful substances, as the flower petals give away the most useful things in the powder.

The excipients used in the development of the capsules are shown in Table 5.

Table 5

Excipients used in the development of tablet composition and technology

Excipient name	Functional purpose
1	2
AEROSIL® 200 Pharma	Moisture adsorbent Slip agent
Sodium chloride	Enzyme preservative
Sodium croscarmellose (Primelose)	Baking powder
Sodium starch glycolate	Baking powder
Microcrystalline cellulose	Molding device
Lactose monohydrate	Molding device
Water is purified	Solvent

2.2. Methods for evaluating the pharmaco-technological characteristics of the powders and tablets under study.

In order to theoretically substantiate the composition, standardize the quantitative characteristics of the dosage form components, optimize the technological parameters of stepwise processing of intermediates and manufacture of tablets, the substances of biologically active compounds (dry clover and calendula extracts), which provide the main pharmacotherapeutic effect and expand the spectrum of action of dosage forms, as well as excipients (as tablet fillers), tablet mixtures, and tablets based on them, were subject to research.

The shape and surface of the particles of the active substances of dosage forms, as well as the average linear size of their dominant fractions.

These characteristics were determined by microphotography using a Microphot D16B microscope at high magnification.

Dispersibility of powders.

They were evaluated by a combination of two characteristics: average particle size and fractional composition.

The following were also determined: powder flowability, bulk volume and bulk density, moisture content, slope angle, pressability, and the force of pushing the pressed tablet out of the die.

2.3. Methods for assessing drug quality indicators.

The technologies, modes and optimal technological parameters of tableting were tested on typical laboratory equipment that models the basic principles of industrial equipment.

The appearance of the tablets was determined visually in daylight by taking a sample of 20 tablets. The color, shape of the tablets and surface uniformity were controlled by examining the tablets on a white background.

The average weight of a tablet was determined by weighing 20 tablets on

an analytical or electronic balance to the nearest 0.001 g and dividing the result by 20. The weight of individual tablets was determined by weighing 20 tablets separately to the nearest 0.001 g. Only two tablets out of 20 may have a deviation from the average weight of 5%, no tablet may have a deviation from the average weight of more than ±10%.

Disintegration studies of tablets were performed in accordance with the SFS on a laboratory disintegration process identifier.

To obtain a quality finished product in all respects, it is necessary to control the intermediate product for the following indicators: appearance, average weight, weight uniformity, crush resistance, and abrasion.

The tablets were assessed as of high quality if they showed no signs of chipping or cracking, and the abrasion rate was no more than 1.0%.

CONCLUSIONS TO SECTION II

1. When developing the tablets, dry clover and calendula extracts and excipients were chosen as the object of study, which were selected taking into account their pharmacological properties.

2. Modern physical, chemical and pharmacotechnological methods of research were used to objectively evaluate the quality characteristics and technological properties of the starting materials, excipients, tablet mixtures and tablets and to determine the optimal parameters of their production.

SECTION III.

DEVELOPMENT OF COMPOSITION AND TECHNOLOGY OF TABLETS WITH DRY CLOVER EXTRACT AND STUDY OF THE EFFECT OF EXCIPIENTS ON TABLET QUALITY INDICATORS

The choice of dosage form is of great importance in the implementation of the absorption processes of active substances, which are determined by the physicochemical, pharmaceutical, and technological properties, as well as the therapeutic dose of active biologically active substances. The choice of tablet form is due to a few advantages over other forms of solid dosage forms: precise dosage of the drug substance, the ability to vary the dosage, ease of use, full mechanization of the manufacturing process, cost-effectiveness, and portability, which ensure ease of dispensing, storage and transportation.

This section highlights the research on the development of the composition and production technology of tablets for the treatment of cardiovascular diseases with dry clover extract. The components were selected, their quantitative characteristics were studied, and the technological parameters of production were determined, considering the results of experimental studies of the pharmacological, technological, physical, and chemical properties of dry extracts and products during production.

3. 1. Determination of the shape and particle size of the dry extract powder and study of physicochemical and pharmacotechnological properties

In order to develop and determine the optimal quantitative indicators of the composition and technological parameters and modes of preparation of tablets, the crystallographic and basic pharmacological, technological, physicochemical properties of dry clover extract and calendula were studied.

The shape and particle size of the dry extract was studied by microscopy. To do this, a small amount of powder was applied to a glass slide and examined under a microscope.

Microscopy of clover extract powder and calendula powder are shown in Fig. 6 and 7.

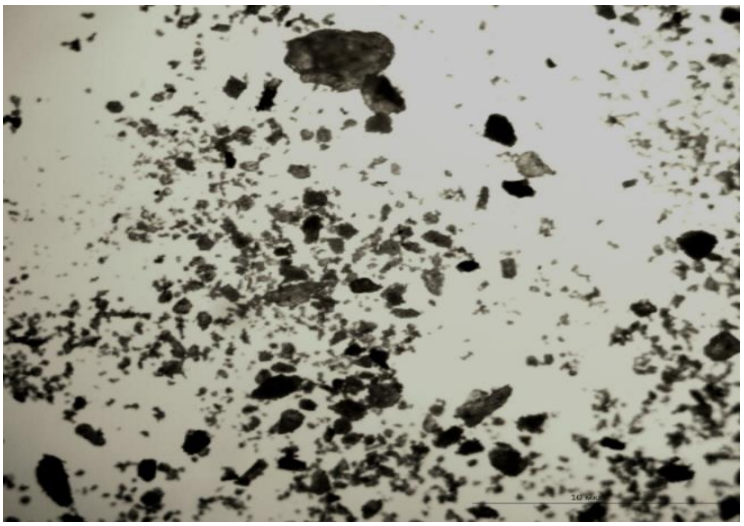


Figure 6. Micrograph of clover extract powder dry (magnification 100 times)

Studies have shown that the powder of the dry extract is a moderate particle with a size of 500 to 1000 microns, uniform in shape.

Figure 7. Micrograph of calendula extract dry

It should be noted that the extract is hygroscopic and can agglomerate under the influence of environmental moisture, and also has a specific odor.

The next stage was the study of pharmacological, technological, physical and chemical properties: fluidity, angle of natural slope, bulk density before compaction and after compaction, compressibility, force of pressing out the pressing from the matrix, moisture content, etc. of the tested substances were carried out according to the methods described in Section 2. The results of the research are presented in Tables 6 and 7.

Table 6

Pharmacotechnological properties of clover extract dry

Moisture content, %	1,5 ± 0,15
Flowability, c/100g	45 ± 1,14
Bulk density, g/cm^3	0,75
Natural bevel angle, degrees	38^o
Pressing, H	40,0 ± 1,04

The analysis of the pharmacotechnological properties of dry clover extract (Table 6) showed that the powder has satisfactory fluidity values (45 ± 1,14), as evidenced by the angle of natural slope. The obtained pressability needs to be adjusted as it is extremely important in the technology of tablet dosage forms.

Dry calendula extract has quite satisfactory flow characteristics (Table 7), but the resistance to pressing is unsatisfactory, which requires the introduction of excipients.

Table 7

Pharmacotechnological properties of dry calendula extract

Moisture content, %	4,68 ± 0,12
Flowability, c /100g	52 ± 2,1
Bulk density, g/cm^3	0,71
Pressing, H	35,0 ± 1,13

We also studied the fractional composition of the clover extract, which is shown in Fig.7

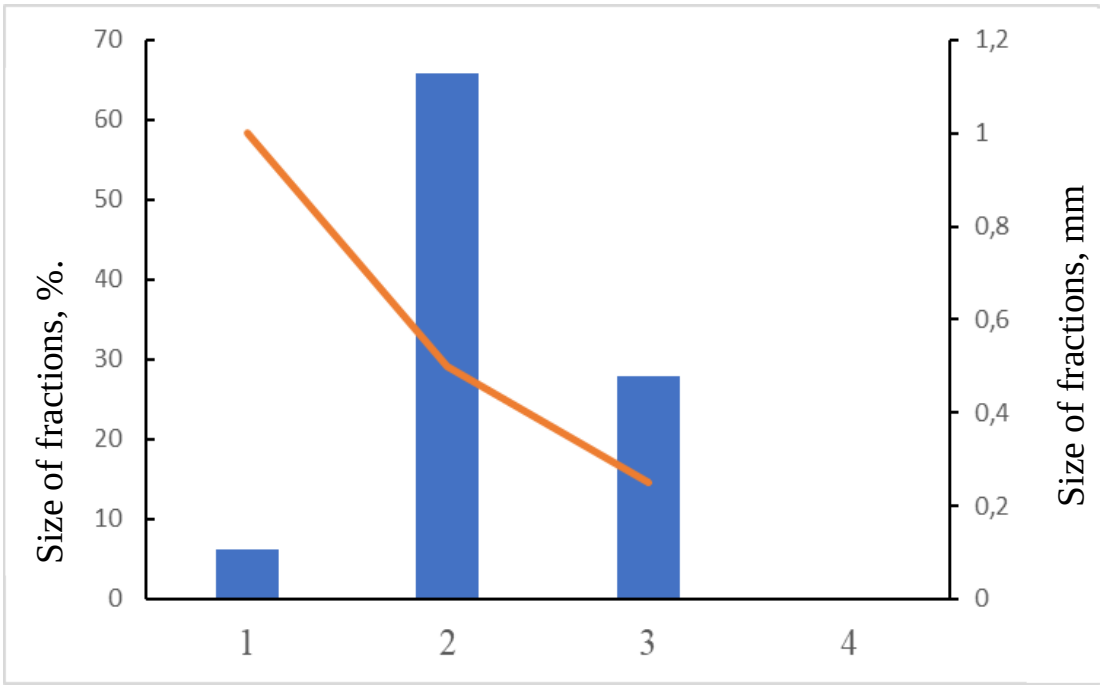


Figure 7. Fractional composition of clover extract

Fig. 7 shows that the main fraction of the extract consists of particles with a size of 0,5 mm, 30% are particles with a size of 0,25 mm or less. That is, the powder is quite homogeneous. The study of dry calendula extract is shown in Fig. 8

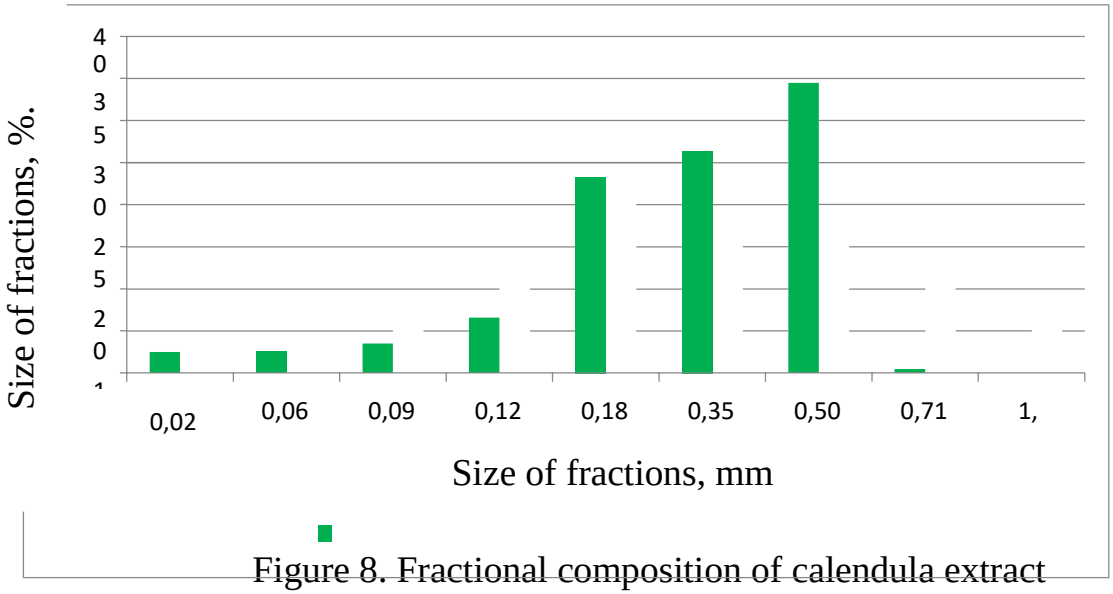


Figure 8. Fractional composition of calendula extract

We also studied the hygroscopicity of phytosubstances using the following solutions: water (100% humidity) and sodium chloride (75,5% humidity).

The studies carried out during the day showed that there is an intensive increase in moisture, both at 75% - by 10% and at 100% - by 20%.

Thus, the dry extracts are highly hygroscopic, which should be considered when developing a dosage form. We selected the substances for the development of the composition and considered their technological properties (Table 8).

Table 8

Technological properties of excipients

№	Excipients	Bulk density, g/cm^3	Flowability, c/100g
1	Lactose monohydrate	0,843±0,18	42,59±0,09
2	MCC 101	0,449±0,10	44,21±0,05
3	AEROSIL® 200 Pharma	0,61±0,08	1,2±0,05
4	Starch glycolate	0,99± 0,03	34,10±0,11
5	Sodium croscarmellose	0,83± 0,02	30,11±0,01

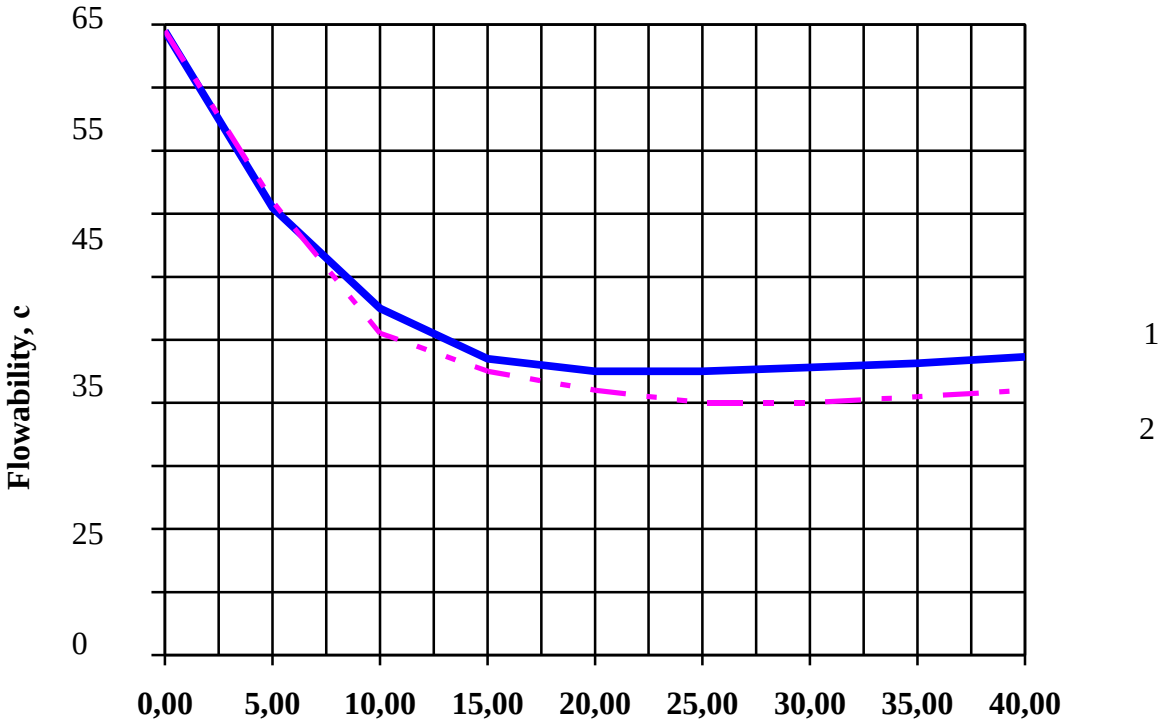
Universal excipient compositions prepared for direct tableting are widely described in the literature, usually including lactose, microcrystalline cellulose (MCC), potato or corn starch, sliding and lubricating components (aerosil, stearic acid salts, etc.). Lactose is one of the most used fillers in the pharmaceutical industry.

In direct pressing, dry binders, such as MCC, are most often introduced to increase the compressibility of medicinal substances in the powder mixture [5].

Aerosil, depending on the brand, is a moisture-absorbing and slip agent. Slip agents, adsorbing on the surface of particles, eliminate or reduce roughness,

increasing their fluidity [5]. The starch sodium glycolate absorbs water quickly and swells, so it is used as a common fast-acting disintegrator [5].

We studied the effect of each indicator separately on tablet weight and then on tablet yield. First, we studied the effect of lactose and MCC on flowability. (Fig. 9).



Lactose and MCC content in tablet weight, %.

1 - lactose, 2 - MCC

Figure 9. The results of studies of the dependence of tablet yield mass on the ratio of milk sugar and MCC in them

From Fig. 9 shows that with the increase of lactose and MCC content in the tablet mass, the fluidity slowly increases. The optimal values of fluidity are in the range of 10-20 %. To optimize the content of MCC in the tablet mass, its effect on abrasion was determined (Fig. 10).

Thus, it was determined that 10-11% of milk sugar and 15% of MCC provide the necessary technological parameters to produce tablets.

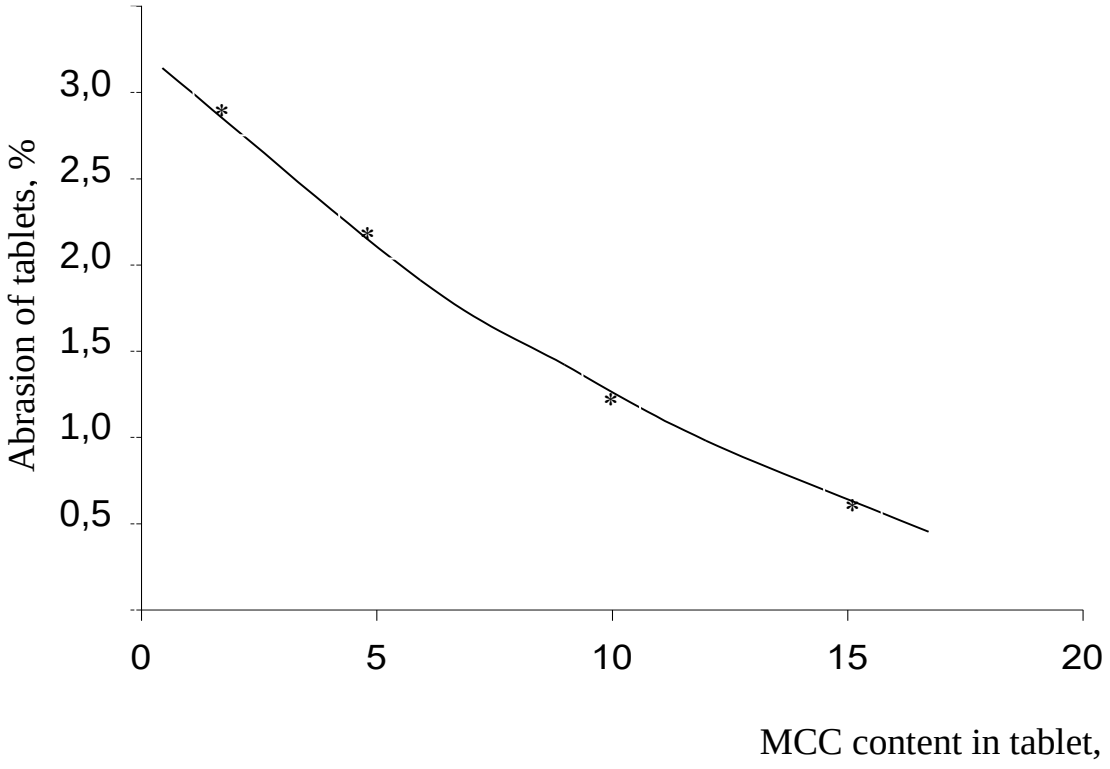


Figure 10. Dependence of tablet abrasion on the content of MCC in the tablet

The next step was to choose the amount of leavening agent, and the results of the study are presented in Table 8. When choosing a leavening agent, we selected the most used ones, which, according to the literature, are used to produce tablets by direct pressing.

Table 8

Results of studies of the dependence of tablet mass fluidity and quality indicators of the obtained tablets on the type of baking powder

The ratio of of sodium croscarmellose and sodium starch glycolate	Fluidity of tablet mass, s/100 g of sample	Quality indicators of the tablets produced	
		Resistance to crushing, H	Decay time, min
1 : 1	30	63±1,1	10,2±0,34
2 : 2	22	65±1,4	6,5±0,15
2 : 0	28	68±1,5	6,1±0,15
0 : 2	24	70±1,7	5,4±0,33

The studies showed that we had slightly better disintegration of tablets (5-6) minutes when using sodium starch glycolate, which was added to the final formulation. None of the leavening agents significantly affected the resistance of tablets to crushing.

Given that the dry extract is a hygroscopic substance, the effect of AEROSIL® 200 Pharma on moisture absorption was studied by adding different concentrations from 0.5 to 1.5% to the composition. The data obtained are shown in Fig. 11.

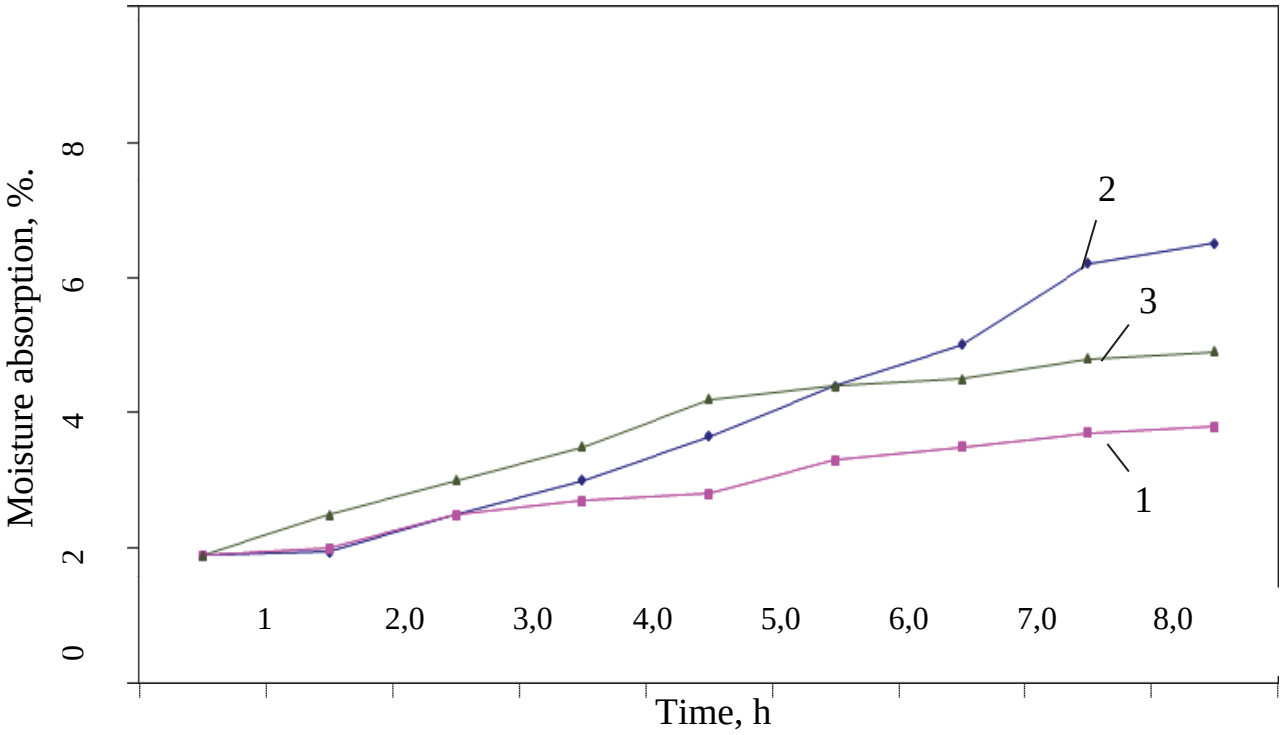


Figure 11. Dependence of moisture absorption on the moisture regulator content

1- 1,5%; 2- 1% and 3- 0,5 %

Studies have shown that the addition of 0.5% to the composition of the mass already gives a positive result when compared with the weight gain of the dry extract itself over a similar period. When 1-1.5% is used, the increase per day stabilizes and is within 3%, which is optimal for the tablet mass.

We also studied the effect of pressing pressure on crush resistance, abrasion, and disintegration. The results are shown in Fig. 12.

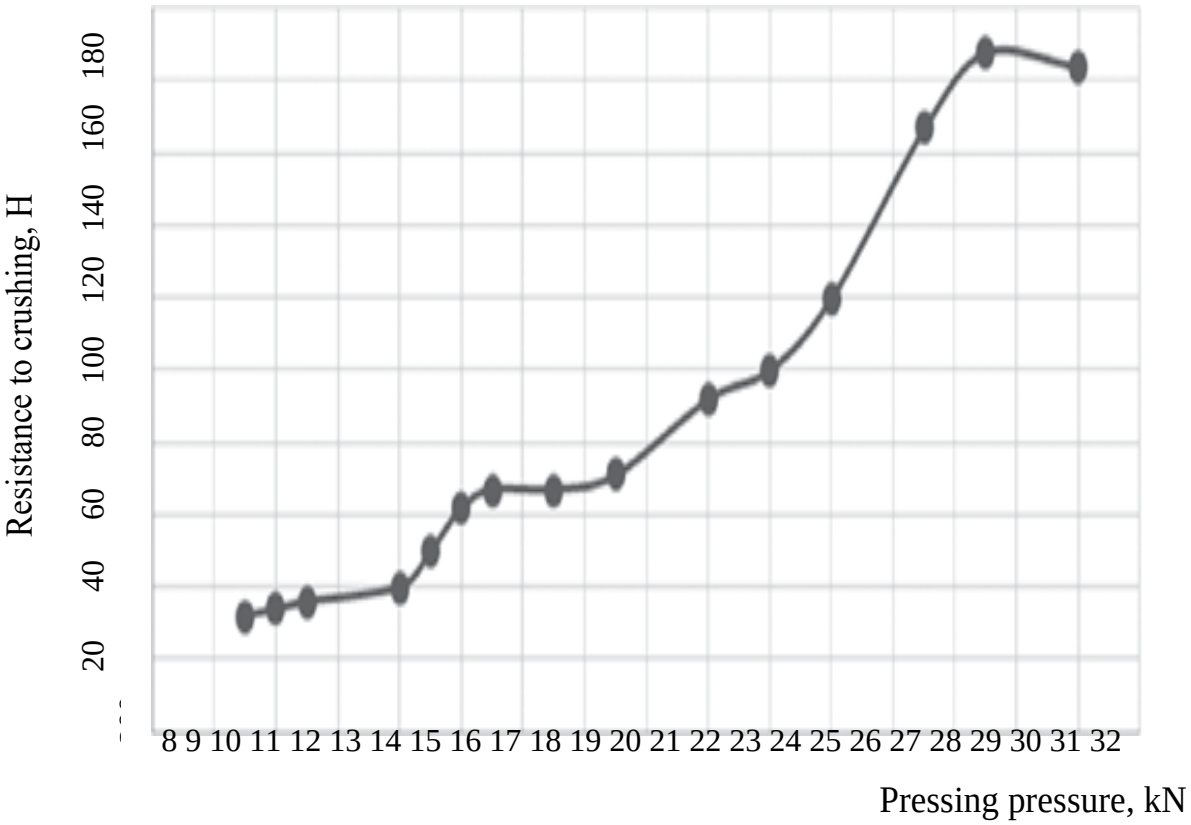


Figure 12. Effect of pressing pressure on tablet resistance to crushing

As can be seen from Figure 12, with increasing values of pressing pressure in the range from 8 to 30 kN, a linear increase in the resistance of tablets to crushing is observed. This value ranges from 36 to 200 N. From the study (Fig. 12), we can see that an increase in pressing pressure leads to a deterioration in abrasion. In subsequent studies, pressing pressures ranging from 8 kN to 22 kN were used.

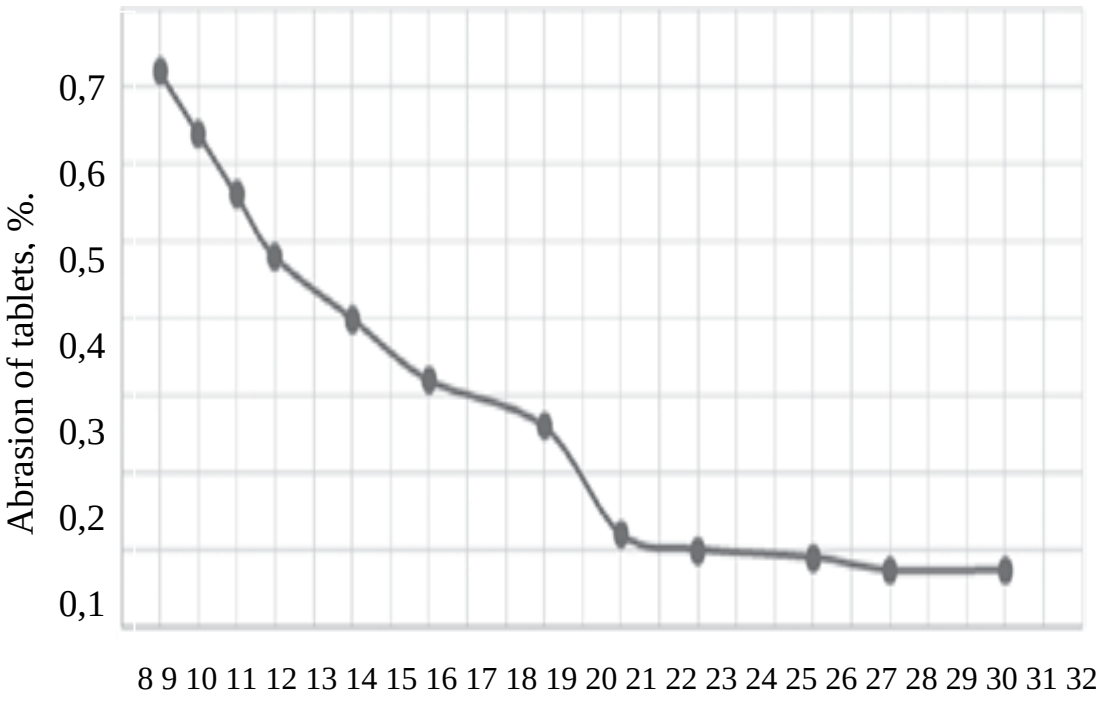


Figure 12. Effect of pressing pressure on tablet abrasion

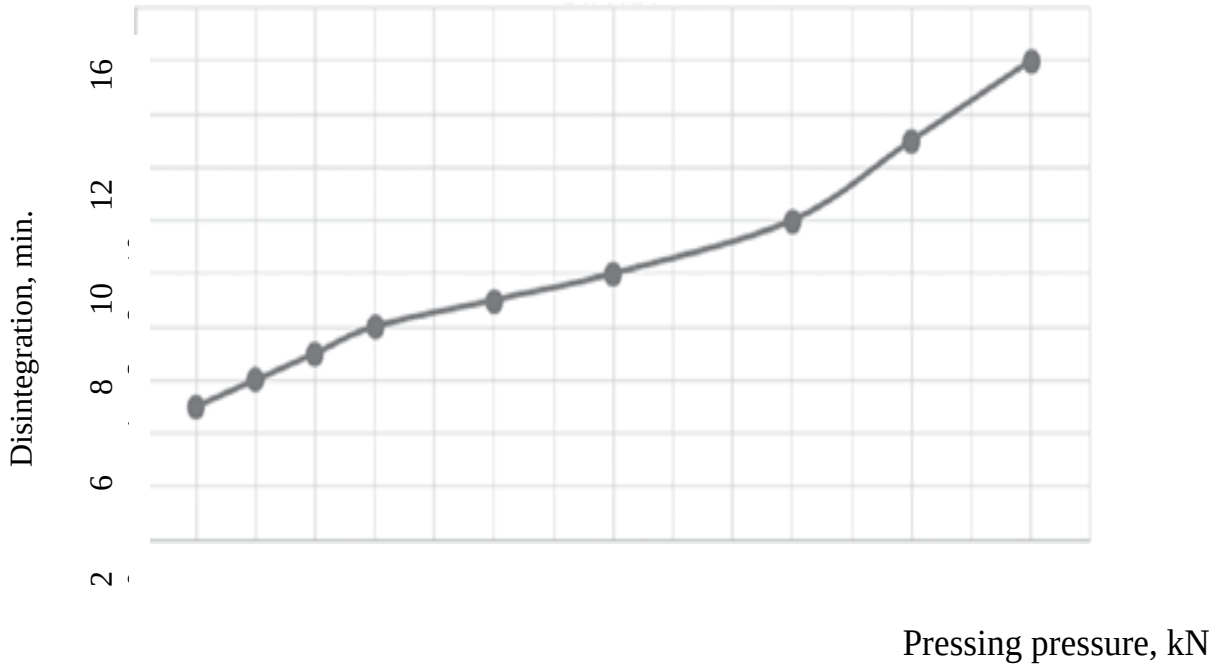


Figure 13. Effect of pressing pressure on tablet disintegration

Increasing the pressing pressure to 22 kN leads to an increase in disintegration time to 16 minutes, which does not meet the requirements of the FDA for uncoated tablets. Thus, we optimized the pressing pressure from 18 to 20

kN.

Based on the results obtained, we developed a tablet formulation for the treatment of cardiovascular diseases:

Composition per 1 tablet, g:

Clover extract dry	0,0750
Calendula extract dry	0,0500
MCC	0,0675
Lactose monohydrate	0,1850
AEROSIL® 200 Pharma	0,0450
Sodium starch glycolate	0,0090
Total weight	0,450

The quality indicators of the obtained tablets are shown in Table 9.

Table 9

Tablet quality indicators

Description	Result
Appearance	Homogeneous, green, round, uncoated tablets
Weight, g	0,45 ± 0,01
Diameter, mm	10,00 ± 0,01
Abrasion resistance, %	0,30 ± 0,02
Resistance to crushing, N	68 ± 1
Decomposition time, s	360 ± 2

We also conducted experimental studies on the effect of moisture content of the tablet mass.

At different values of moisture content, tablets were compounded and the strength and appearance of the tablets were observed. The data obtained are shown in Table 10.

Table 10

Dependence of tablet compressibility and appearance on the moisture content of the tablet mass

Indicators and units of measurement measurement	Number of the laboratory series						
	1	2	3	4	5	6	7
Pressability (Determined by the resistance of tablets to crushing, H	40,1 ±0,93	50,3 ±2,7	61,0 ±2,3	70,1 ±0,41	73,2 ±1,02	72,0 ± 1,69	60,3 ±3,05
Moisture content, %.	4,2 ±0,66	5,4 ±0,6	3,41 ±0,28	2,0 ±0,50	2,3 ±0,58	1,4 ±0,44	0,5 ±0,25
Appearance	P	P	NP	NA	NA	NA	RS

Notes: The data are taken from five definitions.

"P" - adhesion of the tablet mass to the press tool.

"NP" - slight adhesion.

"NA" - no adhesion.

"RS" - rough surface.

The analysis of the data in Table 10 shows that the optimum residual moisture content of the tablet mass is between 2% and 3%. If the value exceeds 3%, the tablet has poor pressability, and sticking of the tablet mass to the press tool is observed.

3.2. Brief description of the manufacturing technology of tablets with dry clover and calendula extract

The tablet manufacturing process must be carried out in compliance with sanitary and hygienic requirements aimed at preventing microbial contamination of raw materials, intermediates and finished products (Figure 14).

Stage 1: Preparation of raw materials.

Powder of dry extracts and excipients, according to the regulatory documentation (calculation for a series) is weighed on an electronic balance.

Stage 2: Preparation of the tablet mass.

The pre-weighed powders are loaded into the mixer and mixed thoroughly for 5-10 minutes. Control the homogeneity of the mass. After that, the resulting mass for pressing is powdered with AEROSIL® 200 Pharma, stirring the mixture for no more than 3 minutes.

Stage 3: Tableting and dedusting.

In industrial production conditions, tablets are obtained on rotary tablet presses, using punches with a diameter of 10 mm, and then dedusted. Control of the intermediate product is conducted in accordance with the requirements of the DFU.

Stage 4. Packaging of tablets.

Tablets are packed in ten pieces in contoured cellular packaging on a filling machine. In the process, the quality of heat sealing, the number of tablets in a blister, and the correctness of labeling are controlled.

Stage 5. Packing in packs.

During the packaging process, the labeling on the packs (which must match the labeling of the original packaging) and the completeness of the package are checked.

Stage 6. Packing the packs in boxes.

It is conducted on a packing table (cardboard packs are placed in boxes - group

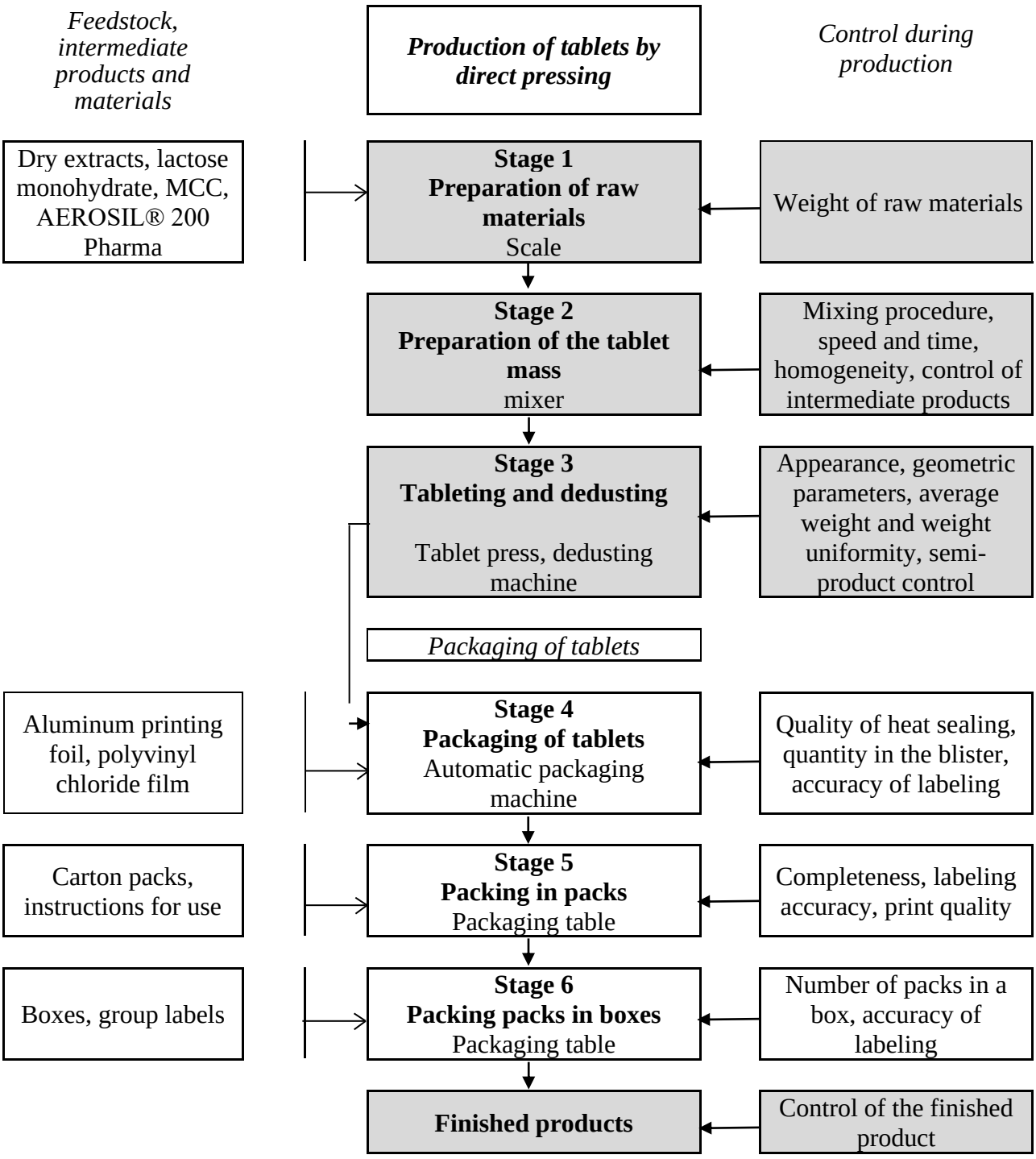


Figure 14. Flow chart of production of tablets with dry extracts of clover and calendula

packaging) with appropriate labels and markings.

Finished products.

Quality control is conducted in the quality control department of the pharmaceutical enterprise in accordance with regulatory documents.

CONCLUSIONS TO SECTION III

1. As a result of technological studies, the shape and particle size of dry clover and calendula extract were studied. The physicochemical and pharmacotechnological properties of the substance and the kinetics of moisture absorption were studied. The results of the study made it possible to predict the possibility of using the direct pressing method in the production of tablets.
2. Excipients were selected as the most commonly used in direct pressing. The concentration of each component was selected experimentally and the effect of each excipient on the quality of tablets was studied.
3. AEROSIL® 200 Pharma was chosen as a moisture-absorbing agent in the amount of 1%. The amount of aerosil is sufficient to obtain a fluid mass.
4. The method of obtaining tablets - direct pressing - was substantiated, the technology of their production was developed, and the corresponding technological scheme was drawn up.

GENERAL CONCLUSIONS

1. The study of the scientific literature made it possible to establish the prevalence of cardiovascular diseases and to prove the relevance of creating new effective drugs.

2. An analysis of the range of drugs based on plant materials for the treatment of cardiovascular diseases in the Ukrainian market was carried out and the creation of a solid dosage form with plant materials was substantiated.

3. In solving this problem, medicines of plant origin play an important role, therefore, dry clover extract was chosen as an active ingredient as a promising raw material of this direction of action.

4. The conducted research allowed us to substantiate the method of tablet preparation and select excipients. The influence of each excipient on the quality of the obtained tablets was studied.

5. The technology for the preparation of tablets was developed and a technological scheme for their production using the direct pressing method was drawn up. The obtained tablets meet the requirements of the State Food Administration in all respects.

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APPENDIXES

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 Industrial Technology of Drugs
Olena RUBAN

_____

" 15 " of May 2022

ASSIGNMENT
FOR QUALIFICATION WORK
OF AN APPLICANT FOR HIGHER EDUCATION

Ibtissam ELUZZANI

1. Topic of qualification work: «Selection of excipients and study of their influence on quality indicators of tablets with dry extract of clover and calendula», supervisor of qualification work: Halyna SLIPCHENKO Ph, 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: dosage form: tablets, active ingredients: dry clover and calendula extract, tablet masses, finished tablets.

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 – 8
figures – 14

6. Consultants of chapters of qualification work

Chapters	Name, SURNAME, position of consultant	Signature, date	
		assignment was issued	assignment was received
I Chapter	Halyna SLIPCHENKO, associate professor of the of higher education of the department of Industrial Technology of Drugs	20.05.2022	20.05.2022
II Chapter	Halyna SLIPCHENKO, associate professor of the of higher education of the department of Industrial Technology of Drugs	15.12.22 - 21.01.2023	15.12.22 - 21.01.2023
III Chapter	Halyna SLIPCHENKO, associate professor of the of higher education of the department of Industrial Technology of Drugs	18.02.2023	18.02.2023

7. Date of issue of the assignment: 15 of 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 _____Ibtissam ELUZZANI

Supervisor of qualification work _____Halyna SLIPCHENKO

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

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

Прізвище студента	Тема кваліфікаційної роботи		Посада, прізвище та ініціали керівника	Рецензент кваліфікаційної роботи
• **по кафедрі заводської технології ліків**				
Елюззані Ібтіссаме	Вибір допоміжних речовин та вивчення їх впливу на показники якості таблеток з сухим екстрактом конюшини та календули	Selection of excipients and study of their influence on quality indicators of tablets with dry extract of clover and calendula	доц. Сліпченко Г.Д.	доц. Буряк М.В.

Підстава: подання, заява, згода ректора

Ректор

Вірно. Секретар

Ф А2.8-47-110

ВИСНОВОК

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

№ 112912 від « 2 » травня 2023 р.

Проаналізувавши випускну кваліфікаційну роботу за магістерським рівнем здобувача вищої освіти денної форми навчання Елюззані Ібтіссаме, 5 курсу, __1 англ._ групи, спеціальності 226 Фармація, промислова фармація, на тему: «Вибір допоміжних речовин та вивчення їх впливу на показники якості таблеток з сухим екстрактом конюшини та календули / Selection of excipients and study of their influence on quality indicators of tablets with dry extract of clover and calendula», 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**

10%
28%

F A 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

Ibtissam ELUZZANI

on the topic: «Selection of excipients and study of their influence on quality indicators of tablets with dry extract of clover and calendula»

Relevance of the topic. Cardiovascular diseases, mainly coronary heart disease and stroke, are the leading causes of death and one of the main factors of disability worldwide. In Ukraine, cardiovascular diseases are the leading cause of mortality. The development of new drugs based on plant materials is an urgent issue.

Practical value of conclusions, recommendations and their validity. The article analyzes the scientific literature on the prevalence of cardiovascular diseases, their causes, methods of treatment and the range of medicines for the treatment of this disease. The author proves that the range of domestic drugs based on plant materials is not large, which indicates the feasibility of developing a new domestic drug in the form of tablets. The excipients for the creation of tablets were selected experimentally and their influence on the quality indicators of tablets was studied.

Assessment of work. The qualification work was performed at a high scientific level. The results of the experiments are statistically processed and presented in the paper in the form of tables and figures. The conclusions are summarized, which is the logical conclusion of theoretical and experimental studies.

General conclusion and recommendations on admission to defend. The qualification work of Ibtissam ELUZZANI 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 _____ Halyna SLIPCHENKO

«05» of April 2023

F A 2.2.1-32-356

REVIEW
for qualification work of the master's level of higher education, specialty 226
Pharmacy, industrial pharmacy
Ibtissam ELUZZANI
on the topic: «Selection of excipients and study of their influence on quality indicators of tablets with dry extract of clover and calendula»

Relevance of the topic. The author of the paper proves the high prevalence of cardiovascular diseases. The occurrence and course of cardiovascular and cerebrovascular diseases are closely related to the presence of risk factors, the main ones being high blood pressure, impaired lipid metabolism, overweight, and unhealthy lifestyle. Dry clover and calendula extracts were chosen as active ingredients.

Theoretical level of work. Based on the literature data, the author discusses the etiology and pathogenesis of diseases, identifies existing drugs and characterizes the main directions of solving this problem.

Author's suggestions on the research topic. The concentrations of API (dry clover extract) and excipients (AEROSIL® 200 Pharma, lactose monohydrate and MCC) were proposed and experimentally confirmed. The pharmacotechnological properties of the active substance were studied and the technology of its preparation was substantiated.

Practical value of conclusions, recommendations and their validity. The scientific positions, conclusions and recommendations formulated in this paper are based on experimental data and logically follow from the results obtained. The reliability of the results obtained is confirmed by the significant amount of research performed and the statistical methods of their processing.

Disadvantages of work. There are spelling and grammatical mistakes in the work.

General conclusion and assessment of the work. The qualification work of Ibtissam ELUZZANI 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. Maryna BURYAK

«10» of 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 Ібтіссаме ЕЛЮЗЗАНІ про представлення до захисту в Екзаменаційній комісії НФаУ кваліфікаційної роботи на тему: «Вибір допоміжних речовин та вивчення їх впливу на показники якості таблеток з сухим екстрактом конюшини та календули».

(Керівник: д.фарм.н., доцент Галина СЛІПЧЕНКО).

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

УХВАЛИЛИ: рекомендувати до захисту в Екзаменаційній комісії НФаУ кваліфікаційну роботу здобувача вищої освіти факультету з підготовки іноземних громадян групи Фм18(4,10д)англ-1 Ібтіссаме ЕЛЮЗЗАНІ тему: «Вибір допоміжних речовин та вивчення їх впливу на показники якості таблеток з сухим екстрактом конюшини та календули».

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 здобувачка вищої освіти Ібтіссаме ЕЛЮЗЗАНІ до захисту кваліфікаційної роботи

за галуззю знань 22 Охорона здоров'я

спеціальністю 226 Фармація, промислова фармація

освітньою програмою Фармація

на тему: Вибір допоміжних речовин та вивчення їх впливу на показники якості таблеток з сухим екстрактом конюшини та календули».

Кваліфікаційна робота і рецензія додаються.

Декан факультету _____ / Світлана КАЛАЙЧЕВА /

Висновок керівника кваліфікаційної роботи

Здобувачка вищої освіти Ібтіссаме ЕЛЮЗЗАНІ у процесі своєї роботи розробив таблетки з сухими екстрактами конюшини та календули. Технологія отримання відповідає усім вимогам ДФУ. Ібтіссаме ЕЛЮЗЗАНІ допускається до захисту кваліфікаційної роботи в Екзаменаційній комісії Національного фармацевтичного університету.

Керівник кваліфікаційної роботи
_____ Галина СЛІПЧЕНКО

« 5 » квітня 2023 року

Висновок кафедри про кваліфікаційну роботу

Кваліфікаційну роботу розглянуто. Здобувач вищої освіти Ібтіссаме ЕЛЮЗЗАНІ 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 Examination commission on

« ___» of June 2023

With the grade _____

Head of the State Examination commission,

DPharmSc, Professor

_____/ Oleh SHPYCHAK /