Ф А 2.2.1-32-367

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QUALIFICATION WORK

on the topic: «**RESEARCH ON THE COMPOSITION AND TECHNOLOGY OF A HYPOLIPIDEMIC DRUG»**

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Фм20(4,10d)англ-02
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Kharkiv – 2025

ANNOTATION

This work is aimed at the development of hard gelatin capsules based on a liquid extract obtained from a tincture. Extraction methods for tincture were compared, a liquid extract was obtained, and the adsorption properties of the filler were investigated to ensure the technological process. The work carried out showed the possibility of improving the existing drug.

The work consists of the following parts: review of literary sources, materials and methods of research, experimental part, general conclusions, list of sources used, appendices. The total volume of the work is 47 pages, contains 9 tables, 3 figures, 34 sources of literature.

Keywords: liquid extract, medicinal plant raw materials, technology, hard gelatin capsules, cardiovascular diseases.

АНОТАЦІЯ

Дана робота спрямована на розробку твердих желатинових капсул на основі рідкого екстракту отриманого з настойки. Порівняно методи екстракції для настойки, отримано рідкий екстракт та досліджено адсорбційні властивості наповнювача для забезпечення технологічного процесу. Проведена робота показала можливість вдосконалення існуючого препарату.

Робота складається з наступних частин: огляд літературних джерел, матеріали та методи дослідження, експериментальна частина, загальні висновки, список використаних джерел, додатки. Загальний обсяг роботи 47 сторінок, містить 9 таблиць, 3 рисунки, 34 джерел літератури.

Ключові слова: рідкий екстрак, лікарська рослинна сировина, технологія, тверді желатинові капсули, серцево-судинні захворювання.

CONTENTS

LIST OF USED ABBREVIATIONS

API – Active pharmaceutical ingredients;

CHD – Coronary heart disease;

CVD – Cardiovascular diseases;

GMP – good manufacturing practice;

HDL – High-density lipoproteins;

LDL – Low-density lipoproteins;

MCC – Microcrystalline cellulose;

MPRM – medicinal plant raw materials;

NCDs – Noncommunicable diseases;

SPU – State Pharmacopoeia of Ukraine;

WHO – World Health Organization.

INTRODUCTION

Actuality of theme. Cardiovascular diseases (CVD) remain a serious health problem in Ukraine and around the world. Sad statistics show that they are the main cause of disability and premature death. Diverse in nature, from rhythm disorders to heart defects, CVD are united by a common target - the heart and vessels that provide vital blood flow. Violation of their function causes a whole wave of negative consequences for the entire body. Therefore, for the effective operation of the health care system, timely forecasts of the incidence of CVD and the implementation of effective preventive measures are necessary. Among the many factors contributing to the development of heart disease, atherosclerosis occupies a special place. This chronic process of damage to the arteries is characterized by the deposition of lipids, primarily cholesterol, on the walls and the formation of atherosclerotic plaques. Over time, these plaques increase, narrowing the lumen of the vessels and preventing normal blood flow. Research into the mechanism of atherosclerotic plaque formation is crucial for developing effective therapeutic approaches, and modern medicine requires a deeper understanding of this process.

The consequences of atherosclerosis are extremely dangerous. Restriction of blood flow leads to insufficient supply of organs and tissues with oxygen and nutrients. If the coronary arteries that feed the heart are affected, ischemic disease develops, manifested by angina attacks. Complete blockage of such an artery by a thrombus can cause myocardial infarction - irreversible damage to the heart muscle. Similarly, atherosclerosis of cerebral vessels can cause stroke, which leads to severe neurological disorders. Accordingly, timely detection and treatment of atherosclerosis significantly reduces the risk of serious complications.

Thus, atherosclerosis is a fundamental problem that underlies the development of many heart diseases. Understanding its essence, knowledge of risk factors, and development of effective prevention and treatment strategies are an urgent need to preserve the health of the nation. In this context, along with traditional medical approaches, increasing attention is being paid to the possibilities of using medicinal

plants in the complex fight against atherosclerosis. Systematic research on the various biologically active compounds contained in medicinal plants and their complex effects on the cardiovascular system, including the regulation of lipid metabolism, strengthening the vascular wall, improving microcirculation and antioxidant protection, opens new horizons in the development of natural remedies for maintaining heart and vascular health, offering the potential for both prevention and adjuvant treatment of cardiovascular pathologies.

The purpose of the study. Develop the composition and technology of hard gelatin capsules using components of a complex tincture.

Research tasks:

1. To review the literature on cardiovascular diseases and determine their current status

2. To present information on the incidence of atherosclerosis and describe current knowledge about the disease;

3. To justify the course of the study, to describe the main components of the objects and research methods;

4. To investigate the feasibility of changing the extraction method, to check and compare the main quality indicators of the obtained samples;

5. To experimentally substantiate excipients for forming the mass for filling capsules.

6. To propose a production technology in the form of a technological flowchart and to present its brief description.

Research objects. Composition and production technology of hard gelatin capsules using liquid extract as an active pharmaceutical ingredient.

The subject of research. Medicinal plant raw materials, complex tincture, liquid extract, excipients, hard gelatin capsules.

Research methods. A complex of scientific research methods was applied, which included theoretical analysis of literary sources, synthesis of data, a logical approach to constructing hypotheses and conclusions, and the formation and conduct

of an experiment, which included physical, chemical, technological, computational, and statistical methods.

Practical significance of the obtained results. An existing drug has been improved by obtaining a more convenient dosage form.

Approval of research results and publication. A fragment of the work was published as a thesis: Трутаєв С. І., Халід Л. Аналіз фармацевтичного ринку гіполіпідемічних засобів та обґрунтування розробки фітопрепарату для корекції гіперліпідемії. The XXI International scientific and practical conference «Modern technologies and science: problems, new and relevant developments», May 26-28, 2025, Zaragoza, Spain.

Structure and scope of qualification work: The work consists of the following parts: review of literary sources, materials and methods of research, experimental part, general conclusions, list of sources used, appendices. The total volume of the work is 47 pages, contains 9 tables, 3 figures, 34 sources of literature.

CHAPTER 1. REVIEW OF LITERARY SOURCES

1.1 Overview of cardiovascular disease and risk factors

Noncommunicable diseases (NCDs) are chronic conditions caused by a complex interaction of genetic, physiological, environmental and behavioural factors. The main types of NCDs include cardiovascular diseases, cancer, chronic respiratory diseases and diabetes. Of particular concern is that NCDs disproportionately affect low- and middle-income countries, where almost three-quarters of all deaths from these diseases occur worldwide, highlighting global health inequalities [1]. The global problem of noncommunicable diseases, known as ‘cardiovascular disease’ (CVD), continues to be the leading cause of death worldwide, claiming the lives of almost 18 million people each year. According to the STEPS study conducted in 2019, CVDs account for 63% of deaths from NCDs in Ukraine, one of the highest rates in the world [2].

CVD is a large and diverse group of diseases affecting the heart and circulatory system, including conditions such as coronary heart disease, cerebrovascular disorders, rheumatic heart disease and a range of other pathological processes. Unfortunately, more than four out of five deaths from CVD are due to acute heart attacks and strokes, and it is alarming that a third of these premature deaths occur in people under the age of 70, highlighting the problem of premature loss of human potential [2,3]. The primary risk factors that need to be addressed in the development of heart disease and stroke, according to the World Health Organization (WHO), are indifferent patterns of behavior of people towards their health, which include unhealthy diets, insufficient physical activity, tobacco addiction and harmful use of alcohol. Along with this, adverse environmental conditions, among which air pollution plays a key role, have a significant impact on the occurrence of CVD. The negative consequences of these factors are reflected in a number of measurable physiological indicators, such as a persistent increase in blood pressure, an increase in blood glucose levels, impaired lipid profile, excess body weight, which is subsequently expressed as obesity. Such risk factors can be

easily detected in primary health care institutions and are a reliable indicator of an increased likelihood of developing myocardial infarction, stroke, heart failure and other serious complications from the cardiovascular system [4].

According to the WHO Noncommunicable Diseases Data Portal, "Noncommunicable Diseases and Key Risk Factors", section "Cardiovascular diseases" for Ukraine are [5]:

- Probability of premature mortality from NCDs – from 30 to 40%;
- Percentage of total mortality from NCDs – more than 90%;
- Age-standardized mortality rate:
  - from NCDs – from 600 to 750 per 100,000 population;
  - from CVDs – from 400 to 500 per 100,000 population;
- Percentage of deaths among people under 70 years of age:
  - from NCDs – from 30 to 40%;
  - from CVDs – less than 30%.
- For people aged 30 to 79, the following is defined:
  - Elevated blood pressure – 35 to 40 percent;
  - Hypertension (30-79 years) – 40 to 45 percent;
  - Diagnosed hypertension – 60 – 70%;
  - Taking medication for hypertension – 40-50%;
  - Controlled hypertension – 10-15%.

Unhealthy diets are also a global health problem, driven by the overproduction and consumption of unhealthy foods. Excessive consumption of sodium, sugar and unhealthy fats, as well as a lack of whole grains, vegetables and fruits, are particularly dangerous. An estimated 1.89 million deaths per year are attributed to excess sodium, which leads to hypertension and cardiovascular disease. Reducing sodium intake is a cost-effective way to improve health. The WHO recommends reducing the sodium content of foods, introducing labelling, conducting information campaigns and controlling public food procurement. These measures will help prevent a wide range of cardiovascular diseases and reduce health care costs [6]. Hypertension, or high blood pressure, affects a large number of adults worldwide,

especially in low- and middle-income countries. Many people do not know they have hypertension because it is often asymptomatic. Diagnosis and treatment of hypertension remain inadequate, and only a small proportion of patients control their condition. Hypertension is a serious health threat that leads to premature death. Risk factors include age, genetics, overweight, physical inactivity and poor diet. Lifestyle changes and drug treatment can help reduce blood pressure. The global community aims to reduce the prevalence of hypertension by 2030 [7].

International experience demonstrates that blood pressure control can be successfully integrated into primary care, providing cost-effective treatment. This reduces the risk of cardiovascular complications such as heart attacks and strokes. For effective treatment, patients must have unhindered access to modern medical technologies and essential medicines. Such drugs include aspirin, beta-blockers, ACE inhibitors and statins. Ensuring the availability of these medicines at the primary care level is key to improving population health and reducing the burden of cardiovascular disease [8].

Ukraine supports the global trend of helping patients with CVD and, according to the data published by the Ministry of Health of Ukraine on the official website for World Heart Day 2024, included the following achievements. In 2024, the National Health Service of Ukraine actively finances the treatment of acute myocardial infarction, cooperating with 78 hospitals throughout Ukraine. About 23 thousand patients have already received the necessary treatment, and the total amount of payments to hospitals exceeded 844 million hryvnias. 49 heart transplants have been performed in Ukraine, which have been financed by the Medical Guarantees Program since 2024, and 36 medical institutions provide organ transplantation services, and payment for post-transplant support services for patients is also available. The Affordable Medicines program plays a key role in providing patients with the necessary drugs for the treatment of cardiovascular diseases. Currently, the program includes 229 trade names of medicines, and from September 2024 the list will expand to 241 items. More than 1.6 million patients have already used e-prescriptions to obtain the necessary medications [9].

1.2 Atherosclerosis

According to the WHO, the most common cause of death in the world as of 2021 was coronary heart disease, accounting for 13% of all deaths worldwide. Coronary heart disease (CHD) is caused by atherosclerotic plaques in the arteries that supply blood to the heart. It can be either partially or completely blocked. CHD can be controlled through lifestyle changes, medications, and invasive procedures that slow its progression. CHD can be stable, but at any time an acute complication can occur due to plaque rupture. It is a chronic disease that progresses even in the absence of symptoms [10].

Atherosclerosis (from the Greek "athere" - porridge and "skleros" - hard) is a chronic systemic inflammatory disease characterized by the appearance of foci of lipid infiltration in the walls of the arteries and the growth of connective tissue with the formation of fibrous plaques that narrow the lumen of the arteries, which leads to organ and general circulatory disorders. It is generally accepted that atherosclerosis develops under the influence of a number of risk factors. Among them are [11]:

- high levels of «bad» cholesterol (Low-density lipoproteins, LDL): this is a key factor contributing to the formation of atherosclerotic plaques;
- arterial hypertension: high blood pressure damages the walls of the arteries, creating conditions for the development of atherosclerosis;
- diabetes: impaired glucose metabolism negatively affects the condition of the vessels;
- smoking tobacco products: toxins in tobacco smoke damage the endothelium of the arteries;
- age: the risk increases in men over 45 years of age and women over 55 years of age;
- gender of the patient: men are more prone to atherosclerosis;
- heredity: the presence of cardiovascular diseases in close relatives increases the risk of developing atherosclerosis.

There is currently no generally accepted classification of atherosclerosis, so we will present some that are accepted in medical practice.

1. By localization:

- atherosclerosis of the aorta;
- atherosclerosis of the precerebral, cerebral arteries;
- atherosclerosis of the coronary arteries;
- atherosclerosis of the renal arteries;
- atherosclerosis of the mesenteric arteries;
- atherosclerosis of the vessels of the lower extremities.

2. By origin: clinicopathogenetic forms:

- hemodynamic (in arterial hypertension and other vascular disorders);
- metabolic;
- mixed.

3. By periods and stages of the disease:

- preclinical, latent period;
- period of clinical manifestations:
    - ischemic stage;
    - necrotic (thrombonecrotic) stage;
    - sclerotic (fibrotic) stage.

4. By phases of disease progression:

- progression;
- stabilization of the process;
- regression.

Atherosclerosis develops in four stages [12]. In the first stage, cholesterol begins to accumulate in the inner lining of the arteries, forming a fatty layer. This most often occurs in young people and is reversible with lifestyle changes and medication.

In the second stage, a fibrous plaque forms, which narrows the lumen of the artery. This stage is usually irreversible and requires medical treatment or medical procedures such as angioplasty or stenting.

In the third stage, a complicated plaque is formed, which can rupture, causing a heart attack or stroke. Treatment includes blood-thinning drugs and surgery to remove or strengthen the plaque.

In the fourth and final stage, the artery is completely blocked and blood flow is stopped. This condition is life-threatening and requires urgent surgery such as bypass surgery or a heart transplant. The development of atherosclerosis is schematically presented in Fig. 1.1.

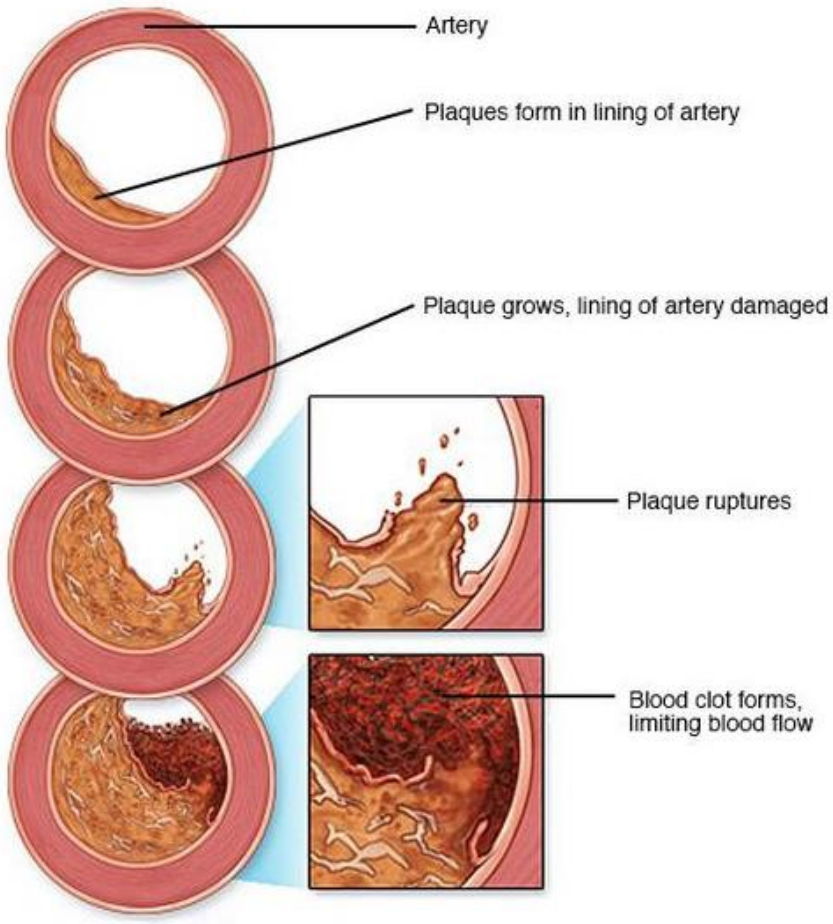

Fig. 1.1 Stages of atherosclerosis development

The formation of atherosclerotic plaque is a complex and gradual process that occurs in the walls of arteries. It begins with damage to the inner layer of the arterial

wall, called the endothelium. The damage can be caused by various risk factors related to both hypertension and atherosclerosis: high blood pressure, smoking, high blood cholesterol, diabetes, obesity, or chronic inflammation [13].

After damage to the endothelium, lipids, especially low-density lipoproteins, begin to penetrate the vascular wall. They become oxidized and cause a local inflammatory response. The immune system responds by recruiting monocytes, blood cells, to the site of damage, which migrate into the tissue and transform into macrophages. Macrophages actively absorb the oxidized lipids, transforming into so-called foam cells. These cells accumulate in the vessel wall and form a fatty streak - an early stage of atherosclerotic plaque. Over time, a fibrous capsule of connective tissue develops around the fatty streak. Smooth muscle cells from the deeper layers of the artery are involved in the process, which migrate to the inner layer, multiply and secrete components of the intercellular substance. As a result, a mature atherosclerotic plaque is formed, consisting of a lipid core and a dense fibrous shell. An atherosclerotic plaque can increase in size over time, narrowing the lumen of the vessel and disrupting blood flow. In addition, the surface of the plaque can be destroyed, which leads to the formation of a thrombus - a blood clot that can partially or completely block the artery. This can cause serious consequences, such as myocardial infarction or stroke [14].

1.3 Phytotherapy in the treatment of atherosclerosis

Phytotherapy, or herbal medicine, goes beyond the simple use of plants. It is a holistic approach that considers the relationship between physical, emotional, and spiritual well-being. Unlike conventional medicine, which focuses on specific symptoms, herbal medicine seeks to restore harmony to the body as a whole. Herbs in herbal medicine are not considered “medicines” in the individual sense, but rather as agents that stimulate natural self-regulatory processes. However, despite their natural origin, they can be potentially toxic if misused. Therefore, it is important to consult qualified specialists with knowledge of herbal medicine [15].

Although the mechanisms of action of many herbs are not fully understood, most are known to have antioxidant properties. These properties play a key role in protecting cells from damage and may be beneficial in various diseases, including cardiovascular, neurodegenerative, and cancer. In addition, herbs can help detoxify the body, reducing the harmful effects of toxins and drugs. Thus, phytotherapy is not just an alternative to traditional treatment, but a comprehensive approach to health that can be effective in combination with other methods [16].

For centuries, natural remedies have played an important role in the fight against cardiovascular diseases. In recent decades, with the growing interest in natural products, especially medicinal herbs, natural compounds that can effectively counteract atherosclerosis have been actively studied. In modern medicine, in addition to the traditional strategy of lowering cholesterol levels, methods of combating atherosclerosis at the cellular level are actively studied. New studies of the pathogenesis of atherosclerosis show that the disease begins with damage to the inner layer of large and medium-sized arteries, especially at the branches. Turbulent blood flow in these areas creates an increased load, damaging endothelial cells. This leads to the involvement of immune cells, which, in turn, contribute to the accumulation of modified low-density lipoproteins in the walls of the arteries. Oxidized LDLs are taken up by macrophages, which, when cholesterol metabolism is disturbed, transform into foam cells, enhancing the atherosclerotic process [17].

Medicinal plants that are effective in combating atherosclerosis act in a complex manner, providing anti-inflammatory, antioxidant, hypolipidemic, hypotensive and antithrombotic effects. The combined effect of biologically active substances allows for simultaneous influence on several risk factors of atherosclerosis. Pharmacological components isolated from plants are relatively safe and have fewer side effects, which makes them promising for the development of new anti-atherosclerotic drugs. Clinical trials confirm the direct anti-atherosclerotic effect of a number of medicinal plants [18].

Some examples of proven anti-sclerotic activity of medicinal plants are presented below from scientific articles from the PubMed database.

Study Yang, J. X. et al. It was found that the hypolipidemic activity and anti-atherosclerotic effect of *Polygonatum sibiricum* have significant potential in the fight against atherosclerosis, acting at two key levels: directly reducing blood lipid levels and indirectly protecting endothelial cells from apoptosis and necrosis. In addition, PPGS has a positive effect on smooth muscle cells and other cytokines, which together provide a pronounced anti-atherosclerotic effect. This effect has been confirmed both at the cellular level and in animal studies [19].

A review article on the potential uses of hawthorn Wu, M. et al. shows that they have pronounced anti-atherosclerotic properties, due to four main mechanisms: lowering blood lipid levels, antioxidant, anti-inflammatory effects and protection of the vascular endothelium. These properties make hawthorn a promising tool for the prevention and treatment of atherosclerosis, which confirms the need for further research into its therapeutic potential [20].

Regarding Mistletoe (*Viscum album L.*), there are many scientific reports on its therapeutic activity. It is also known that it has long been used in folk medicine to treat cardiovascular diseases. Modern studies confirm the presence of cardioprotective properties in mistletoe, but most experiments were conducted in vitro or on animals. Clinical trials are necessary to determine the effectiveness and safety of mistletoe for humans. A debatable fact is the chemical composition of mistletoe extracts, which can vary depending on many factors, which complicates the standardization of drugs. The mechanisms of the cardioprotective action of mistletoe have not been fully studied, but researchers attribute it to the synergistic effect of various components [21, 22].

Sophora japonica L. contains rutin, a flavonoid with potent antioxidant properties that has the potential to treat cardiovascular diseases. Rutin effectively reduces inflammation by reducing pro-inflammatory markers. Although clinical data are limited, natural sources of rutin have shown positive effects on metabolic function. Rutin improves endothelial function, promotes vasodilation, and supports vascular homeostasis. Despite the large amount of information, researchers

recommend further clinical studies to confirm the therapeutic properties of rutin [23, 24].

Aesculus hippocastanum contains escin, which is a valuable phytocompound with proven efficacy in the treatment of cardiovascular diseases. Its anti-edematous, anti-inflammatory, and venotonic properties make it a promising agent for the prevention and treatment of atherosclerosis. Escin reduces vascular permeability in inflamed tissues, preventing the formation of edema, which is especially important in atherosclerosis, which is often accompanied by inflammation and impaired microcirculation. It also improves venous vascular tone, which may be useful in cases of venous insufficiency associated with atherosclerotic changes [25, 26].

Mushrooms have received a new direction in the study of natural raw materials with therapeutic potential for the prevention and/or treatment of atherosclerosis. Studies by Ramakrishnan M. et al. (2017) show that edible oyster mushrooms, such as *Pleurotus ostreatus, Hypsizygus ulmarius* and *Agaricus djamor*, contain lovastatin, a substance that lowers cholesterol levels. The content of lovastatin varies depending on the type of mushroom and cultivation conditions, with the maximum amount found in *P. ostreatus*. The analysis was performed using UV spectrophotometry and high-performance liquid chromatography for the quantitative and qualitative determination of lovastatin. These studies aim to investigate the potential of mushrooms in the treatment of hypercholesterolemia, although the mechanisms and efficacy require further study [27].

In another example, Katarzyna Kała, et al. (2020) reported that edible mushrooms such as *Agaricus bisporus*, *Cantharellus cibarius, Imleria badia*, and *Lentinula edodes* contain lovastatin, a cholesterol-lowering substance. The highest lovastatin content was found in *C. cibarius* and the lowest in *L. edodes*. However, the release of lovastatin into the digestive juices from the mushrooms was relatively low. Interestingly, the mycelium of *L. edodes* grown in laboratory conditions showed the ability to accumulate lovastatin from the culture medium, making it potentially useful for the creation of products with hypolipidemic activity. Thus, these mushrooms may be promising for the prevention of hypercholesterolemia [28].

Conclusions to chapter 1

1. The key areas of modern scientific knowledge in the field of cardiovascular diseases are summarized, which allowed us to determine the current state of the problem.

2. A review of the literature on the general picture of the incidence of atherosclerosis and its prevalence among the population is provided.

3. Modern fundamental and clinical knowledge of atherosclerosis is described, including development mechanisms, risk factors and possible complications.

4. An analysis of the literature on the use of phytotherapeutic agents in the treatment of atherosclerosis is presented, with an emphasis on their potential benefits and limitations.

5. Promising areas of further research in the field of prevention and complex treatment of cardiovascular diseases, in particular atherosclerosis, using medicinal plants are identified.

CHAPTER 2. RESEARCH OBJECTS AND METHODS

2.1 Justification for the creation of a new dosage form

The creation of a solid dosage form based on tincture is a reasonable and promising approach to improving herbal medicines. Despite the widespread use of tinctures in the form of liquid dosage forms, their use is associated with a number of limitations that can be eliminated by developing an alternative form, in particular, hard gelatin capsules containing a liquid extract [29, 30].

Tinctures contain a significant amount of ethanol, which limits their use in certain groups of patients: children, pregnant women, people with liver and central nervous system diseases. The transition to a solid form allows either to completely eliminate or significantly reduce the alcohol content by removing the liquid phase and stabilizing the extract.

Also, the inconvenience of dosing liquid forms can be difficult for the patient and require the use of measuring utensils. The solid form, in turn, provides an accurate and reproducible dose, which improves control over treatment and helps to increase patient compliance.

In addition, solid dosage forms, especially capsules, have better masking of organoleptic properties compared to tinctures, which is especially important when using bitter taste or specific smell of plant components. This makes taking the drug more comfortable and acceptable even for sensitive patients.

Solid dosage forms have advantages in terms of storage and transportation. They are more resistant to external conditions (light, air, temperature fluctuations), do not require special dosage conditions and have a standardized content of the drug composition.

Thus, the transfer of a herbal medicine from a tincture to a solid dosage form allows you to increase its pharmaceutical and consumer value, ensure safety and convenience of use, and also expand the target audience. All this makes the development of solid dosage form with a liquid extract a rational direction for improving the technology of herbal medicines.

Among the dosage forms, hard capsules occupy a special place, which is due to their pharmaceutical versatility, which determines the high degree of their adaptability to different groups of medicinal substances. A comparative analysis of capsules and tablets as forms of solid medicinal products allows us to highlight a number of key facts [29, 30].

First of all, it is possible to note the expanded possibilities of the capsule form in terms of the composition and aggregate state of encapsulated substances. Unlike tablets, which require mandatory pressing and most often preliminary granulation, capsules allow the encapsulation of not only powdery, but also liquid, pasty and oily systems. This feature significantly expands the range of pharmacologically active substances suitable for inclusion in the composition of this form. Also, compared to tableting, capsules usually require a smaller number of excipients in industrial production.

The organoleptic characteristics of capsule preparations are usually more favorable than tablets, since the gelatin shell provides effective isolation of the taste and smell of the contents from the receptor zones of the oral cavity. This circumstance is of particular importance when using compounds with pronounced organoleptic properties, as well as in pediatric and geriatric practice, where high taste sensitivity of patients can make it difficult to comply with the drug intake regimen.

In some cases, capsules are characterized by a higher rate of release of the active substance. This is especially true when using intracapsular fillers in the form of solutions or powders with a high specific surface area. Similar pharmacokinetic features can be useful in the creation of drugs that require a rapid onset of therapeutic effect.

Capsules have improved swallowing characteristics compared to tablets. Their smooth surface, streamlined shape and the absence of sharp edges facilitate intake, reducing the likelihood of discomfort when swallowing.

It should be noted that capsules have found their place in the manufacture of individual drugs, as they provide great flexibility in individualizing the dosage.

This combination of the above factors allows us to consider hard capsules as a promising dosage form, which has a number of advantages compared to tablets, which suggests their feasibility in creating a drug based on a liquid extract of MPRM.

2.2 Objects of research

The prototype for the creation of hard gelatin capsules was an existing drug from the group of hypolipidemic drugs in the form of a tincture based on medicinal plant raw materials called "Ravisol". In the experimental part, we plan to use the finished tincture, MPRM, which is part of the tincture, a water-alcohol mixture of ethanol (40%), hard gelatin capsules and excipients for forming the mass for encapsulation. The composition of the tincture is given in Table 2.1.

Table 2.1

Composition of the tincture "Ravisol"

№	Composition components		Quantity, g
1	Mistletoe shoots and leaves	*Visci albi cormi et folia*	1,5
2	Horsetail grass	*Equiseti arvensis herba*	1,0
3	Sophora japonica fruits	*Sophora japonica fructus*	1,5
4	Horse chestnut seeds	*Hippocastani semina*	1,5
5	Hawthorn fruits	*Crataegi fructus*	2,0
6	Clover flowers	*Trifolii flores*	1,0
7	Periwinkle grass	*Vincae minoris herba*	1,5
8	Extractant ethanol 40%		

1. Viscum album. Raw material. Leafy shoots, individual leaves, stems and rarely fruits. Stems are forked-branched, cylindrical, woody, swollen at the nodes. Leaves are simple, short-petiolate, blunt at the apex, entire, thick, naked, with parallel veins. The color of the stems and leaves is from yellowish-green to brownish-green. The smell is weak. The taste is slightly astringent.

Uses. Mistletoe is a medicinal plant with a variety of pharmacological effects, which is traditionally used for the treatment of cardiovascular diseases. The vasodilator and hypotensive effect of mistletoe is due to its effect on vascular smooth muscle cells and vegetative regulation of tone. The plant normalizes heart rhythm and has a mild sedative effect, which is important in atherosclerosis, which is accompanied by tachycardia and emotional lability. Flavonoids and lectins of mistletoe suppress inflammatory processes in the vascular wall and improve microcirculation. The antioxidant effect of mistletoe prevents oxidative modification of lipoproteins and slows the formation of atherosclerotic plaques. The components of mistletoe have a mild immunomodulatory effect, restoring balance in chronic inflammation. Thus, mistletoe has a complex effect on the cardiovascular system, which justifies its use in atherosclerosis.

2. Horsetail. Raw material. Stems are stiff, branched, jointed, hollow, with longitudinal grooves, up to 30 cm long. Branches are green, also jointed, directed obliquely upwards, unbranched 4-5-ribbed, collected 6-18 in rings. Leaves are underdeveloped and transformed into tubular, toothed sheaths that cover the nodes of stems and branches. Stem sheaths are cylindrical, 4-8 mm long. Teeth are fused in 2-3, triangular-lanceolate, dark brown with a white border; sheaths of lateral branches are green with 4-5 brownish bent teeth. At the base of the branches there are small brown sheaths, which when the branches are torn off remain on the stem in the form of a "vagina ring". Color is grayish-green. The smell is weak, peculiar. The taste is sour.

Application. Horsetail is a valuable phytotherapeutic agent that has a comprehensive effect on the body in atherosclerosis. The mild diuretic effect of horsetail helps to eliminate edema and lower blood pressure, which is important in concomitant cardiovascular insufficiency. Silicon compounds in horsetail strengthen the vascular wall, improving its elasticity and reducing capillary permeability. The antioxidant properties of horsetail reduce oxidative stress, which contributes to the development of atherosclerotic plaques. Horsetail stimulates metabolic processes and improves liver and kidney function, which contributes to the detoxification of

the body. The use of horsetail in phytotherapy for atherosclerosis allows for a comprehensive effect on blood vessels, water-salt balance and pathogenetic mechanisms of the disease.

3. Sophora japonica. Raw material. Beans are juicy, flattened-cylindrical, rachis-shaped, many-seeded, up to 10 cm long, up to 1 cm wide, green with a yellow stripe along the edge. Seeds are dark brown or almost black, up to 1 cm long, 0.4-0.7 cm wide; most seeds are immature. Odorless. Bitter taste.

Application. Sophora japonica is a promising source of rutin, a bioflavonoid with pronounced angioprotective properties, which makes it valuable in the pathogenetic therapy of atherosclerosis. Rutin helps stabilize the vascular wall, increasing its resistance to damage and reducing permeability, which prevents the penetration of low-density lipoproteins into the vascular wall. The antioxidant effect of rutin reduces oxidative damage to lipids, reducing the risk of atherosclerotic plaque formation. Sophora japonica also exhibits moderate anti-inflammatory effects, inhibiting the synthesis of anti-inflammatory mediators, which reduces chronic vascular inflammation. The antiplatelet effect of rutin helps reduce platelet aggregation, which is important for the prevention of thrombotic complications. Thus, Sophora japonica has a complex effect aimed at the key mechanisms of atherosclerosis development.

4. Horse chestnut. Raw material. Seeds of irregular spherical shape, up to 2-4 cm in diameter, slightly flattened, tuberculated, often flat on one side, covered with a smooth, shiny, dark brown shell with a large gray spot at the base. There is no smell. The taste is sweetish, then bitter. The escin content should be at least 7%.

Application. Chestnut fruits are used in herbal medicine for cardiovascular diseases, including atherosclerosis, due to their pronounced angioprotective and venotonic action. The main biologically active substance is escin, which strengthens the vascular wall and reduces its permeability. This helps reduce edema and improve microcirculation, especially in cases of impaired venous outflow. Chestnut preparations also improve the rheological properties of blood and reduce the risk of thrombosis. Antioxidant compounds in its composition protect the endothelium from

damage and inhibit the progression of atherosclerotic changes. The anti-inflammatory effect is realized through membrane stabilization and inhibition of hyaluronidase activity. The inclusion of chestnut fruits in medicinal preparations for atherosclerosis is pathogenetically justified and contributes to the comprehensive protection of the vascular system.

5. Hawthorn fruits. Raw material. The fruits are drupes, spherical or broadly ellipsoidal, hard, reticulate-wrinkled, 6-4 mm long, 5-11 mm wide, with a ring-shaped 5-toothed rim (remnants of sepals) on top; in the pulp of the fruit there are 1-5 light yellow woody seeds of irregular triangular shape; their surface is pitted-wrinkled or furrowed. The color of the fruits is yellow-orange, brownish-red to dark brown or black, sometimes with a white coating of crystallized sugar. There is no smell. The taste is sweetish.

Application. Hawthorn fruits, due to their rich composition, have a complex effect on the cardiovascular system, which makes them a valuable component of phytotherapy for atherosclerosis. The cardiotonic and vasodilator properties of hawthorn improve blood circulation and reduce peripheral resistance. The mild hypotensive effect of hawthorn helps to normalize blood pressure, which often accompanies atherosclerosis. The antioxidant activity of hawthorn reduces oxidative damage to lipids, slowing the progression of atherosclerotic changes. The moderate sedative effect of hawthorn helps to reduce emotional stress, which can aggravate the course of atherosclerosis.

6. Meadow clover. Raw material. Dry raw material is represented by whole inflorescences (heads) of meadow clover, consisting of many small flowers of pink or red color. Each inflorescence has a spherical or oval shape with a diameter of 2-3 cm. The flowers are irregularly shaped, 11-14 mm long, with a butterfly corolla and a tubular-bell-shaped calyx covered with hairs. At the base of the inflorescence are two close-fitting leaves. The leaves are trifoliate, with obovate or oval leaflets, finely toothed along the edges, with a characteristic light spot in the center.

Application. Meadow clover is a valuable phytoestrogen complex containing isoflavones, flavonoids and salicylates, which determines its therapeutic potential in

the prevention and treatment of atherosclerosis, especially in women in the menopausal period. Clover isoflavones have an estrogen-like effect, contributing to the normalization of the lipid profile, reducing the level of "LDL" cholesterol and increasing the level of High-density lipoproteins "HDL". Clover flavonoids exhibit antioxidant properties, protecting the vascular endothelium from oxidative damage and slowing the formation of atherosclerotic plaques. The plant has a mild vasodilator and antispasmodic effect, improving regional blood flow and reducing blood pressure. Clover salicylates have an antiplatelet effect, reducing the risk of thrombosis and preventing vascular complications. The hormone-regulating effect of isoflavones is especially important for women in the climacteric period, when endogenous estrogenic protection of vessels decreases.

7. Periwinkle small. Raw material. A mixture of leafy stems with flowers and without flowers, with leathery leaves of an elongated-elliptical shape. The edges of the leaves are entire, slightly rolled down. The color of the leaves is dark green, shiny on top, lighter on the bottom. The stems are light green. The flowers have a dark blue corolla, parts of the branch at the top are bluntly cut, the calyx is bare. There is no smell. The taste is not determined.

Application. Periwinkle small is a medicinal plant that has a pronounced vascular and neurotropic effect, which makes it valuable in the phytotherapy of atherosclerotic disorders, especially cerebrovascular. The main active ingredient of periwinkle is vincamine, an indole alkaloid, which promotes the expansion of cerebral vessels without systemic hypotension, improving microcirculation and oxygenation of neurons. Periwinkle exhibits moderate antiplatelet and angioprotective effects, improving the rheological properties of blood and preventing thrombotic complications. Periwinkle alkaloids have a mild sedative and antispasmodic effect, reducing the symptoms of neurovegetative dysregulation. The antioxidant activity of periwinkle flavonoids protects blood vessels and neurons from oxidative damage. Thus, periwinkle is effective in the complex treatment of atherosclerosis, especially with cerebrovascular manifestations.

Hard gelatin capsules are a solid two-component dosage form consisting of a cylindrical body and a tightly fitting cap. The capsule shell is made mainly of medical gelatin of animal origin, with the possible addition of plasticizers, dyes, preservatives and opaque substances.

Capsules are intended for filling with solid, free-flowing or pasty masses, including powders, granules and pellets. The filling process is carried out in dry conditions. Capsules can be transparent, opaque or painted in different colors. The shell dissolves in the stomach under the influence of gastric juice.

Capsule sizes are standardized and indicated by numbers (from 000 to 5), which allows you to adjust the volume of internal contents depending on the dosage and physicochemical properties of the medicinal substance.

Standard capsule sizes are presented in Table 2.2.

Table 2.2

Standard size of hard gelatin capsules

Capsule size	Volume (ml)	Approximate powder capacity* (mg)	Capsule length (mm)	Diameter (mm)
000	1,37	800–1600	26,1	9,9
00	0,95	600–1100	23,3	8,5
0	0,68	400–800	21,7	7,3
1	0,50	300–600	19,4	6,6
2	0,37	200–450	18,0	6,1
3	0,30	150–300	15,9	5,8
4	0,21	120–240	14,3	5,3
5	0,13	60–130	11,1	4,9

* – The approximate capacity depends on the bulk density of the powder. The lower the density, the less mass of the substance that can be contained in the capsule.

2.3 Research methods

To assess the pharmaco-technological properties of experimental samples of encapsulation masses, standard methods regulated by the State Pharmacopoeia of Ukraine were used. Studies were conducted on such indicators as granulometric

composition, moisture content, bulk density before and after compaction, fluidity, angle of natural slope, and the degree of mixing uniformity.

The determination of moisture content was carried out using an infrared moisture meter. 3 g of powder mass was used as a sample. Measurements were carried out at a temperature of 105 °C with an accuracy of 0.01% (1 mg). According to the requirements established for solid dosage forms, the moisture content should not exceed 5%.

The bulk density of samples of encapsulation masses was estimated as the ratio of the mass of the sample to the volume it occupied in the measuring cylinder. Consideration of the degree of moisture, dispersion, and other factors was mandatory, since they affect the volumetric characteristics of the powder. Calculations were carried out in accordance with clause 2.9.15 of the State Pharmacopoeia of Ukraine 2.0 (SPU).

The density after shrinkage was determined after mechanical compression of the sample in a cylinder using jumps with subsequent measurement of the volume of the layer of compacted material. Based on the data obtained, the bulk density before and after compaction was calculated:

$$m / V_0 = p_0 \text{ (g/ml)} \quad (2.1);$$

$$m / V_{1250} = p_{1250} \text{ (g/ml)} \quad (2.2);$$

where, m - the mass of the sample, g;

V_0 - the free volume of the sample in the cylinder, ml;

V_{1250} - the volume of the sample after 1250 cylinder jumps, ml;

P (0 or 1250) - the corresponding density value.

The fluidity (flowability) of powder masses was assessed by the free flow method through a funnel, with a vibratory drive. Without prior compaction, a 50 g sample was loaded into the funnel, the lower opening was opened 20 seconds after the device was turned on, and the time of complete powder discharge was recorded. Calculations were made per 100 g of substance.

Organoleptic properties and appearance were assessed visually.

Mass uniformity was determined according to the State Pharmaceutical Industry Code, where the permissible deviation should not exceed ± 5% of the average capsule weight.

Disintegration tests were also carried out according to the pharmacopoeial method. The sample was considered to have passed the test if all 6 capsules disintegrated within 30 minutes. In case of failure, the test was repeated on 12 additional samples. The sample is considered to have passed the test if at least 16 out of 18 capsules demonstrated complete disintegration.

Conclusions to chapter 2

1. The feasibility of improving the existing medicinal product by creating a solid dosage form in the form of hard gelatin capsules containing biologically active components of a complex tincture is substantiated;

2. The composition of the medicinal product that was used is given, the pharmacognostic characteristics of the raw material and phytotherapeutic use are presented;

3. The main methods for conducting an experimental study are given.

CHAPTER 3. EXPERIMENTAL PART

3.1 Assortment analysis of the pharmaceutical market of Ukraine of drugs according to the ATS classification "Lipidemic agents"

Hypolipidemic drugs are drugs intended for the correction of lipid metabolism disorders. Their main goal is to reduce the level of cholesterol and triglycerides in the blood, which helps prevent and treat atherosclerosis, and also reduces the risk of cardiovascular complications, which also include myocardial infarction and stroke.

These drugs affect various links in lipid metabolism: they reduce cholesterol synthesis in the liver, increase its excretion, prevent cholesterol absorption from the intestine, or increase the utilization of low-density lipoproteins. Hypolipidemic drugs are an important component of the drug prevention of cardiovascular diseases. Their selection is carried out individually, taking into account the level of lipids, concomitant risk factors and tolerability of therapy. If necessary, combined treatment is prescribed to achieve the optimal effect.

The main groups of hypolipidemic drugs include the following.

Cholesterol synthesis inhibitors. Statins inhibit the activity of the enzyme responsible for the synthesis of cholesterol in the liver. They reduce the level of low-density lipoproteins, triglycerides and increase the content of high-density lipoproteins.

Agonists of receptors that regulate lipid metabolism. Fibrates activate receptors involved in the regulation of fat metabolism, contributing to the breakdown of triglycerides and increasing the level of high-density lipoproteins.

Cholesterol absorption inhibitors. These drugs reduce the intake of cholesterol from food by blocking its absorption in the intestine. They are often used together with other hypolipidemic agents to achieve a better effect.

Bile acid binders. Bind bile acids in the intestine and promote their excretion, thereby activating the use of cholesterol for the synthesis of new bile acids.

Omega-3 polyunsaturated fatty acids. Used for a pronounced increase in triglyceride levels. Reduce their synthesis in the liver and help improve the lipid profile.

PCSK9 protein inhibitors. These are biological drugs that increase the activity of low-density lipoprotein receptors and enhance cholesterol excretion. Used for familial hypercholesterolemia and in patients with a high risk of complications.

The drug "Ravisol" based on biologically active substances LRS in the form of a complex tincture is produced by a Ukrainian manufacturer. The drug belongs to the ATC classification group C10A 19** "other drugs". This group includes the drugs presented in Table 3.1.

Table 3.1

Hypolipidemic drugs of group C10A 19** "" other drugs&quot"

No.	Medicine	Composition of the drug	Manufacturer
1	2	3	4
1	PUMPKIN SEED OIL oil, 100 ml in a bottle in a cardboard box; 2.5 ml or 5 ml in a sachet, No. 20	1 bottle contains pumpkin seed oil – 100 ml; 1 sachet contains pumpkin seed oil	LLC "Corporation "Health", Ukraine
2	PUMPKIN OIL oil 100 ml in bottles; 100 ml in a bottle; 1 bottle in a cardboard pack	1 bottle contains 100 ml of pumpkin oil (Cucurbitae oleum)	SE "Agrofirma "Yan" PE "Yan", Ukraine
3	MUKOFALK ORANGE granules, 3.25 g/5 g, 5 g granules in a bag No. 20	1 packet (5 g of granules) contains 3.25 g of psyllium seed husk	Dr. Falk Pharma GmbH, Germany
4	FISH OIL-TEVA 500 mg capsules; 10 capsules in a blister; 7 or 9 blisters in a box	1 capsule contains 500 mg of fish oil	Teva Ukraine LLC, Ukraine
5	PUMPKIN SEED OIL 50 ml or 100 ml oil in a bottle; 1 bottle in a cardboard pack	1 bottle contains pumpkin seed oil (cucurbitae semina oleum) 50 ml or 100 ml	JSC Lubnypharm, Ukraine

Continuation of table 3.1

1	2	3	4
6	RAVISOL tincture 100 ml in a jar, 1 jar in a cardboard pack; 100 ml in a polymer or glass bottle, 1 bottle in a cardboard pack	Tincture (ethanol 40%, 1:10) from a mixture of LRS: white mistletoe shoots and leaves 1.5 g; horsetail herb 1 g; Japanese sophora fruits 1.5 g; horse chestnut seeds 1.5 g; hawthorn fruits 2 g; clover flowers 1 g; periwinkle herb 1.5 g;	PJSC "Chempharmaceutical Plant "Chervona Zirka", Ukraine
7	OMAKOR soft capsules 1000 mg 20, 28 or 100 capsules in a bottle; 1 bottle in a box	1 capsule contains 1000 mg of omega-3-unsaturated fatty acid ethyl ester 90, which includes 460 mg of eicosapentaenoic acid ethyl ester and 380 mg of docosahexaenoic acid ethyl ester	Abbott Laboratories GmbH, Germany
8	EPADOL NEO soft capsules 5 capsules in a blister, 6 or 12 blisters in a pack; 10 capsules in a blister, 3 or 6 blisters in a pack	1 capsule contains ethyl esters of omega-3 acids 1000 mg, which include: eicosapentaenoic acid 300 mg; docosahexaenoic acid 200 mg; other fatty acids 498 mg; d-alpha-tocopherol (vitamin E) 2 mg	JSC "KYIV VITAMIN FACTORY", Ukraine
9	LIPOBON 10 mg tablets, 10 tablets in a blister; 3 or 6 or 9 blisters in a cardboard box	1 tablet contains ezetimibe 10 mg	CJSC Pharmaceutical Plant EGIS, Hungary
10	EZETREX 10 mg tablets, 7 tablets in a blister, 4 blisters in a carton	1 tablet contains ezetimibe 10 mg	Hetero Labs Limited, India

Continuation of table 3.1

1	2	3	4
11	SIBRAVA solution for injection, 284 mg/1.5 ml; 1.5 ml of solution in a pre-filled syringe; 1 pre-filled syringe in a carton	1 pre-filled syringe contains 1.5 ml of solution containing inclisiran sodium equivalent to 284 mg inclisiran; 1 ml contains inclisiran sodium equivalent to 189 mg inclisiran	Novartis Overseas Investments AG, Switzerland

From the above data, we can conclude that the group of other drugs includes 11 drug items. Taking into account the difference in the compositions of active substances, there are 7 items. The drug based on pumpkin seed oil is produced by 3 Ukrainian manufacturers. The drugs "Omakor" and "Epadol NEO" are based on the ethyl ester of omega-3 acids but have a slightly different qualitative composition. A foreign and domestic manufacturer produces them in relation to Ukraine, respectively. The drugs "Lipobon" and "Ezetrex" have one active ingredient, ezetimibe, in the amount of 10 mg. In this group, these are the only representatives of drugs in the form of tablets. The last representative of this group contains sodium inclisiran in its composition and is available in the form of a pre-filled syringe.

Regarding the tincture "Ravisol", it is the only representative in this dosage form and 1 of 3 drugs that have a natural origin, since almost all representatives of hypolipidemic drugs are synthetic drugs.

As stated in the previous section, the solid dosage form has a number of advantages, so further actions aimed at developing the technology of the optimal process of extracting raw materials in order to obtain a liquid extract with the subsequent selection of excipients for the possibility of filling hard gelatin capsules. This approach should ensure the creation of a medicinal product with a number of advantages over the existing one, as well as ensure patient compliance.

3.2 Research on the optimal extraction of BAS from raw materials

The study is based on the drug "Ravisol". It is a modern phytotherapeutic agent designed to support the cardiovascular system. Its formula contains an extract of natural components that act synergistically, have an effect on reducing the level of total blood lipids, cholesterol, triglycerides, β-lipoproteins, improves blood circulation and strengthens blood vessels. The main active ingredients are hawthorn, mistletoe, sophora, chestnut, periwinkle, horsetail, clover, which are traditionally used in folk and traditional medicine. The drug helps reduce the level of bad cholesterol, reducing the risk of atherosclerotic plaques. It also has a calming effect on the nervous system, easing the course of vegetative-vascular dystonia. It is recommended in complex therapy for elderly people who have problems with blood pressure or memory. The tincture form allows for quick absorption. The drug is of natural origin, so it rarely causes side effects when used correctly. The drug can be part of the prevention of cardiovascular diseases in the early stages. Its effectiveness has been confirmed not only by research, but also by practical application.

Tinctures remain a popular dosage form due to their simplicity and rapid action, but they have a number of disadvantages. The biggest problem is the presence of ethanol, which makes them unsuitable for certain groups of patients - in particular, children, pregnant women, drivers and people with liver diseases. The dosage of the tincture often depends on the individual perception of the patient, which can cause inaccuracies in the intake. The liquid form is inconvenient for transportation, use on the road or at work. In addition, the strong herbal smell and alcohol taste cause disgust in some patients, reducing compliance.

One of the effective ways to improve such drugs is the transition to solid dosage forms, in particular capsules. Capsules allow you to avoid contact with ethanol, ensure accurate dosing and increase convenience in use. They have a neutral taste, which makes their intake more comfortable, especially for sensitive patients. The solid form also greatly facilitates the standardization of the composition and technological control. Thanks to modern extraction and drying methods, the active

components of plants can be effectively encapsulated without losing biological activity. This opens up new possibilities for existing herbal medicines.

At the first stage of the study, a comparison of two extraction methods (maceration and percolation) was carried out in order to determine the maximum depletion of the raw material. The LRS was used dried and crushed according to the requirements of the technological regulations, passing through a sieve with a hole diameter of 7 mm. A grinder and a micromill were used for grinding. The extractant ethanol 40 % was prepared in the calculated amount using alcoholometric tables (SPU 2.0) before use. The ethanol absorption coefficient was investigated for the raw material to enable the experiment to obtain a given amount of tincture.

The ethanol absorption coefficient of the raw material was not taken into account.

The first sample of the tincture corresponded to the technology of obtaining the original preparation, which is prepared by maceration on 40% ethanol in a ratio of raw material: extractant 1:10, infusing for 2 days in a tightly closed container, with periodic stirring.

The second sample was prepared by percolation. The method is based on the continuous passage of the extractant through a layer of crushed raw materials. The process was carried out in a laboratory percolator using 40 % ethanol in a ratio of raw materials: extractant 1:10. The prepared raw materials were placed in a vessel of a suitable size and the raw materials were moistened by adding the extractant in an amount of 100 % of the mass of the raw materials. They were mixed and left for 5 hours to swell. After the swelling time, the mass was transferred to a laboratory percolator, trying to evenly distribute it in the volume of the container without excessive compression. This should ensure uniform passage of the extractant. After that, the extractant was poured into the percolator and left to infuse for 24 hours. After the infusion time, the percolator drain valve was opened to begin collecting the percolate. The leakage rate was calculated based on the recommended 1/24 of the percolator volume per hour, which in the experiment was approximately 1 drop per 4 seconds. The percolate was collected until the extractant was exhausted.

After obtaining the extracts, the tincture samples were settled for 2 days at a temperature of 8±20C. The transparent part was drained as much as possible, the part with the sediment was filtered. Then these parts were combined.

According to the description, the tincture samples were transparent liquids of yellow-brown color, having a pleasant odor. The obtained tincture samples were examined for the following indicators: dry residue (yield of extractive substances), relative density, ethanol content, identification of the main groups of biologically active substances, quantitative content of the sum of flavonoids and quantitative content of the sum of polyphenolic compounds. The methods meet the requirements of the State Federal University of Ukraine and were performed according to the quality control methods for the tincture "Ravisol". The analysis results are presented in Table 3.2. Identification of the main groups of BAS is presented in Table. 3.3.

Table 3.2

Analysis of tincture samples prepared by maceration and percolation methods (n=3)

Indicator	Units of measurement	Sample #1 maceration	Sample #2 percolation
Dry residue	%	2,07±0,02	2,13±0,01
Relative density	г/мл	0,960±0,002	0,962±0,003
Ethanol content	%	39,48±0,28	38,75±0,34
Sum flavonoid content	%	0,124±0,006	0,129±0,004
Sum polyphenolic content	%	0,141±0,007	0,140±0,009

The conducted tests showed that preparation of tincture by different methods leads to obtaining tinctures with almost identical indicators according to the parameters of the study. However, the purpose of further research may be to improve the percolation method, study the reduction of the amount of extractant by dividing it into portions and quantitative analysis of each portion upon completion of passage through the layer of raw materials. Such an approach may result in a reduction of

the amount of extractant, which will accordingly reduce the extraction time, the cost of extraction and the time that will be spent on condensation of the extract to the state of a liquid extract.

Table 3.3

Qualitative analysis of tincture samples made by maceration and percolation methods

	Reagent / observation	Sample #1 maceration	Sample #2 percolation
1	**2**	**3**	**4**
Flavonoids	Aluminum chloride solution in 96% ethyl alcohol / yellow-green fluorescence in UV light at 365 nm	pass	pass
	10% sodium hydroxide solution / yellow color becomes more saturated	pass	pass
	1% vanillin solution in concentrated hydrochloric acid / bright green color	pass	pass
Polyphenols	1% alcohol solution of iron III chloride / dark green color with a brown tint	pass	pass
	10% acetic acid with lead acetate / a brown precipitate forms	pass	pass
	Reaction with iron-ammonium alums / brown-green color	pass	pass
Saponins	Adding water and shaking / a stable foam appears	pass	pass
	10% copper sulfate solution, concentrated sulfuric acid / brown-green color	pass	pass
	10% lead acetate solution / solution turbidity	pass	pass

Continuation of table 3.3

1	2	3	4
Catechin	Stahl's reagent / crimson red color	pass	pass

The conducted tests showed that preparation of tincture by different methods leads to obtaining tinctures with almost identical indicators according to the parameters of the study. However, the purpose of further research may be to improve the percolation method, study the reduction of the amount of extractant by dividing it into portions and quantitative analysis of each portion upon completion of passage through the layer of raw materials. Such an approach can reduce the amount of extractant, which will accordingly reduce the extraction time, the cost of extraction and the time that will be spent on condensing the extract to the state of a liquid extract.

The next stage of the study was to obtain samples of the liquid extract by evaporation in a vacuum evaporator. This will allow the use of extractive substances in the resulting masses for encapsulation.

A rotary evaporator is a laboratory device designed to remove solvents from liquid mixtures by evaporation at reduced pressure and moderate temperature. Its main advantage is the ability to evaporate volatile liquids without overheating the solution, which is especially important when working with heat-sensitive substances, such as extracts of medicinal plants.

The general view of the rotary apparatus is shown in Fig. 3.1.

The device consists of several main elements: a rotating flask, a water heating bath, a cooler (condenser), a vacuum system and a receiving flask. The solution is poured into a rotating flask, which is partially immersed in a heated water bath. At the same time, the rotation of the flask is turned on, due to which the liquid is distributed in a thin layer along the inner wall, which significantly increases the evaporation area.

Fig. 3.1 Rotary evaporator, manufacturer Biobase Meihua Trading Co., Ltd.

At the same time, a vacuum is created in the system, which lowers the boiling point of the solvent. As a result, ethanol evaporates at a much lower temperature than under normal conditions, which allows preserving biologically active substances. The solvent vapors pass through a cooler, where they condense and drain into a special receiving flask. Thus, a concentrated extract without solvent remains in the working flask.

Thus, the tincture samples were evaporated to a liquid extract, which was subsequently used as an active pharmaceutical ingredient for combination with a carrier.

3.3 Formation of the composition of the mass for filling hard gelatin capsules based on a liquid extract

Microcrystalline cellulose (MCC) was chosen as a carrier for the liquid extract. MCC occupies a special place among the excipients used in the production of solid dosage forms. Its popularity is explained by its high stability, biological inertness and excellent binding properties. Due to its porous structure and microcapillaries, MCC actively interacts with liquids. It is able not only to absorb moisture, but also to evenly distribute it over the volume of particles. Such sorption capacity allows for the effective use of MCC as a carrier for liquid extracts, turning them into powders convenient for dosing.

MCC is a finely dispersed powder consisting of purified and partially depolymerized cellulose. Due to its high purity and chemical inertness, it is widely used as an excipient in pharmaceuticals for the production of solid dosage forms. It improves the fluidity of powders, ensures the strength of tablets, and promotes the disintegration of the form in the gastrointestinal tract. In the pharmaceutical industry, the MCC 102 brand can be effectively used as a sorbent for the absorption of liquid pharmaceutical extracts due to its porous structure and large surface area. This property allows you to convert liquid forms of drugs into a free-flowing powder suitable for further filling of hard gelatin capsules. The use of MCC 102 as a sorbent contributes to the uniform distribution of the active substance in the capsule mass. Its chemical inertness guarantees the stability of the dosage form and the absence of undesirable interactions with the extract.

The saturation of the sorbent was carried out in laboratory conditions using a mixer with a rotating body and an open container. At the first stage, the materials were prepared. The required amount of sorbent (MCC 102) and liquid extract were weighed in order to form batches. The batches corresponded to the ratios of liquid extract to sorbent of 1:1, 1:1.5 and 1:2. The purpose of forming different ratios was to determine the optimal degree of saturation. The degree of saturation was checked by visual signs of the resulting mass and by checking the flow properties.

The prepared portion of the sorbent was loaded into the mixer and, with constant stirring, the liquid extract was gradually added. After the prepared portion of the liquid extract was completed, stirring was continued for another 5 min. Such

conditions were to contribute to the uniform distribution of the liquid throughout the mass of the sorbent and to prevent the formation of lumps.

The saturated sorbent should become wet, but not too wet or sticky. To ensure optimal conditions for the flowability of the mass, it is important to find a balance to ensure sufficient absorption of the extract without losing the flowability necessary for subsequent encapsulation.

Drying can be carried out as necessary. This may depend on the type of liquid, in our case, the properties of the extract, and the requirements for the final product. For laboratory conditions using a small amount of material, the wet sorbent can be spread in a thin layer on a tray and left in the air at room temperature or a drying cabinet can be used. However, the latter option may adversely affect the thermolabile components of the extract. The result of sorbent saturation is presented in Table 3.4.

Table 3.4

Analysis of the mass of the sorbent when saturated in different ratios

	Ratio of sorbent : liquid extract	Observation
1	1:1	The mass is moist and flows
2	1:1,5	The mass is moist, does not flow
3	1:2	The mass is lumpy, sticky

Under these conditions, the moistened mass of sample No. 1 (1:1) was used for further experiments. This sample absorbed a larger amount of extract, and accordingly will have a larger bulk mass, which may positively affect the filled capsules. For this sample, technological parameters of the mass were determined in order to establish flowability parameters. The results are presented in Table 3.5.

The flowability indicators for this sample according to the SPU classification were determined at the level of "good". Also, to improve the technological properties of the mixture and adsorb residual moisture, a combination of aerosil (1, 2 and 3%) and magnesium stearate in an amount of 1% was added to the composition. The results of the determination are given in Table 3.5.

Table 3.5

Determination of mass flowability indicators

Experiment	Units of measurement	Obtained values	Classification of fluidity according to the SPU
Bulk density before shrinkage	g/ml	0,83 ± 0,012	-----
Bulk density after shrinkage	g/ml	0,94 ± 0,008	-----
Carr index	-	11,70	good
Angle of natural slope	degree	31	good

The flowability indicators for this sample according to the SPU classification were determined at the level of "good". Also, to improve the technological properties of the mixture and adsorb residual moisture, a combination of aerosil (1, 2 and 3%) and magnesium stearate in an amount of 1% was added to the composition. The results of the determination are given in Table 3.6.

Table 3.6

Pharmaco-technological properties of a mixture
with aerosil and magnesium stearate

№	Aerosil content : magnesium stearate	Bulk density, g/ml	Fluidity (c/100 g)
1	1 : 1	0,84 ± 0,08	42 ± 0,5
2	2 : 1	0,86 ± 0,07	25 ± 0,5
3	3 : 1	0,87 ± 0,05	22 ± 0,5

The fluidity of the mass increased significantly with the addition of aerosil and magnesium stearate in an amount of 2 and 1%, respectively. The addition of 3

percent aerosil did not significantly affect the fluidity index. Thus, the main components for the possibility of filling hard gelatin capsules were established.

Calculation of the dose of the mass for encapsulation showed the possibility of using it for filling capsules of standard size "0" (see Table 2.1). A manual encapsulator manufactured by PP "NPO Gidromash-1" was used to fill the capsules. The use of the encapsulator was carried out in accordance with the manufacturer's instructions. Thus, the obtained hard gelatin capsules had the following composition, which is given in Table 3.7.

Table 3.7

Composition of the mass for encapsulation with liquid extract

Composition per 1 capsule	mg	%
Liquid extract based on tincture "Ravisol"	242,5	48,5
MCT 102	242,5	48,5
Aerosil	10	2
Magnesium stearate	5	1
Total:	500	100

3.4 Development of a technological scheme for the production of capsules based on a liquid extract

The production of capsules as a medicinal product requires the application of GMP rules with compliance with sanitary standards to prevent cross- and microbial contamination at all stages from raw materials to the finished product. Based on the research conducted, a technological scheme for the production of hard gelatin capsules with a liquid extract obtained from a complex tincture has been developed, which is presented in Figure 3.3.

Before the start of production, all raw materials (substances, starting, auxiliary and packaging materials) undergo thorough incoming quality control, which is carried out by the quality control department.

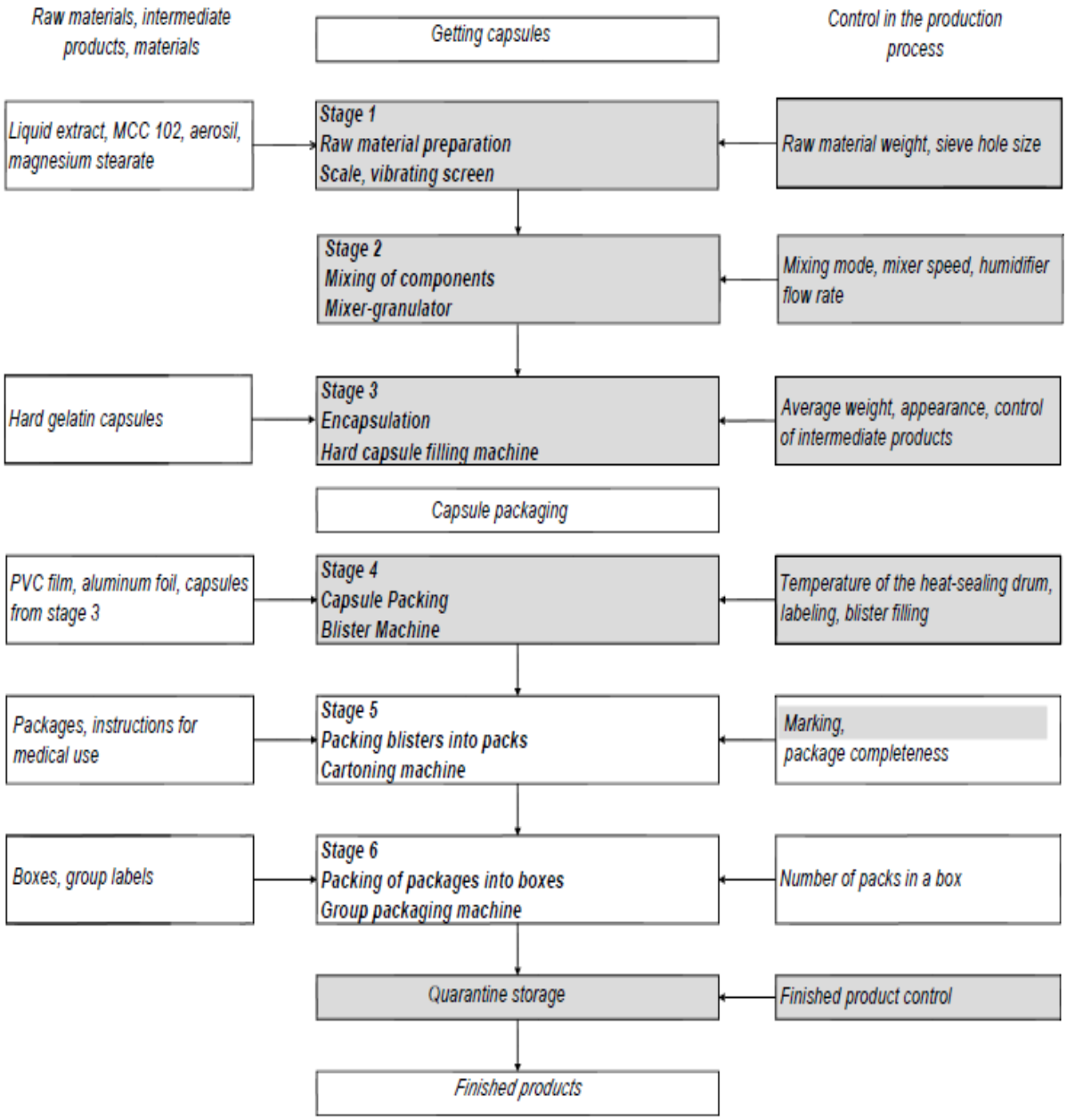

Fig. 3.2 Technological flow chart of capsule production

In accordance with the approved recipe, the components are weighed and placed in separate containers of the required capacity. Next, the bulk materials are sieved using a vibrating screen into prepared collections. Each collection is labeled with a label indicating the name of the raw material, batch number, date, surname and signature of the responsible executor.

The next stage is mixing the components, for which a mixer-granulator is used. The extractant supply system is set up. First, MCC 102 is loaded into the apparatus and, with constant stirring, a liquid extract is fed through the nozzles. After

the extractant is exhausted, mixing is continued for 5 minutes. Then, aerosil and magnesium stearate are added to the container and mixing is carried out for 5 minutes. Upon completion of the mixing process, a sample is taken for intermediate quality control. The finished mixture is unloaded into a labeled collection and transferred to the next stage for encapsulation.

At this stage, hard gelatin capsules are filled with the prepared mass on a capsule filling machine in automatic mode. The capsule filling process on an automatic line usually consists of eight consecutive operations from feeding the capsules into the matrix nests to their dedusting. The encapsulation process is controlled by the average mass of the capsule contents using electronic scales directly at the workplace.

The filled capsules are collected in a marked collection. A sample is taken for analysis by the quality control department for critical quality indicators. In case of a positive conclusion, the filled capsules in the collections are transferred to the next stage for packaging.

The packaging of capsules is carried out in a room with a cleanliness class that meets the conditions for capsule production. Capsules are packed on an automatic machine in 10 pieces in contour cell packaging. Next, blister packaging is carried out on an automatic line or manually on packaging tables. The process includes the formation of a pack, into which two blisters of 10 capsules and instructions for medical use are placed. The packs are placed in a transport container (box) of 100 pieces.

After all stages of packaging, product samples are taken for final quality control. Such products are placed in a warehouse for quarantine storage. After receiving a positive conclusion in the form of a quality certificate, the finished products can be placed on the main (for finished products) and can be intended for sale.

Conclusions to chapter 3

1. An analysis of the range of medicines of the group C10A 19** "other preparations" was carried out, on the basis of which preparations made on a natural basis were established and the feasibility of the planned development was determined.

2. In laboratory conditions, a comparison of extraction methods (maceration and percolation) of plant raw materials included in the composition was carried out and it was established that under the given conditions the percolation method has no advantages. However, for further research it makes sense to adapt it to obtain a liquid extract.

3. A method for obtaining bulk material using a liquid extract for filling hard gelatin capsules was proposed and experimentally studied. The number of excipients was justified and samples of the finished preparation were obtained.

4. In accordance with the progress of the development, a technological scheme of production was proposed and a brief description of the technological process for obtaining hard gelatin capsules based on a liquid extract was given to it.

GENERAL CONCLUSIONS

1. A review of literature on cardiovascular diseases, in particular atherosclerosis, was conducted, which allowed us to understand the current state of the problem and scientific trends in this field.

2. Clinical features, mechanisms of development, risk factors and complications of atherosclerosis were determined, which created a reasonable basis for choosing a research direction.

3. Data on phytotherapeutic agents and the prospects for their use in the treatment of atherosclerosis were considered, including the advantages of medicinal plants as part of complex therapy.

4. The feasibility of creating a new solid dosage form in the form of capsules with a liquid extract as a way to improve existing herbal remedies was substantiated.

5. The composition of the medicinal product and the pharmacognostic characteristics of the plant raw materials included in it were analyzed.

6. As part of the experiment, two extraction methods were compared - maceration and percolation, and it was found that under specific conditions, percolation has no significant advantages.

7. The use of maceration to obtain a liquid extract was justified, which was subsequently adapted to create a loose material for encapsulation.

8. Auxiliary substances were selected that ensured the adsorption of the extract and the stability of the mass for filling hard capsules.

9. Laboratory samples of the finished product were obtained, which met the requirements for shape, structure and technological indicators.

10. A technological scheme for the production of capsules based on a liquid extract was developed, which can be implemented in production and adapted to industrial conditions.

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APPENDICES

АНАЛІЗ ФАРМАЦЕВТИЧНОГО РИНКУ ГІПОЛІПІДЕМІЧНИХ ЗАСОБІВ ТА ОБҐРУНТУВАННЯ РОЗРОБКИ ФІТОПРЕПАРАТУ ДЛЯ КОРЕКЦІЇ ГІПЕРЛІПІДЕМІЇ

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Лаюб Халід
здобувач вищої освіти
Національний фармацевтичний університет, м. Харків, Україна

Гіполіпідемічні лікарські засоби відіграють центральну роль у боротьбі з порушеннями ліпідного обміну. Їхнє основне призначення – зниження концентрації холестерину та тригліцеридів у крові, що є ключовим у запобіганні та лікуванні атеросклерозу. Це, в свою чергу, істотно зменшує ризик розвитку таких серцево-судинних ускладнень, як інфаркт міокарда та інсульт [1].

Механізми дії цих препаратів різноманітні: вони можуть гальмувати синтез холестерину в печінці, посилювати його виведення, блокувати всмоктування з травного тракту або сприяти утилізації ліпопротеїнів низької щільності. Гіполіпідемічні препарати є основою медикаментозної профілактики серцево-судинних захворювань. Вибір оптимальної терапії завжди індивідуальний, враховує ліпідний профіль пацієнта, супутні ризики та переносимість лікування, нерідко передбачаючи комбінований підхід для досягнення максимального терапевтичного ефекту [1, 2].

Гіполіпідемічні засоби класифікуються за специфічними механізмами впливу на ліпідний обмін. До основних груп належать: статини; фібрати; засоби, що знижують всмоктування холестерину; сполучні жовчні кислоти; омега-3 поліненасичені жирні кислоти; інгібітори білка PCSK9.

Аналіз вітчизняного фармацевтичного ринку вказує на те, що підгрупа АТС класифікації C10A 19 «Інші препарати» об'єднує 11 зареєстрованих позицій лікарських засобів. При цьому, вони базуються на 7 діючих речовинах.

Серед представників цієї групи виділяються наступні [3]:

- препарати на основі олії насіння гарбуза, які виробляються трьома українськими компаніями;
- засоби, що містять етилові ефіри омега-3 кислот, зокрема «Омакор» (закордонного виробництва) та «Епадол НЕО» (вітчизняний виробник), відрізняються дещо різним якісним складом;
- препарати з діючою речовиною езетиміб у дозуванні 10 мг («Ліпобон» та «Езетрекс»), які є єдиними представниками у формі таблеток у даній підгрупі;

Ф А 2.2.1-32-366

National University of Pharmacy

Faculty pharmaceutical
Department Industrial Technology of Medicines and Cosmetics
Level of higher education master
Specialty 226 Pharmacy, industrial pharmacy
Educational and professional program Pharmacy

APPROVED
The Head of Department
Industrial Technology of
Medicines and Cosmetics

_____
Olena RUBAN

«26» September 2024

ASSIGNMENT
FOR QUALIFICATION WORK
OF AN APPLICANT FOR HIGHER EDUCATION

Khalid LYOUB

1. Topic of qualification work: «Research on the composition and technology of a hypolipidemic drug»
supervisor of qualification work: Sergiy TRUTAYEV, PhD, assoc. prof.
approved by order of NUPh from "27" of September 2024 № 237

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

3. Outgoing data for qualification work: sources of scientific literature, hypolipidemic drugs, tinctures, extracts, tablet, pharmaceutical technology.

4. Contents of the settlement and explanatory note (list of questions that need to be developed): introduction, review of literary sources, research objects and methods, experimental part, general conclusions, list of references, appendices.

5. List of graphic material (with exact indication of the required drawings):
Figures – 5, table – 2.

6. Consultants of chapters of qualification work

Chapters	Name, SURNAME, position of consultant	Signature, date	
		assignment was issued	assignment was received
1	Sergiy TRUTAYEV, associate professor of higher education institution of department Industrial Technology of Medicines and Cosmetics	26.09.2024 Sergiy TRUTAYEV	26.09.2024 Khalid LYOUB
2	Sergiy TRUTAYEV, associate professor of higher education institution of department Industrial Technology of Medicines and Cosmetics	26.09.2024 Sergiy TRUTAYEV	26.09.2024 Khalid LYOUB
3	Sergiy TRUTAYEV, associate professor of higher education institution of department Industrial Technology of Medicines and Cosmetics	26.09.2024 Sergiy TRUTAYEV	26.09.2024 Khalid LYOUB

7. Date of issue of the assignment: «26» September 2024.

КАЛЕНДАРНИЙ ПЛАН

№	Name of stages of qualification work	Deadline for the stages of qualification work	Notes
1	Review of literary sources	October – December 2024	**done**
2	Research objects and methods	January 2025	**done**
3	Experimental part	February – April 2025	**done**
4	Writing and design of qualification work, Approbation of qualification work	April – May 2025	**done**
5	Submission of the qualification work to the EC of the National University of Pharmacy	May 2025	**done**

An applicant of higher education _____ Khalid LYOUB

Supervisor of qualification work _____ Sergiy TRUTAYEV

ВИТЯГ З НАКАЗУ № 237

По Національному фармацевтичному університету

від 27 вересня 2024 року

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

Прізвище, ім'я здобувача вищої освіти	Тема кваліфікаційної роботи		Посада, прізвище та ініціали керівника	Рецензент кваліфікаційної роботи
по кафедрі промислової технології ліків та косметичних засобів				
Лаюб Халід	Дослідження складу та технології гіполіпідемічного препарату	Research on the composition and technology of a hypolipidemic drug	доц. Трутаєв С.І.	доц. Марченко М.В.

Ректор Віктор Черних

Вик. Секретар

ФА2.8-03-317

ВИСНОВОК

експертної комісії про проведену експертизу
щодо академічного плагіату у кваліфікаційній роботі

здобувача вищої освіти

«03» травня 2025 р. № 331107983

Проаналізувавши кваліфікаційну роботу здобувача вищої освіти Лаюб Халід, групи Фм20(4,10d)англ-02, спеціальності 226 Фармація, промислова фармація, освітньої програми «Фармація» навчання на тему: «Дослідження складу та технології гіполіпідемічного препарату / Research on the composition and technology of a hypolipidemic drug», експертна комісія дійшла висновку, що робота, представлена до Екзаменаційної комісії для захисту, виконана самостійно і не містить елементів академічного плагіату (компіляції).

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

Ф А 2.2.1-32-353

REVIEW

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

Khalid LYOUB

on the topic: «Research on the composition and technology of a hypolipidemic drug».

Relevance of the topic. The relevance of the master's thesis is due to the high prevalence of cardiovascular diseases caused by hyperlipidemia. The development of effective and safe hypolipidemic agents is a priority for modern pharmacy. Phytopreparations are of particular promise due to their complex action and fewer side effects. Research into the composition and pharmaceutical technology of such a drug will contribute to expanding therapeutic opportunities and meeting the growing demand for natural remedies. The work justifies the feasibility of introducing phytopreparations in a convenient form of application for the patient.

Practical value of conclusions, recommendations and their validity. The results of the qualification work contribute to expanding the range of effective, safe, and easy-to-use herbal remedies for the prevention and treatment of hyperlipidemia, allowing patients to improve their quality of life.

Assessment of work. The author has consistently performed the work, demonstrating the ability to apply a scientific approach in solving the tasks set. The results of the work are promising and can be used in further research.

General conclusion and recommendations on admission to defend. The qualification work was completed at a high scientific and practical level, the design meets the requirements for qualification works and can be submitted for defense to the EC of the NUPh, and its performer deserves high praise.

Scientific supervisor _____ Sergiy TRUTAYEV

«13» May 2025

Ф А 2.2.1-32-356

REVIEW

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

Khalid LYOUB

on the topic: «Research on the composition and technology of a hypolipidemic drug».

Relevance of the topic. The relevance of the work is due to the problem of hyperlipidemia, which is the main risk factor for cardiovascular diseases. Effective correction of lipid metabolism is important for the prevention of CVD. In this context, the development of new hypolipidemic drugs is a modern need. Phytopreparations have a perspective due to their complex action and better safety profile. Improving the existing drug will allow to offer a convenient form of application, which should increase patient compliance with treatment.

Theoretical level of work. The theoretical part of the work is done qualitatively and shows the author's ability to work with scientific information.

Author's suggestions on the research topic. Justification of the extraction method and production of hard capsules based on plant components in the form of an extract.

Practical value of conclusions, recommendations and their validity. The results of the work provide a basis for the introduction into industrial production of a new dosage form for an existing drug.

Disadvantages of work. The work is well done and meets its purpose. Some stylistic inaccuracies do not affect the value of the results obtained.

General conclusion and assessment of the work. The work demonstrates proper execution, meets the requirements for qualification works and can be presented for defense at the EC of the NUPh, and its author deserves a high positive assessment.

Reviewer _____ assoc. prof. Mykhailo MARCHENKO

«15» May 2025

Ф А2.2.1-91-287

МІНІСТЕРСТВО ОХОРОНИ ЗДОРОВ'Я УКРАЇНИ
НАЦІОНАЛЬНИЙ ФАРМАЦЕВТИЧНИЙ УНІВЕРСИТЕТ

ВИТЯГ З ПРОТОКОЛУ № 12
від 16 травня 2025 року
м. Харків
засідання кафедри
Промислової технології ліків та косметичних засобів

Голова: завідувачка кафедри, докторка фарм. наук, проф. Рубан О. А.

Секретар: канд. фарм. наук, доц. Січкар А. А.

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

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

СЛУХАЛИ: Про представлення до захисту в Екзаменаційній комісії кваліфікаційної роботи на тему: «Дослідження складу та технології гіполіпідемічного препарату»

здобувача вищої освіти випускного курсу Фм20(4,10д)англ-02 групи НФаУ 2025 року випуску Халід ЛАЮБ
(ім'я, прізвище)
Науковий керівник к.фарм.н., доц. Сергій ТРУТАЄВ
Рецензент к.фарм.н., доц. Михайло МАРЧЕНКО

УХВАЛИЛИ: Рекомендувати до захисту кваліфікаційну роботу здобувача вищої освіти 5 курсу Фм20(4,10д)англ-02 групи Халід ЛАЮБ
на тему: «Дослідження складу та технології гіполіпідемічного препарату»

Голова
завідувачка кафедри,
докт. фарм. наук, проф. _____ Олена РУБАН

Секретар
к. фарм. н., доц. _____ Антоніна СІЧКАР

Ф А2.2.1-32-042

НАЦІОНАЛЬНИЙ ФАРМАЦЕВТИЧНИЙ УНІВЕРСИТЕТ

ПОДАННЯ
ГОЛОВІ ЕКЗАМЕНАЦІЙНОЇ КОМІСІЇ
ЩОДО ЗАХИСТУ КВАЛІФІКАЦІЙНОЇ РОБОТИ

Направляється здобувач вищої освіти Халід ЛАЮБ до захисту кваліфікаційної роботи
за галуззю знань 22 Охорона здоров'я
спеціальністю 226 Фармація, промислова фармація
освітньою програмою Фармація
на тему: «Дослідження складу та технології гіполіпідемічного препарату»

Кваліфікаційна робота і рецензія додаються.

Декан факультету _____ / Микола ГОЛІК /

Висновок керівника кваліфікаційної роботи

Здобувач вищої освіти Халід ЛАЮБ виконав кваліфікаційну роботу на високому рівні, з логічним викладенням матеріалу та обговоренням результатів, оформлення роботи відповідає вимогам НФаУ до випускних кваліфікаційних робіт та може бути рекомендована до захисту в ЕК НФаУ.

Керівник кваліфікаційної роботи

_____ Сергій ТРУТАЄВ

«13» травня 2025 р.

Висновок кафедри про кваліфікаційну роботу

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

Завідувачка кафедри
Промислової технології ліків
та косметичних засобів

_____ Олена РУБАН

«16» травня 2025 року

Qualification work was defended

of Examination commission on

« » of June 2025

With the grade _____

Head of the State Examination commission,

D.Pharm.Sc, Professor

_____ / Volodymyr YAKOVENKO /