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**QUALIFICATION WORK**

on the topic: **«JUSTIFICATION OF THE COMPOSITION AND DEVELOPMENT OF TECHNOLOGY FOR EXTEMPORANEOUS SYRUP FOR THE TREATMENT OF COUGH»**

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## ANNOTATION

The qualification work is devoted to the justification of the composition and development of the technology for the production of extemporaneous syrup for the treatment of cough based on thyme extract and ambroxol hydrochloride, as well as the standardization of the medicinal syrup. The selection of active and auxiliary substances was carried out and a rational technology for the production of syrup in pharmacy conditions was developed, and quality control methods were developed. The qualification work is presented on 43 pages, consists of an introduction, a literature review and 2 sections of the experimental part, general conclusions, includes 8 tables, 6 figures, 33 sources of literature and 5 appendices.

*Key words:* syrup, composition, technology, ambroxol hydrochloride, thyme extract, cough.

## АНОТАЦІЯ

Кваліфікаційна робота присвячена обґрунтуванню складу та розробці технології виготовлення екстемпорального сиропу для лікування кашлю на основі екстракту чебрецю та амброксолу гідрохлориду, а також стандартизації лікарського сиропу. Здійснено підбір діючих та допоміжних речовин та розроблено раціональну технологію виготовлення сиропу в умовах аптечного виробництва, розроблено методики контролю якості. Кваліфікаційна робота представлена на 43 сторінках, складається зі вступу, огляду літератури та 2 розділів експериментальної частини, загальних висновків, включає 8 таблиць, 6 рисунків, 33 джерела літератури та 5 додатків.

*Ключові слова:* сироп, склад, технологія, амброксолу гідрохлорид, екстракт чебрецю, кашель.

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## LIST OF SYMBOLS

BAS – biologically active substances

WHO – World Health Organization

SPhU – State Pharmacopoeia of Ukraine

EU – European Union

OTC – Over-the-Counter

5-LOX – 5-lipoxygenase

COX-2 – cyclooxygenase-2

Ph Eur – European Pharmacopoeia

EMA – European Medicines Agency

HMPC – Herbal Medicinal Products

CFU – colony forming unit

## INTRODUCTION

**Actuality of topic.** One of the main directions in the field of modern practical pharmacy and relevant scientific research is the creation of original expectorant drugs and the search for optimal technological solutions for them.

This aspect has been consistently relevant for many years. In recent years, this position has been consolidated in connection with the increase in infectious diseases of the upper and lower respiratory tract and their consequences. And modern approaches, including those related to the pandemic and related to the preventive direction, provide for increased interest in expectorant drugs created on the basis of medicinal plant raw materials.

There are many medicines for cough therapy, both expectorant and blocking, in the modern world, but their assortment and range cannot be considered exhaustive, since herbal mono-remedies and, especially, their compositions are far from fully realized for this purpose. Synthetic compositions can also be expanded, including in terms of introduction into production and use in medical practice.

However, the modern assessment of herbal medicines, the current structure of pharmaceutical production, and their corresponding equipment provide for the expansion of the technological capabilities of the drug, and therefore the possibilities for its successful use, which makes research in this direction relevant.

Numerous studies of medicinal plants have allowed us to identify one of the most common plants in terms of solving the described problems – *Thymus serpyllum*.

Thus, the creation of original expectorants based on medicinal plant raw materials and the improvement of their technologies is an urgent task of modern medicine and pharmacy.

**The aim** of our research was to develop the composition and rational technology of a liquid dosage form – a syrup based on thyme extract and ambroxol hydrochloride.

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

- to conduct a marketing analysis of the pharmaceutical market of herbal medicines; to characterize the state of research in the field of developing syrups with herbal medicines; to provide a general description of the medicinal plant *Thymus serpyllum*;
- to develop the optimal composition of a syrup based on thyme extract and ambroxol hydrochloride;
- to develop a rational technology for the production of antitussive syrup in pharmacy conditions;
- conduct quality control of the developed syrup according to organoleptic, physicochemical and microbiological indicators.

**Object of research.** Ambroxol hydrochloride, thyme extract, white crystalline sugar, ethanol 95 %, purified water, "Orange" flavoring.

**Subject of research.** Development of a rational composition and justification of the technology of medicinal antitussive syrup and determination of its quality control indicators.

**Research methods.** This qualification work used technological, physicochemical, microbiological and statistical research methods, as well as generalization and observation methods.

**The practical significance of the results obtained.** Based on the results of experimental studies, the composition and technology of a syrup with mucolytic activity were developed. Its standardization methods are proposed.

**Elements of scientific research.** For the first time, an original liquid dosage form – syrup containing thyme extract and ambroxol hydrochloride – was developed. A rational technology for syrup production in pharmacy conditions was proposed.

**Implementation of results.** The main provisions of the qualification work are set out and discussed in the VIII International Scientific and Practical Internet-Conference "Current approaches of pharmaceutical science in development and standardization of medicines and dietary supplements that contain components of natural origin" (April 10, 2026, Kharkiv) and XXXII International Scientific and

Practical Conference of Young Scientists and Students «Topical issues of new medicines development» (April 15-17, 2026, Kharkiv). Abstracts of the report and poster presentation published.

**Structure and scope of qualification work.** The qualification work is presented on 43 pages, consists of an introduction, a literature review and 2 sections of the experimental part, general conclusions, includes 8 tables, 6 figures, 33 sources of literature and 5 appendices.

# **CHAPTER 1. STATE OF THE ART IN COUGH THERAPY AND THE ROLE OF HERBAL SYRUPS IN THE EUROPEAN PHARMACEUTICAL MARKET**

## **1.1. Modern aspects of cough therapy and analysis of the european pharmaceutical market**

Cough occurs when the respiratory receptors are directly irritated by infection (inflammatory diseases of the trachea and bronchi), allergic reactions (urticaria, bronchial asthma), intoxications (tobacco smoke, ammonia, etc.), foreign bodies in the respiratory tract (food), vasomotor disorders (circulatory insufficiency). In addition, the causes of cough can be reflex irritation of the gastrointestinal tract and skin. In rare cases, the cause may be primary excitation of the central nervous system [1, 2].

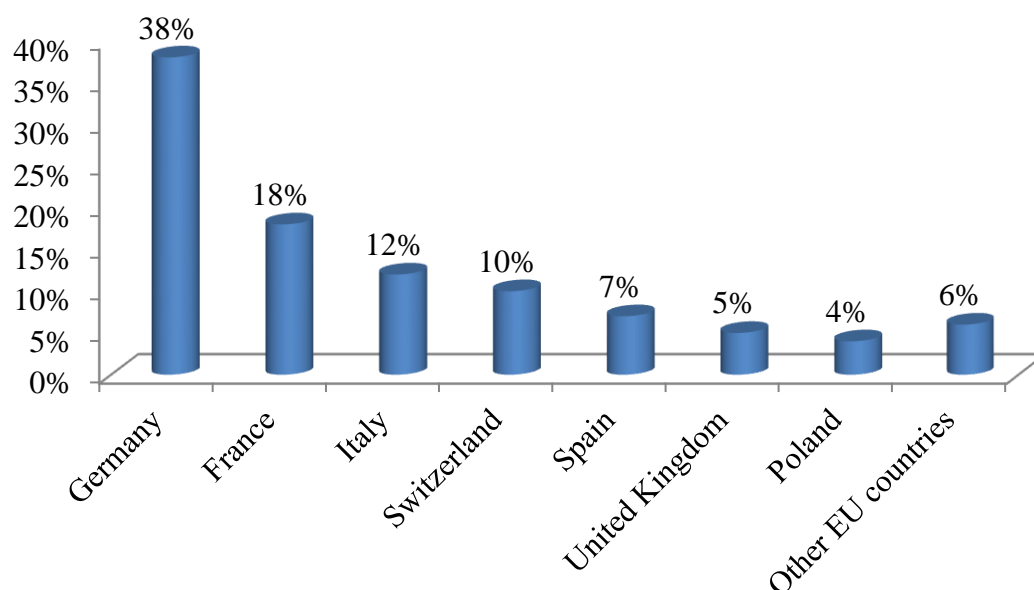
The most important parameter when choosing therapy is the presence of a dry or wet cough. Depending on this, symptomatic therapy is carried out with antitussive, expectorant or combined drugs. Drugs used to treat dry cough affect the suppression of the cough reflex. There are various drugs that act on the cough center (central and reflex action), suppress the sensitivity of cough receptors, or act on afferent regulatory pathways [3].

Expectorant drugs are used in the treatment of «wet» cough. This term refers to a group of drugs that promote the release of bronchial secretions from the respiratory tract. Based on the mechanism of action, there is the following division of drugs – drugs that stimulate expectoration (secretomotor) and drugs that thin sputum (secretolytics or mucolytics). Secretomotor drugs, in turn, are divided into drugs that reflexively stimulate expectoration and drugs with resorptive action. Drugs that reflexively stimulate expectoration affect the gastric mucosa, thereby causing irritation of the cough center and increased severity of the cough reflex (licorice root, sodium benzoate, etc.). Drugs with resorptive action cause increased production of the liquid part of bronchial secretion, which contributes to its

thinning (ammonium chloride, sodium bicarbonate, etc.). This group of drugs is currently almost not used, since quite often there is a side effect from the mucous membranes of the eyes and nose, causing congestion and tearing [1, 3].

Secretolytic (mucolytic) agents are represented by three subgroups – proteolytic enzymes, cysteine derivatives and mucoregulators. The use of proteolytic enzymes is currently limited due to the risk of developing allergies and bronchospasm. Drugs in this group include «Trypsin», «Chymotrypsin», etc. Cysteine derivatives («Acetylcysteine», «Fluimucil», etc.) are most widely used. By breaking disulfide bonds between mucus proteins, they contribute to its breakdown and rapid excretion. Mucoregulators increase the amount of pulmonary surfactant. In addition, they equalize the content of the mucous and liquid parts of sputum by stimulating the synthesis of glycoproteins («Bromhexine», «Ambroxol», etc.) [2, 4].

In Europe, more than a thousand trade names of cough medicines from different manufacturers are registered. We have analyzed the consolidated structure of the cough medicine market in Europe by manufacturing country. For the analysis, averaged data for the European Union (EU) countries were selected, which allows us to assess the pan-european trends in this segment (fig. 1.1) [2].



**Fig. 1.1. Distribution of the pharmaceutical market among manufacturers of cough medicines**

In fig. 1.1, the data demonstrate the dominant position of three key countries – Germany, France and Italy, which together control over two-thirds of the pharmaceutical market for antitussives (68 %).

The expanded data in table 1.1 demonstrates the high degree of therapeutic diversification within the european market [2, 3].

Table 1.1

**Detailed analysis of leading european cough and cold medicines**

<b>№</b>	<b>Country</b>	<b>Active ingredients</b>	<b>Trade name</b>	<b>Pharmacotherapeutic action</b>
1	2	3	4	5
1.	Germany	Ambroxol	Lasolvan	Mucolytic
2.	Germany	Ivy leaf dry extract	Prospan	Herbal secretolytic
3.	Germany	Bromhexine	Bromhexine Berlin-Chemie	Mucolytic, expectorant
4.	Germany	Acetylcysteine	ACC (NAC)	Mucolytic
5.	Germany	Pelargonium sidoides	Umckalor	Antiviral, expectorant
6.	Germany	Cineole, Limonene, Pinene	Gelomyrtol	Secretolytic
7.	Germany	Ambroxol	Ambrobene	Mucolytic
8.	France	Carbocisteine	Fluditec	Mucolytic
9.	France	Carbocisteine	Mucodyne	Mucolytic
10.	France	Oxomemazine	Toplexil	Antihistamine, antitussive
11.	Italy	Levodropropizine	Levopront	Peripheral antitussive
12.	Italy	Butamirate	Sinecod	Central non-opioid antitussive
13.	Italy	Sobrerol	Sobrepin	Mucolytic
14.	Switzerland	Glaucine, Ephedrine	Broncholitin	Antitussive, bronchodilator
15.	Switzerland	Codeine (low dose)	Neo-Codion	Centrally acting antitussive

1	2	3	4	5
16.	Switzerland	Essential oils (Eucalyptus, Rosemary)	Pulmex	Local irritant, expectorant
17.	Spain	Guifenesin	Vicks Expectorant	Expectorant
18.	Spain	Cloperastine	Seki	Antitussive
19.	Austria	Thyme, Primrose extract	Bronchipret	Herbal expectorant
20.	Slovenia	Herb-based combinations	Herbion (Ivy, Primrose)	Herbal mucolytic
21.	Slovenia	Acetylcysteine	Fluimukan	Mucolytic
22.	Poland	Iceland moss extract	Isla-Moos	Demulcent
23.	Poland	Butamirate citrate	Supremin	Non-opioid antitussive
24.	United Kingdom	Dextromethorphan	Benlyn	Centrally acting antitussive

The market is dominated by classic mucolytics such as "Ambroxol" and "Acetylcysteine", with German manufacturers (e.g., Sandoz, Berlin-Chemie) holding the majority of these registrations [1, 3].

There is a growing trend toward standardized herbal medicines (Phytoneering). Products like "Prospan" (Germany) and "Herbion" (Slovenia) represent a significant market share due to their high safety profile, especially in pediatric practice [3].

Southern European countries (Italy, Spain) contribute significantly with peripheral antitussives like "Levodropropizine", which specifically targets the cough reflex without affecting the central nervous system, highlighting a shift toward more specialized therapy.

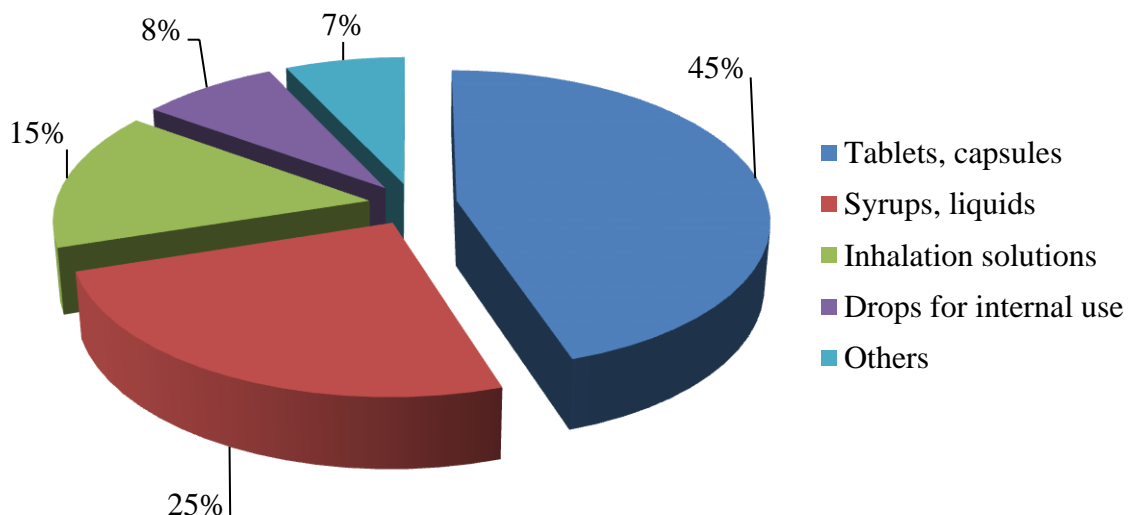
Most of these products are classified as Over-the-Counter (OTC), which explains their high sales volume and the necessity for clear pharmacist-led patient counseling [2, 3].

The group of expectorants occupies the largest share in the category of drugs for the treatment of cough. In the production of these drugs, both extracts from plant raw materials and synthetic substances are used. In the pharmaceutical industry, extracts from thyme herb, licorice root, marshmallow herb, ivy leaves and violet herb are most often used [4, 5, 6].

The group of synthetic mucolytic and antitussive agents in the European pharmaceutical market is strictly regulated and standardized. The leading position in this category belongs to Ambroxol hydrochloride, which serves as the gold standard for secretolytic therapy. It is represented by more than 10 major European brands, with German reference products such as "Lasolván", "Ambrobene", and "Flavamed" defining the quality benchmarks for the region [5, 6].

Based on the analysis of drugs for the treatment of cough, it can be stated that there is a high prevalence of drugs obtained on the basis of medicinal plant raw materials, which are used both in mono-composition and in its complex combination with other substances [6].

Medications for the treatment of cough are presented in various dosage forms (fig. 1.2).



**Fig. 1.2. Distribution of cough medications by dosage form**

The data presented in fig. 1.2 show that the largest share of cough medicines is in solid dosage forms (45 %). The next most common is the liquid dosage form – syrups (25 %).

## **1.2. Modern trends in the composition, technology, and distribution of medicinal syrups in the EU**

Syrups, as a dosage form, are very relevant for use by the population of all age categories due to the presence of indisputable factors – the exclusion of pain during administration, the uniformity and speed of absorption of medicinal substances, their distribution [7].

Syrups are a dosage form intended for internal use, mainly a concentrated (solution of various sugars containing active and excipients) [8].

Syrups are obtained by dissolving sugars (sucrose) or other syrup-forming substances (e.g., polyalcohols) in water and heating to boiling point. Usually, the concentration of sugar or other syrup-forming substance in the finished syrup is not less than 45 % (m/m). The finished syrup is filtered. The addition of active ingredients, tinctures, extracts, juices, etc., as well as excipients is carried out after the syrup has cooled to a temperature of  $(55 \pm 5)$  °C. To prevent crystallization of the syrup-forming component and to adjust other parameters, glycerin, various polyalcohols, surfactants and other excipients permitted for internal use can be added to syrups [8].

As antimicrobial preservatives, excipients are usually introduced into the composition of syrups: ethanol, methyl parahydroxybenzoate, propyl parahydroxybenzoate, sorbic acid, potassium sorbate, sodium benzoate, etc. Syrups in the form of reconstituted dosage forms can also be obtained from granules or powders by dissolving in a suitable solvent [9].

From the point of view of application, syrups are divided into two groups - flavoring and medicinal. Flavoring syrups serve as the basis for the preparation of

medicinal syrups, are used as a means for adjusting and correcting the taste, smell, and sometimes the color of drugs [8, 10].

The group of flavored syrups includes sugar syrup (*Sirupus simplex*), as well as fruit and berry syrups – cherry (*Sirupus Cerasi*), raspberry (*Sirupus Rubi idaei*), tangerine (*Sirupus Citri unshiu*), etc [9].

Medicinal syrups contain biologically active substance that give them therapeutic value (syrups with vitamins, antibiotics, antihistamines and antiemetics, tranquilizers, antitussives, etc.). They can be included in the composition of syrups as dry substances, aqueous solutions, tinctures, extracts, and extracts from dried or fresh raw materials [8, 11].

The basic excipients in syrups are sweeteners. The main sweeteners include sucrose, fructose, maltose, sorbitol, dextrose, honey [12].

A large role in the development of the composition of medicinal products belongs to excipients. Many scientific works are devoted to research on expanding the range, technological nuances of using excipients and other aspects, depending on the tasks set [13].

To prevent redox processes during storage and use, stabilizers are added to the syrups – citric, lactic, ascorbic, hydrochloric, tartaric acids, sodium citrate, sodium hydroxide, sodium metabisulfite [12].

To prevent crystallization of the syrup-forming component and to adjust other parameters, glycerin, various polyalcohols, surfactants and other excipients permitted for internal use can be added to syrups. To improve solubility, cosolvents are added to syrups – polysorbate-80, polyethylene glycol, glycerin, propylene glycol, ethanol [12, 13].

Malt extracts, stevia, sodium saccharinate and aspartame are used as sweeteners. Peppermint, anise, clove oil, pineapple and cherry flavors, levomenthol are used as flavorings.

Syrups as pharmaceuticals allow the introduction of both synthetic drugs and herbal remedies, while providing fairly high organoleptic indicators [12, 14].

Based on the characteristics of the chemical composition of plant raw materials, specific taste characteristics, as well as the features of the production of intermediate products, syrups are undoubtedly one of the optimal dosage forms in the production of preparations from medicinal plant raw materials. For example, the mucolytic effect of plantain and marshmallow is due to the presence of polysaccharides in their composition, during extraction with water. However, it is widely known that water extracts are prone to rapid microbial decomposition, and therefore, in order to achieve product stability during storage, it is advisable to introduce the obtained extracts into sugar syrup [15, 16].

Several technological operations are used to introduce extracts of medicinal plant raw materials into syrup:

- dissolving liquid extracts in a sugar solution;
- dissolving the extract in a suitable solvent and introducing the resulting solution into the syrup [14].

When introducing tinctures and liquid extracts into sugar solutions, due to a change in solvent, a precipitate of oily substances solubilized by alcohol may form. Therefore, after the extract is introduced, its additional settling and filtration are provided.

Dry extracts are pre-dissolved in a portion of water or other solvent, then the finished solution is introduced into the syrup. The schematic diagram of obtaining medicinal syrups with synthetic components provides for two main methods of their introduction, depending on the solubility of the substances [15, 17].

For active substances and excipients that are easily soluble in water, their introduction into the finished sugar solution is provided.

For slowly soluble substances in water, it is advisable to pre-dissolve the substance in hot water (or part of it) and then boil the syrup with the resulting solution of the medicinal substance. In some cases, it is possible to pre-dissolve the substances in other solvents (for example, paracetamol in propylene glycol) with subsequent introduction into the syrup base [18].

The European pharmaceutical market offers a diverse range of medicinal syrups with various pharmacological targets. While syrups are traditionally associated with pediatric practice, their role in adult therapy is also significant due to the ease of administration and rapid absorption of active ingredients [4, 12, 15]. A comparative analysis of the leading syrups registered in the EU is presented in table 1.2.

Table 1.2

**Nomenclature of syrups presented on the European pharmaceutical market**

<b>№</b>	<b>Trade name</b>	<b>Manufacturer</b>	<b>Pharmacological group</b>
1	2	3	4
1.	Lasolván	Sanofi / Boehringer Ingelheim (Germany)	Mucolytics, expectorants
2.	ACC (NAC) Syrup	Sandoz / Hexal AG (Germany)	Mucolytics
3.	Fluditec	Innotech International (France)	Mucolytics
4.	Sinecod	GSK / HALEON (Switzerland/Italy)	Antitussives
5.	Prospan	Engelhard Arzneimittel (Germany)	Herbal expectorants
6.	Herbion Ivy	KRKA (Slovenia)	Herbal mucolytics
7.	Bronchipret	Bionorica SE (Germany)	Herbal expectorants
8.	Bronchostop	Kwizda Pharma (Austria)	Herbal antitussives, expectorants
9.	Toplexil	Sanofi (France)	Antihistamines, antitussives
10.	Depakine	Sanofi Winthrop Industrie (France)	Antiepileptics
11.	Duphalac	Abbott Biologicals (Netherlands)	Laxatives

1	2	3	4
12.	Aerius	Schering-Plough (Belgium)	Antihistamines
13.	Claritine	Bayer / Schering-Plough (Belgium)	Antihistamines
14.	Levopront	Dompé Farmaceutici (Italy)	Peripheral antitussives
15.	Neo-Codion	Bouchara-Recordati (France)	Antitussives
16.	Grintuss	Aboca (Italy)	Protective mucosal barriers
17.	Eurespal	Servier (France)	Anti-inflammatory respiratory
18.	Gaviscon	Reckitt Benckiser (UK)	Antacids
19.	Nurofen for Children	Reckitt Benckiser (UK)	Analgesics, antipyretics
20.	Maltofer	Vifor (Switzerland)	Anti-anemic preparations
21.	Umckaloabo	Dr. Willmar Schwabe (Germany)	Herbal antivirals
22.	Stoptussin	Teva / Ivax (Czech Republic)	Combined antitussives, expectorants
23.	Atarax	UCB Pharma (Belgium)	Anxiolytics, sedatives
24.	Zodac	Zentiva (Czech Republic)	Antihistamines
25.	Isla Moos Liquid	Engelhard (Germany)	Demulcents

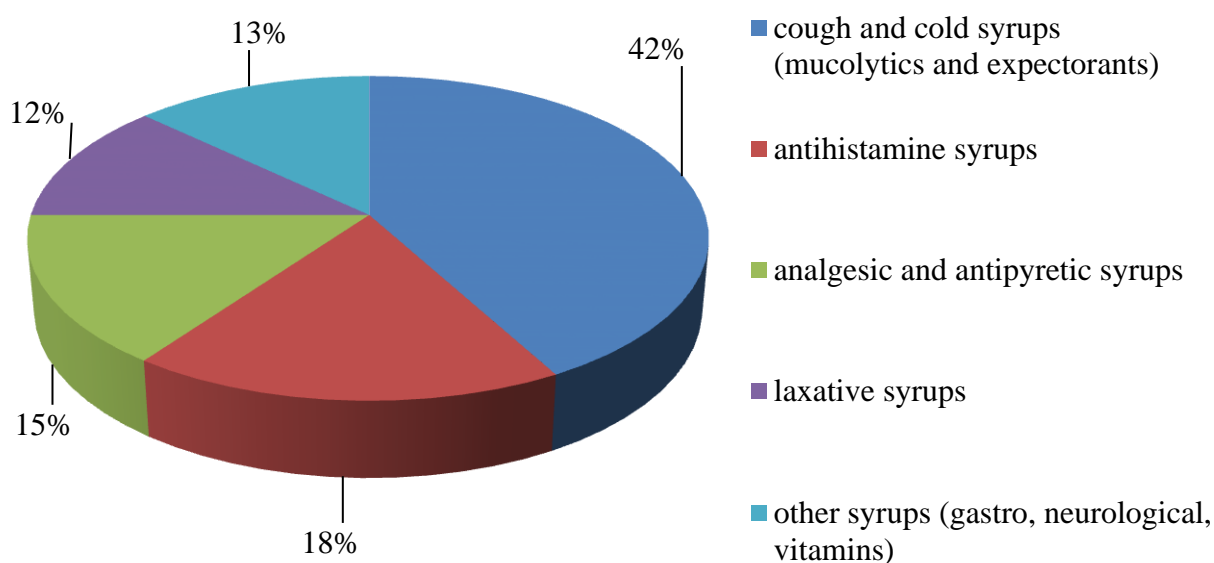
As demonstrated in table 1.2, the european syrup market is highly segmented, with a significant portion dedicated to respiratory care. Within this category, mucolytic and expectorant syrups represent the largest market share, which correlates with the high clinical demand for effective cough management tools [15].

A distinctive feature of the european market compared to others is the high prevalence of standardized herbal syrups (e.g., "Prospan", "Bronchipret", "Herbion"). These products are often preferred in european clinical practice due to their balanced safety-to-efficacy ratio. Additionally, the presence of specialized

neurological (e.g., "Depakine") and gastrointestinal (e.g., "Duphalac") syrups highlights the versatility of this dosage form in european pharmacy.

The pharmaceutical market for syrups in Europe is characterized by high therapeutic diversity [4, 5, 12, 15].

The majority of syrups in the european market are intended for the treatment of cough and respiratory diseases (approximately 42 %). Within this category, 92 % are mucolytic and expectorant agents (fig. 1.3) [5, 15].



**Fig. 1.3. Distribution of pharmaceutical syrups by therapeutic indication in the european market**

The second largest group in the syrup category is antihistamines ( $H_1$ -receptor blockers), which account for 18 % of the total assortment of syrups registered in Europe. This share is due to the widespread use of liquid forms for managing pediatric allergies and chronic dermatological conditions in EU countries. Laxatives in the form of osmotic syrups (primarily based on lactulose) constitute about 12 % of the market, while analgesics and antipyretics (such as ibuprofen and paracetamol suspensions) hold 15 % share [15].

Analysis of cough medicines derived from medicinal plant raw materials confirms their stable demand and high market share in the EU. Unlike the tendency

toward mono-component formulations often seen in other regions, the European pharmaceutical industry focuses on standardized complex extracts with multi-target therapeutic effects [19].

According to our analysis, the most frequently utilized herbal extracts in European respiratory syrups are: Ivy leaf (*Hedera helix*) – the absolute leader in the secretolytic segment (e.g., "Prospan", "Herbion"); Thyme (*Thymus vulgaris/serpyllum*) – primarily used for its potent bronchospasmolytic and antibacterial properties; Primrose root (*Primula veris*) – often combined with thyme to enhance expectoration; Ribwort Plantain (*Plantago lanceolata*) – a key component for soothing non-productive coughs; Iceland Moss (*Cetraria islandica*) – widely used in Central Europe for its demulcent and mucosal protective effects; Pelargonium (*Pelargonium sidoides*) – a specific European trend for treating acute bronchitis with antiviral support [12, 15].

In contrast to markets that prefer simple herbal syrups (like Licorice or *Althaea* mono-syrups), European manufacturers prioritize complex formulations. These often include essential oil fractions such as Anise, Peppermint, and Eucalyptus, which provide a secondary secretolytic effect through the activation of the ciliary epithelium [17].

The European approach is characterized by "Phytoneering" – using high-tech extraction methods to ensure a constant concentration of active markers (such as hederacoside C in ivy or thymol in thyme). This ensures that herbal syrups like Bronchipret or Tussavit provide clinical results comparable to synthetic mucolytics while maintaining a superior safety profile [15, 16, 19].

One of the main priorities for the development of pharmaceutical science and the industry is to expand the range of domestic drugs. Therefore, the analysis and reassessment of already known raw material sources, along with the search for new ones, as well as the study of opportunities for optimizing the production of drugs based on them, is an integral part of the development of pharmacy and medicine in general.

### 1.3. Pharmacognostic characteristics and therapeutic potential of *Thymus serpyllum*

*Thymus serpyllum* L. belongs to the family Lamiaceae (fig. 1.4). This is a perennial strongly branched subshrub up to 15 cm high, ending in recumbent shoots. The leaves are elliptical or oblong-elliptical, 5-10 mm long, 1.5-3.5 mm wide, located on a short petiole, with glands filled with essential oil. Long hairs are noticeable at the base of the leaf. The inflorescences are compactly collected in heads at the ends of the branches. The calyx is narrowly bell-shaped, about 4 mm long. The peduncle is shorter than the calyx. The corolla is pinkish-purple (purple-red), bright, 6-8 mm long. The fruit is small, an ellipsoidal nut, about 0.6 mm long. The plant is fragrant. *Thymus serpyllum* blooms, depending on the environment, from late May to late August. The fruits ripen in June-September. It is found in the temperate climate of Eurasia. Mostly in the steppe zone [20, 21].



**Fig. 1.4. *Thymus serpyllum* L.**

The main components of thyme herb are essential oil, which consists of approximately 34-42 % of phenols, of which up to 40 % is thymol, as well as carvacrol, n-cymene, L- $\alpha$ -pinene,  $\gamma$ -terpinene, terpineol, L-borneol, caryophyllene, linalool. Phenolic acids, where the dominant compound is rosmarinic acid, which acts as a powerful antioxidant and anti-inflammatory agent. Other present acids

include caffeic, chlorogenic, and lithospermic acids. Flavonoids represented by luteolin, apigenin, scutellarein, and their glycosidic derivatives (such as rutin and quercitrin) [20, 22].

The herbal drug contains pentacyclic triterpenes, primarily ursolic acid and oleanolic acid, which contribute to its hepatoprotective and anti-inflammatory activities. Thyme herb also contains tannins, bitterness, gums, triterpene compounds – ursolic and oleanolic acids; flavonoids, a large number of mineral salts, macroelements (mg/g): K, Ca, Mn, Fe; microelements: Mg, Cu, C, Mo, Cr, Al, Se, Ni, Sr, Pb [22].

Many researchers have studied flavonoids in plants of the genus *Thymus*, and many authors suggest standardizing thyme according to the content of flavonoids in their composition. Rutin and quercetin are most often offered as comparison samples. The literature describes studies devoted to the study of triterpene compounds, the amino acid composition, the complex of mineral elements were studied, and fatty oil was found in the seeds [20].

According to the European Pharmacopoeia (Ph Eur), the official herbal drug (*Serpylli herba*) consists of the whole or cut, dried, flowering aerial parts of *Thymus serpyllum* L. The pharmacopoeial quality standards require a minimum essential oil content of 3.0 ml/kg (for the whole drug) and 2.0 ml/kg (for the cut drug) on an anhydrous basis [21].

Healing properties of thyme herb is used to improve the functioning of the intestines, stomach, pancreas, blood vessels and heart. It has a positive effect on the genitourinary, respiratory and endocrine systems. For colds: laryngitis, tonsillitis, pharyngitis, sore throats, the antiseptic properties of this plant are used, and a decoction based on thyme is also used for sinusitis and rhinitis, as drops [22].

In medical practice, thyme herb is used as an expectorant and anti-inflammatory agent. Thyme herb extract increases the amount of secretory secretion of the mucous membranes of the upper respiratory tract, helps to thin sputum and accelerate its excretion. Thyme extract is a part of the drug "Evkabal",

"Bronhipret" (Germany), "Tusavit" (Austria), "Echinasal" (Poland), "Stoptusin-phyto" (Czech Republic) [4, 5, 6, 12, 15].

Without preliminary processing, fresh thyme is used to treat wounds, ulcers, and skin diseases. For this purpose, crushed herb is used, which is applied to the affected areas of the skin. In a similar way, it is used to reduce swelling, pain, and itching after insect bites – bees, wasps, gadflies, etc. [23].

It is believed that preparations with thyme have a positive effect on sexual function. Infusions and thyme oil are used in folk medicine for the treatment and prevention of prostatitis and impotence. Infusions are drunk on an empty stomach, and the oil is rubbed into the perineum. Baths with thyme decoction can also be used for this purpose. Similar baths and compresses (poultices) with thyme are also used for skin diseases, rheumatism, dislocations, bruises, and edema [23, 24].

The therapeutic efficacy of *Thymus serpyllum* preparations in respiratory diseases is mediated by a synergetic multi-target action.

The active constituents (primarily volatile phenols) stimulate the ciliary activity of the ciliated epithelium in the respiratory tract. This accelerates the upward transport of mucus (mucociliary clearance). At the same time, the administration of thyme preparation stimulates the secretory glands of the bronchial mucosa, increasing the liquid volume of the bronchopulmonary secretion, thereby thinning viscous sputum [22].

Thymol and carvacrol exert a direct spasmolytic effect on the smooth muscle of the bronchi. This effect is mediated by the inhibition of calcium ion influx through voltage-dependent calcium channels and the stimulation of  $\beta_2$ -adrenergic receptors, effectively relieving bronchospasms associated with obstructive bronchitis and pertussis [24].

Due to the high lipophilicity of thymol and carvacrol, they easily penetrate the cell membranes of pathogens (including *Streptococcus pneumoniae*, *Haemophilus influenzae*, and *Moraxella catarrhalis*). This disrupts membrane permeability, leading to the leakage of essential intracellular contents and subsequent cell death [24].

Rosmarinic acid and flavonoids inhibit key inflammatory mediators, such as cyclooxygenase-2 (COX-2) and 5-lipoxygenase (5-LOX), reducing the production of prostaglandins and leukotrienes. This effectively decreases mucosal edema and irritation of the respiratory cough receptors [23, 24].

In modern European medical and pharmaceutical practice, raw extracts of *Thymus serpyllum* are rarely used in their crude form. Instead, the industry relies on standardized liquid, soft, or dry extracts. Due to its safety profile, *Thymus serpyllum* is a key ingredient in several registered European OTC cough formulations: "Bronchipret" (Germany) – highly standardized combination of thyme dry extract and ivy leaf liquid extract, clinically proven to reduce cough severity; "Tussavit" (Austria) – a liquid formulation combining liquid thyme extract with plantain leaf extract, designed to treat both productive and non-productive coughs; "Stoptussin-Phyto" (Czech Republic) – a combined syrup containing thyme and plantain extracts, showing strong secretolytic and anti-inflammatory properties; "Echinasal" (Poland) – a complex syrup containing thyme extract alongside *Echinacea purpurea* juice, providing immunomodulatory and expectorant therapy [4, 5, 6, 12, 15].

## CONCLUSIONS

Based on the analysis of the European pharmaceutical market, it was established that respiratory medications constitute a significant segment, with syrups being the preferred liquid dosage form. In the EU, the market is characterized by a high degree of therapeutic diversification, where Germany, France, and Italy are the leading manufacturers, controlling approximately 68 % of the cough medicine sector. It was demonstrated that syrups remain a highly relevant dosage form for all age categories due to their non-invasive administration, uniform absorption, and high patient compliance.

The literature review confirmed a global trend toward the use of standardized herbal preparations. Unlike the prevalence of mono-extracts in some regions, the European market prioritizes "Phytoneering" – the use of high-tech, complex herbal compositions (e.g., "Bronchipret", "Prospan", "Herbion") that ensure consistent concentration of active markers and clinical efficacy comparable to synthetic mucolytics. *Thymus serpyllum* L. was identified as a strategically important raw material for the development of expectorant drugs. Its multi-target action – combining secretomotor, spasmolytic, and antimicrobial effects – is mediated by a unique phytochemical complex of phenolic monoterpenes (thymol, carvacrol), rosmarinic acid, and flavonoids.

The generalization of technological and pharmacognostic data confirms that the integration of standardized thyme extracts into syrup bases is an optimal approach for creating stable and effective domestic medications. This substantiates the relevance of the chosen research topic and provides a theoretical foundation for the subsequent experimental development of the new cough syrup composition.

## CHAPTER II. OBJECTS AND METHODS OF RESEARCH

### 2.1. Objects of research

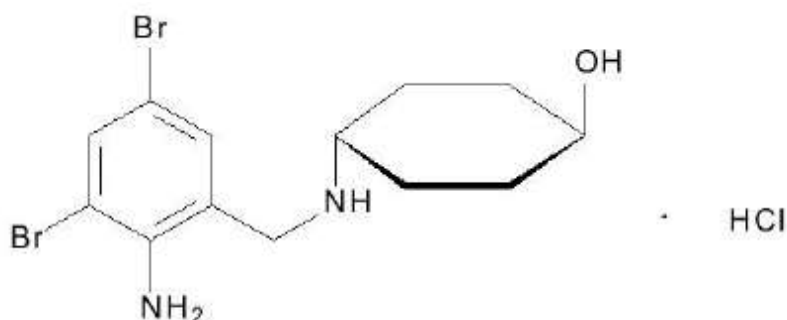
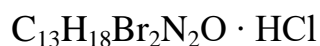
The following were used in experimental studies:

*Research objects:*

Liquid extract of thyme herb – rich in biologically active substances – it contains bitter and tannins, triterpenoids, gum, resin, flavonoids, organic acids, essential oil, vitamins (A, B<sub>1</sub>, B<sub>2</sub>, PP, B<sub>5</sub>, B<sub>6</sub>, B<sub>9</sub>, C), macroelements (potassium, calcium, magnesium, sodium, phosphorus) and microelements (iron, manganese, copper, selenium, zinc). The medicinal properties of thyme extract are determined by the presence of essential oil in it, the component of which is thymol, which has a bactericidal effect on coccal pathogenic flora and a bacteriostatic effect on gram-negative microorganisms [25].

Ambroxol hydrochloride

trans-4-[[[(2-Amino-3,5-dibromophenyl)methyl]amino]cyclohexan-1-ol hydrochloride



**Fig. 2.1. Structural formula of ambroxol hydrochloride**

Ambroxol hydrochloride (SPhU 2.0, Vol. 2, P. 26; CAS: 23828-92-4; PubChem SID: 329770608) is a white or white with a yellowish tinge crystalline powder. Slightly soluble in water, practically insoluble in methylene chloride. Molecular weight: 414.6 [7, 32].

*Excipients:*Ethanol 95 %

A clear, colorless, mobile liquid with a characteristic alcoholic odor. Miscible with water, chloroform, acetone, and glycerin in all proportions. It is used as an extractant in the preparation of extractive drugs, as well as as a co-solvent in the preparation of various dosage forms [7, 32].

White crystalline sugar

White, homogeneous, free-flowing mass of crystals with a characteristic sugar-sweet taste. Without foreign flavors or odors. Very easily soluble in water, slightly soluble in ethanol 96 %, practically insoluble in chloroform. It melts at a temperature of 186-188 °C, forming complex substances colored brown (caramelization). It is used as an auxiliary component in the preparation of both solid and liquid dosage forms [7].

Purified water

Colorless, clear, odorless liquid [7, 32].

Aromatic food essence "Orange"

A natural food flavoring used in industrial food production, intended to impart a pleasant citrus flavor and orange aroma to various food products. The flavoring is intended to impart flavor and aroma to food products and to enhance existing flavor and aroma. The substances used to produce the flavoring are identical to the corresponding substances found in nature [12].

## **2.2. Research methods**

The work used physicochemical and technological research methods. The research was conducted in accordance with the requirements of the pharmacopoeial articles of the State Pharmacopoeia of Ukraine 2.0 and European Pharmacopoeia [7, 32].

Appearance. The syrup was tested according to organoleptic indicators: color, transparency of the solution, smell, taste.

Solution transparency. A flat-bottomed, colourless, transparent neutral glass tube with an internal diameter of 15 mm to 25 mm was used. The determination was carried out in diffuse daylight, viewed along the vertical axis against a black background [7, 32].

Color of the solution. It was determined visually by comparing the color of the tested samples with purified water. The comparison was carried out in identical test tubes made of colorless transparent glass in diffused daylight, viewing the samples horizontally on a white background [7, 32].

Refractive index was determined using an IRF 545B refractometer [7].

The pH value was determined by the potentiometric method using a pH meter of the pH-340 type [7, 32].

Relative density was determined using a pycnometer [7, 32].

Ethanol content determined by the pycnometric method [7, 32].

Determination of microbiological purity syrup was carried out in accordance with the requirements of the SPhU. The developed syrup belongs to the microbiological purity category 3B – for oral administration from raw materials of natural origin (animal, vegetable or mineral), the level of microbial contamination of which cannot be reduced during pre-treatment [7, 32].

Definition of flavonoids. Cyanidin test. To 1 ml of the test sample, 2-3 drops of concentrated hydrochloric acid and 0.1 g of magnesium metal were added. The resulting color (red) was observed. 1/3 of butanol by volume was added to the colored product and diluted with water until the layers separated, shaken and the transition of pigments to the aqueous or organic phase was noted. Pigments of glycosides remained in water, and aglycones passed into the organic solvent layer [32].

Determination of ambroxol hydrochloride. Qualitative reaction to chloride ion. To 2 drops of the test sample containing chloride ion, add 1 drop of dilute nitric acid and 3 drops of silver nitrate solution. Observe a white curdled precipitate soluble in ammonium hydroxide [32].

Methodology for comprehensive evaluation of organoleptic properties of syrup. This is a method of comprehensive assessment of appearance, color and taste, proposed by Andreeva I. M. for the purpose of assessing the organoleptic properties of a liquid dosage form [10, 20]. The assessment is based on 3 criteria: appearance; color range and taste and smell in the full range. Indicators, their characteristics, possible assessments and the general assessment scale are presented in table. 2.1 and 2.2.

Table 2.1

**Method for comprehensive assessment of appearance, color and taste**

<b>Quality indicator</b>	<b>Characteristic</b>	<b>Score</b>
Appearance	Transparent solution	7 (good)
	Weak opalescence, consistent with regulatory documentation	5 (good)
	Strong opalescence or stable suspension that meets regulatory documentation	4 (satisfactory)
	Opaque aqueous solutions	1 (unsatisfactory)
Color	Bright color that matches the smell and taste	7 (excellent)
	Brightly expressed color, but does not combine with either taste or smell	5 (excellent)
	A subtle color that matches the taste and smell	4 (satisfactory)
	Dirty color that does not match the smell and taste	1 (unsatisfactory)
Taste and aroma	Characteristic full taste, matching the aroma with a long pleasant aftertaste	12 (excellent)
	Good taste, matching the aroma. Another aftertaste appears after 2 minutes.	10 (good)
	Strong taste but weak aroma, with another aftertaste appearing in less than 2 minutes.	8 (satisfactory)
	Poorly expressed taste with an off-putting feel and an unpleasant aftertaste	6 (unsatisfactory)

According to the scoring system on this scale, the upper score limit is 26 points, the lower is 15. The overall score is based on the sum of the points obtained according to the three criteria [26, 27].

Table 2.2

**General rating scale**

Rating	Total score
Perfectly	23-26
Good	19-22
Satisfactorily	15-18
Unsatisfactorily	Below 15

Statistical processing. Statistical analysis of the obtained results was carried out in accordance with the methods given in the SPhU 2.0, Vol. 1. Calculations of the results were carried out using the Microsoft Excel computer program. Changes in the studied indicators were considered statistically significant at  $p < 0.05$  [7].

## CONCLUSIONS

1. The objects of the study are presented and described – a plant phytosubstance – liquid extract of thyme herb and a synthetic substance – ambroxol hydrochloride, as well as excipients (ethanol 95 %, purified water, glycerin, white crystalline sugar), which were used in the justification and development of the composition of the medicinal syrup with antitussive action.

2. Organoleptic and physicochemical methods of research of the developed medicinal syrup, as well as identification methods, are described. Pharmacopoeial methods were used to assess the quality of the prepared syrup.

## CHAPTER 3. DEVELOPMENT OF THE COMPOSITION, TECHNOLOGY AND STANDARDIZATION OF MEDICINAL SYRUP

### 3.1. Research on the selection of a rational syrup composition

#### *Choosing a rational composition of active ingredients*

To create a medicinal syrup, a liquid herbal extract of thyme herb (1:1) was used on a water-alcohol basis (a mixture of 30 % ethanol and 10 % propylene glycol). Propylene glycol is traditionally added to the extract to increase the viscosity of the extractant solution, which provides for improved mechanical properties of the extractant, including lower volatility and ease of mixing. It removes surface tension, improves the wettability of the raw material, and also the penetration of the extractant into cells [28].

At the first stage of the research, a rational concentration of liquid thyme extract in the syrup was selected. It was selected based on the calculation of appropriate doses of complex preparations containing liquid thyme extract.

In the current pharmaceutical market of the EU, thyme-based medicines (*Thymus serpyllum* and *Thymus vulgaris*) occupy leading positions in the segment of OTC medicines for the treatment of respiratory diseases. According to the EU Register of Medicinal Products and the monographs of the Committee on Herbal Medicinal Products (HMPC) of the European Medicines Agency (EMA), thyme is recognized as a remedy with a "well-established medical use" [9].

In European medical practice, complex syrups, where thyme extract is a key component in combination with other herbal or synthetic ingredients, have become widespread. In particular, a number of highly effective liquid dosage forms have been registered on the markets of Germany, Austria, Poland and the Czech Republic: "Bronchipret" (Germany), "Tussavit" (Austria), "Bronchostop" (Austria), "Echinasal" (Poland), "Herbion Thyme" (Slovenia), "Stoptussin-Phyto" (Czech Republic) (table 3.1) [15].

Table 3.1

**Liquid medicinal preparations based on thyme extract**

<b>Trade name</b>	<b>Manufacturer</b>	<b>Composition</b>
Bronchipret	Bionorica SE (Germany)	Thyme herb liquid extract ( <i>Thymus vulgaris</i> ), Ivy leaf liquid extract ( <i>Hedera helix</i> ), 7 % ethanol, maltitol liquid, potassium sorbate, citric acid monohydrate, hydroxypropyl betadex.
Herbion Thyme	KRKA, d.d. (Slovenia)	Thyme herb liquid extract ( <i>Thymus vulgaris</i> ), levomenthol, sucrose, methyl parahydroxybenzoate.
Evkabal	Esparma GmbH (Germany)	Plantain liquid extract ( <i>Plantago lanceolata</i> ), Thyme herb liquid extract ( <i>Thymus vulgaris</i> ), methylparahydroxybenzoate, propylparahydroxybenzoate, invert sugar syrup.
Tussavit	Montavit Ges.m.b.H. (Austria)	Thyme herb liquid extract ( <i>Thymus vulgaris</i> ), Plantain liquid extract ( <i>Plantago lanceolata</i> ), sucrose, glycerin 85 %, caramel, sodium benzoate.
Bronchostop	Kwizda Pharma (Austria)	Thyme herb liquid extract, Marshmallow root liquid extract ( <i>Althaea officinalis</i> ), raspberry juice concentrate, saccharin sodium, methyl parahydroxybenzoate.
Stoptussin- Phyto	Teva Czech Industries (Czech Republic)	Thyme herb liquid extract ( <i>Thymus serpyllum</i> ), Plantain liquid extract, Thyme liquid extract ( <i>Thymus vulgaris</i> ), honey, sodium benzoate, sucrose, glycerin 85 %.
Echinasal	Herbapol (Poland)	Thyme herb liquid extract, <i>Echinacea purpurea</i> juice, Plantain extract, Rosary fruit extract, blackcurrant concentrate, sucrose, citric acid.

The presence of thyme extract in the composition of these medicines determines their mucolytic properties – it thins phlegm and promotes its removal

from the lungs. In our formulation, the concentration of the extract is set at 12.0 g per 100 g of the finished product. This concentration is scientifically justified as optimal for stimulating ciliary activity and providing a significant anti-inflammatory effect without causing gastrointestinal irritation [27].

Thyme extract is an excellent secretolytic and is often used to treat productive cough. However, technological and pharmacological improvements in the formulation are relevant for drugs in this pharmacotherapeutic group [29].

We plan to increase the effectiveness of the therapeutic effect by introducing ambroxol hydrochloride into the dosage form.

Ambroxol stimulates serous cells of the glands of the bronchial mucosa, increases the content of mucous secretion and the release of surfactant in the alveoli and bronchi, normalizes the ratio of the serous and mucous components of sputum; by activating hydrolyzing enzymes and enhancing the release of lysosomes from Clark cells, it reduces the viscosity of sputum [30].

Ambroxol remains the "gold standard" for secretolytic therapy in Europe. table 3.2 presents the leading european preparations that served as benchmarks for our technological and quality standards [30].

Table 3.2

### Ambroxol-based liquid medications in the EU

Trade name	Manufacturer	Composition
1	2	3
Mucosolvan® (Lasolvan)	Sanofi / Boehringer Ingelheim (Germany/France)	Ambroxol hydrochloride; sucralose, benzoic acid, hydroxyethylcellulose, forest berry flavor, purified water.
Ambrobene	Merckle GmbH / Ratiopharm (Germany)	Ambroxol; sorbitol 70 %, propylene glycol, saccharin sodium, raspberry flavor, purified water.
Ambrolitin	Sopharma (Bulgaria)	Ambroxol hydrochloride; sorbitol, citric acid, methyl/propyl parahydroxybenzoate, glycerin, propylene glycol.

1	2	3
Ambrohexal	Salutas Pharma / Hexal AG (Germany)	Ambroxol; benzoic acid, sodium metabisulfite, sodium cyclamate, sorbitol solution, glycerin, raspberry essence.
Ambroxol- Teva	Teva Pharmaceuticals (Germany/EU)	Ambroxol hydrochloride; sorbitol solution, propylene glycol, saccharin, raspberry flavor, purified water.
Ambrohim	Hemofarm (Serbia/EU)	Ambroxol hydrochloride; benzoic acid, glycerin (85 %), sorbitol solution, hydroxyethylcellulose, raspberry flavor.

A comprehensive analysis of the European pharmaceutical market reveals that while both components are widely used individually, a combined drug containing both thyme and ambroxol is currently unavailable in the EU. This lack of a combined formulation provides a significant opportunity for the development of a unique, "two-in-one" therapeutic solution that targets both mucus production and its mechanical clearance [6, 12, 15].

In European clinical practice, the standard oral dosage of ambroxol for adults is 30 mg three times daily. For the pediatric population (aged 6 to 12 years), the dose is 15 mg three times daily, and for children aged 3 to 6 years, it is 7.5 mg three times daily [30].

To ensure precise dosing using standard pharmaceutical measuring tools (spoons or measuring cups), we calculated the content of ambroxol hydrochloride per 100 ml of syrup (standard vial volume). Taking into account the density of the syrup base and the required therapeutic window, the concentration of ambroxol hydrochloride was set at 0.2 g per 100 ml. This concentration allows for a convenient and safe dosing regimen, aligning the new product with the safety profiles of existing European OTC medications while offering enhanced efficacy through herbal synergy [31].

### *Selection of auxiliary composition for syrup*

Choosing the optimal combination of excipients is undoubtedly an important part of the technological process.

As the primary carrier for the combined composition of thyme liquid extract and ambroxol hydrochloride, a classical sucrose-based syrup was selected. The rationale for this choice is based on several technological factors: provides natural antimicrobial stability, ensures a stable matrix for the highly concentrated Thyme extract (12.0 %), creates the necessary texture for prolonged contact with the oropharyngeal mucosa, which is beneficial for soothing irritation [31].

Thyme extract possesses a distinct, pungent, and spicy aroma with a characteristic herbal bitterness due to high concentrations of thymol and carvacrol. Additionally, the bitter profile of ambroxol hydrochloride requires effective taste masking to ensure compliance, particularly in pediatric practice [28].

To determine the optimal flavor profile, technological studies were conducted to select flavoring agents that align with the specific chemical nature of the active complex. According to established pharmaceutical guidelines, bitterness is best corrected by a combination of high sweetness and aromas that naturally possess a subtle bitter or spicy undertone [31].

Based on these principles, three experimental samples were formulated with the addition of the following flavor-aromatic compositions: "Cherry" (to mask herbal bitterness through deep fruit notes); "Orange" (to harmonize the citrus-fresh profile with the spicy aroma of Thyme); "Cocoa/Chocolate" (to neutralize the sharp taste of the active ingredients using a masking effect) [31].

The sensory evaluation of the experimental syrups was conducted using the methodology described in chapter 2. This comprehensive method assesses the liquid dosage form across three distinct criteria: appearance (transparency, presence of sediment); color profile (homogeneity and intensity); taste and odor (full spectrum analysis, including aftertaste) [7, 32].

The evaluation was performed by a panel of five experts of varying ages and genders. The final score was calculated as the arithmetic mean of the points

awarded for each indicator. This structured approach allows for an objective selection of the flavoring system that best masks the active ingredients' bitterness while preserving the syrup's aesthetic appeal. The results of the organoleptic assessment are presented in table 3.3.

Table 3.3

**Results of the organoleptic evaluation of the syrup samples**

<b>Composition</b>	<b>Total score</b>			
	<b>Appearance</b>	<b>Color profile</b>	<b>Taste and odor</b>	<b>Rating</b>
Syrup with the composition "Cherry"	7 Clear, viscous solution	4 Yellow-brown	10 Sweet with bitterness, with a cherry aroma	21 good
Syrup with the composition "Orange"	7 Clear, viscous solution	7 Yellow-brown	12 Sweet with a slight bitterness, with an orange aroma	26 perfectly
Syrup with the composition "Cocoa"	7 Clear, viscous solution	5 Brown	11 Sweet with bitterness, with a cocoa aroma	22 good

As can be seen from the data in table 3.3, the highest organoleptic properties were shown by the syrup with the flavor-aromatic-floral composition "Orange", which we accepted as optimal for the syrup under development.

The resulting composition has the following advantages: sugar corrects the bitter taste of thyme extract. It complements the composition "Orange", which is successfully combined with the bitter taste of the original syrup. The aroma "Orange" covers the characteristic sharp smell of thyme essential oil. We have adopted this composition as optimal for the composition of the syrup with thyme extract and ambroxol hydrochloride.

Thus, we selected the following syrup composition based on thyme liquid extract and ambroxol hydrochloride.

**Composition per 100 g:***Active ingredients:*

Thyme liquid extract	12.0 g
----------------------	--------

Ambroxol hydrochloride	0.2 g
------------------------	-------

*Excipients:*

Flavoring "Orange	0.02 g
-------------------	--------

Ethanol 95 %	4.06 g
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Purified water	0.94 g
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Sugar syrup	up to 100.0 g
-------------	---------------

**3.2. Development of technology for the production of medicinal syrup**

The technological process of syrup production consists of the following stages: preparation of production, preparation of raw materials and materials, preparation of sugar syrup, preparation of syrup with thyme extract and ambroxol hydrochloride, filtering of syrup, packaging and labeling of syrup.

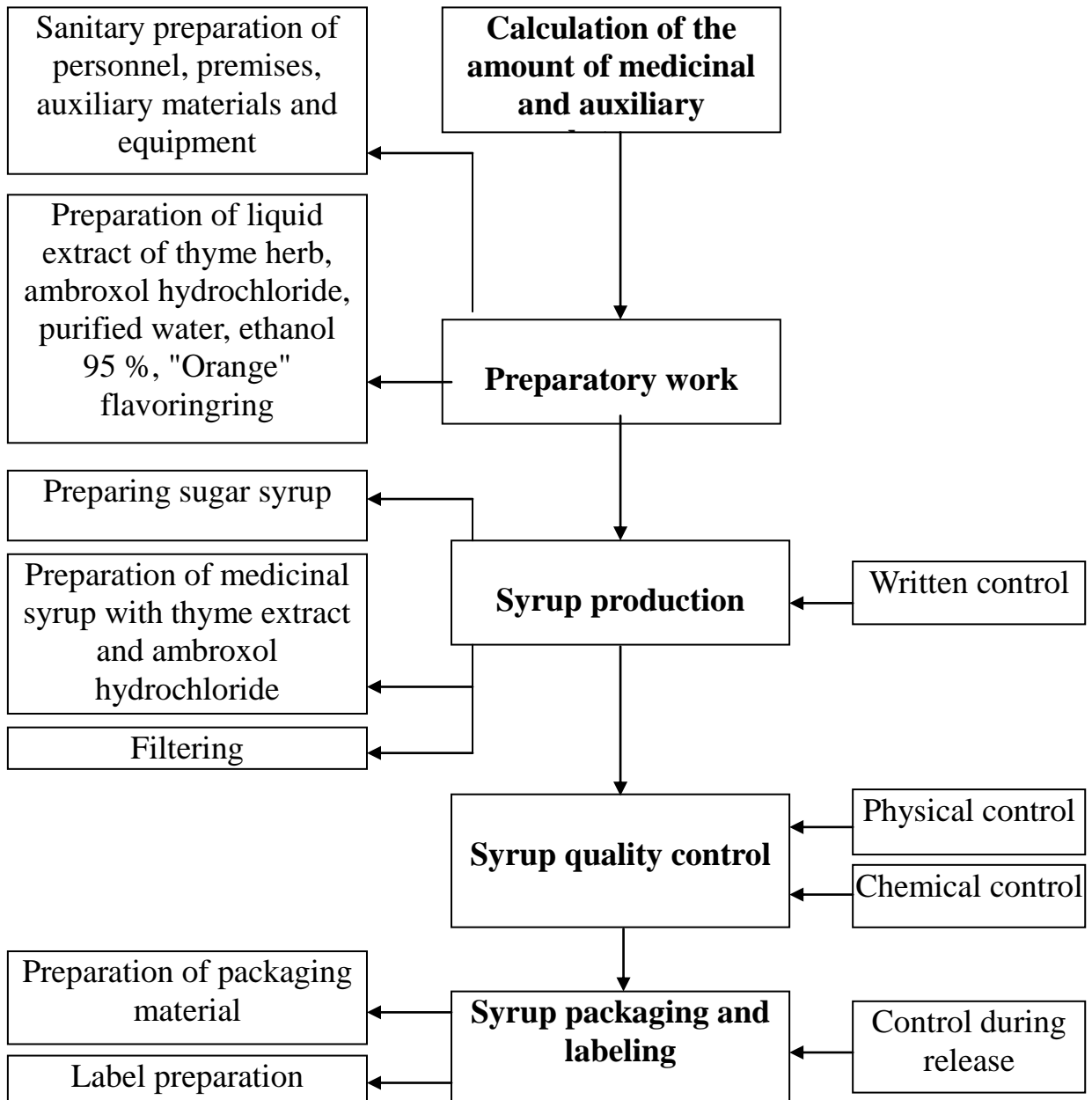
Production preparation includes the following processes: preparation of production facilities and equipment, preparation of ventilation air, preparation of technological clothing, personnel training, preparation of containers [26].

Preparatory work includes measures to carry out a complex of sanitary and hygienic works aimed at preventing microbial contamination of products. The cleanliness class of the premises for syrup preparation is 3B [32].

Preparation of sugar syrup. Sugar syrup was prepared in the ratio of 64 parts of sugar to 36 parts of water. When heating the water to a temperature of 60-70 °C, the calculated amount of sugar was added in portions with continuous stirring. After dissolving the sugar, the syrup was allowed to boil 2 times (but not more than 25 minutes), while collecting the foam that formed. The cessation of foam formation on the surface of the syrup indicated its readiness.

Preparation of medicinal syrup with thyme extract and ambroxol. The resulting sugar syrup was cooled to a temperature of 45-55 °C, after which, with

constant stirring, the calculated amount of ambroxol hydrochloride was added to it. It was mixed well. Then, the food essence-flavoring agent "Orange" was added and mixed again. After that, the syrup was cooled to 20-25 °C and the calculated amount of thyme extract was added (12.0 extract per 100 ml of syrup). Mixing was carried out until a homogeneous mass was obtained. The resulting syrup was filtered through a paper filter and sent for packaging. The technological scheme for the production of cough syrup in a pharmacy is shown in fig. 3.1.



**Fig. 3.1. Technological scheme of cough syrup production in a pharmacy**

The resulting syrup is a viscous liquid from light brown to brown in color.

The final stage of the production process is packaging and labeling of finished products. Packaging and packaging consists of the following stages: packaging and labeling, packaging. The finished syrup is packed in dark glass bottles, sealed with polyethylene stoppers and screw caps. A label made of label paper is glued to each bottle and placed in a cardboard pack [26].

### **3.3. Development of quality indicators for medicinal syrup**

We determined the quality of the syrup according to the SPhU "Liquid preparations for oral use" and Ph Eur according to the following indicators: appearance, identification of biologically active substance, relative density, pH, ethanol content, refractive index, microbiological purity [7, 32].

Appearance of syrup. As a result of the experiments, we obtained a syrup, which is a viscous, transparent liquid of yellow-brown color, bitter-sweet taste with a specific orange smell.

The identification of the syrup was confirmed by a qualitative reaction to chloride ion (determination of ambroxol hydrochloride) and cyanidin test (determination of flavonoids) [32].

Qualitative reaction to chloride ion. To 2 drops of syrup solution containing chloride ion, 1 drop of dilute nitric acid and 3 drops of silver nitrate solution were added. A white curdled precipitate soluble in ammonium hydroxide was observed.

Qualitative analysis of flavonoids. 0.5 g of syrup was dissolved in 1 ml of 70 % ethanol, 2-3 drops of concentrated hydrochloric acid and 0.1 g of magnesium metal were added. The red color that appeared indicates the presence of flavonoids. 1/3 part of butanol is added to the colored product and diluted with water until the layers are separated, shaken and the transition of pigments. Pigments of glycosides remain in water, and aglycones pass into the organic solvent layer [33].

The relative density of the syrup was determined according to the SPhU 2.0, method 1, which is used to determine the density of liquids with an accuracy of

$\pm 0.01 \text{ g/cm}^3$  using a pycnometer. As a result of the conducted studies, the norm for this indicator was established within the range of  $1.050\text{-}1.450 \text{ g/cm}^3$  [7].

The ethanol content in the resulting drug was determined by distillation. When determining the alcohol content, taking into account the fact that an alcohol extract is introduced into the syrup, where the ethanol content may vary, we decided not to average the results obtained and set the norm for this indicator in the range from 8 to 11 % [32].

The pH of the syrup was determined by the potentiometric method using a pH meter of the pH-340 type. As a result of experimental studies, the norm for this indicator was established within the range of 5.5-6.0. Refractive index (refractive index) was determined using an 545B refractometer, according to the SPhU methodology, 2.2.6. As a result of the conducted studies, the norm for this indicator was established as not less than 1.450 [7, 32].

In accordance with the requirements of the SPhU, the syrup we developed belongs to the microbiological purity category 3B – for oral administration from raw materials of natural origin (animal, plant or mineral), the level of microbial contamination of which cannot be reduced during pre-treatment [7].

We conducted a study to determine whether the resulting syrup meets the requirements of the SPhU and Ph Eur. The results are presented in table 3.4.

Table 3.4

#### Results of determining the microbiological purity of syrup

Indicators	Research results	Norm
Total number of aerobic microorganisms, colony forming unit (CFU), in 1 ml	Less than $4 \cdot 10^1$	No more than $10^4$
Total number of yeast and mold fungi, CFU in 1 ml	Not detected	No more than $10^2$
Bile-resistant enterobacteria, CFU in 1 ml	Not detected	No more than $10^2$
Escherichia coli, in 1 ml	Not detected	Absence
Salmonella spp., in 10 ml	Not detected	Absence
Staphylococcus aureus, in 1 ml	Not detected	Absence

Thus, bacteriological studies of the resulting syrup confirmed that the object under study meets the requirements of the SPhU and Ph Eur category 3B [7, 32].

Therefore, we have developed quality standards for syrup with thyme extract and ambroxol hydrochloride (table 3.5).

Table 3.5

### Quality control indicators of medicinal syrup

<b>Indicators</b>	<b>Methods</b>	<b>Norms</b>
Appearance	Visual, SPhU, 2.2.1, 2.2.2; Ph Eur	viscous, clear liquid of yellow-brown color, bitter-sweet taste with a specific smell of orange
Flavonoids	Cyanidine test	red color
Ambroxol hydrochloride	Silver nitrate in the presence of nitric acid solution	white precipitate
Relative density	SPhU, 2.2.5; Ph Eur	1.050-1.450
Ethanol	SPhU, 2.9.10; Ph Eur	from 8 to 11 %
pH	SPhU, 2.2.3; Ph Eur	from 5.5 to 6.0
Refractive index	SPhU, 2.2.6	at least 1.450
Microbiological purity	SPhU, 5.1.4; Ph Eur	category 3B
Storage conditions		in a dry place, protected from light

## CONCLUSIONS

1. A study was conducted to substantiate the composition of the syrup with extract of thyme and ambroxol hydrochloride. Based on the results of technological research to evaluate taste qualities, the optimal flavor enhancers were selected: sugar syrup, which corrects the bitter taste of the plant, the "Orange" flavoring, which covers the characteristic strong, pungent smell of essential oil.

2. The technology of syrup with thyme extract and ambroxol has been developed. Technological schemes for the production of medicinal syrup in pharmacy and industrial production conditions and their detailed description are presented.

3. The quality standards for medicinal syrup with thyme extract were established taking into account all technological features. The quality was determined using the following indicators: description, relative density, identification, ethanol content, pH, refractive index.

4. The necessary microbiological studies were performed. The syrup met the following requirements: total number of aerobic microorganisms - no more than 10<sup>4</sup> CFU in 1 g (ml); total number of yeast and mold fungi no more than 10<sup>2</sup> CFU in 1 g (ml); bile-resistant enterobacteria, no more than 10<sup>2</sup> CFU in 1 g (ml); absence of *Escherichia coli* in 1 g (ml); absence of *Salmonella* spp. 10 g (ml); absence of *Staphylococcus aureus* in 1 g (ml) when stored for 10 days in the open form.

5. A specification has been developed for the resulting syrup with thyme extract and ambroxol, according to which the syrup is a viscous, transparent liquid of yellow-brown color, bitter-sweet taste with a specific smell of orange.

## GENERAL CONCLUSIONS

1. A marketing analysis of the pharmaceutical market of expectorant drugs was conducted. The nomenclature of syrups was presented and the state of research in the field of developing syrups with herbal preparations was studied. Literature data on the pharmacological action, range of preparations and spectrum of application of *Thymus serpyllum* were summarized. The prospects of developing syrups based on medicinal plant raw materials for their introduction into pharmaceutical and medical practice were substantiated.

2. A combined medicinal syrup based on thyme extract has been developed, containing ambroxol hydrochloride as an additional medicinal component. The composition of the syrup per 100 g (1 bottle) has been established: thyme liquid extract – 12.0 g, ambroxol hydrochloride – 0.2 g (active ingredients), "Orange" flavoring – 0.02 g, ethanol 95 % – 4.06 g, purified water – 0.94 g, sugar syrup – up to 100.0 g (excipients).

3. Based on the conducted experimental studies, the technology of syrup with thyme extract and ambroxol hydrochloride in pharmacy production conditions was developed, and a technological scheme was also developed.

4. The physical and physicochemical quality indicators of the syrup were investigated. It was found that the pH value (4.0) and the mass fraction of sugar (64.4 %) in the developed syrup correspond to a decrease in microbial contamination. The quality standards of the proposed syrup with thyme extract and ambroxol hydrochloride were established according to the following indicators: appearance, identification, pH, relative density, refractive index, ethanol content. Microbiological studies of the syrup confirmed its compliance with the requirements of category 3B when stored for 10 days in an open form.

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## **APPENDIXES**

**СУЧАСНІ ДОСЯГНЕННЯ  
ФАРМАЦЕВТИЧНОЇ НАУКИ  
В СТВОРЕННІ ТА СТАНДАРТИЗАЦІЇ  
ЛІКАРСЬКИХ ЗАСОБІВ І  
ДІЄТИЧНИХ ДОБАВОК, ЩО  
МІСТЯТЬ КОМПОНЕНТИ  
ПРИРОДНОГО  
ПОХОДЖЕННЯ**

*Матеріали VIII Міжнародної  
науково-практичної  
інтернет-конференції*



**10  
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***CONTINUATION OF APPENDIX A***

МІНІСТЕРСТВО ОХОРОНИ ЗДОРОВ'Я УКРАЇНИ  
МІНІСТЕРСТВО ОСВІТИ І НАУКИ УКРАЇНИ  
НАЦІОНАЛЬНА АКАДЕМІЯ НАУК ВИЩОЇ ОСВІТИ УКРАЇНИ  
НАЦІОНАЛЬНИЙ ФАРМАЦЕВТИЧНИЙ УНІВЕРСИТЕТ  
КАФЕДРА ФАРМАКОГНОЗІЇ ТА НУТРИЦІОЛОГІЇ

MINISTRY OF HEALTH OF UKRAINE  
MINISTRY OF EDUCATION AND SCIENCE OF UKRAINE  
NATIONAL ACADEMY OF HIGHER EDUCATION OF SCIENCES OF UKRAINE  
NATIONAL UNIVERSITY OF PHARMACY  
DEPARTMENT OF PHARMACOGNOSY AND NUTRICIOLOGY

**СУЧАСНІ ДОСЯГНЕННЯ ФАРМАЦЕВТИЧНОЇ НАУКИ  
В СТВОРЕННІ ТА СТАНДАРТИЗАЦІЇ ЛІКАРСЬКИХ ЗАСОБІВ  
І ДІЄТИЧНИХ ДОБАВОК, ЩО МІСТЯТЬ КОМПОНЕНТИ  
ПРИРОДНОГО ПОХОДЖЕННЯ**

**CURRENT APPROACHES OF PHARMACEUTICAL SCIENCE IN  
DEVELOPMENT AND STANDARDIZATION OF MEDICINES AND  
DIETARY SUPPLEMENTS THAT CONTAIN COMPONENTS OF  
NATURAL ORIGIN**

**Матеріали VIII Міжнародної науково-практичної  
інтернет-конференції**

**The Proceedings of the VIII International Scientific and Practical  
Internet-Conference**

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KHARKIV  
2026

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**С 89**

*Електронне видання мережне*

**Редакційна колегія:** О. С. Кухтенко, О. А. Рубан, Н. П. Половко,  
В. С. Кисличенко, О. О. Іосипенко

*Конференція зареєстрована у Державній науковій установі  
«Український інститут науково-технічної експертизи та інформації»  
(УкрІНТЕІ), посвідчення № 818 від 17 листопада 2025 р.*

*Сучасні досягнення фармацевтичної науки в створенні та  
стандартизації лікарських засобів і дієтичних добавок, що містять  
С 89 компоненти природного походження: матеріали VIII Міжнародної  
науково-практичної інтернет-конференції (м. Харків, 10 квітня 2026 р.).  
– Електрон. дані. – Х.: НФаУ, 2026. – 330 с. – Назва з тит. екрана.*

У збірнику розглянуто теоретичні та практичні аспекти розробки, виробництва лікарських засобів рослинного походження і дієтичних добавок, контролю якості, стандартизації лікарських засобів рослинного походження та визначення безпечності дієтичних добавок, а також їх реалізації в умовах сучасного фармацевтичного ринку.

Для широкого кола науковців, магістрантів, аспірантів, докторантів, викладачів вищих фармацевтичних та медичних навчальних закладів, співробітників фармацевтичних підприємств, фармацевтичних фірм.

*Друкується в авторській редакції. Автори опублікованих матеріалів несуть повну відповідальність за підбір, точність наведених фактів, цитат, економіко-статистичних даних, власних імен та інших відомостей. Матеріали подаються мовою оригіналу. Матеріали пройшли антиплагіатну перевірку за допомогою програмного забезпечення StrikePlagiarism.*

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**CONTINUATION OF APPENDIX A**

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**CONTINUATION OF APPENDIX A**

the 'Alva' cultivar exhibited the highest proportions of essential amino acids, indicating that this cultivar may represent a particularly valuable source of EAAs.

**Conclusions.** Using the UHPLC–ESI–MS/MS method, 15 amino acids were identified and quantified in apple peel and flesh samples, including five essential amino acids—valine, lysine, phenylalanine, threonine, and leucine. The results revealed notable differences in amino acid composition among the studied apple cultivars and between tissues. Among the analyzed cultivars, 'Alva' showed the highest proportion of essential amino acids in both peel and flesh, indicating its potential as a valuable dietary source of these nutritionally important compounds.

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**SYNERGY OF THYME EXTRACT AND AMBROXOL IN THE THERAPY  
OF RESPIRATORY DISEASES**

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**Introduction.** The modern approach to the treatment of inflammatory diseases of the respiratory tract is based on the epithelium and local immunity. Cough, as a complex protective reflex, requires not only suppression, but also correction. The most promising solution in this direction is the creation of combined agents, where time-tested plant substances are enhanced by high-tech synthetic molecules. Such a combination allows you to achieve a rapid clinical effect with minimal doses of ingredients [1].

**Materials and methods.** An analysis of world scientific publications contained in professional databases was conducted, and the mechanisms of interaction between terpenes and mucolytics at the cellular level were studied.

**Results and discussion.** The therapeutic activity of the medicinal plant *Thymus vulgaris* is determined by phenolic compounds - thymol and carvacrol. In addition to the direct bactericidal effect, these substances are able to irritate the nerve endings of the gastric mucosa, which reflexively stimulates the secretion of bronchial glands. This makes sputum less viscous even before direct contact with the lungs. In addition, the flavonoids of *Thymus vulgaris* provide a mild antispasmodic effect [2].

Ambroxol in combination with *Thymus vulgaris* acts as a powerful mucokinetic. Its uniqueness lies in the ability to activate prenatal and postnatal surfactant synthesis. Ambroxol not only thins mucus, but also prevents alveolar adhesion and improves the drainage function of the lungs. It has been clinically

proven that Ambroxol has an antioxidant effect, neutralizing free radicals formed in the area of inflammation [3].

The combination of these two components in the form of a syrup promotes rapid mucus thinning thanks to Ambroxol, acceleration of sputum excretion under the action of *Thymus vulgaris* terpenes. Complementing each other, these components allow you to create a medicine that is simultaneously effective for both dry and wet coughs.

It is important to note that the use of syrup as a dosage form provides an enveloping effect, which instantly reduces throat irritation, which often provokes new coughing attacks [1].

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#### VARIATION OF FLAVONOLS IN THE FRUITS OF *SAMBUCUS NIGRA* L. CULTIVARS

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**Introduction.** *Sambucus nigra* L. is a well-known medicinal plant which has an old history of use in folk medicine. This species is adapted to different soil types and is native to temperate regions of Europe and Asia. Many studies revealed that its fruits and flowers accumulate anthocyanins, flavonoids, phenolic acids and other biologically active compounds [1]. It was substantiated that the amounts of biochemical compounds depend on genotype. This became a reason to compare fruits of certified cultivars and wild genotypes in order to background the biological potential of different accessions and to offer insights for the development of practical use, and to propose genotypes for future breeding.

**Materials and methods.** Samples of elderberry cultivars and wild clones were collected at the full ripening stage in September and October. The fruits were lyophilised and ground into powder. The data were expressed on a dry weight (DW). The quantitative and qualitative composition of flavonols was determined using UHPLC mass spectrometry as described by González-Burgos et al. [2].

**Results and discussion.** Fruits of *S. nigra* accumulated eight flavonols: rutin, isoquercitrin, quercetin, kaempferol-3-*O*-rutinoside, kaempferol-3-*O*-glucoside, isorhamnetin-3-*O*-rutinoside, isorhamnetin-3-*O*-glucoside, and phloridzin. The flavonol rutin was detected in the largest amounts. Fruits of the investigated



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**"CURRENT APPROACHES OF PHARMACEUTICAL SCIENCE IN DEVELOPMENT AND STANDARDIZATION OF MEDICINES AND DIETARY SUPPLEMENTS THAT CONTAIN COMPONENTS OF NATURAL ORIGIN"**

(duration 6 hours)  
April 10, 2026, Kharkiv, Ukraine

Rector of the National University of Pharmacy,  
professor, doctor of pharmaceutical sciences



Oleksandr KUKHTENKO

Head of the department of pharmacognosy and nutriciology,  
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Viktoriia KYSLYCHENKO

МІНІСТЕРСТВО ОХОРОНИ ЗДОРОВ'Я УКРАЇНИ  
НАЦІОНАЛЬНИЙ ФАРМАЦЕВТИЧНИЙ УНІВЕРСИТЕТ

**АКТУАЛЬНІ ПИТАННЯ СТВОРЕННЯ  
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МАТЕРІАЛИ  
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**Укладачі:** Комісаренко М.А., Сурікова І. О., Боднар Л. А.,

Актуальні питання створення нових лікарських засобів: матеріали XXXII міжнародної науково-практичної конференції молодих вчених та студентів (15-17 квітня 2026 р., м. Харків). – Харків: НФаУ, 2026. – 453 с.

Збірка містить матеріали міжнародної науково-практичної конференції молодих вчених та студентів «Актуальні питання створення нових лікарських засобів, які представлені за пріоритетними напрямками науково-дослідної роботи Національного фармацевтичного університету. Розглянуто теоретичні та практичні аспекти синтезу біологічно активних сполук і створення на їх основі лікарських субстанцій; стандартизації ліків, фармацевтичного та хіміко-технологічного аналізу; вивчення рослинної сировини та створення фітопрепаратів; сучасної технології ліків та екстемпоральної рецептури; біотехнології у фармації; досягнень сучасної фармацевтичної мікробіології та імунології; доклінічних досліджень нових лікарських засобів; фармацевтичної опіки рецептурних та безрецептурних лікарських препаратів; доказової медицини; сучасної фармакотерапії, соціально-економічних досліджень у фармації, маркетингового менеджменту та фармакоекономіки на етапах створення, реалізації та використання лікарських засобів; управління якістю у галузі створення, виробництва й обігу лікарських засобів; суспільствознавства; фундаментальних та мовних наук.

УДК 615.1

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XXXII Міжнародна науково-практична конференція молодих вчених та студентів  
«АКТУАЛЬНІ ПИТАННЯ СТВОРЕННЯ НОВИХ ЛІКАРСЬКИХ ЗАСОБІВ»

---

**JUSTIFICATION OF THE COMPOSITION AND TECHNOLOGY  
OF THE SYRUP FOR THE TREATMENT OF RESPIRATORY TRACT DISEASES**

Bumakhruta Brakhim, Oliinyk S.V.

Scientific supervisor: Polovko N.P.

National University of Pharmacy, Kharkiv, Ukraine

sveta\_oleinik@ukr.net

**Introduction.** Respiratory diseases accompanied by cough consistently occupy one of the leading places in the structure of the general morbidity of the population. Despite the diversity of the pharmaceutical market, there is a constant need to create combined drugs that would combine high secretolytic activity of synthetic molecules with a mild therapeutic effect of plant components. The use of liquid dosage forms, in particular syrups, is most appropriate due to their high bioavailability, ease of dosing and better compliance, especially in pediatric and geriatric practice.

**Aim.** Scientific justification for the selection of active ingredients and auxiliary components for the development of the composition and manufacturing technology of a combined antitussive syrup.

**Materials and methods.** The work uses the method of systematic analysis of scientific sources and the results of marketing research on the modern market of mucolytic agents. The objects of the study were thyme extract and ambroxol hydrochloride.

**Results and discussion.** Analysis of the pharmacological properties of the ingredients has proven the feasibility of combining them in one dosage form. Thyme extract (*Thymus vulgaris*) contains essential oils (thymol, carvacrol), which provide expectorant, anti-inflammatory and antiseptic effects. Ambroxol hydrochloride, as a powerful mucolytic, stimulates the synthesis of surfactant and reduces the viscosity of sputum.

It was established that the synergistic interaction of these components allows to achieve a complex effect on the pathological process: thinning of the secretion, facilitating its removal and stopping inflammation of the mucous membrane. A sucrose solution was chosen as the sugar base, which provides the necessary consistency and preservative effect. The study of technological aspects showed that the optimal method is the dissolution of active compounds in the finished sugar syrup at a certain temperature regime, which allows to maintain the stability of thermolabile components of the plant extract.

**Conclusions.** The composition of the combined syrup based on thyme extract and ambroxol is theoretically substantiated. The proposed technology ensures the production of a stable dosage form with high consumer properties.



МІНІСТЕРСТВО ОХОРОНИ ЗДОРОВ'Я УКРАЇНИ  
НАЦІОНАЛЬНИЙ ФАРМАЦЕВТИЧНИЙ УНІВЕРСИТЕТ



**СЕРТИФІКАТ УЧАСНИКА**  
Цим засвідчується, що  
**Bumakhruta Brakhim, Oliinyk S.V.**  
**Scientific supervisor: Polovko N.P.**  
брав(ла) участь у роботі  
XXXII Міжнародної науково-практичної конференції молодих вчених та студентів  
**«АКТУАЛЬНІ ПИТАННЯ СТВОРЕННЯ НОВИХ ЛІКАРСЬКИХ ЗАСОБІВ»**

Ректор  
Національного фармацевтичного  
університету



Олександр КУХТЕНКО

15-17 квітня 2026 р., м. Харків, м. Ужгород



МІНІСТЕРСТВО ОХОРОНИ ЗДОРОВ'Я УКРАЇНИ  
НАЦІОНАЛЬНИЙ ФАРМАЦЕВТИЧНИЙ УНІВЕРСИТЕТ

# ГРАМОТА

нагороджується

**Бумахрута Брахім**

за участь у секційному засіданні студентського наукового  
товариства кафедри  
аптечної технології ліків

**XXXII МІЖНАРОДНОЇ НАУКОВО-ПРАКТИЧНОЇ  
КОНФЕРЕНЦІЇ  
МОЛОДИХ ВЧЕНИХ ТА СТУДЕНТІВ  
«АКТУАЛЬНІ ПИТАННЯ СТВОРЕННЯ НОВИХ  
ЛІКАРСЬКИХ ЗАСОБІВ»**

Ректор закладу  
вищої освіти



**Олександр КУХТЕНКО**

15 квітня 2026 р. м. Ужгород





**МІНІСТЕРСТВО ОХОРОНИ ЗДОРОВ'Я УКРАЇНИ  
НАЦІОНАЛЬНИЙ ФАРМАЦЕВТИЧНИЙ УНІВЕРСИТЕТ  
РАДА МОЛОДИХ ВЧЕНИХ  
СТУДЕНТСЬКЕ НАУКОВЕ ТОВАРИСТВО  
ГО «УКРАЇНСЬКА ФАРМАЦЕВТИЧНА СТУДЕНТСЬКА АСОЦІАЦІЯ»**

## **ПРОГРАМА**

**XXXII Міжнародної науково-практичної конференції  
молодих вчених та студентів  
«АКТУАЛЬНІ ПИТАННЯ СТВОРЕННЯ НОВИХ ЛІКАРСЬКИХ  
ЗАСОБІВ»**

**15-17 квітня 2026 р.**



# **аптека**



**Харків, Ужгород – 2026**

XXXII Міжнародна науково-практична конференція молодих вчених та студентів  
«АКТУАЛЬНІ ПИТАННЯ СТВОРЕННЯ НОВИХ ЛІКАРСЬКИХ ЗАСОБІВ»

---

## Засідання гуртків СНТ на кафедрах

### Кафедра аптечної технології ліків

Час проведення: 17.04.2026 р. 12:05

Ідентифікатор: 502 808 8479

Код доступу: 1539

- 1. Розроблення складу стоматологічного гелю з ефірною олією чебрецю звичайного**  
Доповідач: Юсіфов Сурхай Аділ огли,  
Науковий керівник: Олійник С. В., к. фарм. н., доцент
- 2. «PHARMASY OS GOLD» Комплексна цифрова система управління екстемпоральною аптекою**  
Доповідач: Ковальчук Артем,  
Науковий керівник: Олійник С. В., к. фарм. н., доцент
- 3. Development of the composition of extemporaneous cough syrup**  
Доповідач: Бумахрута Брахім,  
Науковий керівник: Половко Н. П., д. фарм. н., проф.
- 4. Development of the composition of an extemporaneous cream intended for the treatment of dermatitis in diabetes mellitus**  
Доповідач: Аман Аллах Секкат,  
Науковий керівник: Половко Н. П., д. фарм. н., проф.
- 5. Дослідження складу засобів для схуднення**  
Доповідач: Лимаренко Єлизавета  
Науковий керівник: Ковальова Т.М., к. фарм. н., доцент
- 6. Дослідження складу ветеринарних засобів на суспензійній основі**  
Доповідач: Ємець Анастасія  
Науковий керівник: Ковальова Т.М., к. фарм. н., доцент
- 7. Аналіз складу засобів корегувальної відбілювальної косметики**  
Доповідач: Ємець Анастасія  
Науковий керівник: Ковальова Т.М., к. фарм. н., доцент
- 8. Перспективи розроблення екстемпоральної суспензії для лікування інфекцій сечових шляхів**  
Доповідач: Грабіна Марія  
Науковий керівник: Зуйкіна С. С., д. фарм. н., проф.

**National University of Pharmacy**

Pharmaceutical Faculty  
Drug Technology Department  
Level of higher education master  
Specialty 226 Pharmacy, industrial pharmacy  
Educational and professional program Pharmacy

**APPROVED**  
**The Head of Drug**  
**Technology Department**

---

**Liliia VYSHNEVSKA**  
“07” of October 2025

**ASSIGNMENT**  
**FOR QUALIFICATION WORK OF AN APPLICANT FOR HIGHER EDUCATION**

**Brahim BOUMAKHROUTA**

1. Topic of qualification work: «Justification of the composition and development of technology for extemporaneous syrup for the treatment of cough»,  
supervisor of qualification work: Natalia POLOVKO, Doctor of Pharmacy, Professor,  
approved by order of NUPh from “6<sup>th</sup>” of October 2025 № 266
2. Deadline for submission of qualification work by the applicant for higher education: May 2026.
3. Outgoing data for qualification work:  
The aim of research was to develop the composition and rational technology of a liquid dosage form – a syrup based on thyme extract and ambroxol hydrochloride.
4. Contents of the settlement and explanatory note (list of questions that need to be developed):
  - to conduct a marketing analysis of the pharmaceutical market of herbal medicines; to characterize the state of research in the field of developing syrups with herbal medicines; to provide a general description of the medicinal plant Thymus serpyllum;
  - to develop the optimal composition of a syrup based on thyme extract and ambroxol hydrochloride;
  - to develop a rational technology for the production of antitussive syrup in pharmacy conditions;
  - conduct quality control of the developed syrup according to organoleptic, physicochemical and microbiological indicators.
5. List of graphic material (with exact indication of the required drawings):  
Tables – 8, figures – 6

6. Consultants of chapters of qualification work

Chapters	Name, SURNAME, position of consultant	Signature, date	
		assignment was issued	assignment was received
1 Chapter	Natalia POLOVKO, Doctor of Pharmacy, Professor	10.10.2025	10.10.2025
2 Chapter	Natalia POLOVKO, Doctor of Pharmacy, Professor	05.12.2025	05.12.2025
3 Chapter	Natalia POLOVKO, Doctor of Pharmacy, Professor	14.01.2026	14.01.2026

7. Date of issue of the assignment: «07» of October 2025

**CALENDAR PLAN**

№ з/п	Name of stages of qualification work	Deadline for the stages of qualification work	Notes
1.	Topic selection	October 2025	<b>done</b>
2.	Analysis of literature data	November - December 2025	<b>done</b>
3.	Conducting experimental studies	January - March 2026	<b>done</b>
4.	Registration of work	March - April 2026	<b>done</b>
5.	Submission of finished work to the commission	May 2026	<b>done</b>

**An applicant of higher education**

\_\_\_\_\_ Brahim BOUMAKHROUTA

**Supervisor of qualification work**

\_\_\_\_\_ Natalia POLOVKO

**ВИТЯГ З НАКАЗУ**

По Національному фармацевтичному університету

«06» жовтня 2025 р.

№ 266

Фармацевтичний факультет

Затвердити теми кваліфікаційних робіт здобувачам вищої освіти 5 курсу 2025-2026 н. р., група ФМ21(4,10д)англ-01, освітньо-професійна програма «Фармація», спеціальність «226 Фармація, промислова фармація», галузь знань «22 Охорона здоров'я», рівень вищої освіти другий (магістерський), денна форма здобуття освіти, термін навчання 4 роки 10 місяців, мова навчання англійська.

Прізвище, ім'я здобувача вищої освіти	Тема кваліфікаційної роботи (українською мовою)	Тема кваліфікаційної роботи (англійською мовою)	Керівник кваліфікаційної роботи	Рецензент кваліфікаційної роботи
<b>Кафедра аптечної технології ліків</b>				
Бумахрута Брахім	Обґрунтування складу та розроблення технології екстемпорального сиропу протикашльової дії	Justification of the composition and development of technology for extemporaneous syrup for the treatment of cough	проф. Половко Н.П.	проф. Хохленкова Н.В.

**Підстава:** подання декана фармацевтичного факультету доцента Олександра ГОНЧАРОВА

Ректор  
Вірно. Секретар



**ВИСНОВОК**  
**експертної комісії про проведену експертизу**  
**щодо академічного плагіату у кваліфікаційній роботі**  
**здобувача вищої освіти**  
«11» травня 2026 р. № 333812580

Проаналізувавши кваліфікаційну роботу здобувача вищої освіти БРАХІМ Бумахрута, групи ФМ21(4,10д)англ-01, спеціальності 226 Фармація, промислова фармація, освітньої програми «Фармація» очної (денної) форми здобуття освіти на тему: «Обґрунтування складу та розроблення технології екстемпорального сиропу протикашльової дії / Justification of the composition and development of technology for extemporaneous syrup for the treatment of cough», експертна комісія дійшла висновку, що робота, представлена до Екзаменаційної комісії для захисту, виконана самостійно і не містить елементів академічного плагіату (копіляції).

Заступник голови Комісії,  
заступник директора інституту  
в складі ЗВО ННПФ,  
доцент



Олена НОВОСЕЛ

## REVIEW

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

**Brahim BOUMAKHROUTA**

**on the topic: «Justification of the composition and development of technology for extemporaneous syrup for the treatment of cough»**

**Relevance of the topic.** Respiratory tract diseases accompanied by cough and difficulty in expectoration are one of the most common problems of modern medicine. The relevance of the work is due to the need to create combined drugs that combine the secretolytic effect of plant extracts with the powerful mucolytic effect of synthetic molecules. The combination of thyme extract and ambroxol hydrochloride in one dosage form allows you to achieve a synergistic effect and provide a comprehensive effect on the pathological process. The development of extemporaneous syrup allows you to expand the range of available products for personalized therapy of respiratory diseases.

**Practical value of conclusions, recommendations and their validity.** During the work, the higher education applicant conducted a thorough marketing analysis of the expectorant market; scientifically substantiated the choice of active components and their dosage. The author studied the influence of excipients on the stability and organoleptic properties of the drug, developed a rational technology for the manufacture of syrup in a pharmacy. Of particular practical importance is the proposed technological scheme and developed methods for quality control of the finished medicinal product, which allows for standardization of the extemporaneous drug.

**Assessment of work.** The qualification work is performed at a high scientific level. The results of theoretical and experimental studies (organoleptic, physicochemical) are logically structured and clearly presented in the form of

tables and figures. The author demonstrated the ability to analyze modern literary sources and interpret the obtained data. The conclusions fully correspond to the set goal and objectives of the study.

**General conclusion and recommendations on admission to defend.** Qualification work of Brahim BOUMAKHROUTA can be submitted for defense to the Examination Commission of the National University of Pharmacy for the assignment of the educational and qualification level of a master.

Scientific supervisor \_\_\_\_\_ prof. Natalia POLOVKO

«12<sup>th</sup>» of May 2026

**REVIEW**

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

**Brahim BOUMAKHROUTA**

**on the topic: «Justification of the composition and development of technology  
for extemporaneous syrup for the treatment of cough»**

**Relevance of the topic.** Respiratory tract diseases accompanied by cough are one of the most common pathologies that require effective and safe treatment. The creation of combined drugs that combine the mucolytic effect of synthetic compounds with the secretolytic properties of plant extracts is a priority area of modern pharmacy. Ambroxol hydrochloride and thyme extract have proven clinical efficacy, but their combination in one extemporaneous form requires scientific justification. Due to the need for individualization of treatment and expansion of the range of pharmacy production, the development of the composition and technology of a new syrup for the treatment of cough is an urgent and timely task.

**Theoretical level of work.** The work provides a thorough analysis of modern literature on the etiology of cough and the pharmacological properties of active ingredients. The range of expectorants on the pharmaceutical market is analyzed and the choice of ambroxol and thyme as a synergistic combination is justified. The author demonstrates a deep understanding of the physicochemical processes that occur during the creation of liquid dosage forms and the principles of selection of excipients.

**Author's suggestions on the research topic.** The author scientifically substantiated the composition of the combined syrup and developed a rational technology for its manufacture in a pharmacy. A production flow chart was created, the optimal sequence of components was determined, and methods for controlling the quality of the finished product by key indicators (organoleptic properties, pH, density, etc.) were proposed.

**Practical value of conclusions, recommendations and their validity.** During the work, the higher education applicant mastered modern methods of pharmaceutical development, marketing analysis and organoleptic evaluation. The results obtained have practical significance for pharmaceutical institutions, as they allow the production of a stable and effective drug for the treatment of respiratory diseases in children and adults.

**Disadvantages of work.** The work is characterized by a high level of execution, however, among the shortcomings, it should be noted the presence of certain stylistic inaccuracies and isolated errors in the list of sources used.

**General conclusion and assessment of the work.** Qualification work of Brahim BOUMAKHROUTA can be submitted for defense to the Examination Commission of the National University of Pharmacy for the assignment of the educational and qualification level of a master.

Reviewer \_\_\_\_\_ prof. Natalia KHOKHLENKOVA

«14<sup>th</sup>» of May 2026

МІНІСТЕРСТВО ОХОРОНИ ЗДОРОВ'Я УКРАЇНИ  
НАЦІОНАЛЬНИЙ ФАРМАЦЕВТИЧНИЙ УНІВЕРСИТЕТ

**ВИТЯГ З ПРОТОКОЛУ № 14**

«15» травня 2026 року

м. Харків

засідання кафедри

аптечної технології ліків

(назва кафедри)

**Голова:** завідувачка кафедри, проф. Вишневська Л. І.

**Секретар:** докт. філ., ас. Боднар Л. А.

**ПРИСУТНІ:**

проф. Половко Н.П., проф. Семченко К.В., проф. Зуйкіна С.С.,  
доц. Ковальова Т.М., доц. Буряк М.В., доц. Олійник С.В., доц. Марченко М.В.,  
ас. Іванюк О.І.

**ПОРЯДОК ДЕННИЙ:**

1. Про представлення до захисту кваліфікаційних робіт здобувачів вищої освіти.

**СЛУХАЛИ:** проф. Вишневську Л. І. – про представлення до захисту до Екзаменаційної комісії кваліфікаційних робіт здобувачів вищої освіти.

**ВИСТУПИЛИ:** Здобувач вищої освіти групи Фм21(4,0д)англ-01 спеціальності 226 «Фармація, промислова фармація» Брахім БУМАХРУТА з доповіддю на тему «Обґрунтування складу та розроблення технології екстемпорального сиропу протикашльової дії» (науковий керівник: проф. Наталя ПОЛОВКО).

**УХВАЛИЛИ:** Рекомендувати до захисту кваліфікаційну роботу.

**Голова**

Завідувачка кафедри, проф.

\_\_\_\_\_

(підпис)

**Лілія ВИШНЕВСЬКА**

**Секретар**

Асистент

\_\_\_\_\_

(підпис)

**Любов БОДНАР**

## НАЦІОНАЛЬНИЙ ФАРМАЦЕВТИЧНИЙ УНІВЕРСИТЕТ

### ПОДАННЯ ГОЛОВІ ЕКЗАМЕНАЦІЙНОЇ КОМІСІЇ ЩОДО ЗАХИСТУ КВАЛІФІКАЦІЙНОЇ РОБОТИ

Направляється здобувач вищої освіти Брахім БУМАХРУТА до захисту кваліфікаційної роботи за галуззю знань 22 Охорона здоров'я спеціальністю 226 Фармація, промислова фармація освітньо-професійною програмою Фармація на тему: «Обґрунтування складу та розроблення технології екстемпорального сиропу проти кашльової дії»

Кваліфікаційна робота і рецензія додаються.

Декан факультету \_\_\_\_\_ / Олександр ГОНЧАРОВ /

#### Висновок керівника кваліфікаційної роботи

Здобувач вищої освіти Брахім БУМАХРУТА представив кваліфікаційну роботу, яка за об'ємом теоретичних і практичних досліджень повністю відповідає вимогам до оформлення кваліфікаційних робіт.

Керівник кваліфікаційної роботи

\_\_\_\_\_

Наталя ПОЛОВКО

«12» травня 2026 року

#### Висновок кафедри про кваліфікаційну роботу

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

Завідувачка кафедри  
аптечної технології ліків

\_\_\_\_\_

Лілія ВИШНЕВСЬКА

«15» травня 2026 року

Qualification work was defended

of Examination commission on

« 09 » of June 2026

With the grade \_\_\_\_\_

Head of the State Examination commission,

Doctor of Pharmacy, Professor

\_\_\_\_\_ / Volodymyr YAKOVENKO /