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QUALIFICATION WORK

on the topic:

COMPOSITION SUBSTANTIATION AND TECHNOLOGY DEVELOPMENT OF EXTEMPORANEOUS GEL WITH LEMON BALM AND WILLOW BARK EXTRACTS

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ANNOTATION

Qualification work is devoted to the compositional substantiation, technology development and study of its technological properties of extemporaneous gel with Lemon balm and Willow bark extracts.

The work is presented on 42 pages of printed text, consists of an introduction, 3 chapters, general conclusions, a list of sources used, appendices. The list of used sources contains 38 items, including 20 English and 9 on Ukrainian. The work is illustrated with 3 tables and 14 figures.

Key words: gel, extemporaneous, extract, technology, Lemon balm, *Melissa officinalis*, Willow bark, *Salix Viminalis*.

АНОТАЦІЯ

Кваліфікаційна робота присвячена обґрунтуванню складу, розробці технології та вивченню технологічних властивостей екстемпорального гелю з екстрактами меліси та кори верби. Робота викладена на 42 сторінках друкованого тексту, складається зі вступу, 3-х розділів, загальних висновків, списку використаних джерел, додатків. Перелік використаних джерел містить 38 джерел, серед яких 20 англійською мовою та 9 українською мовою. Роботу ілюстровано 3 таблицями і 14 рисунками.

Ключові слова: гель, екстемпоральний, екстракт, технологія, меліса лікарська, *Melissa officinalis*, кора верби, *Salix viminalis*.

CONTENT

INTRODUCTION

Relevance of the topic. The rational treatment of wounds represents a significant contemporary challenge, the effective resolution of which will necessitate the collaborative efforts of multiple generations of medical professionals, including doctors and pharmacists. Despite the extensive array of proposed methodologies and pharmaceutical agents for wound treatment, this problem persists as a salient one.

Prolonged postoperative infections have been demonstrated to increase the mortality rate, the cost of treatment, and the number of additional days spent in the hospital. This finding underscores the profound medical and socio-economic implications of the problem of prevention and underscores the necessity to enhance the efficacy of treatment [35, 36].

The therapeutic value of medicinal plants is determined by the biologically active substances included in their composition. Concurrently, a multitude of active pharmaceutical ingredients (APIs) are synthesized in each medicinal plant, resulting in a collective pharmacological effect. Further examination of medicinal plants that have been the subject of prior study and long-standing utilization can, on occasion, unveil hitherto unobserved facets of their biological activity [15, 26, 28].

The purpose of the research is compositional substantiation, technology development and study of extemporaneous gel with Lemon balm and Willow bark extracts technological properties.

To achieve the set goal, it was necessary to solve the following **research tasks:**

• To study the relevance of developing an extemporaneous gel with Lemon balm and Willow bark extracts.

• Based on the analysis of the literature, identify APIs Lemon balm and Willow bark extracts and justify the choice of dosage form;

• Theoretically substantiate the optimal composition of extemporaneous gel;

• Substantiate the composition of the gel base;

• Develop the technology of extemporaneous gel;

• Determine the technological properties of extemporaneous gel.

Object of research. extemporaneous gel with plant components.

Subject of research. Extemporaneous gel with Lemon balm and Willow bark extracts

Research methods. To achieve the set goal, general scientific research methods were used: generalization, systematization, synthesis, analysis, analogy, comparison for processing literature data; observation, comparison, measurement, modeling, experiment for the preparation and study of ointment gel; as well as physicochemical and technological methods.

Practical significance of the results obtained. Based on the conducted research, an extemporaneous gel with Lemon balm and Willow bark extracts was proposed for practical implementation. The work carried out can be used to further improve the composition of the ointment in order to expand the range of preparations based on plant components.

Elements of scientific research. Based on literature data, the composition and manufacturing technology of extemporaneous gel with Lemon balm and Willow bark extracts of willow were substantiated.

Approbation of research results and publication. The results of the work were presented at: XXXI International Scientifical and Practical Conference of Young Scientists and Students «Topical issues of new medicines development» on April 23-25, 2025.

Scope and structure of work. The work is presented on 42 pages of printed text, consists of an introduction, 3 chapters, general conclusions, a list of sources used, appendices. The list of used sources contains 38 items, including 20 English and 9 on Ukrainian. The work is illustrated with 3 tables and 14 figures.

CHAPTER 1
APPROACHES TO THERAPY OF INFECTED WOUNDS

1.1. Wounds and wound process

Currently, due to the success of antibiotic therapy for soft tissue infections, insufficient attention is paid to the surgical aspects of wound treatment and wound infection in modern recommendations.

A wound is a mechanical violation of the integrity of the skin, mucous membranes, deep tissues, internal organs with the development of local, regional and general disorders of vital activity [1, 36].

The surgeon experiences the greatest difficulties in the treatment of infected wounds. The frequency of surgical infections in the structure of surgical diseases has not decreased in recent years, remaining at the level of 24-36%. Inadequate management of patients with surgical infection is one of the reasons for the high mortality in this patient population - 25-50%.

Classification of the wound process

A wound is a complex biological system and goes through certain stages in its development. Classification of the wound process (according to M. I. Kuzin) [40]:

I - phase of inflammation, divided into the period of vascular changes and the period of cleansing the wound from necrotic tissues;

II - phase of regeneration, formation and maturation of granulation tissue;

III - phase of scar reorganization and epithelialization [1, 4, 36].

There is an alternative four-stage classification of the wound process BYRP (Black Yellow Red Pink).

In this system, different colors imitate different phases of the wound process.

In the BYRP classification, the following stages are distinguished:

Black (black) - necrosis,

Yellow (yellow) - fibrin in the wound,

Red (red) - granulation tissue,

Pink (pink) - epithelialization of the wound. The graphic scheme is close to the real clinical picture, since the color of the wound changes depending on the processes occurring in it. In this case, stages B and Y correspond to phase I of the wound process according to M. I. Kuzin. Stages R and P correspond to phases II and III. This classification is based on the allocation of three degrees of exudation.

Regarding fresh (acute) wounds without signs of infection, a single approach has been developed, the essence of which is the rapid surgical closure of the tissue defect. The need for a long stay of patients in the hospital, repeated surgical interventions and the use of additional treatment methods arises only when the wound "chronicizes". A chronic wound is a wound that exists for more than 4 weeks (the exception is large granulating superficial wounds after a burn) [1, 7, 36].

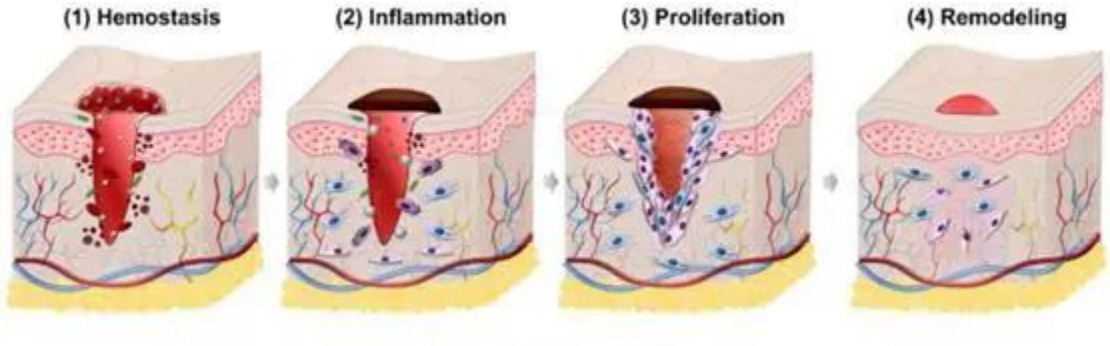

Fig. 1.1. Phases of wound healing

The modern treatment of wound infection is based on the principles of complex therapy, which include surgical intervention with rational drainage, general and local use of antibiotics and drugs that provide detoxification, necrolytic action, and increase the body's immune defense.

First of all, it should be noted that surgical tactics in the treatment of wounded and sick people with surgical infection cannot be templated, since patients come for treatment at different times from the onset of the disease or injury and in different phases, both of the inflammatory process itself and of wound healing. Wound healing "through suppuration" is a natural and phylogenetically justified course of

the wound process. When treating this category of wounded and sick people, secondary surgical treatment of wounds is usually not carried out, but measures are taken aimed at active preparation of wounds and their early closure with sutures or autodermoplasty. Wounded and sick people with clinical manifestations of surgical wound infection or primary purulent diseases require different treatment principles, including the following measures:

1) surgical treatment of purulent wounds and other purulent foci;

2) rational drainage and programmed washing of wounds;

3) active preparation of unsutured wounds for closure and their closure;

4) prevention of auto- and reinfection by strict adherence to the rules of asepsis and antiseptics when performing surgical interventions and dressings in this category of wounded and sick people;

5) targeted antibacterial treatment (local and general);

6) correction of immune defense, microvascular disorders, hypoxia and other disorders of homeostasis;

7) general treatment (infusion-transfusion therapy, hemosorption, hemodialysis, blood UVF, hyperbaric oxygenation); 8) treatment of concomitant diseases [1, 4, 36].

1.2. Principles of choosing a local antiseptic for the treatment and prevention of wound infection

Wounds are one of the most common traumatic injuries. Victims receive injuries in various conditions, including as an operative access during surgery. The wound can be complicated by the development of secondary infections of the skin and soft tissues, which are a consequence of tissue infection in primary violations of anatomical integrity, as well as trophic and / or innervation in systemic diseases (e.g., diabetes mellitus, chronic venous insufficiency). Infected burns, infected traumatic wounds and infections of the surgical area have as their primary cause a wound that is easily contaminated and then infected with both its own microorganisms and nosocomial pathogens [4, 7, 32].

The microbial status of wounds can be classified as follows:

1) contamination - microorganisms are present and fixed to the tissue without multiplication (initially);

2) colonization - microorganisms are present and multiply, a clinically significant immunological response of the host organism is (initially) absent;

3) critical colonization - multiplication of microorganisms without classical signs of infection, but with delayed wound healing due to the formation of toxins or the wound is colonized by antibiotic-resistant strains without signs of infection;

4) local infection - clinically observed immunological reaction of the host organism with typical signs of infection, including hyperemia (erythema 1-2 cm from the wound edge), with a tendency to increase (may be equivalent to the spread of infection with the risk of generalization), edema, increased local temperature of the skin / deep tissues, pain, dysfunction, increased amount of exudate and its viscosity, in some cases the appearance of an unusual odor, delayed wound healing;

5) systemic infection - in addition to symptoms of local infection, signs of systemic reaction of the host organism are observed, such as leukocytosis, increased level of C-reactive protein in the blood and fever [4, 26, 33].

The presence of closed cavities, foreign bodies, necrotic tissues in the wound contributes to the development of wound infection. The proliferation of pathogenic microflora in the wound and the absorption of decay products of non-viable tissues contribute to the stimulation of blood cells and connective tissue, leading to the release of cytokines and other inflammatory mediators with a wide range of biological effects.

In the local treatment of infected wounds, the following strategy is followed:

- surgical treatment of the wound, including necrotectomy;
- adequate drainage;
- maintaining the wound with a moist environment;
- use of optimal antiseptics, refusal of cytotoxic agents;
- use of modern dressings according to the stages of the wound process;

• transport of necessary substances into the wound using ointments and dressings;

• use of additional agents with proven effectiveness for wound treatment [4, 33].

The main indications for the use of antiseptics are:

1. Use for prophylaxis, in the presence of uninfected wounds with a high risk of infection (immunodeficiency patients, wounds in the perineum, burns);

2. Use for the treatment of:

• local infection;

• widespread infection (in combination with systemic antibacterial therapy). Treatment with antiseptics is discontinued in the following cases:

• when the infection resolves;

• when undesirable drug reactions associated with the antiseptic develop;

• when the wound begins to heal clinically [1, 4, 27].

The main role of antiseptics is to eliminate or reduce the number of viable microorganisms in the wound. Most solutions that are used even for many years cope with this task. The secondary goal is to have a positive effect on tissue proliferation and regeneration. Not all currently widely used drugs cope with this task.

Treatment of purulent wounds in modern conditions, with increasing resistance of microorganisms, is the subject of close attention of doctors of various specialties. Currently, this problem should be solved on the basis of a multidisciplinary approach involving not only surgeons, but also clinical pharmacologists [1, 4, 26].

Given the shortcomings of the first antiseptics (carbolic, acetic acid, chlorine preparations), surgeons enthusiastically began to use local forms of antibiotics in practical health care. Until recently, the creation of a new local remedy against pathogens of surgical infections consisted in simply transferring an effective antibiotic to the medium for application to wounds (erythromycin, tetracycline ointment, synthomycin emulsion).

Manufacturers often neglected the problems of drug interaction, the risk of resistance formation. With the emergence of resistance in pathogens and, accordingly, the ineffectiveness of local drugs containing antibiotics, surgeons again began to give preference to antiseptics [1, 4, 33].

The appointment of antiseptics in the treatment of wound infection is a procedure aimed at suppressing the wound microflora by using solutions of non-selective action.

Antiseptics used for the local treatment of purulent wounds have potential advantages and disadvantages.

Advantages: 1) high local concentration of antiseptic in the focus of surgical infection; 2) relatively small amount of the drug used; 3) minimal systemic antibacterial effect; 4) minimal systemic toxicity; 5) the possibility of using drugs that are not available for systemic therapy; 6) low risk of resistance formation; 7) ease of use.

Disadvantages: 1) small selection of effective antiseptics for local use; 2) low penetration into the tissue, which limits use in the depth of the wound; 3) with a large wound area, a systemic effect of drugs is possible; 4) the possibility of developing dermatitis of surrounding tissues; 5) the potential ability to slow down tissue regeneration; 6) the complexity of dosing; 7) the need for multiple applications [1, 4, 27].

When treating wounds locally, it is necessary to take into account the phases of the wound process (phase I - inflammation (vascular changes, cleansing), phase II - regeneration, phase III - scar reorganization and epithelialization). Currently, there are no means and methods that are equally effective in all phases of the wound process. However, as before, drugs for treating wounds in general are offered, without indicating for which phase they are intended. Only such local drug treatment can be considered justified, which is carried out in strict accordance with the pathogenesis of the wound process, that is, taking into account its phase.

Naturally, local drug treatment cannot fully provide a sufficiently effective effect on the wound process. In other words, no treatment can completely replace

surgical treatment of the wound with its early closure. But with the extensiveness of the lesion, the involvement of vital structures, it is not always possible to completely clean the wound and complete the operation by applying primary sutures. In such cases, it is necessary to prepare the wound for closure with secondary sutures or skin grafting, conducting local drug treatment. It is important to emphasize that active surgical treatment is impossible without local and general use of chemotherapy drugs (antiseptics and antibiotics) [1, 4].

Antiseptics. Various antiseptics are offered to the surgeon, the effectiveness of which in relation to wound infection has been confirmed by studies. The task of antiseptics is to eliminate or reduce the number of microorganisms in the wound and exclude negative effects on tissue proliferation and regeneration. Not all traditionally used drugs perform this task, some of them negatively affect the late phases of the wound process.

Existing recommendations for the use of antiseptics are as follows: 1) do not use alcohol solutions of antiseptics, which cause burns of immature granulations; 2) avoid the use of antiseptics that stain tissues (diamond green, methylene blue, etc.), which complicates the visual assessment of the course of the wound process (most colored antiseptics are cytotoxic); 3) do not use hydrogen peroxide (except for the I phase of the wound process) due to the harmful effect on granulation tissue and foci of epithelialization; 4) strictly according to indications, use potassium permanganate solutions, which have a pronounced drying effect, up to necrosis of granulation tissue, and the ability to stain tissues; 5) do not use antiseptics in the III phase of the wound process [1, 4, 33].

Despite the simplicity of using antiseptics, it is necessary to determine the place of each of them in order to balance their positive and negative sides, and they should not be used constantly during the treatment process. Their positive effect prevails over the cytotoxic effect only within a few days to two weeks from the start of use. Thus, an incorrect approach to the use of antiseptics can have a negative impact on the healing time of wounds. An alternative may be the appointment of a local form of antibiotic [1, 4].

1.3. Extemporaneous gels

Extemporaneous dosage forms are drugs that are manufactured in a pharmacy individually for a specific patient.

Extemporaneous (from Lat. * ex tempore — as needed, immediately before use) medicinal forms represent by yourself drugs prepared in pharmacies individually for a specific patient [34].

Gels are soft medicinal forms that are a homogeneous or homogeneously dispersed system containing a liquid phase and a gelling agent that creates a viscous structure. They are easy to use, provide rapid release of active substances and are well tolerated by patients. Geli is one of popular extemporaneous forms used externally or less often - for internal use use.

The gel consists of a liquid phase (water, alcohols, glycerin) and a gelling agent. Typical gelling agents include natural (gelatin, alginates, pectin, agar), semi-synthetic (methylcellulose, CMC), and synthetic (carbopol, PEO, acrylic polymers) polymers. The gelling agent swells in the liquid, forming a three-dimensional network that holds the components and gives the gel stability.

This structure allows evenly distribute active substances and control their release [11, 16, 20].

Advantages of gels:

- Rapid release of active substances - Ease of application and good distribution - Gentle effect on the skin and mucous membranes

- Minimum irritating action compared to ointments and creams.

- Possibility of individualization of the composition

- Thermal stability

Opportunity regulation viscosity and degree penetration of the current substances.

Application: dermatology (antiseptic, anti-inflammatory, wound healing) gels, gynecology (antiseptic and hormonal gels), dentistry (anesthetic and anti-inflammatory gels), pain relief, cosmetology.

Table 1.1.

Comparative characteristics of gelling agents

Gelling agent	Origin	Conc. (% by weight)	Peculiarities	Example of application
Carbopol (Carbomer)	Synthetic	0.5–1.5	Requires neutralization, high transparency, stability	Gels with NSAIDs, cosmetics
Methylcellulose (MC)	Semi-synthetic	1–5	Slowly swells, viscosity increases with heating	Eye, dental, rectal gels
Hydroxyethylcellulose	Semi-synthetic	0.5–2	pH stable	Gels for mucous membranes
Pectins, alginates	Natural	1–3	Biocompatible, require stabilizers	Wound healing gels
Polyethylene oxide (PEO)	Synthetic	Up to 95%	Compatible with fat-soluble substances	Combined external

Gels technology:

1. Preparation of the base. Gelling agent preliminary swells in liquid (usually within 1–24 hours at room temperature) temperature).

Process Maybe be accompanied stirring (manual or mechanical) until reaching necessary consistency.

2. Introduction of active substances - in dissolved or suspended form

3. Adjustment of pH and viscosity - for most gelling agents, when working with carbopol required neutralization solution (more often total triethanolamine) to achieve desired viscosity.

4. Packaging and storage - in sealed containers. from light-protective glass or plastic.

Term storage Extemporaneous Gels - limited (usually up to 10 days), depending on the composition - with mandatory indication dates manufacturing.

For mucous membranes preferably use more soft thickeners - hydroxyethylcellulose, pectin, etc. Sorbitol increases viscosity and improves taste [20, 25, 29].

Extemporaneous gels production allows:

- change concentration current substances depending on age patient.
- combine some active substances (for example, antiseptic with painkiller).
- produced without preservatives and flavorings, which especially important for children and allergy sufferers.
- create rectal, vaginal, dental gels.
- majority gelling agents demand room temperatures for swelling (exception - agar, gelatin). Speed mixing: avoid excessive whipping so that they do not form bubbles. pH control important for conservation stability current substances and viscosities gel. Use preservatives: if term storage gel supposed more than 2-10 days, you need to add preservatives (for example, sorbate potassium benzoate sodium, nipagin, nipazol) - but this is requires pharmaceutical justifications and verifications compatibility [12, 13, 14, 34].

Quality control extemporaneous gels.

When manufactured in pharmacies conditions gels are subject to to all main types of control:

Quality control includes all types of intra-pharmacy control:

- written;

- interview;
- organoleptic - homogeneity, absence bubbles, foreign inclusions, odor.
- physical (accuracy packaging and dosing);
- chemical control (pH environment - especially important when applied to mucous membranes or sensitive areas skin);
- stability - being checked visually during storage (stratification, sediment, change colors).
- microbiological purity - if the drug is stored more than 7 days or used on mucous membranes.
- control during release.

Terms and Conditions Storage: - in a coolplace protected from light place (8–15°C).

Packaging: tubes, jars of dark glass or medical plastic.

Term shelf life: determined depending on the composition, but no more than 10 days without preservatives. If available unstable substances - up to 3 days.

Prospects and relevance. Taking into account individualization therapy and development personalized medicine, extemporaneous gels become All more in demand form. They allow: Fast adjust the composition to a specific patient, Use unstable substances not available in industrial production Pharmacy, Apply new or rare active substances in minimal doses [11, 13, 14, 34].

Conclusions to chapter 1

The feasibility of developing soft dosage forms using modern bases and APIs, effective against resistant pathogens of inflammatory processes and affecting the main pathogenetic processes in complicated wounds, has been repeatedly proven by clinical studies. Even taking into account the successes achieved by the pharmaceutical industry, the creation and improvement of drugs for the local treatment of purulent wounds are among the urgent tasks of the pharmaceutical industry. Considering the above, there is an ongoing active search for effective antimicrobial substances, including those of plant origin, which can be used for this purpose.

EXPERIMENTAL PART

SECTION 2. JUSTIFICATION OF THE GENERAL CONCEPT OF RESEARCH

2.1. Description, chemical composition and use of Lemon balm

Melissa officinalis is a perennial herbaceous plant of the Lamiaceae family. The stem is straight, tetrahedral, branched, up to a meter high. The whole plant is covered with soft hairs. The leaves are petiolate, heart-shaped, large-toothed, wrinkled, dark green on top, light, pubescent on the bottom. When the leaf is crushed, a lemon aroma is felt. Small white or white with a pinkish tint flowers with a red spot are collected at the top of the stem in inflorescences. The fruit is dry, breaks up into four one-seeded nuts. It blooms in June-August [2, 17, 21].

Fig. 2.1. Lemon balm (*Melissa officinalis*)

Lemon balm (*Melissa officinalis*) is a common species in the countries of the Mediterranean basin and Central Europe. In Ukraine, this plant is cultivated on homestead plots, and it also often grows wild, in particular in the Crimea, where it grows along river banks, in meadows and in forests.

Lemon balm leaves are harvested before flowering, when the essential oil content in the leaves is highest. They are harvested during the day in dry, cloudy

weather. Repeated harvesting is possible 20-25 days after the first, and under favorable weather conditions of a humid, warm autumn - for the third time. The collected leaves are dried in a thin layer at a temperature of up to 35°C without turning. The yield of dry raw materials is about 20%. Store in a dark, dry place in metal containers [3, 8, 27].

Lemon balm leaves contain essential oil (up to 0.33%), tannins (up to 5%), bitterness, mucus, sugars, caffeic, succinic, chlorogenic, oleanolic and ursolic acids, and mineral salts.

The plant is used for general nervous excitement, vegetative-vascular dystonia, insomnia, heart rhythm disturbances, changes in blood pressure under the influence of emotional factors, as well as for disorders that accompany them: digestive disorders, vegetative neurosis, gastritis, colitis, etc.

It is more often used with other herbs - mint, chamomile, valerian, lavender, cumin, etc. [6, 18, 28].

Melissa (herb) lowers blood pressure, slows breathing and heart rate. Its diaphoretic, sedative, antifungal and bactericidal properties are known. It exhibits antispasmodic, astringent, hypoglycemic, diuretic, choleretic, anti-inflammatory, mild hypnotic and analgesic effects.

Melissa strengthens the nervous system, increases salivation, improves metabolism, appetite, and digestive system activity. Promotes lymph and blood renewal, helps with headaches.

Lemon balm herb is used to treat nervous, cardiovascular, gastrointestinal diseases, bloating, constipation, flatulence. Helps with gout, anemia, gum disease, dizziness, tinnitus and general weakness.

The beneficial properties of lemon balm make it a means for weight loss. Tea from the plant will help improve metabolism, remove excess fluid and serve as a mild laxative. The sedative and antispasmodic properties of the herb will help you survive diet-related restrictions, calming the nervous system and relieving hunger cramps in the stomach [7, 18, 21].

Lemon balm stimulates menstruation, relieves dysmenorrhea, helps with

inflammatory diseases of the genitourinary system, especially with diseases of the uterus. As a female herb, it was popularly called "motherwort". The herb is suitable for women with increased sexual arousal, as it soothes and regulates the activity of the female body.

According to the ancient Greeks, lemon balm herb was the best remedy for baldness, which is still useful for men who have encountered this problem. Women use lemon balm to improve hair growth, strengthen bulbs, restore damaged roots, regulate the work of the sebaceous glands, reduce oiliness and smooth hair along the entire length.

Lemon balm is used for taking aromatic restorative baths, as well as for furunculosis, dermatitis, skin rashes [3, 8, 27].

The herb of the plant lowers blood pressure. It has a bactericidal effect and is able to destroy some pathogenic fungi and tuberculosis pathogens. Lemon balm herb has anti-inflammatory and antioxidant effects. Taking preparations from it has a restorative effect on the body. Lemon balm helps strengthen the nervous system and normalize sleep. At the same time, it is not depressing and practically not addictive. Lemon balm also enhances the effect of synthetic sedatives and allows you to reduce their dosage.

You can not take lemon balm during pregnancy and breastfeeding, with hypotension and intolerance to the components in the herb.

In folk medicine, lemon balm infusion is used externally for paralysis and gout. Young leaves of the plant are added to salads.

Lemon balm is also used in cosmetology for baths and compresses [2, 6, 8 17].

2.2. Use of Willow and the chemical composition of its BAS

The study of the chemical composition of various species of willow (*Salix L.*) began in the 18th century. The history of use and the chemical composition of some species of willow are quite fully described in scientific publications.

Fig. 2.2., 2.3. *Salix Viminalis L.*

At the moment it is known that the main active substances of the studied species of willow are phenolic glycosides, flavonoids, tannins, and also include phenolic acids, ascorbic acid, amino acids, saponins, essential oils and polysaccharides, which can contribute to the overall pharmacological effect. It is known that the quantitative content of BAS in the bark and leaves can change in different phases of vegetation and depends on the growth conditions [5, 10, 26].

One of the main representatives of biologically active substances of the willow family is phenolic glycosides, the aglycone of which is salicylic alcohol. The first phenolic glycoside isolated from plants - salicin (salicoside), is a β-glucoside of salicylic alcohol. It was obtained from willow bark by the French scientist A. Leroux (1829). It is with Salicin that the main types of action of willow are associated - anti-inflammatory, analgesic and antipyretic [9, 22].

A representative of flavones in willow is luteolin, which was found in the bark of *S. purpurea*, the leaves of *S. acutifolia, S. caprea, S. acutifolia, S. alba, S. triandra, S. vestita, S. berberifolia, S. myrtilloides, S. saxatilis, S. pyrolifolia*. In a hybrid of Babylonian willow with white willow, luteolin-7-glycoside was found, which is also found in the leaves of *S. purpurea, S. acutifolia, S. caprea, S. elburensis, S. acutifolia, S. alba*. Another representative of flavones is apigenin, found and

quantified in the leaves of *S. saxatilis* and *S. recervigemmis*. Flavonols have more pronounced choleretic properties, represented by quercetin, found in S. triandra (leaves and inflorescences) and leaves of *S. acutifolia, S. alba, S. caprea, S. vestita, S. berberifolia, S. myrtilloides, S. nummularia, S. recervigemmis, S. krylovii, S. sphenophylla*, and rutin, found in leaves and inflorescences of *S. triandra, Salix alba* and *Salix alba* var. vitellina, and leaves of *S. acutifolia* and *S. songarica Anderss* [9, 10, 26].

It has been proven that such flavones as diosmetin and its glycosides (ca preoside and salicaprioside), found in goat willow, have venotonic activity and are used for varicose veins, phlebitis and hemorrhoids, as well as in gynecological practice. Flavonoids have a pronounced antiallergic effect, which is explained by the violation of the release of allergy mediators. They restore the functions of cell membranes through direct biochemical interaction, while simultaneously inhibiting the activity of phosphodiesterase, which contributes to the accumulation of cAMP in the cell. At the same time, more effective phosphodiesterase inhibitors are flavones and flavonols contained in the above-listed willow species. Flavonoids, as specific phosphodiesterase inhibitors, are powerful regulators of nucleotide metabolism and in this regard are of potential pharmacological interest [5, 9, 26].

Some species of willow, for example, *S.caprea*, contain ascorbic acid. This compound is a powerful antioxidant and is also necessary for the regeneration of other antioxidants, such as tocopherols and carotenoids. Ascorbic acid contributes to the formation of connective tissue in the human body, exhibits enzymatic activity, promotes the absorption of iron in the body, and has an antisclerotic effect. Carbohydrates are natural compounds widely distributed in the plant world.

Willow has also been found to contain such biologically active substances as essential oils, lipids and resinous substances, and enzymes. The amino acid composition of the leaves of *S.acutifolia, S.caprea,* and *S. alba* has been studied. It is known that chemical elements are the most important catalysts of various biochemical processes and metabolism, and play a significant role in the adaptation of the body in normal and pathological conditions. The elemental composition of the

bark of the willow has been studied. Important micro- and macroelements such as nitrogen, phosphorus, calcium, magnesium, sodium, and potassium have been identified [5, 10, 22, 26].

The chemical composition of white willow shoots was studied, showing the presence of a rich complex of BAS (a high content of condensed group tannins (epigallocatechin, catechin, epicatechin, epicatechin gallate, catechin gallate) was established - in the amount of 3.5 to 9.0% at different periods of harvesting; flavonoids (rutin, quercetin and 2 unidentified substances) in the amount of 0.5-1.5% in terms of rutin; phenolic acids (ferulic, salicylic, cinnamic) in the amount of 0.8% in terms of ferulic acid; triterpene saponins (0.53%); the salicin content was 0.05-0.19%.).

Pharmacological studies have shown a pronounced antiexudative and antiproliferative activity of a decoction of white willow shoots, comparable to acetylsalicylic acid [10, 22, 26].

The use of willow shoots is attractive from an economic point of view, since it allows to significantly expand the raw material base. In addition, the damage caused to the plant during harvesting is reduced compared to traditional raw materials (bark). It is important to note the large number of domestic willow species, which belong to the dominant landscape species in places of increased humidity, especially along the banks of reservoirs and in river valleys, and are also successfully cultivated, including on an industrial scale. At the same time, a characteristic feature of plants of the genus Willow is the ability to grow rapidly, settle the substrate and reproduce [5, 9, 10, 22, 26].

2.3. Characteristics of the research objects

The object of the research work was an extemporaneous gel of complex action with water-soluble *Melissa* and Willow bark extracts. Excipients used in its development: Methylparaben, Glycerin, Noveon®, Triethanolamine, Purified water.

Active pharmaceutical ingredients are Willow bark extract and Lemon balm extract.

Lemon balm extract is known for its properties to calm the nervous system and improve mood. It is a natural adaptogen that helps reduce stress, anxiety and depression. It can help ease sleep and reduce tension levels.

Fig. 2.4. Lemon balm extract

Lemon balm extract also has anti-inflammatory properties and can support skin health. It can help reduce skin inflammation, as well as soothe irritation and redness [3, 21, 27].

Lemon balm extract is rich in various vitamins and minerals: vitamins C, E and B-group vitamins. Vitamin C is a powerful antioxidant that supports the immune system and protects cells from free radical damage.

Vitamin E promotes healthy skin, strengthens hair and nails, and supports eye health. B vitamins are important for the normal functioning of the nervous and cardiovascular systems.

Lemon balm extract contains amino acids and flavonoids. Amino acids, (gamma-aminobutyric acid) help reduce stress levels and improve mood. Flavonoids are powerful antioxidants that help reduce inflammation and protect cells from damage [3, 27].

Lemon balm extract helps maintain the overall condition of the body, reduces stress, and improves mental state.

Melissa extract has antispasmodic, analgesic, and vasodilating effects (dilates the lumen of blood vessels), reducing blood pressure. Decoctions and teas are mainly used for treatment. *Melissa* is part of herbal preparations for the treatment of various diseases of the cardiovascular system, nervous system, and gastrointestinal tract problems. It can be combined with calming herbal preparations based on peppermint, lavender, and valerian [21, 27].

It has antispasmodic, analgesic, hypotensive, sedative, diuretic, carminative, bactericidal effects, improves digestion, slows down breathing rate, helps slow down heart rate, reduces the tension of intestinal smooth muscles, stimulates the secretion of digestive enzymes. Research results have shown the effectiveness of lemon balm extract in the treatment of acne. Oral and topical application of lemon balm extract accelerates the healing process of wounds and can act as a cardioprotective agent.

Lemon balm is used in medicine, perfumery, cosmetics, food, etc., in many countries of the world [3, 21, 27].

Willow Bark Extract is a hydrophilic thick liquid of light brown color with a faint specific odor.

Fig. 2.5. White willow bark extract

Willow Bark Extract is rich in tannins, vitamin C, glycosides salicin and salingrin, lactic acid and other biologically active substances. The combination of the astringent action of tannins with the antiseptic properties of salicin allows you to use Willow Bark Extract as an anti-inflammatory, tonic, hemostatic component [5, 26].

The main active substances are glycoside salicin (which consists of salicylic alcohol and glucose), flavones, ascorbic acid, tannins, pectins, lignin, anthocyanins.

Willow bark extract, has recently been noted to have the ability to inhibit pathogenic bacteria and modulate inflammation. Willow bark extract is rich in bioactive compounds such as salicin, flavonoids, and tannins, which are known to disrupt cell membrane of bacteria, inhibit biofilm formation and interfere with metabolic processes. Its anti -inflammatory activities, inhibiting NF-κB and oxidative stress, provide a more comprehensive way to manage infected wounds.

Willow Bark Extract is used as a part of elixirs and toothpastes, extracts have a healing and disinfecting effect on the gums and mucous membrane; in foot and hand creams they contribute to the healing of wounds and cracks on the skin, in face creams they have a light whitening effect [5, 26].

Willow Bark Extract activities:

• reduces rashes by inhibiting the action of P.acnes and S.aureus bacteria

• accelerates cell renewal

• has an anti-inflammatory effect

• brightens and evens out skin tone

• improves skin tone, helps increase collagen synthesis and reduce wrinkles.

Used in creams, masks, scrubs, bath products, lotions and deodorants for excessive sweating (hyperhidrosis), foot baths for varicose veins and muscle fatigue, for sweating feet. In shampoos, hair masks it is used for dandruff, itchy skin, hair loss [5, 26].

Excipients:

Methylparaben (Nipagin) - preservative (E218), colorless crystals or white powder, molecular weight 152.15 g/mol. It is a methyl ester of para-hydroxybenzoic acid. Soluble in organic solvents, poorly soluble in water. Used as an antimicrobial preservative in pharmacy, cosmetology and food industry.

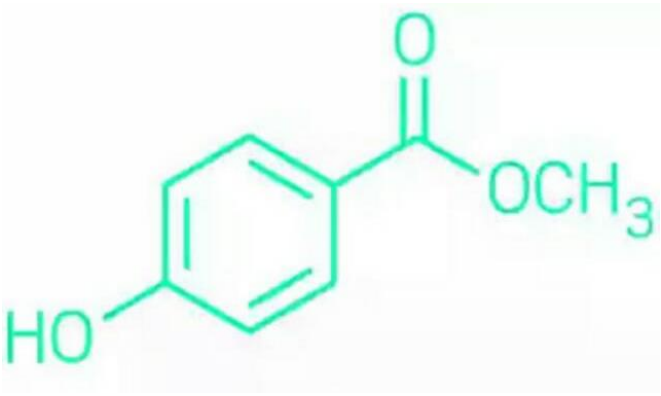

Fig. 2.6. Nipagin (structural formula)

Chemical formula: C8H8O3

Description: colorless crystals or white transparent powder.

Methylparaben (methyl-4-hydroxybenzoate, methyl-p-hydroxybenzoate) - an organic compound, methyl ester of para-hydroxybenzoic acid. Under normal conditions, it is a white powder, poorly soluble in water. It dissolves well in acetone, ethanol, chloroform [19].

Triethanolamine (TEA) is a colorless organic compound, readily soluble in water, and exhibits the properties of a weak base.

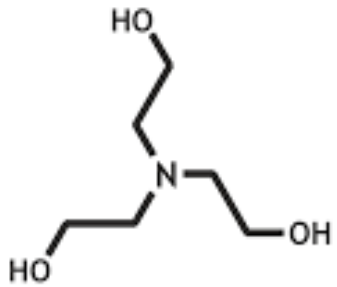

Fig. 2.7. Triethanolamine (structural formula)

Description - colorless liquid, miscible with water in all respects, weak base.

Chemical formula: (HO-CH2CH2)3N

Systematic name: N, N- (2-hydroxyethyl) -2-aminoethanol.

Physical properties: molar mass - 149.19 g / mol, density - 1.124 g / cm³, melting point - 22 ° C, boiling point - 335 ° C, • flash point - 179 ° C

Solubility in water 149 g / 100 ml. Used as a stabilizer and pH regulator in pharmaceuticals [30].

Noveon® polycarbophil

Fig. 2.8. Noveon

Noveon® AA-1 Polycarbophil, USP is a high molecular weight acrylic acid polymer crosslinked with divinyl glycol. This polymer serves as an excellent mucoadhesive excipient and is widely used for the delivery of active ingredients to mucous membranes. Noveon can provide enhanced lubrication for ophthalmic drug products and excellent controlled release characteristics for oral drug products. This excipient is suitable for use in bioadhesive LFs for nasal, vaginal, and rectal applications and is effective for use in both aqueous and non-aqueous systems. It is used as a mucoadhesive excipient for the delivery of active pharmaceutical ingredients to mucous membranes. Effective in both aqueous and non-aqueous systems [12, 23, 38].

Glycerin

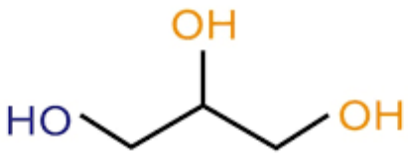

Fig. 2.9. Glycerin (structural formula)

CH2(OH)CH(OH)CH2OH Mol. m. 92.09

Glycerin - (DFU), glycerol, Glycerolum (Ph Eur), Glycerol (BP), Glycerin (USP), Propane-1,2,3-triol, (CAS No. 56-81-5). C3H8O3. G is a syrupy liquid, sticky to the touch, sweet to the taste, odorless, transparent, colorless or almost colorless, very hygroscopic, absorbs moisture from the air (up to 40% by weight).

Physicochemical properties:

- Melting point: 17.9°C
- Boiling point: 290°C (with slight decomposition)
- Density: 1.260 g/cm3
- Miscible with water, alcohols; poorly - with organic solvents.

Contained in natural fats and oils in the form of triglycerides. Industrially obtained by hydrolysis of fats or synthetically. In pharmacy, it is used as a softener, moisturizer, increases adhesion, affects the rheological properties of drugs. Improves the penetration of substances through the skin. Exhibits antimicrobial properties at high concentrations. Store in a sealed stainless steel container.

Used as a solvent for some APIs, is part of suppository bases. Has a laxative and dermatoprotective effect [38].

Purified water, Aqua purificata (Ph Eur), Purified Water (BP; JP; USP), Water (CAS No. 7732–18–5); syn.: Aqua; hydrogen oxide.

Fig. 2.10. Purified water

Purified water is a transparent, colorless liquid without taste and smell., chemical formula H_2O, Mol. m.18.02

Main physical and chemical characteristics:

- Boiling point: 100°C
- Melting point: 0°C
- Density: 0.9971 g/cm3 (at 25°C)
- Refractive index: 1.3330
- Surface tension: 71.97 mN/m (25°C)

Mixes well with polar solvents. Can interact with some substances to form hydrates. Used in pharmacy as an auxiliary substance, solvent. Obtained by purifying drinking water by distillation, ion exchange, reverse osmosis. Stored in tightly closed containers for 3 days under conditions that prevent microbial contamination [24, 31, 37].

2.4. Research methods

During the work, research methods were used, which allow for an objective assessment of the gel samples.

Determination of pH of aqueous gel solutions

A 2.5 g portion of gel was dissolved in 22.5 ml of purified water, the solution was stirred with a glass rod for 10 min for sedimentation, the pH was measured using a pH meter with a glass electrode. Measurements were carried out at room temperature, in 6 parallel determinations, after which the pH of the resulting aqueous dispersion was determined potentiometrically (SPU 2.0.) [37].

Optical microscopy

Microscopy of gels was carried out using a Granum R-40 laboratory microscope with a built-in digital video camera, at magnifications of 40, 100 and 400 times.

Study of antimicrobial activity of ointments

Microbiological studies were conducted in the laboratory of biochemistry of microorganisms and nutrient media of the State Institution "IMI named after I.I. Mechnikov of the National Academy of Sciences of the Republic of Ukraine" under the supervision of senior researcher Osolodchenko T.P.

For the study, reference test cultures of gram-positive and gram-negative bacteria belonging to different taxonomic groups were used: *Staphylococcus aureus* ATCC 25923, *Escherichia coli* ATCC 25922, *Pseudomonas aeruginosa* ATCC 27853, *Bacillus subtilis* ATCC6633, *Proteus vulgaris* ATCC 4636. The antifungal effect of the sample was studied on the reference strain *Candida albicans* ATCC 885-653.

Conclusions to chapter 2

2.1. Taking into account the therapeutic activity of BAS, the use of Lemon balm and Willow bark extracts as the main APIs are theoretically justified.

2.2. The properties of excipients necessary for the preparation of extemporaneous gel are presented.

2.3. Methods for studying samples of the developed extemporaneous gel are presented.

CHAPTER III
DEVELOPMENT OF EXTEMPORANEOUS GEL WITH LEMON BALM AND WILLOW BARK EXTRACTS AND ITS TECHNOLOGICAL PROPERTIES INVESTIGATION

3.1. Theoretical substantiation of the extemporaneous gel composition with Lemon balm and Willow bark extracts

The problem of diagnosis and treatment of infected wounds, despite the rich experience and constant scientific research in this direction, does not lose its relevance. Infectious complications increase the postoperative mortality rate, the amount of treatment costs, the number of additional days spent in the hospital. This indicates the significant medical and socio-economic significance of the problem of prevention and the need to increase the effectiveness of treatment [1, 36].

The therapeutic value of medicinal plants is determined by the biologically active substances included in their composition. At the same time, hundreds of BAS are synthesized simultaneously in each of the medicinal plants, which have a total pharmacological effect. Additional study of previously studied and long-used medicinal plants sometimes allows us to identify a new aspect of their biological activity [6, 15, 22, 21].

Considering the above, the development of modern delivery systems of plant extracts or phytocompounds for local treatment of wounds of various etiologies remains an urgent task for modern scientists[12, 20].

The study of the chemical composition of various species of willow (*Salix L.*) began in the 18th century. The history of use and the chemical composition of some species of willow are quite fully described in scientific publications.

At the moment, it is known that the main active substances of the studied species of willow are phenolic glycosides, flavonoids, tannins, and also include phenolic acids, ascorbic acid, amino acids, saponins, essential oils and polysaccharides, which can contribute to the overall pharmacological effect. It is known that the quantitative content of BAS in the bark and leaves can vary in

different phases of vegetation and depends on growth conditions. The rich chemical composition is characteristic not only of willow bark, but also of leaves, inflorescences, and shoots. The use of this raw material is attractive from an economic point of view, as it allows to significantly expand the raw material base [5, 22, 26].

Willow Bark Extract is a source of salicylic acid-like substances. Willow bark extract has established itself as one of the main herbal remedies for pain management and acts as an anti-inflammatory analgesic. In the cosmetic industry, willow bark extracts are used as a natural source of salicylic acid. Willow bark extract provides the benefits of salicylic acid, such as exfoliation and antimicrobial action, without irritation.

Willow Bark Extract is water soluble and can be used to improve cell renewal, act as a natural antimicrobial agent or as a substitute for synthetic salicylic acid.

Willow Bark Extract accelerates cell renewal, acts as a natural antimicrobial agent, or can be a substitute for synthetic salicylic acid. Therefore, it is excellent for anti-acne products, to reduce inflammation and associated redness, to normalize sebum secretion, suppress unpleasant body odors. According to the Society of Investigative Dermatology, willow bark extract offers significant benefits over salicylic acid, such as exfoliation and antimicrobial action, without any of the irritation that typically accompanies its use [9, 22].

The natural salicylates found in black willow bark provide UV protection and reduce irritation. In addition, willow is useful for increasing the rate of cellular turnover, allowing for the exfoliation of dull, dead skin cells. In standardized form, black willow bark extract provides consistent levels of salicylic acid, allowing it to be used as an active ingredient. Results show that ACB willow bark extract was able to increase cell turnover by 27% compared to an untreated control.

Main properties:

- Antibacterial action (especially against microorganisms involved in acne formation: Propionibacterium acnes, Staphylococcus aureus)

- Anti-inflammatory and anti-acne: reduces symptoms associated with inflammation
- Smoothing and regenerating: a powerful exfoliant with a "peeling" effect that gently stimulates cell regeneration, improving the overall appearance of the skin and eliminating damage left by acne and pigmentation spots, wrinkles, fine lines and uneven skin tone
- Reduces roughness, prevents keratinization, smoothes and softens the skin, prevents the appearance of calluses
- Dandruff: keratolytic (eliminates dandruff), antibacterial (cleanses the scalp)
- Used as an antiseptic, preservative
- Strong antibacterial activity [9, 22].

The properties of lemon balm extract are due to the rich composition of medicinal plant raw materials. Lemon balm herb (*Herba Melissae*) contains essential oil (up to 0.33%), tannins (up to 5%), bitterness, mucus, sugars, caffeic, succinic, chlorogenic, oleanolic and ursolic acids, mineral salts. Lemon balm leaves contain essential oil - up to 1%, which includes: citral - 60%, citronellal, myrcene, geraniol, linalool, cineole, aldehydes; tannins - about 5%; resins; organic acids: succinic, caffeic, chlorogenic; triterpenic acids: oleanolic, ursolic; vitamin C - 150 mg%, carotene - 7 mg%; not less than 5% of hydroxycinnamic acid derivatives, which have the common name rosmarinic acid; mucus; bitterness; macro- and microelements: K, Ca, Mg, Fe, Mn, Cu, Zn, Mo, Cr, Al, Ba, S, Pb, B; concentrate Se. The seeds contain up to 20% fatty oil. The extract of lemon balm contains flavonoids (quercitrin, rhamnocitrin, luteolin), polyphenolic compounds (rosmarinic, caffeic and protocatechuic acids), monoterpenoid aldehyde, monoterpene glycosides, triterpenes (ursolic acid, essential and oleanolic acids). When applied externally, the extract exhibits antispasmodic, analgesic, antimicrobial, antihistamine, antiviral activity, and is an antioxidant. The plant juice is used to treat allergic dermatitis. The leaf extract has an effective sedative effect. It is also used externally for furunculosis, rheumatism, bruises and ulcers, gingivitis and toothache [2, 8, 17, 21].

In the process of technological research, an important stage is to establish the compatibility of active pharmaceutical ingredients (API) and excipients in the composition of soft dosage forms. For this purpose, the properties of potential ointment bases were analyzed. For example, vaseline-lanolin ointments with antibiotics for the treatment of burns show only a short-term effect, since such a base prevents the outflow of wound exudate, does not sufficiently release the API and does not promote deep penetration of substances into the skin. This can lead to the transition of acute inflammation into a chronic form [1, 4, 36].

For the treatment of wounds in phase III, gels based on carbomers have become widespread due to their low toxicity and ability to effectively moisturize damaged tissues. Therefore, the development of carbomer-based gels with extracts of medicinal plants is relevant [20, 25, 29].

Thus, the use of extracts Lemon balm and Willow bark as APIs for the preparation of extemporaneous gel is relevant.

Result composition of the studied extemporaneous gel:

Melissa extract	0,5
Willow bark extract	0,5
Methylparaben	0,01
Glycerin	1,0
Noveon®	0,1
Triethanolamine	up to pH 5,0
Purified water	up to 10,0

Characteristic:

The given medicine is a extemporaneous gel containing soluble in water API Lemon balm and Willow bark extracts.

3.2. Gel technology in laboratory conditions

Stages of the technological process

1. Preparatory stage: (pharmaceutical examination of the recipe; calculations; preparation of auxiliary materials, API and excipients).

2. Technology:

2.1. Measuring water in a measuring cylinder and transferring to a stand.

2.2. Weighing out API (extracts of *Melissa* and Willow bark) and dissolving them in water.

2.3. Weighing out excipients (methylparaben, Glycerin, Noveon) and dissolving them in water.

2.4. Mixing.

2.6. Adding triethanolamine to pH 5.0 of the aqueous solution. Gel formation.

2.7. Mixing until homogeneous.

3. Quality control: written control, physical control (weight deviation), organoleptic control, checking the PPC.

4. Packaging. Labeling (labeling).

5. Control during release.

3.3. Establishment of absence of microbial contamination of extemporaneous gel

The team of authors (V. V. Kovalev, N. V. Borodina, V. M. Kovalev, V. M. Kovalev) studied the antimicrobial activity of ointments with the lipophilic extract from *Salix viminalis L*. Shoots and proved pronounced antimicrobial activity against strains of *Staphylococcus aureus, Escherichia coli, Proteus vulgaris, Pseudomonas aeruginosa, Bacillus subtilis* and *Candida albicans* extract *Salix viminalis L*. [32].

The results of the study of microbial contamination of a gel samples containing extracts of *Melissa* and Willow bark when stored for a month in dark glass jars are given in Table 3.1. To level out the inherent levels of antimicrobial activity of the ointment, it was analyzed at a dilution of 1:100. Drug category 2.

According to the results of microbial contamination control, the number of colony-forming bacteria in the ointment solution 1:100 did not exceed 50, and fungi 100 per 1 g of the drug, for the entire storage period. Bacteria of the families *Staphylococcus aureus, Enterobacteriaceae, Bacilus subtilis, Pseudomonas aeruginosa* were not detected in the test samples.

Table 3.1.

Results of microbial contamination of the studied extemporaneous gel

Shelf life, months	Number of CFU\g		Availability in 1 g			
	bacteria	mushrooms	*St. aureus*	*Esch. coli*	*Bac. subtilis*	*Ps. aeruginosa*
7 days	<50	<100	Missing	Missing	Missing	Missing
15 days	<50	<100	Missing	Missing	Missing	Missing

Note n=6, P=95%

Thus, the conducted studies allow us to state that the manufactured samples of of extemporaneous gel remain stable throughout the entire storage period, and the deviations are within the norms. Based on the conducted studies, the shelf life of the drug is set at 14 days.

3.4. Determination of the size of gel particles

Microscopic examination and measurement of the linear dimensions of gel particles were carried out using a Granum R-40 laboratory microscope with a built-in digital camera DCM 310 and achromatic objectives with a magnification of 4x, 10x, 40x.

The use of this equipment allowed us to visualize the particles and conduct their morphometric analysis using the Toup View 3.7 program. To prove the homogeneity of the gel, its microscopy was performed according to the method given in section 2, the results are presented in Fig. 3.9. and 3.10.

Fig. 3.1. Gel sample at a magnification of x40

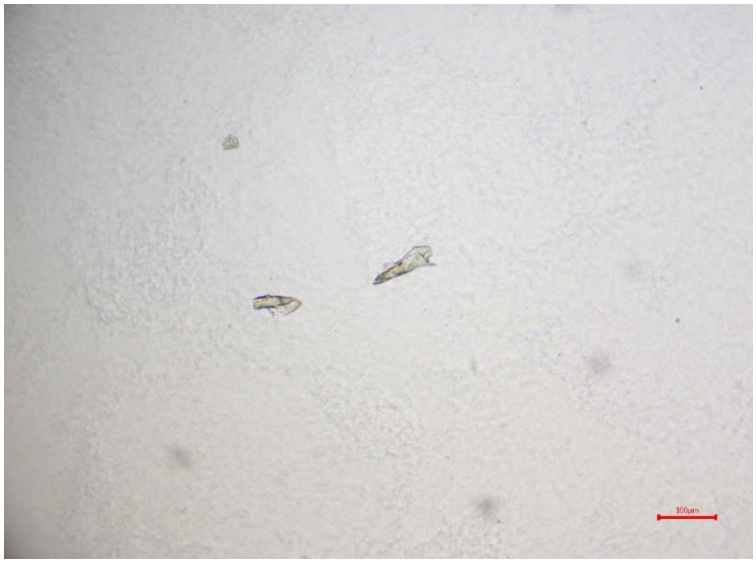

Fig. 3.2. Gel sample at a magnification of x100

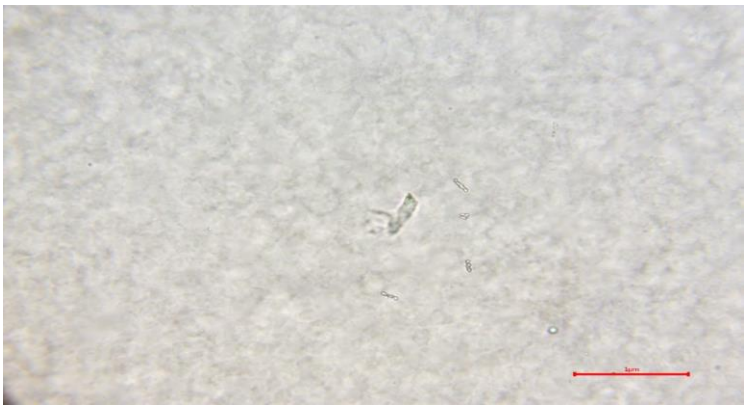

Fig. 3.3. Gel sample at x400 magnification

According to the results of microscopy, it can be concluded that the distribution of API particles in the gel is uniform, there are single insoluble particles, the size of which does not exceed 100 micrometer.

3.5. Determination of pH of gel samples

The pH value is a pivotal indicator that influences the stability of gel systems during storage, the nature of the interactions between components, as well as the biological activity and therapeutic efficacy of the drug [37].

Table 3.2.

The results of the extemporaneous gel pH determinition

m	n	X_i	X_{cp}	S^2	S_{cp}	P	t(P, n)	Confidence interval			ε_, %
1	2		3	4	5	6	7	8			9
6	5	5,11 5,15 5,14 5,14 5,06 4,99	5,0983	0,003896667	0,0255	0,95	2,78	5,0983	±	0,0708	1,3896

The pH of 10% aqueous solutions of the gel samples was measured by potentiometric method in accordance with the generally accepted methodology and requirements of the State Pharmacopoeia of Ukraine [20, 30].

The findings of the studies indicated that the pH level was 5.1 ± 0.07.

Conclusions to chapter3

1. The composition of the gel containing Lemon balm extract 5%, Willow bark extract 5%, glycerin 10%, methylparaben, triethanolamine, purified water and Noveon® 1% was theoretically substantiated. The gel technology was developed.

2. The absence of microbial contamination of extemporaneous gel samples for 14 days was established.

3. The uniform distribution of gel particles and the presence of single insoluble particles were proven by the sieve microscopy method.

4. When determining the pH of the gels, it was established that the pH value is within 4.99-5.15.

5. Based on the conducted research, the technology of extemporaneous gel with Lemon balm and Willow bark extracts was developed.

GENERAL CONCLUSIONS

1. The problem of treating wounds complicated by an infectious component remains relevant for modern pharmaceutical science.
2. Based on the analysis of literary sources, the feasibility of developing soft dosage forms using modern bases containing APIs of natural origin has been substantiated.
3. The BAS complex containing Lemon balm and Willow bark extracts allows us to consider this plant APIs as promising for use in the development of SMF.
4. Based on the analysis of literary sources, the relevance of developing an extemporaneous gel with Lemon balm and Willow bark extracts was substantiated.
5. The conducted studies allow us to state that the manufactured samples of extemporaneous gel remain stable throughout the storage period 14 days and the deviations are within the norms.
6. According to the results of microscopy, it can be concluded that the distribution of API particles in the gel is uniform, there are single insoluble particles.
7. In determining of extemporal gel pH found that the pH value is 5.1 ± 0.07.
8. Based on the conducted studies, a sample of extemporaneous gel with Lemon balm and Willow bark extracts can be recommended for further research in order to expand modern SMFs intended for the treatment of purulent-inflammatory skin diseases and infectious-complicated of wound processes.

LIST OF REFERENCES

1. An intra-individual surgical wound comparison shows that octenidine-based hydrogel wound dressing ameliorates scar appearance following abdominoplasty / J. Matiasek et al. *Int Wound J*. 2018. Vol. 15(6). P. 914-920. DOI: 10.1111/iwj.12944.
2. An Updated Review on The Properties of Melissa officinalis L.: Not Exclusively Anti-anxiety / W. Zam et al. *Front. Biosci. (Schol Ed)*. 2022. Vol. 14(2). P. 16. DOI: 10.31083/j.fbs1402016.
3. Anti-inflammatory and Antioxidant Effects of Melissa officinalis Extracts: A Comparative Study / N. Draginic et al. *Iran J Pharm Res*. 2022. Vol. 21(1). P. e126561. DOI: 10.5812/ijpr-126561.
4. Antimicrobial resistance and primary health care: brief / World Health Organization. 2018. URL: https://apps.who.int/iris/bitstream/handle/10665/328084/WHO-HIS-SDS-2018.57-eng.pdf (Date of access: 12.02.2025).
5. Antioxidant Activity and Chemical Characteristics of Supercritical CO2 and Water Extracts from Willow and Poplar / M. Ostolski et al. *Molecules*. 2021. Vol. 26(3). P. 545. DOI: 10.3390/molecules26030545.
6. Antiviral Potential of Melissa officinalis L.: A Literature Review / A. Behzadi et al. *Nutrition and Metabolic Insights*. 2023. Vol. 16. P. 11786388221146683. DOI: 10.1177/11786388221146683.
7. Carvalho F., Duarte A. P., Ferreira S. Antimicrobial Activity of Melissa officinalis and Its Potential Use in Food Preservation. *Food Biosci*. 2021. Vol. 44. P. 101437. DOI: 10.1016/j.fbio.2021.101437.
8. Clinical Efficacy and Tolerability of Lemon Balm (Melissa officinalis L.) in Psychological Well-Being: A Review / I. M. Mathews et al. *Nutrients*. 2024. Vol. 16(20). P. 3545. DOI: 10.3390/nu16203545.
9. Content of Enzymatic and Nonenzymatic Antioxidants in Salix viminalis L. Grown on the Stebnyk Tailing / A. Fetsiukh et al. *Acta Agrobotanica*.

2022. Vol. 75. P. 752. DOI: 10.5586/aa.752.

10. Curtasu M. V., Nørskov N. P. Quantitative distribution of flavan-3-ols, procyanidins, flavonols, flavanone and salicylic acid in five varieties of organic winter dormant Salix spp. by LC-MS/MS. *Heliyon*. 2024. Vol. 10. P. e25129. DOI: 10.1016/j.heliyon.2024.e25129.
11. Development of an extemporaneous preparation formulation using a simple and non-solubilizing matrix for first in human clinical study / C. W. Chiang et al. *International Journal of Pharmaceutics*. 2024. Vol. 653. P. 123868. DOI: 10.1016/j.ijpharm.2024.123868
12. Emulgel: An effective drug delivery system / M. Talat et al. *Drug Development and Industrial Pharmacy*. 2021. Vol. 47(6). P. 1-11 DOI: 10.1080/03639045.2021.1993889
13. Evaluation of the type and frequency of extemporaneous formulations dispensed in hospital and community pharmacies / Z. Ramtoola et al. *Exploratory Research in Clinical and Social Pharmacy*. 2023. Vol. 12. P. 100380. DOI: 10.1016/j.rcsop.2023.100380
14. Falconer J. R., Steadman K. J. Extemporaneously compounded medicines. *Aust Prescr*. 2017. Vol. 40. P. 5–8. DOI: 10.18773/austprescr.2017.001
15. Formulation and evaluation of herbal-based antiacne gel preparations / J. A. Ansong et al. *Biomed Research International*. 2023. Vol. 18. P. 783-829.
16. Gel Formulations for Topical Treatment of Skin Cancer: A Review / M. Slavkova et al. *Gels*. 2023. Vol. 9(5). P. 352. DOI: 10.3390/gels9050352
17. Melissa officinalis L. as a nutritional strategy for cardioprotection / N. Draginic et al. *Frontiers in Physiology*. 2021. Vol. 12. P. 661778. DOI: 10.3389/fphys.2021.661778.
18. Melissa officinalis: Composition, Pharmacological Effects and Derived Release Systems—A Review / G. Petrisor et al. *International Journal of Molecular Sciences*. 2022. Vol. 23(7). P. 3591. DOI: 10.3390/ijms23073591.
19. Methylparaben. *Wikipedia The Free Encyclopedia*. URL:

https://en.wikipedia.org/w/index.php?title=Methylparaben&oldid=775428890. (Date of access: 12.02.2025).

20. Patil P. B., Datir S. K., Saudagar R. A Review on Topical Gels as Drug Delivery System. *Journal of Drug Delivery and Therapeutics*. 2019. Vol. 9(3). P. 989–994.
21. Phytochemical Composition and Bioactive Potential of Melissa officinalis L., Salvia officinalis L. and Mentha spicata L. / B. N. Silva et al. *Extracts. Foods*. 2023. Vol. 12(5). P. 947. DOI: 10.3390/foods12050947.
22. Phytoremediation Potential of Different Genotypes of Salix alba and S. viminalis / J. Urošević et al. *Plants*. 2024. Vol. 13(5). P. 735. DOI: 10.3390/plants13050735.
23. Polyacrylic acid. *Wikipedia The Free Encyclopedia*. URL: https://en.wikipedia.org/w/index.php?title=Polyacrylic_acid&oldid=756608959. (Date of access: 12.02.2025).
24. Purified water. *Wikipedia The Free Encyclopedia*. URL: https://en.wikipedia.org/w/index.php?title=Purified_water&oldid=778551486. (Date of access: 12.02.2025).
25. Rathod H. J., Mehta D. P. A review on pharmaceutical gel. *International Journal of Pharmaceutical Sciences*. 2015. Vol. 1(1). P. 33–47.
26. Salix spp. Bark Hot Water Extracts Show Antiviral, Antibacterial, and Antioxidant Activities-The Bioactive Properties of 16 Clones / J. Tienaho et al. *Front. Bioeng. Biotechnol*. 2021. Vol. 9. P. 797939. DOI: 10.3389/fbioe.2021.797939.
27. The Antimicrobial Potency of Mesoporous Silica Nanoparticles Loaded with Melissa officinalis Extract / G. Petrișor et al. *Pharmaceutics*. 2024. Vol. 16(4). P. 525. DOI: 10.3390/pharmaceutics16040525.
28. The effects of lemon balm (Melissa officinalis L.) on depression and anxiety in clinical trials: A systematic review and meta-analysis / J. Ghazizadeh et al. *Phytotherapy Research*. 2021. Vol. 35(12). P. 6690–6705. DOI: 10.1002/ptr.7252.

29. Theoretical Basis of Creation of Soft Medicinal Products of Local Application / V. Tarasenko et al. *Archives of Pharmacy Practice*. 2020. Vol. 11, Is. 2. P. 130–136.
30. Triethanolamine. *Wikipedia The Free Encyclopedia*. URL: https://en.wikipedia.org/w/index.php?title=Triethanolamine&oldid=779057283(Date of access: 12.02.2025).
31. Water for pharmaceutical purposes. URL: http://www.uspbpep.com/usp29/v29240/usp29nf24s0_c1231.html (Date of access: 12.02.2025).
32. Вивчення антимікробної активності мазей з ліпофільним екстрактом пагонів верби кошикової / В. В. Ковальов та ін. *Вісник фармації*. 2020. № 2(100). С. 31-36. DOI: 10.24959/nphj.20.29
33. Глущенко О. М. Вивчення асортименту м'яких лікарських засобів, що сприяють загоєнню ран, на фармацевтичному ринку України. *Фармацевтичний часопис*. 2020. № 1. С. 75-81.
34. Екстемпоральна рецептура (технологія, аналіз, застосування) : метод. рек. / О. І. Тихонов та ін. Київ : Агентство Медичного Маркетингу, 2016. 352 с.
35. Порівняльний аналіз асортименту м'яких лікарських засобів на фармацевтичному ринку України / Т. А. Грошовий та ін. *Фармацевтичний часопис*. 2020. № 4. С. 40–46. DOI: 10.11603/2312-0967.2020.4.11647
36. Технологічні аспекти створення м'яких лікарських засобів для лікування гнійних ран (огляд літератури) / О. П. Шматенко та ін. *Український журнал військової медицини*. 2020. Т. 1, № 1. С. 50-63. DOI: 10.46847/ujmm.2020.1(1)-050.
37. Державна Фармакопея України : в 3 т. / ДП «Український науковий фармакопейний центр якості лікарських засобів». 2–ге вид. Харків : ДП «Український науковий фармакопейний центр якості лікарських засобів», 2015. Т. 1. 1128 с.

38. Допоміжні речовини у виробництві ліків : навч. посіб. для студентів вищ. фармацевт. навч. закл. / О. А. Рубан т ін. ; за ред. І. М. Перцева. Харків : Золоті сторінки, 2016. 720 с.

APPLICATIONS

Appendix A

МІНІСТЕРСТВО ОХОРОНИ ЗДОРОВ'Я УКРАЇНИ
НАЦІОНАЛЬНИЙ ФАРМАЦЕВТИЧНИЙ УНІВЕРСИТЕТ

АКТУАЛЬНІ ПИТАННЯ СТВОРЕННЯ НОВИХ ЛІКАРСЬКИХ ЗАСОБІВ

МАТЕРІАЛИ
XXXI МІЖНАРОДНОЇ НАУКОВО-ПРАКТИЧНОЇ
КОНФЕРЕНЦІЇ МОЛОДИХ ВЧЕНИХ ТА СТУДЕНТІВ

23–25 квітня 2025 року
м. Харків

Харків
НФаУ
2025

THE RELEVANCE OF DEVELOPING AN EXTEMPORANEOUS GEL WITH LEMON BALM AND WILLOW BARK EXTRACTS

Ayoub Choukri Hamioui, Kovalova T.M., Oliinyk S.V.
Scientific supervisor: Kovalov V.V.
National University of Pharmacy, Kharkiv, Ukraine
volodyakw@gmail.com

Introduction. Rational wound treatment is one of the most acute and complex problems of our time, the effective solution of which will concern more than one generation of doctors and pharmacists. The problem of wound treatment, despite the great variety of proposed methods and drugs, remains relevant.

Infectious complications increase the postoperative mortality rate, the amount of treatment costs, the number of additional days spent in the hospital. This indicates the significant medical and socio-economic significance of the problem of prevention and the need to increase the effectiveness of treatment.

The therapeutic value of medicinal plants is determined by the biologically active substances included in their composition. At the same time, hundreds of active pharmaceutical ingredients (APIs) are synthesized simultaneously in each of the medicinal plants, which have a total pharmacological effect. Additional study of previously studied and long-used medicinal plants sometimes allows us to identify a new aspect of their biological activity.

Aim. To study the relevance of developing an extemporaneous gel with Lemon balm (Melissa officinalis) and Willow bark (Salix Viminalis L.) extracts.

Materials and methods. To achieve this goal, we used general scientific research methods: analysis, synthesis, comparison, generalisation, comparison, systematisation to process the literature data.

Results and discussion. The properties of Lemon balm extract are due to the rich composition of medicinal plant raw materials. Lemon balm herb (Herba Melissae) contains essential oil (up to 0.33%), tannins (up to 5%), bitterness, mucus, sugars, caffeic, succinic, chlorogenic, oleanolic and ursolic acids, mineral salts. Lemon balm leaves contain essential oil – up to 1%, which includes: citral – 60%, citronellal, myrcene, geraniol, linalool, cineole, aldehydes; tannins – about 5%; resins; organic acids: succinic, caffeic, chlorogenic; triterpenic acids: oleanolic, ursolic; vitamin C – 150 mg%, carotene – 7 mg%; not less than 5% of hydroxycinnamic acid derivatives, which have the common name rosmarinic acid; mucus; bitterness; macro- and microelements. The extract of lemon balm contains flavonoids (quercitrin, rhamnocitrin, luteolin), polyphenolic compounds (rosmarinic, caffeic and protocatechuic acids), monoterpenoid aldehyde, monoterpene glycosides, triterpenes (ursolic acid, essential and oleanolic acids). When applied externally, the extract exhibits antispasmodic, analgesic, antimicrobial, antihistamine, antiviral activity, and is an antioxidant. Lemon balm water is a component of anticonvulsant mixtures, and essential oil is a component of Sanitas liniment. The plant juice is used to treat allergic dermatitis. Leaf extract has an effective sedative effect. It is also used externally for furunculosis, rheumatism, bruises and ulcers, gingivitis, and toothache.

The study of the chemical composition of various species of willow (Salix L.) began in the 18th century. The history of use and the chemical composition of some species of willow are quite fully described in scientific publications.

At the moment, it is known that the main active substances of the studied species of willow are phenolic glycosides, flavonoids, tannins, and also include phenolic acids, ascorbic acid, amino acids, saponins, essential oils and polysaccharides, which can contribute to the overall pharmacological effect. It is known that the quantitative content of BAS in the bark and leaves can change in different phases of vegetation and depends on the growing conditions.

One of the main representatives of biologically active substances of the willow family is phenolic glycosides, the aglycone of which is salicylic alcohol. The first phenolic glycoside isolated from plants – salicin (salicoside), is a β-glucoside of salicylic alcohol. It was obtained from willow bark by the French scientist A. Leroux (1829). The main types of action of willow – anti-inflammatory, analgesic, and antipyretic – are associated with salicin.

Thus, the use of Salix Viminalis L. extract as an API for the preparation of gels is relevant. Further studies are planned to clarify the concentration of the extract and investigate the severity of antimicrobial activity.

Conclusions. Considering the above, we consider it rational and relevant to develop soft dosage forms with extracts of Lemon balm and Willow bark for the treatment of wounds of various etiologies. The focus on natural APIs with antimicrobial, anti-inflammatory, soothing and moisturizing properties emphasizes the transition to a more holistic and effective treatment of wounds and demonstrates a strategic approach to creating a stable and suitable semi-solid dosage form.

PROSPECTS FOR THE DEVELOPMENT OF MEDICINAL PRODUCTS WITH IMPROVED SOLUBILITY OF THE ACTIVE SUBSTANCE

Dilai Fadwa
Scientific supervisor: Vyshnevska L.I.
National University of Pharmacy, Kharkiv, Ukraine
atl@nuph.edu.ua

Introduction. Oral route of drug administration is the simplest and most convenient, but at the same time there is a problem of bioavailability of active substances, in particular poorly soluble in water. One of the options for solving this problem is the introduction of poorly soluble substances in the composition of self-emulsifying compositions (SEC). In this case, the possibility of oral administration is preserved, and solubility, absorption in the gastrointestinal tract and bioavailability are increased. This effect is achieved by proper ratio of excipients such as solvent, surfactant (surfactant) and co-surfactant (co-surfactant).

Aim. Research of prospects for the development of medicinal products with improved solubility of the active substance.

Materials and methods. Literature sources were analyzed in order to study the peculiarities of composition, technology, research of SEC, as well as the prospects for the development of a new drug based on SEC.

Results and discussion. SEC are special drug delivery systems f or oral administration, the active pharmaceutical ingredients (API) of which are insoluble or poorly water-soluble substances. In a classical embodiment, an SEC consists of a solvent, a surfactant and a co-surfactant. The solvents depend on the nature of the AFI. They can be fatty acids, vegetable oils, more modern – acetylated mono-, di-, triglycerides of fatty acids. Among surfactants, sodium lauryl sulfate and polysorbates are more common. Co-surfactants are polyethylene glycol-400 and poloxamers.

Additional substances found in modern literature are emollients and enhancers (glycerin, isopropyl myristate, diethylene glycol). They accelerate the absorption of active substances in the stomach. Due to this composition, when entering the stomach, SEC under the action of gastric juice spontaneously emulsifies, forming a microemulsion of oil-in-water type. Reduction of the particle

Appendix B

МІНІСТЕРСТВО ОХОРОНИ ЗДОРОВ'Я УКРАЇНИ
НАЦІОНАЛЬНИЙ ФАРМАЦЕВТИЧНИЙ УНІВЕРСИТЕТ

СЕРТИФІКАТ УЧАСНИКА

Цим засвідчується, що

Ayoub Choukri Hamioui, Kovalova T.M., Oliinyk S.V.
Scientific supervisor: Kovalov V.V.

брав(ла) участь у роботі
XXXI Міжнародної науково-практичної конференції молодих вчених та студентів
«АКТУАЛЬНІ ПИТАННЯ СТВОРЕННЯ НОВИХ ЛІКАРСЬКИХ ЗАСОБІВ»

В.о. ректора
Національного фармацевтичного
університету

Алла КОТВІЦЬКА

23-25 квітня 2025 р, м. Харків

Ф А 2.2.1–32-366

National University of Pharmacy

Faculty pharmacy
Department drug technology

Level of higher education master

Specialty 226 Pharmacy, industrial pharmacy
Educational and professional program Pharmacy

APPROVED
The Head of Department
Liliia VYSHNEVSKA

_____
"_30_" August 2024

ASSIGNMENT
FOR QUALIFICATION WORK
OF AN APPLICANT FOR HIGHER EDUCATION

Ayoub Choukri HAMIOUI

1. Topic of qualification work: «Composition substantiation and technology development of extemporaneous gel with Lemon balm and Willow bark extracts», supervisor of qualification work: Volodymyr KOVALOV, PhD, assoc. prof.,

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

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

3. Outgoing data for qualification work: compositional substantiation, technology development and study of extemporaneous gel with Lemon balm and Willow bark extracts technological properties.

4. Contents of the settlement and explanatory note (list of questions that need to be developed): to study the relevance of developing an extemporaneous gel with Lemon balm and Willow bark extracts; based on the analysis of the literature, identify APIs Lemon balm and Willow bark extracts and justify the choice of dosage form; theoretically substantiate the optimal composition of extemporaneous gel; substantiate the composition of the gel base; develop the technology of extemporaneous gel; determine the technological properties of extemporaneous gel.

5. List of graphic material (with exact indication of the required drawings): tables 3 , pictures 14.

6. Consultants of chapters of qualification work

Chapters	Name, SURNAME, position of consultant	Signature, date	
		assignment was issued	assignment was received
1	Volodymyr KOVALOV, associate professor of higher education institution of department drug technology	06.09.2024	06.09.2024
2	Volodymyr KOVALOV, associate professor of higher education institution of department drug technology	19.10.2024	19.10.2024
3	Volodymyr KOVALOV, associate professor of higher education institution of department drug technology	01.02.2025	01.02.2025

7. Date of issue of the assignment: "30" August 2024

CALENDAR PLAN

№ з/п	Name of stages of qualification work	Deadline for the stages of qualification work	Notes
1	The topic selection	September 2024	done
2	Analysis of literary sources	September-November 2024	done
3	Conducting experimental research in	October-January 2024	done
4	Designing the work	February-April 2025	done
5	Submission of finished work to the examination commission	May 2025	done

An applicant of higher education _____ Ayoub Choukri HAMIOUI

Supervisor of qualification work _____ Volodymyr KOVALOV

ВИТЯГ З НАКАЗУ № 237

По Національному фармацевтичному університету

від 27 вересня 2024 року

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

Прізвище, ім'я здобувача вищої освіти	Тема кваліфікаційної роботи		Посада, прізвище та ініціали керівника	Рецензент кваліфікаційної роботи
по кафедрі аптечної технології ліків				
Шукрі-Хаміуі Аюб	Обґрунтування складу та розроблення технології екстемпорального гелю з екстрактами меліси та кори верби	Composition substantiation and technology development of extemporaneous gel with Lemon balm and Willow bark extracts	доцент Ковальов В.В.	доцент Солдатов Д.П.

Ректор

Вірно. Секретар

ФА2.8-03-317

ВИСНОВОК

експертної комісії про проведену експертизу
щодо академічного плагіату у кваліфікаційній роботі

здобувача вищої освіти

«05» травня 2025 р. № 331116471

Проаналізувавши кваліфікаційну роботу здобувача вищої освіти Шукрі-Хаміуі Аюб, групи Фм20(4.10)англ-02, спеціальності 226 Фармація, промислова фармація, освітньої програми «Фармація» навчання на тему: «Обґрунтування складу та розроблення технології екстемпорального гелю з екстрактами меліси та кори верби / Composition substantiation and technology development of extemporaneous gel with Lemon balm and Willow bark extracts», експертна комісія дійшла висновку, що робота, представлена до Екзаменаційної комісії для захисту, виконана самостійно і не містить елементів академічного плагіату (компіляції).

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

Ф А 2.2.1-32-353

REVIEW

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

Ayoub Choukri HAMIOUI

on the topic: «Composition substantiation and technology development of extemporaneous gel with Lemon balm and Willow bark extracts »

Relevance of the topic. Rational wound treatment is one of the most acute and complex problems of our time, the effective solution of which will concern more than one generation of doctors and pharmacists. The problem of wound treatment, despite the great variety of proposed methods and drugs, remains relevant. Infectious complications increase the postoperative mortality rate, the amount of treatment costs, the number of additional days spent in the hospital. This indicates the significant medical and socio-economic significance of the problem of prevention and the need to increase the effectiveness of treatment. The therapeutic value of medicinal plants is determined by the biologically active substances included in their composition. At the same time, hundreds of active pharmaceutical ingredients are synthesized simultaneously in each of the medicinal plants, which have a total pharmacological effect. Additional study of previously studied and long-used medicinal plants sometimes allows us to identify a new aspect of their biological activity. Master's thesis of Ayoub Choukri HAMIOUI dedicated to this topical issue.

Practical value of conclusions, recommendations and their validity. In the course of composing the thesis, the master's student conducted a thorough analysis of extant literature concerning the relevance of formulating an extemporaneous gel comprising lemon balm and willow bark extracts. This analysis encompassed the identification of active principles, the rational selection of dosage form, and the theoretical substantiation of the optimal gel composition. Additionally, the analysis addressed the substantiation of the gel base composition and the development of the extemporaneous gel technology, along with the determination of its technological

properties.

Assessment of work. The master's work was completed at a high modern level. The master's student successfully solved all tasks. The results of the work are of practical interest.

General conclusion and recommendations on admission to defend. Ayoub Choukri HAMIOUI's Master's thesis can be submitted for defense to the Examination Commission of the National Pharmaceutical University for the assignment of the educational qualification level of Master of Pharmacy.

Scientific supervisor _____ Volodymyr KOVALOV

«13» of May 2025

Ф А 2.2.1-32-356

REVIEW

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

Ayoub Choukri HAMIOUI

on the topic: «Composition substantiation and technology development of extemporaneous gel with Lemon balm and Willow bark extracts »

Relevance of the topic. The rational treatment of wounds represents a significant contemporary challenge, the effective resolution of which will necessitate the collaborative efforts of multiple generations of medical professionals, including doctors and pharmacists. Despite the extensive array of proposed methodologies and pharmaceutical agents for wound treatment, this problem persists as a salient one.

Prolonged postoperative infections have been demonstrated to increase the mortality rate, the cost of treatment, and the number of additional days spent in the hospital. This finding underscores the profound medical and socio-economic implications of the problem of prevention and underscores the necessity to enhance the efficacy of treatment. The therapeutic value of medicinal plants is determined by the biologically active substances included in their composition. Concurrently, a multitude of active pharmaceutical ingredients are synthesized in each medicinal plant, resulting in a collective pharmacological effect. Further examination of medicinal plants that have been the subject of prior study and long-standing utilization can, on occasion, unveil hitherto unobserved facets of their biological activity.

Theoretical level of work. The research conducted by Ayoub Choukri HAMIOUI is focused on the development of an extemporaneous gel comprising lemon balm and willow bark extracts. This endeavor involves a comprehensive analysis of extant literature to establish the theoretical underpinnings of the optimal gel composition. Additionally, the study aims to substantiate the composition of the

gel base, thereby ensuring its efficacy and safety.

Author's suggestions on the research topic. The master's student conducted theoretical and experimental studies on the justification of the choice of active and auxiliary substances of extemporaneous gel with Lemon balm and Willow bark extracts, studied its stability during storage, proposed a rational technology of gel.

Practical value of conclusions, recommendations and their validity. On the basis of the conducted research, extemporaneous gel with Lemon balm and Willow bark extracts, is proposed for practical implementation. The obtained results can be used for the purpose of expanding the assortment of extemporaneous preparations.

Disadvantages of work. According to the text of the work there are some typographical errors, bad expressions. However, this does not reduce the value of the work and does not call into question the results obtained.

General conclusion and assessment of the work. The qualification work of the applicant deserves high marks, meets the requirements and can be submitted for official defense to the examination commission of the National University of Pharmacy.

Reviewer _____ assoc. prof. Dmytro SOLDATOV

«15» of May 2025

Ф А2.2.1-91-287

МІНІСТЕРСТВО ОХОРОНИ ЗДОРОВ'Я УКРАЇНИ
НАЦІОНАЛЬНИЙ ФАРМАЦЕВТИЧНИЙ УНІВЕРСИТЕТ

ВИТЯГ З ПРОТОКОЛУ № _17_
«_19_» _травня_2025_
року м. Харків

засідання кафедри
аптечної технології ліків
(назва кафедри)

Голова: завідувачка кафедри, професор Вишневська Л. І.
Секретар: докт. філ., ас. Бондар Л.А.

ПРИСУТНІ:

проф. Половко Н.П., проф. Семченко К.В., проф. Зуйкіна С.С., доц. Ковальова Т.М., доц. Буряк М.В., доц. Ковальов В.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 Phm19(4,10d) eng 04 спеціальності 226 «Фармація, промислова фармація» Ayoub Choukri HAMIOUI – з доповіддю на тему «Composition substantiation and technology development of extemporaneous gel with Lemon balm and Willow bark extracts» (науковий керівник, доц. Володимир КОВАЛЬОВ).

УХВАЛИЛИ: Рекомендувати до захисту кваліфікаційну роботу.

Голова
Завідувачка кафедри, проф. _____ Лілія ВИШНЕВСЬКА
(підпис)

Секретар
Асистент _____ Любов БОДНАР
(підпис)

Ф А2.2.1-32-042

НАЦІОНАЛЬНИЙ ФАРМАЦЕВТИЧНИЙ УНІВЕРСИТЕТ

ПОДАННЯ
ГОЛОВІ ЕКЗАМЕНАЦІЙНОЇ КОМІСІЇ
ЩОДО ЗАХИСТУ КВАЛІФІКАЦІЙНОЇ РОБОТИ

Направляється здобувач вищої освіти Ayoub Choukri HAMIOUI до захисту кваліфікаційної роботи
за галуззю знань 22 Охорона здоров'я
спеціальністю 226 Фармація, промислова фармація
освітньою програмою Фармація
на тему: «Composition substantiation and technology development of extemporaneous gel with Lemon balm and Willow bark extracts»

Кваліфікаційна робота і рецензія додаються.

Декан факультету _____/ Микола ГОЛІК /

Висновок керівника кваліфікаційної роботи

Здобувач вищої освіти Ayoub Choukri HAMIOUI представила кваліфікаційну роботу, яка за об'ємом теоретичних та практичних досліджень повністю відповідає вимогам до оформлення кваліфікаційних робіт.

Керівник кваліфікаційної роботи

_____ Володимир КОВАЛЬОВ

«13» травня 2025 р.

Висновок кафедри про кваліфікаційну роботу

Кваліфікаційну роботу розглянуто. Здобувач вищої освіти Ayoub Choukri HAMIOUI допускається до захисту даної кваліфікаційної роботи в Екзаменаційній комісії.

Завідувачка кафедри
аптечної технології ліків

_____ Лілія Вишневська

«19» травня 2025 р.

Qualification work was defended

of Examination commission on

« ___ » of June ___2025

with the grade _____

Head of the State Examination commission,

D.Pharm.Sc, Professor

_____ / Volodymyr YAKOVENKO/