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**MINISTRY OF HEALTH OF UKRAINE**
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# QUALIFICATION WORK

on the topic: **«DEVELOPMENT OF COMPOSITION AND TECHNOLOGY OF EXTEMPORANEOUS ANTI-INFLAMMATORY OINTMENT»**

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## ANNOTATION

The qualification work is devoted to the development of the composition and manufacturing technology of an extemporaneous anti-inflammatory ointment in the conditions of pharmacy production for use in dental practice. A rational composition has been developed and manufacturing technology has been substantiated, methods for controlling the quality of anti-inflammatory ointment have been proposed. The qualification work is set out on 43 pages, consists of an introduction, literature review and 2 sections of the experimental part, general conclusions, includes 5 tables, 4 figures, 59 references and 4 appendices.
*Key words:* dental medicines, soft dosage forms, furazolidone, novocaine, Kalanchoe juice, composition, technology.

## АНОТАЦІЯ

Кваліфікаційна робота присвячена розробці складу та технології виготовлення екстемпоральної протизапальної мазі в умовах аптечного виробництва для застосування в стоматологічній практиці Розроблено раціональний склад та обґрунтовано технологію виготовлення, запропоновано методики контролю якості протизапальної мазі. Кваліфікаційна робота викладена на 43 сторінках, складається зі вступу, огляду літератури та 2 розділів експериментальної частини, загальних висновків, включає 5 таблиці, 4 рисунки, 59 джерел літератури та 4 додатки.
*Ключові слова:* стоматологічні лікарські засоби, м’які лікарські форми, фуразолідон, новокаїн, сік каланхое, склад, технологія.

**CONTENT**

# INTRODUCTION

**Actuality of topic.** With the progress of civilization, the prevalence of dental diseases has increased dramatically and has acquired the significance of both a general medical and a social problem. According to WHO, the results of a survey of the population of 53 countries showed that only 12 % of the population have periodontal health, 53 % have initial inflammation, 23 % have initial destructive changes, and 12 % have moderate and severe lesions.

The modern nomenclature of drugs used in dental practice is quite diverse. It includes a wide range of drugs intended for the treatment and prevention of periodontal and oral mucosa diseases. Medicines used in dentistry belong to different pharmacotherapeutic groups; differ in the nature of active substances and a number of other characteristics, in particular, in the type of dosage form.

As you know, the choice of dosage form is essential to ensure the effectiveness of pharmacotherapy for various diseases. Many clinicians note the expediency of developing long-acting dosage forms that provide a long period of therapeutic effect with a gradual release of medicinal substances. Such dosage forms include soft dosage forms.

Compared with other dosage forms, they have a number of advantages: they are easily applied to the surface of the oral mucosa, are well retained on it and provide long-term contact with the treated surface, significantly prolonging the effect of the drug.

In this regard, the development of an extemporaneous soft dosage form that meets modern requirements for the effectiveness and safety of a drug for use in dental practice is an important area of scientific research that involves solving a number of issues related to the study and systematization of dental diseases, the choice of active and excipients, providing the necessary biopharmaceutical and rheological properties of the composition, standardization of the quality of the dosage form, etc.

The **aim** of our research is devoted to the substantiation of the composition and the development of technology for the preparation of an ointment for use in dental practice.

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

- to study the literary sources about the characteristics and distribution of dental inflammatory diseases; to analyze the range of soft dosage forms for the treatment of dental diseases and the relevance of their use; characterize excipients used for the preparation of soft dosage forms;
- to scientifically substantiate the rational composition of dental ointment with furazolidone, novocaine and Kalanchoe juice;
- theoretically develop a technology for the manufacture of an anti-inflammatory ointment based on furazolidone, novocaine and Kalanchoe juice in a pharmacy;
- calculate of the cost of the developed anti-inflammatory ointment.

**Object of research.** Furazolidone, novocaine, Kalanchoe juice, dental ointment based on furazolidone, novocaine and Kalanchoe juice, anhydrous lanolin.

**Subject of research.** Scientific substantiation of the rational composition, as well as the calculation of the cost and the development of technology for the manufacture of anti-inflammatory dental ointment in a pharmacy.

**Research methods.** In the qualifying work, the following methods were used: marketing methods of descriptive and structural analysis, mathematical, organoleptic, physicochemical and statistical.

**The practical significance of the results obtained.** Rational composition of an anti-inflammatory ointment based on furazolidone, novocaine and Kalanchoe juice for use in dental practice has been proposed. The optimal production technology is scientifically substantiated for the manufacture of dental ointment in a pharmacy used. The estimated cost of the proposed anti-inflammatory ointment made in a pharmacy was determined.

**Elements of scientific research.** The composition is scientifically substantiated, the cost of extemporaneous ointment is calculated, technology are developed dental ointment of anti-inflammatory action in the conditions of pharmaceutical production.

**Implementation of results.** The main provisions of the qualification work are set out and discussed in the 5th International Scientific and Practical Conference «Scientific Paradigm in the Context of Technologies and Society Development» (April 16-18, 2023; Geneva, Switzerland) and XXIX International Scientifical and Practical Conference of Young Scientists and Students «Topical issues of newmedicines development» (April 19-21, 2023, Kharkiv). One abstracts of the report and one article have been published.

**Structure and scope of qualification work.** Qualification work consists of an introduction, literature review (Chapter 1), the experimental part (chapter 2 and 3), general conclusions, references, appendices. The work is presented on 43 pages, includes 5 tables, 4 figure, 59 sources of literature and 4 appendices.

# CHAPTER 1. OVERVIEW OF DENTAL DISEASES AND THE RELEVANCE OF THE USE OF SOFT DOSAGE FORMS FOR THEIR TREATMENT

## 1.1. Characteristics of dental diseases

The level of dental morbidity in the population of Ukraine has crossed the epidemiological threshold. In terms of the intensity of the increase in the number of dental diseases, our country is significantly ahead of the EU countries. That is why the dental health of society requires special attention. Concern is caused by the consistently high prevalence of dental diseases in the population of all ages, and especially the prevalence of dental caries, which is confirmed by the results of various epidemiological studies [16].

In 2005, the World Health Organization (WHO) set European targets for 2020 (Liverpool Declaration), which provides specific measures to improve dental health, define clear indicators of the intensity and prevalence of dental diseases. Most of the EU countries that have introduced these principles have already achieved their goals for improving oral health. The changes that have taken place in these states have shown significant social and medical effectiveness of improving and maintaining a high level of dental health of the population. Decree of the President of Ukraine dated May 21, 2002 No. 475/2002 approved the Programs for the Prevention and Treatment of Dental Diseases for 2002–2007, which defines national tasks for the prevention and treatment of dental diseases.

The oral cavity can be called the "entrance gate" of the body, so maintaining a person's overall health is impossible without healthy teeth. The World Dental Federation (FDI) notes that caries and oral diseases remain the most common diseases worldwide – 98 % of the world's population suffer from them. Dental health is directly related to the quality of life and working capacity of the individual and in some cases even has a significant impact on the level of professional suitability and self-realization (creative professions, public activities,

etc.). Therefore, the prevention of dental diseases and high-quality dental care are a priority of the state health policy [3, 34].

Inflammatory diseases of the oral cavity are among the most common human diseases. Periodontal pathology in the structure of dental diseases occupies a leading place and is a very acute problem of modern medicine. According to WHO, 69% to 99% of patients who visit a dentist have periodontal disease. The most common inflammatory periodontal disease among young people (83.6-96.6% in the age group 18-24 years) and without proper treatment can lead to premature tooth loss. Due to the high prevalence, rapid progression and ambiguity of treatment regimens, it is important to study the assortment composition of dental medicines [54].

Early manifestations of diseases of the inflammatory nature of the oral mucosa are recorded at the age of 10 to 20 years, 80% of children have gingivitis. A severe form of periodontitis is detected in 15-20% of patients aged 35 to 44 years. According to experts, carious and inflammatory diseases of the oral cavity are the main causes of tooth loss. Globally, approximately 30% of older people are completely missing natural teeth. In addition, almost half (40-50%) of HIV-positive people develop fungal, bacterial or viral infections of the oral cavity [1].

The cause of the defeat of the oral cavity can be both infectious diseases associated with the penetration of viruses, bacteria and fungi into the human body, as well as general causes that occur when the functioning of various organs and systems of the body is disrupted.

The risk factors that predetermine the occurrence of major diseases of the oral mucosa include:

- entry of pathogenic microorganisms (viruses, bacteria, fungi) into the oral cavity or their circulation in the body;

- violation of oral hygiene;

- malnutrition, including inadequate nutrition in vitamins, microelements, proteins;

- dehydration of the body, as well as a condition leading to over drying of the mucosa;

- mucosal trauma (for example, dentures), including chemical and thermal burns;

- hormonal fluctuations leading to immune changes (pregnancy, menopause, etc.);

- anemia;

- chronic diseases (respiratory, oncological and cardiovascular diseases, diabetes, allergies);

- smoking and alcohol abuse.

Inflammatory diseases of the oral mucosa are more often caused by microbial flora, in the structure of which the role of opportunistic microbes and pathogens of a specific infection has increased in recent years. These diseases develop through the interaction of macro- and microorganisms, which, together with the nature, quantity and virulence of the microbial flora, affect the immunological characteristics and the general condition of the body. Of great importance is the significant increase worldwide in the number of strains of microorganisms resistant to antibiotics [6, 16, 30].

The results of the study of the etiology and epidemiology of inflammatory diseases of the oral mucosa show that along with the constant pathogens of infections (staphylococci, streptococci, aerobic and anaerobic cocci, etc.), there are pathogens of respiratory, venereal, fungal infections, etc. (viruses, gonococci, chlamydia, mycoplasmas) is the most common cause of inflammatory diseases of the oral mucosa.

An important feature of these types of pathogens of inflammatory diseases of the oral mucosa is the transformation of their biological properties with the development of antibiotic-resistant forms, which determines the diversity of clinical forms and greatly complicates treatment. The rapid development of resistance of many bacterial pathogens to antibacterial agents makes traditional therapy ineffective [47].

Dysbiosis of the microflora of the oral cavity, activation of chronic bacterial infections, allergization of the human body, etc. lead to inflammatory and destructive dental diseases - caries, gingivitis, periodontitis, stomatitis, candidiasis, leukoplakia, etc. In addition, dysbacteriosis and immunodeficiency have a significant impact on the duration and severity of acute and chronic diseases of the oral cavity complicate their diagnosis and treatment.

Periodontal diseases are the second most common among all dental diseases. These include, in addition to periodontal disease, also gingivitis (inflammation of the gums) and the loss of all periodontal tissues together - periodontitis.

According to statistics, periodontal disease affects 86% of adults and 65% of children. In addition, among the child population, the prevalence for gingivitis is 80%, for periodontal disease - 3-5%. Most often, periodontal diseases in children are detected from the age of 9-10 years [3, 57].

The pathogenesis of inflammatory periodontal diseases (gingivitis, periodontitis) is based on an immunologically conditioned inflammatory response in periodontal tissues, which is influenced by a specific microflora. The system of non-specific, specific immunity (cellular and humoral immunity), an inflammatory mediator, takes part in the reaction.

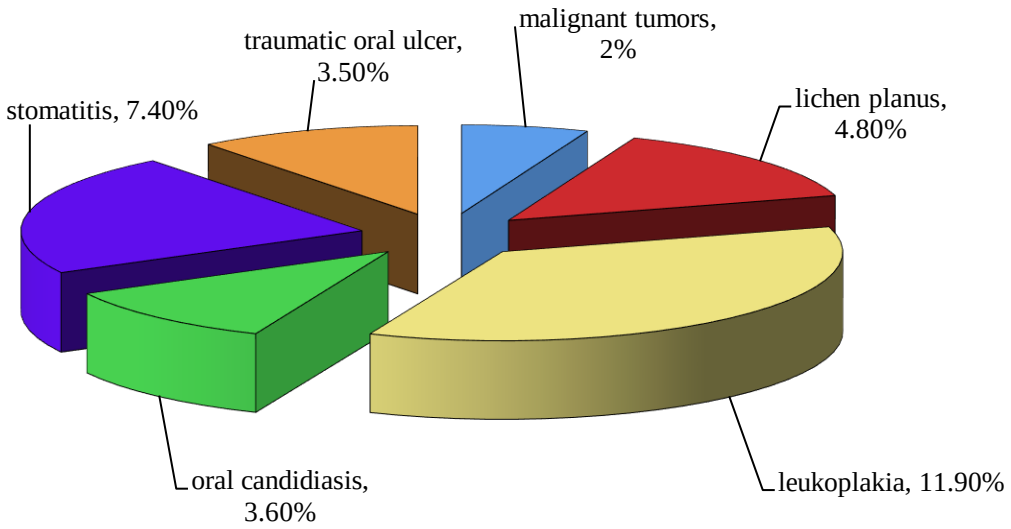



**Fig. 1.1. The prevalence of lesions of the oral mucosa**

Inflammatory diseases of periodontal tissues are most often accompanied by oral dysbiosis, the severity of which corresponds to the degree of periodontal damage. At the same time, against the background of a pronounced growth of pathogenic and conditionally pathogenic microorganisms, the concentration of representatives of the normal microflora decreases [6].

The causes of inflammation of the gums (gingivitis) can be both a general disorder in the body (allergies, diseases of the blood and cardiovascular system, toxicosis of pregnant women, etc.), as well as poor-quality brushing of teeth, tartar, deformation of teeth and jaws. In the development of gingivitis and periodontitis, the main role is played by anaerobic microorganisms and in the first place - bacterioids that produce aggressive enzymes that destroy connective tissue proteins, as well as bone tissue. In the microbial flora of the oral cavity of a healthy person, bacterioids are practically absent - their number is 1.0–2.5%. It contains more “friendly” coca (70–80%) and spirochetes (7–9%) [16, 36, 59].

An equally common disease of oral mucosa is stomatitis (inflammation of the oral mucosa). By the nature of the impression of oral mucosa, stomatitis is divided into infectious (viral, bacterial, fungal) and non-infectious stomatitis associated with a pathological reaction of the immune system, mucosal injury, as a manifestation of hypo- and beriberi. There are common causes of all types of stomatitis: immunodeficiency, diseases of the gastrointestinal tract, changes in the normal microflora of the oral cavity, etc.

In recent years, the incidence of oral candidiasis has increased significantly. This is due to the fact that a fungal infection is opportunistic and, under certain immunodeficiency conditions, can be activated in the oral cavity. The pathogenesis of candida infection depends on exogenous and endogenous factors that contribute to the development of various types of mucosal inflammation with characteristic clinical signs. Various types of yeast-like fungi live on the oral mucosa, most often pathological changes are caused by C. albicans, C. tropicalis, C. pseudotropicalis, C. krusei, C. guilliermondis.

Therapy for inflammatory diseases of the oral cavity includes drugs, both local and systemic, with antimicrobial, antifungal, anti-inflammatory, analgesic, anti-allergic, immunocorrective, and others actions. In the complex of therapeutic measures, an important role belongs to drugs that exhibit a combined effect [47].

Modern antibiotics and antiseptic preparations used in dental practice totally affect all parts of the oral cavity biocenosis. However, their bacteriostatic effect persists for a short time, and often as a result of antibacterial treatment, the biocenosis of the oral cavity changes and the resistance of pathogenic microflora to antibiotics increases. Inflammatory dental diseases are usually accompanied by oral dysbiosis. At the same time, against the background of a pronounced growth of pathogenic and conditionally pathogenic microorganisms, the concentration of representatives of the normal microflora decreases [55].

## 1.2. Analysis of the range of soft dosage forms for the treatment of dental diseases

According to the anatomical and therapeutic classification (ATC), group A01A "Means for use in dentistry" is assigned to group A "Means affecting the digestive system and metabolism", according to the State Register of Medicines of Ukraine as of 01.11.2020, it contains 62 drugs (Table 1.1).

Table 1.1

**The structure of the A01A group according to the ATS code "Means for use in dentistry"**

| *Name of drugs* | *Release form* | *Manufacturer* |
|---|---|---|
| **1** | **2** | **3** |
| *A01A B Antimicrobial and antiseptic preparations for local use in dentistry* | | |
| *A01A B 03 Chlorhexidine* | | |
| Periochip | Dental inserts, 2.5 mg №10, №20 (10 x 2) in blisters | Dexel Pharma Technologies Ltd., Israel |
| *A01A B 11* | | |
| Proposol-KM | Dental spray 25 g in bottles, one bottle contains propolis 1.5 g | JSC Stoma, Ukraine |

| 1 | 2 | | 3 |
|---|---|---|---|
| Proposol | Aerosol of 50 g in cylinders, one cylinder contains 2.1 g of propolis. | | |
| Proposol-N | Oral spray 20 or 60 g in containers with a mechanical pump, 1 bottle contains propolis 1.2 g or 3.6 g | | Micropharm LLC, Ukraine |
| Proposol Zdorovye | Oral spray 25 g in bottles, 50 g in bottles with a spray device, 1 bottle contains a phenolic hydrophobic preparation of propolis in terms of 100% content of the sum of phenolic compounds 0.75 g or 1.5 g | | LLC "Pharmaceutical company " Zdorovye"", Ukraine |
| *A01A B 18 Clotrimazole* | | | |
| Candide | Solution for local use 1%, 15 ml in a vial | | Glenmark Pharmaceuticals Ltd, India |
| *A01A B 12 Hexetedine* | | | |
| Stomatidin | Solution 0.1%, 200 ml in vials | | Bosnalek d.d., Bosnia and Herzegovina |
| Hexoral | Mouth spray 0.2%, 40 ml bottles | | Farmar Orleans, France |
| | Solution 0.1%, 200 ml in vials | | |
| Hexosept | Spray for the oral cavity 0.2%, 25 g per bottle. | | JSC Stoma, Ukraine |
| *A01A B 67 Metronidazole, combinations* | | | |
| Metroviol Denta | Gel for gums 20 g in tubes (in 1 g of metronidazole benzoate gel in terms of metronidazole 10 mg, chlorhexidine gluconate solution in terms of chlorhexidine digluconate - 0.5 mg) | | PrJSC Pharmaceutical factory "Viola", Ukraine |
| Dentagel | | | PJSC Fitopharm, Ukraine |
| Metrogil-Denta | | | Unique Pharmaceutical Laboratories, India |
| Dental Gel Zdorovye | | | LLC "Pharmaceutical company " Zdorovye"", Ukraine |
| Metrodent | Original lemon flavor | Gel for gums 20 g in tubes (in 1 g of metronidazole benzoate gel in terms of metronidazole 10 mg, chlorhexidine gluconate solution in terms of horhexidine gluconate 2.5 mg) | Synmedic Laboratories, India |
| | Pineapple flavor | | |
| | Strawberry flavor | | |
| *A01A D Other topical agents in dentistry* | | | |
| *A01A D 02 Benzidomin* | | | |
| Tantum Verde | Oral solution, 1.5 mg/ml, 120 ml vial. | | A.K.R.A.F. – S.P.A., Italy |
| | Mouth spray 1.5 mg/ml, 30 ml vial | | |

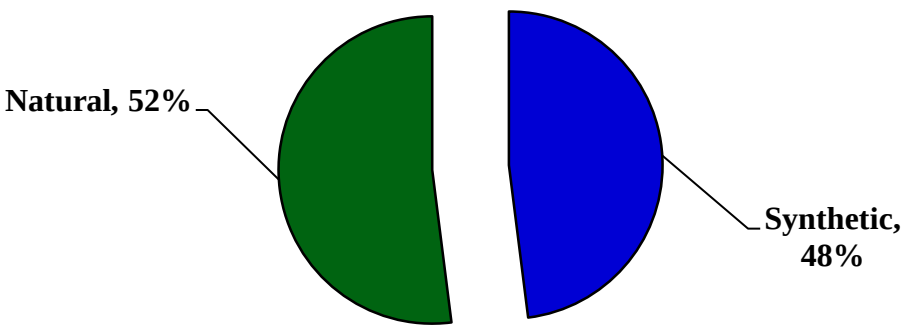
| 1 | 2 | 3 |
|---|---|---|
| T-sept | Lozenges 3 mg №10 (10x1), №20 (10x2) in blisters | ICN Polfa Rzeszow S.A., Poland |
| | Mouth spray, solution, 1.5 mg/ml, 30 ml in vial with nebulizer №1 | |
| Forteza | Oral solution 0.15%, 60 ml or 120 ml in bottles №1 | ABDI IBRAHIM Ilach Sanay ve Tijaret A.S., Türkiye |
| | Mouth spray 0.15% 15 ml or 30 ml bottle №1 with spray | |
| *A01A D 11 Others* | | |
| Holisal | Oral gel 10 g in a tube (in 1 g of gel 87.1 mg of choline salicylate and 0.1 mg of cetalkonium chloride) | Pharmaceutical plant Elfa A.T., Poland |
| Rotokan | Liquid 55 ml or 100 ml in vials (in 1 ml liquid extracts 1:1: chamomile 0.5 ml, calendula 0.25 ml, yarrow 0.25 ml) | JSC "Lubnyfarm", Ukraine |
| Komident-Zdorovye | Gel 10 g or 20 g in tubes (in 1 g of gel 20 ml of lidocaine hydrochloride, 200 mg of tincture of chamomile flowers in ethanol 70% (1: 8.5), 1 mg of thymol) | LLC "Pharmaceutical company " Zdorovye", Ukraine |
| Komistad-gel | Gel 10 g in tubes (in 1 g of gel 20 mg of lidocaine hydrochloride, 185 mg of chamomile flower extract) | STADA, Germany |
| Phytodent | Tincture of 100 ml in vials (100 ml obtained from 2 g of calamus rhizome, 1.5 g of calendula flowers, 1.0 g of nettle leaves, 1.0 g of chamomile, 2.0 g of Japanese Sophora fruit, 1.5 g of celandine herb , 1.0 g rose hips) | PJSC “Khimfarmzavod “Krasnaya Zvezda””, Ukraine |
| Maraslavin | Gingival solution, 100 ml in vials (decoction of wormwood herb - 4.196, thyme herb - 0.728, clove buds - 3.646, black pepper fruits - 1.199, ginger rhizomes - 4.196) | Sopharma JSC, Bulgaria |
| Hypericum herb | Grass 50 g in packs | OOO "Fitolik", Ukraine |
| | Grass 75.0 g in a pack with a filter bag | Ternopharm LLC, Ukraine |
| | Grass 50.0 g or 75.0 g in packs or in filter bags 1.5 g №20 | JSC "Lubnyfarm", Ukraine |
| | | ZAO Lektravy, Ukraine |
| Eucalyptus tincture | Tincture of 25 ml in bottles LLC "Ternopharm", Ukraine | LLC GKP Pharmaceutical Factory, Ukraine |
| | | PJSC Fitopharm, Ukraine |

| 1 | 2 | 3 |
|---|---|---|
| Salvia leaves | Leaves 40.0 or 50.0 g | JSC "Lubnyfarm", Ukraine |
| | | Ternopharm LLC, Ukraine |
| | Leaves 40.0, 50.0 or 60.0 g in packs or in filter bags 1.5 g №20 | PrJSC Pharmaceutical factory "Viola", Ukraine |
| | | ZAO Lektravy, Ukraine |
| Phytosept | Spray in a bottle of 15 ml with a sprayer (in 1 ml of capsicum tincture (1:10) 0.025 ml | PJSC Fitopharm, Ukraine |
| Bronspray | Spray in a 15 ml spray bottle (in 15 ml spray thyme tincture (1:4-6) 4.35 g, sage tincture (1:4-6) 4.35 g, peppermint tincture (1:4-6) 4.35 g) | Kwizda Pharma GmbH, Austria |
| Quercus cortex | Bark 50.0 or 100.0 g in packs or in filter bags 1.5 g №20 | JSC "Lubnyfarm", Ukraine |
| | | PrJSC Pharmaceutical factory "Viola", Ukraine |
| | Bark 100.0 g in packs or filter bags 2.5 g №20 | ZAO Lektravy, Ukraine |
| | Bark 100 g in a pack | Ternopharm LLC, Ukraine |
| Eucalyptus leaves | Leaves 50 g in a pack or in filter bags of 1.5 g №20 | PrJSC Pharmaceutical factory "Viola", Ukraine |
| | | ZAO Lektravy, Ukraine |
| | Leaves 50 or 75 g per pack | JSC "Lubnyfarm", Ukraine |
| Tooth drops | Drops of 10 ml in vials | PJSC Fitopharm, Ukraine |
| Salvia | Lozenges №20 (10 x 2) in blister packs | Herkel B.V., The Netherlands |
| Solcoseryl dental adhesive paste | Paste 5 g in tubes | Legacy Pharmaceuticals Sweetselend GmbH, Switzerland |
| Dentinox-gel N | Gel for gums 10 g in tubes | Dentinox Geselschaft pharmaceutical preparations Lenk and Schuppan, Germany |
| Stomatofit | Oral solution of 45, 50, 100 or 120 ml in vials (in 100 g of solution - liquid extract (0.65: 1) from a mixture of raw materials: chamomile flowers 13 g, oak | Fitofarm Klenko S.A., Poland |

| | | |
|---|---|---|
| | bark 13 g, sage leaves 13 g, herbs arnica 6.5 g, calamus rhizomes 6.5 g, peppermint herb 6.5 g, common thyme herb 6.5 g) | |
| Denta drops | Drops of 10 ml in vials or 20 ml in dropper bottles (1 ml contains chloral hydrate 333 mg, camphor 333 mg) | Ternopharm LLC, Ukraine |
| Stomatofit A | A solution of 25 ml in vials (in 100 g of a solution -50 g of a liquid extract (0.65: 1) from a mixture of raw materials: chamomile flowers 6.5 g, oak bark 6.5 g, sage leaves 6.5 g, arnica herb 3.25 g, calamus rhizomes 3.25 g, peppermint herbs 3.25 g, common thyme herbs 3.25 g, anesthesin 2 g) | Fitofarm Klenko S.A., Poland |

Most of all in the A01A group drugs produced in Ukraine are represented. In addition to domestic drugs, the group is widely represented by drugs manufactured in the EU countries - 15 drugs (25%, of which 5 are from Poland) and India - 6 drugs [11].

In total, drugs of the A01A group of manufacturers from 13 countries are registered in Ukraine. Of the analyzed number of drugs, 23 drugs with 16 different compositions are classified as combined drugs. They are 4 combinations of synthetic ingredients, 6 combinations of synthetic ingredients with natural ones, as well as 6 herbal preparations, which are mixtures of tinctures or extracts from medicinal plant materials (Fig. 1.2).



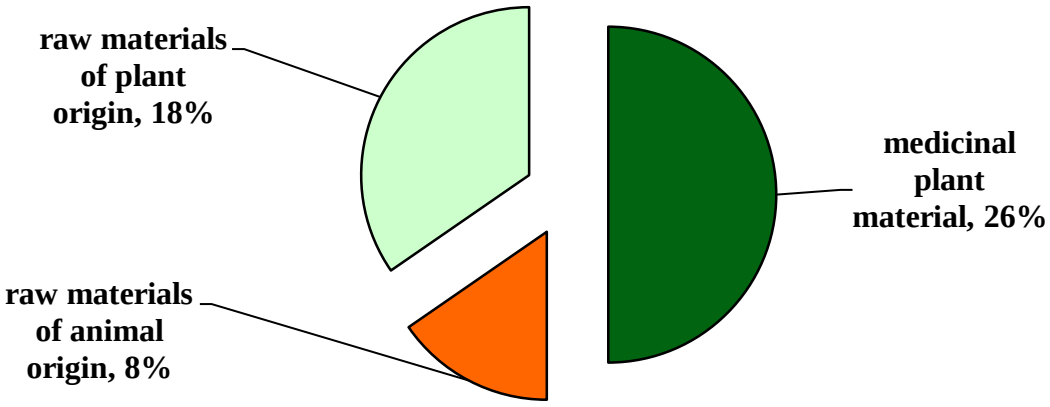



**Fig. 1.2. The structure of the ATC group A01A "Means for use in dentistry" by origin.**

These drugs are assigned to different groups according to the dispersological classification (Fig. 1.3).

Most of them are preparations with a liquid (48.4%) dispersion medium. And 25.8% is medicinal plant raw materials for self-preparation of water lifts by patients. The therapeutic effect of these drugs is short (usually the use is shown every 1.5-3 hours). In addition, self-preparation of water lifts by patients can cause a violation of the technology of preparation or storage and, as a result, a decrease in the therapeutic effect [11, 15, 44].

Drugs with a plastic- or elastic-viscous dispersion medium in the group are mainly represented by gels. Their share among dental drugs registered in Ukraine is 22.6% (14 drugs). They have a longer effect compared to liquid dosage forms, but, nevertheless, require application 1-2 times a day, because they are quickly washed off with saliva.

According to the instructions for use, of the analyzed 62 drugs, only 26 are indicated for the treatment of diseases of the oral mucosa. Of these, 6 - with a liquid dispersion medium, 8 - without a dispersion medium (collections), 12 - soft dosage forms (10 - gels, 1 - paste, 1 - dental inlays). Only 3 soft dosage forms of

domestic productions have been identified, indicated for the treatment of diseases of the oral mucosa [2, 29, 56].

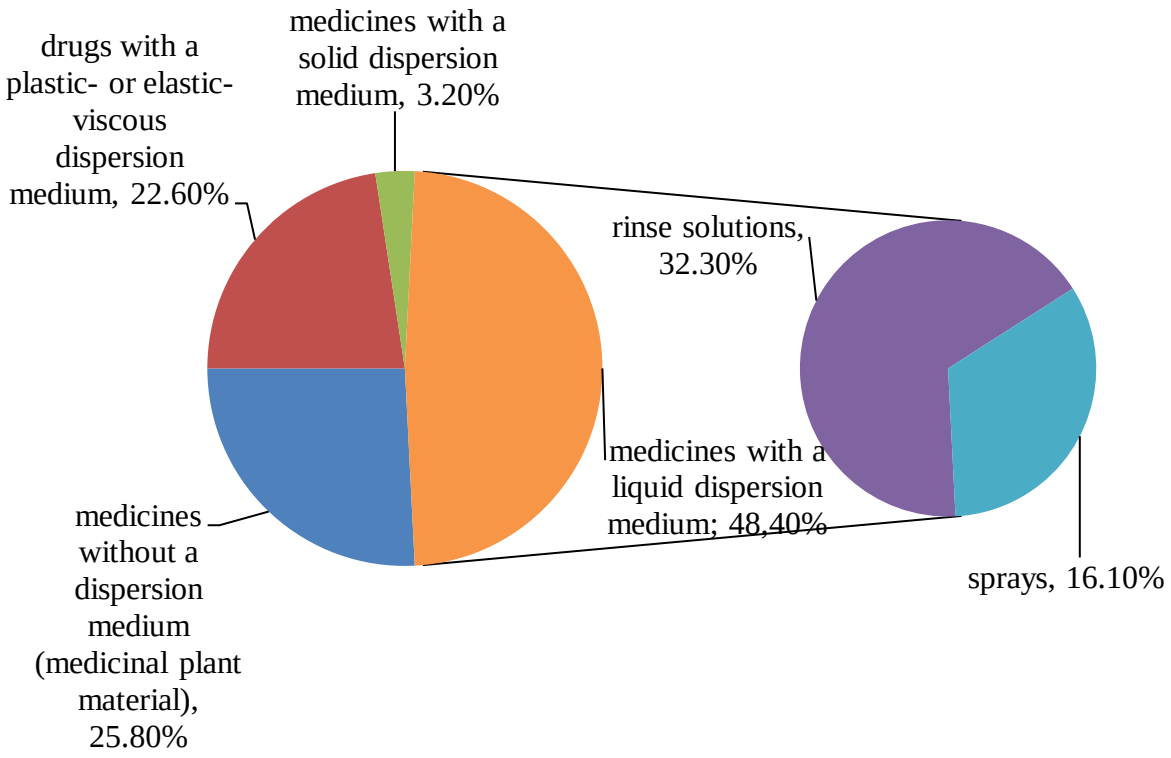



**Fig. 1.3. The structure of ATC group A01A "Means for use in dentistry" by type of dispersion medium.**

Only 5 preparations of group A01A contain local anesthetic components, 3 of them are combined soft drugs with lidocaine, one of which is intended to facilitate teething. The absence of local anesthetic ingredients in medicines can lead to a decrease in the quality of life of patients with inflammatory diseases of the oral cavity. Only one dental preparation containing lidocaine is produced in Ukraine [25].

Therefore, the development of domestic dental drugs with a combined antimicrobial and anti-inflammatory action for the treatment of oral mucosa, as well as combined drugs with antiseptic and local anesthetic effects can be defined as relevant today. A particularly promising direction is the development of prolonged LF, such as ointments, gels [36].

## 1.3. Overview of excipients for the preparation of soft dosage forms

The ointment base is an integral part of the ointment and determines its properties - consistency, storage stability, pH, appearance, color, smell, as well as the speed and completeness of the release of substances.

Today, in the world pharmaceutical practice, there are about 250 individual or complex ointment bases that have certain properties and meet certain requirements. There is no ideal base, therefore, in most cases, in order to obtain a base with the necessary properties; several excipients are combined [25].

Recently, there has been a tendency to expand the range of soft drugs in the pharmaceutical market of Ukraine.

Soft drugs, according to the State Pharmacopoeia of Ukraine, drugs for external use in the form of ointments, creams, gels, pastes, liniments, which have specific rheological properties and in most cases are heterogeneous dispersed systems [9].

Despite the fact that ointments are one of the most ancient dosage forms, they have not lost their significance in modern pharmacotherapy. If about 50 years ago ointments were considered as dosage forms for external use, mainly for the treatment of a number of dermatological diseases, they are currently widely used in surgery, ophthalmology, gynecology, dentistry, proctology and other areas of clinical medicine.

For the preparation of ointments with antibiotics that are sparingly soluble and unstable in water, the bases "Esilon-1" are recommended (Esilon-aerosil base - 45%, hydrolin - 5%, polyethylene oxide-400 - 20%, purified water - 30%) and "Esilon-2" (Esilon-aerosil base - 45%, hydroline - 5%, purified water - 50%).

During their preparation, the esilon-aerosil base is mixed with hydroline at a temperature of 50-60 °C (in a water bath) and hydrophilic components are added with constant stirring [28].

Bases containing emulsifiers pentol deserve attention: (pentol - 2.0 g, vaseline - 38.0 g, purified water - 60.0 g) and sorbitan oleate (sorbitan oleate - 2.5

g, vaseline - 47.5 g, purified water - 50.0 g). The bases are prepared by fusing the emulsifier with petroleum jelly and gradually adding water to the semi-cooled alloy while stirring. The bases are stable to room storage and have a thick consistency [12].

Emulsion bases of the oil/water type easily release medicinal substances mix with aqueous solutions of substances and wound secretions, cause a cooling effect and moisturizing effect. Ointments prepared on these bases can be applied to large areas of the skin without disturbing perspiration (excretion of water vapor and gases by the skin), medicinal substances are easily absorbed from them.

The emulsion base type oil / water most often includes non-ionic (theines) or ionic (emulsifier № 1, emulsion waxes, sodium lauryl sulfate, sodium stearyl sulfate) emulsifiers. Emulsifier № 1 can be used as part of ointments, which include aloe juice, vegetable oils, vaseline oil, petroleum jelly, paraffin, glycerin, sodium-carboxymethylcellulose, alcohol and aqueous solutions of medicinal substances. One part emulsifier № 1 is capable of emulsifying nine parts of water. Tween-80 (ointments with amphotericin B, decamine, propolis) are used much less frequently [12, 53].

For the preparation of ointments with anesthetics (anesthesin, lidocaine, novocaine, dicaine), bases based on emulsion waxes are used.

According to the ability of medicinal substances to be absorbed from ointments through the skin, all ointment bases can be placed in the following sequence: hydrophilic gels - oil / water emulsion bases - water / oil emulsion bases - absorption - hydrophobic. However, as practice shows, there may be exceptions. First of all, the effect of the drug substance, its properties, possible interaction with the components of the ointment, and other factors should be taken into account [28].

Polyethylene oxide bases have a weak bacteriostatic effect and have the ability to increase the activity of many antibiotics (especially chloramphenicol), sulfonamides and other medicinal substances. Polyethylene oxides are

recommended in the manufacture of ointments with hydrocortisone, antibiotics, sulfonamides, local anesthetics, vitamins, enzymes and other medicinal substances.

A characteristic feature of polyethylene oxides is their good solubility in water. It has been established that the addition of water up to 2% to polyethylene oxide further strengthens its structure. This is explained by the fact that water, using hydrogen bonds, “crosslinks” polyethylene oxide macromolecules into new formations, which are highly polymeric substances with more limited mobility [12, 28].

Ointments containing polyethylene oxide are highly effective, especially for exudative dermatoses, for the treatment of which compositions based on fatty and hydrocarbon bases cannot be used.

State Pharmacopoeia of Ukraine divides excipients in ointments into the following groups (taking into account their functional purpose):

- soft carrier bases (vaseline, lanolin, etc.);

- substances that increase the melting point and viscosity of the bases (paraffin, spermaceti, hydrogenated vegetable oils, waxes, high molecular weight polyethylene glycols, etc.);

- hydrophobic solvents (mineral and vegetable oils, isopropyl palmitate, isopropyl myristate, benzyl benzoate, etc.);

- hydrophilic solvents (ethyl and isopropyl alcohols, polyethylene oxide 200-600, propylene glycol, propylene carbonate, glycerin, dimexide);

- oil/water emulsifiers (sodium lauryl sulfate, emulsifier № 1, tweens, polyethylene glycol ethers of higher fatty alcohols, etc.);

- emulsifiers of the water/oil type (higher fatty alcohols, cholesterol, wool wax alcohols, span, glyceryl monooleate, glyceryl monostearate);

- gelling agents (carbomer, alginic acid and its salts, cellulose derivatives, polyethylene, proxanol, polyethylene oxide 1500-8000, gelatin, etc.);

- antimicrobial preservatives (benzalkonium chloride, miramistin, chlorhexidine, benzoic and sorbic acids, parabens, benzyl alcohol, cresol, propylene glycol, ethyl alcohol, etc.);

- antioxidants (α-tocopherol, ascorbic acid, butylhydroxyanisole, citric acid, sodium metabisulphite, etc.);

- solubilizers (α-cyclodextrin, hydrophilic surfactants, etc.);

- fragrances (menthol, essential oils, phenylethyl alcohol, etc.);

- pH stabilizers (citric acid, sodium phosphate salts).

Some excipients can simultaneously perform several of the above functions, as well as be included in the composition as softening and moisturizing additives, wetting agents, etc. Emulsifiers and substances that increase the temperature and viscosity of the bases are also stabilizers of disperse systems. Some excipients are mixtures of excipients: aqueous lanolin, emulsifier № 1, non-ionic wax, vaseline alloy with wool wax alcohols, etc. [7, 53].

Of the solid components that play the role of thickeners, polyethylene oxide-1500, polyethylene oxide-4000, paraffin, beeswax, etc. are most often used.

An important role in the production of ointments is played by surfactants, which provide a directed increase in their therapeutic activity and are used as a solubilizer (hydrophilic-lipophilic balance 15-18), emulsifiers for obtaining emulsions of the oil / water type (hydrophilic-lipophilic balance 8-18) or water / oil type (hydrophilic-lipophilic balance 3-6). In addition, surfactants (mainly cationic) can be used as preservatives and antiseptics [35].

Thus, according to biopharmaceutical and pharmacokinetic indicators, excipients must provide the full range of pharmacological properties of medicinal substances in order to meet the modern requirements of pharmacotherapy.

# CONCLUSIONS

1. Dental morbidity of the population remains high and does not tend to stabilize. The most common are dental caries and periodontitis, which affect almost 80% of the world's population. It has been established that dental diseases are more often recorded in patients with harmful working conditions, characterized by a variety of nosological forms and the activity of pathological processes. Among the urgent problems of modern dentistry, the diagnosis, treatment and prevention of diseases of the oral mucosa occupy one of the most important places. Due to the peculiarities of etiology and pathogenesis, the tendencies to recurrence of the disease, oral mucosa occupy a special place in the structure of dental morbidity. At the same time, the disease of oral mucosa is still a less studied medical and social problem of dentistry both in our country and abroad.

2. The analysis of the range of soft dosage forms for the treatment of dental diseases was carried out using the data of the State Register of Medicines, as well as instructions for drugs registered in Ukraine for dentistry. We used marketing methods of descriptive and structural analysis. The conducted marketing analysis shows that the A01A group includes 23 combined drugs of 16 different compositions and 39 single-component 12 international generic names. It has been established that among the preparations produced in Ukraine, only 3 soft combined medicines have indications for the treatment of the oral mucosa. Therefore, it is advisable to create combined prolonged dental drugs (ointments, gels) with antibacterial and anti-inflammatory effects.

# CHAPTER II. OBJECTS AND METHODS OF RESEARCH

## 2.1. Objects of research

### *Characteristics of the main substances*

**Furazolidone** State Pharmacopoeia X, P. 324; British Pharmacopoeia 2009 Volume I & II) - yellow or greenish-yellow powder, odorless, bitter in taste. Practically insoluble in water and ether, very slightly soluble in 95% alcohol. API of synthetic origin. Contains not less than 97.0% and not more than 103.0% $C_8H_7N_3O_5$ in terms of dry matter [48].

**Novocaine** (Procaine hydrochloride) (State Pharmacopoeia of Ukraine, 2nd ed., Vol. 2, P. 558) - white crystalline powder or colorless crystals. The language evokes a sense of occupation. Very easily soluble in water, soluble in 96% alcohol, practically insoluble in ether [10].

**Kalanchoe juice** (Kalanchoes succus) (monograph 42-1782-82) is a transparent or slightly opalescent liquid from light brown to yellow in color with a specific odor. A fine suspension is allowed, pH 3.8 - 5.0.

**Ointment with furazolidone, novocaine and Kalanchoe juice** - homogeneous ointment of yellow or light brown color with a specific smell. The preparation for microbiological purity must meet the requirements specified in the State Pharmacopoeia of Ukraine, 2nd ed. and current regulatory documents The content of furazolidone in 100.0 g of the drug should be from 0.24 to 0.26 g.

### *Characteristics of excipients*

**Lanolin Anhydrous** (State Pharmacopoeia X, P. 393) - a purified fat-like substance, consisting of esters of macromolecular alcohols and acids and free macromolecular alcohols (mixtures of aliphatic, stearic and triterpene alcohols). Thick viscous mass of brownish-yellow color, a slight peculiar smell. Practically insoluble in water, very sparingly soluble in 95% alcohol, freely soluble in ether,

chloroform, acetone and gasoline. When rubbed with water, the drug absorbs about 150% of water without losing the ointment-like consistency.

## 2.2. Research methods

*Furazolidone identification.*

General reactions:

1. About 0.005 g of the substance is dissolved in a mixture of 0.5 ml of water and 0.5 ml of a 10% sodium hydroxide solution, the liquid is heated, a red-brown color is observed.

2. 0.005 - 0.01 g of the substance is dissolved in 3 ml of dimethylformamide. 1-2 drops of a 1M aqueous-alcoholic solution of potassium hydroxide are added to the resulting solution, a red-violet color is observed, turning into dark blue, then into violet.

Table 2.1

**Physico-chemical properties of furazolidone**

| | |
|---|---|
| *General properties* | |
| Systematized name | 3-{[(5-nitro-2-furyl)methylene]amino}-1,3-oxazolidin-2-one |
| Medicinal substances | furan derivatives |
| CAS number | 67-45-8 |
| ATC code | G01AX06 |
| Latin name | Furasolidonum |
| Chemical formula | $C_8H_7N_3O_5$ |
| Highest single oral dose | 0.2 g |
| Highest daily oral dose | 0.8 g |
| *Physical properties* | |
| Characteristics | yellow or greenish yellow powder |
| Smell | without smell |
| Taste | bitter taste |
| Molar mass | 225.16 g/mol |
| Melting temperature | 252–256 °C (with decomposition) |
| *Chemical properties* | |
| Solubility in water | practically insoluble |
| Solubility in ether | practically insoluble |
| Solubility in ethanol 95% | very slightly soluble |

3. To 0.005 g of the substance, add 2 drops of 96% alcohol, 10% copper (II) sulfate solution and 10% sodium hydroxide solution, a color change is observed.

Weight loss on drying. About 0.5 g of the substance (accurately weighed) is dried at a temperature of 100-105 0C to constant weight. The loss in mass should not exceed 0.5% [9].

Storage. List B. Store in a tightly closed container, protected from light.

*Identification of novocaine.*

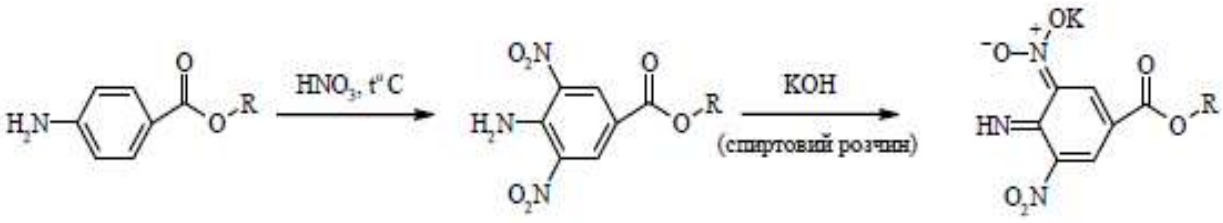
Table 2.2

**Physico-chemical properties of novocaine**

| | |
|---|---|
| *General properties* | |
| Systematized name | procaine, β-diethylaminoethyl ester of para-aminobenzoic acid hydrochloride |
| CAS number: | 59-46-1 |
| ATC code | N01BA02 |
| Latin name | Novocainum |
| Chemical formula | $C_{13}H_{20}N_2O_2$ |
| Highest single oral dose | 0.25 g |
| Highest daily oral dose | 0.75 g |
| *Physical properties* | |
| Characteristics | white crystalline powder or colorless crystals. |
| Smell | without smell |
| Taste | causes numbness on the tongue |
| Molar mass | 236.31 g/mol |
| Melting temperature | 373.6 °C |
| *Chemical properties* | |
| Solubility in water | very easily soluble |
| Solubility in ether | practically insoluble |
| Solubility in ethanol 95% | soluble |

General reactions:

1. Nitrate fuming acid is added to the substance and evaporated to dryness in a water bath, cooled and the residue is dissolved in acetone. To the resulting solution is added a solution of alcohol hydroxide; only a brownish-red color appears:




2. Reaction from potassium permanganate. A solution of novocaine, acidified with dilute sulfate acid, quickly discolors a 0.1 M solution of potassium permanganate (unlike other anesthetics).

Storage. In well-sealed dark glass jars.

*Identification of Kalanchoe juice.*

Amino acids. The resulting mixture is kept for 10 min, and then filtered through a white tape filter paper. The filtrate is placed in a porcelain cup and evaporated in a water bath or in a vacuum oven at a temperature of (100-105) °C to dryness. 0.5 ml of a 0.25% ninhydrin solution is added to the dry residue, mixed and heated in an oven at a temperature of (100-105) $^0$C; a blue-violet to light red color should be observed [22].

Table 2.3

**Physico-chemical properties of Kalanchoe juice**

| | |
|---|---|
| *General properties* | |
| Pharmaceutical group | drugs that promote healing (scarring) of wounds |
| ATC code | D03AX17 |
| *Physical Properties* | |
| Color | Light brown to yellow liquid |
| Transparency | Clear or slightly opalescent liquid |
| Smell | Specific |
| Molar mass | 225.16 g/mol |
| Dry residue | Not less than 2.0% |
| Density | 0.98 to 1.00 g/cm3 |
| *Chemical properties* | |
| Solubility in water | practically insoluble |
| Heavy metals | Not more than 0.01% |
| Ethanol content | Not less than 20.0% |
| Methanol content | Not more than 0.05% |
| Contents of 2-propanol | Not more than 0.05% |
| pH | 3.8 to 5.0 |

Flavonoids. Place 20 ml of the test preparation in a separating funnel, add 20.0 ml of ethyl acetate and shake for 2 minutes. After phase separation, the lower (aqueous) layer is discarded; the ethyl acetate hoist is placed in a porcelain dish and evaporated to dryness on a water bath. 3.0 ml of 70% alcohol is added to the dry residue and filtered through a paper filter. To the resulting filtrate is added drop wise 0.5 ml of a solution of aluminum chloride 2% in alcohol 70%; a yellow color should be observed.

Storage. In a place protected from light at a temperature of 15 to 25 °C.

*Quality control of ointment with furazolidone, novocaine and kalanchoe juice.*

Homogeneity of content (2.9.6). Oromucose drugs in single-dose containers with an active ingredient content of less than 2 mg or less than 2% of the total mass must pass tests for uniformity of the content of the active ingredient in a unit of dosed drug (test A for drugs prepared by pressing or molding or test B for capsules), if not other instructions in a separate article. If the medicinal product contains more than one active substance, the requirements apply only to substances whose content meets the above conditions [9, 10].

*Statistical processing.* Statistical analysis of the obtained results was carried out in accordance with the methods given in the State Pharmacopoeia of Ukraine 2.0, Volume 1, paragraph 5.3.

# CONCLUSIONS

1. Brief data on the properties of active pharmaceutical ingredients (furazolidone, novocaine), medicinal plant materials (kalanchoe juice) and excipients used in the development and research of soft medicines for dentistry are given.

2. Methods of experimental studies have been processed, namely physical and physico-chemical, technological, microbiological, statistical, which made it possible to objectively evaluate the properties of active substances and a medicinal product for skin use in the development of their composition and technology.

3. For technological control, modified methods for the detection and determination of active pharmaceutical ingredients in the composition of dental ointment are presented.

# CHAPTER 3. SUBSTANTIATION OF THE COMPOSITION AND DEVELOPMENT OF ANTI-INFLAMMATORY OINTMENT TECHNOLOGY

## 3.1. Substantiation of the composition of the ointment with furazolidone, novocaine and Kalanchoe juice

The human oral cavity is a unique ecological system for a wide variety of microorganisms that form a permanent microflora that plays an important role in human health and disease.

Today there is a steady increase in the level of erosive and ulcerative lesions of the oral mucosa. This is due to an undifferentiated approach to the choice of drugs for local therapy of erosive and ulcerative lesions of the oral mucosa. Doctors use the same local therapy, and especially antibacterial ones, for all diseases of the oral mucosa, without paying due attention to the etiological factor [16].

In this regard, the purpose of our study was to substantiate and develop a prolonged dental drug in the form of an ointment for the treatment of erosive and ulcerative diseases of the oral mucosa of various etiologies based on an extemporaneous prescription by a doctor [36].

Antiseptics are widely used in dental practice. Antiseptics - drugs that are prescribed for disinfection of the skin, mucous membranes, burn and wound surfaces [17].

Antiseptics must meet the following requirements: have a wide spectrum of action and sufficient activity, including in the presence of biological substrates; should not have a local irritating, toxic effect on the microorganism; should be chemically resistant, available for wide use.

Furazolidone is a synthetic antimicrobial and antiprotozoal drug, a derivative of nitrofuran. It inhibits the growth and reproduction of staphylococci,

streptococci, dysentery, Escherichia coli, pathogens of paratyphoid and other microorganisms.

Side effect. When using furazolidone, the following side effects are possible: infrequent skin rash, pruritus, hives, nausea, vomit, diarrhea, color of urine in dark yellow color; rarely peripheral headache, dizziness, acute toxichepatitis, hypoglycemia, orthostatic hypotension, arterial hypertension, fever.

Release forms. Furazolidone is available in the form of tablets of 0.05 g and granules for the preparation of a suspension of 50 g.

Thus, given the breadth of bactericidal and bacteriostatic action, as well as a small list of side effects that rarely appear in the clinical picture, the furazolidone substance is a promising substance in the development of a dental ointment composition for the treatment of inflammatory diseases of the oral mucosa.

The next stage of our work was the selection and justification of the component of the combined ointment, which exhibits a moderate analgesic effect.

In the treatment of dental diseases, painkillers are often prescribed. The list of such drugs includes anesthetics.

For effective and safe use in practice, the following requirements are imposed on anesthetics: drugs must have high analgesic properties and selectivity of action, sufficient duration of effect and range of therapeutic action, do not irritate tissues and do not constrict blood vessels [4, 37].

For local application anesthesia in dentistry, novocaine, anestezine are used. The anesthetic novocaine has attracted our attention because it causes fast-onset, deep and prolonged anesthesia, and, very importantly, causes superficial anesthesia. It is widely used in dental practice in the form of solutions, irrigations, applications, films.

Novocaine is an anesthetic. It has a wide spectrum of activity and helps to reduce pain.

Pharmacological properties. When absorbed and directly introduced into the blood, it affects the entire body as a whole. Reduces the formation of acetylcholine and reduces the excitability of peripheral cholinergic systems. Blocks autonomic

ganglia. Reduces spasms of smooth muscles, reduces the excitability of the heart muscle.

Novocaine quickly reduces the excitability and automatism of the myocardium. At the same time, spasm of smooth muscles is reduced, a ganglionic blocking effect occurs and the excitability of the motor zones located in the brain is inhibited. It has a generating effect on nerve impulses. Thanks to this ability, novocaine quickly and effectively eliminates acute pain in a person. The drug has a pronounced anti-shock effect.

The substance is completely excreted with the help of the active work of the kidneys along with urine. It is known that unchanged novocaine enters the urine in an amount of not more than 2% of the initial state.

Novocaine ointment, getting on the diseased organ, has a local anesthetic effect. At the same time, polysynaptic unwanted reflexes are inhibited. Anesthetic ointment with novocaine eliminates vascular hypertonicity due to the inhibition of nerve impulses in the fibers. Therefore, soft dosage forms with novocaine can effectively and quickly relieve even severe pain [5].

Novocaine, when applied externally, quickly begins to act, penetrating the skin and blocking impulses flowing from the nerve endings to the brain. The substance is almost instantly absorbed into the bloodstream, so the pain syndrome disappears and relief comes. Experts attribute this to a decrease in the excitability of peripheral systems and to a reduction in the formation of acetylcholine from nerve endings.

The above proves the rationality of including novocaine in the composition of an anti-inflammatory ointment, in order to alleviate the pain of the patient in the treatment of inflammatory diseases of the oral mucosa.

To ensure the complex action of the dental ointment in its composition, in addition to furazolidone, it was advisable to introduce an additional active pharmaceutical ingredient of plant origin - Kalanchoe juice, which has pronounced anti-inflammatory properties, low toxicity, promotes rapid cleansing of wounds and ulcers from necrotic tissues, accelerating the epithelization of wounds.

Kalanchoe juice is used both as an individual drug and as part of extemporaneous formulations in the treatment of long-healing wounds, trophic ulcers, bedsores, and purulent processes [49].

In medical practice, in particular, dentistry, drugs from plant materials and plant materials themselves are widely used, but with the simultaneous use of several drugs, physicochemical or technological incompatibilities are possible, as well as the occurrence of side effects. Each plant consists of hundreds of different organic and inorganic compounds, which are either components of living cells (proteins, amino acids, enzymes, fats, acids, etc.) or its structural elements (cellulose, pectin, lignin, etc.).

Juices, decoctions, infusions and tinctures of medicinal substances, baths, rinses for the treatment of infectious and inflammatory processes of oral mucous membranes and throat, periodontal tissues, to improve wound healing and burn lesions.

Kalanchoe juice is successfully used for local treatment of periodontal disease. The drug is very effective for the treatment of acute and chronic catarrhal gingivitis, ulcerative necrotic ulcers. Kalanchoe juice has a pronounced anti-inflammatory effect, stimulates epithelialization, increases the protective properties of tissues, and normalizes the emigration of leukocytes [58].

Kalanchoe pinnata (Kalanchoe pinnata Lam. Pers.), a family of thick-leaved (Crassulaceae), is widely used in domestic medicine, in particular in dental practice, due to the presence of such biologically active substances as flavonoids (quercetin, kaempferol and their glycosins), polysaccharides ( from 35 to 40%), organic acids and trace elements. Kalanchoe juice from fresh leaves and the green part of the stems of Kalanchoe pinnate has an anti-inflammatory effect, helps cleanse wounds from necrotic tissues, stimulates their healing (aphthous stomatitis, gingivitis, complicated periodontal disease, etc.). The juice of Kalanchoe pinnate has antibacterial activity against a wide range of gram-positive and gram-negative microorganisms [50].

The determining factor that ensures the effective effect of biologically active substances in the ointment is the base. The base of the ointment should be multifunctional: fully release the biologically active substances that are part of the ointment, be indifferent to tooth enamel and periodontal tissues and oral mucosa, but at the same time provide a certain therapeutic effect on the tissues of the oral mucosa, create a prolonged effect. The prolonged action of the ointment implies that the dosage forms is in the oral cavity for a sufficiently long time, so the medicinal substances should not be washed out with saliva, and constant wetting should serve as additional moisturizing to maintain the consistency of the ointment [20, 28, 37].

Given the above, we can conclude that the proposed extemporaneous anti-inflammatory composition is rational and appropriate for the treatment of ulcerative erosive lesions of the lips and oral mucosa:

Novocaine 0.25;

Furazolidone 0.25;

Kalanchoe juice 40.0;

Anhydrous lanolin 60.0.

It is clear that the systemic use of antibacterial and antifungal drugs in patients with diseases of the oral mucosa is inappropriate, because it is extremely difficult to create an effective concentration of drugs in the lesion locus. Therefore, the most effective in the treatment of ulcerative-erosive lesions of the oral mucosa is local antibacterial, analgesic and reparative therapy.

### 3.2.Substantiation of anti-inflammatory ointment technology

The preparation of ointments in pharmacies consists of preparatory work and the main technological stages. The preparatory work includes preventive measures, checking the correctness of the prescription, checking the compatibility of ingredients, the norms for one-time dispensing of medicines.

Preventive measures include compliance with sanitary norms and rules of sanitary-hygienic and anti-epidemic regimes, pharmaceutical order in accordance with the current regulatory and methodological documents and orders (Order of the Ministry of Health of Ukraine № 139 from 14.06.93 «On the approval of the instructions on the sanitary-epidemic regime of pharmacies» [7, 18].

The next step in the preparation of ointments is to calculate the percentage of medicinal substances and the base. The corresponding calculations are made on the reverse side of the written control passport (WCP).

In our case, the amount of substances and bases are indicated by the doctor. To select the optimal technology, it is necessary to calculate the percentage of dry matter in the total mass of the ointment. The amount of furazolidone is about 0.4%, novocaine - about 0.4%. The emulsifying ability of anhydrous lanolin to water is 180-220 ml of liquid per 100.0 g of base. In our prescription, the content of Kalanchoe juice is 40.0 g, that is, it does not exceed the permissible norm.

The process of preparation of dosage forms is preceded by the preparation of the workplace, the selection of dishes, auxiliary and container-closure material, as well as the preparation of medicinal and excipients.

Based on the technology, the assistant selects the necessary working utensils: a mortar of the appropriate size with a pestle (taking into account the prescribed amount of ointment), a porcelain cup (if necessary, fusing the base components or dissolving the prescribed ingredients in it) [21, 23].

Packaging materials used in the pharmacy for packaging and storing ointments are glass or plastic jars with screw-on plastic lids. The assistant selects a container of the appropriate size with a capacity of 10.0 to 100.0 g. In addition, parchment or paraffin paper or a ready-made cardboard lining must be selected under the lid or cork. At this stage, it is necessary to prepare materials for the design of the finished dosage form (main label or signature and additional labels) [39].

The actual preparation of ointments consists of several successive technological stages: melting, dissolving, dispersing, emulsifying, mixing,

packaging and dispensing. In addition, the pharmacy controls individual stages, as well as evaluates the finished ointment according to technological quality indicators [14, 28].

*Description of dental ointment technology*

Rp.: Furasolidoni 0.25
Novocaini 0.25
Succi Kalanchoes 40.0
Lanolini anhydrici 60.0
Misce ut fiat unguentum.
Da. Signa. Ointment for erosive and ulcerative lesions of the lips and oral mucosa.

According to this recipe, an ointment of a combined type is formed. In relation to furazolidone - suspension type ointment, to novocaine and Kalanchoe juice - emulsion type.

For the preparation of an emulsion ointment, purified water is not indicated in the prescription, in addition, anhydrous lanolin is prescribed. According to the rules for the preparation of emulsion ointments, the use of up to 5% of the total mass of the ointment is allowed. But in our case, Kalanchoe juice can be used to dissolve novocaine. For finer grinding of furazolidone, it is rational to use vaseline oil in the amount of 2 drops (according to the Deryagin rule).

Weigh 60.0 g of anhydrous lanolin per parchment capsule. Weigh 0.25 g of furazolidone, place in a mortar and grind. Then add 2 drops of vaseline oil and rub thoroughly. Anhydrous lanolin is added in an amount of about 0.5 g, mixed and the resulting suspension ointment is pushed to the edge of the mortar.

Kalanchoe juice is weighed into a tared porcelain cup, slightly heated in a water bath. Then placed on the bottom of the mortar and add 0.25 g of novocaine. Mix thoroughly until complete dissolution of novocaine (visually control the completeness of dissolution). Add a part of anhydrous lanolin (25-30 g), emulsify, and add ointment from the wall of the mortar, mix. The remaining anhydrous lanolin is added to the mortar and mixed until smooth.

The data obtained made it possible to substantiate the method of manufacturing an ointment with furazolidone, novocaine and Kalanchoe juice and to develop a production flowchart (Fig. 3.1).

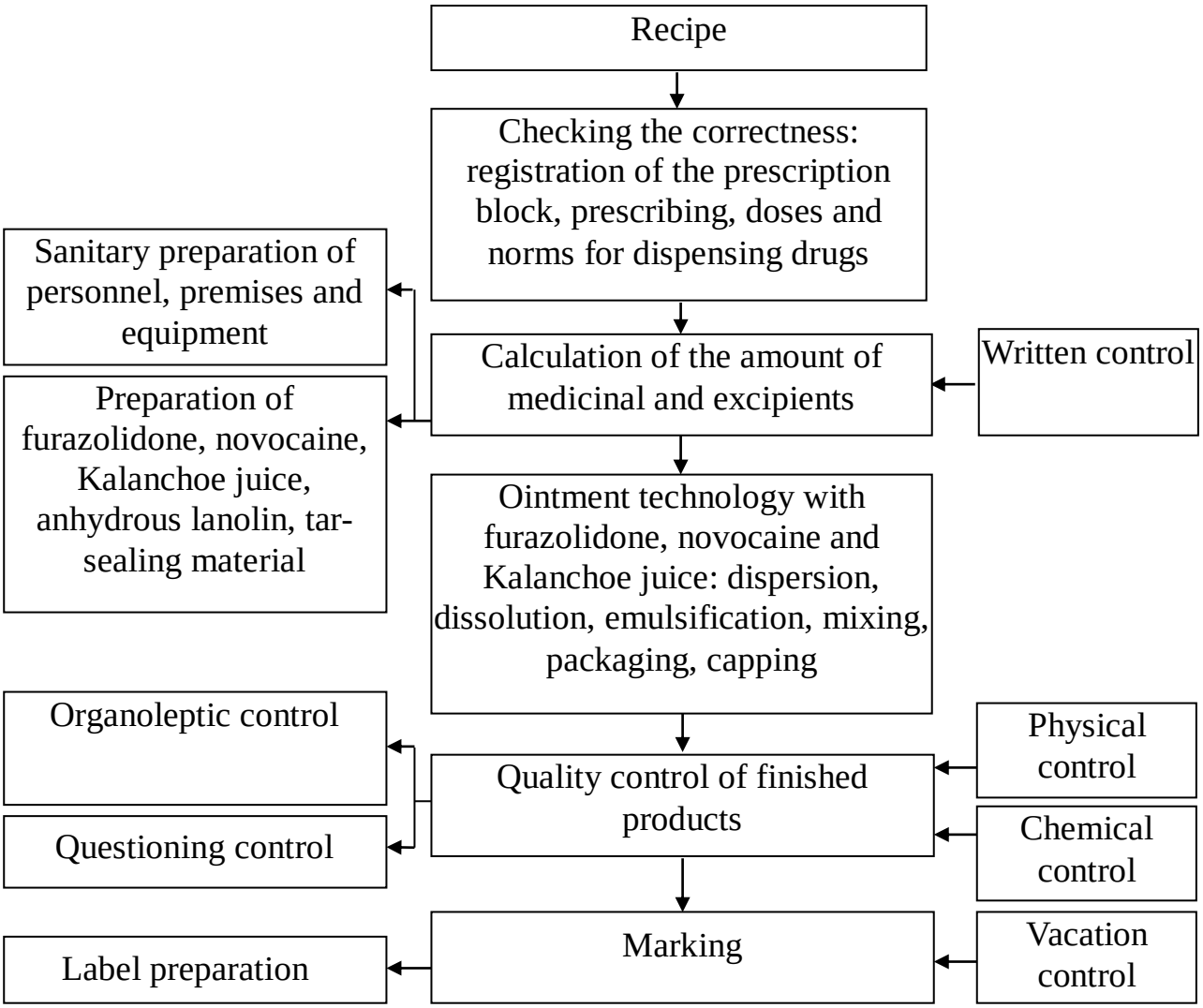



**Fig. 3.1 Manufacturing technology of anti-inflammatory ointment**

Carry out a visual inspection of homogeneity. Technological quality control of the developed drug is carried out in accordance with the State Pharmacopoeia of Ukraine, 2nd ed. "Soft drugs for local use" and existing guidelines [9].

Further, the ointment is standardized according to the following indicators: qualitative and quantitative determination of novocaine, furazolidone, organic acids in terms of malic acid.

Description. They control the appearance and characteristic organoleptic properties of the ointment (color, smell, consistency, etc.), as well as signs of physical instability (aggregation of particles, coalescence, coagulation, separation).

Definition of homogeneity. The determination is carried out according to the method given in the State Pharmacopoeia, 2nd ed. The ointment should be homogeneous in consistency.

pH determination. The pH level of the samples under study is determined potentiometrically (State Pharmacopoeia of Ukraine, 2nd ed., 2.2.3) using an universal ionometer at a temperature range of 15–25 °C [9, 10].

A sample of the ointment in the amount of 2.5 g is added to a 100 ml beaker and 50 ml of purified water (pH 6.2–7.0) is added while stirring with a glass rod for 10 minutes. After that, the pH of the aqueous extract of the sample is measured potentiometrically.

Content uniformity. The determinations are made in accordance with the requirements of the article of the State Pharmacopoeia of Ukraine (2.9.6) "Uniformity of the content of the active substance in a unit of dosed medicinal product", using test A.

The mass of the contents of the container. Ten containers together with the contents were weighed, each separately, with an accuracy of 0.01 g, emptied of the contents, washed with hot water, carefully removed the remaining water with filter paper and weighed again. The weight of the contents of each container must be from 95.0 to 101.0 g according to the normative documents.

Determination of the tightness of the container was carried out according to the method described in State Pharmacopoeia of Ukraine [7, 9, 10].

Determination of the degree and rate of release of furazolidone, novocaine and organic acids in terms of malic acid is carried out by dialysis through a semipermeable membrane.

The weight of the test sample of the ointment is 1.0 g, the medium for dialysis is purified water 30 ml. Sample for analysis - 5 ml. Dialysis is carried out

in a thermostat at a temperature of 37±1°C. Exposure 15'; thirty'; 45'; 60'; 90' min. A 5 ml sample taken for analysis is filled with 5 ml of purified water t = 37°C.

After obtaining positive test results, the bulk ointment is transferred to a dispensing container and sealed with a screw cap.

According to the requirements of the Far Eastern Federal University, aluminum tubes with a membrane for medical purposes according to specifications 25463020-01-98 with an internal lacquer coating or aluminum tubes with a lacquer-coated membrane intended for packaging pharmaceutical products that meet the requirements of the sanitary legislation of Ukraine can also be used as the primary packaging of the ointment [9, 39].

The finished product - a packaged ointment with furazolidone, novocaine and Kalanchoe juice is issued before the release with the labels "External", "Keep away from children", "Store in a cool, dark place."

### 3.3. Calculation of the cost of the developed anti-inflammatory ointment

In the manufacture of medicines for extemporaneous prescriptions in pharmacies with different forms of ownership, a tariff (“taxa laborum”) is charged, which includes the amount to cover costs (labor costs, used electricity, depreciation of equipment, etc.), as well as the formation of a certain profit [32 ]. There are general rules for taxing prescriptions:

- when setting the price for an individual dosage form, the price of medicines included in the prescription, packaging and manufacturing tariff is taken into account;

- taxation is made on the left side of the recipe;

- before determining the cost of each ingredient prescribed in the recipe, its quantity is calculated;

- the cost of each ingredient is put down on the left opposite its name; - when establishing the cost of ingredients, both whole and tenths of kopecks are counted;

- the calculated price of all taken ingredients is recorded in a separate line;

- the price of the package is indicated on a separate line;

- the tariff for the manufacture of the dosage form is recorded in a separate line;

- the total cost of ingredients, packaging and tariff is calculated;

- rounding of a penny share is allowed only in the final price; - on the prescription for preferential leave, in addition to the total cost of the dosage form, indicate the amount that the patient must pay;

- water purified or for injection is considered a separate component;

- auxiliary materials (labels, signatures, corks, etc.), as well as auxiliary substances, are not evaluated, their cost is included in the tariffs [32, 33].

*Formation of the price of anti-inflammatory ointment for use in dental practice (Table 3.1)*

1. Calculation of the number of ingredients

   Furazolidoni 0.25 g

   Novocaini 0.25 g

   Lanolini anhydrici 60.0 g

   Succi Kalanchoes 40.0 g

2. Cost of ingredients (price list)

| | |
|---|---|
| Furazolidoni | 1.0 g - 1-10 |
| | 0.25 g - 0-28 |
| Lanolini anhydrici | 10.0 g - 1-00 |
| | 60.0 g - 6-00 |
| Novocaini | 1.0 g - 1-60 |
| | 0.25 g - 0-40 |
| Succi Kalanchoes | 20.0 g - 10-36 |
| | 40.0 g - 20-72 |
| In total | 27-40 |

3. Tariff definition

   Tariff for the manufacture of eye ointment (1 glass jar) 9.38

Features of the price calculation - 5 component prescription

The addition of each subsequent (operations) 1.22 * 2 = 2-44

Taxa laborum = 9.38 + 2.44 = 11-82

Table 3.1

**An example of calculating the cost of a developed ointment on a prescription form**

| | | | |
|---|---|---|---|
| ***0-28***<br>***0-40***<br>***20-72***<br>***6-00***<br>***27-40***<br>***t.l. 11-82***<br>***pack. 1-58***<br>***40-80***<br>***8-16 VAT***<br>***48-96 at the checkout*** | ***Rp.:*** | ***Furasolidoni***<br>***Novocaini***<br>***Succi Kalanchoes***<br>***Lanolini anhydrici***<br>***Misce ut fiat unguentum.***<br>***Da. Signa.*** *Ointment for erosive and ulcerative lesions of the lips and oral mucosa.* | ***0.25***<br>***0.25***<br>***40.0***<br>***60.0*** |

4. Package

   1 glass jar with strained plastic cover = 1-58

5. Retail price of anti-inflammatory ointment

   The sum of the cost of ingredients 27-40

   Tariff 11-82

   Packing cost 1-58

   Price without VAT 40-80

   Price including VAT (20%) 48-96.

# CONCLUSIONS

1. Based on the results of the studies and analysis of scientific literature data, the expediency of using furazolidone and novocaine as substances in the manufacture of drugs for the treatment of inflammatory diseases of the oral mucosa of various etiologies is substantiated.

Based on theoretical and experimental studies, the relevance of using raw materials of plant origin - Kalanchoe juice, as part of an anti-inflammatory ointment, was determined in order to increase its reparative characteristics. The quality indicators of furazolidone, novocaine and Kalanchoe juice were determined and methods for their control were proposed.

2. A rational technology for the manufacture of anti-inflammatory ointment for use in dental practice has been substantiated, critical production parameters have been determined, and a technology for the pharmacy production of an ointment based on furazrolidone, novocaine and Kalanchoe juice has been developed.

The results obtained open up the possibility of using the proposed soft dosage form in dental practice in order to increase the effectiveness of the treatment of erosive and ulcerative changes in the oral mucosa of microbial etiology.

3. The estimated cost of an extemporaneous anti-inflammatory ointment was determined and a technological instruction was developed for the manufacture of a soft dosage form with furazolidone, novocaine and Kalanchoe juice for use in dental practice under the conditions of pharmacy production.

# GENERAL CONCLUSIONS

1. The data of literary sources on the characteristics and distribution of dental inflammatory diseases were studied. The range of soft dosage forms drugs registered on the pharmaceutical market of Ukraine for use in dentistry was studied. The limitation of the nomenclature of multicomponent soft dosage forms for the treatment of inflammatory diseases of the oral mucosa has been established, and the prospects for creating an extemporaneous medicinal ointment of combined action have been determined.

2. Theoretically generalized and substantiated scientific approaches to the development of the composition of dental soft dosage forms in the form of an ointment with anti-inflammatory, analgesic and reparative activity. The composition of the ointment includes furazolidone (0.25 g), novocaine (0.25 g), raw materials of plant origin - Kalanchoe juice (40.0 g), anhydrous lanolin (60.0 g).

3. The technology for the production of dental ointment has been scientifically substantiated. A block diagram of manufacturing in a pharmacy is proposed. As criteria for the quality of the ointment, indicators were taken: description, identification, and quantitative content, mass uniformity, impurities and pH determination.

4. A method is proposed for calculating the estimated cost, taking into account "taxa laborum" and VAT of the proposed anti-inflammatory ointment. The expediency of creating and extemporaneous production of an ointment for use in dental practice has been confirmed.

5. Theoretically substantiated and developed a technological instruction for the preparation of a drug in the form of an anti-inflammatory ointment based on furazolidone, novocaine and Kalanchoe juice in pharmacies.

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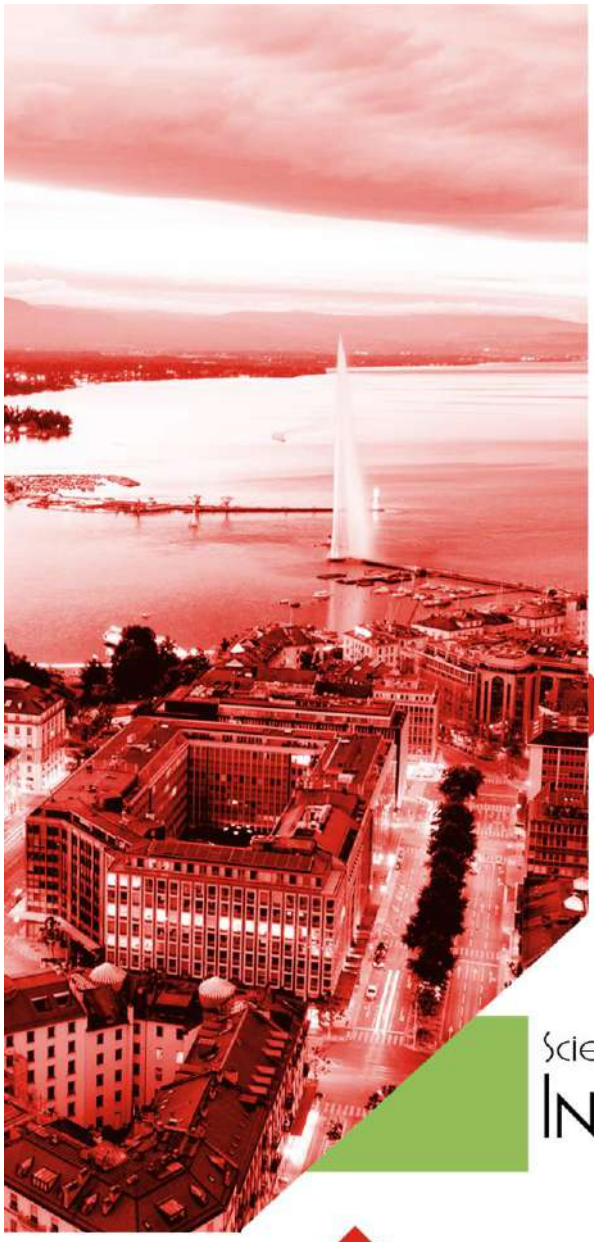
# APPENDIXES

***APPENDIX A***



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GENEVA, SWITZERLAND
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2023

*CONTINUATION OF APPENDIX A*

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No 154

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## BIOLOGY AND BIOTECHNOLOGY



## MEDICINE AND PHARMACY

*CONTINUATION OF APPENDIX A*

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No 154

MEDICINE AND PHARMACY

# Substantiation of composition of the anti-inflammatory ointment

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**Abstract.** The human oral cavity is a unique ecological system for a wide variety of microorganisms that form a permanent micro flora that plays an important role in human health and disease. Today there is a steady increase in the level of erosive and ulcerative lesions of the oral mucosa. This is due to an undifferentiated approach to the choice of drugs for local therapy of erosive and ulcerative lesions of the oral mucosa. Doctors use the same local therapy, and especially antibacterial ones, for all diseases of the oral mucosa, without paying due attention to the etiological factor.
**Keywords:** *oral mucosa, composition, ointment.*

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The composition of a medicinal product for the local treatment of inflammatory diseases of the oral mucosa should include a composition of active pharmaceutical ingredients, one of which has a directed antimicrobial effect, the second - anti-inflammatory, the third - dehydration. All these components must be compatible with each other in one dosage form and not change the pharmacological activity during storage [1].

When treating dental diseases, there is a need for anesthesia, and to reduce pathological microflora, an available antiseptic is needed, for example, furazolidone, which, along with antimicrobial action, has anti-edematous properties and is widely used in the form of applications and therapeutic dressings.

Antiseptics are widely used in dental practice.

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Antiseptics are medicines that are prescribed for the disinfection of the skin, mucous membranes, burn and wound surfaces [2].

Antiseptics must meet the following requirements: have a wide spectrum of action and sufficient activity, including in the presence of biological substrates; should not have a local irritating, allergenic and toxic effect on the macroorganism; should be chemically stable, available for wide application.

Nitrofuran derivatives - antiseptics of the group of nitrofuran derivatives are characterized by high antimicrobial activity and relatively low toxicity, they are used as antiseptics and chemotherapeutic drugs [1].

Furazolidone is a synthetic antimicrobial and antiprotozoal drug, a derivative of nitrofuran. It inhibits the growth and reproduction of staphylococci, streptococci, dysentery, Escherichia coli, pathogens of paratyphoid and other microorganisms.

The drug has both a bactericidal and bacteriostatic effect, which depends on the concentration of the drug and the type of pathogen. The mechanism of action of furazolidone is to inhibit the activity of dehydrogenase and inhibit the respiratory cycles of microbial cells and disrupt protein synthesis in the cells of pathogenic bacteria. The following pathogens are sensitive to furazolidone: staphylococci, streptococci, Escherichia coli, Enterobacter spp., Salmonella, Klebsiel, Shigella, Vibrio cholerae, Serratia spp. The simplest Trichomonas and Giardia are also sensitive to furazolidone [3].

When using furazolidone, the following side effects are possible: skin rash, pruritus, urticaria, nausea, vomiting, diarrhea, dark yellow urine color; headache, dizziness, arterial hypertension [1].

Thus, given the breadth of bactericidal and bacteriostatic action, as well as a small list of side effects that occur infrequently in the clinical picture, the substance furazolidone is a promising substance in the development of the composition of a dental ointment for the treatment of inflammatory diseases of the oral mucosa.

In the treatment of dental diseases, painkillers are often prescribed. The list of such drugs includes anesthetics.

For effective and safe use in practice, the following requirements are imposed on anesthetics: drugs must have high analgesic properties and selectivity of action, sufficient duration of effect and range of therapeutic action, do not irritate tissues and do not constrict blood vessels [4].

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For local application anesthesia in dentistry, novocaine, anesthesin, trimecaine, lidocaine, pyromecaine, articaine are used. The anesthetic novocaine has attracted our attention because it causes fast-onset, deep and prolonged anesthesia, and, very importantly, causes superficial anesthesia. It is widely used in dental practice in the form of solutions, irrigations, applications, films.

Novocaine is a local anesthetic agent. It has a wide spectrum of activity and helps to reduce pain.

When absorbed and directly introduced into the blood, it affects the entire body as a whole. Reduces the formation of acetylcholine and reduces the excitability of peripheral cholinergic systems. Blocks autonomic ganglia. Reduces spasms of smooth muscles, reduces the excitability of the heart muscle.

In the body, novocaine hydrolyzes relatively quickly, forming p-aminobenzoic acid and diethylaminoethanol. Sulfonamides are similar in chemical structure to p-aminobenzoic acid (PABA), which, entering into competition with them, weakens their antibacterial effect. Novocaine as a derivative of PABA also has an antisulfanilamide effect. Diethylaminoethanol exhibits moderate vasodilation properties [3, 4].

Novocaine quickly reduces the excitability and automatism of the myocardium. At the same time, spasm of smooth muscles is reduced, a ganglionic blocking effect occurs and the excitability of the motor zones located in the brain is inhibited. It has a generating effect on nerve impulses. Thanks to this ability, novocaine quickly and effectively eliminates acute pain in a person.

Novocaine ointment, getting on the diseased organ, has a local anesthetic effect. At the same time, polysynaptic unwanted reflexes are inhibited. Anesthetic ointment with novocaine eliminates vascular hypertonicity due to the inhibition of nerve impulses in the fibers. Therefore, soft dosage forms with novocaine can effectively and quickly relieve even severe pain [5].

Novocaine, when applied externally, quickly begins to act, penetrating the skin and blocking impulses flowing from the nerve endings to the brain. The substance is almost instantly absorbed into the bloodstream, so the pain syndrome disappears and relief comes. Experts attribute this to a decrease in the excitability of peripheral systems and to a reduction in the formation of acetylcholine from nerve endings.

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The above proves the rationality of the inclusion of novocaine in the anti-inflammatory ointment, in order to alleviate the pain of the patient in the treatment of inflammatory diseases of the oral mucosa.

To ensure the complex action of the dental ointment in its composition, in addition to furazolidone, it was advisable to introduce an additional active pharmaceutical ingredient of plant origin - Kalanchoe juice, which has pronounced anti-inflammatory properties, low toxicity, which contributes to the rapid cleaning of wounds and ulcers from necrotic tissues, accelerating the epithelization of wounds. Kalanchoe juice is used both as an individual drug and as part of extemporaneous prescriptions in the treatment of trophic ulcers, bedsores, and purulent processes [6].

In medical practice, in particular, dentistry, medicinal preparations from plant materials and plant materials themselves are widely used, but with the simultaneous use of several drugs, physicochemical or technological incompatibilities are possible, as well as the occurrence of side effects. Each plant consists of hundreds of different organic and inorganic compounds, which are either components of living cells (proteins, amino acids, enzymes, fats, acids, etc.) or its structural elements (cellulose, pectin, lignin, etc.).

Juices, decoctions, infusions and tinctures of medicinal substances (Hypericum officinalis, Kalanchoe pinnata, Plantago major, Calendula officinalis, Gnaphálium uliginósum, Sophora japonica, etc.) stimulate regeneration processes, exhibit antibacterial and anti-inflammatory effects, with which they are prescribed in the form of applications, baths, rinses for the treatment of infectious and inflammatory processes of the mucous membrane of the mouth and throat, periodontal tissues, to improve the healing of wounds and burn lesions.

Kalanchoe juice is successfully used for local treatment of periodontal disease. The drug is very effective for the treatment of acute and chronic catarrhal gingivitis, ulcerative necrotic ulcers. Kalanchoe juice has a pronounced anti-inflammatory effect, stimulates epithelialization, increases the protective properties of tissues, and normalizes the emigration of leukocytes [7].

Kalanchoe pinnata is widely used in medicine, in particular in dental practice, due to the presence of such biologically active substances as flavonoids (quercetin, kaempferol and their glycosins), polysaccharides (from 35 to

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40 %), organic acids and trace elements. The juice of Kalanchoe from fresh leaves and the green part of the stems of Kalanchoe pinnate has an anti-inflammatory effect, helps cleanse wounds from necrotic tissues, and stimulates their healing. The juice of Kalanchoe pinnate has antibacterial activity against a wide range of gram-positive and gram-negative microorganisms [8].

Considering the foregoing, it can be concluded that the extemporaneous anti-inflammatory composition, which contains novocaine, furazolidone and Kalanchoe juice as active pharmaceutical ingredients, is rational and appropriate for the treatment of ulcerative erosive lesions of the lips and oral mucosa.

In patients with diseases of the oral mucosa, the systemic use of antibacterial and antifungal drugs is not advisable, because it is extremely difficult to create an effective concentration of drugs in the lesion locus. Therefore, the most effective in the treatment of ulcerative-erosive lesions of the oral mucosa is local antibacterial, analgesic and reparative therapy.

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We are honored to present this certificate to
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for participation in the
V International Scientific and Practical Conference
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***APPENDIX C***

МІНІСТЕРСТВО ОХОРОНИ ЗДОРОВ'Я УКРАЇНИ
НАЦІОНАЛЬНИЙ ФАРМАЦЕВТИЧНИЙ УНІВЕРСИТЕТ

# АКТУАЛЬНІ ПИТАННЯ СТВОРЕННЯ НОВИХ ЛІКАРСЬКИХ ЗАСОБІВ

МАТЕРІАЛИ
XXIX МІЖНАРОДНОЇ НАУКОВО-ПРАКТИЧНОЇ
КОНФЕРЕНЦІЇ МОЛОДИХ ВЧЕНИХ ТА СТУДЕНТІВ

19-21 квітня 2023 року
м. Харків

Харків
НФаУ
2023

***CONTINUATION OF APPENDIX C***

УДК 615.1

**Редакційна колегія**: проф. Котвіцька А. А., проф. Владимирова І. М.
**Укладачі**: Сурікова І. О., Боднар Л. А., Григорів Г. В. Литкін Д. В.

Актуальні питання створення нових лікарських засобів: матеріали XXIX міжнародної науково-практичної конференції молодих вчених та студентів (19-21 квітня 2023 р., м. Харків). – Харків: НФаУ, 2023. – 606 с.

Збірка містить матеріали Всеукраїнської науково-практичної конференції «Youth Pharmacy Science», які представлені за пріоритетними напрямами 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

*CONTINUATION OF APPENDIX C*

## Секція 5.
## БІОФАРМАЦЕВТИЧНІ АСПЕКТИ СТВОРЕННЯ ЕКСТЕМПОРАЛЬНИХ ЛІКАРСЬКИХ ЗАСОБІВ

## Section 5.
## BIOPHARMACEUTICAL ASPECTS OF THE DEVELOPMENT OF EXTEMPORAL MEDICINES

***CONTINUATION OF APPENDIX C***



For the treatment of inflammatory diseases of the female half of the sphere use advantageously local and antibacterial drugs.

**Results and discussion.** Oils are part of many medicines.. Anti-inflammatory, antispasmodic, bacteriostatic action have drugs "Urolesan," "Cystenal."

In medical practice, essential oils of such plants as eucalyptus, mint, sage, pine, anise have become the most common. Companies of such leading countries as Austria, USA, Canada produce the substance of tea tree oil. Essential oils inhibit the activity of pathogenic microorganisms and contribute to the penetration of antibiotics into the human cell, thereby providing opportunities to reduce doses of antibiotics. One of the main producers of essential oils in Ukraine is Aromatica Ltd. The products of this company meet international standards and have international quality certificates. Thus, the development and justification of the composition of the anti-inflammatory medicine in the form of pessaries on the basis of substances of natural and synthrtic origin is an actual task of medicine and pharmacy.

**Conclusions.** The rates of inflammatory gynecological diseases are quite high all over the world, so the need to study the problem of treating these diseases is very actual.

Therefore, the expansion of the range of schemes and methods of treatment of inflammatory pathologies in gynecology is promising through the wide study and use of biologically active substances of essential oils, and will also expand the range of medicines.

## FEATURES OF THE USE OF THE BASE IN THE DEVELOPMENT OF SOFT MEDICINAL FORM

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**Introduction.** Despite the fact that ointments are one of the oldest LF, they have not lost their importance in modern pharmacotherapy. If approximately 50 years ago, ointments were considered as LF for external use, mainly for the treatment of a number of dermatological diseases, now they are quite widely used in surgery, ophthalmology, gynecology, dentistry, proctology and other fields of clinical medicine.

**Aim.** Study of the characteristics and features of the use of bases for the manufacture of soft dosage forms.

**Materials and methods.** Generalization of literature data on the characteristics of ointment bases.

**Results and discussion.** The ointment base is a component of the ointment and determines its properties – consistency, stability during storage, pH, appearance, color, smell, as well as the speed and completeness of the release of substances.

Today, in global pharmaceutical practice, there are about 250 individual or complex ointment bases that have certain properties and meet certain requirements. There is no ideal basis, therefore, in most cases, to obtain a basis with the necessary properties, several auxiliary substances are combined.

For the preparation of ointments with antibiotics that are difficult to dissolve and unstable in water, the bases "Esilon-1" (Esilon-aerosil base – 45 %, hydrolin – 5 %, PEO-400 – 20 %, purified water – 30 %) and "Esilon-2" are recommended (esilon-aerosol base – 45 %, hydrolin – 5%, purified water – 50 %). When preparing them, the esilon-aerosol base is mixed with hydrolin at a temperature

of 50-60 °C and hydrophilic components are added with constant stirring. Bases that contain pentol emulsifiers deserve attention: (pentol – 2,0 g, petrolatum – 38,0 g, purified water – 60,0 g) and sorbitan oleate (sorbitan oleate – 2,5 g, petrolatum – 47,5 g, purified water – 50,0 g). The bases are obtained by fusing the emulsifier with petroleum jelly and gradually adding water to the semi-cooled alloy while stirring. The foundations are stable when stored in room conditions and have a thick consistency.

Emulsion bases of the o/w type easily release medicinal substances, mix with aqueous solutions of substances and wound secretions, cause a cooling effect and a moisturizing effect. The emulsion base of the o/w type most often includes nonionic (theins) or ionic (emulsifier № 1, emulsion waxes, sodium lauryl sulfate, sodium stearyl sulfate) emulsifiers. Emulsifier № 1 can be used as part of ointments, which include aloe juice, vegetable oils, petroleum jelly, petroleum jelly, paraffin, glycerin, sodium-CMC, alcohol and aqueous solutions of medicinal substances. One part of emulsifier № 1 can emulsify nine parts of water.

To prepare ointments with anesthetics (anesthesia, lidocaine, novocaine, dicaine) a base based on emulsion waxes is used.

According to the ability of medicinal substances to be absorbed from ointments through the skin, all ointment bases can be placed in the following sequence: hydrophilic gels – emulsion bases of the o/w type – emulsion bases of the o/o type – absorption – hydrophobic. However, as practice shows, there may be exceptions. First of all, the action of the medicinal substance, its properties, possible interaction with the components of the ointment, and other factors should be taken into account.

Polyethylene oxide bases have a weak bacteriostatic effect and have the ability to increase the activity of many antibiotics (especially chloramphenicol), sulfonamides and other medicinal substances. A characteristic feature of PEOs is their good solubility in water. It was established that adding water up to 2 % to PEO strengthens its structure even more. This is explained by the fact that water, with the help of hydrogen bonds, "stitches" PEO macromolecules into new formations, which are highly polymeric substances with more limited mobility.

Ointments containing PEO are highly effective, especially for exudative dermatoses, for the treatment of which formulations based on fat and hydrocarbons cannot be used.

**Conclusions.** A literature review of the bases used for the production of soft dosage forms was conducted. Their characteristics and manufacturing methods are given. It was determined that emulsion bases of the o/w type cause a cooling and moisturizing effect, and polyethylene oxide bases have a weak bacteriostatic effect.

## RELEVANCE OF THE DEVELOPMENT OF PREPARATION WITH ADAPTOGENIC EFFECT

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**Introduction.** Currently, one of the urgent problems of medicine is the problem of human adaptation to the environment, which is associated with increased environmental and social pressure, an increase in the number of stressogenic factors operating at the current stage of society's development. So, according to statistics in Ukraine, only 5-7% of the population can be classified as


МІНІСТЕРСТВО ОХОРОНИ ЗДОРОВ'Я УКРАЇНИ
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# СЕРТИФІКАТ УЧАСНИКА

Цим засвідчується, що

**Salma Ghled, Yarnykh T.G., Oliinyk S.V., Rukhmakova O.A.**

брав(ла) участь у роботі
XXIX Міжнародної науково-практичної конференції молодих вчених та студентів
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МІНІСТЕРСТВО ОХОРОНИ ЗДОРОВ'Я УКРАЇНИ Національний фармацевтичний університет №02010936

19-21 квітня 2023 р, м. Харків

*Ф А 2.2.1–32-366*

**National University of Pharmacy**

Faculty for foreign citizens' education
Department Technology of Drugs

Level of higher education master

Specialty 226 Pharmacy, industrial pharmacy
Educational program Pharmacy

**APPROVED**
**The Head of Department**
**Technology of Drugs**

**Tatyana YARNYKH**
" 28 " of September 2022

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

**Salma GHLED**

1. Topic of qualification work: «Development of composition and technology of extemporaneous anti-inflammatory ointment», supervisor of qualification work: Svitlana OLIINYK, candidate of pharmaceutical sciences, assistant,

approved by order of NUPh from "6th" of February 2023 № 35

2. Deadline for submission of qualification work by the applicant for higher education: April 2023.

3. Outgoing data for qualification work:
The aim is devoted to the substantiation of the composition and the development of technology for the preparation of an ointment for use in dental practice

4. Contents of the settlement and explanatory note (list of questions that need to be developed):
- to study the literary sources about the characteristics and distribution of dental inflammatory diseases; to analyze the range of soft dosage forms for the treatment of dental diseases and the relevance of their use; characterize excipients used for the preparation of soft dosage forms;
- to scientifically substantiate the rational composition of dental ointment with furazolidone, novocaine and Kalanchoe juice;
- theoretically develop a technology for the manufacture of an anti-inflammatory ointment based on furazolidone, novocaine and Kalanchoe juice in a pharmacy;
- calculate of the cost of the developed anti-inflammatory ointment.

5. List of graphic material (with exact indication of the required drawings):
Tables – 5, pictures – 4

6. Consultants of chapters of qualification work

| Chapters | Name, SURNAME, position of consultant | Signature, date | |
|---|---|---|---|
| | | assignment was issued | assignment was received |
| 1 Chapter | Svitlana OLIINYK, assistant of department technology of drugs | 28.09.2022 | 28.09.2022 |
| 2 Chapter | Svitlana OLIINYK, assistant of department technology of drugs | 17.11.2022 | 17.11.2022 |
| 3 Chapter | Svitlana OLIINYK, assistant of department technology of drugs | 19.12.2022 | 19.12.2022 |

7. Date of issue of the assignment: «28» of September 2022

**CALENDAR PLAN**

| № з/п | Name of stages of qualification work | Deadline for the stages of qualification work | Notes |
|---|---|---|---|
| 1. | Topic selection | September 2022 | **done** |
| 2. | Analysis of literature data | October 2022 | **done** |
| 3. | Conducting experimental studies | October December 2022 | **done** |
| 4. | Registration of work | January March 2023 | **done** |
| 5. | Submission of finished work to the commission | April 2023 | **done** |

**An applicant of higher education** _____ Salma GHLED

**Supervisor of qualification work** _____ Svitlana OLIINYK

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

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

| Прізвище студента | Тема кваліфікаційної роботи | | Посада, прізвище та ініціали керівника | Рецензент кваліфікаційної роботи |
|---|---|---|---|---|
| • **по кафедрі технології ліків** | | | | |
| Хлед Сальма | Розробка складу та технології екстемпоральної мазі протизапальної дії | Development of composition and technology of extemporaneous anti-inflammatory ointment | ас. Олійник С.В. | проф. ХохленковаН. В. |

Підстава: подання декана, згода ректора

Ректор

**Вірно.** Секретар

*Ф А2.8-47-110*

**ВИСНОВОК**

**Комісії з академічної доброчесності про проведену експертизу**

**щодо академічного плагіату у кваліфікаційній роботі**

**здобувача вищої освіти**

№ 113096 від « 8 » травня 2023 р.

Проаналізувавши випускну кваліфікаційну роботу за магістерським рівнем здобувача вищої освіти денної форми навчання Хлед Сальма, 5 курсу, _____ групи, спеціальності 226 Фармація, промислова фармація, на тему: «Розробка складу та технології екстемпоральної мазі протизапальної дії / Development of composition and technology of extemporaneous anti-inflammatory ointment», Комісія з академічної доброчесності дійшла висновку, що робота, представлена до Екзаменаційної комісії для захисту, виконана самостійно і не містить елементів академічного плагіату (компіляції).

**Голова комісії,**
**професор** **Інна ВЛАДИМИРОВА**

**0%**

**24%**

*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**

**Salma GHLED**

**on the topic: «Development of composition and technology of extemporaneous anti-inflammatory ointment»**

**Relevance of the topic.** Among the urgent problems of modern dentistry, the diagnosis, treatment and prevention of diseases of the oral mucosa occupy one of the important places. Therefore, it is advisable to create combined prolonged dental drugs (ointments, gels) with antibacterial and anti-inflammatory effects..

**Practical value of conclusions, recommendations and their validity.** During the work, the applicant for higher education analyzed the range of soft dosage forms for the treatment of dental diseases, developed a manufacturing technology and technological instructions for the production of anti-inflammatory ointment in a pharmacy for use in dental practice, and calculated the estimated cost of the developed ointment.

**Assessment of work**. Qualification work in terms of theoretical and practical research fully meets the requirements for qualification work.

**General conclusion and recommendations on admission to defend.** Qualification work of Salma GHLED 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 _____ Svitlana OLIINYK

«12th» of April 2023

*Ф А 2.2.1-32-356*

**REVIEW**

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

**Salma GHLED**

**on the topic: «Development of composition and technology of extemporaneous anti-inflammatory ointment»**

**Relevance of the topic.** The development of an extemporaneous soft dosage form that meets modern requirements for the effectiveness and safety of a drug for use in dental practice is an important area of scientific research that involves solving a number of issues related to the study and systematization of dental diseases, the choice of active and excipients, and the regulation of the quality of the dosage form. etc.

**Theoretical level of work.** The paper analyzes the range of soft dosage forms for the treatment of dental diseases using the data of the State Register of Medicines, as well as instructions for medicines for dentistry registered in Ukraine. A literature review of excipients used for the preparation of soft dosage forms was carried out.

**Author's suggestions on the research topic.** The author proposes a rational composition of an anti-inflammatory ointment based on furazolidone, novocaine and Kalanchoe juice for use in dental practice. The optimal production technology is scientifically substantiated and a technological instruction for the manufacture of dental ointment in a pharmacy is proposed. The estimated cost of the proposed ointment has been determined.

**Practical value of conclusions, recommendations and their validity.** In the course of work, the applicant for higher education mastered marketing methods of descriptive and structural analysis, mathematical, organoleptic, physico-chemical, statistical research methods of practical interest.

**Disadvantages of work.** There are spelling and grammatical mistakes in the work. It is desirable to add justification for the choice of packaging of the developed dental ointment.

**General conclusion and assessment of the work.** Qualifica-tion work of Salma GHLED 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

«20th» of April 2023

**МІНІСТЕРСТВО ОХОРОНИ ЗДОРОВ'Я УКРАЇНИ**
**НАЦІОНАЛЬНИЙ ФАРМАЦЕВТИЧНИЙ УНІВЕРСИТЕТ**

**ВИТЯГ З ПРОТОКОЛУ № _11_**
«28» квітня 2023 року
м. Харків

**засідання кафедри**
**___технології ліків___**

**Голова:** завідувачка кафедри, доктор фарм. наук, професор Тетяна ЯРНИХ
**Секретар:** канд. фарм. наук, асистент Світлана ОЛІЙНИК

**ПРИСУТНІ:** професор Тетяна ЯРНИХ, професор Олександр КОТЕНКО, професор Юлія ЛЕВАЧКОВА, професор Ріта САГАЙДАК-НІКІТЮК, доцент Марина БУРЯК, доцент Володимир КОВАЛЬОВ, доцент Наталія ЖИВОРА, асистент Світлана ОЛІЙНИК, асистент Єлизавета ЗУЙКІНА

**ПОРЯДОК ДЕННИЙ**
1. Про представлення до захисту до Екзаменаційної комісії кваліфікаційних робіт здобувачів вищої освіти.

**СЛУХАЛИ**: проф. Тетяну ЯРНИХ – про представлення до захисту до Екзаменаційної комісії кваліфікаційних робіт здобувачів вищої освіти.

**ВИСТУПИЛИ:** Здобувач вищої освіти 5 курсу групи Фм18(5,0д)англ-01 спеціальності 226 Фармація, промислова фармація Сальма ХЛЕД з доповіддю на тему «Розробка складу та технології екстемпоральної мазі протизапальної дії» (науковий керівник: асистент Світлана ОЛІЙНИК).

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

**Голова**
Завідувачка кафедри, проф. _____ **Тетяна ЯРНИХ**
(підпис)

**Секретар**
асистент _____ **Світлана ОЛІЙНИК**
(підпис)

*Ф А2.2.1-32-042*

# НАЦІОНАЛЬНИЙ ФАРМАЦЕВТИЧНИЙ УНІВЕРСИТЕТ

## ПОДАННЯ
## ГОЛОВІ ЕКЗАМЕНАЦІЙНОЇ КОМІСІЇ
## ЩОДО ЗАХИСТУ КВАЛІФІКАЦІЙНОЇ РОБОТИ

Направляється здобувач вищої освіти Сальма ХЛЕД до захисту кваліфікаційної роботи
за галуззю знань 22 Охорона здоров'я
спеціальністю 226 Фармація, промислова фармація
освітньою програмою Фармація
на тему: «Розробка складу та технології екстемпоральної мазі протизапальної дії»

Кваліфікаційна робота і рецензія додаються.

Декан факультету _____ / Світлана КАЛАЙЧЕВА /

### Висновок керівника кваліфікаційної роботи

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

Керівник кваліфікаційної роботи

_____ Світлана ОЛІЙНИК

«12» квітня 2023 року

### Висновок кафедри про кваліфікаційну роботу

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

Завідувачка кафедри
технології ліків

_____ Тетяна ЯРНИХ

«28» квітня 2023 року

Qualification work was defended

of Examination commission on

« _____ » ___of June____ 2023

With the grade _____

Head of the State Examination commission,

DPharmSc, Professor

_____ / Oleh SHPYCHAK /