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MINISTRY OF HEALTH OF UKRAINE
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faculty for foreign citizens' education

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QUALIFICATION WORK

on the topic

DEVELOPMENT OF THE COMPOSITION AND TECHNOLOGY OF EXTEMPORANEOUSE TOPICAL GEL FOR THE TREATMENT OF BURN WOUNDS

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SUMMARY

The relevance of the development of topical gel with homeopathic calendula tincture and dexpantenol for use in the treatment of burns is theoretically and experimentally substantiated in the master 's thesis. Based on the results of experimental studies, in particular organoleptic, physical, chemical, biopharmaceutical, the optimal composition of the new drug is substantiated. Quality parameters of model samples were determined according to methods of SPhU. The work is presented on 47 pages, includes 10 tables, 7 figures, 90 sources of literature.

Key words: gel, composition, technology, burn wounds, homeopathy, tincture.

АННОТАЦІЯ

У магістерській роботі теоретично та експериментально обґрунтовано актуальність розробки гелю для місцевого застосування з гомеопатичною настойкою календули та декспантенолом для застосування при лікуванні опіків. За результатами експериментальних досліджень, зокрема органолептичних, фізико-хімічних, біофармацевтичних, обґрунтовано оптимальний склад нового препарату. Показники якості модельних зразків визначали за методиками ДФУ. Робота представлена на 47 сторінках, містить 10 таблиць, 7 малюнків, 90 джерел літератури.

Ключові слова: гель, склад, технологія, опікові рани, гомеопатія, настоянка.

CONTENTS

INTRODUCTION

Actuality of topic.

Burns are a global public health problem, accounting for an estimated 180 000 deaths annually. The majority of these occur in low- and middle-income countries and almost two thirds occur in the WHO African and South-East Asia regions.

In many high-income countries, burn death rates have been decreasing, and the rate of child deaths from burns is currently over 7 times higher in low- and middle-income countries than in high-income countries.

Non-fatal burns are a leading cause of morbidity, including prolonged hospitalization, disfigurement and disability, often with resulting stigma and rejection.

Burns are among the leading causes of disability-adjusted life-years (DALYs) lost in low- and middle-income countries.

In 2014, nearly 11 million people worldwide were burned severely enough to require medical attention.

In India, over 1 000 000 people are moderately or severely burnt every year.

Nearly 173 000 Bangladeshi children are moderately or severely burnt every year. In Bangladesh, Colombia, Egypt and Pakistan, 17% of children with burns have a temporary disability and 18% have a permanent disability.

Burns are the second most common injury in rural Nepal, accounting for 5% of disabilities.

In 2018, over 410 000 burn injuries occurred in the United States of America, with approximately 40 000 requiring hospitalization.

For 2020, direct costs for care of children with burns in the United States of America exceeded US$ 211 million. In Norway, costs for hospital burn management in 2017 exceeded €10.5 million.

In South Africa an estimated US$ 26 million is spent annually for care of burns from kerosene (paraffin) cookstove incidents. Indirect costs such as lost wages, prolonged

care for deformities and emotional trauma, and commitment of family resources, also contribute to the socioeconomic impact.

The treatment of burns requires careful attention to the wound surface, timely treatment and the use of highly effective drugs of combined action with pronounced anti-inflammatory, antimicrobial and healing properties.

Among them, a special place is occupied by an active pharmaceutical ingredient of natural origin - calendula tincture. Also considered an effective remedy is dexpanthenol, known for its anti-inflammatory and antipruritic properties, as well as the ability to accelerate granulation and re-epithelialization, which contributes to rapid healing properties, and due to its physical and chemical properties it can be used in soft dosage forms on hydrophilic bases.

Research purpose and objectives

Theoretically and experimentally substantiate the composition and technology of extemporaneous gel with calendula tincture and dexpanthenol for use in the treatment of burn wounds.

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

- to analyze the literature data on the prospects of using calendula tincture and dexpanthenol in the treatment of burns;
- to analyze the pharmaceutical market of Ukraine for the availability of medicines for the treatment of burn wounds;
- theoretically and experimentally substantiate the composition of the gel with anti-inflammatory, antimicrobial action;
- to carry out physicochemical, biopharmaceutical and microbiological studies of gel sections;
– to develop a technology for the manufacture of the gel in pharmacy.

Scientific novelty

The composition and technology of extemporaneous gel with calendula tincture and

dexpantenol for use in local therapy of burns have been developed.

Theoretical and practical significance of the work

The theoretical and practical significance of the master's work lies in the fact that the choice of the gel base and excipients were experimentally substantiated and the composition and technology of the extemporaneous drug in the form of topical gel were proposed in the treatment of burns.

The structure and size of the qualifying work.

The qualifying work consists of an introduction, a literature review (Chapter 1), an experimental part (Chapters 2 and 3), general conclusions, a list of references. The work is presented on 47 pages, includes 10 tables, 7 figures, 90 references.

CHAPTER I.
RATIONALE FOR THE USE OF CALENDULA MEDICINES AND DEXPANTHENOL IN THE THERAPY OF BURN WOUNDS

1.1. Burns: characteristics, classification and modern approaches to pharmacotherapy

Burn - damage to the skin or mucous membranes, often with tissues, due to exposure to high temperature (thermal burn), chemically active substances (chemical burn) or physico-chemical factors such as electric current and radiation (electric and radiation burns).

Most burns affect only the skin. In the case of severe burns, deeper tissues such as bones, muscles, and blood vessels may also be injured. A burn wound of the skin leads to the loss of the protective function as a barrier to microorganisms, which leads to a high risk of infection [35, 53].

Thus, patients with burn wounds face more morbidity due to infection of large open burns; wound healing occurs over a long period, which leads to deformities and contractures. Problems such as infection, electrolyte imbalance, shock, and respiratory injury may occur [40].

Burn treatment includes removal of dead tissue, wound dressing, fluid replacement, administration of antibiotics, and, in some cases, skin grafting [42, 78].

A wound is a violation of the integrity of anatomical tissues caused by the influence of any factor [15]. Wounds are divided into two groups:

Closed wounds: this group includes contusion, hematoma and abrasion. Contusion involves damage to soft tissues, deep tissue layers, and small blood vessels, resulting in their separation, but the anatomy of the skin remains intact. Edema is observed in the wound, and in the later stages, atrophy and a pigmentation defect, healing is slowed

down. A rupture of a vessel due to damage is called a hematoma, and wounds such as scratches are called abrasions.

Open wounds: This group includes lacerations, cutting wounds, gunshot wounds, surgical wounds and metabolic wounds. Wounds, with the exception of lacerations, severely damage tissue under the skin. In lacerated wounds, the skin and subcutaneous tissue are destroyed, but the deep tissues remain healthy. The integrity of tissue anatomy is violated when cutting with a prickly instrument without tissue damage along the edges of the wound [22, 80, 85].

In medicine, burns can be divided into 4 groups depending on the depth and affected layers of the skin (fig. 1.1.).

1. First-degree burns (usually caused by brief contact with heat or flames or prolonged exposure to intense sunlight). The burn is accompanied by redness and swelling. There is a local increase in body temperature, moderate pain, which may increase with movement

2. Second-degree burns (deeper than first-degree burns and necrosis extends to the dermis). Damage covers the entire epidermis and part of the dermis. The burn is accompanied by the appearance of blisters. There is inflammation around the wound. Over time, the shell of the bubbles disappears, and in its place a new epithelium is formed.

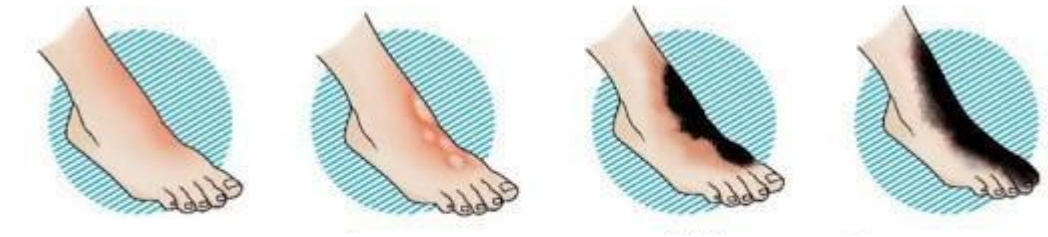
3. Third degree burns. The skin is deeply damaged. Sometimes even subcutaneous tissue suffers. The burn is accompanied by tissue necrosis, so the wound may be black and even black. The victim is in severe pain, tissue recovery is slow. Sometimes a skin graft is needed.

4. Fourth degree burns. The skin is charred, muscles and even bones suffer. Characterized by unbearable pain. The wound is covered with a dark gray eschar due to tissue necrosis [79].

Burns can be caused by various substances and external sources such as contact with electricity, chemicals, friction, radiation and heat [53, 78].

Chemicals

Most chemicals that cause chemical burns are strong acids or alkalis. Chemical compounds such as sodium hydroxide and sulfuric acid cause chemical burns. Depending on the time of contact, the potency of the substance, and other factors, chemical burns can be first, second, or third degree burns.



I degree – redness of the skin

II degree – blistering of the skin

III -IV degrees – charring of skin and tissues

Fig. 1.1. Types of burns.

Electrical

Electrical burns are caused by electric shock. A common occurrence of electrical burns includes injuries in the workplace. Lightning is also a rare cause of electrical burns.

Radiation

Radiation burns are caused by long-term exposure to ultraviolet light, radiation therapy, sunlamps, radioactive fallout, and X-rays. The most common radiation-related burn is from the sun, especially the two wavelengths UVA and UVB, the latter being more dangerous.

Scalding:

Scalding burns are caused by hot liquids (water or oil), gases (steam), high temperature tap water in the bath or shower. A fluid-filled blister forms on the skin as a result of the body's reaction to heat and the subsequent inflammatory response. The top of the blister is dead and the fluid contains toxic inflammatory substances [78, 79].

Usually burns are first or second degree, but due to prolonged contact, this may be a third-degree burn.

Burns are the fourth most common injury worldwide. Approximately 11 million people worldwide seek medical attention for burns each year.

According to the American Burn Association (ABA), most burns are small: 67% are burns with less than 10% of the total body area [40]. The average burn size is decreasing, especially in high-income countries, but despite these statistics, large burns still occur.

The prevalence of burns has a bimodal distribution according to age groups, with children (especially young children) accounting for 24 % of burns and 55 % for people aged 20 to 59 years.

Flame contact is the most common cause in people over 5 years of age. Steam burns are more common in children under 5 years of age. More burns (75%) occur at home, while 13% occur at work. Approximately 95 % of burns are accidental, and about 2 % of burns are related to the abuse of security measures.

Burn injuries require a long period of treatment due to the complexity of the multidimensional clinical course. Patients require precise treatment, from initial trauma and immediate life support, to clinical stabilization processes including intensive care, conservative management and surgical wound reconstruction, followed by long-term rehabilitation. Treatment should take place under appropriate conditions, depending on the severity of the burn injury. In addition, infrastructural conditions and staff qualifications are vital for the treatment of burns [45].

Sepsis is a major risk after any large burn, as the skin, as the main barrier to microbial invasion, becomes degraded. Sepsis can develop at any time after resuscitation, and the risk persists throughout the entire period because the wound remains open.

Unfortunately, antibiotics are not effective in preventing infection. And their use leads to more resistant microorganisms.

Bandages, ointments, creams, gels, etc. are more often used as local dosage forms for the treatment of burns.

Because trauma disrupts the protective barrier function of the skin, dressings are essential to protect the body from environmental flora. The burn dressing also protects against evaporative heat loss.

An ideal burn dressing should be inexpensive, comfortable, and not require frequent changes. Changing the bandage daily allows the burn caregiver not only to apply clean bandages, but also to clean the wounds. The selection of an appropriate dressing for a given wound is determined by the physician for specific purposes.

In superficial wounds, the goal is always to create a moist environment that enhances the epithelialization process. This is achieved by applying an ointment or lotion. For wounds of partial or full thickness, it is necessary to include agents that protect against microbial colonization.

Topical antimicrobials are used to prevent and treat burn infections compared to other traumatic, surgical, and medical conditions that may be susceptible to infection. Most agents are intended to be used prophylactically to prevent the development of infection, while others are intended to kill the actual microbial cells that proliferate in the burn site when an infection develops [43].

1.2. Calendula, its chemical composition and use in allopathy and homeopathy

Calendula officinalis (Calendula), belonging to the family of *Asteraceae*, commonly known as English Marigold or Pot Marigold is an aromatic herb which is used in traditional system of medicine for treating wounds, ulcers, herpes, scars, skin damage, frostbite and blood purification. It is mainly used because of its various biological activities to treat diseases like analgesic, anti–diabetic, anti-ulcer and anti-inflammatory. It is also used for in gastro-intestinal, gynecological, eye disease, skin injuries and in some cases of burn.

Calendula officinalis (fig. 1.2) is a short-lived aromatic herbaceous perennial, growing to 80cm (31in) tall, with sparsely branched lax or erect stems. The leaves are oblong-lance. The disc florets are tubular and hermaphrodite, and generally of a more intense orange olate, 5–17cm (2–7in) long, hairy on both sides, and with margins entire or occasionally waved or weakly toothed. The inflorescences are yellow, comprising a thick capitulum or flower head 4–7cm diameter surrounded by two rows of hairy bracts; in the wild plant they have a single ring of ray florets surrounding the central disc florets-yellow colour than the female, tridentate, peripheral ray florets. The flowers may appear all year long where conditions are suitable. The fruit is a thorny curved achene.

Fig. 1.2. Calendula officinalis

Organoleptic properties

The odour of Calendula officinalis is faint and aromatic. The taste of Calendula officinalis is bitter.

Cultivation

The plant is native to Central and Southern Europe, Western Asia and the US.

Calendula officinalis is widely cultivated and can be grown easily in sunny locations in most kinds of soils. Although perennial, it is commonly treated as an annual, particularly in colder regions where its winter survival is poor and in hot summer locations where it also does not survive. Calendulas are considered by many gardening experts as among the easiest and most versatile flowers to grow in a garden, especially because they tolerate most soils. In temperate climates, seeds are sown in spring for blooms that last throughout the summer and well into the fall. In areas of limited winter freezing, seeds are sown in autumn for winter color. Plants will wither in subtropical summer. Seeds will germinate freely in sunny or half-sunny locations, but plants do best if planted in sunny locations with rich, well-drained soil. Pot marigolds typically bloom quickly from seed

(in under two months) in bright yellows, golds, and oranges.

Uses of calendula

Sedative drugs: In early animal studies, high doses of ingested calendula preparations were reported to act as sedatives. Therefore, combination use with sedative agents may lead to additive effects. In rats, calendula was shown to increase hex barbital sleeping time. A systemic effect after topical use of calendula in human is not clear.

Antihypertensive drugs: In early animal studies, high doses of calendula preparations were reported to possess hypertensive effects. Therefore, combination use with hypertensive agents may lead to additive effects.

Hypoglycemic drugs: Calendula may increase the activity of hypoglycemic medications or insulin.

Cholesterol-lowering drugs: Calendula may have an additive effect with agents that decrease lipids and triglycerides.

A number of phytochemical studies have well reported about the presence of several classes of chemical compounds, the main ones being terpenoids, flavonoids, coumarines, quinines, volatile oil, carotenoids and amino acids in the plant.

Terpenoids: Various terpenoids have been reported from the petroleum ether extract of C. officinalis flowers. They include sitosterols, stigmasterols, diesters of diols, 3-monoesters of taraxasterol, lupeol, erythrodiol, brein, ursadiol, faradiol-3-O-palmitate, faradiol-3-Omyristate, faradiol-3-O-laurate, arnidiol-3-O-palmitate, arnidiol-3-O-myristate, arnidiol-3-O-laurate, calenduladiol-3-Opalmitate, calenduladiol-3-O-myristate, oleanolic acid saponins: calenduloside AH, oleanane triterpene glycoside: calendula glycoside A, calendulaglycosideA6-O-n-methylester, calendulaglycosideA6‟-O-n-butylester, calendula glycoside B, calendulaglycosideB6-O-n-butylester, calendula glycoside C, calendula glycoside C 6-O-n-methyl ester, calendula glycoside C 6- O-n-butyl ester, calenduloside F6-O-n-butyl ester, calenduloside G6-O-n-methyl ester, glucoside of oleanolic acid (mainly found in roots of grown and senescing plants) I, II, III, VI, VII, and glucu-

ronides (mainly found in flowers and green parts) F, D, D2, C, B and A. One new triterpenic ester of oleanane series has been isolated from flowers was cornulacic acid acetate from flowers.

Flavonoids: Various flavonoids have been isolated from the ethanol extract of the inflorescence of C. officinalis. They include quercetin, isorhamnetin, isoquercetin, isorhamnetin-3-O-D-glycoside, narcissin, calendoflaside, calendoflavoside, calendoflavobioside, rutin, isoquercetin neohesperidoside, isorhamnetin-3-Oneohesperidoside, isorhamnetin-3-O-2G- rhamnosyl rutinoside, isorhamnetin-3-Orutinoside, quercetin-3-O-glucoside and quercetin-3-O-rutinoside.

Coumarins: The ethanol extract of the inflorescence of the C. officinalis reported to contain coumarins-scopoletin, umbelliferone and esculetin.

Quinones: Quinones reported from C. officinalis were plastoquinone, phylloquinone, and tocopherol in the chloroplast, ubiquinone, phylloquinone, tocopherol in mitochondria, and phylloquinone in the leaves.

Volatile oil: C. officinalis flowers contain maximum volatile oil at full flowering stage (0.97 %) and minimum during the pre-flowering stage (0.13%). The composition also showed different patterns at different phases of vegetative cycles.

Various monoterpenes and sesquiterpenes have been reported in the volatile oil : α-thujene, α-pienene, sabinene, β-pienene, limonene, 1,8-cineol, p-cymene, trans-β-ocimene, ϒ-terpenene, δ-3-carene, nonanal, terpene-4-ol, 3-cylohexene-1-ol, α-phellandrene, α-terpeneol, geraniol, carvacrol, bornyl acetate, sabinyl acetate, α-cubebene, α-copaene, α-bourbonene, cubebene, α-gurjunene, aromadendrene, β-aryophyllene, α-ylangene, α-humulene, epibicyclosequiphellandrene, germacrene D, allo aromadendrene, β-saliene, calarene, muurolene, δ-cadinene, cadina 1,4-diene, α-cadinene, nerolidol, palustron, endobourbonene, oplopenone, α-cadinol, Tmuurolol. The essential oil was found to be rich in α-cadinene, α-cadinol, t-muurolol, limonene, and 1,8-cineol with p-cymene at lower levels at the post-flowering periods.

Carotenoids: The methanol extract of leaves, petals and pollens of C. officinalis flowers showed a number of carotenoids. The carotenoids found in the pollens and petals were neoxanthin, 9Z-neoxanthin, violaxanthin, luteoxanthin, auroxanthin, 9Z-violaxanthin, flavoxanthin, mutatoxanthin, α-cryptoxanthin, β-cryptoxanthin, z-cryptoxanthin, lycopene, α-carotene, and β-carotene.

Total carotenoid (mg/g dry weight) was 7.71% for petals and 1.61% for pollens. Carotenoid compositions of the leaves and stems were reported as neoxanthin, violaxanthin, luteoxanthin, antheraxanthin, mutatoxanthin epimer 1, mutatoxanthin epimer 2, lutein, α-cryptoxanthin, β-cryptoxanthin, β-carotene.

Total carotenoids (mg/g dry weight) for the leaves is 0.85% and for stems 0.18%. Glycosides of quercetin and isorhamnetin were the predominant components of the flavonoids, while beta-carotene and lutein were the most abundant carotenoids. Analysis of carotenoid composition in petals of Calendula officinalis was made. Nineteen carotenoids were identified in extracts of petals of orange and yellow flowered cultivars of calendula.

Amino acids: The ethanol extract of the flowers of the plant is reported to show the presence of 15 amino acids in free form: Alanine, arginine, aspartic acid, asparagines, valine, histidine, glutamic acid, leucine, lysine, proline, serine, tyrosine, threonine, methionine and phenylalanine. Amino acid content of the leaves is about 5%, stems 3.5% and flowers 4.5%.

Carbohydrates: The ethanol extract of the inflorescence of plant showed the presence of polysaccharides, PS-I,-II, and III having a (1_3)-D-galactam backbone with short side chains at C-6 comprising -araban(1_3)-araban and alpha-L-rhamnan-(1_3)- araban along with monosaccharide's.

Lipids: The lipids in the petroleum ether extract of the seeds, leaves and flowers of C. officinalis have been analyzed. The amount of neutral lipids in the seeds was 15.7%, phospholipids 0.6% and glycolipids 0.9%. Fatty acids of monols, sterol esters, 3-monoesters, 3-monoester diols reported in flowers were lauric, myristic, palmitic, stearic,

oleic, linoleic and linolenic acid. The fatty acids of marigold seeds contain about 59% of an conjugated trienic acid and about 5% of 9-hydroxy- acid-dimorphecolic acid, one oxygenated fatty acid also reported from the seed oil of C. officinalis was D-(+)-9-hydroxy, octadecadienoic acid.

Other constituents: Other phytochemicals include the bitter constituent, loliolide (calendin), calendulin and paraffins.

Calendula preparations are widely used in both allopathy and homeopathic practice (table 1.1) [34, 76, 81, 83].

Table 1.1

The use of calendula in medicine

In allopathy	In homeopathy
Calendula flowers are used. Preparations from calendula flowers have anti-inflammatory, choleretic, reparative and antiseptic effects. • cuts, purulent wounds, furunculosis, burns, proctitis, paraproctitis, for gargling with inflammatory diseases of the upper respiratory tract, sore throat, etc. • with gingivitis, periodontitis, bleeding gums, conjunctivitis. • for the treatment of cervical erosion. • gastritis, peptic ulcer of the stomach and duodenum, colitis, enterocolitis.	Herb collected during flowering or flower baskets are used. • Eyes - inflammation of the eyes after surgery. • Ears - deafness. • Tonsillitis. • Teeth - bleeding after extraction. • Stomatitis. • Uterus - erosion of the cervix. • Childbirth - the consequences of tissue rupture. • Muscles - ruptures of muscles, ligaments. • Ulcers - obsolete ulcers, incl. varicose. • Burns - I and II degree. • Frostbite - I and II degree. • Suppuration - prevents suppuration and accelerates scarring of the wound. • Wounds - wounds and abrasions with ulcers. • Fever - traumatic fever. • Cancer - as an adjuvant in case of surgical cancer of the skin, breast, uterus and rectum.

In homeopathy, herbs collected during flowering are used [19, 50-52, 54-57]. In dermatology it is used to prevent suppuration of wounds as a substitute for iodine tincture, in dentistry - as a hemostatic agent; for tonsillitis, sore throat and stomatitis - for rinsing; in gynecology - in endometritis [49, 62, 66, 69].

The main dosage forms of calendula used in homeopathy:

- Homeopathic granules D3, C3, C6 and above.
- Drops, tincture D2, D3, C3 and above.
- Calendula ointment 10%.
- Suppositories with calendula [10-12, 89].

1.3. Prospects and prevalence of dexpanthenol in the treatment of burn wounds

Many medical and cosmetic interventions, such as ablative laser treatment, dermabrasion, microneedling, or tattooing, result in superficial/minor wounds; this affects the integrity of the epidermis and requires postprocedural wound care to assure a proper healing process of the damaged skin [17, 23].

Topical compounds that support all three phases of wound healing (inflammation, proliferation, and remodeling) are considered particularly useful for the treatment of minor and superficial wounds [2].

Recently, it has been suggested that dexpanthenol exhibits activity across all three wound healing phases [38].

Dexpanthenol is well absorbed when applied topically to the skin and rapidly converted to pantothenic acid [1, 45, 46].

The latter is a coenzyme A constituent and essential for the physiological function of epithelia [13, 30].

Dexpanthenol supports skin regeneration by enhancing epidermal differentiation and facilitates wound healing [18, 29, 32]; it also showed activity in the prevention of biofilm formation and has anti-inflammatory effects [6].

Furthermore, dexpanthenol acts as a moisturizer and skin barrier enhancer. In dry skin conditions, it compensates for reduced hydration by increasing water content and by beneficially influencing the molecular mobility of the stratum corneum lipid lamellae and proteins [4, 36, 37]

These features triggered the development of various topical dexpanthenol-containing galenical formulations which are widely used in the dermatological field. Topical dexpanthenol has also been recommended for the treatment of minor and superficial wounds, especially in the form of ointments or gels.

They form a semi-occlusive breathable film that protects the wound from external influences (e.g., pathogens or contaminants), keeps the injured area hydrated but avoids moisture congestion, and supports a successful skin barrier restoration [24].

For the care of epidermal wounds, an air interface and appropriate partial pressure of oxygen are considered important for achieving rapid re-epithelialization. It has been suggested that semi-occlusion of epidermal injuries results in a superior epidermal response and an earlier achievement of skin barrier function compared to an occlusive wound management [47].

Historically, a 5 % dexpanthenol-containing ointment has been used in the postprocedure wound care despite the fact that supporting studies in this setting were lacking for many years. Recently, clinical data were generated which provide scientific evidence for the use of a 5% dexpanthenol ointment in the wound aftercare of freshly tattooed skin [26]. For the wound care following ablative laser treatments of the skin, petroleum jelly is currently recommended by the manufacturers of ablative laser systems until encrustation of the affected skin area decreases. However, petroleum jelly is a wax-like, difficult-to-handle material, particularly when larger skin areas have to be covered. In addition, petro-

leum jelly has rather strong occlusive effects following topical application. In fact, it is used as positive reference product when the occlusion properties of new topical developments are studied. Results from a recent head-to-head comparative trial provided evidence that a 5% dexpanthenol-containing ointment is superior to petroleum jelly in the wound care after fractional ablative laser treatment as reflected by a faster wound closure and higher re-epithelialization rate as well as better cosmetic outcomes.

Today, different topical dexpanthenol formulations exist (cream, emollient, drops, gel, lotion, oil, ointment, solution, spray), developed to meet individual requirements [20]. There is cumulative evidence, that out of this product range, the ointment is a suitable option for postprocedure wound care.

Today, the pharmaceutical market of Ukraine consists of 24 drugs containing dexpanthenol, among which soft dosage forms (ointment, cream) and foams (Fig. 1.3.) [15, 20].

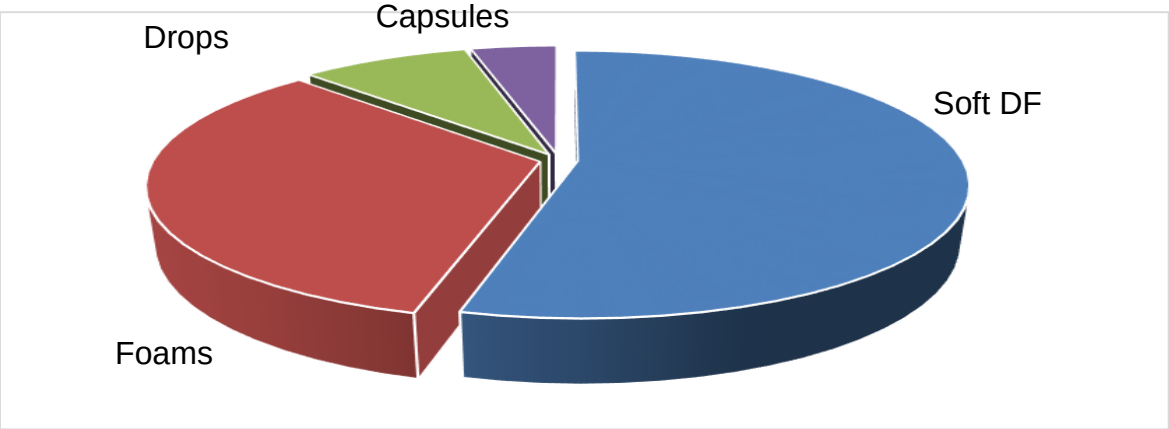


Fig. 1.3. Distribution of dexpanthenol drugs by dosage forms.

The distribution of drugs by country of origin is shown in fig. 1.4. As can be seen from the figure, drugs of domestic production (Ukrainian) are 58.3%, and foreign production - 41.7%.

It should be noted that there is duplication of dosage forms by different manufacturers with the same content of dexpanthenol, in particular in creams and ointments, the concentration of dexpanthenol is 5%.

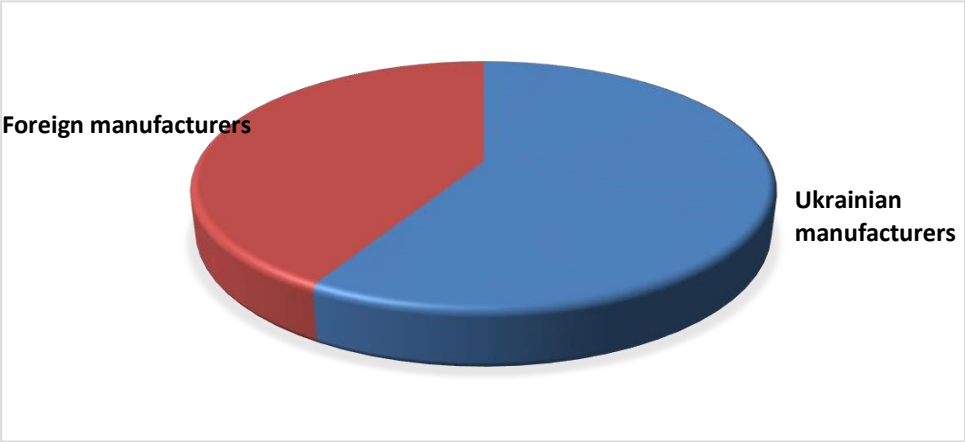


Fig. 1.4. Distribution of dexpanthenol drugs by producer countries.

Therefore, given the high pharmacological activity and effectiveness of dexpanthenol and the limited range of drugs based on it, we consider it appropriate to develop a combined drug, in particular, a gel with a tincture of calendula and dexpanthenol for the treatment of burn wounds.

CONCLUSIONS

1. Information about burns, their types; the classification and basic pharmacotherapeutic approaches to their treatment with the help of local medicines are generalized and considered on the basis of literature data.
2. A literature search about characteristics and chemical composition of calendula drugs was carried out, and information on its use in allopathy and homeopathy was summarized.
3. The prospects and prevalence of dexpanthenol in the treatment of burn wounds are considered, the pharmaceutical market of dexpanthenol drugs is studied.
4. Prospects for the introduction of calendula tincture and dexpanthenol, which promote healing (scarring) of wounds, into the composition of the gel for the treatment of burn wounds as active pharmaceutical ingredients has been substantiated.

EXPERIMENTAL PART

CHAPTER II

OBJECTS AND METHODS OF RESEARCH

In the course of research on the creation of a gel with calendula tincture and dexpanthenol, substances and excipients that meet the requirements of the SPhU and NTD were used.

2.1. Objects of researches

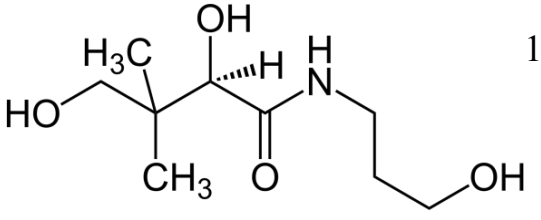
Objects of research were active pharmaceutical ingredients - calendula tincture and dexpanthenol, which met the requirements of the State Pharmacopoeia of Ukraine, as well as model gel samples with different substances that form gels and the content of excipients..

2.1.1. Characteristics of active substances

Marigold flowers (SPhU, 1, ed, suppl 2, p. 511) are dried inflorescences of a basket up to 5 cm in diameter. Grayish-green wrapper, one-, two-line; leaflets linear, pointed, densely pubescent. Receptacle slightly convex, glabrous. Marginal flowers reed, pistillate, 12-23 mm long, 3-5 mm wide, with a curved short pubescent tube, twice the length of the involucre, and four to five veins. The flowers are arranged in two or three lines in non-double forms and in 10-15 lines in double forms. Median flowers are tubular with a five-toothed corolla. The color of marginal flowers is reddish-orange, orange, bright or pale yellow; median - orange, tan or yellow.

Calendula tincture (PhS 42U-11-661-00) is a yellow-brown liquid with a specific odor and bitter taste. Store in tightly closed dark glass bottles in a dry, cool and well-ventilated place.

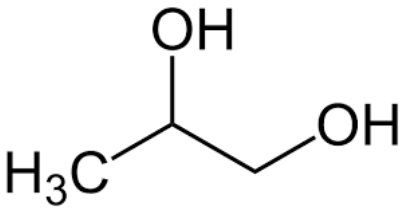
Dexpanthenol (CAS No. 81-13-0; 205.25 g/mol) is a clear, viscous liquid with almost no odor. Density 1.20. The boiling point is 118-120 ºC. Refractive index (589 nm): 1.495–1.502. High-



ly soluble in water, freely soluble in alcohol, soluble in glycerol, slightly soluble in ether, insoluble in vegetable oil, mineral oil and fats.

2.1.2. Characteristics of excipients

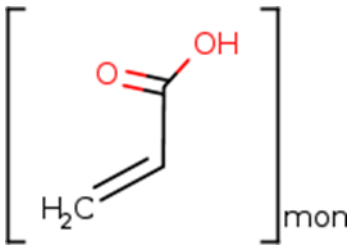
Propylene glycol (CAS 57-55-6) is a colorless thick liquid with a slight characteristic odor, miscible with water and alcohol, and has hygroscopic properties. Boiling point -187.4°C, freezing point -60°C. One of the important properties of propylene glycol is its ability to dissolve both hydrophilic and hydrophobic substances, which makes it possible to mix with it substances that do not mix by themselves.



Glycerin (SPhU 1.2, p. 409) is a viscous, oily to the touch, colorless or almost colorless, transparent liquid; very hygroscopic; miscible with water and 96% ethyl alcohol, slightly soluble in acetone, practically insoluble in fatty and essential oils.

Purified water (SPhU 1.1, p. 308-309) is a colorless, transparent liquid, odorless and tasteless, pH 5.0-7.0.

Carbopol 980 NF (CAS No. 9007-20-9) is a rare cross-linked acrylic polymer derived from acrylic acid. White fluffy powder with a slight acetic smell. The polymer is a high performance thickener and is ideal for creating clear aqueous and hydroalcoholic gels. The polymer has a short fluid rheology. Store in tightly closed containers in a cool, well-ventilated place. Temperature: 12.5°C. Molecular weight: 72.02 g/mol.

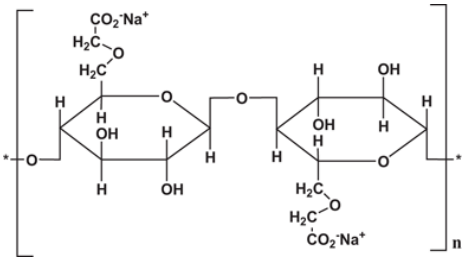


Carbopol 934 P (CAS No. 9003-01-4) is a rare cross-linked acrylic polymer derived from acrylic acid. It mixes well with water and oils. Gels formed by Carbopol are used in pharmacy and cosmetology as bases for soft dosage forms. At a concentration of carbopol 934P in an aqueous solution of 0.56-1.5%, a highly viscous gel is formed at pH

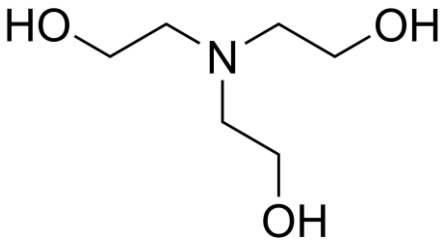
values of 6.0-7.0. The initial pH level is 3.0 -3.3, however, with an increase in this indicator, the mass turns. into a gel structure [49].

Sodium alginate (CAS No. 9005-38-3) is a polysaccharide. Natural hydrophilic colloid derived from brown algae. The main ability of alginates is the formation of homogeneous solutions with different properties, the formation of gels resistant to heating and cooling. Fine powder of white, pale yellow-brown color, pH (1% solution) 6.50-7.00. Slowly soluble in water to form a viscous solution, practically insoluble in alcohol and ether.

Sodium carboxymethylcellulose (EPh 5.0, p. 1189) is a white or almost white granular powder, hygroscopic. After drying, it is practically insoluble in acetone, ethanol and toluene. It mixes easily with water to form a colloidal solution.



Triethanolamine (CAS No. 102-71-6) is an organic amine containing at least 99%. White or almost white crystalline powder or colorless crystals. Easily soluble in water, sparingly soluble in ethanol, very slightly soluble in ethyl acetate. The aqueous solution has a pH of 10.0 to 11.5.



Ethyl alcohol 96 % (SPhU 1.1, pp. 339-343) is a colorless, transparent, volatile, combustible liquid, hygroscopic. Miscible with water. Ignites a blue smokeless flame. Boils at about 78°C. Relative density from 0.805 to 0.812.

2.2. Methods of researches

In the process of creating and studing an пgel with calendula tincture and dexpanthenol for external use on various ointment bases, a complex of physical, chemical, struc-

tural-mechanical, technological and biopharmaceutical research methods based on the qualitative and quantitative indicators of API and excipients were used.

Study of **organoleptic indicators** (SPhU 2.0).

The appearance and organoleptic characteristics of the samples (color, odor, consistency, etc.) were monitored.

Determination of homogeneity (SPhU 1.1, p. 511). Conducted determination of the homogeneity of the model samples of the studied gel according to a known method.

Determination of osmotic activity.

Osmotic activity characterizes the ability of the gel to clean wound surfaces, providing a restorative effect. To determine the osmotic activity, 0.25 g of the gel was placed on the cellophane membrane of the tube and weighed in an analytical balance with an accuracy of 0.0001 g.

50 ml of purified water was placed in a beaker and the tube was installed in such a way that the membrane was immersed to a depth of 2-3 mm. The system was weighed at certain intervals. Mass measurements were recorded and osmotic activity was calculated using the formula:

$X = \Delta m_1 \times 100\ \% / m$

where: X is an osmotic activity, %;

m is the mass of the gel taken for analysis, g;

m_1 is the amount of absorbed liquid, g.

Determination of colloidal stability.

For the test, a laboratory centrifuge with a set of test tubes, a mercury thermometer with a range of measured temperatures from 0 to 100 °C and a division value of 1 °C, as well as a stopwatch and a water bath were used. The tubes were filled to 2/3 of the volume (approximately 9.0 g) with the studied samples (so that the masses of the tubes with the drug did not differ by more than 0.02 g) and weighed to the nearest 0.01 g. Then the tubes were placed in a water bath at a temperature of 42.5 ± 2.5 ° C for 20 minutes, after

which they wiped dry from outside, placed in the centrifuge nest. Centrifuged for 5 min at 6000 rpm. A sample was considered stable if no demixing was observed in the tubes after centrifugation. If at least one of the test tubes was determined to separate the sample or precipitate, the analysis was repeated with new portions of the gel base. If at least one tube with separation was detected during the repeated test, the sample was considered unstable.

Determination of thermal stability.

For determination, 5-6 glass test tubes with a diameter of 15 mm and a height of 150 mm were taken. The tubes were filled with 8-10 ml of the test samples and placed in a thermostat at a temperature of 40-42°C for 1 week, then in a refrigerator at a temperature of 10-12°C for 1 week, after which they were kept for 3 days at room temperature. Stability was determined visually by the absence of delamination.

The average weight of the пуд was determined according to SPhU weighing 30.0 g to the nearest 0.01. Deviations in mass should not exceed ± 5 %.

Determination of pH (SPhU 1.2, paragraph 2.2.3, p. 46).

The pH value was adjusted using the extraction method: 1.0 g of gel was placed in a conical flask with a capacity of 150 ml, added 100 ml of water, stirred for 10 min with a glass rod. The resulting solution was filtered through a blue tape filter, and the first portions of the filtrate were discarded. The pH of the aqueous extract was determined according to the method described in the SPhU, paragraph 2.2.3 "Potentiometric determination of pH".

Identification of BAS

To detect *tannins* used the following qualitative reactions:

Reaction with gelatin:

To 1 ml of tincture add dropwise 1% gelatin solution. A turbid solution is formed, which disappears with the addition of excess gelatin.

Reaction with alkaloids:

To 1 ml of tincture add a few drops of 1% quinine hydrochloride solution. An amorphous precipitate is formed.

Reaction with lead acetate:

To 1 ml of tincture add 2 ml of 10% acetic acid and 1 ml of 10% medium salt of lead acetate. A precipitate is formed.

Reaction with bromine water:

To 1 ml of tincture add drops of bromine water to a noticeable odor of bromine. Precipitation precipitates (in the presence of condensed tannins).

Reaction with sodium nitrite in the presence of hydrochloric acid:

To 1 ml of tincture add a few crystals of sodium nitrite and 2 drops of 0.1 M hydrochloric acid. In the presence of tannins, a brown color appears [82].

To detect *saponins* used the following qualitative reactions:

Foaming reaction:

Take two test tubes: one is filled with 5 ml of 0.1 M hydrochloric acid solution, the other with 5 ml of 0.1 M sodium hydroxide solution. Then in two test tubes add 3 drops of calendula tincture and shake vigorously. Foam appears, equal in volume and stability.

Reaction with lead acetate:

To 1 ml of tincture add 3-4 drops of lead acetate solution. A precipitate is formed.

Reaction with cholesterol:

To 1 ml of tincture add 3-4 drops of 1% alcohol solution of cholesterol. A precipitate is formed.

Reaction with acetic anhydride and sulfuric acid:

To 1 ml of tincture add a mixture of acetic anhydride and *sulfuric acid P* (50:1). After some time, the color is formed from pink to green and blue.

Reaction with sodium nitrite in an acidic environment:

To 1 ml of tincture add 1 ml of 10 % sodium nitrite solution and 1 drop of hydrochloric acid. A blood-red color appears.

Reaction with sulfuric acid and iron (III) sulfate solution:

To 1 ml of tincture add 1 ml of sulfuric acid *P*, 1 ml of ethyl alcohol and 1 drop of iron (III) sulfate solution. When heated, a blue-green color is formed.

To detect *flavonoids* use the following qualitative reactions:

Cyanidin test:

To 1 ml of tincture add 2-3 drops of hydrochloric acid P and 0.1 g of magnesium powder. A red color is formed.

Reaction with a solution of aluminum chloride:

To 1 ml of tincture add 1 ml of 2% solution of aluminum chloride in 95% ethyl alcohol. When viewing the solution in ultraviolet light at a wavelength of 366 nm, yellow-blue fluorescence is observed.

Reaction with alkali solutions:

To 1 ml of tincture add 1-2 drops of 10% alcohol solution of sodium. A yellow-orange color appears.

Reaction with lead acetate:

To 1 ml of tincture add 3-4 drops of lead acetate solution. An orange precipitate is formed.

Reaction with ammonium hydroxide:

Up to 1 ml of tincture 0.5 ml of 10% ammonium hydroxide solution. A yellow color appears.

Reaction from iron (III) chloride:

To 1 ml of tincture add 2-3 drops of 1% alcohol solution of iron (III) chloride. A dark green or brown color is formed.

Wilson's reaction:

To 2 ml of tincture add 1 ml of 2% boric acid solution and 1 ml of 2% alcoholic citric acid solution. A bright yellow color appears [82].

The **ethyl alcohol content** is at least 65 %.

Place 25 ml of the drug in a round bottom flask with a capacity of 200-250 ml, add 50 ml of water purified. For uniform boiling, capillaries or pieces of calcined porcelain are placed in the flask with liquid. The flask is tightly closed and connected to a refrigerator. The receiver (a volumetric flask with a capacity of 50 ml) is placed in a vessel with cold water, about 48 ml of distillate is collected, brought to a temperature of 20 ^{0}C, and brought purified water to the mark. The distillate should be clear or slightly cloudy.

The **density** of the tincture was determined with a pycnometer; found the alcohol content as a percentage by volume.

Alcohol content in the medicine (X, %) by volume:

$X = 50 \times A/B$

Where: 50 is the distillation volume, ml;

A is the alcohol content, % (by volume);

B is the volume of the test preparation taken for distillation, ml.

Ash definition.

About 1.0 g (accurately weighed) of homeopathic calendula tincture was placed in a pre-calcined and weighed crucible. The crucible was then gently heated so that the substance evaporated at a lower temperature. After the coal residue burned completely, the fire was increased. The calcination was carried out at a weak red glow (about 5000 C) to a constant mass, avoiding the fusion of the ash and its sintering with the walls of the crucible. After the calcination was completed, the crucible was cooled in a desiccator and weighed.

Quantitative determination of tannins was carried out by the titrimetric method:

25 ml of the tincture were placed in a 1 L conical flask, 750 ml of purified water and 25 ml of indigo sulfonic acid solution were added, and titrated with constant stirring with 0.1 M potassium permanganate solution until golden yellow.

In parallel, a control experiment was carried out.

1 ml of 0.1 M solution of potassium permanganate corresponds to 0.004157 g of tannins in terms of tannin.

The content of tannins (X) in percent in terms of absolutely dry matter is calculated by the formula:

$$X = (V - V_1) \times 0.004157 \times 250 \times 100 \times 100 / m \times 25 \times (100\text{-}W),$$

Where: V is the volume of potassium permanganate solution (0.1 M) used for titration of extracts, ml;

V_1 is the volume of potassium permanganate solution (0.1 M) used for titration in the control experiment, ml;

0.004157 is the amount of tannins, which corresponds to 1 ml of a solution of potassium permanganate (0.1 M) (in terms of tannin), g;

m is the mass of raw materials, g;

W is a weight loss during drying of raw materials,%;

250 is the total volume of extract, ml;

25 is the volume of extract for titration, ml.

Quantitative determination of flavonoids was carried out by spectrophotometric method.

1 ml of the drug was placed in a volumetric flask with a capacity of 25 ml, 10 ml of 70 % alcohol, 2 ml of 5 % alcohol solution of aluminum chloride, stirred, after 10 min 2 ml of 5% acetate acid solution was added, the volume of the solution was made up to the mark with 70 % alcohol and stirred.

After 1 hour, the optical density of the solution was measured on a spectrophotometer at a wavelength of 408 nm in a cuvette with a layer thickness of 10 mm.

As a reference solution, a solution of the following composition was used:

1 ml of the drug was placed in a 25-ml volumetric flask, 1 ml of 70 % alcohol was added, stirred, after 10 min 2 ml of 5 % acetate acid solution was added, the volume of

the solution was made up to the mark with 70 % alcohol, and mixed. The content of the sum of flavonoids (%, in terms of rutin) in the preparation was calculated by the formula:

$X = A \times 25/220 \times 1$,

where A is the optical density of the test solution;

220 - specific absorption index of rutin from aluminum chloride in 70% alcohol at a wavelength of 408 nm.

25 is a amount of solution, ml

The content of the flavonoids sum in terms of rutin must be at least 0.06 %.

Preparation of 5 % acetic acid solution:

Acetic acid (5 ml) was placed in volumetric flask 100 ml, the volume of the solution was made up to the mark with 70 % alcohol, and mixed. The shelf life of the solution is 7 days.

CONCLUSIONS

1. Calendula tincture, dexpanthenol, as well as model gel samples on different bases were used as the object of study.

2. When developing a gel with calendula tincture and dexpanthenol, we used organoleptic, physicochemical and biopharmaceutical research methods.

CHAPTER III.
DEVELOPMENT OF THE COMPOSITION AND TECHNOLOGY OF GEL WITH CALENDULA TINCTURE AND DEXPANTENOL FOR THE TREATMENT OF BURN WOUNDS

3.1. Development of technology of homeopathic matrix tincture of calendula

Matrix tincture of calendula was prepared according to method 4a SPhU using 70% ethyl alcohol. Preparation was carried out by maceration method in a ratio of 1:10 [58, 59, 89].

Dried flowers were pre-ground into a coarse powder. 10 g of crushed calendula flowers, which meets the requirements of NTD, weighed into a mortar and poured half the amount of prepared 70 % alcohol (50.0), mixed thoroughly. The resulting mass was transferred to a glass vial, the remaining alcohol was added and left to settle for 8 days with frequent stirring (for the most complete impregnation of raw materials with alcohol) in a dark and cool place at 16 °C. After 8 days, the liquid was drained, and the mass was pressed out with a press strainer. The resulting liquid was left to settle for 8 days, after which the liquid was filtered. The block scheme of the preparation of homeopathic calendula tincture is presented in fig. 3.1.

Calendula tincture is a yellowish-green liquid, a peculiar odor, with a bitter taste, without mechanical inclusions. The content of medicinal substances in calendula tincture is 1:10. This tincture corresponds to the first decimal dilution and is the source for further dilutions and other dosage forms preparation.

The results of organoleptic, physical and chemical study of the obtained tincture of calendula X1 are presented in table 3.1.

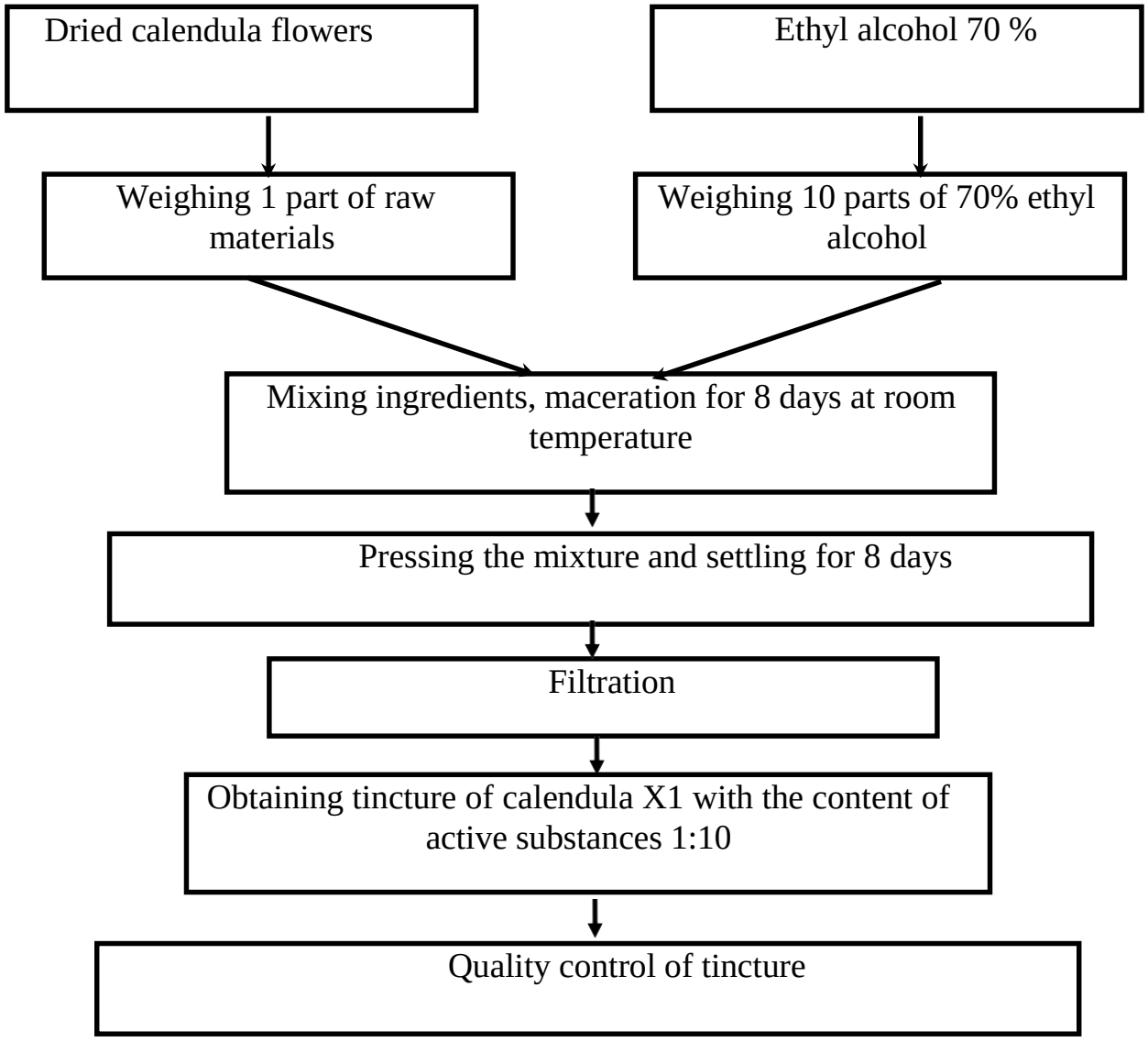


Fig. 3.1. Block scheme of making a matrix tincture of calendula X1

Table 3.1

Organoleptic, physical and chemical quality indicators of homeopathic calendula tincture

№	Indicators	Result
1.	Appearance	Yellow-green liquid
2.	Taste, smell	Odorless, bitter taste
3.	Density, kg/m^3	0.8679 ± 0.0054

4.	Alcohol content, %	68.50 ± 0.05
5.	Dry residue, %	2.8 ± 0.3
6.	Quantitative content of tannins, %	3.53 ± 0.08
7.	Quantitative content of flavonoids, %	0.41 ± 0.05

In order to determine the main groups of biologically active substances in the composition of the obtained calendula tincture, their identification was carried out using well-known color reactions. The results are presented in table 3.2.

Table 3.2

Results of identification reactions for tannins, saponins and flavonoids

№	Reactant	Observations
1.	1 % gelatin solution	The appearance of turbidity, which disappears when an excess of reagent is added
2.	Solution of lead acetate	Formation of a yellow precipitate
3.	1 % quinine chloride solution	The appearance of an amorphous precipitate
4.	Foaming reaction	Foam is formed, equal in volume and stability
5.	Cyanidin test	Pink coloring
6.	10 % ammonium hydroxide solution	Pale yellow coloring

Based on the results of qualitative reactions in the obtained calendula tincture X1 by maceration method, tannins, saponins and flavonoids were identified.

The proposed reactions are highly sensitive and can be recommended for standardization of matrix calendula tincture X1.

Capillary analysis of the obtained calendula tincture X1 was carried out by the Plan method according to the guidelines of Dr. W. Schwabe [89].

Filter paper was cut into strips 2 cm wide and 25 cm long in the direction perpendicular to the paper texture and hung in a cylindrical glass vessel 5 cm high and 3 cm in diameter so that the ends of the paper strips touched the bottom of the vessel.

5 ml of calendula tincture X1 was placed in the vessel. They put it in a moderately warm room for 24 hours, took out the strips, dried them and examined them in daylight. Capillary analysis gave the following results: rise height - 10.2 cm at 56 % relative humidity and 20°C. The data are presented in table 3.3.

Table 3.3.

Results of capillary analysis of calendula tincture X1

Zone	**Color in visible light**
Upper 5.5 cm	4 cm - water zone, pale brown; 0.3 cm - transparent, greenish-brown area; 0.2 cm - opaque dark green stripe; 1 cm - green area, opaque
Lower 2.5 cm	1 cm - yellowish-green zone; 1 cm - green area, opaque; 0.5 cm - the yellowish area
Base 2.2 cm	colorless

Luminescence: blue with greenish and light red stripes.

As can be seen from the results of capillary analysis, the tincture meets the requirements of management and can be used for the preparation of other dosage forms, including gel for the treatment of burn wounds.

3.2. Development of gel composition with calendula tincture

In order to substantiate the composition of the gel for the treatment of burns, which includes two APIs - calendula tincture and dexpanthenol, we have produced 6 model samples of bases on different agents in the concentration range from 0.5 to 5 % (table 3.4).

The calculated amount of gel agents was weighed and distributed on the surface of purified water in a thin layer for swelling and dissolution, the required amount of neutralizer was added to obtain a homogeneous gel mass [48, 49].

The bases of CMC sodium and sodium alginate were prepared according to general rules.

Table 3.4

Compositions of samples of gel bases

Components	**Sample number**					
	1	**2**	**3**	**4**	**5**	**6**
Carbopol 980 NF	0.5	-	-	-	-	1.0
Carbopol 934P	-	0.5	-	-	1,0	-
Sodium alginate	-	-	2.0	-	-	-
Sodium carboxymethylcellulose	-	-	-	5.0		-
Triethanolamine	0.5	0,5	-	-	1,0	1.0
Purified water	up to 100.0	up to 100.0	up to 100.0	up to 100.0	up to 100.0	up to 100.0

The obtained gel bases were checked in terms of organoleptic control within 1 month, in particular, homogeneity of the gel, color, signs of delamination, as well as the growth of bacteria and mold fungi has been observed (table 3.5).

Table 3.5

Quality indicators of the obtained gel samples during storage

Sample	Observation results
1	Homogeneous, transparent colorless gel
2	Homogeneous, transparent colorless gel
3	Drying during storage
4	Destruction of the gel structure. Growth of microorganisms
5	Homogeneous, transparent colorless gel
6	Homogeneous, transparent colorless gel

According to the results of experimental studies of base samples, samples containing gelling agents 980 NF and 934 P were selected for further research. Samples 1, 2, 5, 6 had satisfactory properties that did not change throughout the entire observation period. On the basis of the conducted studies, we proposed gel compositions with selected gelling agents and APIs, the concentration of which was selected according to the literature data (table 3.6).

Table 3.6

Compositions of model gel samples

Components, g	Sample number					
	1	**2**	**3**	**4**	**5**	**6**
Calendula tincture X1	5.0	5.0	5.0	5.0	5.0	5.0
Dexpanthenol	4.0	4.0	4.0	4.0	4.0	4.0
Carbopol 980 NF	0.5	1.0	-	-	-	1.0
Carbopol 934P	-	-	0.5	1.0	1.0	-
Propylene glycol	-	5.0	-	5.0	-	-
Triethanolamine	0.5	1.0	0.5	1.0	1.0	1.0

Purified water	up to 100.0	up to 100.0	up to 100.0	up to 100.0	up to 100.0	up to 100.0

The obtained samples were prepared by adding calendula tincture to the gel base by mixing (samples 1, 3, 5, 6) and after dissolving dexpanthenol in propylene glycol (samples 2 and 4).

Propylene glycol is known to be an effective moisturizing and moisture-retaining component, so it is very often added to the composition of medicines. The main feature is its ability to maintain the required level of moisture, extracting moisture from the environment, including from the wound, preventing drying [63].

The prepared gel samples were tested for colloidal and thermal stability immediately after preparation and after 1, 14 and 30 days of storage. The results are presented in table 3.7.

Table 3.7

Stability results of model gel samples

Stability	**Shelf life, days**	**Sample number**					
		1	**2**	**3**	**4**	**5**	**6**
Colloidal	1	+	+	+	+	+	+
	14	-	+	-	+	+	+
	30	-	+	-	+	+	+
Thermal stability	1	+	+	-	+	+	+
	14	-	+	-	+	+	+
	30	-	+	-	+	-	-

According to the results of the study of the stability of model samples, satisfactory performance was observed for samples 2 and 4, where propylene glycol was introduced into the composition. The stability indicators of samples 5 and 6 had satisfactory characteristics, but on the 30th day they showed signs of stratification of the system. Thus, we chose samples 2, 4, 5, and 6 for further research.

It is known from the literature that one of the important indicators of the quality of gels intended for application to mucous membranes is osmotic activity and pH. The optimal pH range is 5.5-6.0. Therefore, we have determined these indicators for selected gel formulations (table 3.8).

Table 3.8

Physical and chemical parameters of model gel samples

Indicator	**Results for samples**			
	2	**4**	**5**	**6**
Appearance	Transparent yellowish gel with a specific odor			
Homogeneity	Homogeneous	Homogeneous	Homogeneous	Homogeneous
pH	5.80 ± 0.05	5.85 ± 0.05	6.10 ± 0.05	6.05 ± 0.05
Osmotic activity,%	62.4 ± 0.5	68.5 ± 0.5	44.8 ± 0.5	48.1 ± 0.5

Based on the indicators of osmotic activity and pH, for further studies, samples 2 and 4 were selected. The compositions are presented in table 3.9.

Table 3.9

Compositions of model samples of gel with calendula tincture

Components, g	**Sample number**	
	1	**2**
Calendula tincture X1	5.0	5.0
Dexpanthenol	4.0	4.0
Carbopol 934P	1.0	-
Carbopol 980 NF	-	1.0
Propylene glycol	5.0	5.0
Triethanolamine	1.0	1.0
Purified water	up to 100.0	up to 100.0

Therefore, our further research will be aimed at choosing the optimal composition of the developed gel.

3.3. Biopharmaceutical studies of gel with calendula tincture and dexpanthenol

The next stage of our research was to study the bioavailability of the developed samples of gels based on carbopol of different brands, which was tested by the degree of release of flavonoids in agar gel (diffusion method).

Iron (III) chloride was used as an indicator for the identification of flavonoids contained in the tincture [24]. The degree of release of phenolic compounds from the gels was assessed by the size of the colored zone (yellow color) formed around the well, which was measured using a ruler. The results are presented in fig. 3.2.

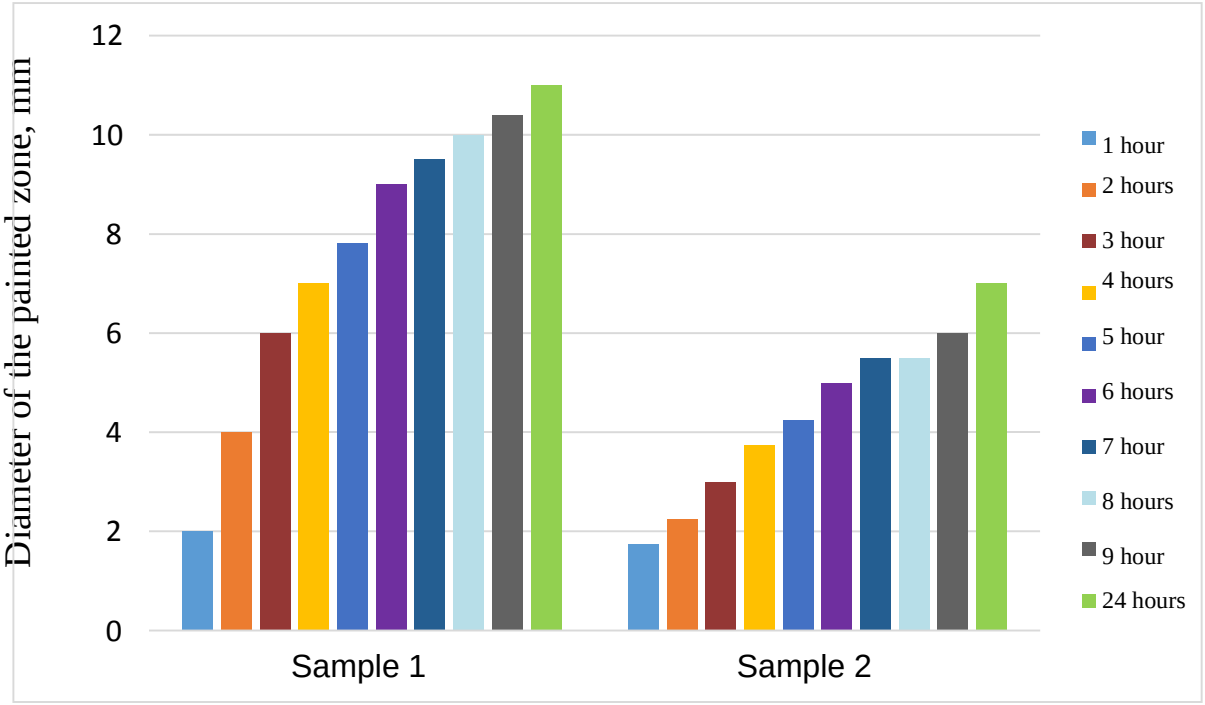


Fig. 3.2. Dynamics of phenolic compounds release from gel samples: Sample № 1 - carbopol 934 P; Sample № 2 - carbopol 980 NF.

As can be seen from the data presented in fig., in general, we can note the positive dynamics of the release of phenolic compounds from gels based on selected brands of carbopol. The maximum release was observed from gels based on carbopol 934 P, a slightly lower degree of release from the gel based on the brand of carbopol 980 NF.

Thus, the results of the research made it possible to substantiate the composition of the gel with calendula tincture for use in the treatment of burn wounds.

The composition of the extemporaneous gel (g):

Calendula tincture X1 - 5.0

Dexpanthenol - 4.0

Carbopol 934P - 1.0

Propylene glycol - 5.0

Triethanolamine - 1.0

Purified water - up to 100.0

3.4. Development of the technology of topical gel with calendula tincture and dexpanthenol in pharmacy condition

On the basis of the conducted studies, the composition of the gel is theoretically and experimentally substantiated. It is known that the therapeutic efficacy, quality and stability of the drug is directly dependent on the technology of its manufacture as one of the most important biopharmaceutical factors.

The main stages of gel preparation include: preparation of the gel base, preparation of the API mixture in propylene glycol, its introduction into the gel composition, homogenization, packaging and labeling. The scheme of gel preparation in the conditions of pharmacy production is given on fig. 3.3.

The gel production technology consists of the following stages:

Preparatory works. The first stage of the technological process of any medicinal product, regardless of its dosage form, is the sanitary preparation of the premises, equipment and personnel. The premises where homeopathic medicines are manufactured must be subjected to wet cleaning using detergents and disinfectants registered and approved for use by the Ministry of Health of Ukraine. All surfaces of workplaces, equipment, apparatus used in drug technology must be washed and treated with disinfectants.

Preparation of the gel base

The calculated amount of purified water is measured into a beaker, and a weighed amount of carbopol 934P is distributed on its surface in a thin layer, left to swell and dissolve. The calculated amount of triethanolamine is added to the resulting cloudy solution with stirring until a transparent gel mass is formed.

Preparation of the API mixture in propylene glycol

Propylene glycol is weighed, in which dexpanthenol and calendula tincture X1 are dissolved. Mix thoroughly by a mixer.

Preparation of gel

A mixture of propylene glycol solution of APIs is added to the gel base. Thoroughly mixed with a pharmacy mixer RT-2 until a homogeneous gel mass is formed.

Gel quality control

Gel quality control is carried out by appearance, uniformity, absence of mechanical inclusions, pH value, identification of the main groups of biologically active substances.

Packing, packaging and labeling of the gel

The gel is packaged in dark glass jars or suitable containers of the appropriate weight. They are issued with an “External” label, on which the name of the medicinal product, weight and date of manufacture are indicated. Also comes with an additional label “Keep in a cool place”, “Keep out of reach of children”.

Thus, a complex of physical, chemical and biopharmaceutical studies contributed to the selection of the optimal composition and the development of gel technology recom-

mended for the treatment of burn wounds.

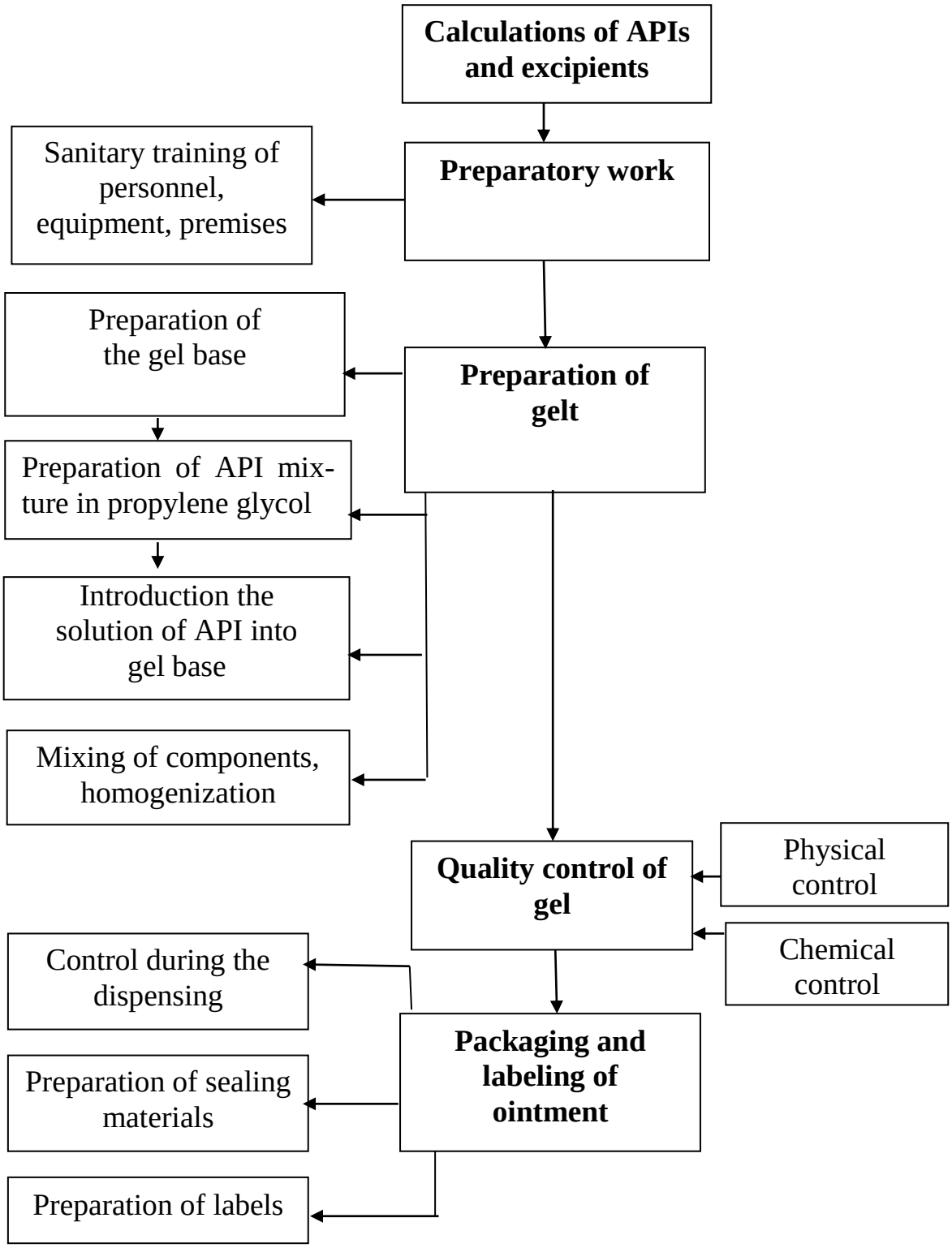


Fig. 3.3. Technological scheme for the production of gel in a pharmacy condition

CONCLUSIONS

1. Technology for obtaining homeopathic tincture of calendula X1 using the maceration method has been developed
2. Methods for qualitative and quantitative analysis of the active ingredients of calendula tincture, in particular: flavonoids, tannins, saponins, have been developed. The main physico-chemical parameters of the obtained calendula tincture were studied.
3. Theoretically and experimentally substantiated the composition of the gel with calendula tincture and dexpantnol, which provides the highest degree of release of phenolic compounds from the gel based on the results of diffusion into the agar gel. Carbopol 934P was chosen as a gelling agent, which meets the quality requirements of gels.
4. On the basis of experimental studies, a technology has been developed for the manufacture of a gel with calendula tincture and dexpanthenol in a pharmacy condition

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GENERAL CONCLUSIONS

1. Based on the results of the analysis of literature sources, the prospects of creating a combined drug based on calendula tincture and dexpanthenol in the form of topical gel in the treatment of burn wounds are substantiated.
2. The information on the properties of calendula medicines, their advantages and the main groups of BAS is generalized.
3. The most commonly used substances as the gel agent, namely: carbopol, sodium alginate, sodium carboxymethylcellulose were selected. According to the results of research, carbopol 934P was selected.
4. Based on the study of organoleptic, physicochemical and biopharmaceutical properties of gel samples, the rational composition of the gel with API - calendula tincture and dexpanthenol is substantiated.
5. Developed drug in the form of topical gel with anti-inflammatory, healing, antimicrobial action may be recommended to expand the range of extemporaneous drugs for the treatment of burn wounds.

REFERENCES

1. Abiko, Y.; Tomikawa, M.; Shimizu, M. Enzymatic conversion of pantothenylalcohol to pantothenic acid. *J. Vitaminol. (Kyoto)* 1969, *15*, 59–69.
2. Baron, J.M.; Glatz, M.; Proksch, E. Optimal support of wound healing: New insights. Dermatology 2020, 1–8.
3. Biro K., Thaci I. D., Ochsendorf F. R. et al. Efficacy of dexpanthenol in skin protection against irritation: a double-blind, placebo-controlled study. *Contact Dermatitis.* 2013; 49: 80-84.
4. Björklund, S.; Pham, Q.D.; Jensen, L.B.; Knudsen, N.Ø.; Nielsen, L.D.; Ekelund, K.; Ruzgas, T.; Engblom, J.; Sparr, E. The effects of polar excipients transcutol and dexpanthenol on molecular mobility, permeability, and electrical impedance of the skin barrier. *J. Colloid Interface Sci.* 2016, *479*, 207–220.
5. Camargo F. B. Jr., Gaspar L. R., Maia Campos P.M. Skin moisturizing effects of panthenol-based formulations. *J Cosmet Sci.* 2011; 62: 361-370.45
6. Camargo, F.B., Jr.; Gaspar, L.R.; Maia Campos, P.M. Skin moisturizing effects of panthenol-based formulations. *J. Cosmet. Sci.* 2011, *62*, 361–370.
7. Dinda M., Mazumdar S., Das S., Ganguly D., Dasgupta U.B., Dutta A., Jana K., Karmakar P. The Water Fraction of Calendula officinalis Hydroethanol Extract Stimulates In Vitro and In Vivo Proliferation of Dermal Fibroblasts in Wound Healing. *Phytother. Res.* 2016; 30:1696–1707.
8. Ebner F., Heller A., Rippke F., Tausch I. Topical use of dexpanthenol in skin disorders. *Am J Clin Dermatol*. 2012; 3: 427-433.
9. Efstratiou E., Hussain A.I., Nigam P.S., Moore J.E., Ayub M.A., Rao J.R. Antimicrobial activity of Calendula officinalis petal extracts against fungi, as well as Gram-negative and Gram-positive clinical pathogens. *Complement. Ther. Clin. Pract.* 2012; 18:173–176.

10. Ernst E. A systematic review of systematic reviews of homeopathy / E. Ernst// Blackwell science LTD. – 2012.-№54.-P. 577-582.
11. European Pharmacopoeia. – 7-th ed. – Strasbourg: European Directorate for the Quality of Medicines & Healthe Care, 2011. – Suppl. 7.2. – 3774 p.
12. Extreme homeopathic dilutions retain starting materials: a nanoparticulate perspective / P. S. Chikramane, A. K. Suresh, J. R. Bellare, S. G. Kane. Homeopathy. 2012. Vol. 99, № 4. P. 231–242.
13. Giménez-Arnau, A. Standards for the Protection of Skin Barrier Function. Curr. Probl. Dermatol. 2016, 49, 123–134.
14. Givol O., Kornhaber R., Visentin D., Cleary M., Haik J., Harats M. A systematic review of Calendula officinalis extract for wound healing. *Wound Repair Regen*. 2019;27: 548–561.
15. Gonzalez A. C., Costa T. F., Andrade Z. A., Medrado A. R. Wound healing—A literature review. *An. Bras. Dermatol*. 2016; 91: 614–620.
16. Heise R., Scazik C., Marquardt Y. et al. Dexpanthenol modulates gene expression in skin wound healing in vivo. *Skin Pharmacol Physiol*. 2012; 25: 241-248.
17. Heise, R.; Schmitt, L.; Huth, L.; Krings, L.; Kluwig, D.; Katsoulari, K.V.; Steiner, T.; Hölzle, F.; Baron, J.M.; Huth, S. Accelerated wound healing with a dexpanthenol-containing ointment after fractional ablative CO_2 laser resurfacing of photo-damaged skin in a randomized prospective clinical trial. *Cutan. Ocul. Toxicol.* 2019, *38*, 274–278.
18. Helaly, G.F.; Abd El-Aziz, A.A.; Sonbol, F.I.; El-Banna, T.E.; Louise, N.L. Dexpanthenol and propolis extract in combination with local antibiotics for treatment of Staphylococcal and Pseudomonal wound infections. *Arch. Clin. Microbiol.* 2011, *2*, 1–15.
19. Herbert A. R. The Principles and Art of Cure by Homoeopathy. 3ed. –New Delhi, 2015. – 325 p.

20. Hormozi M., Gholami M., Babaniazi A., Gharravi A.M. Calendula officinalis stimulate proliferation of mouse embryonic fibroblasts via expression of growth factors TGFβ1 and bFGF. *Inflamm. Regen.* 2019; 39:7.
21. Jahdi F., Khabbaz A.H., Kashian M., Taghizadeh M., Haghani H. The impact of calendula ointment on cesarean wound healing: A randomized controlled clinical trial. *J. Fam. Med. Prim. Care*. 2018;7:893–897.
22. Klasen H. History of burns. – 2004. – 632 p.
23. Kluger, N.; De Cuyper, C. A practical guide about tattooing in patients with chronic skin disorders and other medical conditions. Am. J. Clin. Dermatol. 2018, 19, 167–180.
24. Kuhlmann, M.; Wigger-Alberti, W.; Mackensen, Y.; Ebbinghaus, M.; Williams, R.; Krause-Kyora, F.; Wolber, R. Wound healing characteristics of a novel wound healing ointment in an abrasive wound model: A randomised, intra-individual clinical investigation. *Wound Med.* 2019, *24*, 24–32.
25. Nicolaus C., Junghanns S., Murillo R., Merfort I. Triterpene alcohols from Calendula officinalis L. flowers and in vitro studies on their wound healing activity. *Planta Med.* 2014;80: P 2B63.
26. Olsavszky, R.; Nanu, E.A.; Macura-Biegun, A.; Kurka, P.; Trapp, S. Skin barrier restoration upon topical use of two 5% dexpanthenol water-in-oil formulations on freshly tattooed skin: Results from a single-blind prospective study. *Wounds Int.* 2019, *10*, 33–39.
27. Preethi K. C., Kuttan R. Wound healing activity of flower extract of Calendula officinalis. *J. Basic Clin. Physiol. Pharmacol*. 2009; 20:73–79.
28. Proksch E., Nissen H.P. Dexpanthenol enhances skin barrier repair and redusec inflammation after sodiom lauryl sulphate-induced irritation. *J Dermatolog Treat*. 2012; 13: 173-178.
29. Proksch, E.; Berardesca, E.; Misery, L.; Engblom, J.; Bouwstra, J. Dry skin

management: Practical approach in light of latest research on skin structure and function. *J. Dermatol. Treat.* 2019, 1–7.

30. Proksch, E.; de Bony, R.; Trapp, S.; Boudon, S. Topical use of dexpanthenol: A 70th anniversary article. J. Dermatol. Treat. 2017, 28, 766–773.
31. Proksch, E.; de Bony, R.; Trapp, S.; Boudon, S. Topical use of dexpanthenol: A 70th anniversary article. *J. Dermatol. Treat.* 2017, *28*, 766–773.
32. Proksch, E.; Nissen, H.P. Dexpanthenol enhances skin barrier repair and reduces inflammation after sodium lauryl sulphate-induced irritation. *J. Dermatol. Treat.* 2002, *13*, 173–178.
33. Research on homeopathy: state of the art / H. Walach, W. B. Jonas, J. Ives et al. *Journal of Alternative and Complementary Medicine*. 2015. Vol. 11, № 5. P. 813-829.
34. Ross S., Simpson C. R., McLay J. S. Homoeopathic and herbal prescribing in general practice in Scotland. *Br. J. Clin. Pharmacol*. 2016. Vol. 62, № 6. P. 647-652.
35. Sen C. K. Human Wounds and Its Burden: An Updated Compendium of Estimates. *Adv. Wound Care*. 2019; 8:39–48.
36. Stettler, H.; Kurka, P.; Lunau, N.; Manger, C.; Böhling, A.; Bielfeldt, S.; Wilhelm, K.P.; Dähnhardt-Pfeiffer, S.; Dähnhardt, D.; Brill, F.H.; et al. A new topical panthenol-containing emollient: Results from two randomized controlled studies assessing its skin moisturization and barrier restoration potential, and the effect on skin microflora. *J. Dermatol. Treat.* 2017, *28*, 173–180.
37. Stettler, H.; Kurka, P.; Wagner, C.; Sznurkowska, K.; Czernicka, O.; Böhling, A.; Bielfeldt, S.; Wilhelm, K.P.; Lenz, H. A new topical panthenol-containing emollient: Skin-moisturizing effect following single and prolonged usage in healthy adults, and tolerability in healthy infants. *J. Dermatol. Treat.* 2017, *28*, 251–257.

38. Stüttgen, G.; Krause, H. Die percutane Absorption von Tritium-markiertem Panthenol bei Mensch und Tier. *Arch Klin. Exp. Derm.* 1960, *209*, 578–582.
39. Udompataikul M., Limpa-O-Vart D. Comparative trial of 5% dexpanthenol in water-in-oil formulation with 1% hydrocortisone ointment in the treatment of childhood atopic dermatitis: a pilot study. *J Drugs Dermatol.* 2014; 11: 366-374.
40. Van Koppen C.J., Hartmann R.W. Advances in the treatment of chronic wounds: A patent review. //Expert Opin. Ther. Pat. - 2015; 25:931–937.Verma D. K. Homeopathy - The Science of Ultra-Dilution and its PossibleMechanism. *Homoeopathic Links.* 2017. Vol. 24, № 4. P. 254-258.
41. Vowden K. Wound management: the considerations involved in dressing selection. In: Trends in Wound Care Volume 4. – 2006. Cutting, K (Ed) London,Quay Books.
42. Vyas K., Vasconez H.C. Wound healing: Biologics, skin substitutes, biomembranes and scaffolds. /Healthcare. 2014;2: 356–400.
43. Wiederholt T., Heise R., Skazik C. et al. Calcium pantothenate modulates gene expression in proliferating human dermal fibroblast. *Exp Dermatol.* 2019; 18: 969-978.
44. Wilkins RG, Unverdorben M. Wound cleaning and wound healing: a concise review. // Adv Skin Wound Care. 2013 Apr; 26(4):160-3.
45. Wollina, U. Zur klinischen Wirksamkeit von Dexpanthenol. *Kosm Med.* 2001, *4*, 180–184.
46. Wollina, U.; Kubicki, J. Multiaktive Eigenschaften von Dexpanthenol-haltigen Externa. *Kosm Med.* 2007, *3*, 14–18.
47. Zhai, H.; Maibach, H.I. Effect of occlusion and semi-occlusion on experimental skin wound healing: A reevaluation. Wounds 2007, 19, 1–8. Available online: https://www.woundsresearch.com/article/7894 (accessed on 23 April 2020).
48. Анурова М. Н., Бахрушина Е. О., Демина Н. Б. Обзор современных гелеоб-

разователей в технологии лекарственных форм. Химико- фармацевтический журнал. 2015. Т. 49. № 9. С. 57–64.

49. Багатофункціональні інгредієнти для створення м'яких і рідких лікарських форм - Київ, 2017. – Карборол ETD 2020 NF – ИМСД України.
50. Варпаховская И., Серебряков С. Гомеопатический ренессанс. *Ремедиум*. 2010. №11. С. 3-14.
51. Ганеман С. Лечение хронических болезней и гомеопатическая доктрина: пер. с исп., нем., англ. Калининград: ОЛЛО, 2003. 230 с.
52. Ганеман С. Органон врачебного искусства. М.: Атлас, 2012. 206 с.
53. Герасимова Л. И., Жижин В. Н. и др. Термические и радиационные ожоги. – М.: Медицина, 1996. – 246 с.
54. Гомеопатическая фармация сегодня: проблемы и пути их решения / Т.А. Сокольская [и др.]. *Фармация*. 2012. №1. С. 40-42.
55. Гомеопатические лекарственные средства / А.В. Патудин [и др.]. М.: Знак, 2011. 352 с.
56. Гомеопатические препараты в терапии острых респираторных инфекций у детей /Абрамович М. Л [и др.]. *Практика педиатра*. 2013. №5. С. 15 - 19.
57. Гуцол Л. П., Мощич О. П. Актуальність застосування гомеопатії як холістичного методу в діяльності лікаря загальної практики – сімейної медицини. *Сімейна медицина*. 2013. 4 (48). С. 112-114.
58. Державна Фармакопея України : в 3 т. / ДП «Український науковий фармакопейний центр якості лікарських засобів». 2-е вид. Харків : Державне підприємство «Український науковий фармакопейний центр якості лікарських засобів», 2014. Т. 3. 732 с.
59. Державна Фармакопея України : в 3 т. / ДП «Український науковий фармакопейний центр якості лікарських засобів». 2-е вид. Харків : Державне-підприємство «Український науковий фармакопейний центр якості лікарсь-

ких засобів», 2014. Т. 2. 724 с.

60. Державна Фармакопея України. Допов. 1. / ДП «Науково-експертний фармакопейний центр». 1–е вид. Харків : РІРЕГ, 2004. 520 с.
61. Державна Фармакопея України. Допов. 2. / ДП «Науково-експертний фармакопейний центр». 1–е вид. Харків : РІРЕГ, 2008. 618 с.
62. Державний реєстр лікарських засобів України / МОЗ України, 2018. URL: http://www.drlz.com.ua/ (дата звернення: 01.05.2021).
63. Допоміжні речовини в технології ліків: вплив на технологічні, споживчі, економічні характеристики і терапевтичну ефективність: навч. посіб. для студ. вищ. фармац. навч. закл. / І. М. Перцев та ін. Харків : Золоті сторінки, 2010. – 600 с.
64. Зубицька Н. П., Желясков Р. П. Лікуємо нагідками. Тернопіль: Навчальна книга-Богдан, 2003. 88 с.
65. Иванов В. И. Лекарственные средства в народной медицине. М. : Военное издательство, 1992. 448 с.
66. Кожевникова, Е.В. Гомеопатия для всех. Волгоград: изд-во ВолгГМУ, 1999. 176 с.
67. Компендіум. Лікарські препарати, 2021. URL: https://compendium.com.ua (дата звернення: 01.05.2021).
68. Корвякова О. А. Создание концепции гомеопатической фармации. *Новая аптека.* 2000. №4. С.8-14.
69. Криошина Н. А. Приверженность пациентов гомеопатическому методу лечения и их оценка эффективности применения гомеопатических лекарственных средств. *Вестн. новых мед. технологий*. 2012. Т 19, № 2. С. 166-167.
70. Куркин В. А. Фармакогнозия: Учебник для студентов фармацевтических вузов (факультетов). Самара: ООО «Офорт», 2019. 1278 с.
71. Куркина А. В. Флавоноиды фармакопейных растений: монография; Самара:

ООО «Офорт», ГБОУ ВПО СамГМУ Минздравсоцразвития России, 2012. – 290 с.

72. Лебеда А. П., Осетров В. Д. Здоров’я ділової людини: практичний посібник з фітотерапії і гомеопатії. К. : Академперіодика, 2002. 174 с.
73. Лікарські рослини в таблицях та схемах: Навчальний посібник. / Укдадачі: А68 О. О. Аннамухаммедова, А. О. Аннамухаммедов. - Житомир: Вид-во ЖДУ ім. І. Франка, 2016 - 187 с.
74. Лікарські рослини: Енциклопедичний довідник / Відп. ред. А. М. Гродзінський.— К.: Видавництво «Українська Енциклопедія» ім. М. П. Бажана, Український виробничо-комерційний центр «Олімп», 1992. 544 с.
75. Марчишин С. М., Сушко Н. О. Лікарські рослини Тернопільщини. Тернопіль : Навчальна книга–Богдан, 2007. 312 с.
76. Мифтахутдинов С. Г. Гомеопатия и аллопатия: от противопоставления к интеграции. *Поликлиника*. 2016. №4. С.29-31.
77. Нагідки лікарські//Лікарські рослини: Енциклопедичний довідник/ Відп. ред. А.М. Гродзінський.- Київ: Видавництво «Українська Енциклопедія» ім. М.П. Бажана, Український виробничо-комерційний центр «Олімп», 1992.- С.291.
78. Ожоги: Руководство для врачей / Под ред. Б.С. Вихриева, В.М. Бурмистрова. – 2-е изд. перераб. и доп. – Л.: Медицина, 1986. – 272 с.
79. Парамонов Б.А., Порембский Я.О., Яблонский В.Г. Ожоги: Руководство. – М.: СпецЛит., 2000. 480 с.
80. Петров С.В. Общая хирургия: Учеб. пособие. – 3-е изд., перераб. и доп. – М.: ГЭОТАР-Медиа, 2007. – 768 с.
81. Семенова А.И. Душа гомеопатии. М.: Знак, 2000, 185 с.
82. Фармакогнозия : базовый учеб. для студентов высш. фармац. учеб. заведения (фармац. фак.) IV уровня аккредитации ; изд. дораб. и доп. [авториз. пер. с укр. яз.] / В.С. Кисличенко, И.А. Журавель, С.М. Марчишин, О.П.

Хворост ; под ред. В.С. Кисличенко. — Харьков :НФаУ : Золотые страницы, 2017. 776 с.

83. Фармацевтическая гомеопатия: Методические рекомендации для самостоятельной работы студентов медицинского факультета / Т.А. Лотош, О. В. Жукова, И. А. Виноградова. Петрозаводск: Издательство ПетрГУ. 2014. 56 с.
84. Хамаганова И. В., Кашеваров Д. Ф. Топические средства в терапии аллергодерматозов у детей. *Медицинский Совет*. 2014; (6):46-53.
85. Хірургія / За ред. Я.С. Березницького, М.П. Захараша, В.Г. Мішалова, В.О. Шідловського. – Дніпропетровськ: РВА „Дніпро-VAL”, 2006. – Т.1. – 443 с.
86. Цимбал Н. М. Основи фітопрофілактики: навчальний посібник для вузів. Тернопіль : ТДПУ, 2000. 144 с.
87. Чикин В. В. Метилпреднизолона ацепонат и декспантенол в топической терапии больных атопическим дерматитом. *Вестник дерматологии и венерологии.* 2014 №5. С. 112-116.
88. Шаршунова М., Шварц В., Михалец Ч. Тонкослойная хроматография в фармации и клинической биохимии пер. с словацк. под. ред. В.Г. Березкина, С.Д. Соколова, в 2 ч. М.: Мир, 1980. 622 с.
89. Швабе В. Гомеопатические лекарственные средства. Руководство поописанию и приготовлению / под ред. В. И. Рыбака; пер. с нем. – М. : Московское научное общество врачей-гомеопатов, 1967. – 373 с.
90. Шелудько Л. П. Куценко Н. І.. Лікарські рослини (селекція і насінництво). Полтава, 2013. 476 с.

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APPROVED
The Head of Department
Technology of Drugs
Tatyana YARNYKH

" 18 " of June 2021

ASSIGNMENT
FOR QUALIFICATION WORK
OF AN APPLICANT FOR HIGHER EDUCATION

Mohamed Medkhat Ahmed Mohamed ELBANNA

1. Topic of qualification work: «Development of the composition and technology of extemporaneouse topical gel for the treatment of burn wounds», supervisor of qualification work: Ganna YURYEVA, PhD, assoc. prof.,

approved by order of NUPh from "17th" of February 2022 № 76.

2. Deadline for submission of qualification work by the applicant for higher education: April 2022.

3. Outgoing data for qualification work: Object of researches: homeopathic tincture calendula D1, dexpanthenol, model samples of gel with calendula tincture and dexpanthenol.

4. Contents of the settlement and explanatory note (list of questions that need to be developed):
- to analyze the literature data on the prospects of using calendula tincture and dexpanthenol in the treatment of burns; - to analyze the pharmaceutical market of Ukraine for the availability of medicines for the treatment of burn wounds; - theoretically and experimentally substantiate the composition of the gel with anti-inflammatory, antimicrobial action; - to carry out physicochemical, biopharmaceutical and microbiological studies of gel sections; – to develop a technology for the manufacture of the gel in pharmacy.

5. List of graphic material (with exact indication of the required drawings):
tables – 4
figures – 3

6. Consultants of chapters of qualification work

Chapters	Name, SURNAME, position of consultant	Signature, date	
		assignment was issued	assignment was received
I Chapter	Ganna YURYEVA, ass. prof. of higher education institution of department Technology of Drugs	18 June 2021	18 June 2021
II Chapter	Ganna YURYEVA, ass. prof. of higher education institution of department Technology of Drugs	10 September 2021	10 September 2021
III Chapter	Ganna YURYEVA, ass. prof. of higher education institution of department Technology of Drugs	5 December 2021	5 December 2021

7. Date of issue of the assignment: ___18 of June 2021_____

CALENDAR PLAN

№ з/п	Name of stages of qualification work	Deadline for the stages of qualification work	Notes
1.	Analysis of literature data. Treatment of nervous system diseases, analyze of pharmaceutical market of homeopathic drugs and their dosage forms.	September – November 2021	**done**
2.	Researches of active substances and excipients	December 2021 – February 2022	**done**
3.	Justification of the results	March 2022	**done**
4.	Registration of qualification work	April 2022	**done**

An applicant of higher education_____ Mohamed Medkhat Ahmed Mohamed ELBANNA

Supervisor of qualification work _____ Ganna YURYEVA

ВИТЯГ З НАКАЗУ № 76

По Національному фармацевтичному університету
від 17 лютого 2022 року

1. нижченаведеним студентам 5-го курсу 2021-2022 навчального року, навчання за освітньо-кваліфікаційним рівнем «магістр», галузь знань 22 охорона здоров'я, спеціальності 226 – фармація, промислова фармація освітня програма – фармація, денна форма навчання (термін навчання 4 роки 10 місяців), які навчаються за контрактом, затвердити теми магістерських робіт:

№ з/п	Прізвище студента	Тема магістерської роботи	Посада, прізвище та ініціали керівника	Рецензент магістерської роботи
по кафедрі технології ліків				
1.	Ельбанна Мохамед Медхат Ахмед Мохамед	Розробка складу та технології екстемпорального гелю для місцевого застосування у лікуванні опікових ран Development of the composition and technology of extemporaneouse topical gel for the treatment of burn wounds	доц. Юр'єва Г.Б.	доц. Степаненко С.В.

Підстава: подання декана, згода ректора.

Ректор

Вірно. Секретар

F A 2.2.1-32-353

REVIEW

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

Mohamed Medkhat Ahmed Mohamed ELBANNA

on the topic: «Development of the composition and technology of extemporaneouse topical gel for the treatment of burn wounds»

Relevance of the topic. According to the World Health Organization, it is estimated that each year approximately 11 million people suffer from burn wounds, 180,000 of whom die because of such injuries. Regardless of the factors causing burns, these are complicated wounds that are difficult to heal and are associated with high mortality rates. Medical care of a burn patient requires a lot of commitment, experience, and multidirectional management, including surgical activities and widely understood pharmacological approaches. Despite many preventive measures, various types of complications may arise during the therapeutic process. The moist wound environment itself promotes adhesion, the multiplication of microorganisms, and the development of infection, which can be both exogenous and endogenous. Additionally, the appearance of secondary infections negatively affects the general condition of the patient, prolongs hospitalization and convalescence, while significantly increasing the cost of treatment. Currently, burn wounds still pose many difficulties. This is because the wound itself requires frequent dressing changes. Some of the dressings adhere tightly to the wound, especially to the burned wound surface. Changing the dressing can lead to new epithelial injuries, delayed healing, and suffering of the patient. In addition, the process of changing the dressing itself is lengthy and, on average, takes one hour. In this aspect, the use of drugs in the form of a gel is promising and reasonable.

Practical value of conclusions, recommendations and their validity. Obtained results became the basis for the creation of a new extemporaneous gel based on homeopathic tincture calendula and dexpanthenol with anti-inflammatory, antimicrobial and wound healing activity.

Assessment of work. The research methodology is based on the main principles reflected in the works of domestic and foreign authors. The study used a complex of physical, chemical, microbiological and biopharmaceutical studies of researches.

General conclusion and recommendations on admission to defend. The work was carried out at a high level, meets all requirements and can be submitted to the Examination Commission.

Scientific supervisor _____ Ganna YURYEVA

«12» of April 2022

F A 2.2.1-32-356

REVIEW
for qualification work of the master's level of higher education, specialty 226 Pharmacy, industrial pharmacy
Mohamed Medkhat Ahmed Mohamed ELBANNA
on the topic: «Development of the composition and technology of extemporaneouse topical gel for the treatment of burn wounds»

Relevance of the topic. Burns are a serious condition, irrespective of the origin, type, depth, or extent of the wound. Burns may occur due to a moment of inattention, and in situations beyond the victim's control. Because of the clinical conditions they present, they undoubtedly constitute a great challenge for people who provide professional care and help to injured patients. Patients with burns are at risk of developing various infectious and systemic complications. In addition to local changes, burns can also lead to systemic disturbances in the form of shock and burn disease, which is caused by pain, loss of blood plasma, and poisoning from the absorption of tissue protein breakdown products by the body. The infectious process and the type of infection in a burn is strongly related to the extent and depth of the burn, as well as the general condition of the patient, their age, comorbidities, and general lifestyle.

Theoretical level of work. To analyzed the pharmaceutical market of Ukraine for the availability of medicines for the treatment of burn wounds. The prospects for the use of homeopathic tincture of calendula and dexpanthenol in the treatment of burns are substantiated. The expediency of creating a gel of combined action has been considered.

Author's suggestions on the research topic. A complex of physical, chemical, biopharmaceutical and microbiological studies of gel samples was carried out in order to develop the optimal composition. On the basis of the results obtained, the technology of gel preparation in pharmacy condition was proposed.

Practical value of conclusions, recommendations and their validity. During this work, the literature data has been analyzed, the physical, chemical, and biopharmaceutical methods of research have been mastered. Results are of practical interest for the purpose to expand the range of available medicines.

Disadvantages of work. There are spelling mistakes, technical errors in the work.

General conclusion and assessment of the work. Qualification work of Mohamed Medkhat Ahmed Mohamed ELBANNA can be submitted to the Examination Commission for defense.

Reviewer _____ assoc. prof. Serhii STEPANENKO

«19» of April 2022

МІНІСТЕРСТВО ОХОРОНИ ЗДОРОВ'Я УКРАЇНИ
НАЦІОНАЛЬНИЙ ФАРМАЦЕВТИЧНИЙ УНІВЕРСИТЕТ

ВИТЯГ З ПРОТОКОЛУ № _10_
«28» квітня 2022 року
м. Харків

засідання кафедри
___технології ліків___

Голова: завідувачка кафедри, доктор фарм. наук, професор Тетяна ЯРНИХ
Секретар: канд. фарм. наук, доцент Володимир КОВАЛЬОВ

ПРИСУТНІ: професор Олександр КОТЕНКО, професор Юлія ЛЕВАЧКОВА, доцент Марина БУРЯК, доцент Оксана Данькевич, доцент Ганна ЮР'ЄВА, доцент Вікторія ПУЛЬ-ЛУЗАН, асистент Світлана ОЛІЙНИК

ПОРЯДОК ДЕННИЙ

1. **Про представлення до захисту до Екзаменаційної комісії кваліфікаційних робіт другого (магістерського) рівня вищої освіти**

СЛУХАЛИ:
Здобувача вищої освіти 5 курсу групи Фм17 (4.10д)англ-07 спеціальності 226 Фармація, промислова фармація Мохамеда Медхат Ахмед Мохамед ЕЛЬБАННА з доповіддю на тему «Розробка складу та технології екстемпорального гелю для місцевого застосування у лікуванні опікових ран» (науковий керівник: доцент Ганна ЮР'ЄВА).
УХВАЛИЛИ:
Рекомендувати до захисту кваліфікаційну роботу.

Голова засідання **Тетяна ЯРНИХ**

Секретар **Володимир КОВАЛЬОВ**

Ф А2.2.1-32-042

НАЦІОНАЛЬНИЙ ФАРМАЦЕВТИЧНИЙ УНІВЕРСИТЕТ

ПОДАННЯ
ГОЛОВІ ЕКЗАМЕНАЦІЙНОЇ КОМІСІЇ
ЩОДО ЗАХИСТУ КВАЛІФІКАЦІЙНОЇ РОБОТИ

Направляється здобувач вищої освіти Мохамед Медхат Ахмед Мохамед ЕЛЬБАННА 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 екстемпорального гелю для місцевого застосування у лікуванні опікових ран».

Кваліфікаційна робота і рецензія додаються.

Декан факультету _____ / Світлана КАЛАЙЧЕВА /

Висновок керівника кваліфікаційної роботи

Здобувач вищої освіти Мохамед Медхат Ахмед Мохамед ЕЛЬБАННА представив магістерську роботу, яка за об'ємом теоретичних та практичних досліджень повністю відповідає вимогам до оформлення магістерських робіт.

Керівник кваліфікаційної роботи

_____ Ганна ЮР'ЄВА

«12» квітня 2022 року

Висновок кафедри про кваліфікаційну роботу

Кваліфікаційну роботу розглянуто. Здобувач вищої освіти Мохамед Медхат Ахмед Мохамед ЕЛЬБАННА допускається до захисту даної кваліфікаційної роботи в Екзаменаційній комісії.

Завідувачка кафедри технології ліків

_____ Тетяна ЯРНИХ

«28» квітня 2022 року

Qualification work was defended

of Examination commission on

« ___ » of June 2022

With the grade _____

Head of the State Examination commission,

DPharmSc, Professor

_____ / Oleh SHPYCHAK /