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QUALIFICATION WORK

on the topic: «**JUSTIFICATION OF THE COMPOSITION OF THE OINTMENT WITH PHYTOCOMPONENTS»**

Prepared by: higher education graduate of group Phm19(4.10)-05
specialty 226 Pharmacy, industrial pharmacy
educational program Pharmacy
Aya SAYEGH
Supervisor: associate professor of higher education institution of department pharmaceutical drugs technology, PhD, associate professor Marina BURYAK
Reviewer: professor of department of industrial technology of drugs, doctor of pharmacy, professor Vita GRYTSENKO

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ANNOTATION

As a result of the research, the composition of the extemporaneous ointment for the treatment of skin diseases were substantiated. The stability and technological properties of the ointment for local use were studied.

The organoleptic and physico-chemical indicators of model samples of the ointment were determined in accordance with the methods of the pharmacopeia. According to the results of the conducted research, the stability of the developed ointment was established.

The work is laid out on 40 pages, includes 3 tables, 6 figures, and 31 literature sources.

Key words : skin diseases, symptomatic therapy, technology, composition, extemporaneous ointment.

АНОТАЦІЯ

В результаті проведених досліджень обґрунтовано склад екстемпоральної мазі для лікування шкірних захворювань. Вивчено стабільність та технологічні властивості мазі для місцевого застосування.

Органолептичні та фізико-хімічні показники модельних зразків мазі визначали згідно з методиками фармакопеї. За результатами проведених досліджень встановлено стабільність розробленого гелю.

Робота викладена на 40 сторінках, включає 3 таблиці, 6 малюнків та 31 літературне посилання.

Ключові слова: захворювання шкіри, симтоматична терапія, технологія, склад, екстемпоральний гель.

Content

INTRODUCTION

Actuality of theme. In the field of dermatological health, it is difficult to overestimate the importance of early recognition of symptoms and timely medical intervention. A proactive approach not only ensures optimal skin condition, but also prevents more serious complications, mitigates possible psychological consequences, and reduces long-term medical costs.

The relevance of the problem is determined not only by the constant growth of this disease, but also by the inconsistency in the assessment of various pathogenetic mechanisms of its development and, as a result, not always effective treatment results, as well as its high cost.

Therefore, today it is relevant to create a dermatological ointment based on plant raw materials for the treatment of such a skin disease as atopic dermatitis. The most effective in this case is an emulsion ointment, which will not interfere with the natural functions of the skin, will moisturize the absorption surface and eliminate such symptoms of atopic dermatitis as inflammation and itching. At the same time, it is necessary to search for and rationally select both active substances and auxiliary substances in the composition of the carrier.

The Department of Pharmaceutical Drug Technology of the National Pharmaceutical University is developing an extemporaneous ointment that includes phytocomplex for the treatment of skin diseases.

The purpose was to develop the composition and technology of an extemporaneous ointment intended for the treatment of dermatitis using plant raw materials.

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

- analyze and summarize modern literary data on the current state of treatment of dermatological diseases;
- • conduct an analysis of the extemporaneous formulation of soft drugs for the treatment of dermatological diseases;

- • to theoretically and experimentally justify the composition of extemporaneous ointment based on plant raw materials (herbs, rosehip and chamomile oils);
- • to develop the optimal technology of extemporaneous ointment for the treatment of dermatological diseases.

Research objects. herbs, rosehip and chamomile oils, glycerin, purified water; model samples of ointment bases.

Subject of study. Pharmaco -technological studies of ointment bases and model samples of ointmentfor the treatment of dermatological diseases.

Research methods. Organoleptic, physicochemical, pharmacotechnological , statistical

Practical significance of the obtained results. Physico-chemical studies (description, homogeneity, pH) of the ointment for the treatment of dermatological diseases were conducted .

The obtained results of experimental studies can be used in the development of the technology of this medicinal product .

Scientific novelty. For the first time, the main physicochemical parameters of the new ointment for the treatment of dermatological diseases were investigated.

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CHAPTER 1. RELEVANCE OF THERAPY OF INFLAMMATORY SKIN DISEASES

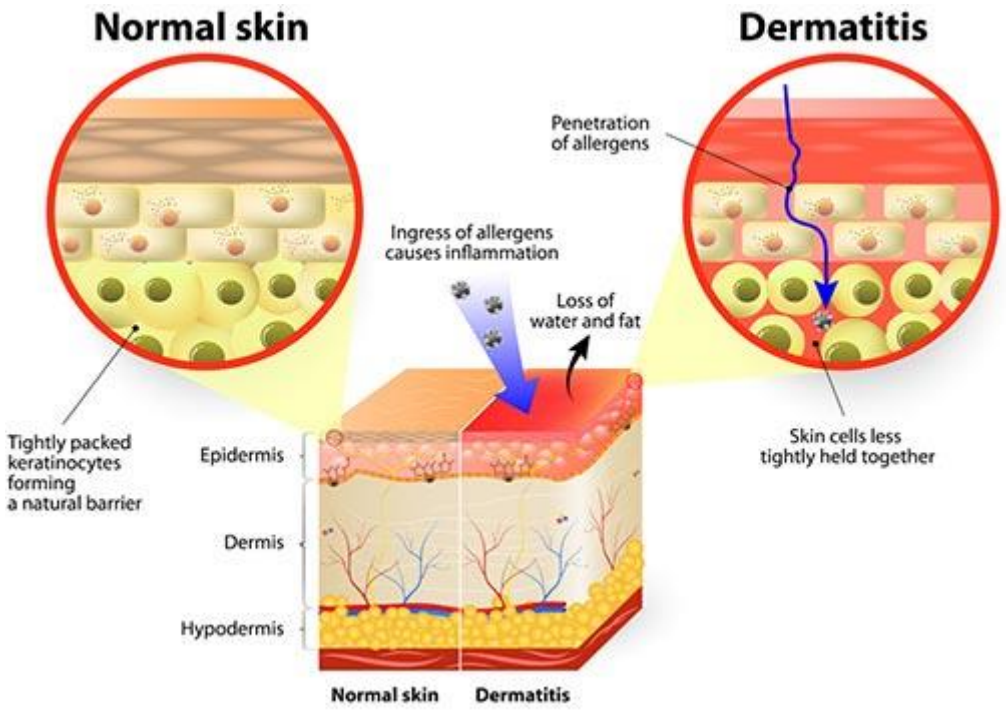
1.1. Principles of local treatment in dermatology.

The skin is the largest human organ; its weight is 11-15% of body weight. The skin provides several important functions: it is a barrier separating the environment from the inside; protects against mechanical, thermal, chemical damage; regulates the amount of water in the body; provides a sense of touch; protects against invasion of pathogens, ensures persistence of symbiotic microorganisms; helps produce vitamin D and a number of hormones.

The dermis is permeated with sweat and fat glands and pores, blood vessels, nerve fibers and hair follicles. The epidermis consists of stratified keratinizing epithelium, represented by keratinocytes . The top layer is formed by “dead” cells (stratum corneum), called corneocytes . The formation of the stratum corneum is ensured by the differentiation and death of keratinocytes of the upper layer by apoptosis, called cornification .

During the process of keratinization, the synthesis of a number of proteins (keratins, loricrin , involucrin , filaggrin) is activated in keratinocytes ; the cell membrane thickens; aggregate keratin intermediates filaments ; lipids and proteins are released into the extracellular space as part of lamellar bodies (Odland bodies); organelles are released, which as a result causes flattening of cells connected to each other by a layer of lipids, which provides an additional barrier impermeable to water [1, 2].

One of the most important proteins involved in and regulating keratinization is filaggrin . During the differentiation of keratinocytes into corneocytes filaggrin is formed from a protein precursor, profilaggrin , which is stored in keratohyalin granules. The release and modification of profilaggrin into filaggrin causes aggregation of keratin filaments and cell death. Mutations in the filaggrin gene are often detected in patients with AD , asthma and other dermatological diseases [3, 4].



Pic.1.1 Clinical characteristic of normal skin and patological

The surface layer of the epidermis already consists of particles that gradually exfoliate (see figure, d). To hold the scales together and maintain the integrity of the barrier, the skin produces a lipid glue consisting primarily of ceramides .

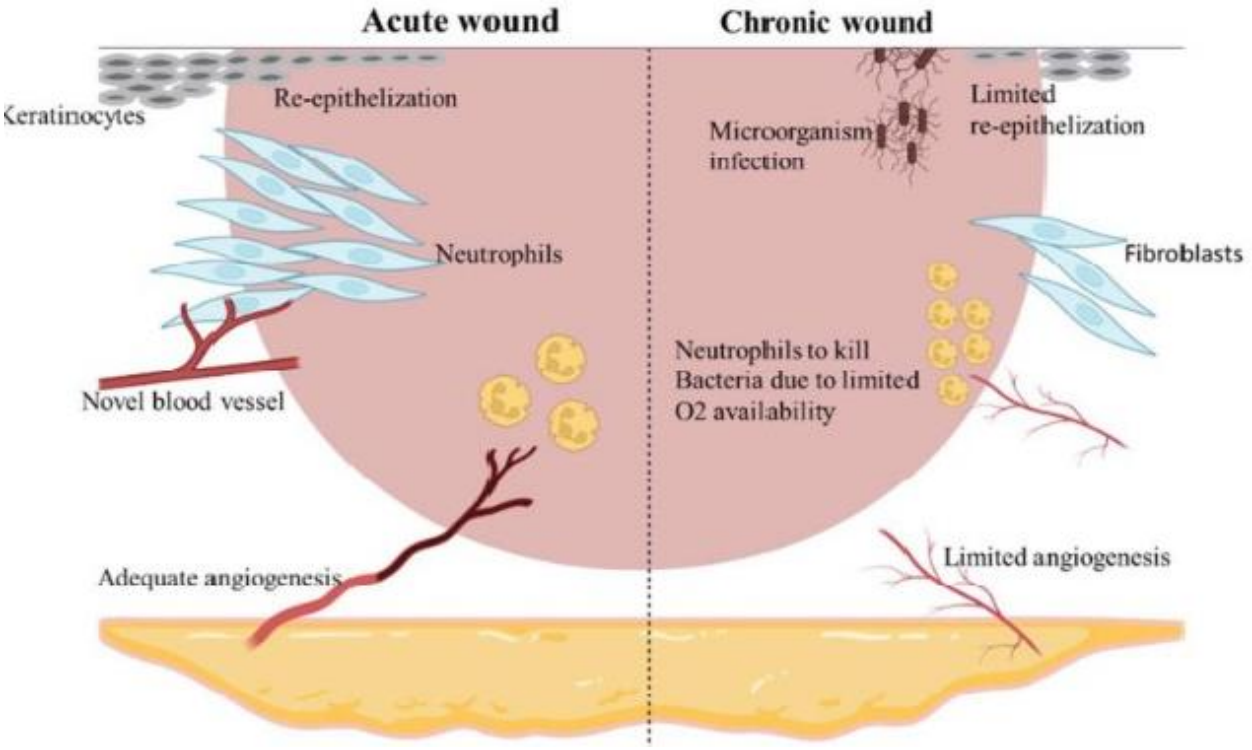
Ceramides and other lipids of the stratum corneum

The lipid layer between “dead” cells consists of 50% molecules called ceramides , 30% cholesterol, 20% free fatty acids (FFA; including omega-3, -6, -9), as well as enzymes (proteases, phosphatases, glucosidases , lipases), as well as proteins (corneodesmosin , cathepsin D). The membrane of lamellar bodies has contact with the Golgi apparatus [5]. The lipids of the lamellar bodies (LBs) of the stratum corneum differ significantly from the lipids of the membranes of living cells. They contain phospholipids and sphingolipids , from which ceramides are synthesized under the action of phospholipase A2 and beta- glucocerebrosidase .

Structurally, ceramide consists of two molecules: a sphingoside polar base and a fatty hydrophobic acid, connected by an amide bond (see figure, 1.2).

Sphingosine is associated with the cells of the stratum corneum through the membrane system of the Golgi apparatus; fatty acids fill the intercellular space

perpendicular to the cell layers. The red line indicates the location of lipids between the cell layers.



Pic. 1.2. Different between wounds

Ceramides in the region of the polar part, attached to “dead” keratinocytes , form a sedentary pseudocrystalline lattice; the middle part of the lipid layer is formed by the tails of fatty acids, which have a smaller volume than sphingosides , which ensures their greater mobility. Between them, the space is filled with cholesterol and FFAs not associated with ceramides , which ensures the fluidity of the middle layer of lipids. Thus, ceramides provide the density of the stratum corneum, and the middle zone ensures its elasticity.

Analysis of the structure of ceramides using reversed -phase liquid chromatography in combination with high-resolution quadrupole time-of-flight mass spectrometry showed that there can be more than 1000 variants of combinations of sphingosines with fatty acids [6, 7]. In general, ceramides are produced by a combination of variants of the sphingosine polar moiety and fatty acids with different numbers of carbon atoms .

In dermatology, agents used for local treatment are grouped according to their therapeutic effect; these include:

cleansers;

moisturizers (emollients , humectants and skin softeners);

drying agents as well as superabsorbent powders

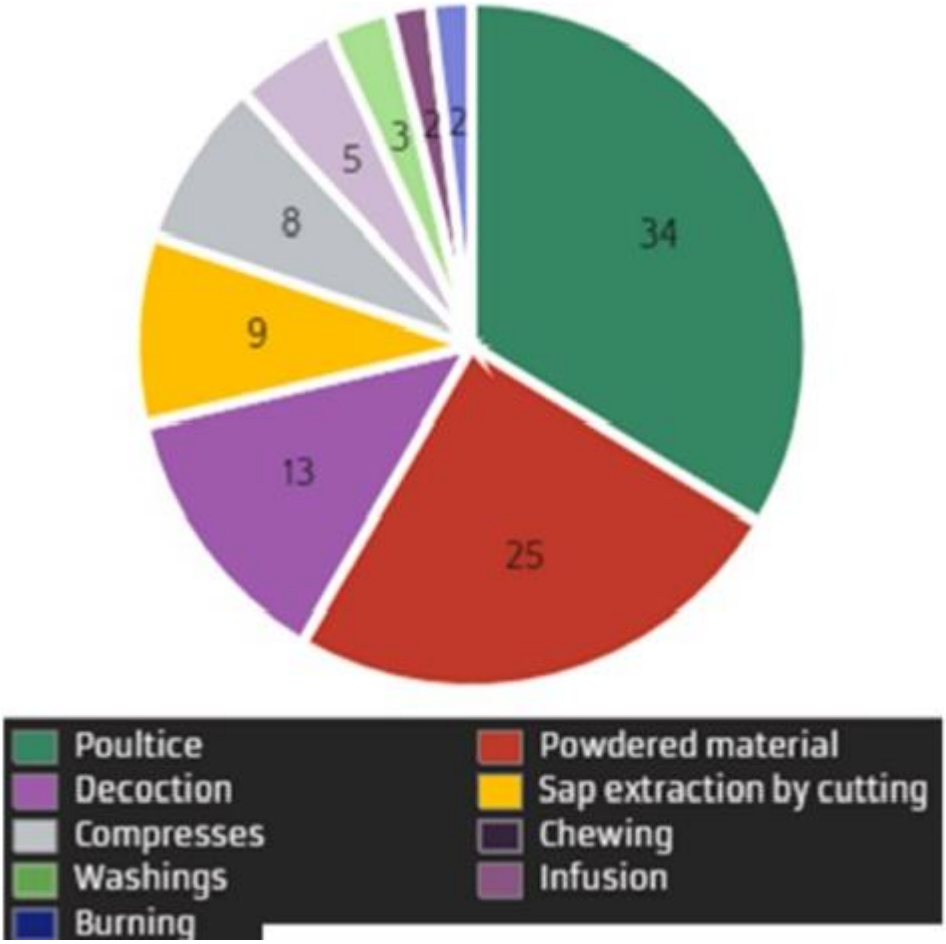
anti-inflammatory drugs;

Antimicrobials

keratolytics (softening, cleansing and facilitating exfoliation of squamous cells of the epidermis)

astringents (drying agents that release proteins that promote contraction and contraction of the skin);

antipruritic



For any given topical treatment, success may depend on:

The basis on which the product is made

dressing used

External preparations can be used in different bases, which include:

Powders

Liquids

Liquid and oil mixtures

The base influences the effectiveness of the treatment and may itself cause side effects (eg, allergic contact dermatitis or irritant contact dermatitis). Typically, water- and alcohol-based preparations are drying due to the evaporation of liquid and are used for acute inflammatory diseases. Powders are also drying agents. Oil-based preparations moisturize the skin and are preferable for chronic inflammation.

When choosing a drug base, one is guided by the localization of application, cosmetic effect and ease of use.

Powders

Inert powders can be mixed with active substances (such as antifungals) to give them a therapeutic effect. These products are prescribed for use for rashes in irritated areas or areas of the skin with high humidity.

Liquids

Liquid media include:

Baths and lotions

Foam

Solutions

Lotions

Gels

Baths and lotions are used when it is necessary to apply the drug to large areas of the skin, such as, for example, with widespread contact dermatitis or atopic dermatitis .

Foams are aerosol preparations based on alcohol or emollients . They are generally quickly absorbed and are used primarily on hairy areas of the body.

Solutions are medications dissolved in a solvent, which is usually ethyl alcohol, propylene glycol, polyethylene glycol , or water. Solutions are convenient

for application (especially on the scalp for diseases such as psoriasis or seborrhea), but they have a drying effect. One common solution is aluminum acetate solution.

Lotions are a water emulsion. They are easily applied to areas of the skin with thick hair growth. Lotions cool and dry areas of acute inflammation and exudation, such as contact dermatitis, tinea pedis and tinea groin .

Gels are a suspension of a drug in a solvent thickened with polymers. Gels are often more effective for the controlled release of active ingredients in topical preparations. They are often used for acne , rosacea and psoriasis of the scalp .

Combined Basics

Combinations include:

Creams

Ointments

Combination bases typically contain oil and water, but may also contain propylene or polyethylene glycol .

Creams are a semi-solid emulsion of oil and water. Creams are used for moisturizing and cooling, as well as in the presence of exudation. They are absorbed into the skin when rubbed.

Ointments are based on oil (for example, Vaseline) with a small amount of water or even without it. Ointments are good lubricants and improve the penetration of the drug into the skin due to their occlusive properties; a certain concentration of the drug, as a rule, has a more pronounced effect when introduced into an ointment base. The use of ointments is preferable for lichenified rashes and lesions covered with thick crusts or accumulations of scales, including psoriasis and lichen simplex chronicus . For erosions and ulcers, ointments irritate the skin less than creams. They are generally best applied after bathing or moisturizing the skin with water.

Dressings protect skin defects, accelerate healing, increase drug absorption and protect the patient's clothing from contamination.

Non-occlusive dressings

The most commonly used non-occlusive dressing is gauze. They are maximally permeable to air, which is sometimes preferable for speedy healing, and allow the lesions to dry out.

Wet-dry dressings are non-occlusive dressings moistened with a solution, usually saline, that are used to cleanse lesions of dead tissue and thick crusts. The dressings are applied wet and removed after the solution evaporates (i.e., wet-dry dressings); in this case, the skin tissue adheres to the dried bandage.

Occlusive dressings

Occlusive dressings increase absorption and effectiveness of topical therapy. The most commonly used are transparent polyethylene films (household plastic bags) or soft transparent semi-permeable dressings. Hydrocolloid dressings absorb excess fluid from the skin to form a gel and can be used under gauze for patients with skin ulcers. Zinc gelatin dressing (Unna boot) is an effective occlusive dressing for patients with stasis dermatitis and ulcers . Plastic tape impregnated with fluranrenolide , a glucocorticosteroid , can be used to treat isolated or refractory lesions.

The application of occlusive dressings over topical corticosteroids to enhance absorption is sometimes used in the treatment of psoriasis , atopic dermatitis , skin lesions due to systemic lupus erythematosus and chronic hand dermatitis , as well as other diseases. Systemic absorption of topical corticosteroids may occur, leading to suppression of adrenal function. Local side effects of topical corticosteroids include the development of miliaria , skin atrophy, striae , bacterial or fungal infections, and acneiform rashes.

Other occlusive dressings are used to protect and treat open wounds such as burns ; special silicone dressings are sometimes used to treat keloids .

The main groups of external medicinal products include:

Disinfection

Moisturizing

Drying

Anti-inflammatory

Antimicrobial

Keratolytic

Knitting

Antipruritic

Cleansers

The main cleaning agents are soaps, surfactants and detergents. Soap is the most widely used skin cleanser, but synthetic detergents are also used. Baby shampoos are generally well tolerated when applied to the eye area and cleansing wounds and abrasions; they help remove crusts and scales from psoriasis, eczema and other forms of dermatitis. But for acute inflammation, eczema and weeping rashes, it is best to cleanse them with water or saline.

Water is the main solvent for cleansing the skin. Organic solvents (eg acetone, hydrocarbon derivatives, propylene glycol) are very drying to the skin and can cause irritation or, less commonly, allergic contact dermatitis . To remove hardened tar and dried paint from leather, you may need to use a petroleum jelly-based ointment or a commercially available waterless detergent.

Moisturizers

Moisturizers (emollients) restore the water and fat content of the skin and help maintain hydration. They usually contain glycerin, mineral oil or petroleum jelly and come in the form of lotions, creams, ointments and bath oils. Stronger moisturizers contain 2% urea , 5-12% lactic acid and 10% glycolic acid (higher concentrations of glycolic acid are used as keratolytics , for example for ichthyosis . They are most effective when applied to already moisturized skin, i.e. after a bath or shower). Cold creams are over-the-counter (OTC) moisturizing emulsions of fats (such as beeswax) and water.

Drying agents

Excess moisture in intertriginous areas (interdigital folds, gluteal fold, axillary areas, inguinal folds, inflamed areas) can cause irritation and maceration.

Powders dry out macerated skin and reduce friction by absorbing liquid. However, some powders can ball up and cause irritation if they become wet. The

most commonly used are cornstarch and talc. Although talc is more effective, talc can cause granulomas if ingested into the lungs, so it is no longer used in baby powders. Cornstarch can encourage fungal growth. Superabsorbent powders (absorbent powders) are in some cases used to dry out very wet areas of the skin (for example, to treat intertrigo).

Another drying agent is aluminum chloride solution (often used for hyperhidrosis).

Anti-inflammatory drugs

Local anti-inflammatory drugs include glucocorticosteroid and non-steroidal drugs.

Glucocorticosteroids form the basis of therapy for most non-infectious inflammatory dermatoses. Lotions are used in areas prone to irritation and on the face. Gels are useful for the scalp and when it is necessary to dry the skin between the toes to treat tinea pedis. Creams are applied to the face and in diaper rash areas, as well as for the treatment of inflammatory dermatoses. Ointments are effective for dry, scaly rashes and when it is necessary to increase the effectiveness of treatment. A patch impregnated with a corticosteroid protects the skin from scratching. It also increases the absorption of glucocorticosteroids and, consequently , the activity of the drug increases.

Topical corticosteroids range in potency from low (Class VII) to very high (Class I—see table Relative Potencies of Some Topical Corticosteroids). The fundamental differences in effectiveness are due to fluoridation or chlorination (halogenation) of the active substance.

Topical corticosteroids are usually applied 2–3 times daily, but high-potency medications may be limited to once daily use or even less frequently. Most dermatoses are treated with moderate and highly active agents; soft preparations are best used for mild inflammation and for application to the face or areas of diaper rash, where the likelihood of the drug entering the systemic bloodstream and developing local side effects is highest. All drugs, when used for > 1 month, can cause local skin atrophy, the appearance of stretch marks and acneiform rash. This

effect is especially pronounced on thinner skin of the face, armpits or genitals. Glucocorticosteroids may also promote fungal growth. Contact dermatitis also often develops in response to preservatives and additional components of the drug, especially with prolonged use. It is possible to develop contact dermatitis due to glucocorticosteroids themselves . Perioral dermatitis develops when using medium- and high-potency products on the facial skin, but is not typical for weak glucocorticosteroids . Highly active agents may suppress adrenal function when used in children, when applied to large areas of skin, under sealed dressings, or when used for long periods of time. Relative contraindications include conditions in which infection plays a role, as well as acneiform diseases.

Nonsteroidal anti-inflammatory drugs include tar preparations. Tar is a product of dry distillation of wood or a product of coking coal, and its use is indicated for psoriasis. Side effects: irritation, folliculitis, staining of clothes and furniture, photosensitivity. Contraindications: infectious skin diseases. A number of herbal preparations are widely used in commercial products, but their effectiveness has not been well studied. Among them, the most popular are chamomile and calendula. Calcineurin inhibitors can be used for atopic dermatitis pimecrolimus and tacrolimus , and the phosphodiesterase-4 inhibitor crisaborole (all topical). The topical Janus kinase (JAK) inhibitor ruxolitinib is also currently in use (1).

Antimicrobial agents

Local antimicrobial agents include:

Antibiotics

Antifungal drugs

Insecticides

Nonspecific antiseptics

Antibiotics have several indications for use. External forms of clindamycin and erythromycin are used as primary or additional therapy for acne vulgaris in patients intolerant to oral forms of antibiotics. For the treatment of rosacea metronidazole and sometimes sulfacetamide , clindamycin , or erythromycin are used topically . Mupirocin has a pronounced effect on gram-positive (mainly

Staphylococcus aureus and streptococci) microorganisms and can be used to treat impetigo if the deeper layers of the skin are not damaged (2). Other topical antibiotics used to treat impetigo are retapamulin (2) and ozenoxacin (3).

Over-the-counter topical antibiotics such as bacitracin and polymyxin have been replaced by topical petrolatum in the postoperative period after skin biopsy and to prevent infection of scrapes, minor burns, and scratches. Topical use of petrolatum is as effective as the above antibiotics, but unlike them (especially neomycin), it does not cause contact dermatitis. Using topical antibiotics and washing the skin with antiseptic soap to treat erosions and ulcers can also slow healing.

Antifungal agents are used to treat candidiasis , a wide range of dermatophytoses , and other fungal infections (see table Treatments for superficial fungal infections*).

Insecticides (eg, permethrin , malathion) are used to treat lice and scabies (see tables Primary Lice Treatment Options and Scabies Treatment Options).

Nonspecific antiseptics include iodine solutions (povidone iodine, clioquinol), gentian blue , silver preparations (silver nitrate, silver sulfadiazine) and zinc pyrithione . Iodine is prescribed to treat the skin before surgery. Gentian violet is used when a chemically and physically stable antiseptic/antimicrobial drug is needed, which must also be very cheap. Preparations containing silver are effective in the treatment of burns and ulcers and have pronounced antimicrobial properties; There are a number of wound dressings impregnated with silver. Zinc pyrithione is an antifungal agent and is a common ingredient in shampoos used to treat dandruff associated with psoriasis or seborrheic dermatitis. Healing wounds should not be treated with local antiseptics, with the exception of silver preparations, as they are irritating and can destroy fragile granulation tissue. In the last few years, sodium hypochlorite has been used as an antiseptic in the form of solutions and sprays.

Keratolytics

Keratolytics soften and cleanse the skin of exfoliated epidermal cells. An example is 3% and 6% salicylic acid and urea.

Salicylic acid is used to treat psoriasis , seborrheic dermatitis , acne and warts . Side effects include burning and systemic toxicity if the drug is applied to a large area of skin. It should not be used frequently in children and infants.

Urea is used to treat plantar keratoderma and ichthyosis . Side effects include irritation and persistent burning. It should not be applied to large areas of the skin.

Astringents

Astringents (drying agents that precipitate exudate proteins, promote contraction and tightening of the skin). A solution of aluminum acetate is most often used as an astringent. Typically applied under a bandage or as a poultice, astringents are used to treat infectious eczema, exudative rashes, and weeping bedsores. A popular over-the-counter astringent is Witch Hazel .

Antipruritics

Doxepin (not registered in the Russian Federation) is a local antihistamine effective in the treatment of itching associated with atopic dermatitis , chronic dermatitis in lichen simplex and nummular dermatitis .

Other antipruritics include camphor 0.5–3%, menthol 0.1–0.2%, pramoxine hydrochloride (not registered in the Russian Federation) and a eutectic mixture of local anesthetics (EMLA), which contains equal parts lidocaine and prilocaine in an oil-water solution. environment. External antipruritics are preferable to systemic medications (oral antihistamines) when smaller areas of the skin are affected and the itch is resistant. Calamine lotion is more soothing than antipruritic .

Topical benzocaine and diphenhydramine (available in certain over-the-counter lotions) sensitize the skin and are not recommended for use.

1.2. Phytotherapy in dermatology

The peculiarities of the existence of society at the present stage include: the ever-increasing intensity of the pace of life and the acute and chronic stresses associated with it, the progressive negative impact on health of harmful environmental factors, the so-called soil diseases and further reduction of the biological value of food, man-made pollution with negative electromagnetic background from various gadgets, hypodynamia, etc.

The consequences of this are the gradual loss of general biological potential, the imbalance of the regulatory systems of the human body, the increase in morbidity, in particular the problem of comorbidity (interdependence of diseases) and polymorbidity [1, 7], which in recent decades has been recognized as one of the main problems in modern world medicine [7, 9, 10, 16, 17].

The majority of current patients with chronic non-communicable diseases have ≥2 pathological conditions, but their number increases with age and may exceed 10 nosologies after 70 years of age [16, 17]. It should be considered that over time, depending on the influence of numerous external and genetic factors, the manifestations of comorbidity can be very different (number, severity of diseases, sequence of their occurrence, etc.).

It is also necessary to consider the increase in life expectancy on Earth and the deterioration of the tolerability of synthetic drugs, especially among elderly patients, the increase in the frequency of side effects and complications [6, 11].

Dermatology is one of the most important causes of forced polypharmacy, which is associated with side effects and complications against the background of the use of a large number of drugs [9, 10]. In particular, according to the State Expert Center of the Ministry of Health of Ukraine, the use of two drugs leads to the development of side effects in 6.0% of patients, five - in 50%, and ten or more - up to 100% [14]. At the same time, there is information in the literature about the appointment of polymorbid patients from 6 to ≥11 drugs for daily use, while potential drug interaction is often not considered, especially in the practice of primary health care [6, 11, 18].

The study of the problem of dermatology involves the search and clarification of common pathophysiological, usually non-specific, links of the main and comorbid pathologies. As a result, a deeper understanding of the essence of the interaction of existing violations is achieved. Academician of the National Academy of Sciences of Ukraine V.M. Kovalenko, focusing on the importance of determining these common pathogenetic links in the formation and progression of comorbid processes, sees in this approach the development and improvement of treatment

technologies that will help reduce the likelihood of polypharmacy [7]. The complexity of treating poly- and comorbid patients is currently a problem that needs an urgent solution. Currently, there are no reliable recommendations, protocols for curation of such patients based on evidence-based medicine, which is a serious challenge and requires the justification of personalized approaches to the treatment process.

This problem is also taken care of by the World Health Organization (WHO) and the European Parliament, which since 2003 have published a number of important recommendation documents regarding the consolidated actions of the world medical community in solving the mentioned challenge [8, 14]. One of the latest documents is the WHO Strategy in the field of traditional medicine for 2014-2024 [23, 31], which, among other things, states that during this decade, methods of traditional medicine (NM) should become integral parts of modern standards of treatment for many pathologies.

Special attention is paid to the formation of NM personnel, increasing their skill level at the postgraduate stage both in specialized higher educational institutions and through self-improvement, including international exchange of experience, formation of the pharmaceutical market for plant products, etc [15]. The achievements of world scientific and practical phytotherapy in recent decades have demonstrated that each medicinal plant contains a wide range of components that have a beneficial effect on the human body weakened by diseases. The use of phytoremedies is a connecting, harmonizing link that optimizes the effect of modern powerful synthetic drugs, prevents the occurrence of side effects or reduces their manifestations. Of course, each medicinal plant contains the main, unique to it, active substances (or a group of medicinal plants similar to it), which determine its main pharmacological properties: cardiotonic, diuretic, choleretic, hypotensive, expectorant, antimicrobial, anti-inflammatory, etc [28, 30].

Pathophysiological studies of the mechanism of the formation of various diseases have demonstrated that frequent common links in the pathogenesis of dermatological processes in the most common and socially significant pathologies

are oxidative stress, endothelial dysfunction and imbalance in the production/metabolism of nitric oxide, systemic inflammation of low intensity and disruption of the regulatory systems of neurogenic, neuroendocrine, immune, metabolic nature. The components of most medicinal plants affect precisely the specified non-specific common pathogenetic links.

In the last 20-25 years, experts in the field of pharmacy have created a whole series of herbal medicinal products of various orientations - both mono- and polycomposite, intended specifically for patients with poly- and comorbidities. It should be noted the annual increase in the assortment of such drugs and the scale of their production [25].

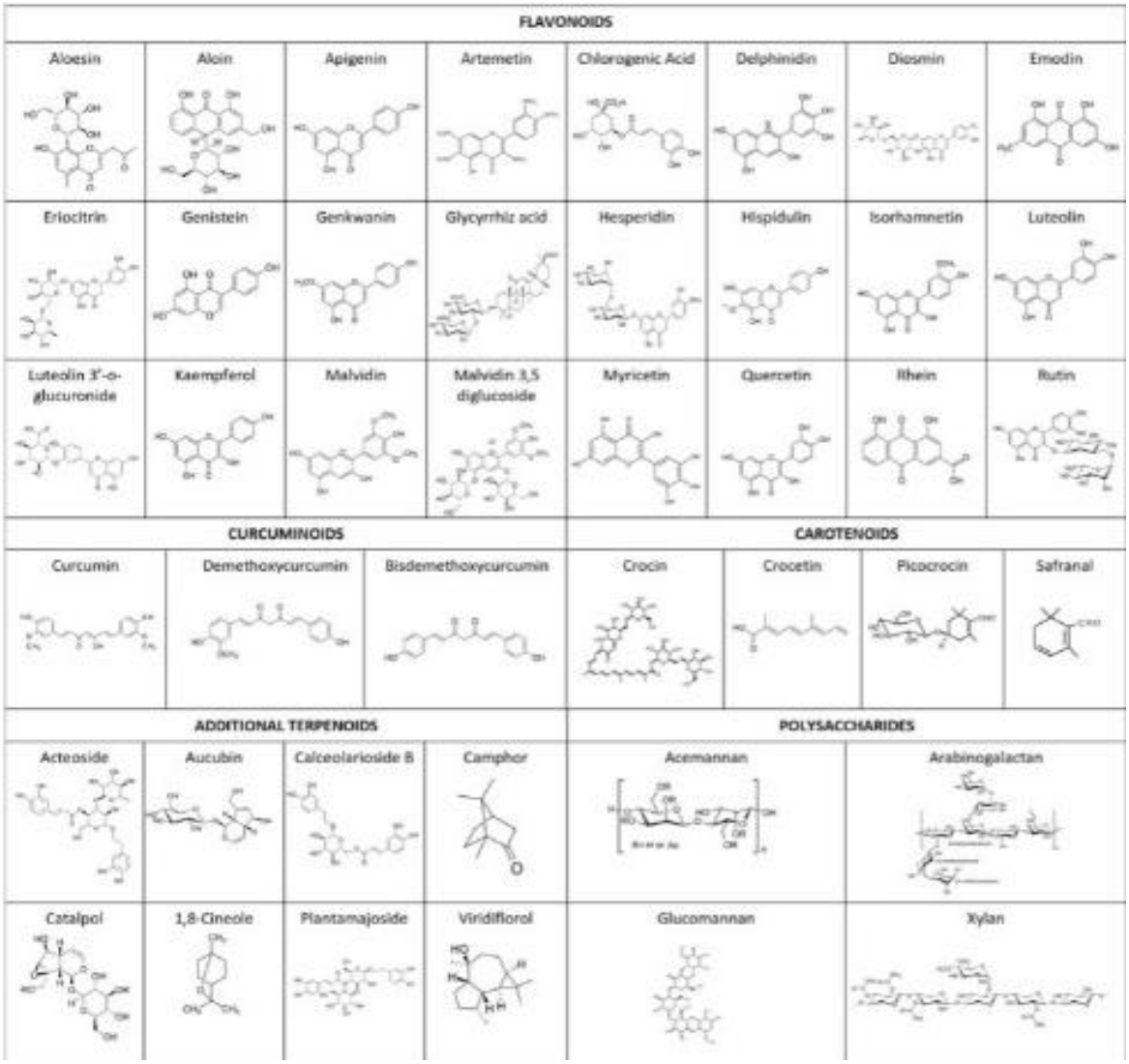
It should be noted that the current stage of using phytotherapeutic agents in everyday practice is significantly different from the previous one. The main reason is the progressive pollution of the environment and the danger of harvesting medicinal plants with anthropogenic toxicants. This requires constant eco-monitoring of the production of plant, which is why galena technologies for manufacturing drugs at home or in a pharmacy are becoming a thing of the past. The reasons for this trend are also the lack of knowledge in pharmacognosy, phytotherapy, ecology, lack of time, personnel, etc [13].

Today, in the world, attention has been significantly increased both to the conditions of growing medicinal plant raw materials and to the production processes of plant in the context of the requirements of Good Manufacturing Practice (GMP) and Good Agricultural Practice (GAP). Phytoniring technology, production of multi-component phytomedicine with pharmacologically diverse and multi-organ mechanisms of action are becoming widespread. Mankind has not yet forgotten the consequences of the thalidomide tragedy. For this reason, all drugs of synthetic origin enter the pharmaceutical market, especially the international one, only after passing a 4-phase test, including on the basis of evidence-based medicine, which requires considerable time and money. However, such approaches are not entirely correct in relation to phytomedicine: a person must responsibly check the plant medicine created by his mind, but is it necessary to so meticulously examine - a

creation of Nature. Apparently, other strategies are needed here, and the international research policy in this aspect is not yet established.

A significant number of new plants are presented on the pharmaceutical market as biologically active supplements. It is no secret that the attitude of most doctors towards such herbal remedies is often skeptical. The explanation is quite simple: in response to the challenges of the era (increasing morbidity, poly- and co-morbidity, etc.), the first to solve this problem were newly created companies such as Herbalife, in which the dietary supplement manufacturing technologies had numerous shortcomings. At the same time, the concept of network marketing, which aimed to enrich the participants of the sale of these products (often without medical education, with a not entirely healthy form of distribution and advertising), discredited the important idea of the need to use nutritional supplements, especially for preventive purposes.

Currently, the production of dietary supplements is carried out mainly by pharmaceutical companies of European countries and Ukraine, which have modern technologies, use certified raw materials and generally meet the requirements, however, most of such products have not been sufficiently tested with the involvement of significant contingents of patients on the basis of evidence-based medicine. Currently, such nutritional supplements are called parapharmaceuticals, since they are produced from the same raw materials as well-known plants, which have the status of drugs, but may differ from the latter in terms of dosage (as a rule, they contain lower concentrations of active substances), combinations of components, etc. Often, in some European countries, certain herbal remedies have the status of nutritional supplements, while in others they are a medicinal product. Often common RLZ from the same plant (from different manufacturing companies) even in the same country, including Ukraine, have different status - dietary supplement or medicine. As an example, we can cite complexes based on ginkgo biloba, St. John's wort, lemon balm, etc.

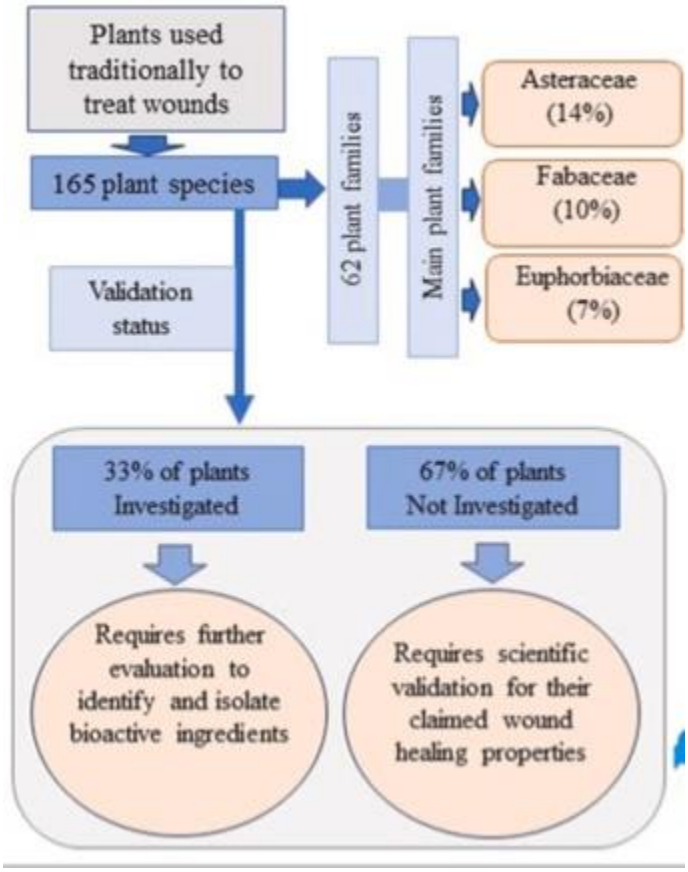


1.3 Biological active substances using for treted dermatological deasesse.

Over time, many of them gain the recognition of doctors and patients due to their effectiveness, wide application and receive the status of RLZ. For example, Neocardil (extracts of ginkgo biloba, hawthorn and pueraria), which was considered a dietary supplement 5-7 years ago, is now a popular drug.

The problem of training personnel in phytotherapy and self-education of doctors in this direction remain relevant. Kyiv Medical University of the Ukrainian Association of Folk Medicine operates in Ukraine, which provides training of specialized specialists and advanced training. Until recently, the Ministry of Health of Ukraine had a Committee for the study and implementation of NM methods in clinical practice, the team of which did a lot for the legislative registration of the activities of this field, coordination, promotion of scientific research, holding

scientific forums, publication of special literature, etc. Unfortunately, it was disbanded for unknown reasons.



Cells and centers of scientific and practical research on phytotherapy were fruitfully developed in Uzhhorod (Research Institute of Phytotherapy at Uzhhorod National University), Kharkiv, Chernivtsi, Lviv, Ivano-Frankivsk. The collectives of these centers have prepared a number of modern publications for self-education of specialists with the additional direction of "phytotherapy" [1, 2, 3, 5], special courses, etc. are also functioning. Today's realities require the activation of this process in Ukraine in the context of the WHO Strategy in the field of traditional medicine 2014-2023, including the organization of new modern phytopharmaceutical productions that are as close as possible to raw materials and meet the requirements of a favorable ecological environment.

Conclusions to chapter 1

1. The main trends of the ecological situation on Earth, the growing pace of life and associated acute and chronic stresses, a decrease in the biological value of food, hypodynamia and other negative factors lead to an increase in population morbidity, poly- and co-morbidity.

2. Comorbidity and polymorbidity require in-depth study in order to develop new treatment methods and technologies.

3. The WHO strategy in the field of traditional medicine for 2014-2024 directs the world medical community and pharmacy to comprehensive research and introduction into clinical practice of herbal remedies, in particular phytotherapy, as necessary components of modern treatment programs for polymorbid patients, which will ensure the development of more effective technologies in medicine

CHAPTER 2

RESEARCH OBJECTS AND METHODS

2.1. Research objects

When developing the composition of the extemporaneous prescription ointment substances approved for use in pharmaceutical and medical practice were used.

The development of the composition of this dosage form is based on various physical-chemical and structural-mechanical studies. The results of the analyzes were processed statistically on the basis of five parallel determinations.

Bidens tripartita herb

It is pieces of leaves, stems, buds and flowers that pass through a sieve with holes with a diameter of 7 мм. The color is green, brownish-green or greenish-purple with muddy yellow drops. The smell is weak. The taste is bitter, a little astringent.

Chamomile oil (TU U 25399227.001-98)

The oil is viscous, deep blue in color with a strong and characteristic bitter aroma. With a chamazulene content of more than 40%, it becomes non-flowable.

The specific gravity at 20°C is 0.910-0.950; refraction is not determined due to the dark color of the oil, nor is optical rotation. The ether number is 0-40 (mainly 6-12), the acid number is 5-50.

Rosehip oil (TU 9374-005-78056148-06)

Brown oily liquid with a greenish tint, bitter in taste and with a specific smell. Contains saturated and unsaturated fatty acids, including linoleic and linolenic, as well as carotenoids, vitamins C and E.

Twin-80 (VFS 42-1676-80)

Oleic acid ester and polyoxyethylation of sorbitan. Liquid substance from lemon to amber color, weak odor and bitter taste. Soluble in water and organic solvents. Synthetic emulsifier.

HALs C_{16} – C_{21} – synthetic fatty alcohols of the primary fraction (TU 64-6-216-82)

Homogeneous mass from white to yellow color, acid number, mg – KOH, 200/225; mass fraction of hydrocarbons, %, no more than 4.0; mass fraction of water, %, no more than 0.4.

Vaseline(SPhU)

Homogeneous viscous ointment-like mass without odor, from white to yellow in color. Practically insoluble in water, slightly soluble in 95% ethyl alcohol, soluble in ether, gasoline, chloroform. It is miscible in all respects with fatty oils and fats. The melting point is from 27 to 50°C.

Glycerin (SPhU I ed., p. 353; EF 4 ed., 2002, p. 1256, Glycerol monograph)

Viscous liquid, sticky to the touch, transparent, colorless, sweet in taste, odorless. Boiling point – 290°C; refractive index - 1.4740. Miscible in any ratio with water, ethanol, methanol, acetone, insoluble in chloroform and ether, soluble in their mixtures with ethanol. Absorbs moisture from the air (up to 40% by weight). When glycerin is mixed with water, heat is released and contraction (volume reduction) occurs.

Glycerin is used as a skin softener, as an auxiliary substance in the technology of medical and cosmetic creams, ointments, suppositories, and as a component of emulsifiers. Due to the increase in viscosity in liquid medicinal forms for local use, it prolongs their effect, increasing the contact time of the active substances with the affected area of the skin or mucous membrane.

The water is purified

(SPhU III ed., p. 276;)

Transparent, colorless liquid without taste or smell.

Solvents, reagents, and solutions used in the work met the requirements of the State Pharmacopeia of Ukraine.

2.2. Research methods

Organoleptic and physicochemical indicators of model samples were determined according to the methods of the Ministry of Defense of Ukraine and DEST 29188.0-91.

Description

The appearance and characteristic organoleptic properties of the samples (color, smell, consistency, etc.) were controlled. The studied dosage forms were monitored for the presence of a bitter smell, as well as signs of physical instability (aggregation of particles, coalescence, coagulation, delamination).

Definition of homogeneity

The determination was carried out according to the methodology given in SPhU I ed., p. 511. Four samples of each sample of 20-30 mg each were taken, two samples were placed on a slide, covered with a second slide and firmly pressed until spots with a diameter of about 2 см.

The obtained samples were viewed with the naked eye (at a distance close 30 смto the eyes). The sample was considered homogeneous if all four samples did not show visible particles, extraneous inclusions and signs of physical instability:

aggregation and coalescence of particles, coagulation. If one of the samples did not pass the test, the determination was made additionally on eight more samples, while all eight samples had to pass the test.

Determination of colloidal stability (for emulsion systems)

To conduct the test, a laboratory centrifuge with a set of test tubes, a mercury thermometer with an interval of measured temperatures from 0 to 100 °C and a division price of 1 °C, as well as a stopwatch and a water bath were used.

The test tubes were filled to 2/3 of the volume (approximately 9 g) with the test samples (so that the weights of the test tubes with the drug did not differ by more than 0.02 g) and weighed to the nearest 0.01 g. Then the test tubes were placed in a water bath at a temperature of (42.5 ± 2.5)°C for 20 minutes, after which they were wiped dry from the outside and placed in the centrifuge nests. Centrifuged for 5 minutes at a speed of 6000 rpm. (the relative force of centrifugation in this case was about 5000 g).

The sample was considered stable if no delamination was observed in the tubes after centrifugation. If at least one of the test tubes showed delamination of the sample or sedimentation, the analysis was repeated with new portions. If at least one tube with delamination was detected during the retest, the sample was considered unstable.

Determination of thermal stability of emulsion systems

For determination, 5-6 glass tubes with a diameter 15 ммand height were taken 150 мм. The test tubes were filled with 8-10 ml of the tested samples and placed in a thermostat with a temperature of (40-42) ° C for 1 week, then in a refrigerator with 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 results of all experimental studies were statistically processed in accordance with the Federal Law of Ukraine.

CHAPTER 3

DEVELOPMENT OF THE COMPOSITION OF THE OINTMENT

3.1. Development of the composition of the ointment

The development of a dermatological ointment is carried out taking into account special requirements and has its own specific features. The ointment should not interfere with the natural functions of the skin, which is involved in metabolism, respiration, excretion, and thermoregulation. In the treatment ointments should moisturize the absorption surface and eliminate inflammation and itching. And if the last action is achieved thanks to the active substances included in the composition of the dermatological ointment, then the moisturizing of the skin surface is entirely the merit of a properly selected foundation.

In addition, it is known from clinical practice that the choice of base directly affects the penetration and assimilation of active components in skin cells. When choosing a base, we took into account the main requirements for dermatological ointments:

- have a positive effect on the skin depending on the purpose;
- easy to squeeze out of tubes;
- easy to apply on the surface of the skin, quickly absorbed;
- be stable during storage at temperatures from -10 ° C to 40 ° C;
- have a pleasant smell.

The type of foundation that best meets the task is the oil/water system. Due to their physical and chemical properties, these carriers ensure high efficiency and stability of the introduced biologically active substances. In addition, due to their high water content (up to 70%), they replenish the skin's moisture loss, are easily applied to its surface, and are quickly absorbed without leaving a greasy sheen on

the skin. They are economical, their production does not cause any particular difficulties.

In connection with this, we set ourselves the following task - the creation of an emulsion base of the first kind.

The best stability, high dispersibility and necessary viscous-plastic properties of emulsions are provided by the use of mixtures of emulsifiers of the first and second kind in certain ratios. Thus, it was established that when stabilizing oil/water type emulsions with a first-class emulsifier in combination with higher fatty alcohols (HALs) of C_{16} - C_{21} fractions , emulsions with viscous-plastic properties of an ointment-like consistency are formed. The rheological properties of these emulsions can be varied due to the ratio between emulsifiers of the first and second kind.

As an emulsifier of the first kind in the composition of the base, we chose twin-80. According to its chemical composition, Tween-80 is a mixture of esters of polyoxyethylated sorbitan and higher fatty acids. These compounds dissolve well in water and organic solvents, are physiologically indifferent, and are stable in a wide pH range .

As an emulsifier of the second kind, we used synthetic alcohols of the primary fraction C_{16}-C_{21} .

The physicochemical stability of oil/water emulsions with a pronounced spatial structure is determined by the colloidal-micellar properties of the adsorption layer formed by emulsifiers, their structural-mechanical properties, and the ability to form a spatial rigid network due to hydrophobic interactions between the coagulation centers of emulsifier molecules.

The choice of optimal concentrations of emulsifiers was carried out taking into account studies on the study of the physical and chemical stability of model emulsions.

Table 3.1

Composition of model emulsions (%)

Model emulsion	Sunflower oil	Glycerin	Twin-80	Vaseline	VJS	Purified water
1	10.0	15.0	10.0	15.0	20.0	30.0
2	10.0	10.0	1,2	15.0	6.8	57.0
3	10.0	10.0	1.5	15.0	8.5	55.0

Glycerin was added to the emulsion base to increase viscosity, as well as to provide a moisturizing effect and as an antifreeze admixture. It is known that the glycerin molecule has small dimensions and easily penetrates into the deep layers of the skin.

Glycerin is an adsorbent, has a hygroscopicity close to the natural moisturizing factor of the horny scales of the skin, it thickens the stratum corneum due to swelling of the stratum corneum and increasing the space between the layers. In addition, glycerol stabilizes cell membranes and activates enzymes that participate in the degradation of demosomes of horny scales. It is introduced into the composition of the ointment in a concentration of about 10%.

Emulsion bases were prepared according to a well-known method. At a temperature of 60-65 ° C, the oil and water phases were heated separately. Emulsifiers were introduced into the oil phase. Vaseline, Tween-80 and HALs were melted in a water bath, after melting all components, sunflower oil was added to the oil phase. Water purified with glycerin was heated to the same temperature. The aqueous phase was added in parts to the oil phase with the stirrer running. It was emulsified with the help of a RT-2 tissue microshredder at 3000 rpm, followed by artificial cooling at a temperature of 30 ° C. The resulting emulsion base was stirred to room temperature.

The colloidal structure and thermal stability of the emulsion bases were evaluated visually according to the methods given in Chapter 2 at room temperature (20 ° C), at temperatures of 40 ° C and 5 ° C, and after freezing and thawing cycles.

As a result of the conducted research, it was established that the model system N1 has a too dense consistency, is poorly applied to the skin and is almost not absorbed. We concluded that there is a large amount of emulsifier in the base.

As for the model emulsion bases No. 2 and No. 3, it was established that they both after manufacturing and after aging for 30 days at temperatures of 5, 20, 40 ° C, as well as after 5 freeze/thaw cycles (temperature interval - from -10 ° C to +45 ° C) were stable. However, the model emulsion base No. 2 was more liquid, therefore, for further study and development of the technology of dermatological ointment for the treatment of atopic dermatitis, we chose an emulsion system with the following composition:

Vaseline 15.0
Vegetable oil 10.0
Glycerin 10.0
Twinu-80 1.5
VZhS 8.5
Purified water up to 100.0 (55.0)

The next stage of our research was the development of the optimal composition of the ointment for the treatment of AD.

using medicinal plant raw materials is relevant today . Such a method can be an emulsion ointment with the following components:

- Bidens tripartita herb;
- chamomile oil;
- rosehip oil.

Let's consider each component of this ointment separately.

In medicine, the herb is often used, which includes: essential oil, tannins, polysaccharides, flavonoids (glycosides of luteolin and butin, auron, sulfuretin), coumarins, bitters, mucilage, vitamin C, carotene, trace elements (iron, chromium, copper , aluminum and manganese).

The plants of the family have pronounced anti-inflammatory, anti-allergic and immunomodulating properties. The wound-healing ability of fresh leaves and oil extracts of sedum grass has been experimentally confirmed. This is partly due to pronounced antiseptic and anti-inflammatory properties of the plant. In addition, biologically active compounds of the herd grass are able to improve regenerative processes. The anti-inflammatory and anti-allergic effect of the extracts of the herd herb is based on the antioxidant properties of biologically active substances, as well as their ability to slow down the synthesis and release of inflammatory mediators. In the experiment, the extracts of the sedum grass reduce the clinical manifestations of anaphylactic shock, slow down the development of passive skin anaphylaxis (Artus phenomenon). An important aspect of the anti-inflammatory and anti-allergic effect of the drugs of the series is also their ability to block the synthesis of prostaglandins.

Preparations of the herb are used externally for various skin diseases, including AD. However, they are also used as diuretics and choleretics when taken internally.

As for chamomile, it belongs to the mildest, but very effective medicinal plants. It is recognized as an official medicinal plant in 26 countries of the world . Chamomile decoction is prescribed even to infants.

Medicinal properties of chamomile have been proven experimentally and confirmed in clinical conditions. Khamazulen and its reduction products - postazulen and besabolol - have an anti-inflammatory effect; choline is a plant hormone substance that precedes fatty liver and excessive deposition of mineral salts. Chamomile essential oils normalize the function of the central nervous system, strengthen the body's reflex activity, improve breathing, and dilate brain vessels. Glycosides activate digestion and bile secretion, as well as block M-cholineractive systems, relax smooth muscles and relieve abdominal spasms.

Chamomile oil, or azulene, inhibits the release of endogenous histamine, stimulates the reticuloendothelial system, activates the phagocytic properties of lymphocytes, which is associated with a pronounced anti-allergic and anti-inflammatory effect in AD.

Domestic specialists note that thanks to its antiseptic, anti-inflammatory and antispasmodic properties, chamomile stimulates tissue regeneration processes in dermatitis and skin ulcers.

Another component - rosehip oil, has the title of "queen of natural oils" for no reason. The properties of this oil are extremely diverse. It eliminates irritation, increases skin elasticity, normalizes the work of sebaceous and sweat glands, promotes skin regeneration and rejuvenation, and gives it an even and beautiful color. It is a mild but powerful antidepressant. Cosmetic rosehip oil perfectly tones blood vessels, has an antimicrobial effect. Rosehip oil is used externally for trophic ulcers, some diseases of the skin and mucous membranes. Rosehip seed oil stimulates the regeneration of skin and mucous membranes.

Rosehip oil contains saturated and unsaturated fatty acids, including linoleic and linoleic, as well as carotenoids and vitamins C and E.

Considering all the above, it can be said that all three components have anti-inflammatory and anti-allergic properties, and their combination in the form of a soft dosage form (MLF) can be used in the treatment of AD.

Thus, we have proposed the following ointment composition:

The infusion of the herb ranges from 3.0 to 30 ml
Rosehip oil 10.0
Chamomile essential oil 5 drops
Glycerin 10.0
Twin -80 1.5
VZhS 8.5
Vaseline 15.0
Purified water up to 100.0 (25.0)

3.2 Development of the technology of extemporaneous ointment based on phytocomponent.

Taking into account all experimental data, we conducted research on the technology of extemporaneous ointment based on plant components for the treatment of atopic dermatitis.

The first stage was obtaining an infusion of the herd grass (1:10) according to a well-known method. To do this, we weighed 3.0 of the herd's grass and placed it in the infuser. 36 ml of purified water was measured using a measuring cylinder (taking into account the water absorption coefficient, which is 2 mg/l for the grass of the herd), and it was added to the infuser with the grass of the herd.

The infusion was placed in a water bath, infused for 15 minutes, and then the resulting infusion was cooled for 45 minutes.

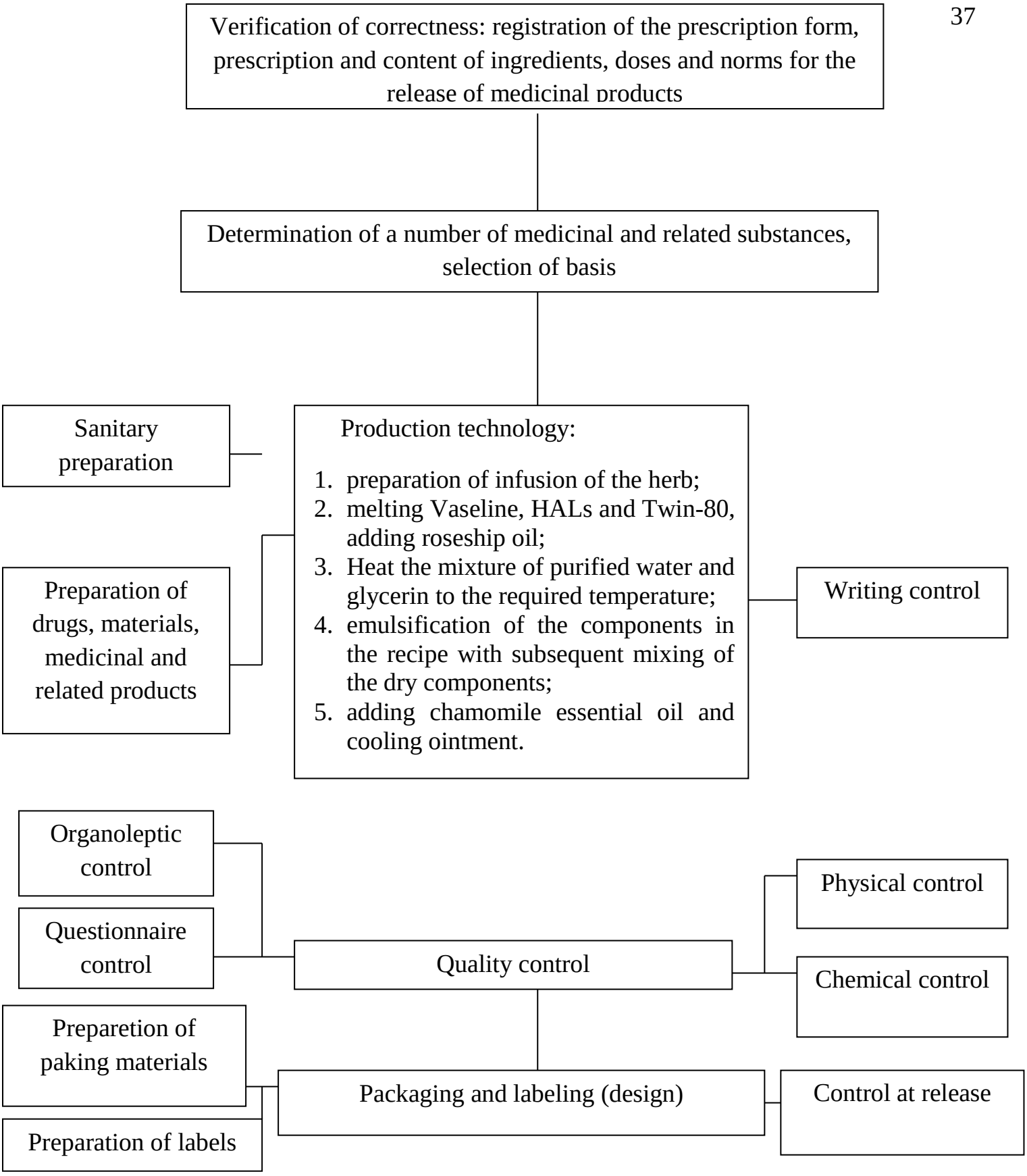
After cooling, the resulting infusion was filtered through a double layer of gauze with a cotton swab placed into a measuring flask. The raw material was squeezed and the volume of the infusion was brought up to 30 ml with purified water.

The next stage was the preparation of extemporaneous ointment. 15.0 vaseline and 8.5 VZhS, weighed on BP-20, were placed in glass No. 1, and 1.5 tween-80 (1.0-16 drops) were also added, and placed in a water bath to melt the components. After their melting, 10.0 rosehip oil was added to the solution.

10.0 glycerin and 25 ml of purified water were placed in beaker #2, the resulting mixture was heated in a water bath to the required temperature.

The final stage of the preparation of the ointment was the combination of all components and their emulsification using the RT-2 device by adding a mixture of glycerin and water and the previously obtained infusion of the grass of the herd to the melt of the components of glass No. 1.

When obtaining an ointment-like consistency, 5 drops of chamomile essential oil were added, after which the finished ointment was artificially cooled and placed in jars, decorated with labels.


Verification of correctness: registration of the prescription form, prescription and content of ingredients, doses and norms for the release of medicinal products
Determination of a number of medicinal and related substances, selection of basis
Sanitary preparation
Production technology:
1. preparation of infusion of the herb;
2. melting Vaseline, HALs and Twin-80, adding roseship oil;
3. Heat the mixture of purified water and glycerin to the required temperature;
4. emulsification of the components in the recipe with subsequent mixing of the dry components;
5. adding chamomile essential oil and cooling ointment.
Preparation of drugs, materials, medicinal and related products
Writing control
Organoleptic control
Questionnaire control
Quality control
Physical control
Chemical control
Preparetion of paking materials
Preparation of labels
Packaging and labeling (design)
Control at release

The physicochemical parameters of the developed preparation are given in Table 3.2, from which it can be seen that the ointment has a light yellow color, a pleasant smell, is homogeneous and stable.

Table 3.2

Physico-chemical indicators of model ointments

Model ointment	color	odor	homogeneity	Colloidal stability (visual)	Thermal stability (visual)
1	light yellow	pleasant	homogeneous	stable	stable
2	light yellow	pleasant	homogeneous	not stable	not stable

We also studied the stability of the ointment during storage. The results are shown in Table 3.3 which shows that the ointment retains its properties for 5 months at two temperature storage conditions.

Stability studies are ongoing. The following studies will be devoted to the development of methods of qualitative and quantitative analysis of active substances, a project of technological instructions and an information sheet on the manufacture of ointment in the conditions of pharmacies.

Table 3.3

Study of the stability of the ointment during storage

At a temperature of 20 °C ± 2.5 °C				
	1 month	2 months	3 months	5 months
Color	light yellow	light yellow	light yellow	light yellow
Odor	pleasant	pleasant	pleasant	pleasant
Homogeneity	homogeneous	homogeneous	homogeneous	homogeneous
Colloidal stability (visual)	stable	stable	stable	stable
Thermal stability (visual)	stable	stable	stable	stable
At a temperature of 10 °C ± 2.5 °C				
Color	light yellow	light yellow	light yellow	light yellow
Scent	pleasant	pleasant	pleasant	pleasant
Homogeneity	homogeneous	homogeneous	homogeneous	homogeneous
Colloidal stability (visual)	stable	stable	stable	stable
Thermal stability (visual)	stable	stable	stable	stable

CONCLUSIONS

1. The development of a dermatological ointment is carried out taking into account special requirements and has its own specific features: it should not interfere with the natural functions of the skin, it should moisturize the absorption surface and eliminate inflammation and itching.
2. The type of foundation that best meets the task is the oil/water system.
3. On the basis of technological and physico-chemical studies, the following base composition was chosen: petroleum jelly 15.0; vegetable oil 10.0; glycerin 10.0; twin-80 1.5; HALs 8.5 and water purified to 100.0.
4. It was established that, taking into account the latest trends and an individual approach to the treatment of patients, it is relevant to create an emulsion ointment based on plant components, as which we proposed: sedum grass, chamomile and rosehip oil.
5. The technology of extemporaneous ointment has been developed based on plant components: bidens tripartita, chamomile and rosehip oil.

LIST OF REFERENCES

1. Phytotherapy for Wound Healing: The Most Important Herbal Plants in Wound Healing Based on Iranian Ethnobotanical Documents / K. Solati et al. *Mini Rev. Med. Chem*. 2021. № 21(4). P. 500–519.

2. Traditional wound-healing plants used in the Balkan region (Southeast Europe) / S. Jarić et al. *J Ethnopharmacol*. 2018. № 211. P. 311–328.

3. Ethnopharmacology of Hypericum species in China: A comprehensive review on ethnobotany, phytochemistry and pharmacology / R. Zhang et al. *J Ethnopharmacol*. 2020. № 254. P. 112–686.

4. Pathak D., Mazumder A. A critical overview of challenging roles of medicinal plants in improvement of wound healing technology. *Daru*. 2024. № 32(1). P. 379–419.

5. Phytochemistry and Biological Activity of Medicinal Plants in Wound Healing: An Overview of Current Research / S. Vitale et al. *Molecules*. 2022. № 27(11). P. 3566.

6. Anitha K. V., Rajkumar K. Management of Denture Infection with Phytomedicine. *Infect Disord Drug Targets*. 2023. № 23(2). P. 290–310.

7. Bromelain: A Potent Phytomedicine / P. Agrawal et al. *Cureus*. 2022. № 14(8). P. 27876.

8. A systematic review of natural products for skin applications: Targeting inflammation, wound healing, and photo-aging / A. Fernandes et al. *Phytomedicine.* 2023. № 115. P. 154–162.

9. Державний реєстр лікарських засобів України. URL: http://www.drlz.com.ua/ibp/ddsite.nsf/all/shlist (дата звернення: 27.11.2023).

10. Компендіум. Лікарські препарати України. URL: https://compendium.com.ua/uk/ (дата звернення: 27.11.2023).

11. Pharmacy – based technology of drugs : the manual for applicants of higher education / O. I. Tykhonov et al. Kharkiv : NUPh, 2019. 488 p.

12. Workbook for Pharmacy-based Technology of Drugs : a tutorial for the 3-rd year English-speaking applicants of higher education of “Pharmacy” specialty / T. G. Yarnykh et al. Kharkiv : NUPh, 2019. 149 p.

13. Workbook for preparation to the licensed examination “KROK-2” in pharmacy-based technology of drugs: for English-speaking applicants of higher education of specialty “Pharmacy” / T. G. Yarnykh et al. Kharkiv : NUPh, 2017. 56 p.

14. Державна Фармакопея України / ДП «Український науковий фармакопейний центр якості лікарських засобів». 2-ге вид. Харків : ДП «Український науковий фармакопейний центр якості лікарських засобів», 2015. Т. 1. 1128 с.

15. Державна Фармакопея України / ДП «Український науковий фармакопейний центр якості лікарських засобів». 2-ге вид. Харків : ДП «Український науковий фармакопейний центр якості лікарських засобів», 2014. Т. 2. 724 с.

16. Державна Фармакопея України / ДП «Український науковий фармакопейний центр якості лікарських засобів». 2-ге вид. Харків : ДП «Український науковий фармакопейний центр якості лікарських засобів», 2014. Т. 3. 732 с.

17. Про затвердження правил виробництва (виготовлення) лікарських засобів в умовах аптеки : Наказ МОЗ України від 17.10.12 р. № 812. *Офіційний вісник України.* 2012. № 87. 28 с.

18. Вимоги до виготовлення нестерильних лікарськіх засобів в умовах аптек : Настанова СТ-Н МОЗУ 42 - 4.5: 2015 / розроб.: О. І. Тихонов та ін. Вид. офіц. Київ : МОЗ України, 2016. 128 с.

19. Gang R., Okello D., Kang Y. Medicinal plants used for cutaneous wound healing in Uganda; ethnomedicinal reports and pharmacological evidences. *Heliyon.* 2024. № 10(9). P. 297–317.

20. Medicinal plants and their components for wound healing applications / A. Sharma et al. *Future Journal of Pharmaceutical Sciences.* 2021. № 53. P. 1–13.

21. Prevalence of chronic wounds in the general population: systematic review and meta-analysis of observational studies / L. Martinengo et al. *Ann. Epidemiol*. 2019. № 29. P. 8–15.

22. Pharmacopea ufficiale della Republica Italiano. XII ed. Roma, 2018. 1568 p.

23. Pharmacopee Française. XI ed. Paris, 2016. URL: https://ansm.sante.fr/Mediatheque/Publications/Pharmacopee-francaise-Substances-d-origine-vegetale. (Date of access: 10.02.2024).

24. The Japanese Pharmacopeia. XVII ed. 2016. URL: http://jpdb.nihs.go.jp/kyokuhou/archives-e.htm. (Date of access: 10.02.2024).

25. U. S. Pharmacopeia. National Formulary USP 38 — NF 33. Rockville : The United States Pharmacopeial Convention. URL: https://www.usp.org/?gad_source=1&gclid=Cj0KCQjwjL (Date of access: 10.02.2024).

26. British Pharmacopoeia. London : The Stationary Office on behalf of the Medicines and Healthcare products Regulatory Agency (MHRA), 2016. 6111 p.

27. Český lékopis. Praga : Grada Publishing, 2017. 4869 p.

28. European Pharmacopoeia 8.0. Strasbourg : Council of Europe, 2014.

29. Wound Healing Properties of Selected Natural Products / N. Ibrahim et al. *Int J Environ Res Public Health.* 2018. № 15(11). P. 2360.

30. Bacterial Metabolites: A Link between Gut Microbiota and Dermatological Diseases / A. Stec et al. *Int. J. Mol. Sci*. 2023. № 24(4). P. 3494.

31. Perspective on the application of medicinal plants and natural products in wound healing: A mechanistic review / O. Yazarlu et al. *Pharmacol Res*. 2021. № 174. P. 105–121.