4.5 Theoretical aspects of creation of soft medicines for treatment of wounds

The study of the wound and the wound process is one of the current problems of surgery. The tendency to increase the number of surgical patients and surgical interventions, increase the level of complexity and duration of operations, as well as the progressive antibiotic resistance of pathogenic microflora complicate the problem of wound prevention and treatment [324, 325].

Wounds are the most common phenomenon in the daily professional activity of doctors of both surgical and non-surgical profiles. The increase in the number of purulent diseases and postoperative purulent complications, cases of generalization of infection indicate the unresolved problem of purulent infection in surgery, as well as its important socio-economic importance. All of the above necessitates an in-depth, detailed study of the wound and the wound process.

The wound process is a set of successive changes that occur in the wound, and related reactions of the body.

Today the treatment of wounds is complex and differentiated. Comprehensive treatment of wounds includes both local and general therapeutic measures. Tactically, wound treatment is carried out simultaneously by local and general measures or local measures on the background of general therapy.

For local therapy use application means, in particular soft medicines. Soft drugs play an important role in the treatment of wounds due to the ability to directly affect the leading factors of pathogenesis - pathogens, necrotic-inflammatory and reparative processes in the wound [326, 327].

According to the State Pharmacopoeia of Ukraine, soft drugs for external use are divided into ointments (water-emulsion, hydrophilic, hydrophobic), creams (lipophilic, hydrophilic), gels (lipophilic, hydrophilic), pastes, poultices, medical and skin patches, as well as liniments (ointments, creams, gels and pastes with the ability to melt at body temperature) [328].

The authors propose integrated classifications of mild drugs. Yes, E.V. Gladukh proposes to classify soft drugs on five grounds: type of production (shapeless, molded);

the nature of the action (superficial, deep); place of application (dermatological, ophthalmic, nasal, rectal, vaginal, urethral, dental); consistency (liniments, ointments, gels, creams, pastes, dry ointments) and the type of dispersed system (homogeneous, heterogeneous) [329].

Shostak T.A. with co-authors [330] based on the differentiation of soft drugs three characteristics: type of dosage form (ointment, gel, cream, paste, liniment, poultice, medical patch, skin patch); affinity for water (lipophilic, hydrophilic); type of dispersed system (homogeneous - ointments-solutions, ointments-alloys, extraction ointments, single-phase gels; heterogeneous - suspension ointments, emulsion ointments, combined ointments, creams, two-phase gels, multiphase gels).

The choice of drug composition, dosage form and technological methods is made at the stage of pharmaceutical development, where the foundations of quality, efficacy and safety of the drug are laid [328, 331, 332]. The main conditions of action of topical drugs are the release of active ingredients from the dosage form and penetration through biological membranes to the lesion [332 - 334]. The release of active ingredients is the initial and very important stage of providing therapeutic action. Crucial at this stage are pharmaceutical factors: physical properties of active ingredients and excipients (degree of dispersion, polymorphism, solubility, viscosity, etc.), nature and amount of base-carrier and excipients that are part of the drug, type of drug forms and technological operations carried out during its manufacture [329, 332, 334].

Carrier bases are important components of soft drugs, as they account for 90% or more of the total mass and affect the activity of active ingredients and rheological properties of the dosage form [329, 330, 334, 334]. Classification of bases of soft medicines, according to requirements of SPU harmonized with the European Pharmacopoeia, is carried out on signs of affinity to water (for ointments - hydrophobic, water-emulsion, hydrophilic; for creams and gels - lipophilic and hydrophilic) and type of dispersed system single-phase or multiphase) [328, 335, 336].

The US Pharmacopoeia, in addition to the above features, also uses the differentiation of the ability to absorb water, which leads to the allocation of four

classes of bases for ointments: hydrocarbons (hydrophobic), absorbent (divided into 2 groups, depending on the type of emulsion formed). or o / v), water-flushing and water-soluble [337]. Carbohydrate bases are anhydrous, although they may include small amounts of aqueous solutions and are able to form a waterproof film on the skin surface. Absorption bases allow to enter aqueous solutions of active ingredients into structure of soft medicines. Water-wash bases are formed from the aqueous phase, emulsifiers and dispersed oil phase, so they are easily washed off with water and have the ability to absorb serous secretions. Water-soluble bases (gels) do not contain hydrophobic components [337, 338].

Rationale for the choice of carrier base in the creation of soft drugs, along with the choice of active ingredients and their concentration, is one of the basic fragments of the study, because it is the base to the greatest extent affects the rate and completeness of API release [329, 331, 334, 335 , 339], and also provides the optimal consistency of the drug and its consumer characteristics [329, 338-341].

The results of numerous studies show that the use of ointments on hydrophilic and emulsion bases, which are characterized by dehydrating action and the ability to effectively conduct active ingredients to wound canals and cavities, is clinically justified for local treatment of the wound process [331, 334, 335, 341 - 344]. Studies by IM Pertsev and co-authors found that the active ingredients, insoluble or slightly soluble in water (chloramphenicol, tetracycline, streptocide, norsulfazole, anesthetic), are less released from hydrophobic ointment bases than hydrophilic, with increasing degree of foundations. It has also been proven that water-soluble APIs are also better released from hydrophilic bases than from hydrophobic or emulsion types in / o [332, 335]. These authors studied the dependence of pharmacokinetic activity of active ingredients in suspension soft drugs on the degree of their dispersion, which allowed to record an increase in the rate and completeness of release of chloramphenicol, aromatic amines, sulfonamides and corticosteroids before their crushing. According to Bhowmik D. and co-authors, water-based bases provide the best absorption of active ingredients from soft drugs through the skin [338]. An important feature of drugs for the local treatment of the wound process is that not only the active ingredients but also

the bases have therapeutic functions due to their osmotic activity [345]. According to research Davtyan LL osmotic activity of soft drugs can be divided into small (up to 83%), medium (up to 193%) and severe (from 240% and above) [346].

According to scientists, in the first phase of the wound process with a significant exudate is rational to use ointments that have a very strong dehydrating effect - ointments based on polyethylene oxide [331, 333, 335, 339, 340, 345]. Research conducted by Bezrukavym EA [344], Grigoryan A.Yu. with co-authors [347], Yaremchuk AA [348], Locksmith OI demonstrated the undeniable advantage of polyethylene oxide (PEO) 400 as a dehydrating agent in ointment bases.

Vernikovsky V.V., based on the results of the study of the osmotic activity of 11 ointment bases, proposed their division into 4 groups: 1) bases with maximum osmotic activity - alloys PEO-400, PEO-1500 in different ratios; 2) bases with pronounced osmotic activity - hydrogels of PEO and propylene glycol or carbopol; 3) bases with moderate osmotic activity - hydrogels of carbopol and sodium alginate; 4) bases with low osmotic activity - chitosan hydrogels [349].

It should be noted that the strong osmotic activity of polyethylene oxide bases prevents their use in the second and third phases of the wound process, because their components in contact with the wound unidirectionally adsorb both wound exudate and intracellular fluid of granulation tissue, causing its dehydration and subsequent death [350, 351].

In order to prevent excessive dehydration of granulation tissue of wounds in the composition of ointment bases should include osmotically active substances of different molecular weight, as well as hydrophilic non-aqueous solvents (MPP) with low molecular weight, such as propylene glycol (PG), whose molecules can penetrate biological bind intracellular water and prevent tissue dehydration under the influence of PEO [351].

Some authors prefer the use of creams and gels of moderate osmotic activity, containing a complex of active ingredients of different directions, for the treatment of purulent-inflammatory phase of the wound process [351, 352].

In the second and third phases of the wound process, it is advisable to use mild drugs that will promote the reparative processes in the wound and provide comfortable conditions for the affected tissues. Such requirements, according to Gladukh EV and Bezrukavy EA, correspond to ointments on two types of combined bases - viscoplastic emulsions of the first kind containing hydrophilic solvents, and viscoplastic gels formed by hydrophilic surfactants and higher fatty alcohols, which include hydrophilic solutions. and osmotically active polymers [351]. The selection of components of the oil phase allows to further enhance the regeneration of wound defect tissues by introducing into the MLZ vegetable oils - corn [344] or castor [350], which have in addition to the necessary technological characteristics, also reparative and anti-inflammatory properties.

For production of modern soft medicines for treatment of wounds use multicomponent ointment bases which contain substances with various physicochemical properties that requires application of various auxiliary substances for formation of the set medical properties and consumer characteristics [353, 354].

According to the functional purpose of excipients that are part of the MLZ, Gladukh EV recommends to divide into: substances that increase the melting point and viscosity of bases; hydrophobic and hydrophilic solvents; emulsifiers type o / v and v / o; gelling agents; antimicrobial preservatives; antioxidants; solubilizers; fragrances and deodorants; pH regulators [329].

Davtian LL with co-authors it is proposed to classify excipients according to the influence on technological and pharmacotherapeutic characteristics of MLZ with the selection of the following groups: carriers of active ingredients - molding substances (gelling agents, film-forming, foaming agents, solvents); stabilizers (emulsifiers, thickeners, preservatives); hydrophilizers; solubilizers; extenders; fragrances; correctors; dyes [355].

However, some excipients may simultaneously perform several functions or change the purpose depending on the quality of the dosage form and the features of its technology. All the above determines the importance of rational choice of excipients

in order to ensure high therapeutic activity and minimize side effects of soft drugs [334, 335, 341, 353].

The main conditions of action of any drug are the release of active ingredients from LF, penetration through biological membranes and transportation to the site of action with the flow of physiological body fluids [356, 357]. This process of release of active substances is the initial and crucial stage of ensuring the therapeutic effect of the drug. Crucial at this stage are a number of pharmaceutical factors, namely: physical properties of ingredients (active ingredients, excipients), nature and amount of carrier base and excipients, type of dosage form and technology of drug production [358 - 360] . Biophysical and biochemical properties of drug ingredients determine its nature, speed and strength of action on the body; is a leading factor in determining the specifics of the pharmacotherapeutic effect (speed, strength, duration), type of dosage form, routes of administration [361, 362].

The choice of method of drug administration is a crucial point in treatment. Administration is possible naturally (enteral, inhalation, dermal), in which the transport of drugs to the body is provided by the physiological absorption capacity of mucous membranes and skin, or by using technical means where there is a violent pathological entry into the body. For example, drugs intended for use in the form of aerosols are administered using a nebulizer; dry powder inhaler or metered dose metered dose inhaler [363 - 365]. The purpose of any drug is to accelerate the cleaning of the wound, suppression of the infectious process in it, providing a protective effect on tissues for further regeneration in the wound, stimulating its healing.

Mild dosage forms. The effectiveness of local wound healing is determined by the rational selection of ingredients (active ingredients and excipients), type of dosage form, sorption characteristics of the base [366]. Unlike no other dosage form, experts emphasize the presence of a leading role of excipients, in particular the carrier base, in relation to soft drugs. These are the main components, because their content is up to 90% of the total mass. The base undergoes a complex interaction with the introduced drugs, which leads to changes in its stability, the order of release and absorption, pharmacological action, largely affects the manifestation of various side effects [367,

368]. In general, today the theoretical foundations of local soft drugs have been studied quite thoroughly [360, 368, 369].

The State Pharmacopoeia of Ukraine in the general pharmacopoeial article "Soft medicines for external use" (Praeparationes molles ad usum dermicum) [370 - 373] makes clear requirements for drugs that conditionally unite the general concept of "Ointments" (Unguenta), on the basis, sterility, production technologies, etc. As noted by Goritsky VM and Smetanina KI (2012), the therapeutic effect of soft drugs is determined mainly by the drug substance, and the ointment base (Basis Unguenti) provides a targeted nature of its biotransformation and the necessary pharmacotherapeutic action [374]. Therefore, at present, considerable attention is paid to the development of new and fundamentally new combined bases with valuable properties [369, 375, 376]. Examples are the following pharmaceutical compositions: multicomponent antimicrobial ointment on a hydrophilic basis levomecol + liasten (immunomodulator muramylpeptide series) with the ability to simultaneously affect several parts of the pathogenetic process [364]; wound cleansing ointments with bases for immobilization of proteolytic enzymes (alloys of polyethylene oxides (PEO 400, PEO 1500)), which differ from traditional drugs in duration of osmotic effect (up to 18 h) and a wide range of antimicrobial activity [377, 378]; multicomponent polyfactor ointment based on enterosgel, containing antiseptic (furacillin, chlorhexidine bigluconate or hexetidine) in combination with a stimulator of the regeneration process - methyluracil in phase I-II of the wound, etc. [379].

The main chemical and pharmaceutical requirement to ointment bases as components of soft medicines for treatment of wounds (especially purulent inflammations) is maintenance of outflow of purulent-necrotic allocation. Literary analysis showed a rather small range of bases with the specified properties. We find interesting the study of Shostak TA on singing. (2014), which conducted a comparative analysis of pharmacopoeias of leading countries and the State Pharmacopoeia of Ukraine on the modern classification of soft drugs and their bases [380 - 382]. It should be noted some revival of the relevant direction of scientific work at the present stage - the development of new ointment bases, the main property of which is osmotic activity

[383, 384]. In general, taking into account the current requirements of good pharmacy practice, domestic scientists consider it necessary to further expand the range of extemporaneous media for pharmacy practice [369, 384, 385, 366, 367].

As the review of the literature showed, the qualitative and quantitative composition of ointment-like forms is constantly being improved [344, 350, 375]. Centuries of competition of dosage forms in this form have honed their range, method of application and manufacturing technology. Carrying out a number of successive technological stages of manufacturing drugs is regulated by the requirements of regulatory documents [386 - 388], prescribed in the basic professional literature [360, 389 - 393] and open information resources [394].

In our opinion, the results of pharmacotechnological studies of soft drugs of complex action for local treatment of wounds in servicemen are widely covered [385], scientists are trying to optimize the technological parameters of this LF [385, 395].

Today, modern technological approaches to the creation of combined ointments [332, 344, 396 - 399] of this direction are unified. Of particular interest are scientific papers on the development of the composition and technology of soft drugs for the treatment of wounds in a certain phase [344, 350, 397, 400].

At present, the rules of control of individual stages and evaluation of the finished product according to technological quality indicators are determined [401]. The results of the study of the microbiological purity of the cream with a phytocomponent [402], toxicological studies of the cream for the treatment of wounds by in vivo [403]. In general, military medical personnel are trying to create an optimal model of local wound healing for the needs of the medical service of the Armed Forces of Ukraine [404]. The choice of ointments as an object of biopharmaceutical research constantly attracts scientists for wide use in medical practice; the ability to incorporate a variety of active ingredients in accordance with therapeutic, physicochemical and structural-rheological properties, concentration, pharmacodynamics and type of therapeutic action (surface, local, local) depending on the purpose; the ability to change the technological methods of manufacture and composition of the ointment base [395, 404, 405 - 407].

The determining factor in the development of new prescriptions for mild dosage forms is to take into account the role of factors that affect the degree of release of substances, speed, completeness of absorption and purpose of the drug. In particular, we are talking about the justification of the optimal temperature factor [375, 395, 408], physico-chemical and structural-mechanical studies of mild dosage forms with subsequent establishment of their compliance with the requirements of the State Pharmacopoeia of Ukraine [355].

Recently, the use of advances in biotechnology to improve wound healing has become widespread. Cellular technologies are being introduced - the cultivation of keratinocytes on collagen gel, created "living equivalents of the skin" (Apligraf, Integra, Epicell, Epidex, Myskin, AlloDerm, etc.), innovative drugs (PolyHeal) [367, 408].

According to Chadayev AP and Klimiashvili AD (2002), in the early 2020's a new development began to take shape in the improvement of local treatment - the development of drug carriers. After all, applying the ointment directly to the wound reduces the effectiveness of healing due to impaired gas, moisture and heat transfer. The positive value of drug carriers was also found in relation to the proteinases immobilized on them (Tolstykh PP et al., 1985; Gostishchev VK et al., 1986). Of particular importance are carriers in the treatment of large wound surfaces, occurring against the background of microcirculation disorders in tissues.

Despite the above, the scientific literature identifies a number of problems that arise in surgical practice with the use of soft drugs, namely:

- Insufficient effectiveness of many drugs due to the shortcomings of the base and / or monocomponent composition [324, 409];
- a small number of drugs that have a specific focus on a particular phase of the wound and the corresponding osmotic activity [366, 410];
- increasing the resistance of wound pathogens to existing drugs [377, 407, 336].

Application dosage forms have recently become increasingly popular [411]. To date, none of the developed methods of drug administration, except transdermal, allows

you to create and simply regulate the high concentration of drugs in the local area. The use of transdermal therapeutic systems minimizes the variability of the therapeutic effect, reduces the effect of systemic metabolism in the liver, the use of substances with a narrow therapeutic index, and eliminates the possibility of overdose in the initial period of therapy and the associated frequency of side effects. This non-invasive method of administration of drugs is convenient to use and economical, because the targeted use of drugs can reduce the need for their number more than 100 times while maintaining the therapeutic effect [412].

Wound dressings. According to the screening analysis, medical dressings are extremely widely available today, many of which have drug impregnation (including biologically active ones). Moreover, the specified impregnation, depending on the intended purpose of the dressing material, may consist of one or more components belonging to different classes of pharmaceuticals [413]. Coatings (bandages), their further development can be considered as a modern direction in improving the local treatment of wounds of various etiologies. The use of fixing materials for these drug carriers has a multi-stage history - from filter paper and gauze wipes to a variety of multilayer multifunctional nanomaterials and dressings [414, 415]. The specified dosage form is quite unique, original, economically affordable, simple to use [330]; varies widely in the chemical composition of the base and the drugs introduced into them. The main structural element is an elastic polymer film (hydrophobic and hydrophilic, insoluble in wound exudate). 1-2 minutes after application of the aerosol composition to the wound, a film-like coating is formed by evaporation of the solvent [416].

Appropriate treatment of patients with skin defects due to purulent soft tissue infection is most effective. For example, the properties of the protective coating have bandages Epigard i Duoderm (USA), Opraflex (Germany), Sincrit and Acutola (Czech Republic), Nobecutan (Sweden), Lifuzol (Russia), Linquidoplast T (Germany), providing close contact with the wound during its healing [417].

Wound dressing components and dressings made from them should ensure the absorption of pathological secretions from the wound (necrobiosis products and

necrotized tissues, microorganisms and their toxins) and the optimal microclimate in the wound (humidity, air access, temperature), to isolate wounds from additional contamination by microorganisms from the external environment. When removed, the bandage should not cause the patient any suffering.

Recently, the range of samples of wound materials and tools on the world pharmaceutical market has significantly increased (over 3,000). Today, only 45 American companies produce about 125 wound dressings and 2,000 varieties. There is a constant expansion of the range of this LF produced in Western Europe and Ukraine (Rudowski W., 2008; Strelli R., 2010) [418].

Possible classification variants of wound dressings are given in the dissertation of Kornienko VV (2016). In particular, according to the form of manufacture and method of application, they are divided into sponges, gel-forming coatings, film coatings and coatings formed by spraying the composition in the form of an aerosol, combined compositions. According to the stability of the coating are considered as biodegradable (absorbable) and bioinert. As a rule, biodegradable coatings are made of natural polymers (gelatin, collagen, chitosan), and bioinert - from synthetic materials [410].

Literary analysis has revealed the introduction in recent years of new dressings, tools and coatings for the treatment of wounds of natural origin. We are talking about different versions of canned skin, amniotic membrane and preparations of the dermis; bandages based on materials of animal origin - collagen-based coatings, "cultured skin", obtained from the epithelial cells of the patient on collagen [378]; materials of plant origin - cotton bandages based on cellulose, viscose or a combination thereof; bandages based on synthetic materials - made of polyurethane foam, polyvinyl chloride, nylon, silicone and polyamide films and other polymeric materials; means on the basis of materials of different origin - as a rule, multilayered, their sorption-active layer is usually a cellulose component, etc. [419].

Volkov AA and Bolshakova GM (2009) emphasize the widespread use of bandages with ointments, which include corticosteroids in low concentrations; local warm baths with potassium permanganate; treatment of RP without bandages in a

sterile isolation or oxyhyperbaric chamber - especially in case of complication of the wound by anaerobic infection, etc. The use of bandages with indifferent and stimulating ointments for the treatment of wounds in the phase of scar formation and reorganization is highly effective. This allows you to significantly accelerate the epithelialization of the wound and protect it from possible trauma [342, 344].

Highly effective is the use of plant-based coatings in the treatment of the wounded, the development of which is a separate area of research. In particular, the dissertation of Voronin AS (2012), who defended the author's method of treatment of wounds and wound infections of the skin using a wound dressing containing phytotherapeutic substrate in the treatment layer (water and alcohol-based), is of interest. The author proved the presence of antibacterial and anti-inflammatory effect of this drug, the ability to optimize the course of reparative processes in the area of the wound defect of the skin; activation of collagenogenesis processes and accelerated formation of connective tissue [402]. Kolsanov AV with singing. (2013) evaluated the effectiveness of wound dressings in the treatment of wounds and wound infections of the skin and soft tissues in the experiment.

Of course, the accumulated experience allows specialists to clearly grade a certain amount of care for the wounded, dressings and tools [333, 334]. In particular, dressings used in clinical practice, depending on the direction of the expected effect, contain certain means of chemical and biological effects on the wound - antiseptics, antibiotics, cleaning agents, irrigators, growth factors, etc. [333, 334].

One of the main factors influencing rapid healing is the maintenance of a moist environment and pH in the wound. Significant advantages of the method of wet wound healing for the first time, even before the publications of Winter in 1962, showed R. Breitman (1960) [333, 334]. Coatings (bandages), their further development can be considered as a modern direction in improving the local treatment of wounds of various etiologies (table 1).

Table 1

Characteristics of some modern wound dressings *

Types of bandages	Indications to application	Functional properties	Examples
Hydro Gel	Infections are purulent and difficult to heal; burns, ulcers (exudation min)	Instant creation of a moist environment, the ability to absorb wound exudate, promote rehydration and rejection of necrosis, reduce pain, do not stick to the wound	Hydrosorb Gell, Hydro-tac, Intrasite Gel, Flaminal Hydro, NuGel, Aqua-Gel®
Hydro - colloid	Chronic uninfected wounds (moderate exudation)	Fluid adsorption, stimulation and protection of granulation, sufficient permeability, self-fixing and hypo-allergenic agent	Hydrocoll, Dermiflex®, Comfeel® Plus, Granuflex®

* Developed by the author based on materials: [335, 341, 420].

The peculiarity of this group of dressings is its versatility, atraumaticity, hypoallergenicity. They have a complex pathogenetically directed action, able to quickly create and maintain optimal conditions in the pathological focus for the normalization of reparative and regenerative processes in the wound. These three-layer bandages (contact, sorption and top insulating) with clearly defined functions of each component. In particular, the contact layer in interaction with the wound surface reduces the adhesion to it; the task of the middle sorption layer is irreversible sorption, retention and inactivation of wound exudate; the outer insulating membrane is able to create a wound occlusion and is occlusive to the wound [333].

The range of these therapeutic dressings is constantly expanding. According to Kovalenko OM (2010), hydrocolloid coatings consist of a self-adhesive mass, which includes polyisobutylene with drops of gelatin, pectin or chitosan. Upon contact with

the exudate of the wound, these drops absorb it, swell and create a semi-liquid mass [334].

Modern third-generation coatings developed by innovative technologies are hydrophilic, polyurethane films and hydrogels. For example, Aqua-Gel® hydrogel coating is a composition of natural and synthetic polymers (polyvinylpyrrolidone, polyethylene glycol and agar), exposed to ionizing radiation, which binds the polymer chains and ensures the sterility of the coating. Coatings of this type retain moisture in the wound, absorb biological exudates, evaporate excess water. At the same time keep on a wound a thin layer of own proteins of the patient (including growth factors) that is considered as the main reason of the accelerated healing of wounds. [333, 334].

Ukrainian scientists have developed a unique technology for the production of sterile hydrogel medical bandages for soldiers, combining all the advantages of foreign counterparts. Means of the Arma-Gel + line (manufacturer Ukrtechmed) are designed for the treatment of gunshot wounds, thermal injuries (of varying severity), bedsores, dermatological problems; have high strength characteristics that allow them to be used on large surfaces and with a longer period of time without bandages [421]. The specified bandage, which consists of 95% water, is fitted with a polymer frame to level its possible leakage. This polypropylene surgical mesh does not affect the absorption capacity of the hydrogel and does not reduce its elastic properties. The transparency of the hydrogel dressings allows you to monitor the condition of the wound and to carry out certain medical manipulations in a timely manner. According to experts, this drug is indispensable at all stages of specialized medical care, such as "Arma-gel with novocaine" (for pain relief and prevention of wound drying), "Arma-gel with nanosilicon" (in the exudation phase), "Arma-gel with furacillin "(to prevent infection of large area burns)," Arma gel with methyluracil "(to create optimal conditions for tissue regeneration and stimulation of the epithelialization process), etc.

Popadyuk's O. Ya. research on singing is interesting. (2019), aimed at studying the therapeutic properties of nanomaterial biopolymer films. In particular, the authors proved that film degradation provides dosed prolonged delivery of active ingredients directly to the affected area (wound) [422].

Blednov AV (2006) reported the creation of a group of dressings with immobilized forms of active substances intended for different phases of the wound. These therapeutic dressings have not only pronounced proteolytic and antibacterial activity, but also sorption properties, which significantly accelerates the cleansing and healing of purulent wounds. Thus, the rapid development of "therapeutic nanotechnologies" continues [414]. In particular, Prokopchuk NR and others. (2017) report on the development of an innovative drug "Wound coatings with nanofibers of chitosan" Chitomed-wound-healing sterile "by NanoSpider technology - capillary electroforming of nanofibers from solutions of biocompatible polymers with antimicrobial and wound-healing action. The new drug is highly effective for the treatment of significant burns, trophic ulcers and wounds that do not heal for a long time.

Analysis of the results of biopharmaceutical studies conducted by IM Pertsev and OA Ruban (2013), made it possible to create drug systems for the treatment of infected wounds and burns, where all components were active and each individually "controlled" a factor of inflammation: unprofitable tissue hydration, necrosis, suppression of infection, pain, evacuation of wound contents in the first phase or stimulation of granulation growth in the second phase, or formation of epithelialization and ensuring complete wound healing in the third phase of inflammation. This prompted the development of new approaches to the creation of pharmaceuticals not only in the form of ointments, gels, emulsions, but also aerosols and polymer films; became a rich visual material for improving the effectiveness and improvement of drug consumption, gave a new impetus to the formation of new thinking about the therapeutic efficacy of drugs [358, 359].

Dosage forms that have been created in recent decades mainly require the use of new excipients that require comprehensive study in order to be included in the composition of drugs. Military medical specialists widely cover the results of research in this area. This concerns the further study of certain properties of aerosols - technological, rheological, physicochemical, toxicological, biopharmaceutical and specific [395, 402, 403].

According to Vyas K.S., Vasconez H.C. (2014), increasing the effectiveness of drugs for the local treatment of purulent wounds is possible through the further development of new combination drugs. In particular, to significantly increase the effectiveness of treatment of wound infection will use the developed Tarasenko VO from singing. (2020) film-forming aerosol of antimicrobial and anesthetic action, the composition of which is scientifically substantiated in accordance with the pathogenesis of the wound, taking into account its phase and the nature of the microflora. Researchers conducted an experimental study of the toxicological characteristics of drugs to determine the degree of its safety in different ways of entry into the body [375, 395].

Despite the dynamic development of medicine and the active introduction of new drugs for the treatment of wounds of various etiologies, including and antibacterial agents, it is important to expand the range of research on the development and implementation in the production and medical practice of alternative drugs of particular interest. For example, Kuznetsova TA, Besednova NN, Kovalev NN, Somova LM and others. (2015) developed gel forms of promising biocompatible wound dressings based on active ingredients from marine aquatic organisms (Hydrobiontes): plankton, jellyfish, mollusks, algae, fish, pinnipeds, etc. The model of thermal burns shows a pronounced effect of appropriate samples of gel coating on wound healing, proved the ability to significantly accelerate the regeneration process. Scientific school of prof. Tikhonova OI (Kharkiv) for the first time theoretically generalized and experimentally developed ideas about biologically active fractions of beekeeping products, high medicinal properties, proved their high medicinal properties and the possibility of integrated use in pharmaceutical and industrial drug production [356, 392].

The results of research on drugs based not only on animal but also on plant origin are widely presented. The study of little-known plants continues. For example, Subsai et al. (2015) reported a pronounced anti-inflammatory and wound-healing effect of the tropical Asian plant Caesalpinia sappan (genus Fabaceae) [344]. Scientific and practical works devoted to the development of the composition, manufacturing technology, experimental and clinical justification and evaluation of the quality of

medicines based on plant extracts of various consistencies are published. In particular: 1) ointments with extracts of Lofant anise (Agastache foeniculum, genus Lamiaceae), foxglove (Pentaphylloides fruticose, genus Rosaceae), Chamomile (Matricaria recutita, genus Asteraceae), cinnamon Populus tremula (genus Salicaceae), hanging birch bark (Betula pendula, genus Betulaceae), oak bark (Quercus robur, genus Fagaceae) and horse chestnut seeds (Aesculus hippocastanum, genus Sapindaceae) [367, 384]; 2) gels with Burdock extract (Arctium lappa, genus Asteraceae) [423], Oman extract and Inula helenium & I. britannica, genus Asteraceae; 3) phytofuels based on dry extracts [326, 327], phytotherapeutic wound dressings for the treatment of wounds and wound soft tissue skin infections [336, 337], etc.

According to experts, many years of experience in folk medicine proves the effectiveness of the use of lipophilic extracts from medicinal substances for the treatment of wounds of various etiologies. Extraction with fatty oils facilitates the removal, retention and delivery of biologically active substances, in particular essential oils, to biological tissue. This is important because the active substances used to treat wounds must have a wide range of antimicrobial activity and prevent secondary infection. Therefore, to ensure a wide range of pharmacological action of drugs, including soft, developed as active ingredients, often choose lipophilic extracts: Yarrow (Achillea millefolium, genus Asteraceae), Dried flowers (Gnaphalium uliginosum, genus Asterapoa, genus Asteraceae). black (Populus nigra, genus Salicaceae), St. John's wort (Hypericum perforatum, genus Clusiaceae), Calendula (Calendula officinalis, genus Asteraceae). The complex of BAS extracts, consisting of essential oils, resins, fat-soluble vitamins, carotenoids and chlorophyll derivatives, will provide the necessary antimicrobial, anti-inflammatory and reparative action of the drug [423]. Relevant patent and licensing work is being carried out quite widely today. This applies to the developed complex pharmaceutical compositions in the form of ointments (anti-inflammatory, antimicrobial, analgesic, reparative action) [384, 395], cream (antimicrobial, anti-inflammatory, anesthetic action), aerosol (antimicrobial, anesthetic action) and so on.

Undoubtedly, the events on the territory of Ukraine have somewhat adjusted the directions of scientific research [403]. The creation of drugs of appropriate pharmacotherapeutic action (anti-inflammatory, wound-healing, anesthetic, antibacterial, reparative, etc.) is very important for medical and rehabilitation work and ensuring high combat capability of servicemen. Also, special attention is paid to the pharmaceutical development of complex drugs for the needs of military medicine, the study of models of their design, clinical and pharmacological evaluation.