Original Article

Theoretical Basis of Creation of Soft Medicinal Products of Local Application

Victoria Tarasenko, Andrew Solomennyy, Alexei Pidlisnyy, Alina Koval*, Valentina Vaschuk, Aleksandr Shmatenko, Lena Davtian, NataliaTakhtaulova, Ivanna Sakhanda, Koziko Natalia, Shumeiko Mykola

Ukrainian Military Medical Academy, Kyiv, Ukraine.

Abstract

The widespread use of firearms in the cells of military conflicts, modern weapons, bullets, and new-generation devices causes an increase in the number of severe wounds, characterized by significant damage to soft tissues, blood vessels and the like.
The creation of soft medicinal products contributes to faster regenerative processes of affected soft tissues.

Keywords: soft medicinal products, local application, wounds

Introduction

On the epic of providing care to the wounded, in the joint Forces Operation in Ukraine, found that in 28% of cases, gunshot wounds are complicated by purulent-infectious processes. The share of polytrauma in the structure of modern trauma is from 25 to 6%.

In today's world, not only combat tactics but also methods and physical methods of wound healing and healing are being improved. However, these methods can not be used both in the advanced and in the stages of medical evacuation of the wounded. During the evacuation stages, dressings and medicines with a resilient viscous medium for topical application, such as ointment, cream, gel, film-forming aerosols and film materials with immobilized medicines, do not lose their relevance. The widespread use of these drugs is due to the simplicity and ease of use, so wound healing by application methods remains a priority in medical practice.

Research Materials

The main conditions of action of drugs are the release of active substances from the dosage form, penetration through biological membranes and transportation to the place of action with the current physiological fluids of the body [1, 2]. The release of drugs from the dosage form is an initial and very important step in ensuring therapeutic action. Pharmaceutical factors are crucial at this stage: physical properties of active and auxiliary substances (degree of dispersion, polymorphism, solubility, viscosity, etc.), nature and amount of carrier base and excipients that are part of the medicinal products, type of dosage form and technological operations performed in its manufacture [3-6].

Soft medicines. EV Gladukh proposes to classify soft drugs according to the features shown in fig. 1 [7].

Signs of classification of soft medicines
Type of receipt: Formless; molded.
Nature of action: surface; deep.
Place of application: dermatological; ophthalmic; nasal; rectal; vaginal; urethral; dental
Consistency: liniment; proper ointment; gels; creams; shepherd; dry ointments.
Type of dispersed system: homogeneous; heterogeneous.

Tab. 1. Classification of soft medicines

Address for correspondence: Alina Koval. Ukrainian Military Medical Academy, Kyiv, Ukraine.
Email: alinasposts @ gmail.com

How to cite this article: Tarasenko, V., Solomennyy, A., Pidlisnyy, A., Koval, A., Vaschuk, V., Davtian, L. and et al. Theoretical Basis of Creation of Soft Medicinal Products of Local Application. Arch Pharma Pract 2020;11(2):130-6.

Soft drugs are distinguished by the following features: they must have a high degree of adhesion; the active ingredients of the drug composition should be well released from the base, ensuring the accuracy of dosing and maintaining the required concentration at the site of application, but not have a resorptive effect; no side effects should be observed; soft medicine should be easy to use; the medicinal product must retain Physico-chemical parameters within the prescribed shelf life [2, 5, 6].

Research Methods

According to the authors of [2], the therapeutic efficacy of drugs should be evaluated not on the composition of active substances, but on the aggregate properties obtained by a certain technology of the pharmaceutical product, since the active and auxiliary substances form a specific system in which each component performs certain functions - active substances provide a therapeutic effect, formative substances - physical-chemical and consumer characteristics of a particular dosage form. Substances that optimize certain technological processes provide a drug capable of storing all of its intended properties for a fixed time.

By function, the excipients included in soft medicines, EV Gladukh recommends dividing into 12 groups: carrier bases; substances that increase the melting point and the viscosity of the substrates; hydrophobic solvents; hydrophilic solvents; oil/water type emulsifiers; water/oil type emulsifiers; gelling agents; antimicrobial preservatives; antioxidants; solubilizers; fragrances and deodorants; pH regulators [7].

Davtian LL and his co-authors proposed to classify excipients by influence on the technological and pharmacotherapeutic characteristics of soft drugs with the following groups: carriers of active substances - forming substances: gel-forming fillers bases; film-forming; foaming agents; solvents; stabilizers: emulsifiers; thickeners; preservatives; hydrophilizers; solubilizers; prolongers; flavorings; correctors; dyes [2].

In the creation of soft drugs, one of the main research fragments is the sound choice of the carrier base, since it has the greatest influence on the speed and completeness of release of active substances [8-10] and provides the optimal consistency of drugs and its consumption characteristics [11, 12].

An important feature of this group of medicines is that the excipients make up more than 90%. However, some excipients may simultaneously perform several functions or change the purpose depending on the qualitative composition of the dosage form and features of its technology. All of the above determines the importance of the rational selection of excipients to ensure high therapeutic activity and minimize the side effects of soft drugs [13].

The above analysis of sources of scientific literature has shown that the main dosage forms used at the present stage to achieve topical effect in the treatment of infectious-inflammatory diseases are hydrophilic and emulsion ointments, as well as creams and gels.

According to EV Gladukh's classification, ointments are completely free dispersion systems with plastic or elastic-viscous dispersion medium [7, 14, 15].

By definition of VA Golovkin with co-authors, ointments are systems with high viscosity, which can form an even layer at the surface of mucous membranes and skin at room temperature, which does not drain, and at high temperature transform into a thick liquid [6, 16].

At the present stage, as a basis for ointments, creams, gels, a large number of components are used to form complex physicochemical systems. Thus, the bases for the manufacture of hydrophilic ointments can be divided into 2 groups: 1) water-soluble containing hydrophilic non-aqueous solvents (polyethylene glycol-400, propylene glycol, etc.) and a sufficiently large number of water-soluble polymers (polyethylene glycol-1500, proxanol-268 and others); 2) water washes containing hydrophilic non-aqueous solvents (polyethylene glycol -400, propylene glycol, etc.), water-soluble polymers (polyethylene glycol-1500, proxanol-268 and others), lipophilic substances (higher fatty alcohols, petrolatum, petrolatum, lanolin), lanolin, and also require v / v emulsifiers as they are oil/water type emulsions [7].

In the manufacture of absorbent ointments, it is possible to use hydrophobic bases of 2 groups: bases which are water/oil or oil/water/oil type emulsions, to which it is possible to enter aqueous solutions of active substances by emulsification; bases consisting of hydrocarbons and emulsifiers of the water/oil type, to which considerable quantities of aqueous solutions of medicinal substances can be introduced with the formation of an emulsion of the type o / o [7, 13-15, 17-20].

Studies conducted by MV Gavrilin and AV Podluzhna found an increase in antifungal activity of ointments made on hydrophilic polymer bases, in particular, with a content of 67.8 h polyethylene glycol-1500 and 30.0 h propylene glycol, compared with ointments on emulsion bases [21, 22].

Of great interest at the present stage are the ointment bases of the class of rare-folded acrylic polymers, the advantages of which are the provision of a prolonged effect of the drug, more complete and uniform release of active substances, the ability to absorb secretory products, high mucoadhesive affinity, related affinity, due to easy washing with water and no contamination of clothing [22, 23].

The feasibility of using a hydrophilic base of a styrene copolymer with maleic anhydride of 2% concentration for the manufacture of ointments for the treatment of inflammatory gynecological processes with the content of propolis oil extract in combination with dibunol [24] is substantiated.

Scientists of Kursk State Medical University have found an increased manifestation of antimicrobial activity of ointments made on such hydrophilic bases as carboxymethyl cellulose, sodium carboxymethyl cellulose, and hydroxymethyl cellulose, alloy polyethylene glycol-1500 and polyethylene glycol, 400 meths, glycol. The use of these bases provides a rapid flow of active substances to microbial cells; also, certain dehydration activity of the base against gram-positive microorganisms reduces their ability to resist, which also contributes to the therapeutic activity of developed ointments [25].

Perspective in the manufacture of ointments, according to S. Inagamov et al., Is the use of a base consisting of 9 parts of 8% aqueous sodium carboxymethylcellulose and 1 part of a synthetic urea-formaldehyde oligomer linear structure. In the aqueous medium, these compounds form a poly complex gel that has a unique feature of structure - the ability to form nanostructures with dimensions that can be adjusted, which allows them to be used as carriers of drug systems with directional transport properties and controlled release of active substances [1, 26].

To increase the sedimentation and aggregative stability of ointments, gels, creams emulsifiers and thickeners are used, to which are derived cellulose, pectins, alginates, bentonite clays, aerosil, and others [2, 7, 8, 12]. The choice of the emulsifier is made taking into account the value of its hydrophilic-lipophilic balance. When stabilizing the oil/water type emulsion bases, emulsifiers with a hydrophilic-lipophilic balance greater than 10 are used: sodium lauryl sulfate, emulsifier No. 1, sodium cytostearyl sulfate, tween, cetylpyridinium chloride, salts of higher fatty acids, polyoxyethylene ethylene ethoxyethylene. I/O type emulsifiers have a hydrophilic-lipophilic balance of less than 10, including higher fatty alcohols, cholesterol, foams, pentol, T-2 emulsifier, glyceryl monooleate, glyceryl monostearate, cetyl oleate and others [8, 12, 14, 18].

Emulsifiers also play an important role in the bioavailability of soft medicines. According to VA Golovkin with co-authors from three classes of emulsifiers, used as emulsifiers - cationic, anionic and nonionic - in the development of drugs, the latter is preferred, since they are characterized by chemical and physical indifference, invariability in environments resistance to electrolytes, as well as other components of the dosage form [27]. The inhibitory effect on the manifestation of antimicrobial and antifungal action of medicinal substances, in particular, metronidazole, Lamisil, Batrafen and clotrimazole, emulsifiers from the group of ionic emulsifiers included in the medicinal product have been proved [21, 27].

Creams are two- or multiphase dispersion systems in which the components of the dispersed phase in the form of small droplets (with a diameter of not more than 1 - 5 microns) are distributed in the dispersion medium; for hydrophobic creams, the dispersion medium is "oil" - vegetable or mineral oils, silicones, water/oil or oil/water/oil type emulsions [27].

Hydrophobic creams are made based on a water/oil or oil/water/oil emulsion and require stabilization by suitable stabilizers.

Hydrophilic creams are made based on an oil/water emulsion or water/oil/water, stabilized with suitable emulsifiers. This group also includes colloidal dispersion systems formed from dispersed in water or mixed water-glycol solvents of higher fatty alcohols or acids, stabilized by hydrophilic emulsifiers [14, 18, 28].

For topical action, creams are traditionally a common dosage form containing Phyto-components [29].

In the manufacture of emulsion creams based on oil extracts from medicinal plant raw materials - herbs St. John's wort, flowers of rowan, rowan fruits - as a carrier-carriers, the expediency of using lipophilic substances (cocoa butter and vaseline) when used as tween-80 emulsifiers, emulsifiers, was confirmed. 2, anhydrous lecithin or lanolin [24]. In the case of the introduction of aqueous extracts of medicinal herbs into the cream, these authors recommended the use of 4% methylcellulose gels with the addition of 10% glycerol to prevent drying of the gel.

The processes of the release of biologically active substances from the cream, the convenience, and ease of their application are significantly influenced by structural and mechanical characteristics. The studied compositions had low values of yield strength, about 40 PA, which indicates the ease of their use. Other rheological characteristics, such as plastic and effective viscosity, were within the generally accepted rheological optimum of consistency, which also confirmed their optimum consistency in terms of consumer properties [30-32].

Authors AB Khlebtsova and S.S. Turchenkov substantiated the feasibility of producing soft dosage forms - cream and gel-based on thick extracts from medicinal plant raw materials with the use as a carrier of a water-glycerol gel of methylcellulose [33]. At the present stage, gels are recognized as the most promising soft dosage form, since they have a pH close to the pH of the skin and mucous membranes, quickly and evenly distributed, providing the release of the therapeutically active components and their topical action. The composition of the gels can be introduced as

hydrophilic and hydrophobic substances, and if necessary - to produce suspension gels [13, 32].

Gels are single, double or multiphase dispersion systems with a liquid dispersion medium in which the particles of the dispersed phase form a spatial grid; they are jelly-like masses characterized by elasticity and plasticity [6]. Gels with aqueous dispersion medium (hydrogels) are made on the bases consisting of water, a hydrophilic mixed or non-aqueous solvent (glycerol, PG, ethyl alcohol, isopropyl alcohol) and a hydrophilic gel-forming agent (carbomer, cellulose derivatives, tragacanth and other).

Non-aqueous dispersion gels (oleogels) are made based on a hydrophobic solvent (petroleum jelly, vegetable oils, etc.) and require the use of lipophilic gelling agents (polyethylene, silicon dioxide, aluminum or zinc soap, etc.) [6].

The effectiveness of gels, as well as other soft dosage forms, is determined by the carrier base and auxiliaries, which requires substantiation of the composition of the gel and its technology, taking into account the physicochemical properties of the medicinal and auxiliary substances to provide a weakly acidic pH environment and the required polarity [34].

Thus, OO Sally as a carrier of vaginal gel with a content of 1.5% metronidazole and mebetizol in a ratio of 1: 1, investigated glycerol gels of sodium carboxymethylcellulose and apple pectin, which provided a high level of release of active substances from the dosage form. It is also experimentally confirmed the feasibility of using hydrophilic solvents - polyethylene glycol-400 for the manufacture of a solution of mebetizol and dimethyl sulfoxide for the manufacture of a solution of metronidazole when introduced into the vaginal gel. Subsequent microbiological studies recorded a 1.5-fold increase in antiprotozoal activity and 1.2-fold greater antifungal activity of sodium-carboxymethylcellulose based gel with the addition of polyethylene glycol-400 and dimethyl sulfoxide compared to Pellin-based gelatin [35].

Carbopol, Arespol gels are being actively explored as gels based on their ability to be well applied to the skin and mucous membranes with the formation of thin smooth films that provide a long-lasting action and high degree of bioavailability [36]. They are traditionally used in concentrations of 0.5-1%, but the addition of components with average polarity or that reduce the pH, reduce the viscoelastic properties of gel systems, so to obtain water-alcohol gels is necessary to increase the concentration of polymer [34, 36].

To expand the range of hydrophilic bases that will provide solubility and stability of water-insoluble or water-insoluble drugs, NP Polovko and AG Bashura studied the properties of gels based on polyacrylic acid derivatives - carbopol of brands 940, 980, Ultrez 10, "Ultrez 21", 2623 on hydrophilic non-aqueous solvents - ethyl alcohol, glycerol, propylene glycol, which made it possible to recommend carbapole brand 980 for the manufacture of gels containing hydrophobic active substances [37, 38].

The study of the dynamics of the release of active substances of antimycotics from the carrier base of the dosage form showed a more complete release of drugs from anhydrous gel base in comparison with the emulsion basis of the cream.

Pulyaev DS with co-authors conducted a study of gels based on carbopol "Ultrez 10", which revealed the feasibility of using carbopol of this brand at a concentration of 1 - 1.5% to obtain gels of acceptable consistency and transparency, constant indicators for the influence of electrolytes, temperature, and mechanical actions and ability to release medicinal substances [39].

As a basis for the development of gels, YN Molchanov proved the possibility of using a 65% aqueous solution of polyvinylpyrrolidone with the addition of 2% plasticizer polyethylene glycol-400. The basics with the content of polyvinylpyrrolidone are inherent in physiological inertness, a high degree of adhesion, lack of toxicity and ability to complex with many classes of drugs, which allows ensuring the prolongation of the therapeutic effect of the drug [40].

The elaboration of the composition and biotechnological aspects of gels containing probiotics for the treatment of purulent-inflammatory processes in gynecological practice by NA Zabokritsky and coauthors recognized the expediency of using gel bases of triazole, ectoderm, and organosilicon glycerol hydrogel [41-43].

Based on the study of the structural and mechanical properties of hydrogels based on a modern gel-forming complex of a copolymer of acrylamide methyl propane sulfonic acid and vinylpyrrolidone (commercial name "Aristoflex AVC") - depending on the concentration of polymer, temperature, pH, a gradient of the shear rate content of 1% gel to create modern soft dosage forms [44].

Comparative study of the structural and mechanical properties of gel bases of apple and citrus pectins, sodium alginate, and hydroxyethylcellulose allowed II Baranov and SM Zaporizhzhya to recommend gel bases of pectins with higher mechanical stability for the development of soft drugs. and therefore allowed to predict the mechanical impact during homogenization and stability during further storage [45].

Thus, II Baranova developed xanthan gel compositions with natural carob-cadmium, guar gels, and confirmed the positive effect of gels of this group on the viscosity increase:

the gels obtained were non-Newtonian flow type and possessed thixotropy [46].

The same author, in collaboration with AG Bashura, investigated the properties of hydrocolloids of the polysaccharide nature of xanthan and dehydroxanthan as gelling agents. Samples with the maximum structural viscosity of such gel bases are formed at a gel-forming concentration of 1 - 2%, whereby the gel systems are resistant to pH change in the range of 3 - 10 and do not lose their viscosity characteristics in the temperature range from 10 to 50°C. which makes them promising for use in the technology of soft medicines for topical use [47, 48].

To develop a vaginal gel containing a solution of bischofite, pyridoxine hydrochloride and tea tree essential oil, Golovkin VA proposed to use proxanol-propylene glycol carrier composition: proxanol-268 - 15.0 - 25.0; twin-80 - 0.05 - 0.1; propylene glycol - up to 100 h, which ensures uniform and fast release of AFI from the gel, as well as optimal lubricity [49].

An important component of gels is non-aqueous solvents that allow them to simulate their osmotic activity when applied topically. Studies conducted by IM Pertsev [50, 51], AI Tikhonov [52, 53] and EV Gladukh [54] with co-authors prove that the introduction into gel bases of such non-aqueous solvents as polyethylene glycol- 400, propylene glycol or glycerol in an amount of from 10 to 40% increases the dehydration properties of the basics. In this case, polyethylene glycol-400 causes the highest, glycerol is moderate, and propylene glycol is the least osmotic activity of the gel bases under study. The duration of the dehydration action also differs: for bases containing glycerol and propylene glycol it lasts up to 5 h, and for bases containing polyethylene glycol-400 - 8 h or more. Thus, for the creation of soft drugs with pronounced dehydrating properties in their composition should be introduced polyethylene glycol-400, and in cases where it is necessary to create gel bases with a long but more moderate dehydrating effect - use a mixture of glycerol (5%) and propylene glycol (10%).

Recently, an active introduction into the therapeutic process of gels with active substances based on medicinal herbal raw materials is noted. This is due to greater bioavailability, less toxicity and, as a rule, a wider range of pharmacological action of bioactive herbal substances compared to synthetic medicinal substances [55]. If necessary, the introduction of the gel of biologically active substances from the group of flavonoids in the form of solutions on hydrophilic solvents, it is advisable to use carbopol-940, which provides a more complete and faster release of this group of biologically active substances in comparison with the bases of methylcellulose or a mixture of polyethylene glycol [56, 57].

Also, the therapeutic activity of soft drugs is significantly influenced by the technology of their production, namely, the method of introducing active and auxiliary substances into the substrate, the temperature regime during certain technological operations, their hardware design, etc., which requires thorough research in the development of new drugs. of this group [2, 7, 14, 15, 18, 20, 27, 58].

Rheological properties significantly affect the effectiveness of all study groups of soft drugs used in gynecology, because they provide the proper consumer properties (lubricity, uniform distribution on the surface of the mucous membrane, fixation on the surface). Also, they determine the parameters of such elements of the technological process as homogenization, transportation during technological processing, packaging, etc. [35, 59-63].

Conclusions

We have concluded that active introduction into the therapeutic process of gels with active substances based on medicinal herbal raw materials. This is due to greater bioavailability, less toxicity and, as a rule, a wider range of pharmacological action of bioactive herbal substances than synthetic medicinal substances. If necessary, the introduction of the gel of biologically active substances from the group of flavonoids in the form of solutions on hydrophilic solvents, it is advisable to use carbopol-940, which provides a more complete and faster release of this group of biologically active substances in comparison with the bases of methylcellulose or a mixture of polyethylene glycol. It should be noted that the therapeutic activity of soft drugs is significantly influenced by the technology of their production, namely, the method of introduction of active and auxiliary substances into the substrate, the temperature regime during certain technological operations, their hardware design, etc., which requires thorough research in the development of new medicines of this group. Rheological properties significantly affect the effectiveness of all study groups of soft drugs used in gynecology, because they provide the proper consumer properties (lubricity, uniform distribution on the surface of the mucous membrane, fixation on the surface). Also, they determine the parameters of such elements of the technological process as homogenization, transportation during processing, packaging, etc.

References

1. Inagamov S. Ya. Polikompleksnye geli na osnove natrij karboksimetilcellyulozy – novye prolongatory lekarstvennyh preparatov / S. Ya. Inagamov, M. Yu. Muhamedzhanova, G. I. Muhamedov // Himiya rast. syrya. – 2011. – № 2. – S. 51–56.
2. Osnovni trendy` rozvy`tku farmacevty`chnogo ry`nku Ukrayiny` po farmakoterapevty`chny`x grupax / za red. : L. L. Davtyan, R. S. Kory`tnyuk, G. M. Vojtenko. – Ky`yiv : Osvita Ukrayiny`, 2015. – 130 s.
3. Biofarmaciya : pidruch. dlya studentiv vy`shh. farmacevt. navch. zakl. i farmacevt. f-tiv vy`shh. med. navch. zakl. IV rivnya akredy`taciyi / O. I. Ty`xonov, T. G. Yarny`x, I. A. Zupanecz` [ta in.]. – Xarkiv : NFAU : Zoloti storinky`, 2010. – 238 s.
4. Cagarejshvili G. V. Biofarmacevticheskie, farmakokineticheskie i tehnologicheskie aspekty sozdaniya myagkih lekarstvennyh form:

(Rektal. preparaty) / G. V. Cagarejshvili, V. A. Golovkin, T. A. Groshovyj. – Tbilisi : Mecniereba, 1987. – 263 s.
5. Farmacevticheskie i mediko-biologicheskie aspekty lekarstv : uchebnik : v 2 t. / pod red. : I. M. Perceva, I. A. Zupanca. – Harkov : Izd-vo NFAU, 1999. – T. 2. – 448 s.
6. Golovkin V. A. Vaginalnye lekarstvennye sredstva: Osobennosti razrabotki, issledovaniya i primeneniya / V. A. Golovkin, V. V. Golovkin, A. V. Golovkin. – Zaporozhe, 2000. – 271 s.
7. Texnologiya likiv promy`slovogo vy`robny`cztva : pidruch. dlya studentiv vy`shh. navch. zakl. : u 2 ch. / V. I. Chuyeshov, Ye. V. Gladux, I. V. Sajko [ta in.]. – Vy`d. 2-ge, pererob. i dop. – Xarkiv : NFaU : Ory`ginal, 2013. – Ch. 2. – 640 s.
8. Vspomogatelnye veshestva, ispolzuemye v tehnologii myagkih lekarstvennyh form (mazej, gelej, linimentov, kremov) (obzor) / O. A. Semkina, M. A. Dzhavahyan, T. A. Levchuk [i dr.] // Him.-farmacevt. zhurnal. – 2005. – № 9. – S. 45–48.
9. Gladysheva S. A. Optimizaciya issledovanij po vyboru osnovy-nositelya myagkih farmakoterapevticheskih sredstv dlya profilaktiki alopecii / S. A. Gladysheva, E. V. Gladuh // Zaporozh. med. zhurnal. – 2008. – № 6. – S. 70–71.
10. Farmacevticheskie i biologicheskie aspekty mazej / I. M. Percev, A. M. Kotenko, O. V. Chueshov, E. L. Haleeva. – Harkov : Zolotye stranicy, 2003. – 288 s.
11. Ankirskaya A. S. Bakterialnyj vaginoz / A. S. Ankirskaya // Akusherstvo i ginekologiya. – 2005. – № 3. – S. 10–13.
12. Dopomizhni rechovy`ny` v texnologiyi likiv: vply`v na texnologichni, spozhy`vchi, ekonomichni xaraktery`sty`ky` i terapevty`chnu efekty`vnist` : navch. posib. dlya studentiv vy`shh. farmacevt. navch. zakl. / avt.-uklad. : I. M. Percev, D. I. Dmy`triyevs`ky`j, V. D. Ry`bachuk [ta in.]. – Xarkiv : Zoloti storinky`, 2010. – 598 s.
13. Texnologichna ta fizy`ko-ximichna xaraktery`sty`ka geliv / R. S. Kory`tnyuk, G. V. Zagorij, V. O. Tarasenko, Ukadike Chy`namere // Farmacevt. zhurnal. – 2012. – # 3. – S. 38–42.
14. Tehnologiya lekarstv promyshlennogo proizvodstva : ucheb. dlya studentov vuzov : v 2 ch. / [V. I. Chueshov, E. V. Gladuh, I. V. Sajko i dr.]. – Vinnica : Nova kn., 2014. – Ch. 2. – 662 s.
15. Texnologiya likiv promy`slovogo vy`robny`cztva : pidruch. dlya studentiv vy`shh. navch. zakl. : u 2 ch. / V. I. Chuyeshov, Ye. V. Gladux, I. V. Sajko [ta in.]. – Vy`d. 2-ge, pererobl. i dopov. – Xarkiv : NFaU : Ory`ginal, 2012. – Ch. 1. – 693, [1] s.
16. Golovkin V. V. Biofarmacevty`chni aspekty` stvorennya likuval`no-profilakty`chny`x zasobiv iz standarty`zovany`m rozchy`nom bishofitu dlya vaginal`nogo zastosuvannya / V. V. Golovkin // Farmacevt. zhurnal. – 2007. – # 3. – S. 95–99.
17. Rozrobka skladu ta texnologiyi pinnogo preparatu bakteriofagu. Povidomlennya 1. Vply`v emul`gatoriv pershogo ta drugogo rodu i yix koncentracij na stabil`nist` ta specy`fichnu akty`vnist` emul`siyi oliya/voda z gidrozolem bakteriofagu stafilokokovogo / O. A. Yereshhenko, L. S. Strel`ny`kov, G. I. Kabachny`j, Ye. I. Kompaniyecz` // Zaporozh. med. zhurnal. – 2008. – # 5. – S. 116–120.
18. Tehnologiya lekarstvennyh form : ucheb. dlya farmacevt. in-tov : v 2 t. / R. V. Bobylev, G. P. Gryadunova, L. A. Ivanova [i dr.]. – M. : Medicina, 1991. – T. 2. – 543 s.
19. Texnologichny`j sposib vvedennya diyuchy`x rechovy`n do osnovy` preparatu / A. O. Drozdova, Yu. P. Polishhuk, L. L. Davtyan [ta in.] // Vijs`k. medy`cy`na Ukrayiny`. – 2012. – # 4. – S. 61–63.
20. Texnologiya likars`ky`x preparativ promy`slovogo vy`robny`cztva : navch. posib. dlya studentiv specz. “Farmaciya” dennoyi ta zaoch. dy`stancz. form navchannya / D. I. Dmy`trivs`ky`j, L. I. Boguslavs`ka, L. M. Xoxlova [ta in.]. – 2-e vy`d., doopracz. i dop. – Vinny`cya : Nova kn., 2008. – 277 s.
21. Gavrilin M. V. Ispolzovanie polietilenoksidov dlya sozdaniya mazi nistatina / M. V. Gavrilin, A. V. Podluzhnaya // Him.-farmacevt. zhurnal. – 2002. – № 3. – S. 51–53.
22. Gavrilin M. V. Primenenie polimerov i sopolimerov proizvodnyh akrilovoj kisloty i etilenoksida v farmacii (obzor) / M. V. Gavrilin // Him.-farmacevt. zhurnal. – 2001. – № 1. – S. 33–37.
23. Slyusar O. I. Izuchenie vliyaniya razlichnyh faktorov na strukturno-mehanicheskie i tehnologicheskie harakteristiki gidrogelevyh osnov polimera akrilovoj kisloty / O. I. Slyusar, T. P. Kalmykova, F. Kermanian // Him.-farmacevt. zhurnal. – 2003. – № 5. – S. 51–53.
24. Razrabotka sostava i tehnologii ginekologicheskih lekarstvennyh sredstv / Yu. V. Shikova, V. A. Lihoded, V. V. Petrova [i dr.] // Innovacionnye tehnologii v farmacii : sb. nauch.-metod. tr. Vseros. nauch.-metod. konf. s mezhdunar. uchastiem, posvyash. 95-letiyu Irkutsk. gos. med. un-ta, 9-10 iyunya 2014 g. – Irkutsk : IGMU, 2014. – S. 172–173.
25. Sravnitelnyj analiz antimikrobnoj aktivnosti novyh biologicheski aktivnyh soedinenij i lekarstvennyh form na ih osnove [Elektronnyj resurs] / O. I. Basareva, S. V. Kostrov, E. M. Bukreeva [i dr.]. – Rezhim dostupa : URL : https://science-education.ru/ru/article/view?id =4815 . – Nazvanie s ekrana.
26. Inagamov S. Ya. Issledovanie reologicheskih svojstv polikompleksov karboksimetilcellyulozy s mochevino-formaldegidnymi oligomerami kak osnov dlya lekarstvennyh preparatov / S. Ya. Inagamov // Farmacevt. vestn. Uzbekistana. – 2006. – № 1. – S. 30–33.
27. Golovkin V. V. Vaginal`ni likars`ki formy`. Povidomlennya III. Rozrobka vaginal`nogo gelyu z kuriozy`nom / V. V. Golovkin, V. O. Bory`shhuk, T. A. Kot // Farmacevt. zhurnal. – 2000. – # 5. – S. 51–54.
28. Tehnologiya lekarstv promyshlennogo proizvodstva : ucheb. dlya studentov vuzov : v 2 ch. / [V. I. Chueshov, E. V. Gladuh, I. V. Sajko i dr.]. – Vinnica : Nova kn., 2014. – Ch. 1. – 695 s.
29. Razrabotka tehnologii i issledovanie lechebno-kosmeticheskih kremov s fitokomponentami [Elektronnyj resurs] / L. K. Babiyan, N. I. Shramm, V. I. Truhina [i dr.]. – Rezhim dostupa : URL : https://science-education.ru/ru/article/view?id=6331 . – Nazvanie s ekrana.
30. Adsorption behavior and dilational rheology of the cationic alkyl trimethylammonium bromides at the water/air interface / C. Stubenrauch, V. B. Fainerman, E. V. Aksenenko, R. Miller // J. Phys. Chem. B. – 2005. – Vol. 109, N 4. – P. 1505–1509.
31. Salij O. O. Rozrobka skladu, texnologiyi ta doslidzhennya supozy`toriyiv i gelyu metronidazolu u poyednanni z mebety`zolom dlya kompleksnoyi terapiyi vaginal`ny`x infekcij : avtoref. dy`s... kand. farm. nauk : 15.00.01 / Salij Olena Oleksandrivna ; Zaporiz. derzh. med. universy`tet. – Zaporizhzhya, 1999. – 15 s.
32. Encyclopedia of pharmaceutical technology [Electronic resource] / ed. by J. Swarbrick. – 3rd ed. – New York ; London : Informa healthcare, 2007. – Vol. 1. – Way of access : URL : https://ru.scribd.com/document/250553175/4-Encyclopedia-of-Pharmaceutical-Technology-Third-Edition-pdf . – Title from the screen.
33. Hlebcova E. B. Razrabotka tehnologii izgotovleniya myagkih lekarstvennyh form na osnove gustogo ekstrakta Lofanta anisovogo / E. B. Hlebcova, S. S. Turchenkov // Materialy 4 ezhegod. itog. konf. profes.-prepod. sost. Chechen. gos. un-ta, 28 fevr. 2015 g. – Groznyj, 2015. – S. 171–174.
34. Sapozhkova M. B. Razrabotka tehnologii polucheniya protivovarikoznogo gelya / M. B. Sapozhkova, T. P. Kalmykova, S. N. Suslina // Him.-farmacevt. zhurnal. – 2012. – № 5. – S. 35–38.
35. Alekseeva I. V. Tehnologicheskie i biofarmacevticheskie osnovy sozdaniya lekarstvennyh form, soderzhashih mestnyj anestetik anilokain : avtoref. dis… d-ra farm. nauk : 15.00.01 / Alekseeva Irina Vladimirovna ; [Perm. gos. farmacevt. akad. Roszdrava]. – Perm, 2007. – 50 s.
36. Alekseev K. V. Teoreticheskoe i eksperimentalnoe obosnovanie primeneniya redkosshityh akrilovyh polimerov v tehnologii myagkih lekarstvennyh form (mazej i gelej) i biopreparatov : avtoref. dis… d-ra farm. nauk : 15.00.01 / Alekseev Konstantin Viktorovich ; NII farmacii. – M., 1993. – 59 s.
37. Pat. 49336 Ukrayina, MPK6 A 61 K 8/00. Geleva osnova dlya likars`ky`x ta kosmety`chny`x zasobiv / O. G. Bashura (UA), N. P. Polovko (UA), A. A. Yaryemchuk (BY). – # u200911528 ; zayavl. 12.11.2009 ; opubl. 26.04.2010, Byul. # 8.
38. Polovko N. P. Vply`v rozchy`nny`kiv i karbomeriv na vlasty`vosti bezvodny`x geliv / N. P. Polovko, O. G. Bashura // Visn. farmaciyi. – 2009. – # 4. – S. 39–41.
39. Pulyayev D. S. Obgruntuvannya koncentraciyi karbomera u skladi gelyu “Al`gozan” / D. S. Pulyayev, I. V. Kovalevs`ka, V. I. Chuyeshov // Visn. farmaciyi. – 2010. – # 2. – S. 22–25.
40. Molchanova Yu. N. Polivinilpirrolidony v proizvodstve myagkih lekarstvennyh form / Yu. N. Molchanova, A. P. Tolstova, A. A.

Trubnikov // Innovacionnye tehnologii v farmacii : sb. nauch.-metod. tr. Vseros. nauch.-metod. konf. s mezhdunar. uchastiem, posvyash. 95-letiyu Irkutsk. gos. med. un-ta, 9-10 iyunya 2014 g. – Irkutsk : IGMU, 2014. – S. 150–151.

41. Zabokrickij N. A. Biotehnologicheskie aspekty razrabotki i konstruirovaniya eksperimentalnyh obrazcov probioticheskih preparatov na osnove trankutannyh provodnikov / N. A. Zabokrickij // Vestn. Bashkir. universiteta. – 2013. – № 3. – S. 730–733.
42. Zabokrickij N. A. Novoe sredstvo intimnoj gigieny Femivit v korrekcii vospalitelnyh zabolevanij organov malogo taza / N. A. Zabokrickij, L. P. Larionov, A. B. Bakurinskih // Biomedicina. – 2010. – № 5. – S. 85–86.
43. Zabokrickij N. A. Razrabotka eksperimentalnyh obrazcov novyh probioticheskih preparatov dlya naruzhnogo primeneniya na osnove transdermalnyh terapevticheskih sistem / N. A. Zabokrickij, O. V. Kolomiec // Zdorove i obrazovanie v XXI veke. – 2014. – T. 16, № 6. – S. 26–40.
44. Baranova I. I. Rozrobka ta vy`vchennya gelevy`x sy`stem na osnovi kompleksnogo sopolimeru “Aristoflex AVC” / I. I. Baranova // Farmacevt. zhurnal. – 2009. – # 5. – S. 112–115.
45. Baranova I. I. Sravnitelnaya harakteristika reoparametrov geleobrazovatelej razlichnogo proishozhdeniya / I. I. Baranova, S. N. Zaporozhskaya // Zaporozh. med. zhurnal. – 2008. – № 4. – S. 81–84.
46. Baranova I. I. Stvorennya opty`mal`ny`x gelevy`x kompozy`cij za dopomogoyu galaktomananiv / I. I. Baranova // Visn. farmaciyi. – 2009. – # 3. – S. 46–48.
47. Baranova I. I. Ekspery`mental`ne vy`vchennya fizy`ko-mexanichny`x vlasty`vostej geliv na osnovi mody`fikovanogo geleutvoryuvacha “Amaze” / I. I. Baranova, O. G. Bashura // Visn. farmaciyi. – 2010. – # 1. – S. 10–12.
48. Proksanoly – vspomogatelnye veshestva v tehnologii lekarstvennyh form / G. S. Bashura, N. A. Lyapunov, A. G. Bashura [i dr.] // Farmakom. – 1994. – № 8/9. – S. 8–14.
49. Golovkin V. V. Biofarmacevty`chne obgruntuvannya skladu, texnologiyi ta doslidzhennya m'yaky`x intravaginal`ny`x likars`ky`x form z mefenamina natriyevoyu sillyu i mebety`zolom : avtoref. dy`s... kand. farm. nauk : 15.00.01 / Golovkin Volody`my`r V'yacheslavovy`ch ; L`viv. derzh. med. universy`tet. – L`viv, 1997. – 18 s.
50. Znachenie osmoticheskih svojstv mazej pri ih ispolzovanii v medicinskoj praktike / I. M. Percev, N. N. Berkalo, S. A. Gutorov, V. V. Postolnik // Visn. farmaciyi. – 2002. – № 2. – S. 7–10.
51. Problemy` stvorennya osmoty`chno akty`vny`x likars`ky`x sy`stem dlya zovnishn`ogo vy`kory`stannya / V. G. Gun`ko, I. M. Percev, B. M. Dacenko, S. G. Byelov // Farmacevt. zhurnal. – 1991. – # 3. – S. 62–67.
52. Kozy`r G. R. Vy`vchennya osmoty`chny`x vlasty`vostej geliv na osnovi karbopolu / G. R. Kozy`r, O. I. Ty`xonov, N. V. Zhy`vota // Farmaciya XXI stolittya : tezy` dop. Vseukr. nauk.-prakt. konf., 23-24 zhovt. 2002 r. – Xarkiv : Vy`d-vo NFaU “Zoloti storinky`”, 2002. – S. 46–47.
53. Tihonov A. I. Izuchenie vliyaniya ryada nevodnyh rastvoritelej na osmoticheskie svojstva kombinirovannogo gelya protivovospalitelnogo dejstviya / A. I. Tihonov, V. V. Mihajlenko // Zaporozh. med. zhurnal. – 2008. – № 4. – S. 142–144.
54. Rozrobka skladu ta texnologiyi pinnogo preparatu bakteriofagu. Povidomlennya 1. Vply`v emul`gatoriv pershogo ta drugogo rodu i yix koncentracij na stabil`nist` ta specy`fichnu akty`vnist` emul`siyi oliya/voda z gidrozolem bakteriofagu stafilokokovogo / O. A. Yereshhenko, L. S. Strel`ny`kov, G. I. Kabachny`j, Ye. I. Kompaniyecz` // Zaporozh. med. zhurnal. – 2008. – # 5. – S. 116–120.
55. Kabishev K. E. Fitopreparaty v otechestvennoj dermatovenerologicheskoj praktike / K. E. Kabishev // Vestn. Voronezh. gos. un-ta. Ser. Himiya. Biologiya. Farmaciya. – 2005. – № 1. – S. 189–204.
56. Bazarkina O. V. Razrabotka novoj lekarstvennoj formy s ranozazhivlyayushej i protivovospalitelnoj aktivnostyu / O. V. Bazarkina, O. A. Semkina, E. I. Gribkova // Ros. nauch. mir. – 2013. – № 2. – S. 5–16, 142.
57. Zhilina I. V. Razrabotka sostava i tehnologiya gelya s ekstraktom iz cvetkov labaznika vyazkolistnogo dlya ispolzovaniya v kachestve dermatoprotektora / I. V. Zhilina, E. F. Stepanova, G. A. Golova // Fundam. issledovaniya. – 2011. – № 9-2. – S. 349–351.
58. Babij O. V. Rozrobka texnologiyi gelyu dlya zovnishn`ogo likuvannya gerpety`chnoyi infekciyi / O. V. Babij, K. F. Vashhenko // Zb. nauk. pr. spivrobitny`kiv NMAPO im. P.L. Shupy`ka. – Ky`yiv, 2016. – Vy`p. 26. – S. 122– 4.
59. Ofner C. M. 3rd Gells and jellies / C. M. Ofner 3rd, C. M. Klech-Gelotte // Encyclopedia of pharmaceutical technology / ed. by J. Swarbrick. – 3rd ed. – New York : Informa Healthcare, 2007. – Vol. 3. – P. 1875–1890.
60. Malkin A. Ya. Reologiya: koncepcii, metody, prilozheniya : avtoriz. per. s angl. / A. Ya. Malkin, A. I. Isaev. – SPb. : Professiya, 2007. – 557 s.
61. Tarasenko V. O. Rozrobka skladu ta texnologiyi stomatologichny`x m'yaky`x likars`ky`x form z nimesulidom ta ceftry`aksonom : avtoref. dy`s… kand. farm. nauk : 15.00.01 / Tarasenko Viktoriya Oleksandivna ; Nacz. med. akad. pislyady`plom. osvity` imeni P.L. Shupy`ka. – Ky`yiv, 2010. – 24 s.
62. Vlasenko I. O. Rozrobka naukovo obgruntovanogo skladu ta tehnologiyi m’yakih likarskih zasobiv protizapalnoyi ta antimikrobnoyi diyi dlya stomatologiyi : avtoref. dis… kand. farm. nauk : 15.00.01 / Vlasenko Irina Oleksiyivna ; Nac. med. akad. pislyadiplom. osviti im. P.L. Shupika MOZ Ukrayini. – Kiyiv, 2009. – 23 s.
63. Volovik N. V. Rozrobka gelevih osnov z karbomerami dlya m’yakih likarskih zasobiv / N. V. Volovik, M. O. Lyapunov // Visn. farmaciyi. – 2001. – № 3. – S. 51.