REVIEWS

ISSN 2307-9266 e-ISSN 2413-2241

Scientific and Practical Journal
PHARMACY & PHARMACOLOGY

USE OF SORPTION PROCESSES IN THE TECHNOLOGY OF DRUG DELIVERY SYSTEMS

A.V. Bondarev, E.T. Zhilyakova

Belgorod State University
85, Pobedy St., Belgorod, Russia, 308015

E-mail: alexbond936@yandex.ru

Received: 23.08.2018 Accepted for publication: 20.02.2019

The aim *of this research is the review of scientific and technical literature regarding possibility of using sorption processes in the technology of drug delivery systems.* ***Materials and methods.*** *The materials are the following electronic resources: eLIBRARY, CyberLeninka, PubMed. The methods of review are analysis and synthesis. The study covers the scientific literature from 1996 up to the present time.* ***Results.*** *Sorbents are used as carriers for various medicinal peroral substances, they are also dispensers of various compounds in the form of polymeric eye films and stents in the human body. The delivery of medicinal substances occurs with the help of sorption processes of mass transfer. Currently, the following medical substances are used as carriers for medicinal substances: activated carbon, mineral sorbents (medical clays, synthetic sorbents), polymers and their biosimilars. 6 groups of pharmaceutical substances are registered for the production of enterosorbents in Russia and they can be used as sorbent carriers in the sorption drug system. They are: activated carbon, colloidal silicon dioxide, polyvinylpyrrolidone, dioctahedral smectite, polymethylsiloxane polyhydrate. As a result of the study, the model of the sorption drug system has been developed. It consists of sorbent carrier, active pharmaceutical ingredient and excipients that provide the desorption. Desorption of the active pharmaceutical ingredient may contribute to its modified release. The technology for obtaining sorption medicinal systems requires further study and development of modeling methods, searching for experimental pharmacological models and technological methods, which make it possible to obtain sorption dosage form with modified release.* ***Conclusion.*** *The review of the sorption processes used in the technology of drug delivery systems has been carried out. The model of the sorption drug system has been developed.*

Keywords: *sorption drug system, release modification, drug delivery*

ИСПОЛЬЗОВАНИЕ СОРБЦИОННЫХ ПРОЦЕССОВ В ТЕХНОЛОГИИ СИСТЕМ ДОСТАВКИ ЛЕКАРСТВЕННЫХ ВЕЩЕСТВ

А.В. Бондарев, Е.Т. Жилякова

Белгородский государственный национальный исследовательский университет
308015, Россия, г. Белгород, ул. Победы, 85

E-mail: alexbond936@yandex.ru

Поступила в редакцию: 23.08.2018 Принята к печати: 20.02.2019

Цель *– обзор научной и технической литературы, касающейся возможности использования сорбционных процессов в технологии систем доставки лекарственных веществ.* ***Материалы и методы****. В качестве материалов исследования использовали электронные ресурсы eLIBRARY, CyberLeninka, PubMed. Методы исследования – анализ и обобщение научной литературы за период с 1996 года по настоящее время.* ***Результаты.*** *Сорбенты выступают в роли носителей для различных лекарственных веществ при приеме per os, а также в роли дозаторов различных соединений в организме человека при использовании полимерных систем доставки в виде глазных пленок и стентов. Доставка*

For citation: YA.V. Bondarev, E.T. Zhilyakova. USe of sorption processes in the technology of drug delivery systems. *Pharmacy & Pharmacology*. 2019;7(1): 4-12. **DOI:**10.19163/2307-9266-2019-7-1-4-12

Для цитирования: А.В. Бондарев, Е.Т. Жилякова. Использование сорбционных процессов в технологии систем доставки лекарственных веществ. *Фармация и фармакология.* 2019;7(1): 4-12. **DOI:**10.19163/2307-9266-2019-7-1-4-12

ОБЗОР
DOI: 10.19163/2307-9266-2019-7-1-4-12

*лекарственных веществ происходит при помощи сорбционных процессов массопереноса. В роли носителей для различных веществ используются следующие сорбенты: активированный уголь, минеральные сорбенты – медицинские глины, синтетические сорбенты – полимеры и их биоаналоги. В России зарегистрировано 6 групп фармацевтических субстанций, предназначенных для производства лекарственных препаратов энтеросорбентов, которые возможно использовать в качестве сорбента-носителя в сорбционной лекарственной системе: активированный уголь, кремния диоксид коллоидный, поливинилпирролидон, смектит диоктаэдрический, полиметилсилоксана полигидрат. Разработана модель сорбционной лекарственной системы, состоящая из сорбента-носителя, активного фармацевтического ингредиента и вспомогательных веществ, обеспечивающих десорбцию. Десорбция активного фармацевтического ингредиента может способствовать его модифицированному высвобождению. Технология получения сорбционных лекарственных систем требует дальнейшего изучения и разработки методов моделирования, поиска экспериментальных фармакологических моделей и технологических методик, позволяющих получить сорбционную лекарственную форму с модифицированным высвобождением. **Заключение.** Проведен обзор использования сорбционных процессов в технологии систем доставки лекарственных веществ, разработана модель сорбционной лекарственной системы.*

Ключевые слова: *сорбционная лекарственная система, модификация высвобождения, доставка лекарственных веществ*

INTRODUCTION

According to the information of Ministry of Health, in 2016 there were 237 million cases of registration of various diseases per 146.8 million people in Russia [1]. The statistical indicators show a high overall morbidity of the population. National security of the country, among other things, implies pharmaceutical security, i.e. the availability of drugs produced in Russia, which is impossible without the introduction of high-tech domestic developments in this area. Currently, specialists are faced with the task of developing and introducing new active pharmaceutical substances, developing new formulations of dosage forms of various directions of action, improving the production technology of dosage forms. These areas are the main ones in the state program "Strategy for the development of the pharmaceutical industry of the Russian Federation for the period up to 2020". The existing range of active pharmaceutical substances on the Russian pharmaceutical market is represented mainly by foreign manufacturers. Domestic development to improve the technology of obtaining new dosage forms are lagging behind foreign ones [2].

The development of a new dosage forms in pharmaceutical technology are going on in two directions:

1. development of new dosage forms with improved characteristics (release modification, low percentage of side effects) based on clinically approved substances. The actual direction is the study and use of mass transfer processes of drugs to modify their release;
2. development of new pharmaceutical ingredients and traditional dosage forms based on them [3, 4].

The promising direction in the development of drug delivery systems is the use of sorption technologies. Sorption methods can be used to inject medicinal substance (MS) into the sorbent under the conditions of reversibility of the process and desorption of the medicinal substance into the organism. The sorbent is pre-saturated with the necessary medicinal substance and the system is used in the desorption mode [5]. A medical substance has a large active area on the sorbent carrier due to the sorption of the monomolecular layer. This effect can reduce the dosage of the medicinal substance while maintaining therapeutic activity. The resulting sorption drug system can perform the function of the transport for delivering medicinal substance to the body.

THE AIM of this research is review of scientific and technical literature on the possibility of using sorption processes in the technology of drug delivery systems. The set up a problem are as follows: to review the use of sorption processes in the technology of drug delivery systems; to develop the sorption drug system model.

MATERIALS AND METHODS

The materials are the following electronic resources: eLIBRARY, CyberLeninka, PubMed. The methods of review are analysis and synthesis. The study covers the scientific literature from 1996 up to the present time.

RESULTS AND DISCUSSION

Modern pharmaceutical technology has the problems, the solution of which will be the new ways of developing effective drugs. The subject of the study is the dosage form with optimal bioavailability and a target action.

Currently, dosage forms are classified into three generations by therapeutic effect (Ischenko V.I., 2016):

1. traditional dosage forms are characterized by systematicity and periodicity of the action, in

which the major part of the injected substance is metabolized and does not reach the target;
2. dosage forms with systemic action and modified drug release (transdermal therapeutic systems, delivery systems based on sorption processes of mass transfer);
3. dosage forms characterized by target action in organs, tissues, cells and even in cell structures and controlled release (liposomes).

Traditional dosage forms are characterized by the immediate and uncontrolled release of drugs. Promising dosage forms are those with modified release and characterized by changes in the mechanism and nature of the release of medicinal substance [6]. Modification of medicinal substance release can be achieved in the following ways:

1. technological and nanotechnological ways mean the production of micro-size dosage forms, production of nanoscale dosage forms with a directed effect on a biological target;
2. physical-chemical ways mean the use of excipients that alter the solubility, absorption, distribution or elimination, as well as the formation of complexes or changes in the structure of the drug molecule [4, 7, 8].

Technological methods of modification consider sorption drug systems in which the drug is physically or chemically bound to a solid carrier in order to modify its release during subsequent desorption. Sorption drug system will reduce the dosage and frequency of drug administration. In this aspect, biopharmaceutical research on the creation of a new-generation of drugs is of particular relevance.

There are several ways to obtain sorption medicinal systems:

1. joint dispersion of drugs with a solid carrier in mills of various types. Grinding a polymer when it is used as a solid carrier can be done in the low temperature range, since it increases its ability for abrasion;
2. mixing drugs with a solid carrier in solvent medium, followed by removal of the solvent by evaporation [9].

Polymeric sorption systems with modified release of active pharmaceutical ingredients is the structure in which the polymeric carrier and the drug are in the complex with physiological activity and regulated pharmacokinetics [10-11]. In gastroenterology, dried cultures of living bacteria – probiotics – are widely used. The biomass of live bacteria adsorbed on the stone activated carbon is improved by dosage forms with respect to traditional lyophilized probiotics. The nomenclature of sorption probiotics is represented in Russia by the following medicinal preparation: “Bifidumbakterin Forte”, “Probifor” and “Florin Forte”. The technology of producing probiotic preparations is based on sorption processes aimed at sorption of microorganisms with activated carbon. Sorption ensures the survival of microorganisms in the acidic environment of the stomach, interaction with the parietal layer of the intestinal mucosa and an increase in the therapeutic effect [12, 13].

The carbon-mineral sorbent “SUMS-1” with bifidobacteria immobilized on its surface, showed a high adsorption activity and the probiotic therapeutic effect [14]. When immobilized on the “SUMS-1”, the sorbent polysaccharide from fucoidan algae, the elution of the latter into an aqueous solution was 50±10%. Combined dosage forms for enteral use have shown high efficacy in the treatment of burn wounds. [15, 16]. “SUMS-1” with an immobilized fibrinolysis inhibitor can be recommended in complex therapy for the treatment of inflammatory periodontal diseases [17].

Experimental studies of the treatment of burns and purulent wound surfaces have shown the effectiveness of using vulneororption by sorption medicinal systems with antibiotics [18–20] and herbal remedies [21–23].

Clinical observations of the last decades indicate side effects of antibiotics, and therefore interest in silver preparations is renewed. Silver-containing sorbents (SIAL-S), which showed good detoxifying and antioxidant properties have been developed [24]. Experimental studies indicate that «SIAL-S» sorbent may be an implant to fill in bone cavities, while maintaining osteoreparative properties in an infected wound [25].

The adsorptive immobilization of inulinase on ultra-crosslinked sorbents makes it possible to reuse the heterogeneous biocatalyst obtained in the enzymatic production of fructose. Protein adsorption was carried out on the polymeric sorbent [26], mesoporous silica [27].

In Babanina et al [28], methods for obtaining medical clays intercalated with Analgin and Amoxicillin are presented, as well as the influence of the synthesis methods (coprecipitation and hydration) on the degree of intercalation and the kinetics of release of active anions are considered. The advantages and disadvantages of using medical clays for oral drug delivery, prolongation of the release and purposefulness of the action of the medicinal substance included in the structure of medical clays, a rational choice of the type of clay as a carrier of medicinal substances are reflected in the works by different scolars [29–32].

The development of carbon sorption drug nanosystems for use in veterinary practice and the study of their physicochemical and toxicological properties are presented in Pyanova et al [33].

ОБЗОР
DOI: 10.19163/2307-9266-2019-7-1-4-12

Polymer carriers, in addition to their use in gastroenterology, are widely used in ophthalmology and surgery [34]. The method of obtaining films and capsules by alternating adsorption of oppositely charged polyions in order to obtain sorption medicinal systems based on chitosan, alginates and albumin are presented in Makarevich et al [35–36].

The sorption drug system has been developed in the form of a contact lens with a prolonged therapeutic effect with the use of computer programming. The dynamics of adsorption and desorption of the drugs have been considered, the time of saturation and therapeutic effect of the lens, i.e. the wearing time during which the drug was transported from the lens and exerted therapeutic effect has been determined [37–41].

The technology of creating the polymer-doxorubicin drug sorption system is presented in [42–43]. Sorbed doskorubitsin on the surface of the polymer stent slows down crystallization of bile. Polycaprolactone polymer is a carrier of doxorubicin and is effective in the treatment of cancer.

Researchers from Helsinki University and the Institute of Theoretical and Experimental Biophysics of the Russian Academy of Sciences have created a bone carcass based on hydroxyapatite, gelatin, polypyrrole and mesoporous silica. The carcass contains adsorbed antibiotics which suppress the infection in the damaged bone and help cells-reducers to work. The adsorption of antibiotics allows them to stretch their release from the carcass to 4 months [44].

Thus, the use of polymers as bases for sorption drug systems is aimed at obtaining controlled pharmacokinetics of sorbed drugs [45]. The release of drugs is due to the processes of mass transfer of drugs from the surface of the polymer. When creating polymer sorption drug systems, the polymer is chosen on the basis of the following properties: biocompatibility, biodegradability, physical properties, porosity, specific surface, type and pore volume, which make a controlled release of the drug possible. Currently, polymeric sorption drug systems are used in the development of materials for stents, ophthalmic films, as well as other systems with targeted drug delivery [46–51].

The review of the literature has shown the widespread use of sorption processes in the technology of drug delivery systems. The following sorbents are used as carriers for various substances: activated carbon, mineral sorbents (medical clays) synthetic sorbents (polymers and their combinations). Fig. 1 shows the recommended structure of the sorption drug system (*sorption drug system – "SDS"*).

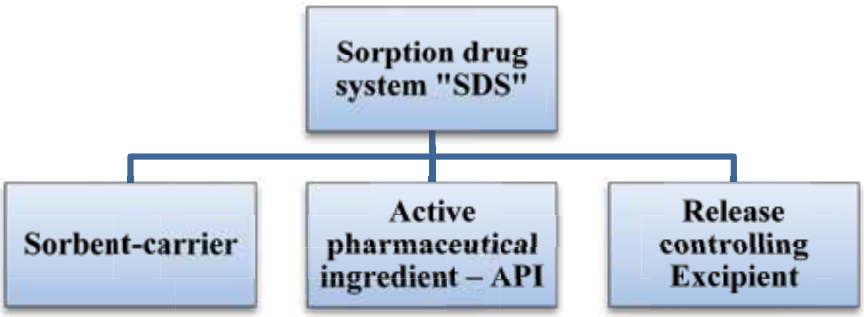

Figure 1. Structure of the sorption drug system

The structure of the sorption drug system consists of a sorbent carrier, an active pharmaceutical ingredient and excipients that provide desorption. Desorption of the active pharmaceutical ingredient may contribute to its modified release. This effect provides a constant therapeutic concentration, the known release rate, elimination of side effects, and stability augmentation [52–54].

Fig. 2 shows the pharmacokinetic model of drug release according to the dose.

ISSN 2307-9266 e-ISSN 2413-2241

Scientific and Practical Journal
PHARMACY & PHARMACOLOGY

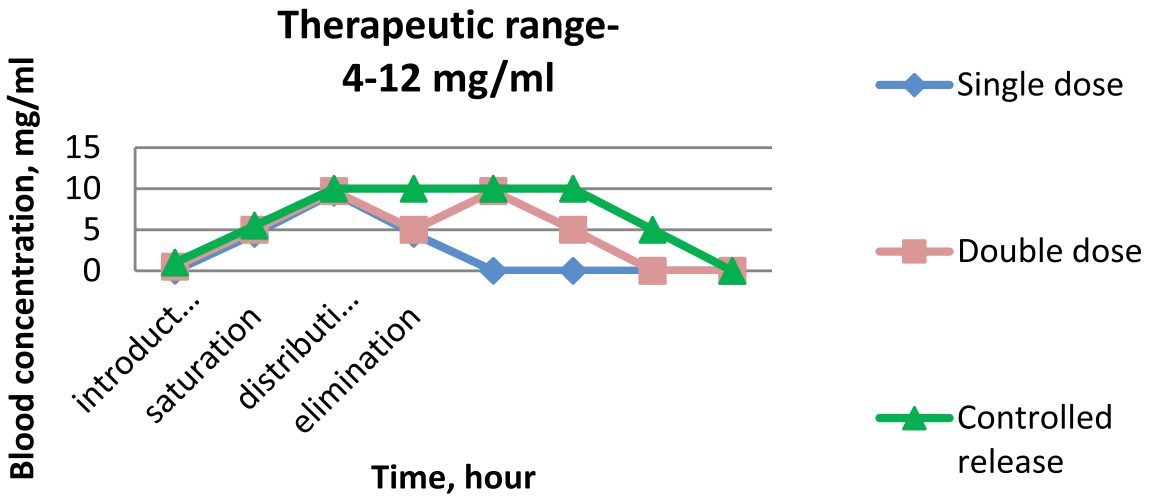

Figure 2. Pharmacokinetic model of drug release

As Figure 2 shows, the dosage form with controlled release is rational, as the active substance is able to have a clinical effect with a pharmacokinetic profile that is different from the one achieved with the use of the dosage form with immediate release at a single or double dosage.

Fig. 3 shows the mechanism of the sorption drug system action of the use *per os*.

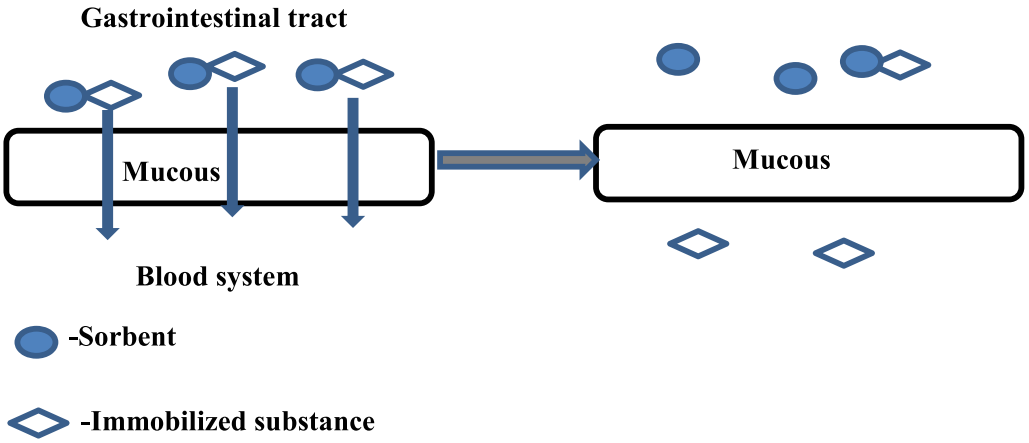

Figure 3. Mechanism of the sorption drug system action of the use per os

As Fig. 3 shows, the sorption drug system desorbs immobilized drug, which, accumulating near the intestinal wall, is absorbed into the blood when ingested into the gastrointestinal tract. The use of carrier sorbents will allow modification of drug release. The following factors may influence the release of drugs: the surface structure of the sorbent carrier, the concentration of drugs in the carrier, type of dosage form, surface area, pore size, adsorption activity.

In the technology of obtaining sorption medicinal systems for use *per os,* it is possible to use only registered pharmaceutical substances with an adsorption pharmacological action. Based on the analysis, the following groups of pharmaceutical substances permitted for use in medical practice, were identified (Table 1) [55–56].

ОБЗОР
DOI: 10.19163/2307-9266-2019-7-1-4-12

Table 1. Characteristics of the main groups of sorbents

№	Group	Characteristic	Specific surface area
1	2	3	4
1	Activated Carbon	Obtained from stone coals by cleaning and steaming to increase porosity. It has a highly developed microporous surface	1,5–200 m²/g
2	Dioctahedral Smectite	Prepared from mineral raw materials by purification. It has a mesoporous surface. Due to the structure of the crystal lattice it has an ion-exchange ability	up to 600 m²/g
3	Colloidal Silicon dioxide	Prepared from highly dispersed silica. It shows sorption properties on the surface in the places of silicon oxide bonding with hydroxyl groups	up to 400 m²/g
4	Hydrolyzed Lignin	Obtained by alkaline processing of lignin. It has a macroporous structure	up to 20 m²/g
5	Polyvinylpyrrolidone	Prepared synthetically from the monomer vinylpyrrolidone. Possesses ion-exchangeable capability	200–400 m²/g
6	Polymethylsiloxane-polyhydrate	Prepared by polycondensation of methylsilicic acid hydrogel. It has a silicone porous structure. Sorbs medium molecular substances.	180–300 m²/g

As Table 1 shows, the 6 groups of pharmaceutical substances are registered in Russia and used in the manufacture of enterosorbents. The following sorbents can be used as carriers: activated carbon, dioctahedral smectite, colloidal silicon dioxide, polyvinylpyrrolidone and polymethylsiloxane polyhydrate. Sorbents have different specific surface indicators. This indicator characterizes the amount of sorption processes on their surface, they can occur simultaneously. Hydrolyzed lignin is obtained in the form of secondary raw material after hydrolysis of hardwood and softwood. Lignin has a macroporous structure.

Medical refined clays are used as carriers, using surface hydroxyl groups for sorption of organic substances, as well as active centers inside the crystal lattice for sorption of inorganic substances. Currently, developed polymer sorption drug systems have limitations *in vivo* due to the biodegradation processes, unexplored metabolism, low solubility or insolubility and toxicity. To solve these problems, additional studies of polymers as carriers for sorption drug systems are required.

The technology for obtaining sorption medicinal systems requires further study and development of modeling methods, searching for experimental pharmacological models and technological methods, which allow obtaining a sorption dosage form with modified release.

CONCLUSION

The review of sorption processes in the technology of drug delivery systems has been carried out. The possibility of using sorption processes in drug delivery systems has been established. Sorbents act as carriers for various medicinal substances when taken *per os*, as well as dispensers of various compounds in the human body when using polymer delivery systems in the form of eye films and stents. A model of the sorption drug system, consisting of a sorbent carrier, an active pharmaceutical ingredient and excipients that provide desorption, has been developed. Desorption of the active pharmaceutical ingredient may contribute to its modified release.

REFERENCES

1. Zdravoohranenie v Rossii. 2017: Stat.sb. [Health care in Russia. Statistical compilation] Rosstat, M. 2017. 170 p.
2. Bondarev AV, Linnikova OV, Novikova NB. Obzor farmacevticheskogo rynka Rossii [Overview of the pharmaceutical market in Russia] International scientific and periodical "New science: current state and ways of development" on the basis of scientific-practical. conf. 2016 Aug: 117-9. Russian.
3. Menshutina NV Nanochasticy i nanostrukturirovannye materialy dlya farmacevtiki [Nanoparticles and nanostructured materials for pharmaceuticals] Publishing House of Scientific. Literature NF Bochkareva, Kaluga. 2008. 192 p.
4. Sysuev BB, Pletneva IV. Sovremennoe sostoyanie issledovanij razrabotok v oblasti innovacionnyh lekarstvennyh form i ih modifikacij [The current state of research in the field of innovative dosage forms and their modifications] Bulletin of Volgograd State Medical University. 2014;4(52):7-12. Russian.
5. Borodin YI, Konenkov VI, Parmon VN, Lyubarsky MS, Rachkovskaya LN, Bgatova NP, Letyagin AY. Biologicheskie svojstva sorbentov i perspektivy ih primeneniya [Biological properties of sorbents and the prospects for their use] Advances in modern biology. 2014; 3(134):236-48. Russian.
6. Sakaeva IV, Vasilyev AN, Bunyatyan ND, Sakanyan EI, Kolganov LA. Sovremennoe sostoyanie vopro-

sa klassifikacii i standartizacii lekarstvennyh form v Rossijskoj Federacii [Current status of the issue of classification and standardization of dosage forms in the Russian Federation] Bulletin of the Scientific Center for Expertise of Medical Products application. 2012;3:52-5. Russian.

7. Leonova MV. Novye lekarstvennye formy i sistemy dostavki lekarstvennyh sredstv: osobennosti peroral'nyh lekarstvennyh form. CH. 2 [New Dosage Forms and Drug Delivery Systems: Peculiarities of Oral Dosage Forms. Part 2] Medical business. 2009;3:18-25. Russian.
8. Kathe K, Kathpalia H. Film forming systems for topical and transdermal drug delivery. Asian Journal of Pharmaceutical Sciences. 2017;12(6):487-97. https://doi.org/10.1016/j.ajps.2017.07.004.
9. Alekseev KV, Tikhonova NV, Blynskaya EV, Karbusheva EY, Turchinskaya KG, Mikheeva AS, Alekseev VK, Uvarov NA. Tekhnologiya povysheniya biologicheskoj i farmacevticheskoj dostupnosti lekarstvennyh veshchestv [Technology of increasing the biological and pharmaceutical availability of medicinal substances] Bulletin of new medical technologies. 2012;4:43-7. Russian.
10. Recommendations of the Collegium of the Eurasian Economic Commission "On the Manual on the Quality of Medicinal Products with Modified Release for Oral Intake". 2018;2.
11. Volova TG, Sevastyanov EI, Shishatskaya EI. Polioksialkanoaty – biorazrushaemye polimery dlya mediciny: Monografiya. 2-e izd., dopoln. i pererabot [Polyoxyalkanoates - biodegradable polymers for medicine: Monograph. Second edition enlarged and revised] Krasnoyarsk. 2006. 288 p. Russian.
12. Korochinsky AV, Privalov IM, Stepanova EF, Sergienko AV. Farmakologicheskie issledovaniya lekarstvennoj formy biosporina, immobilizovannogo na mikrokapsulah [Pharmacological studies of the dosage form of biosporin immobilized on microcapsules] Scientific Bulletin of Belgorod State University. 2012;10(129):114-20. Russian.
13. Khoroshilova NV. Terapevticheskaya ehffektivnost' probiotikov [Therapeutic efficacy of probiotics] New pharmacy. Pharmacy assortment. 2009;6: 100-2. Russian.
14. Borodin YI, Soldatova GS, Burmistrov VA, Rachkovskaya LN. Preparat Biosorb-Bifidum dlya normalizacii ehkologii vnutrennej sredy [Biosorb-Bifidum preparation for the normalization of the ecology of the internal environment] Problems of lymphology and endoecology of the internal environment: materials of international symposium. Novosibirsk. 1998:58-9. Russian.
15. Konenkov VI, Bgatov NP, Borodin YI, Lyubarsky MS, Rachkovskaya LN, Besednova NN. Kuznetsova TA, Shevchenko LM, Zvyagintsev TN. Biologicheskie svojstva ehnterosorbenta specificheskoj napravlennosti v usloviyah ozhogovoj travmy [Biological properties of a specific-purpose enterosorbent in conditions of burn injury] Improving, curative and restorative medicine. Novosibirsk. 2006;1:16-21. Russian.
16. Poristyj sorbent s gepatoprotektornymi svojstvami [Porous sorbent with hepatoprotective properties] Patent 2329864 Russian Federation N. 2006107349/15; declare 09/03/06; publ. 07/27/08, Bull. N. 21.
17. Kovalenko GA, Kuznetsova EV, Vanina MP. Adsorbciya i antifibrinoliticheskaya aktivnost' ehpsilon-aminokapronovoj kisloty na uglerodsoderzhashchih ehnterosorbentah [Adsorption and antifibrinolytic activity of epsilon-aminocaproic acid on carbon-containing enterosorbents] Chemical and pharmaceutical journal. 1998;32(11):39-42. Russian.
18. Pavlov VV, Pleshakov VP. Ispol'zovanie limfotropnoj i sorbcionno-applikacionnoj terapii dlya podgotovki ranevoj poverhnosti k razlichnym vidam kozhnoj plastiki [Use of lymphotropic and sorption-application therapy to prepare the wound surface for various types of skin plastics] Problems wedge and experts. Lymphology: Mater. int. conf. Novosibirsk 1996: 195-9. Russian.
19. Pleshakov VP. Morfofunkcional'naya harakteristika limfaticheskogo rusla bryushnoj polosti pri razlitom gnojnom peritonite ego lechenii s pomoshch'yu limfosorbcionnogo drenazha [Morphofunctional characteristics of the lymphatic bed of the abdominal cavity with purulent peritonitis poured out; its treatment using lympho-sorption drainage] Problems of the wedge and experts. Lymphology: Mater. int. conf. Novosibirsk. 1996:202-6. Russian.
20. Murueva AV, Shershneva AM, Shishatskaya EI, Volova TG. Issledovanie polimernyh mikronositelej, nagruzhennyh protivovospalitel'nymi preparatami, dlya terapii model'nyh defektov kozhnyh pokrovov [The study of polymeric microcarriers loaded with anti-inflammatory drugs for the treatment of model skin defects] Bulletin of experimental biology and medicine. 2014;157(5):614-9. Russian.
21. Bukhanov VD. Shaposhnikov AA, Vezentsev AI. Sravnitel'nyj analiz biohimicheskih i morfologicheskih pokazatelej krovi krys na tret'ej stadii processa ranozazhivleniya pri lechenii fitomineralosorbentami [Comparative analysis of biochemical and morphological parameters of blood in rats at the third stage of the wound healing process in the treatment with phytominelo-sorbents] Scientific Bulletin of Belgorod State University. 2014;26(11):177-80. Russian.
22. Kasanov KN, Popov VA, Uspenskaya MV, Soloviev VS, Makin DN, Vezentsev AI, Ponomareva NF, Mukhin VM. Razrabotka montmorillonit soderzhashchej matricy bioaktivnogo sorbiruyushchego ranevogo pokrytiya [Development montmorillon-

ОБЗОР
DOI: 10.19163/2307-9266-2019-7-1-4-12

ite-containing matrix of bioactive sorbent wound dressing] Scientific Bulletin of Belgorod State University. 2011;3(98):167-73.
23. Lutsenko VD, Shaposhnikov AA, Krut UA, Magolin GF, Lukhanina EM, Ivanchikova KN, Shevchenko TS. Obosnovanie primeneniya bioaktivnyh sorbcionno-gelievyh kompozicij pri lechenii gnojnyh ran [Justification of the use of bioactive sorption-helium compositions in the treatment of purulent wounds] Surgery News. 2016;3:222-6. Russian.
24. Konenkov VI, Borodin YI, Burmistrov VA, Rachkovskaya LN, Bgatova NP. Preparaty vysokodispersnogo serebra dlya ozdorovitel'nyh programm [Highly dispersed silver preparations for health programs] Medical and restorative medicine. Novosibirsk. 2009;2:8-11. Russian.
25. Asanov BM, Beysembaev AA. Zameshchenie kostnyh polostej sorbcionnymi implantantami [Replacement of bone cavities with sorption implants] Problems of lymphology and interstitial mass transfer: Mater. scientific conf. Novosibirsk. 2004:38-9. Russian.
26. Shkutina IV, Stoyanova OF, Selemenev VF. Sverhsshitye sorbenty kak nositeli inulinazy pri poluchenii fruktozy [Superstitched sorbents as carriers of inulinase in the production of fructose] Sorbents as a factor in the quality of life and health: Mater. IV Intern. scientific conf. Belgorod. 2012:189-93. Russian.
27. Sonmez M, Ficai D, Ficai A. Applications of mesoporous silica in biosensing and controlled release of insulin. International Journal of Pharmaceutics. 2018;549(1-2):179-200. https://doi.org/10.1016/j.ijpharm.2018.07.037.
28. Babanina AK, Ryltsova IG, Lebedeva OE. Interkalyacionnye struktury na osnove sloistyh dvojnyh gidroksidov kak sistemy dostavki lekarstvennyh preparatov [Intercalation structures based on layered double hydroxides as a drug delivery system] Sorption and ion-exchange processes in nano- and supramolecular chemistry. Mater. All-Russia scientific conf. 2014 Sept:16-9. Russian.
29. Diab R, Canilho N, Pavel I, Haffner F. Silica-based systems for oral delivery of drugs, macromolecules and cells. Advances in Colloid and Interface Science. 2017;249:346-362. https://doi.org/10.1016/j.cis.2017.04.005.
30. Jayrajsinh S, Shankar G, Agrawal Y, Bakre L. Montmorillonite nanoclay as a multifaceted drug-delivery carrier: A review. Journal of Drug Delivery Science and Technology. 2017;39:200-9. https://doi.org/10.1180/0009855013640007.
31. Graycyelle RS, Cavalcantiac MG, Fonsecaa EC. Thiabendazole/bentonites hybrids as controlled release systems. Colloids and Surfaces B: Biointerfaces. 2019;176:249-255. https://doi.org/10.1016/j.colsurfb.2018.12.030.
32. Beissebekov M, Kayralapova R, Kudaybergenova G. Organo-mineral carriers of medicinal substances. Chemical Bulletin of Kazakh National University. 2012;3:197-202. https://doi.org/10.15328/chemb_2012_3197-202.
33. Pianova LG, Gerunova LK, Liholobov VA, Sedanova AV. Sozdanie i perspektivy ispol'zovaniya modificirovannyh sorbentov v veterinarnoj medicine [Creation and prospects for the use of modified sorbents in veterinary medicine] Omsk State Medical University Bulletin. 2016;2(22):138-46. Russian.
34. Bolotova GV. Polimernye nositeli dlya protivotuberkuleznyh lekarstvennyh sredstv na osnove hitozana [Polymeric carriers for anti-tuberculosis drugs based on chitosan] Young Scientist. 2010;5(2):208-10. Russian.
35. Makarevich NA, Bogdanovich NI, Bubnova II, Lagunova EA. Poliionnaya sborka na osnove biopoliehlektrolitov [Polyion assembly based on biopolyelectrolytes] Sorption and ion-exchange processes in nano- and supramolecular chemistry: Mat. All-Russia scientific conf. 2014 Sept:67-72. Russian.
36. Makarevich NA, Boitsova TA, Brovko OS, Palamarchuk IA. Poliehlektrolitnye kompleksy na osnove lignosul'fonatov i hitozana v sisteme ochistki stochnyh vod cellyulozno-bumazhnyh predpriyatij [Polyelectrolyte complexes based on lignosulfonates and chitosan in the wastewater treatment system of pulp and paper enterprises] Water: chemistry and ecology. 2009;7:23-9. Russian.
37. Zhilyakova ET, Novikov OO, Akopova VV. Issledovanie poverhnosti i morfologii myagkih kontaktnyh linz s cel'yu sozdaniya oftal'mologicheskoj terapevticheskoj sistemy dostavki lekarstvennyh preparatov k tkanyam glaza [Examination of the surface and morphology of soft contact lenses in order to create an ophthalmologic therapeutic drug delivery system to the eye tissues] Scientific Bulletin of Belgorod State University. 2010;22(93):73-6. Russian.
38. Akopova VV. Myagkie kontaktnye linzy kak vozmozhnoe sredstvo dostavki lekarstvennyh sredstv [Soft contact lenses as a possible means of drug delivery] Modern high technology medical and pharmaceutical technologies for ophthalmology: for young scientists: collection of articles. materials of All-Russia. 2009 Sept:7-11. Russian.
39. Akopova VV. Izuchenie poverhnosti i struktury myagkih kontaktnyh linz s cel'yu sozdaniya oftal'mologicheskoj terapevticheskoj sistemy dostavki lekarstvennogo preparata k tkanyam glaza [Study of the surface and structure of soft contact lenses in order to create an ophthalmologic therapeutic drug delivery system to the eye tissues] Nano- and supramolecular chemistry in sorption and ion-exchange processes. 2010 Sept:9-12. Russian.
40. Zhilyakova ET, Naplekov DK. Izuchenie vozmozhnosti sozdaniya kombinirovannogo lekarstvennogo

sredstva dlya lecheniya glaukomy, oslozhnennoj miopiej [Study of the possibility of creating a combined drug for the treatment of glaucoma complicated by myopia] Young Scientist. 2014;19:107-9. Russian.
41. Zhilyakova ET, Novikov OO, Akopova VV, Popov NN, Goncharov IY, Bondarev AV. Issledovanie poverhnosti i morfologii myagkih kontaktnyh linz s cel'yu sozdaniya oftal'mologicheskoj terapevticheskoj sistemy dostavki lekarstvennogo preparata k tkanyam glaza [Study of the surface and morphology of soft contact lenses in order to create an ophthalmological therapeutic system drug delivery to eye tissues] Scientific Bulletin of Belgorod State University. 2010;22(93):73-6. Russian.
42. Beburishvili AG, Zaporotskova IV, Spiridonov EG, Mandrikov VV, Shinkarev RA. O vozmozhnosti sozdaniya novogo lekarstvennogo pokrytiya na poverhnosti biliarnogo stenta [On the possibility of creating a new drug coating on the surface of the biliary stent] Bulletin of Volgograd State Medical University. 2014;2(50):123-30. Russian.
43. Nizaa José E, Castro-Osmaa A. Assessment of doxorubicin delivery devices based on tailored bare polycaprolactone against glioblastoma. International Journal of Pharmaceutics. 2019;558(10):110-9. https://doi.org/10.1016/j.ijpharm.2018.12.079.
44. Grigorieva MV. Polimernye sistemy s kontroliruemym vysvobozhdeniem biologicheski aktivnyh soedinenij [Polymer Systems with Controlled Release of Biologically Active Compounds] Biotechnol. acta. 2011;2:009-23. Russian.
45. Glangchai LC, Caldorera MM, Li Shi Roy K. Nanoimprint lithography based fabrication of shape specific, enzymatically trig gered smart nanoparticles. Journal of Controlled Release. 2008;125:263-72. https://doi.org/10.1016/j.jconrel.2007.10.021.
46. Pengac H, Huangb X, Melleac A. Redox-responsive degradable prodrug nanogels for intracellular drug delivery by crosslinking of amine-functionalized poly(N-vinylpyrrolidone) copolymers. Journal of Colloid and Interface Science. 2019;540:612-622. http://dx.doi.org/10.1016/j.jcis.2019.01.049.
47. Erdoğar N, Akkın S, Bilensoy E. Nanocapsules for Drug Delivery: An Updated Review of the Last Decade. Recent Patents on Drug Delivery & Formulation. 2018;12:252-66. http://dx.doi.org/10.2174/1872211316661901231537 11.
48. Mundargi RC, Babu VR, Rangaswamy V. Nano/micro technologies for delivering macromolecular therapeutics using poly (D,L-lactide co glicolide) and its derivatives. Ibid. 2008;125:193-209. http://dx.doi.org/10.1016/j.jconrel.2007.09.013.
49. Grigoriev MV, Gladiore II, Galatenko NA. Cefazolin-filled polyurethane carriers. Ukrainian chemical journal. 2002;68(4):125-7. Ukrainian.
50. Grigorieva MV, Mazur LN, Galatenko NA. Izuchenie svojstv polimernoj kompozicii na osnove setchatogo poliuretana s prolongirovannym antinarkoticheskim dejstviem [Study of the properties of a polymeric composition based on a netted polyurethane with prolonged anti-drug action] Polymer journal. 2004;26(4):254-9. Russian.
51. Blaesi A, Saka N. Microstructural effects in drug release by solid and cellular polymeric dosage forms: A comparative study Materials Science and Engineering. 2017;80(1):715-27.
52. Bajpai AK, Shukla SK, Bhanu S. Responsive polymers in controlled drug delivery. Progr. Polym. Sci. 2008;33:1088-118. https://doi.org/10.1016/j.progpolymsci.2008.07.005.
53. Sosnov AV, Ivanov RV, Balakin KV, Shobolov DL, Fedotov YA, Kalmykov YM. Razrabotka sistem dostavki lekarstvennyh sredstv s primeneniem mikro- i nanochastic [Development of drug delivery systems using micro- and nanoparticles] High-quality clinical practice: new drugs and technologies. 2008;2:4-12. Russian.
54. Malafaya PB, Silva GA, Reis RL. Natural-origin polymers as carriers and scaffolds for biomolecules and cell delivery in tissue engineering applications. Advanced Drug Delivery Reviews. 2007:207-33. https://doi.org 10.1016/j.addr.2007.03.012.
55. Gosudarstvennyj reestr lekarstvennyh sredstv [The state register of medicines] [Electronic resource] Ministry of Health of the Russian Federation. M., 2018. Access mode: http://grls.rosminzdrav.ru.
56. Zhilyakova ET, Bondarev AV. Obzor rossijskih ehnterosorbcionnyh lekarstvennyh sredstvn [Overview of Russian enterosorption drugs] Remedium. Magazine on the market of drugs and medical equipment. 2014;(10):40-47. https://doi: 10.21518 / 1561-5936-2014-10-40-47. Russian.

Conflict of interest

The authors declare no conflict of interest.

Authors

Bondarev Alexander Vasilievich *– PhD (Pharmacy), Senior Lecturer of the Department of Pharmaceutical Technology, Belgorod State National Research University. E-mail: alexbond936@yandex.ru*

Zhilyakova Elena Teodorovna *– PhD (Pharmacy), Professor, Head of the Department of Pharmaceutical Technology, Belgorod State National Research University. E-mail: ezhilyakova@bsu.edu.ru*