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CHARACTERISTICS OF GEL BASES FOR THE DEVELOPMENT OF GEL WITH ANTI-BACTERIAL ACTIVITY

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Introduction. Import substitution is one of the key directions of domestic pharmaceutical development with the aim of expanding the assortment of dosage forms of already used active substances, which is aimed at reducing the side effects of active substances and increasing the convenience of their use. At the same time, medicinal products must ensure the rapid and complete release of active substances from dosage forms and the penetration of active substances into the target organ, including when applied locally. The high level of antibiotic resistance of modern microorganisms limits the use of many active substances. Therefore, the urgent task is the development of

antimicrobial drugs with a mechanism of action different from that of antibiotics, with proven effectiveness and easy to use.

The main advantages of gels are higher efficiency in application due to increased bioavailability compared to water-insoluble soft dosage forms. Unlike ointments, they are characterized by better penetration of active substances through the skin barrier. An important characteristic is the pH value, which is close to the pH value of the surface of the human skin, which allows you to avoid irritating and toxic effects and not disrupt the physiological functions of the skin. When applied to the surface, gels form the thinnest, uniform film that does not clog pores and evenly and completely releases active substances. Water-soluble soft dosage forms are convenient to use, as they have a pleasant appearance and consistency and do not leave marks on clothes, they are stable during storage. One of the most frequently used groups of auxiliary substances in gel technology are acrylic acid polymers.

The aim of the study. Development of the composition, technology and research of antibacterial gel.

Research methods. Information-searching, information-analytical, organoleptic, physico-chemical.

Main results. Soft dosage forms with a viscous-plastic consistency are one of the most popular and widely used dosage forms on the modern pharmaceutical market. This is due to the high efficiency of representatives of medicinal forms - gels and ointments and a number of their advantages over other medicinal forms.

The advantages of gels and ointments are:

• the possibility of introducing into the composition active substances of different aggregate state (because in a viscous environment, physical and chemical processes proceed slowly);

• the possibility of simultaneous introduction of interacting components into the basis;

• the possibility of introducing active substances in a finely dispersed state without an additional manufacturing stage;

• possibilities of correction of organoleptic properties (smell, color);

• no irritating effect on the skin (especially in soft medicinal forms on hydrophilic bases), since the pH is close to the value of the hydrogen index of healthy skin;

• relative simplicity and safety of use in comparison with injectable, oral dosage forms;

• relative speed of production;

• ease of transportation and storage;

• low probability of developing undesirable reactions;

• comfort of use on the surface of the skin and mucous membranes;

• ease of use [1].

Due to the high viscosity at room temperature, the gels retain their shape. With an increase in temperature or intense mechanical impact, the gels turn into thick liquids, and when external physical influences are weakened, they are able to restore the original structure. The viscosity of gels is due to the formation of bonds between

molecules or colloidal particles of polymers that form a gel network, the cells of which are filled with a solvent.

Due to the viscous structure of gels, physico-chemical processes (redox, hydrolytic interactions) unfavorable for the dosage form proceed slowly. Also, in the viscoelastic environment of gels, there are practically no processes of sedimentation and gluing of particles, which ensures uniform distribution of the active substance in the base.

Depending on the type of dispersion system, gels are classified into hydrogels and oleogels. Hydrogels are a mixture of a small amount of gelling agent (for example, carbopol) with a solvent - purified water or a mixture of water / hydrophilic solvent (polyethylene glycol, glycerin). The presence of a gelling agent determines the rheological properties of gels - the ability to retain shape, elasticity and plasticity over time, as well as a viscous consistency [2].

Oleogels consist of a solvent, for example, vegetable or petroleum jelly, and a gelling agent (zinc or aluminum soap, polyethylene, etc.) of a hydrophobic nature.

General methodological approaches to the pharmaceutical development of soft dosage forms are currently not officially standardized. The European Pharmacopoeia sets out general requirements for their quality and some test methods, which only assume the conduct of relevant research during pharmaceutical development. Due to various biological and pharmaceutical factors, there are different requirements for medicinal products, in particular, for ointments and gels. Gels, like ointments, should:

• provide a pharmacological effect aimed at eliminating the disease;

• have the best dispersion and homogeneity of distribution in the base of the active substance to ensure the optimal therapeutic effect;

• maintain stability of quality indicators during storage, be resistant to adverse factors (microbial contamination, humidity fluctuations, etc.);

• to be able to combine in the composition substances with different aggregate states, as well as chemically incompatible components;

• do not have a toxic and sensitizing effect on the body;

• exclude the possibility of interaction of components of dosage forms and packaging material;

• have a soft consistency, marketable appearance and be convenient to use.

In order for the gels to have satisfactory physico-chemical, pharmaceutical and biological characteristics, it is necessary to choose the optimal gel base. It is a competent approach to the selection of the base during the development and production of soft dosage forms that affects the physical and chemical properties of the drug, the stability of the components. The choice of the optimal base and the selection of a certain combination of auxiliary substances allows to avoid many interphase changes to dosage forms, and that also allows to optimize the technological process of manufacturing dosage forms and obtaining the finished medicinal product.

The main indicators of the quality of gels, described in the leading pharmacopoeias and state standards, are the appearance, uniformity, identification, pH of the aqueous extract, and the content of the active substance [3].

One of the most important indicators of the quality of gels as a medicinal product is the ability to ensure the bioavailability of the active substance. Using different

combinations of auxiliary substances, it is possible to adjust the strength and duration of the therapeutic effect of the gel, and to adjust the bioavailability of the active substance. When creating a drug with high therapeutic activity, the ability of the active substance to be released from the gel and its resorption through the skin should be evaluated.

These possibilities of the gel can be judged by the results of the study of its diffusion, which characterizes the penetration of the active substance through biological membranes upon contact with the skin. Model experiments conducted in vitro can be used for this. There are two types of research methods: diffusion in direct contact of the gel with the environment and diffusion through a semipermeable membrane.

The first type includes diffusion in agar. The essence of the method is that the suspension of the tested soft dosage form is applied to agar gel containing a reagent that forms colored compounds from the active substance. As the active substance diffuses from the gel, the painted area increases. The degree of diffusion of the substance from the gel can be measured by the linear dimensions of this zone. If the active substance has antiseptic or bactericidal properties, a microbiological test is used, which differs in the method of identification. Microorganisms on the nutrient medium do not grow where the minimal bacteriostatic or bactericidal effect of the substance diffused from the gel is formed for them. Thus, an inhibition zone is formed around the gel, which is absent when using an inappropriate base. The diameter or width of the inhibition zone characterizes the degree of diffusion of the active substance from the base [4].

Currently, the most common methods are diffusion through a membrane. The essence of this group of research methods is that a semipermeable membrane is placed between the gel and the medium into which the active substance is released. Dialysis films with different hole diameters can serve as a membrane. At the same time, the thickness of the film has a negligible effect on diffusion. The active substance does not interact with the polymer material of the semipermeable film. During the study, a certain amount of gel is placed in the dialysis chamber. The tank is immersed in a physiological solution, a buffer solution or purified water at a temperature of 32–37 °C. Diffusion of the active substance in the solution is determined at set time intervals by chemical or physico-chemical methods. At the stage of development of the composition and technology of the dosage form, special attention is paid to the study of structural and mechanical characteristics of soft dosage forms, such as viscosity, shear stress. The State Pharmacopoeia of Ukraine does not regulate these indicators, while in a number of foreign Pharmacopoeias, the determination of rheological characteristics is a mandatory requirement. Soft dosage forms must have constant characteristics during storage, as they determine consumer and medicinal properties. Stability during storage is determined over time by a set of parameters that indicate the invariance of the properties of the gel after the expiration date. Control is carried out according to such parameters as appearance, uniformity, pH, quantification, authenticity, container weight, microbiological purity. By structure, carbomeres are divided into 5 groups (table 1).

Table 1

Assortment of carbopols and the area of their use

A group of polymers	Structure	Representatives	Field of application
Carbopol™ homopolymer	acrylic acid polymer cross-linked with allylsucrose or allylpentaerythritol	971PNF; 71GNF; 934PNF; 974PNF; 5984EP; 980NF; 981NF; 934NF; 940NF; 941NF	<u>For internal use:</u> <u>used in</u> in the production of matrix tablets and capsules for modification of release, in the production of oral soft prolonged LF. <u>For external use:</u> production of gels, creams, suspensions, cosmetics, viscous solutions, medical glue; as an active substance for conjunctivitis or dry eyes; as a coating for implants to protect against corrosion.
Carbopol™ polymer	polymer of acrylic acid and C10–C30 alkyl acrylate, cross-linked with allylpentaerythritol	1342 NF	
Carbopol™ interpolymer	carbomer homopolymer or copolymer, including a copolymer of PEG and a complex ester with an alkyl substituent	Ultrez10 NF; ETD 2020NF; ETD 2001; ETD 2050	
Pemulen™ polymer	acrylic acid polymer with C10–C30 alkyl acrylate, cross-linked with allylpentaeritol	TR–1 NF; TR–2 NF	
Noveon™ Polycarbophil homopolymer	polymer of acrylic acid, cross-linked with divinyl glycol	AA–1 USP	

Carbopol™ RAP derivatives can be singled out among the most popular auxiliary substances for the pharmaceutical production of soft dosage forms. Carbopol of the ETD (Easy to Disperse) series should be singled out in a special group. It includes carbopol ETD 2001, carbopol ETD 2020 and carbopol ETD 2050. They are characterized by a number of advantages compared to other brands of Carbopol, which contribute to the simplification of the technological stages of obtaining dosage forms based on them. Carbopol of the ETD series swells and dissolves in water much more easily, forming weakly elastic solutions and few lumps, which simplifies the technological process of mixing.

• Carbopol® ETD 2020 - provides excellent thickening efficiency, suspending ability and absolute transparency in gel systems;

• Carbopol® ETD 2020 NF – forms aqueous dispersions, the viscosity of which before neutralization is significantly lower than that of other carbomers; aqueous dispersions of Carbopol ETD 2020 NF polymer are less susceptible to agglomeration;

• Carbopol® 980 NF – used in the pharmaceutical production of gels and bioadhesive structures;

• Carbopol® ETD 2001 – swells very easily in water, is used in the production of water and water-alcohol based gels, is slightly toxic;

• Arespol - used to thicken polar liquids, which does not have an irritating effect on mucous membranes [5].

Conclusions. Soft hydrophilic dosage forms are widely used in the antimicrobial therapy of skin diseases, expanding their range, due to the creation of new drugs, is an urgent task. Derivatives of acrylic polymers are a group of widespread gelling agents that allow obtaining soft dosage forms with optimal physicochemical and biopharmaceutical properties.

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JUSTIFICATION OF THE EXTRACTION CONDITIONS OF BIOLOGICALLY ACTIVE SUBSTANCES OF UROLOGICAL PHYTOCOMPOSITION

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Introduction. Kidney diseases are the most complex from a clinical and epidemiological point of view. Analysis of uro- and nephrological morbidity in Ukraine according to official statistics in recent years showed an increase in the absolute number of registered patients with diseases of the genitourinary system by 25.8% annually. This is largely due to the important role of the kidneys in maintaining human physiological functions. Phytotherapy, as a method of safe basic treatment of many diseases through the harmonization of natural detoxification processes, is aimed at improving the functional state of the kidneys and can significantly increase both the effectiveness and safety of basic pharmacotherapy due to the advantages of the following nature: polymodality of effects, absence of xenobiotic metabolites, effects of drug therapy.

In this regard, the development of new phytomedicine for the treatment of kidney diseases and the increase in the range of nephroprotective agents on the pharmaceutical market is particularly relevant.

One of the important groups of medicinal substances for phytotherapy of arterial hypertension is the group of flavonoids, which have capillary-stabilizing, anti-edematous, anti-inflammatory and antioxidant activity.

The search for affordable, cost-effective and official medicinal plant raw materials for the treatment of this pathology, which would show the necessary pharmacological effects, led to the well-known medicinal plant raw materials - three-lobe beggartick herd, woundwort herb, and ommon agrimony herb. The peculiarity of this phytocomposition lies in its ability to strengthen the integral local-reflex action, which is accompanied by the expansion of blood vessels (tissue trophicity, fluid outflow and not a sharp decrease in blood pressure are improved) and has a venotonic effect [1].