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DEVELOPMENT OF NEW MEDICINE IN THE FORM OF HYDROGEL PATCHES FOR THE TREATMENT OF SKIN BURNS

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Abstract

In an technological experiment the composition of hydrogel patches with panthenol and hyaluronic acid for the treatment of skin burns has been developed. The concentrations of hyaluronic acid 2% and panthenol 4% have been substantiated and the composition of the base consisting of sodium alginate, polyvinylpyrrolidone, guar gum, gelatin, glycerol, phenoxyethanol and purified water has been selected taking into account the medical and biological requirements for the medicine and physicochemical properties of active pharmaceutical ingredients. The quality of hydrogel patches has been evaluated by organoleptic, physicochemical and pharmaco-technological indicators.

Keywords: *hydrogel patches, panthenol, hyaluronic acid, burns, dermal medicines.*

Introduction

In modern dermatology, increasingly popular medicines that let to achieve the desired results faster and easier, without injuring the skin, but not inferior in effectiveness to other medicines [1].

Burn wounds are one of the most common types of skin injuries; about 6 million people seeking medical help every year, but most are treated on an outpatient basis. Stimulating the healing of burn wounds in medicine remains an urgent problem [2, 3]. Despite the wide nomenclature of highly effective wound-healing medicines, traditional treatment of burns does not always give the desired results, and the frequency of complications can reach 10% [4].

Therefore, it is important to create new dosage forms with high bioavailability of active substances, which will increase the therapeutic efficacy and quality of life of the patient and allow to achieve the desired treatment results faster.

The aim of our work was to develop the composition, technology and quality indicators of new medicine in the form of hydrogel patches for the treatment of skin burns.

Methods

The following study methods have been used to solve the set tasks: technological methods of patches preparation, organoleptic (color, odor, homogeneity); physico-chemical (determination of pH), pharmaco-technological (strength of hydrogel patches, adhesive properties), as well as tactile sensations after contact with the skin for quality control of patches.

Results and Discussion

As a result of our study, we found that in addition to bandages, ointments and gels, in the global pharmaceutical market there are popular in recent years for the treatment of skin burns medicines on water-soluble bases, in particular in the form of patches (hydrogel patches), but in Ukraine, there are no domestic analogs of these medicines, that necessitates the development of such preparations [5, 6, 7].

The term "patches" in Ukraine is mainly used to denote the form of cosmetic products. Korea is the leader in the production of patches sold on the Ukrainian market. There are no medicines in the form of patches on the pharmaceutical market of Ukraine [6]. This problem is due to the ambiguity of the definition and interpretation of this term. The State Pharmacopoeia of Ukraine does not describe patches, but medical plasters and skin plasters are described [8]. In the scientific literature for the designation of products for transdermal drug delivery there are definitions "transdermal therapeutic system", "transdermal plasters", "films", which are similar in content. However, transdermal therapeutic systems are preferably designed to deliver the APIs through the skin and achieve a systemic effect, patches act mainly at the level of the epidermis or penetrate into the deeper layers of the skin without causing a systemic effect.

As a dosage form in the development of a new medicine for the treatment of burns, we have chosen patches as a highly effective and convenient method of skin treatment. This dosage form allows to include a variety of APIs. Ease of use of patches allows their use not only in the hospital and outpatient setting, but also in self-treatment and care [9, 10].

An important step in our study was the development of the basis for hydrogel patches, which is necessary to achieve the desired therapeutic effect.

According to modern requirements, bases-carriers are important components of medicines which in combination with active substances create effective and safe medicines [11].

According to the scientific literature, the basis that would provide the maximum therapeutic effect for the treatment of skin burns must meet the following medical and biological criteria: must be chemically stable (does not change under air, light, temperature) and does not react with active substances; do not show irritating and sensitizing effects; ensure microbiological purity during the shelf life; should be easy to apply to the skin, as well as have moisturizing and emollient effects [12, 13].

In order to choose the optimal basis, we made 6 samples of bases with different concentrations of gelling agents, which were selected on the basis of literature data. Consumer properties of each sample were determined visually before and after their solidification, as well as after 1 month of storage of samples (Table 1).

Considering, that studied hydrogel bases have a high content of the aqueous phase, an antimicrobial preservative was introduced into their composition to prevent microbial contamination of the finished product during storage and use.

Based on a literature search for the purpose of selecting an effective preservative that would ensure the quality and safety of the developed hydrogel patches, phenoxyethanol were introduced at a working concentration 0.6%, which is allowed to use in external applications.

The most important characteristic of the bases immediately after preparation is their ability to pour, which provides pouring into molds. After solidification, the strength of hydrogel patches, adhesive properties, and tactile sensations after skin contact were evaluated.

The prepared samples of hydrogel patch bases were stored in a refrigerator at a temperature of + 5 ° C for 1 month.

Sample 3 was a transparent film, not strong enough, adheres well to the skin, but had not adhesive properties, samples 2, 4, and 6 - opaque, very dense and strong films, adhere well to the skin, had adhesive properties and smooth surface, sample 1 after solidification met the requirements for hydrogel patches, but after a month of storage turned into a transparent very viscous gel. Based on the results of the study, a sample 5 was selected, which had optimal consumer characteristics immediately after preparation, after solidification and after 1 month of storage and met the requirements for hydrogel patches bases. The pH of the studied bases was in the range of 5.2 - 6.4 ± 0.05, which is acceptable for cutaneous preparations.

Whereas moisturizing and wound-healing effects are important in the treatment of burns, such medicines must include active ingredients having this effect. After analyzing the literature data about the development of medicines for the treatment of skin burns, as active pharmaceutical ingredients we used hyaluronic acid, which has moisturizing and anti-inflammatory properties [14], and panthenol, which has regenerating, anti-inflammatory, dermatoprotective properties, and increases the number of fibroblasts, collagen, the frequency of mitosis, accelerating skin regeneration and promoting wound healing [15].

The concentration of active ingredients was selected on the basis of literature data and analysis of the composition of medicines and medicinal cosmetics available on the pharmaceutical market. It has been established that hyaluronic acid is used as a part of medicines and medicinal cosmetics for external use in a concentration from 1% to 3%, and panthenol from 1% to 6%. We selected the working concentrations of hyaluronic acid 2% and panthenol 4% [6].

The composition of the developed hydrogel patches included next ingredients: panthenol, hyaluronic acid, sodium alginate, polyvinylpyrrolidone, guar gum, gelatin, glycerol, phenoxyethanol and purified water.

The quality of hydrogel patches was evaluated by organoleptic, physicochemical and pharmaco-technological indicators [8].

Prepared hydrogel patches are stored for 9 months, during that time we conduct study (after preparation, after 3 months, 6 months, 9 months of storage) of their organoleptic characteristics (color, odor, homogeneity). The results of the study are shown in table 2.

The results of studies of these indicators of hydrogel patches show that this sample can be recommended for further research with a view to implementation in production.

Conclusions

The choice of new medicine for the treatment of skin burns in the form of hydrogel patches has been grounded. Based on theoretical and experimental studies the composition of base for hydrogel patches has been proposed. As the active ingredients of the medicinal hydrogel patches panthenol and hyaluronic acidhave been used. The composition of medicinal hydrogel patches has been developed and organoleptic, physical, chemical, and consumer properties of patches have been studied.

Conflict of interest

The authors declare that they have no conflicts of interest regarding the publication of this paper.

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Table 1. Comparative characteristics of consumer properties of the studied bases

N	Composition, %	Immediately after preparation	After solidification	After 1 month of storage
1	Sodium alginate 1.0 Polyvinylpyrrolidone 1.0 Guar gum 0.5 Glycerol 5,0 Purified water up to 100	Colorless transparent slightly viscous liquid, well poured	Colorless, transparent film, strong, well adjacent to the skin, the touch is pleasant, has a smooth, glossy surface	Colorless very viscous transparent gel
2	Sodium alginate 2,0 Polyvinylpyrrolidone 0,5 Guar gum 0,5 Glycerol 5,0 Purified water up to 100	Colorless transparent thick, viscous homogeneous mass, does not pour out	Transparent, very strong film, well adjacent to the skin, pleasant on the touch, has a smooth, glossy surface	Transparent, very strong film, well adjacent to the skin, pleasant on the touch, has a smooth, glossy surface
3	Sodium alginate 2,0 Guar gum 0,5 Glycerol 5,0 Purified water up to 100	Colorless transparent fluid, viscous, easily poured	Colorless, transparent film, insufficiently strong, well adjacent to the skin, but does not have an adhesive properties, pleasant on the touch, has a smooth surface	Colorless, transparent film, insufficiently strong, well adjacent to the skin, but does not have an adhesive properties, pleasant on the touch, has a smooth surface
4	Gelatin 10 Glycerol 40 Purified water up to 100	Transparent liquid of yellowish color, easily poured	Opaque, dense film with a yellowish shade, strong, well adjacent to the skin, has an adhesive properties, pleasant on the touch, has a smooth, glossy surface	Opaque, a very dense film with a yellowish shade, strong, well adjacent to the skin, does not have sufficient adhesive properties, pleasant on the touch, has a smooth, glossy surface
5	Sodium alginate 1,0 Polyvinylpyrrolidone 1,0 Guar gum 0,5 Gelatin 0,8 Glycerol 5,0 Purified water up to 100	Colorless transparent slightly viscous, yellowish liquid, well poured	Yellowish, transparent film, well adjacent to the skin, has adhesive properties, pleasant on the touch, has a smooth, glossy surface	Yellowish, transparent film, well adjacent to the skin, has adhesive properties, pleasant on the touch, has a smooth, glossy surface
6	Sodium alginate 1,0 Polyvinylpyrrolidone 2,0 Guar gum 0,5 Glycerol 5,0 Purified water up to 100	Colorless, not transparent very thick, viscous homogeneous mass, does not pour out	Colorless, not transparent film, very strong, well adjacent to the skin, pleasant on the touch, the surface is not smooth	Transparent film, very strong, well adjacent to the skin, pleasant on the touch, the surface is not smooth

Table 2. The results of the study of hydrogel patches

Organoleptic indicators								
Color			Odor			Homogeneity		
3 months	*6 months*	*9 months*	*3 months*	*6 months*	*9 months*	*3 months*	*6 months*	*9 months*
Yellowish transparent film, has a smooth, glossy surface	Yellowish transparent film, has a smooth, glossy surface	Yellowish transparent film, has a smooth, glossy surface	Without smell	Without smell	Without smell	Homo-geneous film, without signs of hetero-geneity	Homo-geneous film, without signs of hetero-geneity	Homo-geneous film, without signs of hetero-geneity