Design and researching of biologically active polymeric hydrogel transdermal materials modified by humic acid

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Abstract. Biologically active polymer hydrogel transdermal materials based on gelatin, sodium alginate, modified by humic acids, were designed and researched. Literature review was carried out and it was proved that humic acids using is perspective for the functional effect on the biologically active polymer hydrogel transdermal properties. It has been found that effective processes for receiving biologically active polymer hydrogel transdermal materials based on gelatin, hydroxypropyl cellulose and sodium alginate can be carried out in different humic acids concentration while achieving an effective increase in hydrogel polymers structuring processes. It can be seen efficiently increasing biologically active polymeric hydrogel transdermal materials based on gelatin and sodium alginate conditional viscosity and the specific electrical conductivity with an increase of humic acids content: from 114 to 135 sec and from 2350 to 2850 mkS/cm, respectively. Humic acids modification in biologically active polymeric hydrogel transdermal materials based on gelatin and sodium alginate caused structure formation with high density, and resistance and with larger agglomerates in hydrogels. It was found that the gelatin-based biopolymer hydrogels modification by humic acids makes it possible to receive biologically active polymeric hydrogel transdermal materials with higher swelling degree. It is shown that the application of new biologically active polymeric hydrogel transdermal materials based on gelatin and sodium alginate modified by humic acids allows improving the skin moisture-lipid balance. From the initial values of 34-36% moisture and 8-10 skin fat, they increase to 58-66% and 52-60%. So, designed polymer hydrogel based on gelatin, sodium alginate, modified by humic acids, are transdermal materials with good properties.

1. Introduction

The modern sustainable development trend in area of biologically active polymers and materials based on them is the technology that allows creating effective systems for drugs and active substances transdermal delivery into the human body [1].

Transdermal delivery systems based on biologically active polymer materials cause increased interest in the drugs introduction through the skin, for local therapeutic action on the affected skin during systemic local drugs delivery. They are also widely used as biologically active materials in the form of various polymer hydrogels [2]. Hydrogels are three-dimensional polymer networks held together by cross-linked covalent bonds and weak cohesive forces in hydrogen or

ionic bonds form. This hydrophilic polymeric materials shows an inherent ability to swell in water and some other solvents and is able to absorb and retain more than 10 percents of its weight in water in a gel structure. Hydrogels together with other chemical compounds can form a biologically active composition that can find several local applications on the body and hair surface [3]. Bioadhesive hydrogels using for skin care has important advantages, such as a longer residence time at the application site and a lower product introduction frequency.

Until now, several biologically active hydrogels compositions containing biologically active ingredients have been produced. The selected hydrogels are bioadhesive hydrogel compositions for skin application. Used in biologically active preparations hydrogels can be based on numerous biopolymers, such as collagen, gelatin, hyaluronic acid, alginate, chitosan, xanthan gum, pectin, starch, cellulose and its derivatives.

Based on biopolymers hydrogels are used to design new biologically active agents, such as so-called "beauty masks". It is claimed that these masks moisturize the skin, restore its elasticity and promote rejuvenation. Superabsorbent hydrogels, particularly acrylate-based materials, are widely used in personal hygiene products to absorb liquids because of their ability to lock moisture away from the skin, promoting skin health, preventing diaper rash and providing comfort.

Today, several types of materials are used to design effective biologically active hydrogels. Both synthetic and bio polymers are widely used. Natural biopolymers fully implement the principle of sustainable development and demonstrate higher biocompatibility and activity compared to synthetic polymers [4].

The transdermal delivery mechanism in such biologically active polymeric hydrogel is that active substances in the hydrogel is delivering to the skin by diffusion. The most effective modern biologically active polymeric hydrogel make of hydroxypropylmethylcellulose [5], hyaluronic acid [6], carboxymethyl cellulose [7], polyvinylpyrrolidone [8] and polylactic glycolic acid [9] and other polymers [10]. For high stability and strength while thermal contact with human skin [11], biologically active polymeric hydrogel actively use their functional modification [12] with various inorganic [13]and organic substances [14]. In our previous works, it was determined that humic substances have a functional effect on the hydrogel biopolymer materials based on gelatin and hydroxypropyl cellulose properties [15]. Especially for increasing structuring processes and strength characteristics [16]. Therefore, it is interesting to study the possibilities of effective modification of biologically active polymer hydrogel materials based on gelatin and sodium alginate with humic substances for receiving systems for active substances delivery systems into the human body.

The *aim* of the article is designing and researching of biologically active polymeric hydrogel transdermal materials modification by humic acid.

2. Materials and methods

The study's objects for biologically active polymeric transdermal hydrogel designing were:

- food gelatin brand R-11 (Ukraine);
- sodium alginate (China);
- humic acid, were received by extraction from lignite.

The research conditions are the procedure and determination toluene extract output and free humic acids.

First, a gelatin solution (7 % wt.), a defined amount of polymer was placed in 50 mL of distilled water (preheated at 90 ± 2 °C) and stirred to obtain a clear solution. For the co-mixture of gelatin and sodium alginate, a defined amount of sodium alginate (2.5 % wt.) was added in the previously prepared gelatin (7 % wt.) solution and allowed to mix homogeneously

on a magnetic stirrer (Jisico Co. Ltd., South Korea). After that, by mixing, solutions with humic acids were obtained, in which the concentration of the latter was 2.5, 5 and 7.5 % wt.

Conductometric studies of biologically active polymeric hydrogel solutions were carried out on a combined TDS-meter HM digital COM-100 (USA), scale range: specific conductivity: from 0 to 9990 mkS/cm; temperatures: from 0 to 55 °C; Error: ± 2%.

Microscopic studies of biologically active polymeric hydrogel were carried out using the electron microscope Digital Microscope HDcolor CMOS Sensor (China).

The viscosity of biologically active polymeric hydrogel was determined according to ISO 2431. The method is based on determining the viscosity of a solution of biologically active polymeric hydrogel solution with free flow is taken as the time of continuous flow in seconds test material (50 cm^3) through a calibrated nozzle with 4 mm diameter of a viscometer (VZ-246) at a certain temperature.

The swelling degree of biologically active polymeric hydrogel transdermal materials was calculated according to formula (2) [15]:

$$Q = 100 \cdot \frac{m_1 - m}{m}, \tag{1}$$

where m_1 is the mass of the swollen sample, g.; m is the mass of the sample before standing in an aqueous solution, g.

To determine the moisture-lipid skin balance a professional skin moisture and oiliness analyser SK-92 (China) was used. This device operates on the basis of the Bioelectric Impedance Analysis (BIA) method – measuring the skin resistance tissues under the electric current. The moisture-lipid balance was measured in the area around the eyes before and after applying biologically active polymeric hydrogel transdermal materials for 15 minutes in five 23-year-old women (figure 1).

The skin moisture and oiliness range is from 0 to 99.9%, accuracy: 0.1%.

3. Results

The biologically active polymeric hydrogel transdermal materials based on gelatin and sodium alginate conditional viscosity and conductivity dependence from on the different humic acid content is shown in figure 2.

Next studies were carried out to determine the humic acids modification effect on the most important operational properties of biologically active polymeric hydrogel transdermal materials based on gelatin and sodium alginate: swelling degree and effect on the skin moisture-lipid balance. Table 1 shows the operational properties of biologically active polymeric hydrogel transdermal materials based on gelatin and sodium alginate modified by humic acids.

Table 1. Operational properties of biologically active polymeric hydrogel transdermal materials based on gelatin and sodium alginate modified by humic acids.

Humic acid content (%wt.)	Swelling degree (%wt.)	Moisture/lipid, %
Pure gelatin-sodium alginate composition	19.82	58-60/52-54
2.5	27.17	60-62/55-56
5	26.83	62-64/56-58
7.5	23.21	64-66/58-60

Figure 1. Model (women) with biologically active polymeric hydrogel transdermal materials in the area around the eyes.

4. Discussion

In hydrogel materials for transdermal delivery it is very important to ensure prolonged bioavailability of target biologically active substances through the skin barrier while high adhesion to the skin, stability of their geometric dimensions and shape preservation in temperature conditions throughout the entire period of exposure to human skin. Such properties of hydrogel materials for transdermal delivery can be achieved by researching hydrogels viscosity, electrical conductivity and structural formation optimized level. For example, in [17] it was shown that by increasing the viscosity and structuring of polyacrylamide-polydopamine hydrogels with mesoporous silica nanoparticles, hydrogel patches with high adhesiveness for transdermal drug delivery were obtained. Therefore, the initial studies consisted in determining the conditional viscosity and electrical conductivity dependence of bioactive humic-polymer hydrogel transdermal materials based on gelatin and sodium alginate, as well as based on hydroxypropyl methylcellulose and sodium alginate, on the different humic acids content in them. According to [18], the electrical conductivity of bioactive humic polymer hydrogel transdermal materials, which is related to the content of ionogenic substances, can actually be used as hydration level measure using a high-density and rigid network in water-soluble polymer hydrogel materials. Therefore, it is important to study non-cytotoxic alginate–gelatin hydrogels modified with humic acids as biomaterials with good mechanical strength and biocompatibility, which are advisable to use in transdermal patches, microcapsules for bioactive compounds, cells and preparations, as well as in regenerative medicine (for example, for bone tissue regeneration) or as a soft tissue patch for wound healing. From the data in the figure 2 it can be seen increasing biologically active polymeric hydrogel transdermal materials based on gelatin and sodium alginate conditional viscosity and the specific electrical conductivity with humic acids content increase: from 114 to 135 sec and from 2350 to 2850 mkS/cm, respectively. Such changes

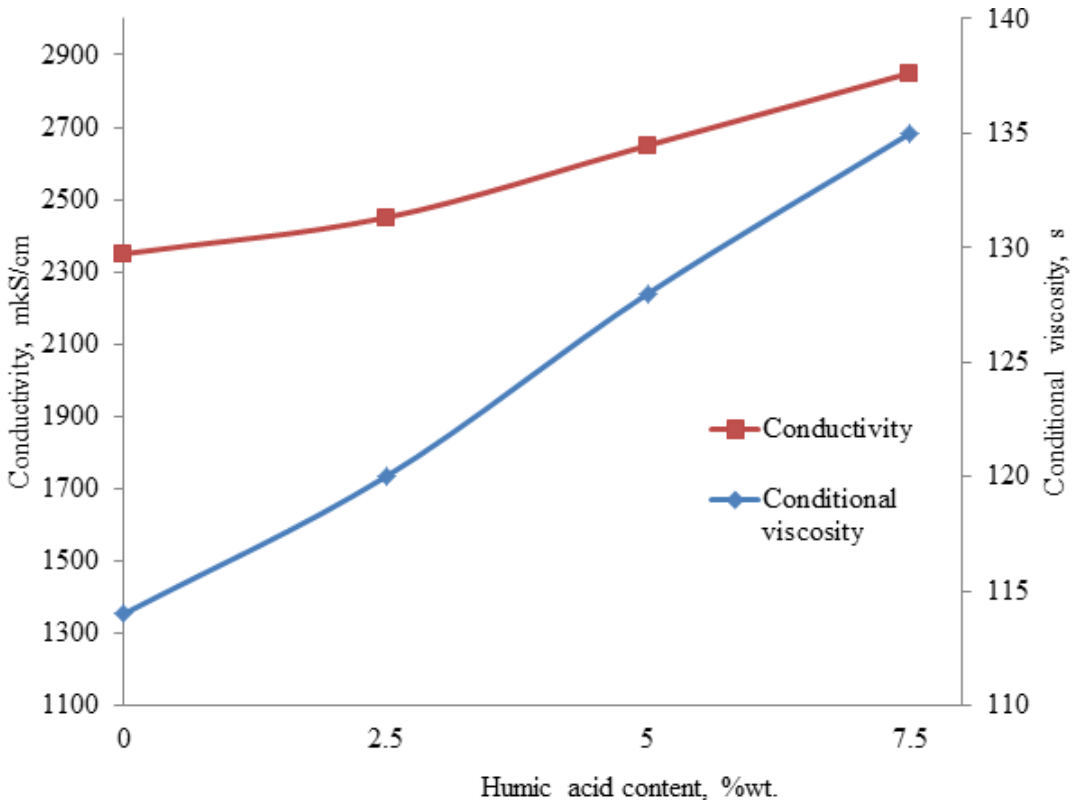

Figure 2. The conditional viscosity and conductivity dependencies of biologically active polymeric hydrogel transdermal materials based on gelatin and sodium alginate with different humic acid content.

indicate the following features humic acids modification of the structure formation processes in biologically active polymeric hydrogel transdermal materials based on gelatin and sodium alginate: more density [19] and rigid network of biologically active polymeric hydrogel [20]. Also the larger number agglomerates formation [21] in biologically active polymeric hydrogel [22] (figure 3).

Table 1 shows that the modification of gelatin-based biopolymer hydrogels by humic acids makes it possible to obtain biologically active polymeric hydrogel transdermal materials with an increased swelling degree. The larger number agglomerates formation in biologically active polymeric hydrogel transdermal materials based on gelatin and sodium alginate on the different humic acid content is clearly visible from the microscopic studies results. It should be noted that the hydrogel delamination in biologically active polymeric hydrogel transdermal materials based on gelatin and sodium alginate on the different humic acid content into the aqueous phase and the structured polymer phase does not occur. Increasing the degree of swelling when modified with humic acids due to more rigid network hydrogels formation makes it possible to achieve long-term prolonged transdermal release of drugs, stability of their geometric dimensions and shape in temperature conditions throughout the entire period of exposure to human skin, and easier separation from the skin after application. So, it is important to note that the using new biologically active polymeric hydrogel transdermal materials based on gelatin and sodium alginate modified by humic acids allows to improve the skin moisture-lipid balance. So, from the initial values of 34-36% moisture and 8-10 skin fat, they increase to 58-66% and 52-60%. As it can be seen in table 1, the improvement in skin moisture-lipid balance became more with an increase in humic substances content. Actually, modification with humic acids makes it possible

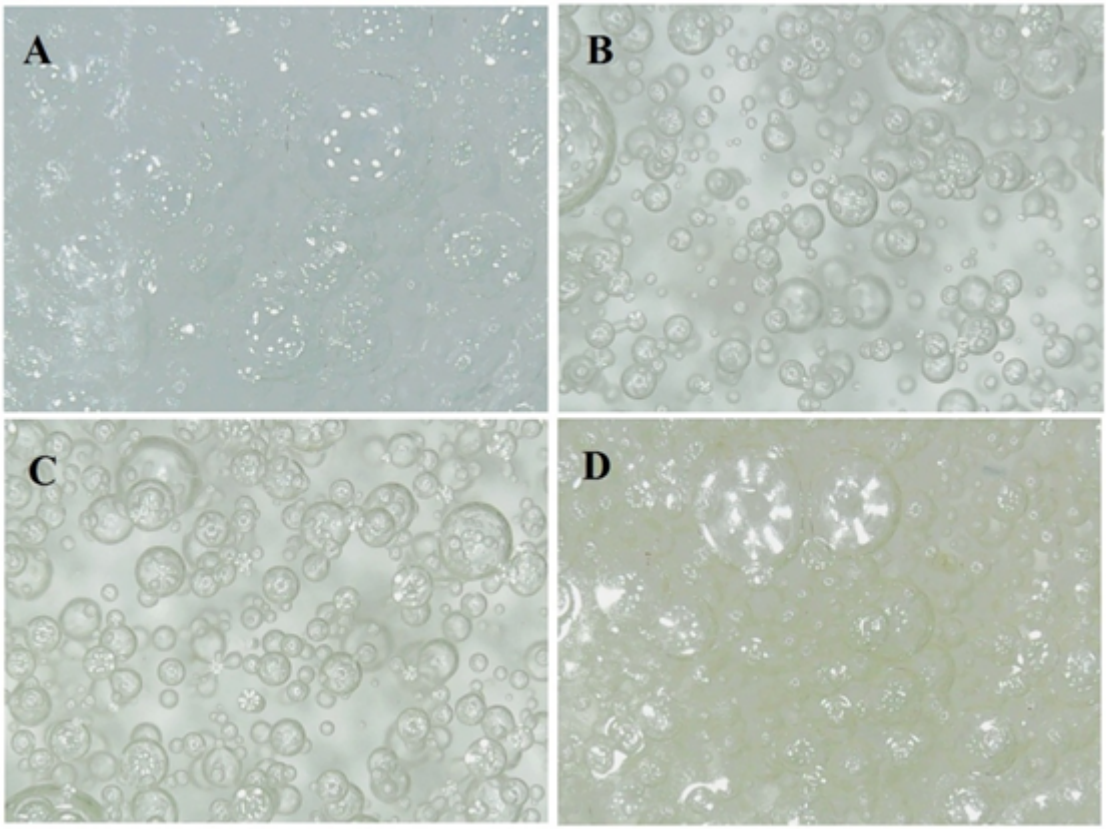

Figure 3. Microscopic studies of of biologically active polymeric hydrogel transdermal materials based on gelatin and sodium alginate on the different content of humic acid: A – pure gelatin and sodium alginate hydrogel; B – gelatin and sodium alginate hydrogel + 2.5 % wt. of humic acid; C – gelatin and sodium alginate hydrogel + 5 % wt. of humic acid; D – gelatin and sodium alginate hydrogel +7. % wt. of humic acid.

to obtain hydrogel transdermal materials, which, when applied to the human body, will allow to regulate skin moisture-lipid balance uniformly and for a long time.

In fact, thanks to the biologically active polymeric hydrogel transdermal materials based on gelatin and sodium alginate modified by humic acids using, it becomes possible to transfer the skin from slightly moist-fatty hard to highly moist-fatty elastic condition. The moisture-lipid balance skin improving increases with increasing the humic substances content.

5. Conclusions

The effective biologically active polymeric hydrogel transdermal materials based on gelatin and sodium alginate, modified by different humic acid content, were received and researched. By carrying out rheological, conductometric and microscopic studies, it was found that the modification of gelatin-sodium alginate systems by humic acids allows receive polymer hydrogels with high structuring degree. Modification of gelatin-based biopolymer hydrogels by humic acids makes it possible to obtain biologically active polymeric hydrogel transdermal materials with an increased swelling degree and ability to improve the skin moisture-lipid balance: from the initial moisture 34-36% and fatness 8-10%, they increase to 58-66% and 52-60%. In future researching is perspective to determine transdermal level of designed biologically active polymer hydrogels for most important medicine and cosmetic biologically active substances.

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