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THE EVALUATION OF NOVEL WOUND DRESSINGS BASED ON HYDROGELS

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Abstract: *Wound dressings gained a significant importance in the development of ideal solutions regarding wound healing therapy. The necessity of novel wound dressings in the clinical flied increased over the years due to the constant occurrence of burns or anti-inflammatory lesions. Skin injuries can compromise the integrity and protective function of the cutaneous tissue, resulting in infections. In this regard, numerous studies have been performed to improve the healing process without scarring, by developing suitable wound dressings based on hydrogels. Hydrogel dressings are an essential component in different categories of wound care strategies. The aim of this study was to develop an ideal hydrogel dressing based on carboxymethyl cellulose/pectin/gelatin in order to provide an ideal environment for both cleaning and protecting the wound, but also to offer a suitable permeability to the wound bed. The addition of Common Comfrey (Symphytum officinale) extract and Aloe Vera oil has been accomplished to enhance the healing capacity of the developed wound dressings. Further, woven fabric made of 100% cotton fibers was treated with the synthesized hydrogels through padding method using different concentrations of glycerin (10-20%). The resulted hydrogels were characterized from their morphological and rheological point of view to evaluate their stability and integrity. The treated fabrics were investigated to confirm the successful deposition on the textile material and comfort of the resulted specimens.*

Key words: *hydrogel, textile material, dressing, swelling degree, permeability.*

1. INTRODUCTION

Skin provides a natural barrier against the environment and employs several essential protective functions. When the skin integrity is compromised, the native protective mechanism is disturbed [1]. Wound healing is a dynamic physiological process that consists of four main phases: hemostasis, inflammation, proliferation, and remodeling phase [2]. An ideal skin wound dressing must accomplish the following requirements: provide a physical barrier to prevent further contaminations and injuries, absorb generated metabolites and enhances wound healing capacity by maintaining a moist environment, removes free radicals and improves the antioxidant properties [3].

Hydrogels represent the most suitable choice as wound dressings for their outstanding properties (biocompatibility, high water retention ability and flexibility). Carboxymethyl cellulose (CMC) is one of the most applied polymers for the development of hydrogels due to their abundance, low cost, transparency and film forming ability. Regardless of its beneficial properties, the relatively decreased cell adhesion, inferior antibacterial activity and low water stability of CMC hydrogels limited their applicability as a wound dressing. To overcome the drawbacks, the combination of CMC with other polymeric materials has been preferred to obtain an ideal wound dressing [4]. Gelatin is an efficient biomaterial for wound dressings, which can absorb wound exudates, provide moist environment that accelerates wound healing and instantaneous hemostasis [5]. Pectin has been widely used in combination with other polymers due to its biocompatibility, strong film forming properties and biodegradability. The high hydrophilicity of these polymers does not maintain their integrity upon exposure to physiologic conditions and therefore, the polymers must be subjected to chemical crosslinking for the improvement of their stability [6].

Furthermore, to enhance the antimicrobial and healing capacity, a combination of bioactive molecules can be incorporated in the developed systems. One of these bioactive molecules is represented by Common Comfrey (*Symphytum officinale*) extract, known for its increased cell proliferation, astringent and anti-inflammatory activity [7]. Another important bioactive substance is Aloe Vera oil, also known for its biological activities (hemostatic, antibacterial and anti-inflammatory), providing an effective solution for the treatment of anti-inflammatory lesions and burns [8]. The main purpose of this study was the development and evaluation of carboxymethyl cellulose/pectin/gelatin hydrogels that incorporate two active substances. Additionally, the obtained hydrogels were further applied on 100% cotton woven fabrics through padding method the treated textile materials being then assessed from the morphological and comfort point of view.

2. MATERIALS AND METHODS

2.1 Materials

For hydrogels synthesis, sodium carboxymethyl cellulose (high viscosity), gelatin (bovine skin ~ 225g Bloom, type B), citrus peel pectin (galacturonic acid ≥74.0%) and glutaraldehyde (50 wt. % in H_2O) were purchased from Sigma Aldrich (Germany). The hydrogel crosslinking was performed using calcium chloride (≥ 93.0%) purchased from Honeywell, (Germany). Vegetable glycerin (99.5% purity) was obtained from SC Herbavit SRL (Romaina). Common Comfrey extract (PlantExtrakt, Romania) and Aloe Vera oil (Mayam, Romania) have been selected as active compounds. For subsequent measurements, the phosphate-buffered saline (PBS) solution (Merck, Germany) has been used.

2.2 Hydrogels Synthesis

The hydrogel films were obtained by preparing 1% (w/v) CMC, gelatin and pectin solutions, under magnetic stirring at 60 ° C. Next, the obtained solutions were cooled and mixed in different concentrations according to Table 1. After complete homogenization, 10-20% (v/v) glycerin was added in the obtained solutions. Furthermore, 1% Common Comfrey extract and 1% Aloe Vera oil were introduced in the obtained solution dropwise and maintained under magnetic stirring for 30 minutes. For crosslinking stage, 0.5% (v/v) glutaraldehyde was used. The developed hydrogels were poured into Petri dishes and kept in the oven for 24 hours at 40 °C. A secondary crosslinking of hydrogels was performed in a 5% (w/v) $CaCl_2$ crosslinking bath, for 24 hours. After crosslinking, the specimens were removed from the Petri dishes, washed and dried at room temperature for 24 hours.

Table 1. *The codification of hydrogels*

Probe	Pectin (%)	Gelatin (%)	CMC (%)	Glycerol (%)	Bioactive substances
F_0-10	1	1	1	10	-
F_0-20	1	1	1	20	-
F_0-10-SA	1	1	1	10	+
F_0-20-SA	1	1	1	20	+

2.3 Functionalization Treatments

For the functionalization treatments, the preparation of hydrogels was repeated. After the homogenization of glutaraldehyde, the hydrogels were cooled and applied on textile fabrics. Simultaneously, the textile materials were sectioned in 20x10 cm variants. Their application was achieved by padding of the selected textile materials with the polymeric solutions under the following conditions: 3 passes through the padder at 2.7 barr and further, the treated textile materials were then dried at 50 ° C for 5 minutes. The secondary crosslinking was performed by the padding the treated fabrics using a $CaCl_2$ crosslinking bath and dryed at 50 ° C for 5 minutes. The treated fabric textiles are presented in Table 2. Additionally, for the evaluation of resulted samples, untreated 100% cotton woven fabric was selected as control (M).

Table 2. *The codification of treated fabrics*

Probe	Pectin (%)	Gelatin (%)	CMC (%)	Glycerol (%)	Bioactive substances	Padding
F-10	1	1	1	10	-	+
F-20	1	1	1	20	-	+
F-10-SA	1	1	1	10	+	+
F-20-SA	1	1	1	20	+	+

2.4 Characterization Methods

2.4.1. Swelling Degree

In order to determine fluid uptake ability, the samples were cut into 2 cm x 2 cm and the initial weight (in dry state) was measured. Each sample was immersed in 25ml PBS (pH= 7.4) at 37°C inside an incubator. Further, samples were gently removed from PBS and the excess fluid was removed with filter paper. Swollen samples were weighted to determine the fluid uptake ability known (swelling degree) by using the following equation:

$$SD\ (\%) = ((W_s - W_d)/W_d) \cdot 100 \qquad \textbf{(1)}$$

Where W_s and W_d are the weights of swollen and dry samples respectively. The fluid uptake ability was evaluated for 2h with 15 min time interval.

2.4.2 Water Retention Capacity

For water retention assessment, each sample was immersed in deionized water. Further, the water excess was removed with filter paper and the weight of each probe is determined (W_0). The hydrogels were maintained at room temperature. After 24h, the specimens were taken out and weighted (W_t). This property is defined by the following equation:

$$WR\ (\%) = (W_t/W_0) \cdot 100 \qquad \textbf{(2)}$$

2.4.3 Scanning Electron Microscopy (SEM)

SEM analysis was used to investigate the deposition of hydrogels on the fabrics surface by using a FEI Quanta 200 Scanning Electron Microscope with a GSED detector and accelerating voltage of 12.5 Kv – 20 Kv.

2.4.4 Comfort Tests

The treated fabrics were characterized in terms of the main comfort parameters, respectively: water vapor permeability (STAS 9005: 1979) and permeability to air (SR EN ISO 9237: 1999).

3. RESULTS AND DISCUSSION

3.1 Swelling Degree

The swelling degree was determined in order to investigate the absorption capacity (Fig. 1) of the system regarding the released exudate in a predetermined period.

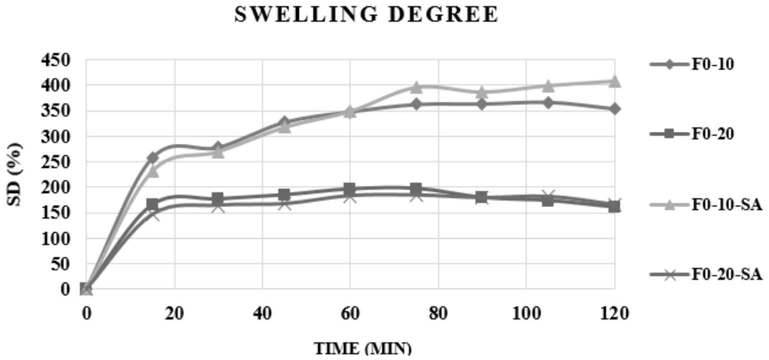

***Fig. 1**: The swelling behaviour of carboxymethyl cellulose/pectin/gelatin hydrogels*

The samples were analyzed in phosphate-buffered saline (PBS) solution, at pH=7.4, similar with the physiological medium. In Fig. 1 it was observed the influence of glycerin in different volume ratios, but also the effect on the encapsulated active substance on the obtained system. The hydrogels with 10% (v / v) glycerin exhibited an increased absorption capacity compared to the sampled with higher glycerin content, which achieved their maximum absorption within a short period of time. Moreover, the entrapment of both active substances does not negatively influenced the stability and integrity of the synthesized hydrogels. Additionally, these polymeric systems exhibited superior swelling degree, ranging between 100 - 400%, an ideal fluid uptake ability that recommends them for wound healing.

3.2 Water Retention Capacity

An ideal wound dressing requires specific properties, such as water retention capacity that is necessary to absorb and maintain the exudate in the polymeric system. This property was assessed by determining the retention capacity as shown in Fig. 2.

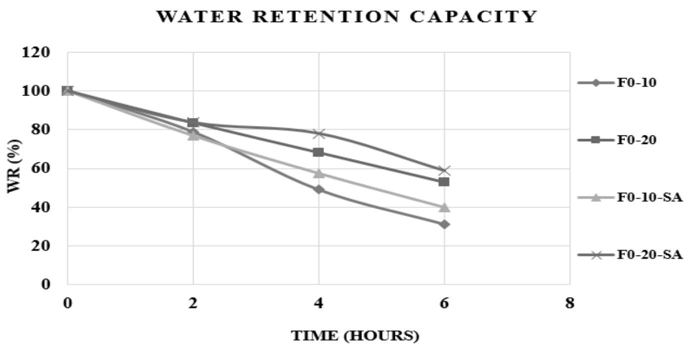

***Fig. 2**: The retention capacity of carboxymethyl cellulose/pectin/gelatin hydrogels*

The increased glycerol content allowed to maintain the absorbed fluid in the hydrogel structure for an increased period (up to 6 hours). Also, the addition of Common Comfrey extract and Aloe Vera oil in the hydrogels does not cause major modifications regarding the retention capacity.

3.3 Scanning Electron Microscopy (SEM)

The morphological evaluation of the obtained wound dressings was accomplished through scanning electron microscopy, as shown in Fig. 3.

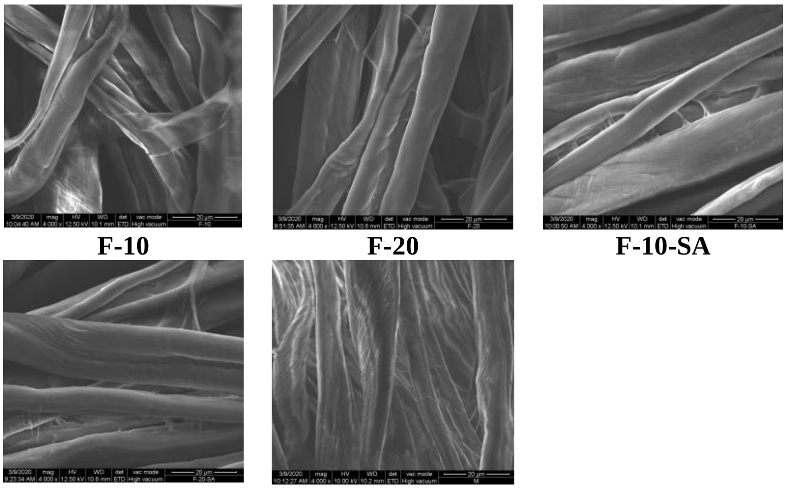

***Fig. 3**: SEM images of the obtained samples*

The SEM images have been recorded at 4000X magnification in order to highlight the successful deposition of hydrogels on the surface of 100% cotton woven fabrics. In all micrographs, the hydrogel film can be observed on the cotton fibers as a thin membrane. Moreover, the incorporation of Common Comfrey extract and Aloe Vera oil does not negatively influence the hydrogel deposition. The developed coatings are presented in a homogeneous slim membrane on the fibers surface suggesting a suitable compatibility between the carboxymethyl cellulose/pectin/gelatin film and cotton fibers.

3.4 Comfort Tests

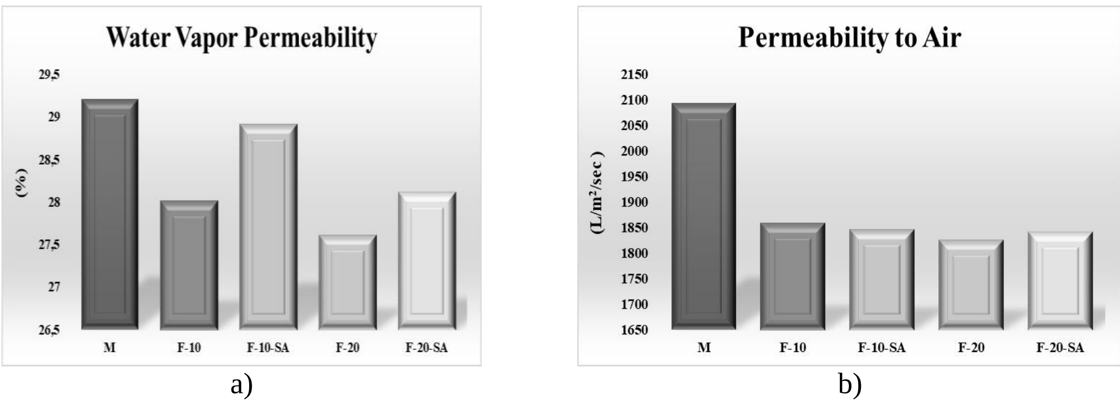

***Fig. 4**: Comfort indices of functionalized fabrics: a) water vapor permeability; b) permeability to air*

Air and water vapor permeability have recorded lower values after functionalization treatment due to the hydrogel deposition on the fabrics surface as a semi-permeable film (Fig. 4).

However, the obtained values are acceptable for the product's destination and does not influence the thermal comfort of end-user, providing proper ventilation for the removal of accumulated exudates.

5. CONCLUSIONS

The developed systems exhibited suitable fluid uptake and water retention capacities, representing a proper solution for wound dressing applications. Moreover, the addition of Aloe Vera oil and Common Comfrey extract has not influenced the main characteristics of hydrogels. Regarding the functionalization treatment, SEM images confirmed the successful deposition of hydrogels on the fabrics surface. Air and water vapor permeability of the treated textile materials decreases after the functionalization treatments, but the obtained values are acceptable for the product's destination. Further research on the potential of hydrogels application as wound dressings must be continued.

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