Evaluation of Film Forming Polymeric Solutions for Skin Wound Dressing

CRISTINA-DELIA NECHIFOR[1], CARMEN-BEATRICE ZELINSCHI[2], DANA-ORTANSA DOROHOI[3]*

[1] "Gheorghe Asachi" Technical University.of Iasi, Department of Physics, Machine Manufacturing and Industrial Management Faculty, 67 Dimitrie Mangeron Bvd, 700050, Iasi, Romania

[2]"Vasile Adamachi" College for Agriculture and Food Industry, 41 Mihail Sadoveanu Alley, Iasi, Romania.

[3] "Alexandru Ioan Cuza" University, Faculty of Physics, 11 Carol I Bvd., 700506, Iasi, Romania,

Film forming polymer solutions for skin wound dressing were developed and characterized. Film forming solutions were prepared by adding polyvinyl alcohol (PVA) and poly (hydroxy) urethane (PHU) in different proportions into a well tolerate volatile solvent. The formulations were in vitro evaluated according to five criteria. Two formulations have proved the ability to form polymeric film. Evaluation of the tensile strength, contact angle and swelling index were made for these formulations. The results showed a positive response of the formulations to be used for skin wound dressing.

Keywords: integrity on skin, swelling index, tensile strength, surface polarity

Films forming polymeric solutions are a new approach chosen for skin wound dressing [1]. These solutions consist in a mixture between a polymer and a well tolerate volatile solvent. When the solution is sprayed on the skin surface, it solidifies and forms a film which is able to protect the wound and to accelerate wound healing [2]. The loaded films applied on skin act as barrier to microorganisms and environmental factors [3].

The film forming solutions provide many advantages over traditional preparations (patches or semisolid) due to the manufacturing process which is fairly simple and due to the costs which can be low depending on the components that are used [4].

The film forming polymer solutions are required to have a low viscosity to be easily applied as spray. The spray will ensure an accurate and flexible dose which dry quickly on the skin. The formed film is required to be non-sticky to avoid adhesion to the clothes, invisible and have to resist long time on the skin in order to protect the wound and to accelerate wound healing [5].

The most applied polymers on skin belong to various classes, for example to cellulose derivatives, chitosan, carrageenan, polyacrylates, poly vinylalcohol, poly vinylpyrrolidone and silicones [6].

In the present study, polyvinyl alcohol (PVA) and poly (hydroxy) urethane (PHU) in different proportions were solved in a volatile solvent (ethanol) to obtain polymeric solutions. The films formed by spraying the solutions were characterized and analyzed taking into account five criteria: viscosity, drying time, cosmetic attractiveness, outward stickiness and integrity on skin. The main goal of this work was to evaluate the ability of formulations to form polymeric film according to these criteria. Another objective of this study was to evaluate the mechanical properties, surface polarity and swelling index of the formulations in order to achieve the best formulation to be used for skin wound dressing.

PVA is a mechanically stable polymer which can be easily manufactured [7, 8]. It has a preferred role in obtaining different biomedical materials due to its simple structure; biodegradability, biocompatibility, and water solubility. The viscosity of PVA water solutions varies with concentration and temperature [9]. PVA is used for biomedical applications, in drug delivery [10], tissue replacement [11] for improving and correction of human organs functionality, immunological kits [12] and for cancer therapy due to their high embolism effect [13]. Due to its transparency, ease of processing and low costs, PVA is an optical polymer widely used as material for various optical devices [14].

Polyurethanes are synthetic polymers which found many applications as biomaterials due to their excellent physical properties and good biocompatibility [15, 16]. Polyurethanes are often used in wound dressings because of their good barrier properties and oxygen permeability. New developments are likely to come from bio-erodible polyurethanes to be used as scaffolds for wound dressings and tissue ingrowths. PHU is an aliphatic polymer from the polyurethane class. These materials are resistant to corrosion and abrasion, they have pores which absorb the humidity of the body and are recommended in hospitals [17].

Blending PVA and PHU in different proportions, materials with specific physico-chemical properties have been obtained in order to use them for biomedical applications [18].

Experimental part

Poly (vinyl alcohol) (hydrolyzed 99%, with average Mw= 22 000) were obtained from Merck – Germany and PHU was obtained from "P. Poni" Institute of Macromolecular Chemistry Iasi. All the chemicals were used as received. 10 wt. % PVA solutions were prepared by dissolving PVA in 70°C distilled water with stirring for 6 h. PHU was synthesized through a well knowing method [19], and then solved in deionized water to obtain 10 wt. % of PHU solution. Six formulations were obtained using polymer content (PVA and PHU in different rations) with 10% water and 75% ethanol.

The film forming solutions were prepared by adding different concentration of PHU with PVA into ethanol (96%) as the volatile solvent. The solutions were blended and subjected to magnetic stirring for half an hour and subsequently centrifuged for another half an hour to remove air bubbles from the samples and ensure blend homogeneity. The formulations were stored in glass vials sealed tightly to prevent evaporation of alcohol.

* *email: ddorohoi@uaic.ro, 0749 641 954.*

Sample	PVA-PHU ratio		Polymer Content		Water Content		Ethanol Content	
	PVA content (%)	PHU content (%)	(grams)	(%)	(grams)	(%)	(grams)	(%)
S I	88	12	1,01	10,03	1.51	15	7,55	74,97
S II	84	16	2,03	10,09	3,00	14,92	15,04	74.99
S III	75	25	2,04	10,05	3,06	15,08	15,19	74,87
S IV	68	32	2,00	9,95	3,00	14,93	15,10	75,12
S V	50	50	1,97	9,84	3,00	14,98	15,05	75,18
S VI	30	70	2,07	10,29	3,01	14,96	15,04	74,75

Table 1
CONTENT OF THE COMPOUNDS IN % (w/w)

The viscosity of the solution was evaluated visually and rated as low (water-like), medium (glycerol-like) or high (syrup-like) [4].

The drying time the formulation was evaluated applying a volume of 10 μL/cm^2 solutions on the inner side of the forearm volunteer. The film was considered dried if no remains of liquid were visible when a glass slide was applied after 5 min. If remains of liquid were observed the test was repeated after 7 min.

The ratio PVA-PHU and compositions of the formulations are listed in table 1.

Pressing cotton wool on the dried film under low pressure the stickiness of the outer surface was tested. If a dense accumulation of fibbers on the film was observed the stickiness was rated high. A medium stickiness was considered for thin fibber layer on the film surface and a low stickiness when occasional or no adherence of fibbers was observed.

Transparent films with a good skin fixation have been considered as cosmetically attractiveness as they were almost invisible. Opaque films and films with a medium skin fixation were considered less attractive.

The integrity on skin of the formulation was tested by applying to the forearm of 10 volunteers as described for the assessment of the drying time. The dried film was worn overnight. After 24 h the tested area was examined with the help of a magnifying glass for completeness of the film, appearance of cracks or flaking.

A score system for the evaluation of the film forming polymeric solutions [4] for five characteristics: viscosity, drying time, stickiness of the outer surface, cosmetically attractiveness and integrity on the skin after 24 h is listed in table 2.

Three grades were assigned to each criterion. Where A is the best rating (meaning that film meets the required features) and B is the worst outcome. The formulations were considered positive when all five criteria were denoted by A.

The resulting solutions were stirred and deposited on glass substrates to evaporate the solvent at ambient temperature for 48 h.

The dried films were cut into samples with dumbbell form of 4 mm X 40 mm with the help of a scalpel. The mechanical properties of the films were determined with a tensile tester TIRA-TEST 2161 apparatus (Germany), at a crosshead speed of 16.8 mm/min.

The tensile strength (σ) and percent elongation at breaking (ε) were evaluated representing abrasion resistance and flexibility, respectively [4].

The tensile strength (σ) was calculated as:

$$\sigma = \frac{F_{max}}{A} \text{ (N/m}^2\text{)} \quad (1)$$

where:

F_{max} (N) is the maximum applied force) and A (m^2) is the cross-sectional area.

The values for percent elongation at breaking were calculated with the following equation:

$$\varepsilon = \frac{L_R}{L_0} \cdot 100 \text{ (\%)} \quad (2)$$

where:

L_R (m) is the extension of the sample in the moment of rupture and L_0 (m) is the original sample length.

Evaluation of the swelling index and contact angle time evolution were made for the formulations which showed a low viscosity, low drying time, and low stickiness being highly cosmetic attractively and maintained intact on the skin for 24 h.

The equilibrium values of the films contact angles were measured with a KSV CAM 101 (USA), using the sessile drop technique. The experiments involved the use of water as test liquid. The formed films were stored in room condition, and water contact angle was measured at different time (1 day, 30 days, and 90 days) to obtain information about the water vapor absorption. Different regions of the sample surface were selected to obtain a statistical result, taking into consideration the contact angle values of 10 measurements with an error of ±1°. Before recording the contact angle, the thermodynamic equilibrium was established by waiting a fixed time (10 seconds). This way, the effect of film dissolution on the measurements was considered equal for all samples.

Swelling index was evaluated to complete the information about water absorption. The test aimed to give information on how a wound dressing can also be influenced by the excessive sweating of the human body.

The dried films were cut into samples of 3 X 3cm^2. Measurements were run in triplicate by immersing films in distilled water, at room temperature. At different time intervals (60 s), the samples were removed, wiped gently

Rating score	A	B	C
Viscosity	Low	Medium	High
Drying time	<5 min	5-7 min	>7 min
Outward stickiness	Low	Medium	High
Cosmetically attractiveness	High	Medium	Low
Integrity on skin (after 24 h)	Complete film, no cracks, no flaking	Complete film, no cracks, no flaking	Film partly or completely missing

Table 2
SCORE SYSTEM FOR THE EVALUATION OF THE FILM FORMING POLYMERIC SOLUTIONS

Sample /Score	Viscosity	Drying time	Outward stickiness	Cosmetically attractiveness	Integrity on skin (after 24 h)
S I	C	A	B	C	C
S II	C	A	B	C	C
S III	C	A	C	C	C
S IV	B	A	C	C	B
S V	A	A	A	A	A
S VI	A	A	A	A	A

Table 3
THE SCORE OBTAINED FOR THE EVALUATION OF THE FILM FORMING POLYMERIC SOLUTIONS

with a tissue to expel surface water, and weighed. The swelling index (SI) was calculated according to equation (3):

$$SI = \left(\frac{M_t - M_0}{M_0} \right) x100 \quad (3)$$

where:

M_o is the initial weight of the films and M_t is the weight of the films at time *t*.

Results and discussions

The grade achieved according to the score system for the obtained films from formulations are listed in table 3.

Formulations with one or more criteria rated B were considered acceptable with limitations, formulations with one or more criteria rated C were not accepted.

The formulations containing a low percent of PHU (S I, S II and S III) are characterized by high viscosity. The optimal solutions are S V and S VI because have a low viscosity and can be easily applied as spray. The sample S IV can be considered acceptable for this criterion.

All the studied formulations exhibit a drying time less than 5 min.

A dense accumulation of cotton fibbers on the film was observed for the formulations SIII and S IV. A medium stickiness was observed for the samples containing low percent of PHU (S I and SII) and a low stickiness characterized with occasional or no adherence of fibbers was observed for S V and S VI formulations.

The cosmetically attractiveness of the films reveal that formulations with high content of PHU (S V and S VI) are accepted. The other films showed a strong skin fixation causing heavy wrinkling of the skin.

An erythematic response of the skin after 1 h of administration, for 9 of the volunteers was observed for the formulation with low content of PHU (all except S V and S VI). Erythema disappeared after approximately 1 hour and no other type of skin irritations were observed.

All the formulations with negative results for skin irritation test were excluded.

According to the score system for the evaluation of the film forming polymeric solutions (table 2) the formulations with 50% PHU (S V) and 70% PHU (S VI) have the essential properties to be used for skin wound dressing.

Materials for skin wound dressing need certain tensile strength, sustainability, flexibility, bending, and elastic properties [4]. The wound dressing must be removed easily without damaging the new formed epithelial tissues. Evaluations of the mechanical properties are very important to establish an equitable balance between flexibility and hardness.

In table 4 are listed the values of tensile strength and percent elongation at break for the tested films

The formulation containing 50% PHU (S V) is hard and tough [20] ensuring the greatest properties appropriate for the intended application. These films are enough flexible to follow the movements of the skin without breaking. In the same time the samples showed an increased tensile strength which can prevent abrasion of the film [4]. The sample S VI (70% PHU) ensure an inferior tensile strength

Table 4
TENSILE STRENGTH AND PERCENT ELONGATION AT BREAKING FOR THE TESTED FILMS

SAMPLE	Tensile strength (N/mm^2)	Elongation at breaking (%)
S I	67.2	107.7
S II	68.4	103.9
S III	77.4	103.7
S IV	65.4	103.9
S V	48.0	105.2
S VI	16.1	140.4

compared with sample S V but it is acceptable as wound dressing material.

Evaluation of the contact angle and swelling index was made for the formulations S V (50% PHU) and S VI (70% PHU). These samples meet the optimal conditions to form polymeric film according to the selected criteria.

Wettability is a very important parameter for the studies on the rate of fluid absorption of a wound dressing material especially for exudates wounds.

The equilibrium water contact angle of the pure PVA is 74 degree and increased when PHU was added at 91 degree for the sample containing 50% PHU and at 94 degree the sample containing 70% PHU. This fact was explained by the presence of the complex branch of PHU which contains polar structures: -CONH- and –NH-COO- able to form hydrogen bonds with water molecules [18].

Evolution of water contact angles as function of stored time (1 day, 30 days, 60 days and 90 days) in normal atmospheric condition is displayed in figure 1.

From figure 1 it can be observed that the water contact angles decrease for all the samples after exposure to the room humidity and temperature. The decrease of the contact angle values indicates an increase in hydrophilicity of the samples.

These effects are also reflected in the surface free energy of hydration, ΔG_w . The ΔG_w values (fig.2) were obtained from equation (4) [21] by using the total surface tension of water as 72.8 mN/m [22] and the contact angle of water for the studied films.

$$\Delta G_w = -\gamma_l \cdot (1 + \cos\theta_w) \quad (4)$$

when:

ΔG_w < -113mJ/m, the studied material can be considered hydrophilic, while, when ΔG_w > - 113mJ/m, it should be considered hydrophobic [21]. The results from

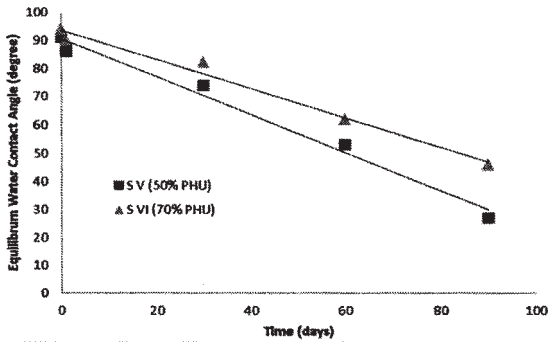

Fig. 1. Evolution of water contact angles versus stored time in normal atmospheric condition

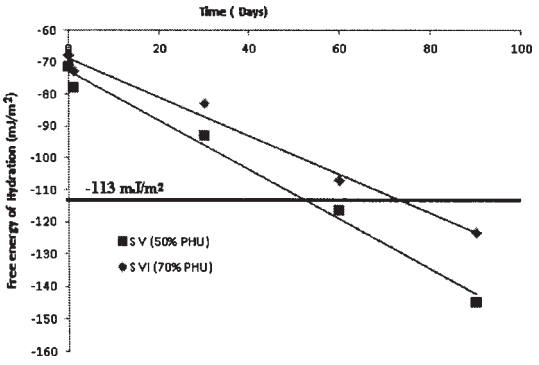

Fig. 2
Evolution of free energy of hydration versus stored time in normal atmospheric condition

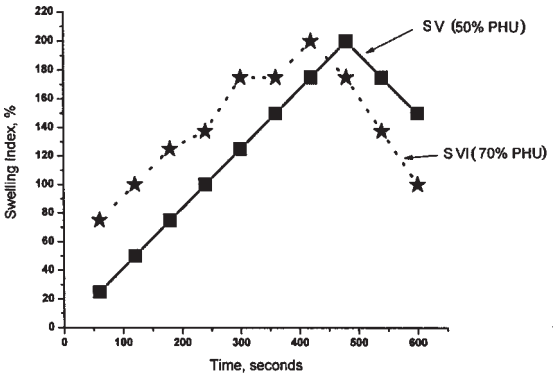

Fig. 3
The swelling index of the sample containing 50% and 70% of PHU, in distilled water, at room temperature as a function of time

the surface free energy reveal that the studied samples possess an increased wettability, which is improved as the stored time is higher. According to figure 2 after 60 days of stored under normal atmospheric condition the values of ΔG_w were almost reaching the limit between hydrophilicity and hydrophobicity. Also, as the storage duration was increased the difference between the surface free energy of hydration values of the samples was smaller.

The swelling profiles of the samples in distilled water at room temperature are shown in figure 3.

The swelling index is an important factor which can give information about the maximum amount of fluid absorption and fluid retention from the wound of a wound dressing material.

The maximum value of SI is 200 for these samples but is obvious that the sample S VI (70% PHU) has the tendency to hydrate more rapidly than the sample S V (50% PHU). The sample with 70% PHU hydrate more rapidly but a loss of material due to dissolution can be seen after 400 seconds. The loss of material can also be seen for the sample with 50% of PHU but after 500 s.

The fluid retention from a wound determines the performance of the wound dressing under very severe conditions. The weight increase of a material after fluid absorption and swelling during a defined time is taken as an indication of water-uptake and retention [4]. The studied samples revealed a rapidly hydration of polymer matrix. The hydration process is accelerated with the increase of PHU content, at the same temperature. The results show that the formulations with high content of PHU matrices can be used in wound dressing applications due their high tendency to absorb vapours of water and due to their high water-uptake.

Conclusions

In the present study, polyvinyl alcohol (PVA) and poly (hydroxy) urethane (PHU) in different proportions were solved in a volatile solvent (ethanol) to obtain polymeric solutions. The films formed by spraying the solutions were characterized and analyzed taking into account five criteria: viscosity, drying time, cosmetic attractiveness, outward stickiness and integrity on skin. The main goal of this work was to evaluate the ability of formulations to form polymeric film according to these criteria. Another objective of this study was to evaluate the mechanical properties, surface polarity and swelling index of the formulations in order to achieve the best formulation to be used for skin wound dressing.

The *in vivo* testing methods reveal that optimal solutions are S V and S VI because have a low viscosity and can be easily applied as spray, have a low stickiness characterized with occasional or no adherence of fibbers was observed. The entire studied formulations exhibit a drying time less than 5 minutes. The cosmetically attractiveness of the films reveal that formulations with high content of PHU are accepted. The other films showed a strong skin fixation causing heavy wrinkling of the skin. An erythematic response of the skin after 1 hour of administration, for the formulation with low content of PHU (all except S V and S VI). Erythema disappeared after approximately 1 hour and no other type of skin irritations were observed.

According to the score system for the evaluation of the film forming polymeric solutions the formulations with 50% PHU (S V) and 70% PHU (S VI) have the essential properties to be used for skin wound dressing.

The formulation containing 50% PHU (S V) is hard and tough ensuring the greatest mechanical properties appropriate for the intended application. The sample S VI (70% PHU) ensure an inferior tensile strength compared with sample S V but it is acceptable as wound dressing material.

The water contact angles decrease for all the samples after exposure to the room humidity and temperature. Wettability of the films increased with the storage time under atmospheric conditions. Also, as the storage duration was increased the difference between the surface free energy of hydration values of the samples was smaller.

The studied samples revealed a rapidly hydration, with high capacity of water-uptake, of polymer matrix and a good capacity to absorb water vapors.

This study evidenced that two of the formulations developed for film forming polymeric solutions are well tolerated by the skin suggesting that PVA/PHU materials might be successfully used as component in the development of skin delivery systems.

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