Journal of
Kerman University of Medical Sciences

https://jkmu.kmu.ac.ir
10.34172/jkmu.2023.04
Vol. 30, No. 1, 2023, 25-32

Original Article

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Preparation and Characterization of Black Pomegranate Peel Extract-Loaded Nanofibers Using Electrospinning

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Abstract

Background: Blended electrospun nanofibrous mats containing black pomegranate peel extract (BPPE) were prepared using different proportions of polyvinylpyrrolidone (PVP) and polycaprolactone as the filament-forming polymers.

Methods: The electrospinning process was conducted by simultaneously injecting PVP and polycaprolactone spinning solutions from two opposite sides on a rotary collector. The films were characterized in morphology, mechanical features, water vapor transmission rate, swelling properties, and drug release profile.

Results: The uniform white porous nanofibrous mats were achieved using the optimized method. As the concentration of PVP in the formula increased, the average diameter of the fibers increased, and fibers containing spindle bodies appeared. Though, the moisture content is one of the most essential issues with a wound dressing to promote the healing process, excessive water absorption by PVP produced highly erodible mats with weak tensile strength and elongation. The higher content of polycaprolactone created narrower and more uniform fibers and improved the mechanical features and water swelling properties of the blended mats. Furthermore, the nanofibrous membrane composed of a 70:30 polycaprolactone/PVP weight ratio resulted in a more sustained drug release.

Conclusion: The favorable properties mentioned above, along with the wound healing effect of BPPE, make it an attractive candidate for application in wound dressing products.

Keyword: Electrospinning, Nanofiber, PCL, Pomegranate peel extract, Wound dressing

Citation: Heydari A, Kouchak M, Raesi Vanani A, Kord Zanganeh A. Preparation and characterization of black pomegranate peel extract-loaded nanofibers using electrospinning. *Journal of Kerman University of Medical Sciences*. 2023;30(1):25-32. doi:10.34172/jkmu.2023.04

Received: April 15, 2022, **Accepted**: September 13, 2022, **ePublished**: February 21, 2023

Introduction

The recent increasing investigations on nanomaterials are due to their outstanding properties, including great relative surface area (lead to increased chemical reactions), inertness, stability, ease of functionalization and novel optical, electrical, and magnetic behaviors (1). Nanofibrous technology is a major innovation in nanomaterial science. Nanofibers, due to their properties such as ease of synthesis, few components, adjustable porosity, surface, and mechanical features, are distinct from other types of nanostructures (2). The primary method for the large- scale production of nanofibers is electrospinning. This technique is a significantly efficient, versatile, and fast method invented about 100 years ago. It is based on charging the viscoelastic fluids (polymers, ceramics, small molecules, and their combinations) by the DC electrode, which at a critical voltage creates a polymer jet that moves toward the collector, and after solvent evaporation, fabricates a nanofibrous polymer.

The advantages of this method include the production of controllable diameter, easy handling, minimal use of the solution, and its cost-effectiveness. Electrospun fibers can easily carry biological molecules and act as a drug delivery system. They can load a wide range of different drugs in an amorphous form. Electrospun mats have engrossed considerable attention for topical drug delivery. Utilization of them as delivery vehicles for wound treatment or other skin diseases could significantly reduce the systemic absorption of the drugs (3). For this reason, the use of nanofibers in the preparation of wound dressings is very promising.

Various polymer solutions such as polyvinylpyrrolidone (PVP) and poly-ε-caprolactone (PCL) are used alone or in combination in the electrospinning technique. PVP is a safe, hydrophilic, chemically inert, and spinning polymer commonly used in the biomedical field (4,5). The hydrophilic and hydrophobic functional groups of PVP are responsible for its solubility in water and some

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organic solvents, such as ethanol, methanol, chloroform or propanol (6). PVP has several benefits for wound dressing, including biocompatibility, good water vapor transfer, and impermeability to bacteria (4). A common problem with wound dressings is absorbing large amounts of water while not being resistant to erosion. This issue has been addressed by using composite membranes (7). The utilization of hydrophobic polymers in the structure of hydrogel (such as PVP) nanofibrous helps to increase the mechanical stability of the film and its resistance to dissolution and erosion in the presence of water.

PCL is a hydrophobic and aliphatic polyester that is nontoxic, adjustable, biodegradable, and compatible with several body tissues. The semicrystalline structure of PCL results in high toughness along with flexibility due to the rubbery state of the amorphous domains. It has a melting point above body temperature (59-64ºC). Degradation of most biodegradable polyesters is slower than natural biopolymers. Among them, PCL has the longest erosion. Its advantages, including tailorable degradation kinetic, high mechanical strength, elasticity, and ability to form electrospun nanofiber, make it valuable for research and use in the design of wound dressings that are made of composite nanofibers (8). The major limitation of PCL polymers is hydrophobicity, which can affect mechanical properties, cell adhesion efficiency, or biodegradability. However, this can be overcome by blending with more hydrophilic components or alkali treatment (9).

Jia et al prepared and characterized nanofiber membranes of PCL/PVP containing silver nanoparticles using the electrospinning method. They found that PVP at molar ratios above 15% presents good hydrophilicity in nanofiber membranes. They suggested that PCL/PVP/Ag nanofibrous membranes could be used to prepare wound dressing (10).

Pomegranate (*Punica granatum L.*), known as a primeval plant from the family of Punicaceae, originates from Iran and India. Iran was the largest producer (47%. of global production) and exporter of pomegranate in 2009 (11,12). Recent research on pomegranate peel has shown that it contains a large number of biologically active compounds such as phenolic compounds, including flavonoids (catechins, anthocyanins, and other complex flavonoids) and hydrolyzable tannins (pedunculagin, punicalin, punicalagin, gallic and ellagic acid) (13,14). The polyphenol content of pomegranate peel is higher than that of seed, leaf, pulp, and flower extract (15). Tannins and flavonoids have been shown to play an essential role in tissue repair and wound healing. In the healing procedure of treated wounds, an improvement in the epithelialization, contraction of the incised wounds, higher hydroxyproline contents, dry weight, and breaking strength of granulated tissues had been observed (14). The gels prepared from pomegranate peel extract (PPE) showed wound healing properties against an excision wound on the skin of Wistar rats. The group that had been treated with 5.0% PPE gel healed entirely after ten days, and hydroxyproline content at the wound area doubled (16). *In vitro* experiments on PPE had also been shown its antimutagenic, antibacterial, and antioxidant activities (17). Indices of organic acid, total phenolic, and antioxidant activity of pomegranate are affected by its cultivar (18).

Black pomegranate (*Punica granatum* var. black peel) is a cultivar of pomegranate with a high amount of tannins in the peel. Omidi Ghaleh Mohammadi and Mirghazanfari conducted a research study on exocarp and pulp of fourteen cultivars of Iranian pomegranates and showed that black pomegranate exocarp has the highest amount of tannin (19). Shams Ardekani et al demonstrated that peel extract of black peel pomegranate is among the three Iranian pomegranate cultivars with the highest amount of polyphenols and flavonoids (20). Therefore, designing an adequate wound dressing containing black pomegranate peel extract (BPPE) is an auspicious approach. However, it is necessary to cover the surface of the wounded skin with an appropriate membrane to prevent microbial infection and loss of skin moisture, which in turn would increase the wound healing process. Notably, the nanofibrous film is an appropriate option for wound dressing (21). Hence, in this study, we fabricated and characterized the PCL/PVP blend nanofibrous mats containing BPPE by electrospinning method to prepare wound dressing.

Materials and Methods

Reagents

Poly-ϵ-caprolactone (MW 80 000), polyvinylpyrrolidone (MW 58 000), Folin-Ciocalteu reagent, and gallic acid were all purchased from Sigma Aldrich (USA). Dichloromethane and dimethylformamide were ordered from Merck (Germany). All chemicals used in this experiment were of analytical grade and were commercially available.

Preparation of BPPE

Black pomegranate was procured from Shiraz, Iran, and authenticated by a Botanist from the Horticulture department, Shiraz University. Fruits were peeled manually, and peels were shade-dried, crushed, and powdered in a food grinder, and soaked in methanol at 30°C for 18 hours with a cover of parafilm and occasional shaking. The solution was filtered through a Whatman No.1 paper, and solvent was then removed under vacuum in a rotary evaporator until dry (15).

The electrospun nanofibrous samples with equal amounts of BPPE were prepared using different weight ratios of PCL to PVP (30:70, 50:50, and 70:30) (Table 1). PCL solution (10% w/v) was prepared using dichloromethane as solvent. Mechanical stirring was applied for 24 hours to obtain a homogeneous solution.

Table 1. Solid components of the nanofiber formulations

Formulation	PCL:PVP ratio (w/w)	PCL/ PVP:Extract ratio (w/w)	Solid components of dry film (%)		
			PCL	PVP	BPPE
F 1	30:70	100:25	24	56	20
F 2	50:50	100:25	40	40	20
F 3	70:30	100:25	56	24	20

PVP: Polyvinylpyrrolidone, PCL: poly-ϵ-caprolactone, BPPE: Black pomegranate peel extract.

Extract solution (10% w/v) was prepared by dissolving the extract in dimethylformamide. Different volumes of these two solutions were mixed to prepare spinning solution I and PVP solution (5% w/v) in ethanol 96% v/v was used as spinning solution II.

Electrospinning process

The process was performed with an electrospinning apparatus (Nano Azma, Iran). The different volume ratios of spinning solution I and II were inserted in two 10 mL separated syringes with 27-G metallic needles. Both solutions were simultaneously electrospun from two opposite sides on a rotary collector covered with aluminum foil. The process was optimized at voltages of 25 kV and feed rates of 1 mL/h. The nozzle distance to the collector was 16 cm. The electrospinning was conducted at 25°C and relative humidity of 40-50%. After fabrication, the nanofibrous membranes were further dried at 50°C and kept in airtight containers until use.

Morphology

The surface morphology of electrospun fibers was assessed by field emission scanning electron microscopy (FESEM, S4160, and Hitachi, Japan). The nanofiber samples were sputter-coated by a thin gold-palladium alloy layer under vacuum.

Evaluation of folding endurance

A strip (3×5 cm^2) was cut from each nanofibrous membrane and folded repeatedly in a fixed-line until it was broken or cracked. The folding endurance value of membranes was expressed as the number of times these films could be folded without breaking or cracking (22).

Mechanical properties

The thickness of five locations of each nanofibrous membrane was measured by a micrometer screw gauge (Shanghai Precision Instrument Co., Ltd., China) to calculate the mean value. Mechanical properties of the electrospun matrix were evaluated by using the Material Testing Machine (Wance, China), equipped with a 5-kN load cell. The sample strips (2×5 cm^2) were held between two clamps at a distance of 3 cm. The crosshead speed in tensile mode was set at 10 mm/min. The tensile strength (formula 1) and elongation at break (formula 2) for all different formulations were obtained from the below equations (23):

Formula 1: Tensile strength (N/mm^2) = Breaking force (N) ÷ Cross sectional area (mm^2)

Formula 2: Elongation at break (%) = $[L_2 \div L_1] \times 100$

L_2 = Increasing in length at breaking point (mm)

L_1 = Original length (mm)

Swelling degree

The wholly dried nanofibrous pieces (2×2 cm^2) were weighed and soaked in 20 mL of distilled water at room temperature for 3 hours. At regular intervals, the weight of swollen samples was determined after removing the excess water with a filter paper. The samples were dried in an oven at 60°C to reach constant weight. Percentages of swelling degree (Sw) (formula 3) and erosion (formula 4) were calculated using the below equations (3):

Formula 3: Swelling degree (%) = $[(W_2\text{-}W_1) \div W_1] \times 100$

Formula 4: Erosion (%) = $[(W_3\text{-}W_1) \div W_1] \times 100$

W_1 is the weight of the nanofibrous piece before soaking (initial weight), and W_2 refers to the maximum weight of the sample after soaking. W_3 is the weight of the samples after drying again and losing weight.

Water vapor transmission rate

Five grams of anhydrous calcium chloride was placed in a round bottle, and the opening was covered firmly by a nanofibrous membrane. The bottles were stored in an oven at 50°C in order to achieve constant weights and then moved to a desiccator containing a saturated solution of sodium chloride (75% RH) at room temperature. Weight changes of containers on the days 1, 2, 3, 4, and 5 were recorded. The diagram of weight gain against time (day) was plotted. The water vapor transmission rate (WVTR) (g/day.m^2) of each formulation was calculated by the below formula (formula 5), which divides the slope of the above plot by the effective area of nanofibrous pieces (m^2) (23).

Formula 5: WVTR = Slope (g/day) ÷ Effective area (m^2)

Assessment of content uniformity

From each mat, five samples with an area of 2×2 cm^2 were separated and after weighing, they were immersed in 10 mL of water and dichloromethane (1:1) mixture for 24 hours. Gallic acid was determined as the main compound of BPPE in the aqueous phase by Folin Ciocalteu colorimetric method (12). For this purpose, 20 µL of each sample was mixed with 20 µL of Folin-Ciocalteu reagent (10% v/v). After 5 minutes, 80 µL of sodium carbonate (7.5% w/w) was added. The mixture was left to react for 30 minutes in the dark at room temperature. The absorbance of the mixture was measured at a wavelength of 600 nm by an Elisa reader (Sunrise Tecan, Switzerland).

Measurement of pH

According to the research design, 10 ml of distilled water was used to immerse a 3 cm diameter piece of each

formula. After one hour, pH has been gauged by pH meter (lab, Mettler Toledo; Switzerland). All experiments have been done three times. The data have been expressed as the mean ± SD.

In vitro drug release

Franz-type diffusion cells (Dorsatech, Iran) with a receiver volume of 25 mL were used for *in vitro* drug release study. The fabricated formulations were mounted as a membrane in the upper part of cells directly contacting the receiver medium. Phosphate buffer (pH 7.4) at 37°C was used as receiver phase, and it was magnetically stirred at 300 rpm. At regular intervals, 20 µL of receiver phase was withdrawn and collected in 5 µL tubes (3). Gallic acid was detected by Folin-Ciocalteu colorimetric method (12).

Statistical analysis

All data are presented as mean ± SD from at least three independent experiments. One-way ANOVA was used to analyze the mean values statistically, and significance was set at $P<0.05$.

Results

Morphology

Three different weight ratios of PCL and PVP were used to fabricate nanofibrous films containing BPPE. As shown in Figure 1, uniform white mats were obtained using the optimized electrospinning method. Despite the red color of BPPE, entirely white films were achieved, indicating that the extract was completely encapsulated in the fibers. Figure 2 depicts SEM images of the BPPE-loaded electrospun nanofibrous membrane surface.

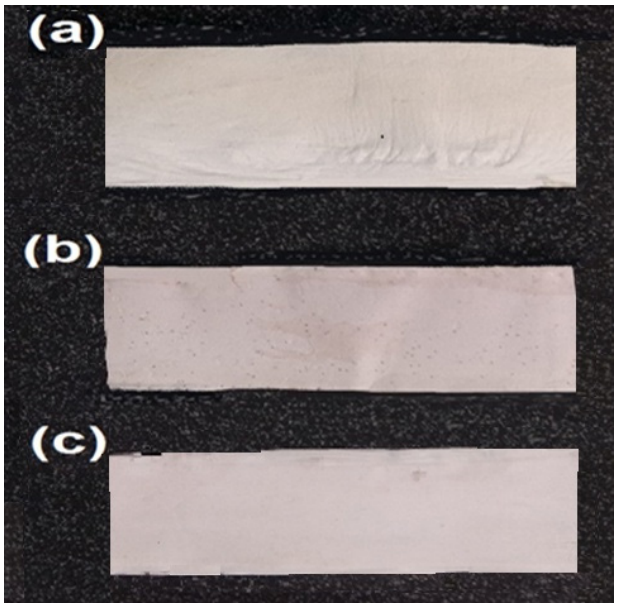

Figure 1. Black pomegranate peel extract-loaded electrospun nanofibrous mats with different PCL: PVP weight ratios: (a) F1 (30:70), (b) F2 (50:50) and (c) F3 (70:30)

Folding endurance

The endurance of the procured nanofibers was evaluated by the folding test, which is frequently used to estimate the ability of a film to withstand repeated bending and folding. Table 2 reports the results of the hand-folding of the nanofibrous films.

Mechanical properties

For evaluating the mechanical properties of nanofibers, thickness, tensile strength, and elongation at break of the films were tested under dry conditions. The data are given in Table 2.

Swelling degree and erosion

Figure 3 shows the profiles of the water uptake of the fabricated nanofibrous films. Moreover, Table 2 indicates the maximum swelling degree and erodibility of each formulation during 3 hours.

Water vapor transmission rate

WVTR is an indicator to show the ability of a dressing to control water loss (24). Table 2 summarizes the water vapor transmission rate through the formulations.

Content uniformity

The gallic acid contents of the different formulations are shown in Table 2. The results confirm the uniform distribution of the extract throughout the nanofibrous mats.

The pH of the nanofibrous films

It is widely accepted that normal skin has an acidic pH between 4.1-5.8, whereas the internal environment of the body retains a near-neutral pH (25). The solutions procured via the immersion of a 3 cm diameter circular section of the nanofibrous films F1, F2, and F3 in 10 mL deionized water possess pH-values 6.42, 5.96, and 6.05, respectively.

In vitro drug release

The release profiles of gallic acid from BPPE -loaded nanofibrous mats are shown in Figure 4. Throughout the first 15-60 minutes, all formulations caused a burst release that continued at a constant and slower rate.

Discussion

Morphology

SEM images of the BPPE-loaded electrospun nanofibrous membrane surface are shown in Figure 2. The microphotographs confirm the formation of nanofibers. No solvent is observed on the surface of the nanofibers, indicating its relatively complete evaporation during the electrospinning process. The fibers consisting of PVP are indistinguishable from those made of PCL, and their entanglement generates an interlinked porous structure.

Table 2. Mechanical properties, SW%, Erosion%, WVTR and content uniformity of different fabricated nanofibrous films (Mean ± SD, n = 5)

Formulations	Thickness (μm)	Tensile strength (MPa)	Elongation (%)	Folding endurance	SW (%)	Erosion (%)	WVTR (g/day.m²)	Content uniformity (%)
F1	536 (±11.4)	1.13 (±0.06)	25.44	n>250	103.70 (±6.22)	81.48 (±4.07)	358.38 (±15.09)	9.673 (±0.52)
F2	440 (±12.2)	1.46 (±0.07)	169.90	n>250	181.48 (±14.51)	66.67 (±5.33)	354.05 (±15.37)	7.475 (±0.29)
F3	306 (±16.7)	2.46 (±0.19)	129.15	n>250	118.52 (±5.92)	62.96 (±4.40)	358.38 (±19.07)	7.139 (±0.10)

F1: weight ratios of PCL to PVP (30:70), F2: weight ratios of PCL to PVP (50:50), F3: weight ratios of PCL to PVP (70:30).

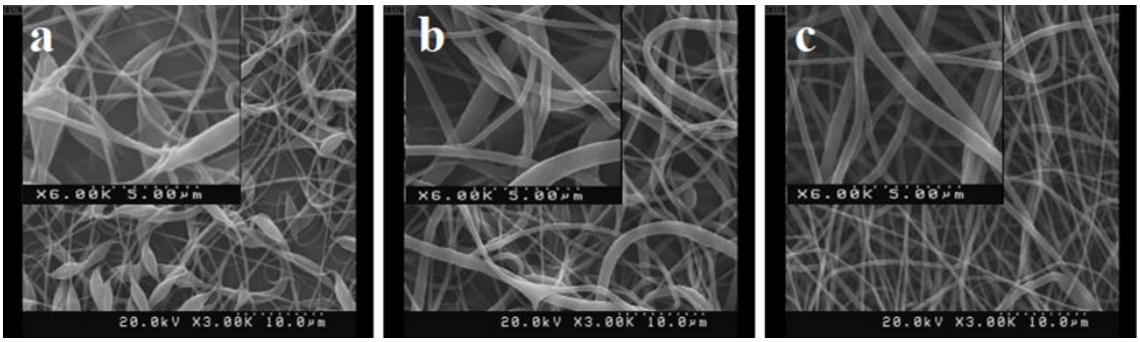

Figure 2. Representative SEM images of black pomegranate peel extract-loaded nanofibrous films with different PCL: PVP weight ratios: (a) F1 (30:70), (b) F2 (50:50) and (c) F3 (70:30)

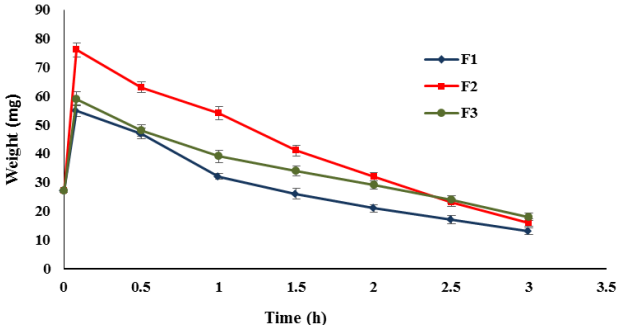

Figure 3. Water uptake profiles of three different nanofibrous mats (Mean ± SD, n = 3)

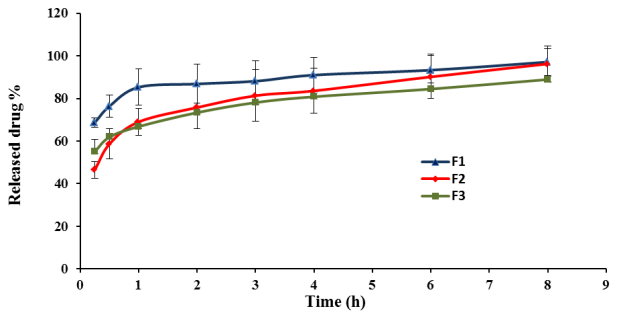

Figure 4. Release profiles of gallic acid from different nanofibrous mats (Mean ± SD, n = 3)

The SEM images of the formulations demonstrate that the diameters of F1, F2, and F3 fibers are 783.8, 535.2, and 309.8 nm, respectively. As the PVP content in the formulations increased, the nanofiber diameters enhanced, so that the F1 strings were relatively thicker than the others. Notably, morphology and diameter of the electrospun fibers would be dependent on some factors such as the spinning solution features (kind of polymer, conductivity, conformity of the polymer chain, molecular weight, concentration, viscosity, and polarity), the solvent surface tension, and electrospinning condition including applied field strength, the nozzle distance to the collector, and the feeding rate (5). It has been found that high-viscosity polymer solution would generally eject with excessive difficulties from the needle for forming nanofibers under an electrostatic force (26). The surface morphology of the F1 formulation revealed that the nanofibers were less uniform in size and surface area than the others. Moreover, spindle-like forms were observed among them (Figure 2a). This formulation had the lowest PCL: PVP ratio, at which high PVP levels could be the reason for the production of spindle bodies. It was reported that high voltage and the improper ratio of polymers might result in the spindle bodies (5). In the electrospinning process, it is necessary to apply high voltage so that the electrostatic force in the solution overcomes its surface tension. However, an excessive increase in voltage causes the jet to accelerate faster, resulting in a larger volume of solution coming out of the needle tip without a corresponding increase in its supply from the supporting source. Therefore, the Taylor cone may draw back into the needle, and the jet becomes unstable. This change causes the creation of the spindle or spherical beads. Studies have shown that as the voltage increases, the density of the beads also increases so that they can coalesce to form thicker fibers (27). The study conducted by Samprasit et al indicated that PVP alone cannot produce suitable nanofibers because PVP fibers are hygroscopic and wet strings to be deposited on the collector, rapidly fused, and subsequently agglomerated under room temperature (28). Employing another polymer such as PCL in a proper concentration along with PVP can help to

produce nanofibers with a uniform structure. However, formulas F2 and F3 share suitable characteristics such as cylindrical shape, random array, smooth surface, and size homogeneity without spindle bodies (Figures 2b, 2c). There was no visible particle apart from the fiber matrix, suggesting that the system could be termed as nano solid dispersions. This characteristic indicates that BPPE has been homogeneously encapsulated in the fiber matrix, and the system possesses a favorable biophysical environment for the drug to stably exist. In general, non-woven nanofibrous structures with the same architectural and morphological characteristics as the natural extra-cellular matrix in the skin, contribute to the cellular adhesion and rapid growth on the scaffold (29). The SEM pictures of PCL/PVP nanofibers show coalescence at the fibers junctions, which provide firm mats. As F3 offers the thinnest nanofibers, it makes greater contact surface available and stronger cohesion between the fibers (30). The nanofibers coalescence is one of the beneficial traits in the electrospun scaffolds that have been developed for tissue engineering due to their high tensile features (31).

Folding endurance

One of the useful features of a film for wound dressing is its strength and relative flexibility. As seen (Table 2), none of the membranes ruptured after folding 250 times on one line, and all formulations preserved their flexibility and retained their continuity.

Mechanical properties

According to the results (Table 2), the highest tensile strength (approximately 2.46 MPa) was detected for F3, which indicated its appropriateness for soft tissue engineering and wound dressing (23). On the contrary, F1 films showed minimum tensile strength and elongation values. The findings demonstrated that the tensile strength of nanofibrous films enhances with an increase in the PCL contents.

Swelling degree and erosion

According to the results (Figure 3 and Table 2), all films reached the maximum water uptake value (maximum swelling capacity) in the first 5 minutes and tended to lose weight due to the erosion phenomenon. Because of the simultaneous process of inflation and erosion, the swelling results were not accurate and comparable. It should be noted that the weight loss of each nanofiber after weight gain is due to the dissolution of PVP and the release of BPPE from the films. F1 formulation, which had the highest PVP content, suffered the most destruction during 3 hours. PVP is a hygroscopic polymer that readily absorbs a lot of water and dissolves in water and other polar solvents (31). The OXO groups of pyrrolidone rings in PVP are responsible for forming hydrogen bonds with water molecules. It has been found that the presence of PVP with PCL leads to the creation of the nanofibers, in which PVP helps absorb water and PCL prevents structural destruction (32). Such a situation improves hydrophilicity and even increases the swelling capacity. For this reason, the application of further amounts of PCL along with PVP in formulations F2 and F3 resulted in higher swelling degree values.

The ability of a film to preserve water is one of the most critical issues in skin tissue engineering, especially for wound healing (23). The researchers also found that cells were more compatible with hydrophilic surfaces than hydrophobic ones (33). Therefore, hydrophobic polymers such as PCL are surface-treated for improving their hydrophilicity (34).

Water vapor transmission rate

As moisture content is an essential factor of the wound dressing to promote the healing process, an ideal dressing should control the evaporation of water from the wound at an optimal rate (35). To prevent desiccation of the wound surface, the dressing should have a limited permeability. Alternatively, an unacceptable low WVTR dressing can lead to wound exudate accumulation (24). The WVTR for normal skin is 204 g/m^2 per day, whereas, for damaged skin, it may be in ranges between 279 g/m^2 per day for the first-degree burn to 5138 g/m^2 per day for a granulated wound (36). However, it is necessary to stop extreme dehydration of the exudates by controlling the water vapor permeability of the wound dressing. Researchers recommend that WVTR at the rate of 2500 g/m^2 per day which is in the average speed range for damaged skin, should exhibit adequate moisture levels without the risk of wound dehydration (37). According to these results (Table 2), no significant difference has been observed between the values of various nanofibrous films ($P>0.05$). Anyway, the range of the WVTR data for our fabricated nanofibrous mat was between 354 to 358 g/m^2 per day. The highly porous structure of the electrospun mats due to the entanglement of nanofibers is beneficial for the circulation of oxygen gas and water vapor. Besides, these pores provide space for storing wound-secreting water.

The pH of the nanofibrous films

The procured solutions of the nanofibrous films F1, F2 and F3 in 10 mL deionized water possess pH-values 6.42, 5.96, and 6.05, respectively. These results show that the electrospun mats in water provided partly acidic solutions that do not require pH adjustment. However, PCL and PVP are non-ionic polymers that do not affect the pH of the solution (31). So, it seems BPPE is responsible for acidic pH.

In-vitro drug release

The rapid dissolution of the drug in these systems can

be partially ascribed to the ability to incorporating of the drug in an amorphous state and solid solution form within nanofibers, the extraordinary high surface area of the fibers, and the interconnecting porous structure of the mat (Figure 4) (38). It is noteworthy that procedures providing fast solvent evaporation or fast supersaturation such as the electrospraying and electrospinning techniques result in forming amorphous solids with a rapid dissolution rate (39). According to the results, F1 experienced more significant levels of drug release in comparison with F2 ($P<0.001$) and F3 ($P<0.01$) at the first 15 minutes. This result confirmed the role of PVP in dissolving and releasing the BPPE from nanofibers. Due to its hydrophilic nature, PVP absorbs water and increasing the volume of solvent exposed to drugs raises the dissolution rate. On the other hand, because of the high solubility of PVP in water, it acts as a pore-forming agent in combination with a hydrophobic matrix to facilitate drug dissolution and release from the system (38,40).

Conclusion

In this study, BPPE as a wound healer could be successfully incorporated into a newly designed PVP/PCL electrospun porous nanofibrous membrane. The visual and microscopic assessment demonstrated that BPPE was homogenously distributed into the fibers in solid solution form. Three weight ratios of PCL: PVP were utilized to fabricate the composite films. All fabricated films were evaluated in terms of various properties, including morphology, folding endurance, mechanical properties, swelling degree, water vapor transmission rate, pH, and *in vitro* drug release. Based on the results, the formula F3 (PCL: PVP ratio 70:30) exhibited narrower nanofibers and more desirable elongation, tensile strength, water swelling, and drug release profile in comparison with the F1 and F2 films. Reduction of initial burst effect and extended-release of drug from F3 film provide longer time for exposing BPPE to the wound skin. Therefore, this formulation is potentially a good candidate as a medicated wound dressing for future animal studies in order to evaluate its protective and healing capability.

Acknowledgements

The work was financially supported by Nanotechnology Research Center, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran (grant Number: N-9503).

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Writing – original draft: Atefeh Raesi Vanani, Ali Kord Zanganeh, and Ali Heydari.

Conflict of Interests

Authors declare that there is no conflict of interest.

Ethical Approval

This article does not contain any test on human participants or animals.

Funding

This work was supported by Nanotechnology Research Center, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran [grant Number: N-9503].

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