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Research Article

Fabrication of innovative wound exudates dissolvable electrospun povidone-iodine loaded poly (Ɛ-caprolactone)-poly (ethylene oxide) composite nanofiber mat based wound bandages

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Abstract

Changing of bandage when nursing chronic wounds is a necessary exercise that encourages effective wound healing but often the bandage gets stuck to the wound, making changing it painful and uncomfortable. Furthermore, most of the wound medicine that is usually smeared on the bandage gets thrown away with the removed bandage unused. To deal with these challenges, we fabricated an innovative, dissolvable, drug releasing bandage based on electrospun povidone iodine (pvpi) blended poly (Ɛ-caprolactone), PCL-poly (ethylene oxide), PEO, composite nanofiber mats. From the experiments, smooth, yellow coloured nanofiber mats of calculated average fiber diameters of 341 nm were obtained from electrospinning an optimized 80:20 (v/v) PCL: PEO composite solution, blended with an optimized quantity of pvpi acting as model medicine incorporated in the structure of the nanofiber mats. From the performance evaluation results, the electrospun composite nanofiber mats excelled in releasing over 50% of the loaded pvpi over prolonged drug release time of 210 min which compared well with 200 min we reported in our previous work. Additionally, the composite nanofiber mats proved to be hydrophilic, influenced by the incorporation of the hydrophilic pvpi and PEO within the composite mats. Furthermore, the nanofiber mats gradually dissolved in phosphate-buffered saline (PBS), that was employed as wound exudate mimic, just under 24 h qualifying them as wound exudates-dissolvable nanofiber bandages that could revolutionize the bandage history and make wound care management free from bandage changes as well as totally removing medicine wastage during bandage changing and improving medicine efficacy during wound dressing.

Keywords: Chronic wounds, Wound exudates, Electrospinning, Polymer composite nanofibers, Electrospun nanofiber bandages, Innovative drug delivery bandages, Dissolvable nanostructured bandages

1. INTRODUCTION

Wound care management through bandage dressing and periodical bandage changing plays a critical role in enabling proper wound healing process and preventing wounds from being septic especially chronic wounds[1,2] by covering them from germs and providing other therapeutic benefits. Since time immemorial, current bandages and wound dressing materials have been based on cotton micro or macro structures with fiber diameters of above 1000 micrometers at molecular level, thus making them morphologically unfavorable and inefficient[3,4,5]. These micro/macro structured wound bandages, such as cotton bandages[5], cotton gauzes[6] and hydrogels[7], are still commonly employed the world over to cover and protect all types of skin wounds[8]. They are usually smeared on their surfaces with wound medicine to enhance their therapeutic benefits towards promoting wound healing. The medicine is always wasted as most of it is commonly thrown away with the used bandage during periodical bandage changing. The inefficient micro/macro structured cotton bandage materials with their; poor design, limited skin compatibility, frequent changing, medicine wasting, poor medicine efficacy and unfavorable morphological attributes which all contribute to wound healing delays, consequently led to our group starting to research in this area to revolutionize wound care management through synthesizing innovative, smarter wound dressing materials with superior properties in wound healing, less medicine wastage and excellent drug efficacy as well better morphologies and designs that better support efficient wound healing.

With the advent of nanostructured materials having a wide range of applicability in various fields, polymer based electrospun nanofibers and their polymer composites, can be taken advantage of in wound care management which is a challenge the world over, to produce the next generation wound bandages loaded with healing drugs that could give them smart drug delivery capabilities and eliminate drug wastage, thus providing cost effective wound care management solutions with improved therapeutic outcomes. Generally, nano fiber-based materials are well known for possessing unique, favorable attributes such as controllable morphologies that can be functionalized, large surface area to volume ratio and small pore sizes compared to the conventional micro-based materials[6,7]. Nanofibers have also been found to resemble extra cellular matrix, (ECM)[9,10,11] which is an integral layer within the human skin's structural composition, which in turn will further make the nanofiber based dressing materials better alternative

dressing materials in terms of bio compatibility to the skin structure for accelerated wound healing and skin cell growth. Recently, we have seen an increasing interest in developing nanofiber based wound dressing materials loaded with drugs and therapeutic agents of natural and synthetic origin. For example, Taymouri et al. made a study on fabrication and evaluation of hesperidin loaded polyacrylonitrile/polyethylene oxide electrospun composite nanofibers specifically for wound dressing applications[12]. From a study reported by Hassiba et al. novel hybrid double layered electrospun mats were developed for wound dressing applications with antimicrobial properties, which consisted of an upper layer of poly (vinyl alcohol) and chitosan loaded with silver nanoparticles (AgNPs) and a lower layer of polyethylene oxide (PEO) or polyvinylpyrrolidone (PVP) nanofibers loaded with chlorhexidine as an antiseptic for killing microbes on wound surfaces[13]. Merrel et al. made investigated the potential of curcumin loaded poly (-ε-caprolactone) (PCL) electrospun nanofibers as a delivery vehicle for wound healing applications. Under optimal conditions, employing electrospinning technology, they showed that bead-free curcumin-loaded PCL nanofibers were developed. The fibers showed sustained release of curcumin for 72 h and could be made to deliver a dose much lower than the reported cytotoxic concentration while remaining bioactive[14]. Farzamfar et al. fabricated taurine-loaded poly (-ε-caprolactone)/gelatin electrospun composite mats as potential wound dressing materials that were tested via both in vitro and in vivo for their performance. Their potential wound dressing mat showed a successful wound closure when applied in vivo[15]. Likewise, Salehi et al. reported on similar work regarding poly caprolactone polymer, and in their study, they fabricated via electrospinning naringin-loaded Poly (-ε-caprolactone)/Gelatin electrospun composite mat as potential wound dressing mats, which were also successfully evaluated via both in vitro and in vivo performance experiments[16].

To the best of our knowledge, as much as no wound dressing material can possess all the attributes needed by a wound to heal, one way of developing electrospun wound dressing materials that have more than one attribute to help enhance their efficiency in promoting wound healing, is to consider polymer composite nanofiber materials, compared to a single polymer-based nanofiber material. Forming polymer composite nanofiber materials as it has been reported by several researchers as outlined above, has proved to result in better materials with enhanced physical, mechanical and chemical attributes coupled with improved advanced morphological structures. Additionally, the type of wound structure and how the wound dressing material would be applied also dictates the design of the proposed wound dressing material. For example, the use of hydrophobic poly (-ε-caprolactone) alone to produce electrospun nanofibers with high mechanical strength and slow degradation abilities would greatly work best as drug delivery systems that needs no fast degradation during their application[17]. To enhance its degradability characteristic so that it degrades fast, this polymer can be optimally mixed with fast degrading polymers such as poly (ethylene oxide), PEO that is known to be naturally hydrophilic , easy to degrade and dissolve under aqueous environments[18]. The resulting composite nanofiber material would now possess enhanced structural morphology and optimized mechanical properties such as toughness, strength, improved degrading and dissolving attributes, hence suitable for their application in fields that need materials with fast degrading and dissolving abilities as in this work, where we aimed to develop through fabrication, innovative wound exdudates_dissolvable medicated electrospun composite nanofiber based wound bandages. Wound exudate is a largely water based (hydrophilic) fluid that is secreted from an open wound during the healing process, thus, helps to provide a moist environment for optimum wound healing, and also contains essential nutrients that nourish the tissues on the surface of the wound[19]. Taking advantage of the hydrophilic nature of the exudates within the wound environment, the expectation for the proposed wound exudates_dissolvable composite fiber based wound bandages, in this work is for them to be compatible with the wound exudates, thus allowing for these bandages to potentially dissolve gradually into the wound matrix, thus, eliminating the need to periodically swap the bandage during scheduled bandage change overs.

Experimentally, electrospinning[20,21,22,23], as a versatile approach for nanofiber material fabrication, was employed in our work to fabricate three separate composite solutions of varying percentage volume ratios of; 80:20, 50:50 and 20:80 (v/v) PCL:PEO into three electrospun poly (ε-caprolactone)-poly (ethylene oxide) composite nanofiber mats (PCL-PEO composite nanofiber mats), incorporated with a model therapeutic agent, povidone iodine (pvpi) within the nanostructures of the composite mats to be potentially employed as innovative and biocompatible wound exudates_dissolvable nanofiber based wound bandages. Incorporation of the therapeutic agent, pvpi into the fabricated composite nanofiber mats was performed through pvpi_blending to finally obtain what we referred to as pvpi_blended PCL-PEO composite nanofiber mats. Previous studies have shown that both the PEO and PCL synthetic polymers have been employed before in clinical research for drug delivery, making surgical sutures and scaffold tissue engineering as they are easy to be chemically modified, degradable, biocompatible and non-toxic to the human skin as approved by the food and drug administration (FDA) center for use by humans[24,25]. It is known that PCL is hydrophobic whereas PEO is hydrophilic in nature, therefore, mixing them in this work attained amphiphilic-like composite nanostructures that exhibited unique hydrophilicity-hydrophobicity behavioral traits, that we took advantage of, to optimally improve the overall performance of the composite nanofiber mats in line with their proposed applicability as the next generation innovative wound bandages. From the three pvpi_blended PCL-PEO composite fiber mats developed, the one that demonstrated the best performance based on excellent; pvpi_blended PCL-PEO composite morphologies, fiber sizes, maximum loading capacities, controlled pvpi release of over 50% of the loaded drug over a reasonably prolonged time and wettability studies was then subjected to invitro dissolubility studies, to check its potential wound exudates compatibility and gradual dissolubility. Overall, the newly developed medicated electrospun PCL-PEO composite nanofiber mats demonstrated remarkable qualities from both characterization and the in vitro performance results, hence they emerged as promising alternatives that could replace the drug wasting old micro structured cotton bandages that are not even wound exudates compatible during wound care management.

2. MATERIALS, ANALYTICAL INSTRUMENTS AND METHODS

2.1 Materials

Reagents employed were; Polycaprolactone (PCL, Average Mw 80 kDa), Polyethylene oxide (PEO, Average Mw 300 kDa), Polyvinylpyrrolidone-iodine complex (pvpi), phosphate buffered saline (PBS), Chloroform (CFM, 99% purity), and N, N-dimethylformamide (DMF, 99.5% purity), all of which were purchased from Sigma-Aldrich (Johannesburg, South Africa).

2.2 Analytical Instruments employed for the preparation and characterization of the prepared materials

Spraybase electrospinning platform that was employed to prepare the electrospun pvpi_blended PCL-PEO composite fiber mats was supplied by Avectas (Maynooth, Ireland). The following pieces of equipment, were all purchased from

Thermo Fisher Scientific (Johannesburg, South Africa): Evolution 201 UV-Vis spectrophotometer that was employed for the determination of pvpi absorbances, Drying oven (TTM-J4) that was employed for the drying of the prepared pvpi_blended PCL-PEO composite fiber mats and a Nicolet iS10 FTIR spectrophotometer for acquiring the FTIR spectra of the starting materials as well as the prepared composite fiber mats. A field emission scanning electron microscope (FE-SEM) JSM-7100F, purchased from JEOL Ltd (Welwyn GardenCity, United Kingdom) was employed to evaluate the morphology and the fiber diameters of the prepared composite fiber mats and the Thermogravimetric analyzer (TGA/DSC 3+ star system) purchased from Mettler-Toledo (Columbus, OH, USA) was employed to evaluate the thermal stability of the prepared pvpi_blended PCL-PEO composite fiber mats.

2.3 Preparation of the electrospun pvpi_blended PCL-PEO composite fiber mats

A modified electrospinning method by Barbak et al.[26] was employed in this work to produce electrospun PCL-PEO composite fiber mats under optimized electrospinning parameters of 4% spinnable polymer concentration, 11.58 kV voltage, 20 µl min^{-1} feeding rate and 20 cm needle tip to collector distance. To medicate the newly prepared electrospun PCL-PEO composite fiber mats in this work, an innovatively optimized approach that was recently published by Tabane et. al, was employed to incorporate a model therapeutic agent, pvpi into the structure of the PCL-PEO composite fiber mats. For this work, optimized quantities of PCL pellets and PEO powder were separately dissolved in (70:30) (v/v) CFM and DMF 40 ml mixture to produce two separate 4% (w/v) of PCL and PEO polymer stock solutions which were stirred overnight at room temperature. From the two polymer stock solutions, Three separate 10 ml composite solutions of varying percentage volume ratios of; 80:20, 50:50 and 20:80 (v/v) PCL:PEO were then prepared by mixing the two stock solutions of PCL and PEO. Thereafter, an optimized quantity of pvpi, 10% (w/w) pvpi was added to each of the three 10 ml composite polymer solutions which were then stirred at room temperature, until all the added pvpi was completely dissolved, to produce pvpi_blended PCL-PEO composite spinnable solutions. The solutions were then electrospun to produce what we referred to as the pvpi_blended PCL-PEO composite fiber mats that were formed on an aluminum foil collector. The pvpi_blended PCL-PEO composite fiber mats were dried in an oven at 40 °C, then stored in a desiccator overnight for subsequent analysis. From the three pvpi_loaded composite fiber mats developed, the one that demonstrated the best performance based on excellent; pvpi_blended PCL-PEO composite morphologies, fiber sizes, loading capacities, pvpi release and wettability studies was then subjected to invitro dissolubility as well as kinetic studies.

2.4 Characterization

2.4.1 SEM characterization of the electrospun pvpi_blended PCL-PEO composite fiber mats

A field emission scanning electron microscope (FE-SEM) was employed to evaluate the morphology of the electrospun pvpi_blended PCL-PEO composite fiber mats and subsequently estimate their fiber diameters. To perform this, round mat pieces of 5 mm radius which were cut from the electrospun PCL-PEO composite fiber mats were supported on 1 cm tall sample holders, then sputter coated with gold and inserted into the system for acquisition of SEM images.

2.4.2 TGA characterization of pure pvpi, electrospun PCL-PEO composite fiber mats and pvpi_blended PCL-PEO composite fiber mats

To qualify the formed electrospun pvpi_blended PCL-PEO composite fiber mats as thermally stable under temperature-controlled conditions, TGA analysis was performed as follows; 5 mg of pure pvpi, electrospun PCL-PEO composite fiber mats and that of the electrospun pvpi_blended PCL-PEO composite fiber mats were placed in separate TGA sample holders then subjected to heat from 25 °C to 400 °C, at a rate of 10 °C min^{-1} under nitrogen gas stream within a monitored timed duration. TGA curves of the electrospun pvpi_blended PCL-PEO composite fiber mats were obtained and compared to that of the pure pvpi and the electrospun PCL-PEO composite fiber mats.

2.5 Loading capacities of the electrospun PCL-PEO composite fiber mats

To evaluate the loading capacities of the three PCL:PEO (80:20, 50:50 and 20:80) composite fiber mats, 10 mg of each of the three pvpi_blended PCL-PEO composite fiber mats were dissolved in 2 ml of 70:30 (v/v) mixture of CFM and DMF which were stirred for an optimized time after which their absorbances were measured in triplicates at an optimal λmax of 364 nm employing a UV-visible spectrophotometer. The obtained absorbances were then employed to calculate the loading capacities in percentages employing equation **1** and the encapsulation efficiencies (EE%) employing equation **2**. The obtained values gave a measure of the pvpi loaded and encapsulated in the PCL-PEO composite fiber mats and all the values were then tabulated.

Eq 1

$$pvpi\ loading\ (\%) = \frac{Meaured\ pvpi\ \ quantity\ (mg)}{mass\ of\ the\ loaded\ mat\ (mg)} x\ 100$$

Eq 2

$$EE\ (\%) = \frac{Measured\ pvpi\ \ quantity\ (mg)}{theoretical\ pvpi\ quantity\ (mg)} x\ 100$$

2.6 pvpi releasing behavior of the electrospun PCL-PEO composite fiber mats

To evaluate the release of the incorporated pvpi from the three pvpi_blended PCL-PEO composite fiber mats into the wound matrix, an invitro experiment involving 10 mg of each of the three pvpi_blended PCL-PEO composite fiber mats were incubated at 37 °C in 5 ml PBS solution resembling wound exudates in three separate reaction vials. At 30 min intervals, 2 ml portions were withdrawn from the incubated solution to determine their absorbances in triplicates using a UV spectrophotometer and subsequently the withdrawn 2 ml PBS solutions were replaced. The absorbances of the withdrawn solutions were recorded in triplicates at an optimal λmax = 364 nm. This was repeated until there was a constant trend in the recorded absorbances for each of the three pvpi blended PCL-PEO fiber mats of different PCL: PEO ratios. The absorbances were employed to calculate the quantities of pvpi released at each time interval. These quantities were then employed to calculate the cumulative pvpi quantities released in percentages via equation **3** which gave an estimation of the quantity of pvpi released into the wound. Corresponding cumulative pvpi release (%) against release time (min), for the three pvpi_blended PCL-PEO composite fiber mats were constructed. A cumulative pvpi release of 50% or more at a particular time from the plots by the prepared materials was described as good enough. Materials that exhibit longer release times for cumulative drug releases of 50% or more are said to possess prolonged releases and are the preferred materials when it comes to wound care management.

Eq 3

$$pvpi\ release\ (\%) = \frac{Cum\ pvpi\ quantity\ (mg)}{initial\ pvpi\ loaded\ (mg)} x\ 100$$

2.7 Contact angle measurements for wettability Studies on the electrospun PCL-PEO composite fiber mats

The wettability of the pvpi_loaded PCL-PEO composite fiber mats that exhibited excellent performance on both the pvpi loading and releasing experiments was studied through contact angle measurements. Typically, 1 x 1 cm^{-2} mats were cut and placed on glass slides on a flat surface. One drop of PBS solution was carefully placed on the mat surfaces. Absorption of the PBS drop by the PCL-PEO composite fiber mat surfaces was monitored, with snapshot image of the drop obtained once the drop was placed on the mat surfaces (initial snapshot) and another snapshot obtained after some time when almost all the drop was absorbed (final snapshot). This was performed in triplicates and the images were uploaded into the image J software which assisted in calculating the initial and final measured contact angles based on the obtained initial and final snapshots respectively. The average initial and final measured contact angles were recorded and used to classify the prepared composite fiber mats as hydrophobic or hydrophilic based on the fact that materials that exhibit average final contact angles of < 90° are said to be hydrophilic and the ones of > 90° are hydrophobic.

2.8 Invitro dissolubility test on the electrospun pvpi_blended PCL-PEO composite fiber mats

The main aim of this work was to evaluate whether the prepared PCL-PEO composite fiber mats could dissolve in hydrophilic wound exudates or similar environments over time or not. To achieve that, an invitro dissolubility test was set up which involved immersing 10 mg of the prepared, optimized electrospun pvpi_blended PCL-PEO composite fiber mats in 5 ml PBS (employed as a wound exudates mimic) at 37 °C in reaction vials. The immersed fiber mats were removed from the PBS solution at 12 h time intervals for 24 h, dried in an oven at 40 °C then left to cool at room temperature for 1 hr before determining their final masses in triplicates. Fiber mat mass losses in (%) at 12 h time intervals were then calculated employing equation **4**, from which a bar graph of mass loss % over time was constructed. The calculated % mass lost of the fiber mats represented the mass that dissolved in the PBS solution hence the % mass of the prepared fiber mats that could dissolve in wound exudates if the prepared fiber mats were to be applied as a bandage on the wound. In a similar manner, electrospun pvpi_blended PCL fiber mats that we recently developed and published were subjected to the same dissolubility test and the two were compared under the same conditions.

Eq 4

$$Fiber\ mat\ mass\ loss\ (\%) = \frac{Initial\ mat\ mass\ (mg) - final\ mat\ mass\ (mg)}{Initial\ mat\ mass\ (mg)} x\ 100$$

2.9 Application of pvpi release data on Higuchi and Korsmeyer peppas kinetic models

Topical medication through medicine carriers for skin wounds treatment follows a diffusion process[27]. Usually, an invitro cumulative drug release from drug delivery systems involving water soluble drugs[28,29,30] follow a drug diffusion mechanism based on Higuchi kinetic model[31,32]. Since the pvpi used in this work is a water-soluble drug, the release data in this work was fitted to the Higuchi kinetic model (Eq **5**) to understand the pvpi release kinetics and mechanisms from the electrospun pvpi_blended PCL-PEO composite fiber mats. It must be noted that only the pvpi release data from the pvpi_blended PCL-PEO composite fiber mats that exhibited best performance on both the pvpi loading and releasing experiments was the one whose data was evaluated. A plot corresponding to the pvpi release data against time was constructed based on the kinetic model equation **5** and corresponding correlation coefficient value (R^2) was determined. Only a linear plot with R^2 value of at least 0.900 confirmed that the pvpi release data fitted the Higuchi kinetic model.

Eq 5, Higuchi model

$$Q = K_H \sqrt{t}$$

Where, Q is the cumulative quantity of pvpi released in time t, and K_H is the Higuchi release constant. The cumulative pvpi percentage releases were plotted against square root of time in minutes.

The pvpi release data for the pvpi_blended PCL-PEO composite fiber mats was also fitted to another kinetic model known as Korsmeyer peppas[30], (Eq **6**) to further establish the type of diffusion mechanism, between fickian and non-fickian, which can clearly be defined by the value of ***n*** from the equation, corresponding to the slope of the graph obtained. A plot corresponding to the pvpi release data against time was also constructed based on the kinetic model equation **6** and corresponding correlation coefficient value (R^2) was determined. Only a linear plot with R^2 value of at least 0.900 confirmed that the pvpi release data fitted the Korsmeyer peppas kinetic model.

Eq 6, Korsmeyer peppas model

$$log \frac{M_t}{M_\infty} = logk + nlogt$$

Where M_t/M_∞ is a fraction of drug released at time t, M_t is the amount of drug released in time t, M_∞ is the amount of drug released after time ∞, ***n*** is the diffusional exponent or drug release exponent, K is the Korsmeyer release rate constant. The following criteria apply for different ***n*** values indicating different release mechanisms, more especially if the release mechanism is unknown.

- n < 0.5 fickian diffusion mechanism
- 0.5 < n < 0.89 anomalous behavior, non fickian diffusion mechanism.
- n > 1 release is independent of time and concentration (zero order)

3 RESULTS AND DISCUSSION

3.1 The prepared electrospun pvpi_blended PCL-PEO composite fiber mats

All the three PCL-PEO composite products were obtained on separate aluminum collectors as thin sheet-like-mats upon electrospinning. The sheet-like-mats were carefully harvested from the collectors and stored for subsequent analysis. All the mats collected exhibited a homogeneous pale-yellow color, thus indicating the successful uniform distribution of the loaded pvpi molecules throughout the surface structure of the obtained mats.

3.2 Characterization results for the electrospun pvpi_blended PCL-PEO composite fiber mats

SEM images and TGA curves for all the three pvpi_blended PCL-PEO composite fiber mats obtained did not show any notable difference, hence only the characterization results of the pvpi_blended PCL:PEO (80:20) ratio composite fiber mats which demonstrated better performance in other parameters that were investigated, were reported.

3.2.1 SEM images of the electrospun pvpi_blended PCL-PEO composite fiber mats

From the SEM image in figure **1**, it was observed that an interconnected PCL-PEO composite structure consisting of randomly aligned smooth fibers with no beads was formed.

Employing the image J software, calculated fiber diameters from the SEM image gave an estimated average diameter of about 341 nm as per the fiber diameter distribution in the range of about 100 nm-900 nm, as illustrated by the histogram in figure **2**. The fiber magnitude of 341 nm confirmed that the obtained electrospun pvpi_blended PCL-PEO composite fiber mats were in the nano scale, hence, were nanofibers.

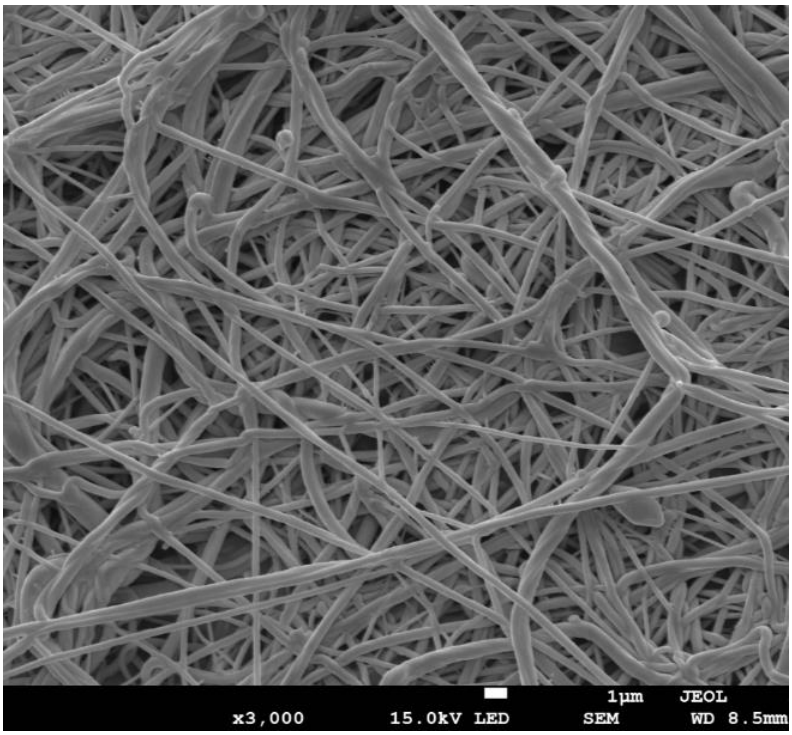

Figure 1 Scanning electron microscope image of the electrospun pvpi_blended PCL-PEO composite fiber mats

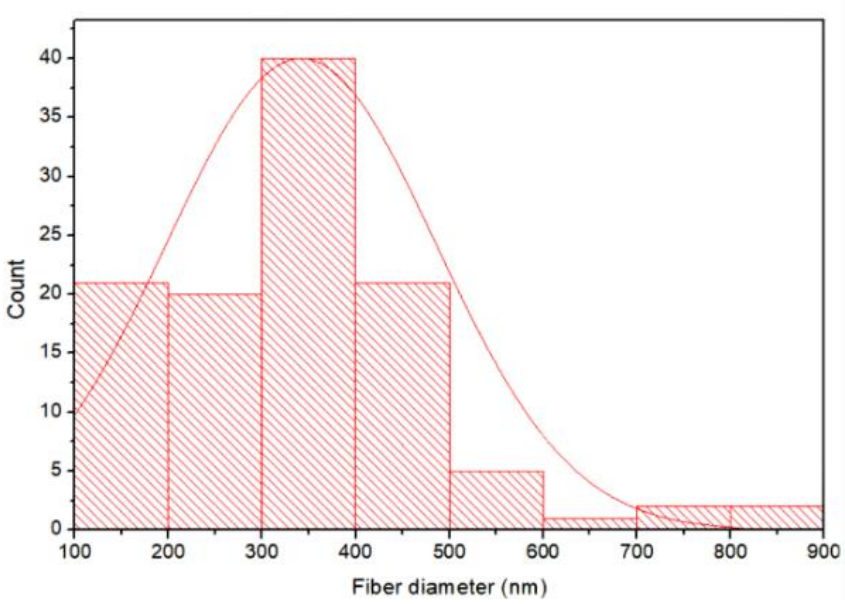

Figure 2 Estimated fiber diameter and distribution of the prepared electrospun pvpi_blended PCL-PEO composite fiber mats as calculated by the image J software from the SEM image in figure 1

3.2.2 TGA curves of pure pvpi, electrospun PCL-PEO composite nanofiber mats and pvpi_blended PCL-PEO composite nanofiber mats

From the results shown in figure **3**, it was observed that the TGA curves (**a** and **b**) for the electrospun PCL-PEO composite nanofiber mats and the pvpi_blended PCL-PEO composite nanofiber mats showed no mass loss change within the temperature range from 25 °C to about 300 °C, thus the mats were stable within the temperature range when compared to the TGA curve (**c**) of the pure pvpi that recorded a mass loss of about 15%, between 80 °C and 100 °C which was attributed to the water moisture content loss by evaporation and boiling processes respectively at those temperatures from the highly hygroscopic pvpi. The PCL-PEO composite nanofiber mats and the pvpi_blended PCL-PEO composite nanofiber mats experienced a huge mass loss change of over 80%, between 300 °C and 450 °C, as observed on the corresponding TGA curves on figure **3** (**a**) and (**b**) respectively. The loss was attributed to possible degradation and/or decomposition of the polymeric structure of the nanofiber mats into products such as carbon dioxide and volatile organic based products such as ethanol and hexanoic acid as per literature[33] hence the two structures including the newly electrospun pvpi_blended PCL-PEO composite nanofiber mats were declared unstable at those temperatures, between 300 °C and 450 °C due to the mass loss and stable at temperatures just below 300 °C.

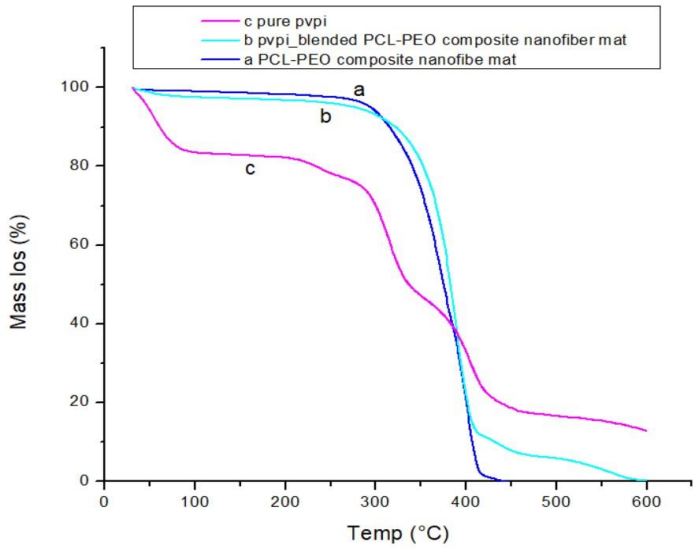

Figure 3 TGA curves of pure pvpi (c), electrospun pvpi_blended PCL-PEO composite nanofiber mat (b) and PCL-PEO composite nanofiber mat(a)

3.3 pvpi loading capacities and encapsulation efficiencies of the electrospun PCL-PEO composite nanofiber mats

Table 1 Table showing pvpi loading capacities and encapsulation efficiencies for all the three electrospun pvpi_blended PCL-PEO composite nanofiber mats

Composite nanofiber mats ratios (PCL:PEO)	Actual pvpi loading capacity (%)	Pvpi encapsulation efficiency (%)
20:80	9.49 ± 0.010	95.5 ± 0.59
50:50	9.57 ± 0.027	96.1 ± 0.61
80:20	9.63 ± 0.017	96.3 ± 0.12

Initially, all the three PCL-PEO composite nanofiber mats were subjected to a total of 10% (w/w) pvpi through pvpi_blended approach. From the results obtained, the pvpi_blended PCL:PEO (80;20) composite nanofiber mats outclassed both the pvpi_blended PCL:PEO (50;50) and (20:80) composite nanofiber mats as marked by pvpi actual loading capacity and encapsulation efficiency percentages of 9.63% out of 10.00% and 96.3%, respectively, which were slightly higher than those of the pvpi_blended PCL:PEO (50;50) composite fiber mats with slightly lower values at 9.57% out of 10.00% and 96.1% and that of the pvpi_blended PCL:PEO (20:80) composite nanofiber mats with slightly lower values at 9.49% out of 10.00% and 94.5% for pvpi actual loading capacity and encapsulation efficiency percentages, respectively, as displayed in table **1**. The obtained reasonable values of the loaded pvpi quantities (9.49-9.63%) and encapsulation capacities (95.5-96.3%) for all the three PCL-PEO composite nanofiber mats were attributed to the polymer-drug interaction during blending[34] which allowed the pvpi molecules to be evenly distributed over the large surface area of the composite nanosized fiber mats, even though all the three composite nanofiber mats were prepared from different PCL-PEO polymer ratios.

3.4 pvpi releasing behavior of the electrospun pvpi_blended PCL-PEO composite nanofiber mats

From the results in figure **4**, all the three electrospun pvpi_blended PCL-PEO composite nanofiber mats, figure **4** (**a**), (**b**) and (**c**) released over 50% of pvpi within a reasonable time, thus exhibiting an excellent pvpi releasing behavior that cannot be attained by the conventional wound bandages as they struggle to release at least 50% of the wound medicine that is usually smeared on them to be used up before the next bandage change over usually scheduled to next 3 to 5 days. Interestingly, it was noteworthy that a change in the polymer ratios resulted in different pvpi release times of different PCL-PEO composite nanofiber mats.

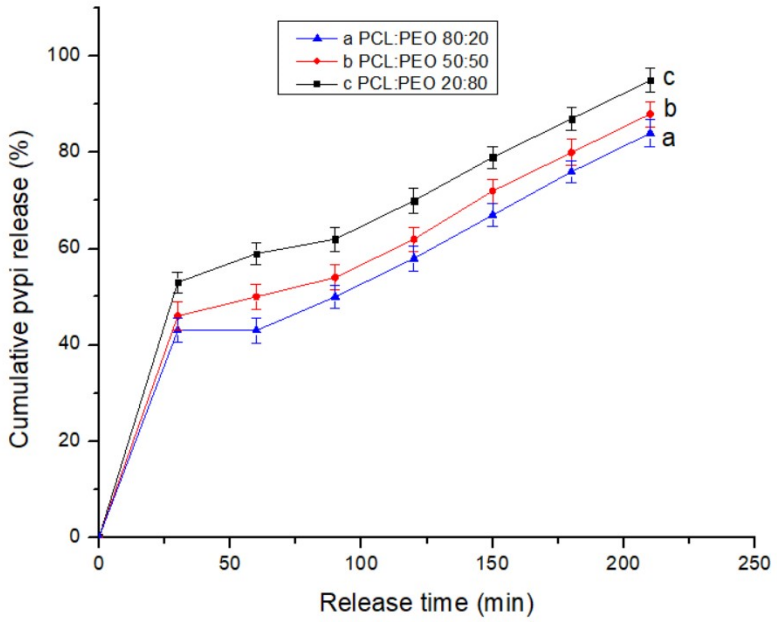

Figure 4 Cumulative pvpi release plots of the electrospun pvpi_blended (PCL:PEO 80:20 (a), PCL:PEO 50:50 (b), PCL:PEO 20:80 (c)) composite nanofiber mats

This was attributed to the hydrophilicity-hydrophobicity behavioral contributions from the two individual polymers, as PCL is hydrophobic whereas PEO is hydrophilic in nature, therefore, mixing them attained an amphiphilic-like composite nanostructure, thus significantly altering the polymer-dug interaction during the drug release. Comparatively, the electrospun pvpi_blended PCL:PEO (80:20) composite nanofiber mat, attained a maximum pvpi release of about 85% within a longer time of about 210 min, compared to shorter times of about 200 min and 180 min taken by the electrospun pvpi_blended PCL:PEO (50:50) and pvpi_blended PCL:PEO (20:80) composite nanofiber mats, respectively to release the same comparable pvpi quantity (85%) as illustrated in figure **4**. This showed that the electrospun pvpi_blended PCL:PEO (80:20) composite nanofiber mat exhibited the prolonged release for the drug to be used up, marked by the relatively longer pvpi releases, thus making it suitable for applications where prolonged drug releases are needed such as in wound care management, an area under study in this article. On the other hand, electrospun pvpi_blended PCL:PEO (50:50) and pvpi_blended PCL:PEO (20:80) composite nanofiber mats with short pvpi release times of about 200 and 180 min, respectively, at the same comparable 85% pvpi release showed that they could be applicable to instances where the medicine is needed swiftly. Even though, the electrospun pvpi_blended PCL:PEO (50:50) and pvpi_blended PCL:PEO (20:80) composite nanofiber mats recorded relatively poor prolonged releases, from figure **5** (**b**) and (**c**) they achieved higher maximum cumulative releases of about 90% and 98% for the electrospun pvpi_blended PCL:PEO (50:50) and pvpi_blended PCL:PEO (20:80) composite nanofiber mats, respectively, which meant that their higher pvpi release percentages were accessible to be used up compared to about 85% of maximum cumulative release by electrospun pvpi_blended PCL:PEO (80:20) composite nanofiber mat, figure (**a**).

3.5 Measured contact angles for wettability studies on the electrospun pvpi_blended PCL-PEO composite nanofiber mats

From the contact angles results, the electrospun pvpi_blended PCL-PEO composite nanofiber mats initially displayed hydrophobic characteristics (due to the presence of hydrophilic PCL within the composite nano structures of the mats), as marked by an initial average measured contact angle of about 110° which changed almost after an hour to a final average measured contact angle of 0°. The change in contact angle from 110° to 0° was due to the presence of hydrophilic pvpi and PEO within the structure of the prepared PCL-PEO composite nanofiber mats, thus making the newly developed pvpi_blended PCL-PEO composite nanofiber mats satisfactorily hydrophilic at 0°. From the literature, Li et al. developed the PCL-PEO composite nanofiber membrane materials and subsequently proved their hydrophilicity behavior through contact angle measurement, which they reported to be 42.25°, thus hydrophilic due to the presence of the PEO within the membranes[35]. Generally, hydrophobic materials are characterized by contact angles above 90° whereas those showing hydrophilic behavior are characterized to have contact angles below 90° [36,37]. Final measured contact angles of 90° and below are said to be hydrophilic and tend to favor wound exudates absorption [38,37,39] The newly prepared composite nanofiber mats were found to have final average measured contact angles below 90°, (0°), thus hydrophilic (water loving) and as wound exudates are largely water based, the two (the newly prepared composite nanofiber mats and the wound exudates) were compatible.

3.6 Invitro dissolubility test results on the electrospun pvpi_blended PCL-PEO composite fiber mats

In figure **5**, this work's aim was attained where the newly prepared electrospun pvpi_blended composite nanofiber mats proved their ability to gradually dissolve in PBS (as wound exudates mimic) within a reasonable time not exceeding 24 h, as marked by the calculated nanofiber mats mass loss change from the initial 100% to a lower value of about 5%, compared to a smaller mass loss change from 100% to about 90%, that was exhibited by the electrospun pvpi_blended PCL nanofiber mats, that we recently developed and published, to be slightly hydrophilic (due to the loaded hydrophilic pvpi).

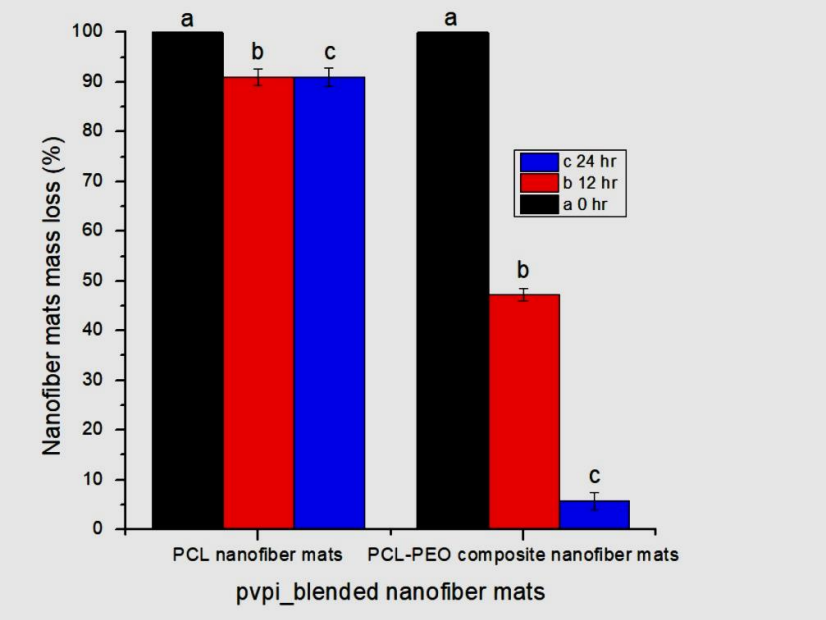

Figure 5 Measured composite nanofiber mat mass loss (%) for invitro dissolubility test on the electrospun pvpi_blended PCL-PEO composite nanofiber mats

To our knowledge, it was noted that the presence of hydrophilic PEO and pvpi within the nano structures of the newly prepared electrospun pvpi_blended PCL-PEO composite nanofiber mats greatly enhanced the invitro dissolubility of the same composite nanofiber mats when compared to the pvpi_blended PCL nanofiber mats that only had hydrophilic pvpi within their nano structure. Overall, the electrospun pvpi_blended PCL-PEO composite nanofiber mats demonstrated their potential ability to dissolve in the largely water based wound exudates, thus, they can be employed as wound exudates dissolvable nanofiber based wound bandages that would not need to be frequently replaced during periodical bandage change overs.

3.7 pvpi release data fitted to Higuchi and Korsmeyer peppas kinetic models In figure **6**, it was noted that the pvpi release kinetics for the electrospun pvpi_blended PCL-PEO composite nanofiber mats followed the Higuchi kinetic model in a linear fashion associated with a correlation coefficient (R^2) value of 0.955. The linear plot in figure **6**, together with the correlation coefficient (R^2) value of more than 0.900, $R^2 = 0.955$, confirmed that the pvpi release was through the diffusion mechanism as our pvpi release data by the electrospun pvpi blended PCL-PEO composite nanofiber mats was successfully fitted to the Higuchi kinetic model.

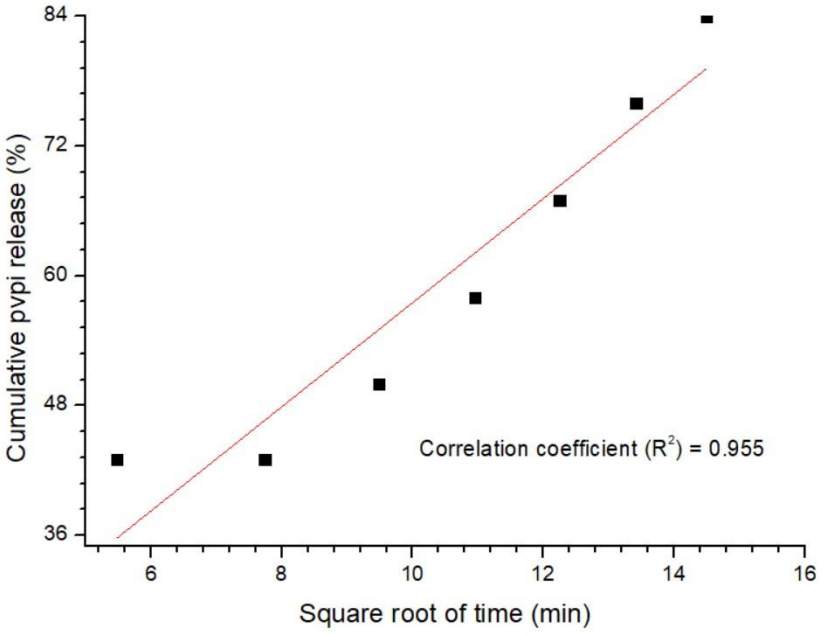

Figure 6 A linear plot representation of the pvpi release data fitted to the Higuchi kinetic model for the electrospun pvpi_blended PCL-PEO composite nanofiber mats

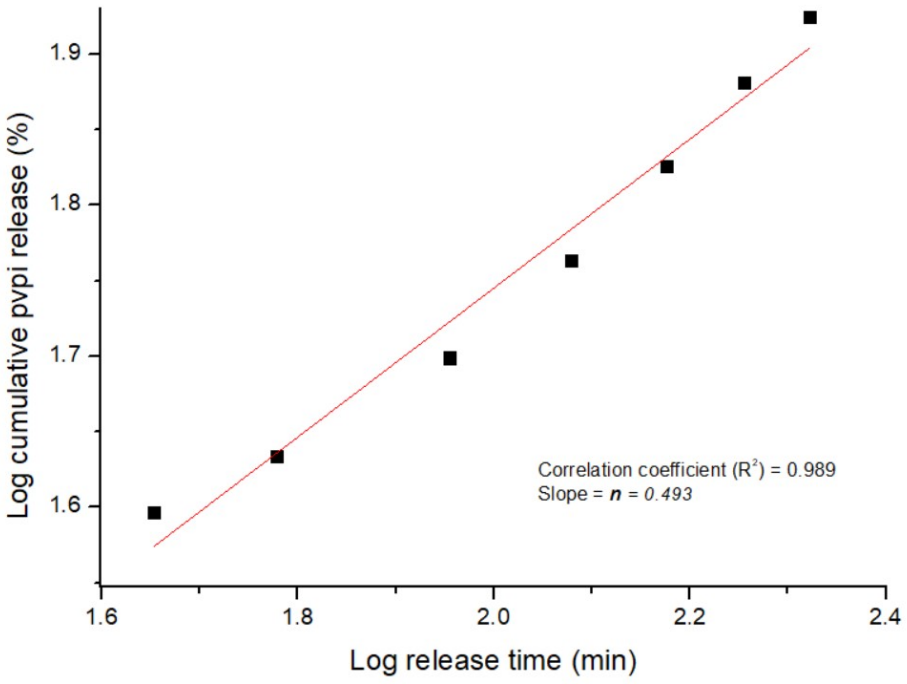

Figure 7 A linear plot representation of the pvpi release data fitted to the Korsmeyer peppas kinetic model for the electrospun pvpi_blended PCL-PEO composite nanofiber mats

From literature, Monteiro et al. reported that the drug release kinetics based on the Higuchi kinetic model are described to be time-dependent diffusion. This means that the quantity of the drug released decreased with time of exposure to the dissolution medium [40]. Moreover, Higuchi model supports the drug release kinetics that involve water soluble drugs such as pvpi in our case, and polymeric based drug loaded vehicles, such as the PCL-PEO composite nanofiber mats in this work.

In figure **7**, it was also observed that the pvpi release kinetics for the electrospun pvpi_blended PCL-PEO composite nanofiber mats followed the Korsmeyer peppas kinetic model in a linear representation associated with a correlation coefficient (R^2) value of 0.989, that was also more than 0.900. The diffusional exponent, ***n*** corresponding to the slope of the line plot in figure **7** was determined to be 0.493, which indicated that between fickian (***n*** < 0.5) and non fickian (***n*** > 0.5) diffusion mechanisms, the loaded pvpi was released from the PCL-PEO composite nanofiber mats through a fickian diffusion mechanism as the ***n*** value was determined to be < 0.5, (0.493).

4. CONCLUSION

In conclusion, we innovatively produced three yellow coloured medicated electrospun pvpi_blended PCL-PEO composite nanofiber mats with the potential to be applied as wound exudates dissolvable bandages, namely; the pvpi_blended PCL:PEO (80:20) composite nanofiber mats, the pvpi_blended PCL:PEO (50:50) composite nanofiber mats and the pvpi_blended PCL:PEO (20:80) composite nanofiber mats. In comparison, the pvpi_blended PCL:PEO (80:20) composite nanofiber mats significantly outperformed both the pvpi_blended PCL:PEO (50:50) composite nanofiber mats and the pvpi_blended PCL:PEO (20:80) composite nanofiber mats when evaluating the results for all the three composite mats regarding pvpi loading capacity and the pvpi releasing behavior even though all three composite mats showed similar, good, controlled releases of over 50% pvpi within a reasonable time of between 180 -210 min inclusive. Furthermore, the pvpi_blended PCL:PEO (80:20) composite nanofiber mats demonstrated a more prolonged pvpi release as was marked by longer time periods (210 min) taken to release 50% or more of the loaded pvpi compared against (< 210 min) for both the pvpi_blended PCL:PEO (50:50) composite nanofiber mats and the pvpi_blended PCL:PEO (20:80) composite nanofiber mats which all took shorter times. From the wettability and the invitro dissolubility results, the pvpi_blended PCL:PEO (80:20) composite nanofiber mats were satisfactorily hydrophilic due to the presence of the hydrophilic pvpi and PEO within the structure of the newly prepared composite nanofiber mats, thus potentiating them as wound exudates absorbers and wound exudates dissolvable within a reasonable time not exceeding 24 h. They were further found to possess excellent morphological attributes such as beadless, smooth and nano-sized fibers as well as hydrophilic traits that supported their potential to function as wound exudates absorbers. Overall, the custom-made medicated electrospun PCL-PEO (80:20) composite nanofiber mats demonstrated more remarkable qualities such as better wound exudates dissolubility, drug delivery and drug efficacy improvement than the other two newly prepared composite nanofiber mats, thus, displaying their potential as promising next generation wound bandage alternatives that could replace the drug wasting and insoluble conventional macro/micro structured cotton bandages.

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Conflict of interest

No conflict of interest was declared from all the authors.

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