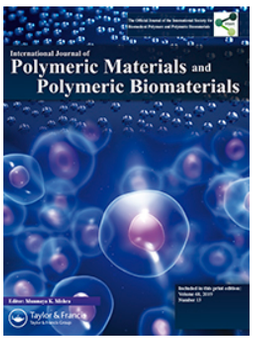

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A novel bilayer drug-loaded wound dressing of PVDF and PHB/Chitosan nanofibers applicable for post-surgical ulcers

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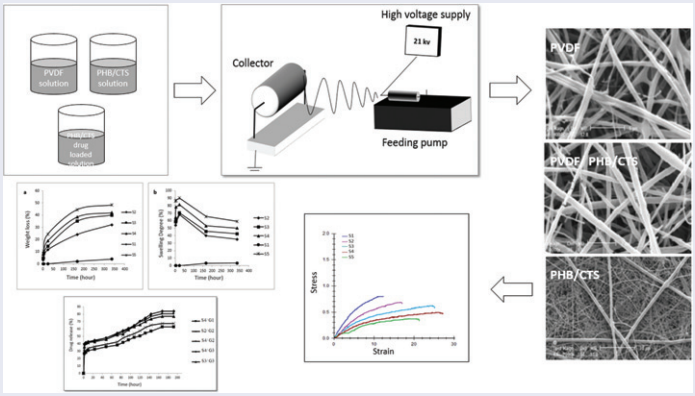
ABSTRACT

A novel bilayer nanofibrous wound dressing, with enhanced mechanical properties is successfully fabricated. This membrane, consisted of polyvinylidenefluoride (PVDF) nanofibers for providing tensile strength and polyhydroxybutyrate/chitosan (PHB/CTS) nanofibers loaded with gentamicin with ability of controlled drug delivery, is a great choice for post-surgical ulcers. Mechanical properties showed dramatically improvement of tensile strength by addition of PVDF layer. Gentamycin release represented both an immediate and a sustained release of about 24 h and 1 week, respectively and release increment with increase of CTS ratio. Results also revealed that drug release in structures follow first order kinetic and Fickian release mechanism.

GRAPHICAL ABSTRACT



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Drug-loaded nanofibers; nanofiber; post-surgical ulcer; wound dressing

1. Introduction

Acute and chronic wounds on the skin, caused by physical, mechanical, chemical and dermal damages, need to be cared clinically[1–3]. The most effective and common way to heal such undesired disease is applying wound dressings[3, 4]. Biocompatibility, non-toxicity, ability to absorb excess wound exudates, maintaining moisture in the wound and prevention it from infections and pain are some essential properties of an appropriate wound dressing[5, 6].

In recent years, electrospun nanofibers have been applied in a wide variety of applications especially in the field of medical engineering such as wound dressing[7, 8]. Possession of unique characteristics like high surface to volume ratio, high porosity, suitable mechanical properties and interconnected pores, make nanofibrous mats to be superior choices as wound dressings[8, 9]. Furthermore, ability of nanofibrous matrices for reserve and delivery of various kinds of drugs is of another valuable advantages which makes them be identified as suitable wound healing dressings with controlled drug delivery[10, 11].

In this area, usage of biodegradable and biocompatible polymers to fabricate nanofibrous wound dressings with these two valuable characters has attracted huge attention by researchers[12, 13]. It is noteworthy that degradation rate of polymers play a significant role in drug delivery systems and must be tuned according to considered application[14, 15].

Poly (hydroxybutyrate) (PHB) is one of the biocompatible polymers with natural origin of polyhydroxyalkanoate groups, which recently has been widely used in tissue engineering and drug delivery systems due to outstanding features such as high elasticity, acceptable mechanical properties, and biocompatibility. However, existence of downsides like hydrophobicity and low rate of degradation have limited its

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applications[16–18]. Blending PHB with other polymers such as chitosan (CTS), an antibacterial, non-toxic, biocompatible and natural polysaccharide with appropriate biodegradability and hydrophilicity, is an efficient and common method to eliminate mentioned obstacles[3, 13, 19]. CTS has been reported to be effective and influential in wound healing and antibacterial activities[20, 21]. In 2016, Sadeghi et al.[22] fabricated PHB/CTS nanofibrous scaffolds applicable as cartilage tissue engineering. According to the results, addition of CTS causes reduction in both water droplet contact angle (from 74° to 67°) and tensile strength (from 87 MPa to 31 MPa). Moreover, Ma et al.[23] applied nanofibrous PHB/CTS mats as skin tissue engineering due to greater cell attachment and proliferation.

Notably, proper mechanical properties are of other significant features for an ideal wound dressing. Polyvinylidene fluoride (PVDF) is a biocompatible synthetic polymer with high tensile strength[24–26]. He et al.[25] electrospun a nanofibrous membrane from PVDF, containing Enrofloxacin antibacterial drugs for wound dressing application. Obtained results represented that this fabricated membrane possesses superior healing effect than commercial gauzes.

In this study, PHB/CTS nanofibrous membranes containing various ratios of CTS were fabricated as wound dressing for postsurgical ulcers. Mechanical properties of produced nanofibrous wound dressings were enhanced by electrospinning a layer of PVDF on manufactured mats. To characterize prepared electrospun mats, scanning electron microscopy (SEM), fourier transform infra-red spectroscopy (FT-IR), tensile strength test, biodegradation test and *In vitro* drug delivery were carried out and investigated.

2. Experimental details

2.1. Material

Polyvinylidene fluoride with average molecular weight of 156000 was purchased from an American company (Elf Atochem, North America). Chitosan and Poly (hydroxyl butyrate) with molecular weight of 1526/464 and 500000 (g/mol), respectively were obtained from Sigma-Aldrich. In addition, trifluoroacetic acid (TFA, 1.48g/cm^3) and dimethyl form amide (DMF, 0.944 g/cm^3) as solvents were supplied by scharlau and Sigma-Aldrich, respectively. Gentamicin sulfate ($M_w = 477.6$ g/mol) was purchased from Sigma-Aldrich.

2.2. Preparation of spinning solution and electrospinning

PVDF powder with a concentration of 10% (w/w) was dissolved in DMF solvent and stirred vigorously for 24 h at room temperature before electrospinning. Then prepared solution was transferred to a 1 ml syringe with a positively charged needle (23 gauge). Feeding rate, applied voltage and distance between the needle tip and the cylindrical collector were adjusted 7 ml/h, 18 kV and 15 cm, respectively.

Afterwards, PHB/TFA solution with concentration of 9% (w/w) was prepared and then CTS with different weight percentages (10, 15 and 20%) were added to it. Subsequently, gentamicin with three various concentrations (1, 2 and 3%), named G1, G2 and G3, were added to the solutions. Finally, prepared solutions were electrospun on fabricated PVDF layer under persistent electrospinnig conditions (flow rate: 8 ml/h, applied voltage: 21 kV and distance: 15 cm).

2.3. Membrane characterization

The morphology of the electrospun membranes were studied by scanning electron microscope (XL-30, SEM; Philips, Amsterdam, The Netherlands) after sputter coating of samples by gold. The average diameter of each membrane was determined from a hundred random measurements using Digimizer software.

Fourier transform infrared (FTIR) spectroscopy was applied for investigation of the reaction between polymers and drug. A FTIR spectrophotometer (BOMEM-MB-series 100) was applied with wavelength in the range of 500–4000 cm^{-1} for analysis of electrospun membranes.

2.4. Degree of Water absorption and weight loss

To observe degree of water absorption and weight loss of prepared samples, phosphate buffered saline (PBS, PH: 7.4) with temperature of 37 °C was utilized. Both tests were carried out in several times including 2, 4, 24, 168 and 336 h. Then, mentioned properties were calculated using following equations.

$$\text{Water absorption } (\%) = \frac{M - M_d}{M_d} \times 100 \quad (1)$$

$$\text{Weight loss } (\%) = \frac{M_i - M_d}{M_i} \times 10 \quad (2)$$

Where M is the weight of swollen membrane, M_d is the dried mass of immersed sample in buffer medium (obtained after locating swollen nanofibrous mat in oven at 40 °C until constant weight was reached, and M_i is the initial mass of dry sample[27, 28].

2.5. Mechanical properties

The tensile test of samples was performed according to ASTM D882-12 using tensile testing machine (Zwick 1446-60) with 20N load cell and cross- head speed of 10 mm/min. Samples were prepared with dimensions of 3 cm ×0.5 cm before measurement.

2.6. In vitro drug release studies and analysis of drug-release kinetics

Drug delivery of electrospun mats was measured by placing samples with approximate dimensions of 1 cm ×6 cm and specific weight in 20 ml of PBS (PH = 7.4 at 37 °C). Afterwards, 2 ml of solution was removed at specific time points and the amount of drug release was determined using a UV Spectrophotometer at $\lambda_{max} = 200$ nm. The release experiment was repeated three times for each sample and average values were considered.

In order to discover the mechanism of drug release in electrospun samples, zero order, first order, Higuchi and Korsmeyer-Peppas models were also examined[28, 29].

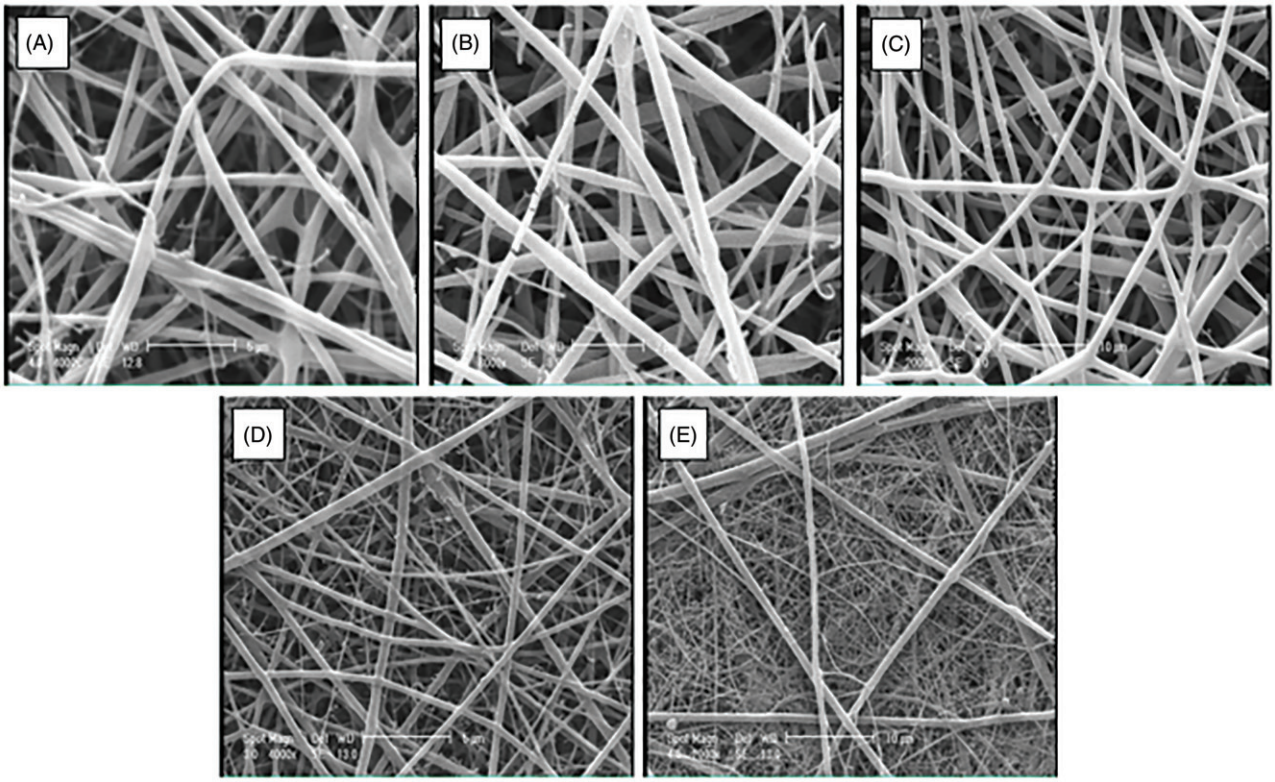

Figure 1. SEM images of electrospun mats: (A) PVDF, (B) PVDF/PHB90%/CTS10%, (C) PVDF/PHB85%/CTS15%, (D) PVDF/PHB80%/CTS20%, (E) PHB85%/CH15%.

Table 1. Average diameter, standard deviation and CV% of samples.

Sample	Material	Average diameter (nm)	Standard deviation (S.D)	CV%
S1	PVDF	207	55.68	26.8
S2	PHB90%/ CTS10%/ PVDF	116	28.26	24.4
S3	PHB85%/ CTS15%/ PVDF	108	28.45	26.34
S4	PHB80%/ CTS20%/ PVDF	149	43.8	29.39
S5	PHB85%/ CH15%	100	26.05	26.05

2.7. Statistics and data analysis

Statistical analysis of obtained data was performed applying SPSS software package (SPSS, Chicago, IL) by one-way analysis of variance (ANOVA), assuming a confidence level at 95% (p-value 0.05) for statistical significance.

3. Result and discussion

3.1. Morphological structure studies

Figure 1 displays a picture of electrospun samples. As it can be seen, uniform nanofibers without beads are formed during electrospinning. However, increase in CTS ratio from 10% to 15% causes nanofiber formation with more monotony that can be related to low viscosity of CTS solution and in addition, it may be associated with the point that CTS is naturally positively charged which help electrospinning process to be improved. Allocated code to electrospun samples and their average diameter is given in Table 1. It is apparent from SEM images and this table that sample S3 containing PVDF as substrate layer and a hybrid nanofibrous layer (PHB/CTS: 85/15) possesses fine and uniform nanofibers in comparison with other fabricated samples.

The FTIR spectra of the polymers, drug and a drug-loaded nanofibrous sample are represented in Figure 2. As it is revealed, PHB has a characteristic absorption peak in 1733 cm^{-1} that is related to tensile absorbance of carbonyl group (υ c = o). CTS displays two characteristic absorption bands in 3434 cm^{-1} and 1611 cm^{-1}, attributed to tensile absorbance of hydroxyl (NH and NH deformation, respectively). PVDF have characteristic peaks at: 1185 cm^{-1} related to tensile absorbance of CF_2 and 838.6 cm^{-1} that can be due to tensile absorbance of CF.

Also Gentamicin have two characteristic absorption peaks at 1539 cm^{-1} that can be related to NH vibration, CH Stretching vibration and CN stretching vibration and at 1068 cm^{-1} (CN and CO stretching vibrations). Hence, due to observation of all characteristic peaks in drug-loaded nanofibrous mat spectra, there were not any specific interactions between materials.

3.2. Mechanical properties

Mechanical properties was conducted to analyze stress, strain and Young's modulus of samples. Figure 3 illustrates typical stress-strain curves of fabricated membranes. As it was predicted, PVDF nanofiber structure owns the highest

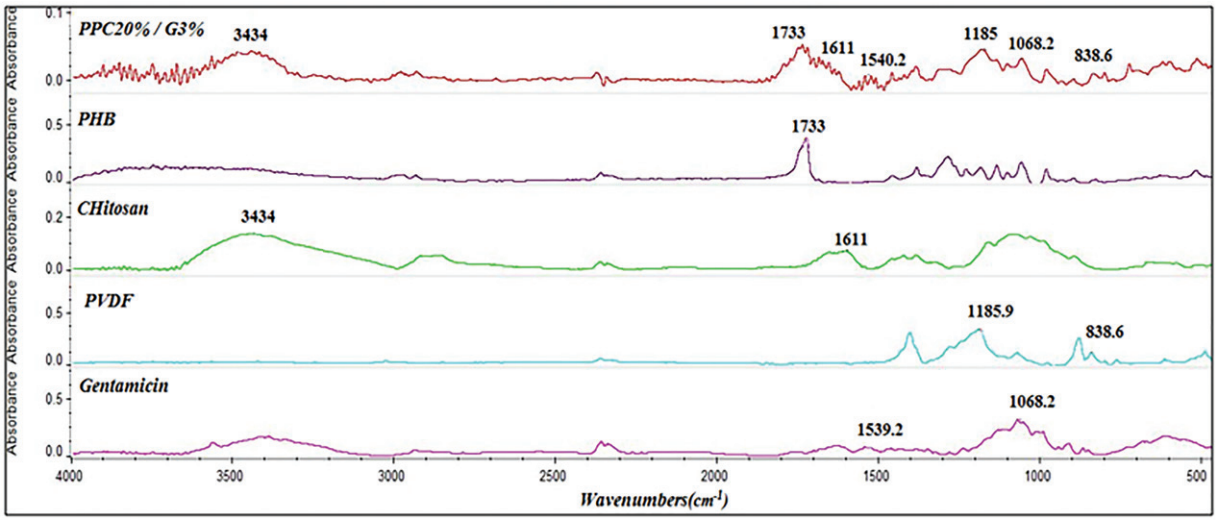

Figure 2. FTIR Spectroscopy of polymers, drug and a drug- loaded electrospun membrane.

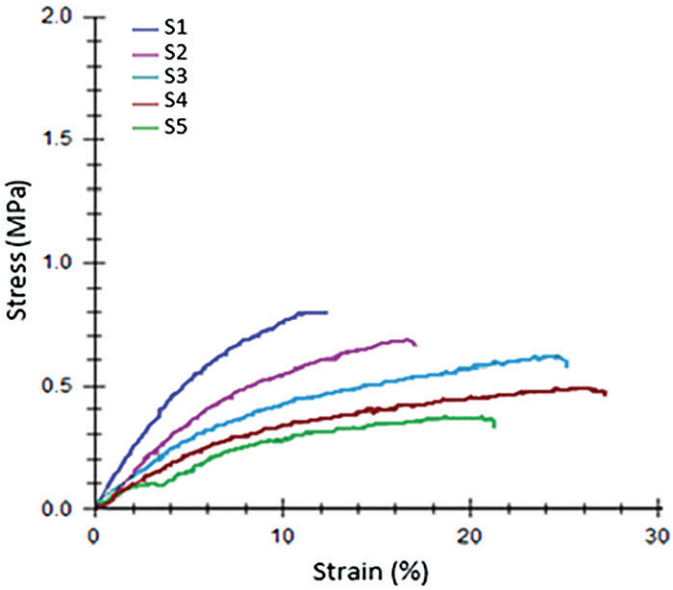

Figure 3. Typical tensile stress-strain curves of samples: S1, S2, S3, S4 and S5.

Table 2. Tensile properties of nanofibrous structures.

number	Stress (MPa)	Elastic modulus (MPa)
S1	0.57	6.60
S2	0.50	5.22
S3	0.49	5.31
S4	0.47	4.97
S5	0.26	2.20

stress and the lowest strain between prepared samples. It is while, addition of CTS to the mixture causes reduction of stress and increase in strain.

Table 2 illustrates some of the main tensile characteristics of samples S1–S5. From the data in Figure 3 and Table 2, it is apparent that S1 containing pure PVDF nanofibers owns greater stress and Young's modulus in comparison to other nanofibrous structures. Also there is a significant difference between tensile properties of sample S5 and other membranes which are formed from two layers. This result could be attributed to the same reason that tensile strength of PVDF nanofibers is much higher than CTS/PHB nanofibers. So this layer plays an effective role in providing adequate mechanical properties that is required for wound dressing application.

3.3. Degree of water absorption and weight loss

Swelling degree and weight loss are two valuable parameters contributing to drug release. Figure 4 provides the results obtained from weight loss and swelling degree of fabricated samples in the release medium (PH 7.4) and several times. What stands out from the figures is rise of weight loss with increase in CTS ratio.

PHB, such as other aliphatic polyesters, is a hydrophobic polymer and as a result water penetration into its polymer chains is actual difficult. Hence, in the presence of phosphate buffer solution, PHB starts to be destructed only from the surface and so it represents slow rate of degradation. By addition of CTS, which is a hydrophilic polymer, water can easily penetrates to the structure and so destruction of the nanofibrous structures happens in both surface and bulk of fabricated membranes.

Data obtained from swelling degree of prepared samples, shown in Figure 4(b), can be compared with the reported data in previous studies[2, 3]. Results show enough degree of swelling that is essential for absorbing excess exudates in wound dressings. In general, samples S2–S5 in the first 24 h represented about 70% of water absorption. However, reduction of water absorption was observed after this time due to destruction of CTS nanofibers during first 24 h. In fact, the destruction rate is greater than swelling degree in CTS nanofibers and thus a lower number of nanofibers are available to absorb phosphate buffer after this period of time.

3.4. In vitro drug release study of nanofibers

Figure 5 exhibits drug release profile of samples in various time intervals. As shown in the figure, in all samples about 30% of gentamicin is released in 2 h and a constant value is

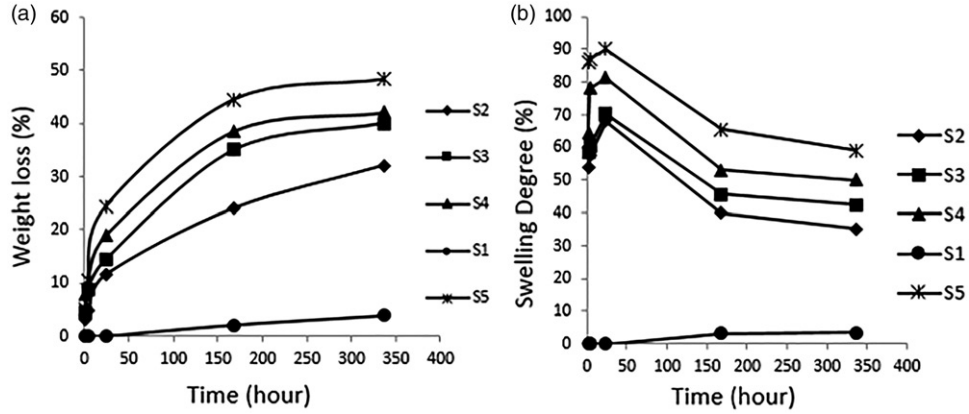

Figure 4. (a) Weight loss and (b) Swelling degree of nanofibrous samples: S1, S2, S3, S4 and S5.

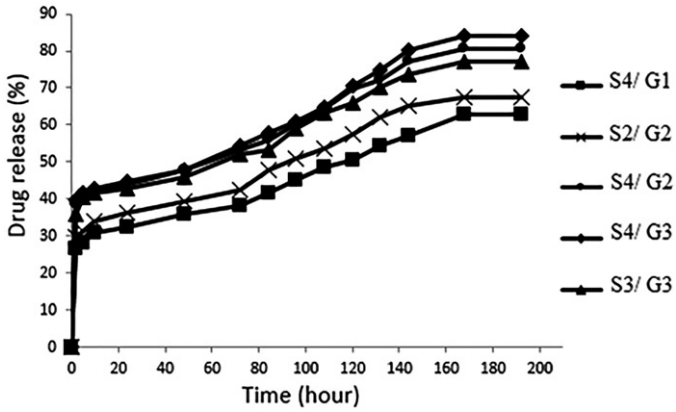

Figure 5. Drug release profile of samples: S4/G1, S2/G2, S4/G2, S4/G3 and S3/G3.

Table 3. Correlation coefficient values of electrospun samples.

	Correlation coefficient value		
Sample	Zero order model	First order model	Higuchi
S1	0.85	0.90	0.80
S2	0.94	0.96	0.65
S3	0.89	0.97	0.9
S4	0.96	0.99	0.88
S5	0.97	0.98	0.95

Table 4. Release component of fabricated samples.

sample	n
S1	0.2
S2	0.3
S3	0.08
S4	0.3
S5	0.1

reached after 132 h. It can be attributed to the high inflation and water permeability of CTS nanofibers. In addition, good solubility of gentamicin in phosphate buffer and presence of soluble molecules through inflation leads to the primary sudden release. This feature makes it suitable for using in various applications specifically in wound dressings, since primary sudden release can improve and accelerate treatment. Also, secretions from the wound is a good place for growth of bacteria, preventing their growth in the early hours inhibits infections of the wound. Furthermore, by comparison between biodegradation and drug delivery results, it is apparent that sample S3 with higher rate of degradation between all prepared samples, have more drug delivery speed as well.

3.5. Kinetics and mechanism of drug release

Correlation coefficients of three models including zero order, first order and Higuchi were calculated to determine the kinetics of drug release. The correlation coefficient values are indicated in Table 3.

Statistical analysis showed that, correlation coefficients of three models have a significant difference together. It appears from Table 3 that the correlation coefficient of first order model is higher than two other models. Actually, the release of gentamicin from nanofibers follow kinetic of first order model.

Moreover, release component "*n*" was calculated following the Peppas equation to obtain mechanism of drug release. Average results are reported in Table 4. From the table it can be seen that release component for all samples is less than 0.5. Therefore mechanism of drug release in nanofibrous samples follows Fickian mechanism and thus publication is more effective in drug release from nanofibers[30].

4. Conclusion

In summary, a novel bilayer nanofibrous wound dressing was successfully prepared by electrospinning method. PHB/CTS hybrid nanofibrous layer was electrospun as one layer to provide controlled drug delivery, while nanofibrous PVDF was fabricated to improve tensile strength of fabricated mats. All prepared samples showed bead free and uniform nanofibers. In addition, mechanical strength of PHB/CTS electrospun layer with various structures were dramatically improved with addition of PVDF nanofibers to fabricated samples. Furthermore, biodegradation rate and weight loss rose with increase in CTS ratio in membranes, which is a hydrophilic polymer. In addition, drug release profile from nanofibrous mats showed that drug delivery increases with addition of CTS ratio and drug-loaded in the structures. Moreover, Gentamycin release from nanofiber wound dressings represented a sustained release for about one week.

Obtained results also showed that gentamicin release from electrospun membranes follows Fickian release mechanism. Based on calculation of correlation coefficients for zero order, first order and Higuchi models, it can be concluded that release kinetic of gentamicin from electrospun mats follows first order model.

References

[1] Kore, S.; Vyavaharkar, M.; Akolekar, R.; Toke, A.; Ambiye, V. Comparison of Closure of Subcutaneous Tissue Versus Non-Closure in Relation to Wound Disruption after Abdominal Hysterectomy in Obese Patients. *J Postgrad Med*. **2000**, *46*, 26.

[2] Lazarus, G. S.; Cooper, D. M.; Knighton, D. R.; Margolis, D. J.; Percoraro, R. E.; Rodeheaver, G.; Robson, M. C. Definitions and Guidelines for Assessment of Wounds and Evaluation of Healing. *Wound Repair Regen*. **1994**, *2*, 165–170.

[3] Zahedi, P.; Rezaeian, I.; Ranaei-Siadat, S.-O.; Jafari, S.-H.; Supaphol, P. A Review on Wound Dressings with an Emphasis on Electrospun Nanofibrous Polymeric Bandages. *Polym. Adv. Technol*. **2010**, *21*, 77–95.

[4] Hanna, J. R.; Giacopelli, J. A. A Review of Wound Healing and Wound Dressing Products. *J Foot Ankle Surg*. **1997**, *36*, 2–14.

[5] Boateng, J. S.; Matthews, K. H.; Stevens, H. N. E.; Eccleston, G. M. Wound Healing Dressings and Drug Delivery Systems: A Review. *J. Pharm. Sci*. **2008**, *97*, 2892–2923.

[6] Dabiri, G.; Damstetter, E.; Phillips, T. Choosing a Wound Dressing Based on Common Wound Characteristics. *Adv. Wound Care*. **2016**, *5*, 32–41.

[7] Abrigo, M.; McArthur, S. L.; Kingshott, P. Electrospun Nanofibers as Dressings for Chronic Wound Care: Advances, Challenges, and Future Prospects. *Macromol. Biosci*. **2014**, *14*, 772–792.

[8] Khil, M. -S.; Cha, D. -I.; Kim, H. -Y.; Kim, I.-S.; Bhattarai, N. Electrospun Nanofibrous Polyurethane Membrane as Wound Dressing. *J. Biomed. Mater. Res. Part B Appl. Biomater*. **2003**, *67*, 675–679.

[9] Cai, Z. –X.; Mo, X. -M.; Zhang, K. –H.; Fan, L. -P.; Yin, A.-L.; He, C. –L.; Wang, H. –S. Fabrication of Chitosan/Silk Fibroin Composite Nanofibers for Wound-Dressing Applications. *Int. J. Mol. Sci*. **2010**, *11*, 3529–3539.

[10] Chen, S.; Liu, B.; Carlson, M. A.; Gombart, A. F.; Reilly, D. A.; Xie, J. Recent Advances in Electrospun Nanofibers for Wound Healing. *Nanomedicine*. **2017**, *12*, 1335–1352.

[11] Sridhar, R.; Lakshminarayanan, R.; Madhaiyan, K.; Barathi, V. A.; Lim, K. H. C.; Ramakrishna, S. Electrosprayed Nanoparticles and Electrospun Nanofibers Based on Natural Materials: Applications in Tissue Regeneration, Drug Delivery and Pharmaceuticals. *Chem. Soc. Rev*. **2015**, *44*, 790–814.

[12] Chong, E. J.; Phan, T. T.; Lim, I. J.; Zhang, Y. Z.; Bay, B. H.; Ramakrishna, S.; Lim, C. T. Evaluation of Electrospun Pcl/Gelatin Nanofibrous Scaffold for Wound Healing and Layered Dermal Reconstitution. *Acta Biomater*. **2007**, *3*, 321–330.

[13] Ignatova, M.; Manolova, N.; Rashkov, I. Electrospun Antibacterial Chitosan-Based Fibers. *Macromol. Biosci*. **2013**, *13*, 860–872.

[14] Ashley, G. W.; Henise, J.; Reid, R.; Santi, D. V. Hydrogel Drug Delivery System with Predictable and Tunable Drug Release and Degradation Rates. *Proc. Natl. Acad. Sci*. **2013**, *110*, 2318–2323.

[15] Hu, X.; Liu, S.; Zhou, G.; Huang, Y.; Xie, Z.; Jing, X. Electrospinning of Polymeric Nanofibers for Drug Delivery Applications. *J. Control. Release*. **2014**, *185*, 12–21.

[16] Correia, D. M; Ribeiro, C.; Ferreira, Jose C. C.; Botelho, G.; Ribelles, Jose L. G.; Lanceros-Méndez, S. and Sencadas, V. Influence of Electrospinning Parameters on Poly (Hydroxybutyrate) Electrospun Membranes Fiber Size and Distribution. *Polym. Eng. Sci*. **2014**, *54*, 1608–1617.

[17] Volova, T.; Shishatskaya, E.; Sevastianov, V.; Efremov, S.; Mogilnaya, O. Results of Biomedical Investigations of Phb and Phb/Phv Fibers. *Biochem. Eng. J*. **2003**, *16*, 125–133.

[18] Wang, A.; Liu, Z.; Hu, M.; Wang, C.; Zhang, X.; Shi, B.; Fan, Y.; Cui, Y.; Li, Z.; Ren, K. Piezoelectric Nanofibrous Scaffolds as in Vivo Energy Harvesters for Modifying Fibroblast Alignment and Proliferation in Wound Healing. *Nano Energy*. **2018**, *43*, 63–71.

[19] Asran, A. S.; Razghandi, K.; Aggarwal, N.; Michler, G. H.; Groth, T. Nanofibers from Blends of Polyvinyl Alcohol and Polyhydroxy Butyrate as Potential Scaffold Material for Tissue Engineering of Skin. *Biomacromolecules*. **2010**, *11*, 3413–3421.

[20] Abdelgawad, A. M.; Hudson, S. M.; Rojas, O. J. Antimicrobial Wound Dressing Nanofiber Mats from Multicomponent (Chitosan/Silver-Nps/Polyvinyl Alcohol) Systems. *Carbohydr Polym*. **2014**, *100*, 166–178.

[21] Chen, J.-P.; Chang, G.-Y.; Chen, J.-K. Electrospun Collagen/Chitosan Nanofibrous Membrane as Wound Dressing. *Colloids Surf. A*. **2008**, *313*, 183–188.

[22] Sadeghi, D.; Karbasi, S.; Razavi, S.; Mohammadi, S.; Shokrgozar, M. A.; Bonakdar, S. Electrospun Poly (Hydroxybutyrate)/Chitosan Blend Fibrous Scaffolds for Cartilage Tissue Engineering. *J. Appl. Polym. Sci*. **2016**, *133*.

[23] Hu, S.-G.; Jou, C.-H.; Yang, M.-C. Antibacterial and Biodegradable Properties of Polyhydroxyalkanoates Grafted with Chitosan and Chitooligosaccharides Via Ozone Treatment. *J. Appl. Polym. Sci*. **2003**, *88*, 2797–2803.

[24] Bouaziz, A.; Richert, A.; Caprani, A. Vascular Endothelial Cell Responses to Different Electrically Charged Poly (Vinylidene Fluoride) Supports under Static and Oscillating Flow Conditions. *Biomaterials*. **1997**, *18*, 107–112.

[25] He, T.; Wang, J.; Huang, P.; Zeng, B.; Li, H.; Cao, Q.; Zhang, S.; Luo, Z.; Deng, D. Y. B.; Zhang, H. Electrospinning Polyvinylidene Fluoride Fibrous Membranes Containing Anti-Bacterial Drugs Used as Wound Dressing. *Colloids Surf. B*. **2015**, *130*, 278–286.

[26] Laroche, G.; Marois, Y.; Guidoin, R.; King, M. W.; Martin, L.; How, T. and Douville, Y. Polyvinylidene Fluoride (Pvdf) as a Biomaterial: From Polymeric Raw Material to Monofilament Vascular Suture. *J Biomed Mater Res A*. **1995**, *29*, 1525–1536.

[27] Johnson, K. C. Dissolution and Absorption Modeling: Model Expansion to Simulate the Effects of Precipitation, Water Absorption, Longitudinally Changing Intestinal Permeability, and Controlled Release on Drug Absorption. *Drug Dev. Ind. Pharm*., **2003**, *29*, 833–842.

[28] Dash, S.; Murthy, P. N.; Nath, L.; Chowdhury, P. Kinetic Modeling on Drug Release from Controlled Drug Delivery Systems. *Acta Pol Pharm*. **2010**, *67*, 217–23.

[29] Fu, Y.; Kao, W. J. Drug Release Kinetics and Transport Mechanisms of Non-Degradable and Degradable Polymeric Delivery Systems. *Expert Opin Drug Deliv*. **2010**, *7*, 429–444.

[30] Brazel, C. S; and Peppas, N. A. Modeling of Drug Release from Swellable Polymers. *Eur. J. Pharm. Biopharm*. **2000**, *49*, 47–58.