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Preparation and characterization of poly(ethylene oxide)-loaded hydroxypropyl-*β*-cyclodextrin nanofibers

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Hydroxypropyl-*β*-cyclodextrin (HP-*β*-CD) is a modified *β*-cyclodextrin (*β*-CD) derivative, which is toxicologically harmless to mammals and other animals. HP-*β*-CD is electrospun from an aqueous solution by blending with a non-toxic, biocompatible, synthetic polymer poly(ethylene oxide) (PEO). Aqueous solutions containing different HP-*β*-CD/PEO blends (50:50–80:20) with variable concentrations (4 wt%–12 wt%) were used. Scanning electron microscope was used to investigate the morphology of the fibers, and Fourier transform infrared spectroscopy analysis confirmed the presence of HP-*β*-CD in the fiber. Uniform nanofibers with an average diameter of 264, 244, and 236 nm were obtained from 8 wt% solution of 50:50, 60:40, and 70:30 HP-*β*-CD/PEO, respectively. The average diameter of the fiber was decreased with increasing of HP-*β*-CD/PEO ratio. However, a higher proportion of HP-*β*-CD in the spinning solution increased beads in the fibers. The polymer concentration had no significant effect on the fiber diameter. The most uniform fibers with the narrowest diameter distribution were obtained from the 8 wt% of 50:50 solution.

Keywords: electrospinning; hydroxypropyl-β-cyclodextrin; poly(ethylene oxide)

INTRODUCTION

Cyclodextrins (CDs) are water soluble biocompatible material composed of cyclic oligosaccharides. The CDs are synthesized by enzymatic degradation of maize, rice, corn husk, potatoes, and sago.[1] A number of CDs have been produced yet, but the most common and popular CDs are αCD, βCD, and γCD, which have 6, 7, and 8 glucose units, respectively. The structure of CDs is formed with a hydrophobic internal cavity that can accommodate suitably sized, generally low molecular weight lipophilic molecules. In general, the CDs are not harmful to animal and human bodies although a minor toxicity is evidenced when dosed orally.[2] Thus, CDs have been used as a good drug-carrying agent for delivering drugs in human body. Besides, these hydrophobic cavities can entrap volatile organic compounds (VOCs) by forming inclusion complexes. Because of its ability to entrap VOCs and low molecular weight lipophilic compounds, it can be used as filters, food ingredients to remove unwanted tastes or smell, odor-absorbing fabrics, odor-absorbing masks, odor-absorbing wound dressings, and odor-absorbing personal products like feminine pads, nappy, underwear, and clothing.[3] Hydroxypropyl-β-cyclodextrin (HP-β-CD) is a modified β-cyclodextrin (β-CD), which can be produced by reacting β-CD with propylene oxide in an alkaline aqueous solution. Conventionally, HP-β-CD is applied on fabrics or other substrates using additional adhesive or resin, which may increase the stiffness of the fabrics or substrates. Application of HP-β-CD by electrospinning can achieve similar function without the negative effect on the stiffness of the substrates. However, HP-β-CD is not suitable for electrospinning because of its low molecular weight and high degree of aggregation in solution.[4] Blending with PEO, a non-toxic biocompatible high molecular weight linear polymer, makes it possible to electrospin HP-β-CD into smooth nanofibers, which can be applied on fabrics or dressing substrates.

EXPERIMENTAL

Materials

2-hydroxypropyl-β-cyclodextrin (Mw = 1460; molecular formula: [C6H9O5]7[C3H7O], brand name: CAVSOL®W7 HP) was supplied by Wacker Chemie AG (Munich, Germany), and poly(ethylene oxide) (PEO) (Mw = 900,000) was supplied by Sigma-Aldrich (Dorset, UK). These chemicals were used without further modification. Purified distilled water was used to prepare spinning solution.

Preparation of electrospinning solution

Predetermined amount of HP-β-CD and PEO powder were dissolved in distilled water in a glass bottle. Then the sealed bottle was transferred to a magnetic stirrer, and the solution was gently stirred at room temperature for 24 h to obtain a homogeneous spinning solution. Solutions with a total polymer concentration of 4–12% (w/w, with respect to solution) of 50:50–90:10 HP-β-CD/PEO blend were prepared.

Electrospinning setup and process

A typical electrospinning setup (Fig. 1) was used to make HP-β-CD/PEO nanofibers. A syringe, filled with a specific amount of

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spinning solution, was fitted to the pump. The process parameters were set as the working distance 12 cm, the feed rate 1 ml/h, and the applied voltage 7 kV. The applied voltage was adjusted at 7 kV because this enabled the formation of a stable fiber jet. The electrospinning was carried out for 30 min to prepare each sample. An aluminum foil was fixed on the metal collector. Samples were collected on the foil and dried for 24 hr at room temperature to remove any residual solvents. All the experiments were carried out at ambient atmospheric conditions.

Characterization of electrospun fibers

Characterization of as-spun electrospun nanofibers was done by a field gun emission scanning electron microscope (SEM; PHILIPS XL30 FEG-SEM, FEI company, Hillsboro, USA) and Fourier transform infrared spectroscopy (FTIR; model: NICOLET5700 FT-IR; manufacturer: Thermo Electron Corporation, Madison, USA). The electrospun fiber mesh on the specimen stub was coated with carbon by using *gatan* Precision Etching Coating System (model: 682). The images were taken at 2000×, 10,000×, and 20,000× magnifications. The SEM operating parameters were set at accelerating voltage 6 kV and spot size 3. The fiber diameters and fibers collection zone were manually measured by using the line-drawing feature of ImageJ [11] software. The measurements of fiber diameters were taken both in beaded and non-beaded places of 30 randomly selected fibers from the 10,000× and 20,000× magnification images at three different focal points. The average diameters of the collection zones were measured from three samples; each sample was measured in two directions—vertically and horizontally. The presence of HP-*β*-CD in the nanofiber was confirmed by FTIR analysis. The infrared spectral of absorption mode of the nanofibers surface was obtained from FTIR spectrometer, which was connected with a PC. The spectra were scanned with a spectral range of 4000–400 cm^{-1} with 32 scans and a resolution of 4 cm^{-1}.

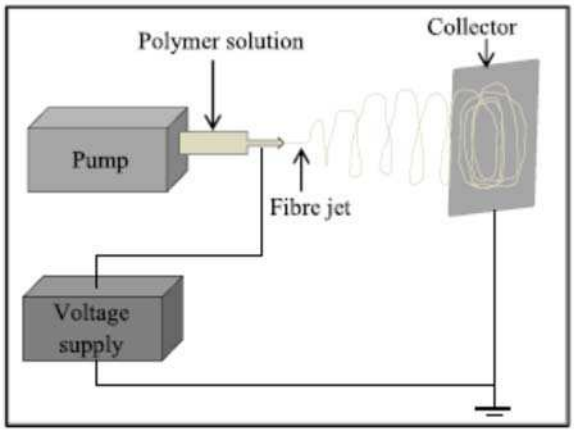

Figure 1. Schematic of electrospinning and laboratory set-up.

RESULTS AND DISCUSSIONS

Electrospinning of HP-*β*-CD/PEO

Electrospinning of HP-*β*-CD/PEO was carried out with varying mass ratios and concentrations at constant electrospinning conditions to obtain smooth nanofibers. Table 1 shows the summary of the spinning solution composition, the properties of yielded nanofibers, and the nanofibers collection zones (nanofibers web). Figure 2 shows the nanofiber webs on the collector obtained from the variable blend ratios and concentrations. The graph, shown in Fig. 3(A), showed that the size of the fiber collection zone increased with increasing proportion of HP-*β*-CD in the solution. The blend of 80:20 or more spread over a large area without making a clear fiber collection zone. This indicates the generation of uncontrolled electrospun jet with increasing blend ratio. This may have happened because of higher content of HP-*β*-CD at higher solution concentration causing molecular aggregation. This may lead to incomplete stretching of the solution jet during electrospinning, which was also seen in a previous study.[4] The solution of 50:50 blend of 4 wt% concentration shows a similar

Table 1. Properties of electrospinning solution of hydroxypropyl-*β*-cyclodextrin/poly(ethylene oxide) (HP-*β*-CD/PEO) and resulting nanofibers

Polymer concentration (wt%)	HP-*β*-CD/PEO ratio	Fiber diameter range (nm)	Average diameter (nm)	Fiber morphology	Average diameter of fiber web (cm)
8	50:50	240–289	264	Smooth fibers	9.2
8	60:40	189–301	244	Smooth fibers	10.5
8	70:30	128–390	236	Very few beads	15.5
8	80:20	80–1628	208	Mainly beads	—
4	50:50	60–972	268	Mainly beads	—
6	50:50	177–362	248	Smooth fibers	12.5
8	50:50	240–289	264	Smooth fibers	9.2
10	50:50	194–302	254	Smooth fibers	7.4
12	50:50	128–328	281	Branched fibers	5.7

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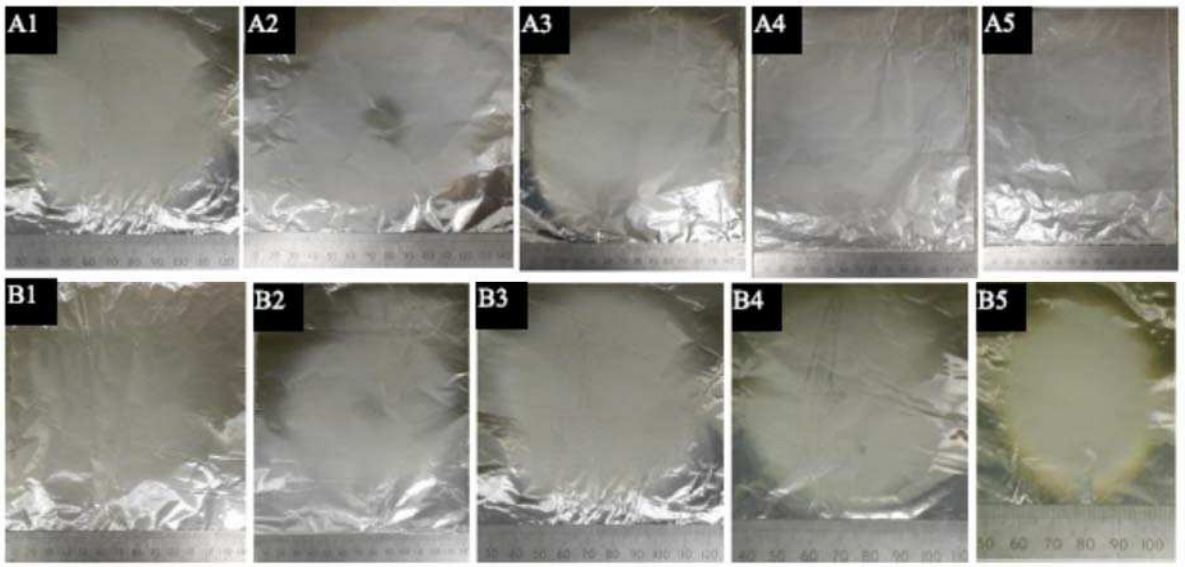

Figure 2. Fibers collection: 8 wt% of (A1) 50:50, (A2)60:40, (A3) 70:30, (A4) 80:20, and (A5) 90:10 hydroxypropyl-*β*-cyclodextrin/poly(ethylene oxide) (HP-*β*-CD/PEO) and (B1) 4 wt%, (B2) 6 wt%, (B3) 8 wt%, (B4) 10 wt%, and (B5) 12 wt% of 50:50 HP-*β*-CD/PEO.

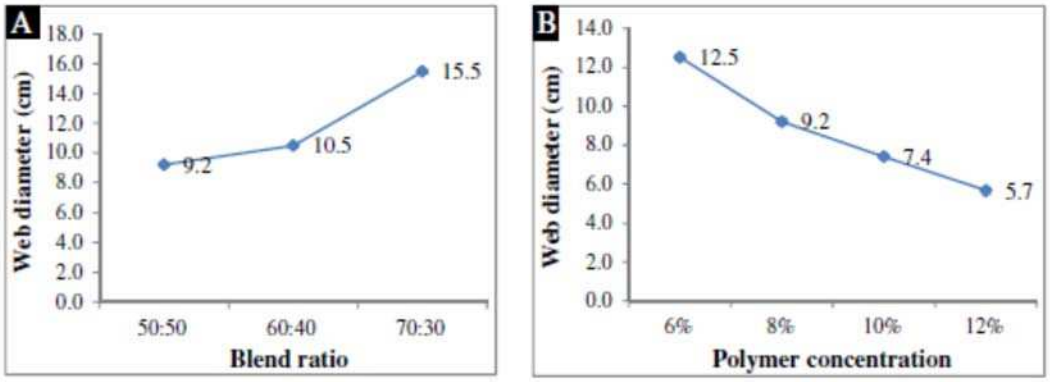

Figure 3. (A) Hydroxypropyl-*β*-cyclodextrin/poly(ethylene oxide) (HP-*β*-CD/PEO) blend ratio versus fiber collection zone and (B) HP-*β*-CD/PEO concentration versus fiber collection zone.

effect. This may be due to insufficient amount of polymer, which results in insufficient viscosity and molecular chain entanglement. In both of these cases, an electrospraying of HP-*β*-CD may have taken place instead of electrospinning. At low polymer concentrations, the solution jet sprayed as droplets or formed bead-on-string fiber structures instead of forming smooth fibers.[12] Moreover, the presence of low molecular weight HP-*β*-CD in the solution deteriorates the viscosity, which causes the electrified solution jet to spread over a large area. Figure 2 shows that the 6–12 wt% solutions produce controlled fiber jets and formed clear circular-shaped fiber webs. It is found that high polymer concentrations produce stable and controlled fiber jets. Figure 3(B) shows that the size of fiber collection zone decreased with increasing the polymer concentration. This indicates that the size of the fiber collection zone is inversely related to the polymer concentration.

Morphological properties of electrospun HP-*β*-CD/PEO nanofibers

Figure 4 shows the SEM images of HP-*β*-CD/PEO nanofibers obtained from 8 wt% of 50:50–80:20 solutions and 50:50 of 4–12 wt% solutions. It was found that 70:30 and lower blends yielded bead-free or less-beaded fibers, and the 80:20 blend yielded beaded fibers with a pearl structure. Table 1 shows that the 50:50, 60:40, and 70:30 HP-*β*-CD/PEO blends yielded fibers with an average diameter of 264 nm, 244 nm, and 236 nm, respectively, and with an increasing distribution of fiber diameter. The graph, shown in Fig. 5(A), provides the relative changes of the fiber diameter with respect to blend ratio. The results indicate that the increase of the fraction of HP-*β*-CD in the solution decreases the fiber diameter and increases bead formation. Uyar *et al.* (2008) have found that uniform fibers are yielded at a low weight content of *α*-CD-poly(ethylene glycol) inclusion complex (50% to 100% w/w with respect to PEO) and beaded fibers were produced at a higher weight content (200% w/w with respect to PEO).[4] They explained that the possible reason for that was the presence of higher content of low molecular weight *α*-CD-poly(ethylene glycol), which showed high crystallinity and degree of aggregation in the solution. The same phenomenon may have happened in the HP-*β*-CD/PEO solution, and the aggregation of HP-*β*-CD causes incomplete stretching during electrospinning. As a result, beads were

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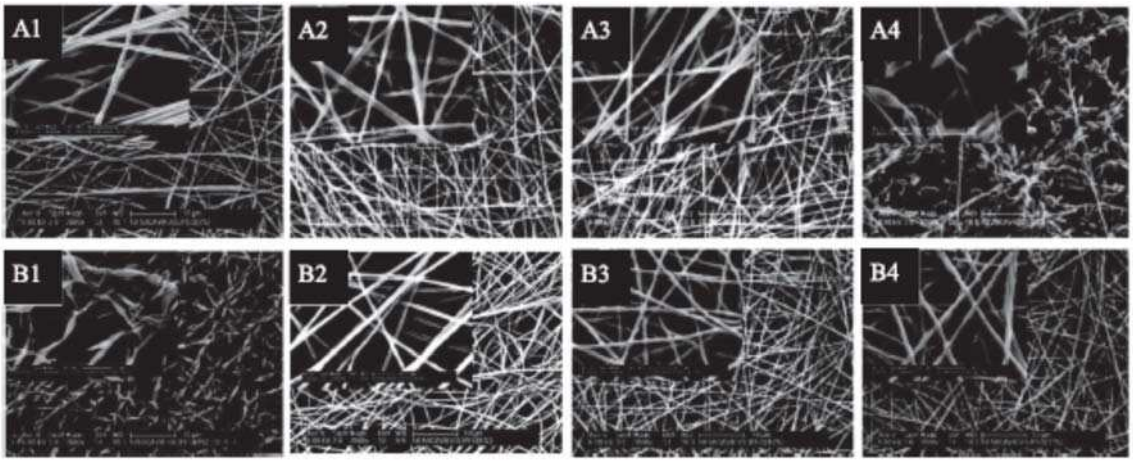

Figure 4. The electrospun nanofibers of 8 wt% of (A1) 50:50, (A2) 60:40, (A3) 70:30, and (A4) 80:20 Hydroxypropyl-*β*-cyclodextrin/poly(ethylene oxide) (HP-*β*-CD/PEO) blend ratios and the nanofibers of 50:50 HP-*β*-CD/PEO from (B1) 4 wt%, (B2) 6 wt%, (A1) 8 wt%, (B3) 10 wt%, and (B4) 12 wt% polymer concentration.

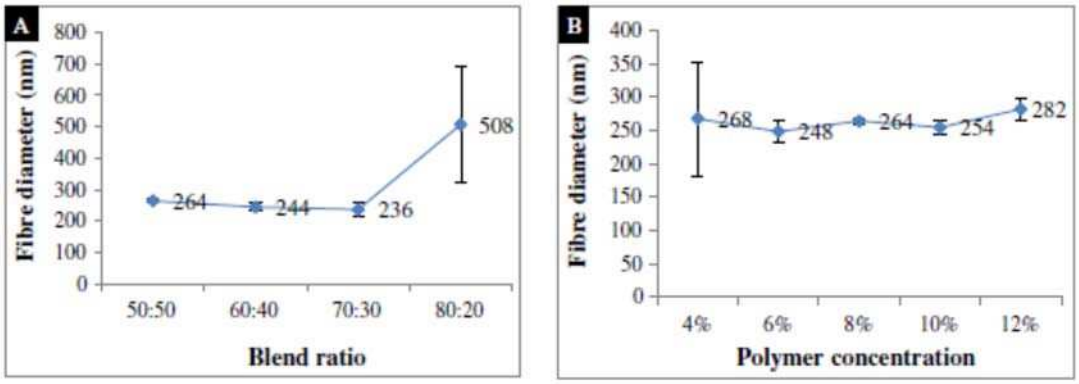

Figure 5. (A) Hydroxypropyl-β-cyclodextrin/poly(ethylene oxide) (HP-β-CD/PEO) blend ratio versus nanofiber diameter and (B) HP-β-CD/PEO concentration versus nanofiber diameter.

formed in the resultant fibers. Other studies have also found that bead formation increased, and average diameter decreased as the proportion of non-spinnable sodium alginate in sodium alginate/PEO blend increased.[13, 14]

The surface morphology of HP-*β*-CD/PEO electrospun nanofiber is greatly influenced by polymer concentration. Several studies have shown the effects of polymer concentration on the diameter and morphology of electrospun fibers.[15-18] Higher polymer concentrations are more likely to be produced uniform fibers with higher diameter. Higher viscosity, which can be achieved by increasing polymer concentration, is essential for yielding continuous fibers. It promotes polymer chain entanglement and increases viscoelastic force, which resists the Coulombic stretching during electrospinning. As a result, a continuous fiber jet travels towards the collector without break up. However, very high or very low concentrations inhibit fiber formation. Figure 4 shows the morphology of fibers obtained from 50:50 HP-*β*-CD/PEO of 4–12 wt% solutions. The 4 wt% solution produces beads and spindle-like fibers. This may have happened because of inadequate viscosity required for molecular chain entanglement of polymer in the thin solution. The solutions of 6, 8, 10, and 12 wt% produced smooth and uniform fibers with an average diameter of 248 nm, 264 nm, 254 nm, and 281 nm, respectively (Table 1). Figure 5(B) shows the relative changes of fiber diameter corresponding to variable polymer concentrations. The results revealed that the 6–10 wt% solutions produce uniform fiber with insignificant effect on fiber diameter. However, the 8 wt% solution produced the most uniform fibers with the narrowest diameter distribution, and the 12 wt% solution produced some irregular and branched fibers.

Fourier transform infrared spectroscopy studies

Fourier transform infrared spectroscopy was used to confirm the presence of HP-*β*-CD in the nanofibers. Figure 6 shows the spectra of PEO, HP-*β*-CD, and HP-*β*-CD /PEO within the 4000–400 cm^{-1} and 1400–800 cm^{-1} spectral range. It shows the spectral peak variation between PEO nanofibers, pure HP-*β*-CD, and HP-*β*-CD/PEO nanofibers. The blending of PEO with HP-*β*-CD led to an interaction between them, which is confirmed by the FTIR study. The prominent absorption bands of the HP-*β*-CD for C-C/C-O stretching vibrations and the antisymmetric stretching vibration are observed at around 1030 cm^{-1}, 1082 cm^{-1}, and 1149 cm^{-1} in the HP-*β*-CD/PEO nanofibers.

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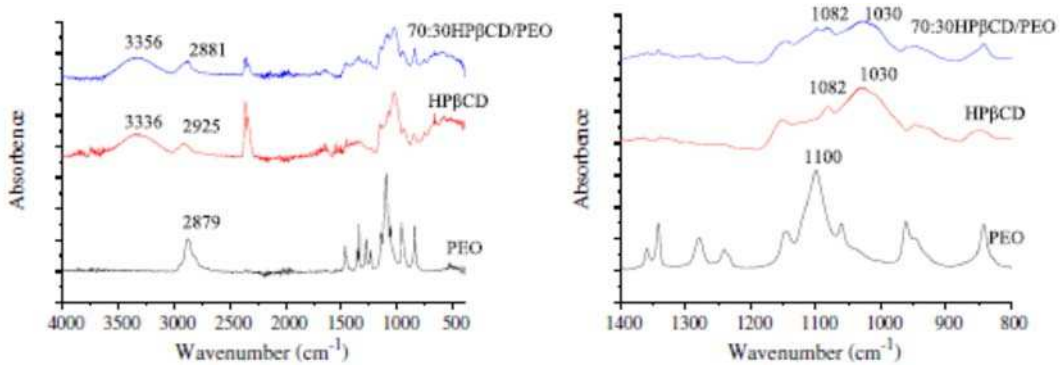

Figure 6. The Fourier transform infrared spectroscopy spectra of poly(ethylene oxide) (PEO), hydroxypropyl-β-cyclodextrin (HP-β-CD), and hydroxypropyl-β-cyclodextrin/poly(ethylene oxide) (HP-β-CD/PEO) nanofibers recorded at room temperature.

These findings are similar to previous studies where CD-functionalized PEO nanofibers were investigated.[3] On the other hand, major bands of PEO for vibration stretching of the ether group (C-O-C) were observed at 1100 cm^{-1}, which shifted to 1082 cm^{-1} in HP-*β*-CD/PEO nanofibers. Moreover, the peaks for –OH group at 3336 cm^{-1} for HP-*β*-CD was moved to 3356 cm^{-1} for HP-*β*-CD/PEO nanofibers because of the incorporation of PEO. The C-H asymmetric stretching band was recorded at 2879 cm^{-1} for PEO and 2925 cm^{-1} for HP-*β*-CD, but it was found at around 2881 cm^{-1} for HP-*β*-CD/PEO nanofiber. These findings confirm the successful electrospinning of HP-*β*-CD/PEO nanofiber.

CONCLUSIONS

This study was carried out to develop functional nanofibers mats from HP-*β*-CD, which would have the ability to accommodate suitably sized target molecules. This nanofiber can be used in controlled drug delivery, tissue engineering applications, filtration, odor absorbing wound dressing, and other personal and healthcare products. These nanofibers can also be incorporated with other substrate to form composite nanofibrous structure that can be used in precise biomedical applications. This study includes the solution properties that are suitable for producing HP-*β*-CD nanofibers. A number of polymer concentrations and blend ratios of HP-*β*-CD/PEO were used in electrospinning experiments to optimize the process. The results reveal that 6–10 wt% concentrations at 50:50 HP-*β*-CD/PEO blend ratio yield bead-free smooth fibers. The blend ratios until 70:30 HP-*β*-CD/PEO at 8 wt% yield bead-free smooth fibers. Overall, the results reveal that electrospinning of 8.0 wt% of 70:30 at 1 ml/hr feed rate, 7 kV applied voltage, and 12 cm working distance provide the best results. The fiber morphology is analyzed by SEM, and FTIR analysis confirmed the presence of HP-*β*-CD in the fibers.

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