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FEATURE ARTICLE

Shuling Shen and Xun Wang
Controlled growth of inorganic
nanocrystals: size and
surface effects of nuclei

Cyclodextrin nanofibers by electrospinning†

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We have demonstrated that cyclodextrin (CD) (a non-polymeric system) can be electrospun into nanofibers by itself; methyl-beta-cyclodextrin (MβCD) nanofibers were electrospun and it was observed that the success of the electrospinning of the CD nanofibers strongly depends on (i) type of solvent, (ii) CD solution concentration and (iii) intermolecular interactions between the CD molecules.

Cyclodextrins (CDs) are cyclic oligosaccharides consisting of α(1,4)-linked glucopyranose units having a truncated cone-shaped molecular structure. Due to their unique molecular structure, CDs can form intriguing supramolecular assemblies by forming non-covalent host-guest inclusion complexes with a variety of small molecules as well as macromolecules. Hence, CDs are applicable in many areas including pharmaceuticals, functional foods, cosmetics and home/personal care, textiles as well as advanced functional systems such as smart materials, sustained/controlled delivery systems, sensor devices, molecular switches or other diagnostic systems.^{1–3} CDs are produced from starch by means of enzymatic conversion and therefore CDs are natural, nontoxic and slowly biodegradable. The most abundant natural cyclodextrins have six, seven or eight glucopyranose units in the cyclic system and are named as α-CD, β-CD and γ-CD, respectively (Fig. 1). Cyclodextrins are capable of self-assembly and form aggregates *via* intermolecular hydrogen bonding in their solutions.^{4,5} Considering the fact that CD molecules form substantial aggregates in their concentrated solutions, such intermolecular interactions can effectively act as chain entanglements in the system and therefore it may be possible to electrospin CD solutions into nanofibers. Cyclodextrins are a very interesting class of molecules and it is anticipated that the electrospinning of such

nanofibers from these supramolecular structures would make them more attractive.

Electrospinning is a very cost-effective and versatile technique for producing functional nanofibers from a variety of materials such as polymers, polymer blends, sol-gels, composites, *etc.*^{6–8} In electrospinning, a continuous filament is spun from a polymer solution under the influence of a very high electrical field, resulting in ultrafine fibers. Electrospun nanofibers/nanowebs have numerous remarkable characteristics such as a very high surface-to-volume ratio with nanoporous structure and they show unique physical and mechanical properties. It has been shown that the very interesting properties and the multi-functional nature of these electrospun nanofibers make them applicable in numerous areas including biotechnology, textiles, membranes/filters, electronics, sensors, energy, *etc.*^{6–8}

In principle, electrospinning involves high molecular weight polymers and high polymer concentrations since chain entanglements and overlapping are necessary for uniform fiber formation,⁹ otherwise, electrospraying occurs which yields beads instead of fibers. During the electrospinning of a polymer solution, the chain entanglements in the charged polymeric fluid provide a stable jet without any break-up into droplets when the electrostatic repulsive forces overcome the surface tension of the polymer solution. Very recently, Long *et al.* showed that low molar mass gemini ammonium surfactant (*N,N'*-didodecyl-*N,N,N',N'*-tetramethyl-*N,N'*-ethanediyl-diammonium dibromide)¹⁰ and phospholipid (lecithin)¹¹ solutions can be electrospun into micron sized fibers since these molecules form cylindrical micelles which can become overlapped and entangled in a fashion similar to polymers in their concentrated solutions. Likewise, highly concentrated cyclodextrin (CD) solutions having considerable aggregates may be electrospun into ultrafine nanofibers. The success of the electrospinning of the CD nanofibers would rely on the presence of substantial aggregates and the sufficient intermolecular interactions between the CD molecules that will effectively act as chain entanglements in the solution. Electrospinning of CD nanofibers is quite a challenge since they are small molecules, yet, the electrospinning of CD nanofibers would be very intriguing due to the exclusive properties obtained by having very large surface area of nanofibers/nanowebs with specific functionality of the CD.

In this communication, we report on the very first studies on electrospinning of CD nanofibers by itself without the use of a carrier polymer matrix. Here, we used methyl-beta-cyclodextrin (MβCD) for the electrospinning since it has a very high solubility when compared to native β-CD.^{12,13} In this study, highly concentrated MβCD solutions (varying from 100% to 160% (w/v)) were prepared by using two types of solvent: water and *N,N*-dimethylformamide (DMF). For all concentrations, MβCD was dissolved and formed clear

Fig. 1 (A) Chemical structure of beta-cyclodextrin (β-CD). (B) Chemical structure of randomly methylated β-CD (MβCD). (C) Schematic representation of truncated cone-shaped molecular structure of CD.

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Table 1 Properties of M β CD solutions, fiber morphology and fiber diameter range (nm) of the resulting electrospun M β CD fibers

Solutions	Solvent	% M β CD (w/v)	Viscosity (Pa·s)	Fiber morphology	Fiber diameter range/nm
100M β CD	Water	100	0.0116	beaded structures	—
120M β CD	Water	120	0.0217	beaded nanofibers	—
140M β CD	Water	140	0.0509	bead-free nanofibers	20–100
160M β CD	Water	160	0.106	bead-free nanofibers	20–100
100M β CD	DMF	100	0.0176	beads only	—
120M β CD	DMF	120	0.0755	beaded nanofibers	—
140M β CD	DMF	140	0.275	bead-free nanofibers	100–1000
160M β CD	DMF	160	0.564	bead-free nanofibers	100–1200
140M β CD + 17.5% Urea	Water	140	0.0323	no fiber formation	—

solutions in water and DMF and the resulting M β CD solutions were electrospun. The experimental procedure, electrospinning parameters and characterization details are given in the Electronic Supplementary Information (ESI).† The properties of the M β CD solutions in water and DMF, the morphology and the fiber diameter range of the resultant electrospun nanofibers are summarized in Table 1.

Representative SEM images of the electrospun M β CD nanofibers obtained from water and DMF solutions having 100%, 120%, 140%, and 160% (w/v) M β CD are given in Fig. 2. Elongated beaded structures were obtained when 100% (w/v) M β CD water solution was electrospun (Fig. 2A). This is possibly because of the insufficient amount of CD aggregates which resulted in destabilization of the electrified jet during the electrospinning process and therefore yielded elongated beads instead of continuous fibers. Very fine fibers with some irregular structures were obtained at 120% (w/v) (Fig. 2B); in addition, some break points were observed between the nanofibers suggesting that the 120% (w/v) M β CD was not sufficient to yield continuous fibers. At 140% and 160% (w/v) M β CD, bead-free nanofibers (Fig. 2C and D) having diameters mostly in the range of 20 nm to 100 nm were obtained. The fiber diameter distributions are given in Fig. 3A and B. In the electrospinning process, the transition from beads to beaded fibers and finally bead-free fibers is very typical for polymeric systems when the concentration and/or viscosity of the polymer solution is increased.⁶ Higher polymer concentrations result in higher chain entanglements which is essential to maintain the continuity of the jet during the electrospinning process. Here, very similar behavior was observed for the electrospinning of M β CD in water. At higher concentrations, M β CD molecules can form considerable aggregates⁴ *via*

Fig. 2 SEM images of the electrospun M β CD nanofibers obtained from water and DMF solutions having different M β CD concentrations. (A) 100% (w/v), (B) 120% (w/v), (C) 140% (w/v) and (D) 160% (w/v) M β CD in water; (E) 100% (w/v), (F) 120% (w/v), (G) 140% (w/v) and (H) 160% (w/v) M β CD in DMF.

Fig. 3 Fiber diameter distribution of the electrospun fibers obtained from (A) 140% (w/v) and (B) 160% (w/v) M β CD in water; (C) 140% (w/v) and (D) 160% (w/v) M β CD in DMF.

hydrogen bonding between the CD molecules and these intermolecular interactions can effectively act as chain entanglements in the system which enables the jet to stretch fully and results in uniform nanofibers. It is known that addition of urea breaks the hydrogen bonds between the CD molecules and causes notable depression of the self-association of the CD molecules in water.⁴ Here, we added urea (17.5% (w/w), with respect to M β CD) to the 140% (w/v) M β CD aqueous solution and we observed that the viscosity of the solution is decreased from 0.0509 Pa·s to 0.0323 Pa·s which is due to the destruction of the hydrogen bonding between the CD molecules. The electrospinning of the solution 140% (w/v) M β CD containing urea did not produce any fibers which is because of the break up of the electrospinning jet due to the lack of sufficient CD aggregates (Fig. S1 of the ESI†). This further proved that the presence of a considerable amount of CD aggregates *via* hydrogen bonding plays an important role in the electrospinning of M β CD into nanofibers from its aqueous solution.

Nanofibers were also obtained when M β CD solutions in DMF were electrospun. At lower M β CD concentration (100%, w/v), micron and nano sized non-uniform droplets were formed (Fig. 2E); at 120% (w/v) M β CD, nanofibers with substantial beaded structures were obtained (Fig. 2F). The transition from beaded nanofibers to bead-free nanofibers was observed in the case of the electrospinning of the 140% (w/v) M β CD solution. At 140% (w/v), bead-free M β CD nanofibers were obtained (Fig. 2G) with diameters in the range of 100–1000 nm (Fig. 3C) and an average fiber diameter of 428 ± 172 nm. When the 160% (w/v) M β CD solution was electrospun, again, bead-free M β CD nanofibers were obtained

(Fig. 2H) and the fiber diameter was in the range of 100–1200 nm (Fig. 3D) having average fiber diameter of 452 ± 197 nm. At higher M β CD concentrations, nanofibers with larger diameters were obtained which is due to high content of the M β CD in the solution and high solution viscosity.⁶

When electrospun M β CD nanofibers obtained from water are compared to the ones obtained from DMF, the nanofibers produced from water solution were much thinner. This may be due to the low viscosity (Table 1) and high conductivity of the M β CD solution in water¹⁴ which yielded thinner fibers owing to more stretching of the jet during the electrospinning process. This behavior is very typical for the electrospinning of polymer solutions in which solutions having low viscosity and high conductivity yield much thinner fibers.^{6,15} On the other hand, SEM and AFM analyses showed that the M β CD nanofibers produced from DMF solution were smoother compared to ones obtained from aqueous solution of M β CD. Representative AFM images and cross-section profiles of M β CD nanofiber obtained from water and DMF solutions are given in Fig. 4. DMF is a high boiling point (153 °C) solvent, thus, slow evaporation of the solvent during the electrospinning resulted in a much smoother fiber surface. This kind of morphological difference is also very common for electrospun polymeric nanofibers where smooth fibers are produced when high boiling point solvents (such as DMF, DMAc, etc.) are used whereas porous and rougher fiber surfaces are obtained in the case of using volatile solvents (chloroform, acetone, THF, water, etc.).^{6,7,15}

β -CD is a crystalline material; however, random substitution of the hydroxyl groups of β -CD with methoxy groups (methyl- β -CD) resulted in amorphous material. Here, we examined the nanofibers of M β CD by X-ray diffraction (XRD) and we observed that the XRD patterns of the M β CD nanofibers are very similar to powder M β CD having amorphous structure (Fig. S2 of the ESI†). We also observed that M β CD nanofibers have a lack of mechanical integrity and they are quite brittle compared to polymeric nanofibers since the nanofibers consist of small molecules (M β CD). Thermogravimetric analysis (TGA) and differential scanning calorimetry (DSC) studies showed that the nanofibers contained ~3%

(w/w) of water and the release of water is between 25–120 °C (Fig. S3 and S4 of the ESI†). We have also investigated the thermal stability of the electrospun M β CD nanofibers by heating up to 200 °C. Fig. S5 of the ESI† shows the SEM images of M β CD nanofibers treated at 100 °C, 150 °C, 175 °C and 200 °C for 2 h in an oven. Up to 150 °C, the M β CD nanofibers kept their fibrous structure, but increasing the temperature to 175 °C, which is very close to the melting point of M β CD (180–185 °C), resulted in deformation of the fibrous structure. At 200 °C, the M β CD nanofibers were melted and totally lost their fiber structure.

In summary, we have achieved the electrospinning of nanofibers from pure cyclodextrin (M β CD) without using any carrier polymeric matrix. We have shown that the success of the electrospinning of the CD nanofibers strongly depends on (i) type of solvent, (ii) CD solution concentration and (iii) intermolecular interactions between the CD molecules. Our findings offer the potential of fabricating new functional nanofibers from cyclodextrins or other supramolecular systems *via* the electrospinning technique. Cyclodextrins are a very interesting class of molecules which are able to form intriguing supramolecular assemblies. Thus, such functional nanofibers obtained from these supramolecular structures can be used as building blocks for constructing distinctive fibrous nanostructures. In addition, having a nanofiber/nanoweb structure may extend the use of cyclodextrins in biotechnology, textiles, filters, or in other advanced functional systems.

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Fig. 4 (A) AFM image and (B) fiber axis cross-section profile of the nanofiber obtained from 160% (w/v) M β CD in water. (C) AFM image and (D) fiber axis cross-section profile of the nanofiber obtained from 160% (w/v) M β CD in DMF.