Cyclodextrins (CDs) are distinctive molecules that can form noncovalent host–guest complexes with a variety of molecules to yield intriguing supramolecular structures. Electrospinning has gained enormous attention since this versatile technique enables production of multifunctional nanofibers made from various polymers, polymer blends, composites, and ceramics. Electrospun nanofibers containing cyclodextrin inclusion complexes are particularly attractive because of the unique properties obtained by combining the large surface area of a polymer nanofiber carrier with the specific chemical structure of the CD complex. Herein we report the first results from electrospinning cyclodextrin inclusion complexes and/or cyclodextrin pseudopolyrotaxanes.

Cyclodextrins are cyclic oligosaccharides with a toroid-shaped molecular structure consisting of α(1,4)-linked glucopyranose units (Figure 1a). The most common natural CDs have either six, seven, or eight glucopyranose units and are referred to as α-, β-, and γ-cyclodextrins, respectively (Figure 1b). The hydrophobic cavity of CDs allows them to form host–guest complexes with various small molecules and macromolecules. The stability of CD complexes depends on many factors such as the size or shape match between host and guest, chemical environment, and the binding forces (e.g., hydrophobic interactions, van der Waals attractions, hydrogen bonding, and electrostatic interactions) between the host CD and guest molecules. Since the physical and chemical properties of incorporated guest compounds can be tailored by CD complexation, CDs are used in a variety of application areas, such as pharmaceuticals (e.g., enhancement of drug solubility and stability, bioavailability, controlled drug delivery, and reduction of drug toxicity), functional food additives (stabilization of volatile or unstable flavors and masking or removal of unwanted tastes and odor), cosmetics and home or personal care (releasing fragrances and masking unpleasant odors), and textiles (stabilization and controlled release of textile additives).

CD pseudopolyrotaxanes, formed by threading a polymer chain or long molecule through many CD rings, have fascinating supramolecular structures with unusual properties. It has been shown that CD pseudopolyrotaxanes can be formed with various synthetic polymers, biopolymers, conducting polymers, dyes, polypeptides, proteins, and enzymes, and that the huge variety of supramolecular structures are extremely useful in many diverse areas. The nanostructure or microstructure and the functionality of the guest molecules are altered when encapsulated by CD molecules; furthermore, CD rings assist the stabilization and protection of the guest molecules and can control or sustain their delivery. CDs are natural, nontoxic, and slowly biodegradable, and consequently CD polyrotaxanes are very attractive candidates for smart materials, controlled or sustained delivery systems, sensor devices, molecular switches, or other diagnostic systems.

Electrospinning is as a versatile and cost-effective technique for producing multifunctional nanofibers. Nanofibers and their mats have several remarkable characteristics such as large surface area to volume ratios, pore sizes in the nanometer range, unique physical and mechanical properties, and the chemical, physical, and functional properties of the nanofiber surfaces are fairly easy to modify. It has been shown that the very interesting properties and the multifunctionality of the nanofibers make them favorable candidates for use in many areas including biotechnology (tissue engineering, controlled or sustained release systems), textiles (delivery and stabilization of additives) and membranes/filters.

The incorporation of CD-pseudopolyrotaxanes into nanofibers is extremely interesting since such the resulting CD-complex-containing nanoweb will have unique character-
istics that can potentially improve and broaden the application areas of cyclodextrins and nanofibers. We have electrospun nanofibers of the poly(ethylene glycol) (PEG) inclusion complex (IC) of alpha-cyclodextrin (α-CD). The pseudopolyrotaxane α-CD–PEG-IC is used as a model system for studying nanofibers formed from CD pseudopolyrotaxanes. The electrospinning of α-CD–PEG-IC was achieved by using a carrier polymer matrix, poly(ethylene oxide) (PEO), to provide α-CD–PEG-IC/PEO nanofibers. To our knowledge, this is the first report to date which deals with the electrospinning of cyclodextrin inclusion complexes and/or cyclodextrin pseudopolyrotaxanes.

CDs are crystalline and have crystal structures referred to as a “cage” or “channel” type (Figure 1c, d).[22, 23] The unmodified α-CD used in this study has a cage structure with a “herringbone” arrangement in which the cavity of each molecule is blocked by neighboring molecules. The channel structure consists of CD molecules that are aligned and stacked on top of each other forming long cylindrical channels. The inclusion of polymers in CD molecules (to form pseudopolyrotaxanes) is therefore supported by the formation of the channel structure. Figure 2a shows an X-ray powder diffractogram of α-CD–PEG-IC, which confirms the channel structure and therefore the formation of the inclusion complex between α-CD and PEG. The powder diffractogram of α-CD–PEG-IC has characteristic strong reflections at 2θ values of approximately 20° and 13°, arising from the channel packing and not the cage structure of unmodified α-CD (Figure 2a).[24, 25]

The electrospinning of α-CD–PEG-IC nanofibers is not possible because of their crystalline nature and the low molecular weight of the PEG. Therefore, the PEO polymer matrix was chosen to be used as a carrier for three reasons: 1) it is easy to electrospin PEO nanofibers, and PEO has been shown to be a good carrier matrix for both inorganic compounds and polymers that cannot be electrospun by themselves.[26–30] 2) it has the same chemical structure as PEG, and 3) PEO nanofibers may have many uses in various applications.[26, 29–32] To facilitate nanofiber formation, α-CD–PEG-IC was premixed with aqueous PEO solutions in different weight ratios (50, 100, and 200% w/w with respect to PEO) prior to electrospinning the resulting suspensions. The conductivity of the PEO solutions did not change with the addition of α-CD–PEG-ICs (in the range of 76–78 μS/cm−1), however, a gradual increase in the viscosity of the polymer solutions was observed as the concentration of α-CD–PEG-IC was increased, which possibly arises from interactions between the CD molecules and PEO chains (Table 1).

The presence of α-CD–PEG-IC in the electrospun nanofibers was confirmed by FTIR studies (see the Supporting Information). The similar structures of α-CD, PEG, and PEO results in an overlap of absorption peaks, which complicates the identification of the individual components in the samples. However, the salient absorption bands of the α-CD at around 1030, 1080, and 1155 cm−1, which correspond to the coupled C–C–O stretching vibrations and the antisymmetric stretching vibration of the C–O–C glycosidic bridge, were observed for all the α-CD–PEG-IC/PEO systems (see Figure S2 in the Supporting Information). The presence of these bands indicates the successful incorporation of α-CD–PEG-IC in the PEO nanofibers.

Representative scanning electron microscopy (SEM) images of the resulting α-CD–PEG-IC/PEO nanofibers are shown in Figure 3 and the morphology and fiber diameter results for the different combinations of solutions are summarized in Table 1. The fiber diameters are in the range 100–250 nm and the average fiber diameters for all systems were approximately 160 nm. The SEM images also show that the fibers change from being very uniform to having beaded structures the content of α-CD–PEG-IC is increased. The electrospun solutions were fully uniform with 50% (w/w) α-CD–PEG-IC, whereas α-CD–PEG-IC nanofibers containing very few beads were obtained at 100% (w/w) α-CD–PEG-IC. However, fibers in which beads of both small and large sizes coexist in the individual nanofibers were formed from 200% (w/w) solutions of α-CD–PEG-IC. A possible explanation for bead formation is that the α-CD–PEG-IC crystals have a

Table 1: Solution properties and morphology and diameter of the resulting nanofibers.

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<td>α-CD–PEG-IC/PEO</td>
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<td>(50)</td>
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<td>2</td>
<td>1908</td>
<td>77.8</td>
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<td>(168±46)</td>
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<tr>
<td>(100)</td>
<td>4</td>
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<td>1925</td>
<td>75.8</td>
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<tr>
<td>(200)</td>
<td>4</td>
<td>8</td>
<td>2272</td>
<td>77.9</td>
<td>nanofibers with beads</td>
<td>(165±16)</td>
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Figure 2. 2D X-ray diffraction patterns of: a) nonmodified α-CD (cage-type structure); b) α-CD–PEG-IC (channel-type structure); and nanowebs of c) PEO; d) α-CD–PEG-IC/PEO (50% w/w); e) α-CD–PEG-IC/PEO (100% w/w); and f) α-CD–PEG-IC/PEO (200% w/w).
higher degree of aggregation at higher solution concentration. Such aggregates remain intact during electrospinning and are not sufficiently elastic to become completely stretched with the PEO matrix; this effect results in bead formation.

A more detailed analysis of the structure of the α-CD–PEG-IC/PEO nanofibers was carried out using transmission electron microscopy (TEM; Figure 3a). Representative TEM images that clearly reveal that the fiber diameter of α-CD–PEG-IC is not uniform are shown in Figure 4. In some cases, large beads incorporated within the nanofiber are observed, possibly because of incomplete stretching of the α-CD–PEG-IC aggregates (Figure 4b), which is consistent with the SEM results. Moreover, in a few fibers, nanosized α-CD–PEG-IC aggregates dispersed in the PEO matrix were observed as defect areas close to the fiber surface region (Figure 4c). This might arise from the fact that some α-CD–PEG-IC crystallites do not get dispersed into the polymer matrix during fiber formation, but, because of some entanglement, remain attached to the PEO matrix and thus get carried with the fibers during the electrospinning process.

It may be possible that the channel structure of α-CD–PEG-IC is destroyed during the electrospinning process as the material is subjected to a high level of stretching. In order to investigate this, 2D X-ray diffraction studies were performed on the α-CD–PEG-IC/PEO nanowebs. The diffraction patterns of these nanowebs containing various weight ratios of α-CD–PEG-IC are shown in Figure 2d–f. PEO is a semicrystalline polymer with diffraction peaks at 2θ = 19° and 23° (Figure 2c). The characteristic peaks of the α-CD channel structure [24, 25] at 2θ values of approximately 20° and 13° were observed for all α-CD–PEG-IC/PEO nanowebs. In addition, an increased peak intensity was observed for the nanowebs containing a high proportion of α-CD–PEG-IC in the matrix. It is thus evident that the α-CD–PEG-IC crystals were incorporated into the nanofibers and the channel structure of α-CD–PEG-IC was preserved during the electrospinning process. Furthermore, there is no evidence for the generation of CD cage structures since no corresponding peaks for this morphology appear in the nanoweb diffractograms.

In conclusion, the first results from electrospinning cyclodextrin pseudopolyrotaxane nanofibers using PEO as a carrier polymer matrix have been reported. We have shown that the α-CD–PEG-IC can be electrospun into nanofibers without destruction of the inclusion complex and its channel packing. The final morphology of the nanofibers is highly dependent on the weight content of α-CD–PEG-IC in the polymer matrix (PEO). Uniform fibers are yielded at low weight content (50% to 100% w/w with respect to PEO matrix) and beaded fibers are generated at higher weight content (200% w/w with respect to PEO matrix). The results are very encouraging and open up a variety of new exciting possibilities for the development of multifunctional nanofibers containing CD pseudopolyrotaxanes and/or CD inclusion complexes. Electrospun nanofibers functionalized with cyclodextrin inclusion complexes are particularly attractive for various application areas, including biotechnology, textiles, and filters.

**Experimental Section**

Materials: Poly(ethylene glycol) (average Mn = 950–1050) and poly(ethylene oxide) (average Mw ~ 900,000) were purchased from Sigma-Aldrich, Germany, while the α-CD was a gift from Wacker Co., Germany. MilliQ water was used as the solvent for PEO in the electrospinning.

Preparation of α-CD–PEG inclusion complex: An aqueous solution of PEG (1 g in 5 mL MilliQ water) was added dropwise to an aqueous solution of α-CD (7.5 g in 45 mL MilliQ water at 50°C) and an immediate suspension was obtained. The suspension was subsequently stirred for 3 h at 50°C and then cooled to RT and stirred for an additional 24 h. The resulting white powder (α-CD–PEG-IC)
was obtained by filtration and washing with water several times to remove noncomplexed CD and PEG.

Electrospinning: The suspensions of α-CD–PEG-IC and PEO were prepared by stirring α-CD–PEG-IC and PEO in MilliQ water at RT for 24 h. PEO is soluble in water, but the α-CD–PEG-IC is not because of complexation. The α-CD–PEG-IC/PEO suspensions were placed in a 3 mL syringe fitted with a metallic needle of 0.6 mm inner diameter. The syringe was fixed horizontally to a syringe pump (Model: KDS 101, KD Scientific) and the electrode of the high voltage power supply (Spellman High-Voltage Electronics Corporation, MP Series) was clamped to the metal needle tip. Flow rate = 1 mL h⁻¹, applied voltage = 15 kV and tip-to-collector distance = 15 cm. A grounded stationary rectangular metal collector covered by a piece of Al foil was used for the fiber collection. The complete electrospinning apparatus was enclosed in a Perspex box, and the electrospinning was carried out at RT.

Measurements and characterization: The viscosity of the polymer solutions was measured at 24°C using a Brookfield DV-III Ultra Rheometer equipped with cone/plate accessory using spindle type CPE-41. The conductivity of the solutions was measured with Multiparameter meter InoLab®Multi 720 (WTW) at room temperature. The morphology of the α-CD–PEG-IC/PEO nanofibers was examined by transmission electron microscopy (TEM) using a Philips CM20 instrument at 200 kV. 2D X-ray diffraction (XRD) data of α-CD and α-CD–PEG-IC powders and nanowebs were collected using a Stoe Stadi P diffractometer applying Cu Kα radiation over the range 2θ = 5–30°. FTIR measurements were performed using a Perkin Elmer Paragon 1000 FTIR Spectrometer. The samples were blended with KBr and pellets were formed under high pressure, spectra were recorded with a resolution of 2 cm⁻¹ and averaged over 16 scans.

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