

Manufacturing Cyclodextrin Fibres using Water

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Abstract

Cyclodextrins are a class of biocompatible and highly water-soluble oligosaccharide polymers, with vast uses in industries ranging from drug delivery to agriculture. Currently, most fibre production relies on using environmentally unfriendly organic solvents and polymeric additions. Cyclodextrins are seldom used on their own without a carrier polymer, however in this work, (2-Hydroxypropyl)- β -cyclodextrin fibres were successfully produced with water, as the “green” solvent with pressurised gyration and electrospinning, without using a carrier polymer. The average fibre diameter of the pressurised gyration produced fibres ranged between 5.5 to 5.8 μm , whilst the average fibre diameter of the electrospun fibres ranged between only 183 - 305 nm. These findings show the thinnest diameter of pure cyclodextrin achieved in the literature. Both techniques had specific advantages, such as electrospinning being able to produce nanofibres, whilst pressurized gyration had productivity of over 1.5 grams per minute. Here we present a pioneering study into the production of cyclodextrin-only fibres with two different fibre production techniques and the creation of a cyclodextrin-super-mat that combines both types of fibres.

1. Introduction

The first reference to cyclodextrin appeared as early as 1891 when a then-unidentified substance was described by Villiers ^[1, 2]. More detailed descriptions of cyclodextrin were provided by Schardinger about 15 years later who found that this same unidentified substance could be produced from the degradation of starch ^[3]. After further investigation, Schardinger was able to identify two major cyclodextrins, namely α and β ^[4]. It was Freudenberg and his coworkers who were able to identify the cyclic structure of these substances ^[5]. It was approximately 1950 when γ -cyclodextrin was

discovered following the clarification of the structures of the different types of cyclodextrin [6].

It is the unique structure of cyclodextrin which makes it appealing for biotechnology applications. Normally, cyclodextrins consist of 6-8 glucopyranoside units which are linked by α -1,4-glycoside bonding [7]. Thus, cyclodextrins have an unusual toroidal shape where the smaller and larger opening portions exposes their primary and secondary hydroxyl groups [8]. As such, the interior of the toroid shape is much less hydrophilic than the surrounding aqueous environment, allowing cyclodextrins to be used to host other hydrophobic molecules. This important feature allows cyclodextrins to exhibit the phenomenon of molecular recognition, where they can include guest molecules of a size and shape which fits the interior of the cavity, leading to a high equilibrium constant [9]. Cyclodextrin can therefore be used to create supramolecular assemblies for gene delivery [10].

The use of cyclodextrin in chemistry is rapidly increasing due to its water solubility which reduces the need for harsh organic solvents which can lead to both human and environmental damage [11]. As cyclodextrins are produced from starch, they are both non-toxic and biodegradable which means they have a wide range of potential uses including in food, pharmaceuticals, textiles and cosmetics [12]. Cyclodextrins are currently most frequently used in the cosmetic and food industries, with less than 10% of produced cyclodextrin being used in pharmaceuticals [13]. In the pharmaceutical industry, cyclodextrins are mostly used in drug formulation and this use is steadily increasing. Cyclodextrin has been found to improve the bioavailability of drugs by increasing the solubility limit and the rate of dissolution of the drug complexes [14, 15]. Cyclodextrins and their derivatives have uses in both synthetic and natural antibacterial agents such as in isocyanates, polyphenols and even itraconazole [16, 17]. Furthermore, cyclodextrin and some of its derivatives have environmental uses in the removal of certain pollutants from soil and water such as pyrene and heavy metals [18].

Recently, cyclodextrins have seen increased prevalence in the food and beverage industries. The incorporation of cyclodextrins in food is facilitated by its ability to keep volatile flavours via the process of complexation and can inhibit light and heat-induced transformation of food by acting as a lipophile carrier [19]. Moreover, cyclodextrin-based adsorbents have attracted worldwide attention as a novel route for wastewater

treatment, owing to their remarkable physicochemical properties [20]. Cyclodextrins are non-toxic and their highly specific cavity structure gives them the suitability to capture particular organic molecules. Cyclodextrins contain an outer surface of hydroxyl groups which could potentially connect to the toxic metal ions with strong covalent bonds, making them a highly specific adsorbent material. Cyclodextrin has also recently been used to develop a smart approach to stimuli-responsive drug delivery systems [21]. These smart delivery systems can detect changes in the physiological microenvironment and respond to several stimuli such as enzyme response, redox response, light, temperature, pH and even electromagnetic fields. Additionally, cyclodextrins have been used with embedded carbon nanotubes to generate an injectable nanocarrier for the reversal of multi-drug resistance in cancer therapy [22]. These cyclodextrin-based nanocarriers demonstrated the ability for an effective combination of cocktail chemotherapy (CCT) and had the anti-angiogenic potential for selective tumour targeting. The nanocarriers were also effective in reversing multidrug resistance (MDR) with minimal toxicological effects to the native cells.

There is very little literature available on the generation of pure cyclodextrin fibres, this is because cyclodextrin is commonly used as an enhancer and seldom required as the bulk material. Forming pure cyclodextrin fibres is therefore difficult and at commonly used concentrations, though to be impossible. Cyclodextrin fibres, however, have previously been manufactured in their pure form by using electrospinning [23, 24]. Pure cyclodextrin fibres were found to be highly dependent on the solvent used and the concentration of the solution produced [15]. Whilst lower concentrations could be used when using a carrier polymer, it was found the concentrations exceeding 140% (w/v) were required to produce bead-free nanofibers when using a solution of pure cyclodextrin using either water or DMF as the solvent [25, 26].

The production of fibres increases the potential uses of cyclodextrin due to the enhanced properties of these fibres such as having a very high surface area-volume ratio. Electrospinning is a widely used method of producing nanofibers [27, 28]. Using a high electric field, continuous fibres are formed on the collection surface. The applied voltage causes the polymer solution to form a Taylor cone, from which a jet is formed and as the solvent evaporates fibres are produced [29, 30]. For example, odour-adsorbent nano-filters have been produced by incorporating cyclodextrin molecules into cellulose acetate fibres spun via electrospinning, in this study β -CD molecules

demonstrated an up to 80% increase in direct adsorption of the odour-producing substance, demonstrating their potential use in filtration ^[31]. The bacteriostatic effect of cyclodextrin was investigated in a β -cyclodextrin/quercetin nanofilm inclusion compound formed via electrospinning ^[32]. The Quercetin was successfully embedded into the nanofilm and allowed a slow release of Quercetin which sustained a potent antimicrobial effect on *E.coli* and *S. aureus*.

Pressurised gyration uses a motor to spin a rotating aluminium vessel with perforations that are attached to a gas outlet which can vary the gas pressure within the vessel. Fibres can then be produced as the vessel rotates, forcing the solution out of the perforations as the centrifugal force and the pressure difference increase. A polymer jet will be produced which forms fibres once dried ^[33]. The pressurised gyration setup incorporates two methods of fibre thinning, the centrifugal force and the applied gas pressure. As the gas pressure is increased within the vessel, the pressure differential between the inside and the surrounding liquid-air interface increases, this causes the polymer jet to be extruded through the orifices at a greater force, leading to increased jet thinning and subsequently thinner deposited fibres ^[34].

In this work, pure (2-Hydroxypropyl)- β -cyclodextrin without a carrier polymer was used to produce fibres with water as a solvent, with both pressurised gyration and electrospinning. Cyclodextrin displays high levels of water solubility and large concentrations are also required for fibre formation, thus cyclodextrin of concentrations ranging from 160 % to 220 % (w/v) was spun in this work using both electrospinning and pressurized gyration and their morphology compared, in order to elucidate mass production features of cyclodextrin fibre generation.

Materials and Methods

Cyclodextrin aqueous solution preparation

For this study, the cyclodextrin source used was (2-Hydroxypropyl)- β -cyclodextrin (CAS: 128446-35-5), which was completely soluble in water even at high polymer concentrations, this was obtained from (MERK, Gillingham, UK). The cyclodextrin was dissolved in deionised water at high concentrations of 160, 180 and 220% (w/v) to ensure sufficient chain entanglement for bead-free fibre production. The cyclodextrin solutions were then subjected to high-speed mixing at 3500 rpm for 5 minutes with a DAC 150.1 FVZ SpeedMixer (Hauschild, Hamm, Germany). The solutions were then

left overnight (24h) to dissolve on their own accord, and then finally subjected to another 5 minutes at 3500 rpm to ensure homogeneous dissolution of all the solutions.

Manufacturing by pressurised gyration

For the pressurised gyration production, 2 mL of 180 and 220% (w/v) cyclodextrin solutions were placed into the aluminium rotating vessel in separate experiments. The working parameters included the addition of pressurised gas infusion of 0.1 - 0.3 MPa and a constant rotational speed of 36000 rpm for the vessel. The collection distance was kept at 8 cm and the spinning process was carried out at ambient conditions of 20-24°C and relative humidity of 45-55 %. At this humidity range, however, the evaporation of water was not sufficient and instead of fibres, droplets would be formed, for this reason, a heat gun was used to increase the heat of the collection chamber to reduce the relative humidity to ~ 30% where fibres could be formed. The immediate temperature of the collection chamber, therefore, was ~ 28-32°C. The fibre yield rate was used as a measurement of production yield and was calculated by weighing the mass of fibre produced with each spin which lasted 20 seconds in duration, this value was converted to minutes by multiplying by 3.

Manufacturing by electrospinning

For the electrospun fibres, 8 mL of the 160 and 180% (w/v) cyclodextrin solutions was taken up with a 10mL syringe (Terumo, Laguna, Philippines), in separate experiments and placed on a PHD 2000 programmable syringe pump (Harvard Apparatus, Massachusetts, USA) where the infusion rate could be controlled. The syringe pump was connected to a metallic nozzle and high-voltage power supply (Glassman Europe Limited, Bramley, UK). The 160% (w/v) polymer solution was spun using a polymer flow rate of 10 $\mu\text{l/hr}$ and using an applied voltage of 23kV, the 180% (w/v) solution was spun at a flow rate of 20 $\mu\text{l/hr}$ and using an applied voltage of 23kV. The collection distance was kept constant at 150 mm from the tip of the nozzle to the grounded stainless steel collection plate. The electrospinning process was carried out at ambient conditions of 20-24°C and relative humidity of 45-55 % and there was no post-processing required. As the productivity of electrospinning is limited by the solution flow, the maximum theoretical production rate is equal to or lower than the flow rate, which was, at most 20 $\mu\text{L/hour}$, producing about 33 nL per minute. Given these values,

the maximum theoretical production rate of the electrospun fibres is about 73 ng per minute.

Combined manufacturing by pressurised gyration and electrospinning

As spun 220% (w/v) cyclodextrin fibre mats were produced by pressurised gyration in the same manner as eluded to before. The fibre mats were then placed on a grounded collection plate 150 mm from the tip of the electrospinning nozzle. the same solution of 220% (w/v) cyclodextrin was used with the electrospinning setup using an applied voltage of 23kV and a solution flow rate of 20 μ l/hr. The electrospun fibres were then directly printed onto the gyro spun cyclodextrin fibre mat and the deposition time was 240 seconds. The resulting structure was a mix between a coarser but more mechanically sound gyration-spun frame, with fine and less dense electrospun fibres at the surface, the structure being referred to as the “super-mat”.

Fibre characterisation

The fibres formed by both pressurised gyration and electrospinning were examined using scanning electron microscopy (SEM). In order to prepare the fibre samples for this technique, they were initially sputter-coated for a duration of 90 seconds using a (Q150R ES, Quorum Technologies, UK). The gold-coated samples were then analysed at a high magnification at an operating voltage of 5kV and a working distance of 7mm (Hitachi S-3400n, Hitachi, Japan). The SEM images were then analysed for their fibre diameter distribution and morphology using Image J software where 100 fibres were measured at random, and the mean diameter was calculated. The frequency distribution of the fibre samples was then plotted using OriginPro software.

Cyclodextrin aqueous solution properties

The cyclodextrin solutions were assessed for their values of surface tension using a pre-calibrated tensiometer (Tensiometer K9, Kruss GmbH, Hamburg, Germany). During the measurement procedure, the Du Nouy ring method was used where a glass vial was filled with cyclodextrin solution and a 60 mm diameter platinum-iridium ring was submerged into each cyclodextrin solution, differing in concentration. This ring was then slowly raised from the solution forming a fluid meniscus, the variation in these forces was measured using a force tensiometer which gave the final surface tension values. Surface tension readings were carried out at ambient conditions with a

temperature between 22–24 °C. The readings have been repeated a total of 5 times in order to find the average surface tension values for each cyclodextrin concentration.

The viscosity of the cyclodextrin solutions was also measured using a Brookfield Viscometer DV-III (Brookfield, Middleboro, MA, USA). For these readings, a small-sample spindle adaptor was used with a cyclodextrin volume of 3 mL. The cyclodextrin solutions were all measured at the same torque values of ~70%. All viscosity measurements were done under ambient conditions (22 ± 2 °C) and repeated three times to give an average value.

The electrical conductivity of the polymer solutions was measured with a Jenway 3540 combined pH and conductivity meter (Cole-Parmer, UK). A conductivity probe was submerged in deionised water for 1 hour before being submerged into a Jenway conductivity standard solution which is produced to have an electrical conductivity of $12880 \mu\text{S cm}^{-1}$ at 25°C, from here, the equipment was calibrated. The three cyclodextrin polymer solutions were then submerged into the conductivity probe and given time for the reading to equilibrate. The measurements were repeated 3 times for reliability and taken at ambient temperature (22-25°C).

Results and Discussion

Table 1: Physical properties of cyclodextrin polymer solutions used in this study.

Polymer Concentration (% w/v)	160	180	220
Surface Tension (mN m^{-1})	51.2 ± 1.0	52.1 ± 1.1	55.2 ± 1.2
Viscosity (mPa s)	423 ± 3	573 ± 5	2423 ± 50
Electrical Conductivity (mS cm^{-1})	59.1 ± 0.4	60.1 ± 0.3	61.4 ± 0.3

Before the process of generating fibres, the physical properties of the polymers need to be taken into consideration as they can have a large effect on the fibre morphology and generally explain well, the characterisation of the produced fibres. **Table 1** shows the physical properties of the cyclodextrin solutions including the surface tension and viscosity measurements. Cyclodextrin is highly water-soluble and even at very high concentrations, the viscosity of its polymer solutions are relatively low. At a concentration of 160% (w/v), the viscosity of the solution in water is only about 420 mPa s, comparatively, most other polymer solutions at this concentration would be too

thick in consistency and difficult to measure [35]. At a concentration of 180 % (w/v), there is a slight increase in viscosity again, but at 220% (w/v), there is a steep increase in measured viscosity indicating a rapid change in polymer chain entanglement [36]. The surface tension of the different cyclodextrin solutions are similar and increase slightly when there is an increase in the concentration amount of polymer, this is typical of most polymer solutions.

Water-based and other non-volatile solvents cause increased difficulty during the fibre manufacturing processes as they take longer for the polymer jet to dry (low evaporation), often leading to beaded morphologies from the inconsistent drying along the jet length. Furthermore, water has a high surface tension, $\sim 70 \text{ mNm}^{-1}$ at room temperature, compared to the surface tension of volatile solvents such as chloroform, which has a room temperature surface tension of about 27 mNm^{-1} [37]. The high surface tension of the polymer solution must be overcome by the formation mechanisms of the fibre production process, with electrospinning, this is the electric field and with pressurised gyration, it is both the centrifugal force and the applied gas pressure [38, 39]. Volatile solvents such as chloroform, dichloromethane and toluene may have lower surface tension values, but they pose risks to human health such as respiratory agitation and also cause environmental damage [40, 41].

Pressurised gyration was used to spin cyclodextrin solution with water as the solvent at a range of applied gas pressures to achieve fibres. Very high concentrations of cyclodextrin were used in this study. At polymer concentrations of less than 180% (w/v), droplets were observed in the pressurised gyration process, explained by the low volatility of water and the solution not having exceeded the critical minimum chain entanglement for these processes [36]. Fibres were successfully produced at concentrations of 180% (w/v) and 220% (w/v), these are shown in **figure 1**. The 180 and 220% cyclodextrin solution both had a solution viscosity of over 500 mPa s. Fibres of 180% (w/v) cyclodextrin spun at 0.1 MPa applied pressure had an average fibre diameter of $5.8 \pm 2.9 \mu\text{m}$. Overall, these microfibres showed good uniformity in their diameter and had excellent interconnectivity. Following post-processing which reduces their water-solubility these fibres may have potential use as tissue scaffolds or as filter medium, given the biocompatibility of cyclodextrin, it is highly suited to the former use [42, 43]. At an applied pressure of 0.2 MPa, the 180% (w/v) cyclodextrin fibres had an average fibre diameter of $5.7 \pm 3.7 \mu\text{m}$. Although there is potential for the fibre

diameter to be reduced with the application of higher pressures, often the instability created by it causes a reduction in uniformity, as witnessed here. Nevertheless, the smallest diameter achieved using the 180% (w/v) cyclodextrin polymer solution was at 0.3 MPa of applied gas pressure, where the fibres had an average diameter of $5.5 \pm 3.5 \mu\text{m}$.

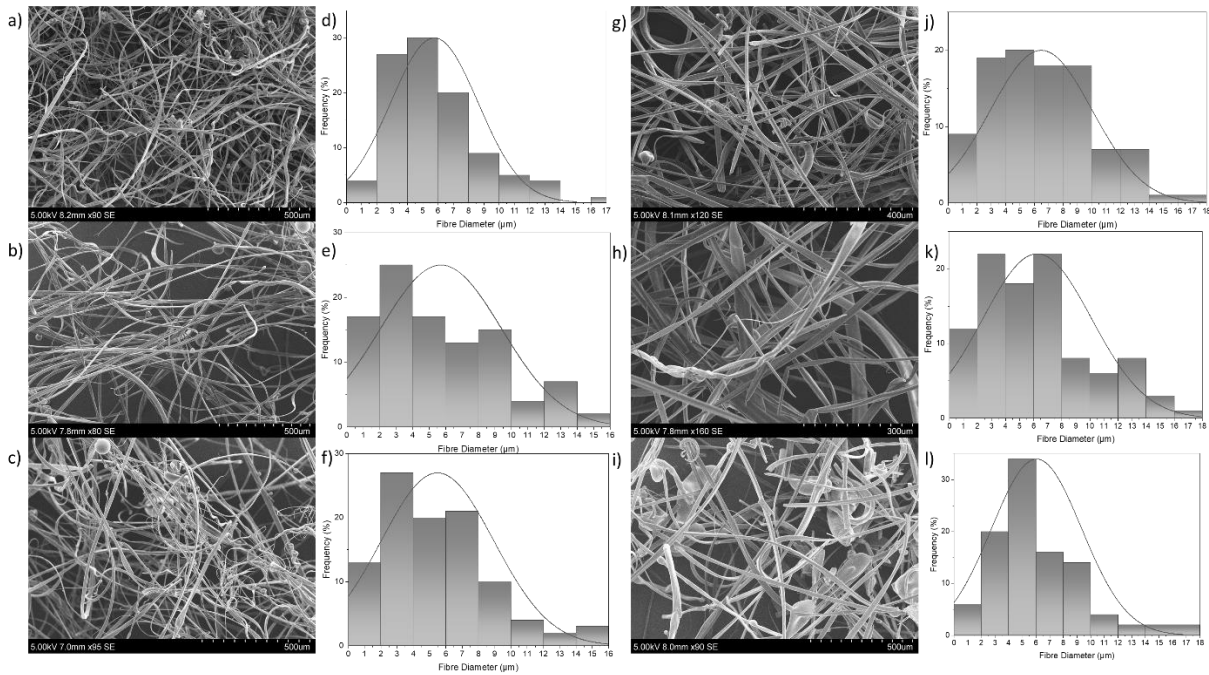


Figure 1: Scanning electron micrographs of 180% (w/v) cyclodextrin fibres spun with pressurised gyration at: a) 0.1 MPa, b) 0.2 MPa, c) 0.3 MPa, 220% (w/v) cyclodextrin fibres spun at g) 0.1 MPa, h) 0.2 MPa, i) 0.3 MPa and their corresponding fibre diameter distribution graphs d), e), f), j), k) and l). For each sample, n=100 fibres.

Although cyclodextrin-water fibres were successfully produced with pressurised gyration, at 180% (w/v), the fibre yield was lower than expected, possibly due to the lower polymer chain entanglement of the polymer matrix at this concentration. For this reason, 220% (w/v) cyclodextrin was also spun with pressurised gyration. At 0.1 MPa of additional pressure, the average diameter of these fibres was $6.5 \pm 3.6 \mu\text{m}$. This increase in fibre diameter compared to the 180% (w/v) fibres is expected due to the higher concentration and higher resulting viscosity of the solution [44, 45]. At 0.2 MPa, the fibres showed an average diameter of $6.2 \pm 3.9 \mu\text{m}$, which showed a slight decrease in the diameter, at the expense of its uniformity. Finally, at 0.3 MPa, the

average fibre diameter was $6.0 \pm 3.93 \mu\text{m}$, showing that there is a potential of achieving thinner fibres at higher pressure values.

The pressurised gyration produced cyclodextrin fibres overall did not have uniaxial alignment as part of their inherent morphology, which is usually seen with gyration produced fibres [35, 46]. This is likely due to the method in which they were collected, which has a large influence on their alignment; air blown from the heat gun could have attributed to the random alignment of the fibres and also a reduction of fibre diameter uniformity [47]. The topography of the fibres showed a smooth surface, devoid of surface pores, due to the fact that a non-volatile solvent was used in the spinning process [48]. There was a difference in the fibre yield of the samples of 180% and 220% cyclodextrin fibres, at 180% only about 50 mg of fibres would be produced in 20 seconds with pressurized gyration, but this number increased to over 500 mg, when using the 220% solution. This behaviour can be attributed to the fact that at 220% (w/v) cyclodextrin, the chain entanglement is much higher, allowing it to spin with more ease and provide a much higher production yield, the fibre yield was therefore calculated to be at 1.5 g/min for the 220% solution using pressurised gyration.

The cyclodextrin solutions were also subjected to electrospinning in order to compare the morphology and yield of the fibres with this manufacturing method. Electrospinning is an excellent fibre manufacturing technique that produced ultrafine fibres with high precision. However, due to the low solution flow rates which must be used, it has a low production rate, and this low productivity can affect its real-world use in many applications [49]. The electrospinning fibre yield was limited by the solution flow rate and was calculated to be a maximum of 73.3 ng/min.

Fibres were successfully produced by electrospinning too; the images of these fibres and their diameter distribution is given in **figure 2**. The applied electric field which is focused on the tip of the single nozzle of electrospinning is capable of overcoming forces such as the surface tension and other viscous forces in a more sustained manner than with pressurised gyration, therefore lower solute concentrations can be utilised [50]. However, very high concentrations of cyclodextrin in water are required to produce any sort of fibrous morphology with electrospinning. In a study that used methyl-beta-cyclodextrin dissolved in water, a minimum of 100% (w/v) cyclodextrin in water was necessary to electrospun fibres, and even then, much higher concentrations

were required in order to achieve bead-free fibres [15]. Typically, with both electrospinning and pressurised gyration, solute concentrations range from 10 - 20 % (w/v), the high requirement of concentration for cyclodextrin emphasises the difficulty of spinning such a polymer.

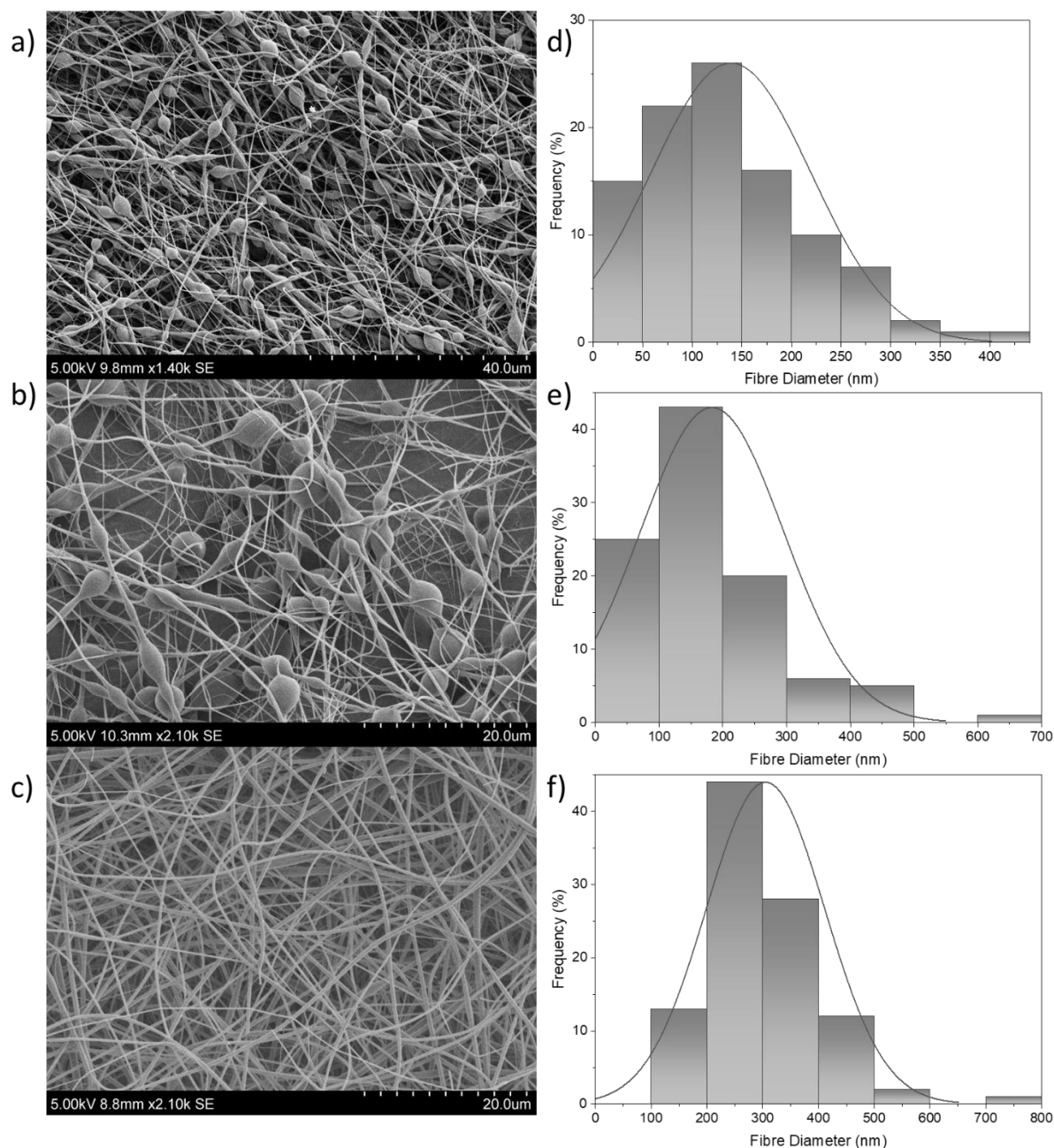


Figure 2: Scanning electron micrographs of electrospun cyclodextrin fibres: a) 160% (w/v), b) 180% (w/v), c) 220% (w/v) and their corresponding fibre diameter distribution graphs; d), e) and f). For each sample, n=100 fibres.

Three differing concentrations of cyclodextrin were used in the electrospinning production in this work, including 160%, 180% and 220% (w/v) polymer solutions. At 160%, the average fibre diameter was 139 ± 81 nm. These fibres can be considered nanofibers with extremely thin fibre diameters and good uniformity. The benefit of having such thinness is that it greatly increases the available surface area to volume ratio which can be advantageous in releasing bioactive or pharmaceutical compounds to be used in a tissue engineering or drug delivery capacity [51, 52]. Furthermore, just like the fibres produced by pressurised gyration, these electrospun fibres have excellent interconnectivity of the pores between the fibre strand, making them highly suitable for use in ultrafiltration, where these fibre mats can filter particulates down to the nanometre range [53]. At a concentration of 180% (w/v), the average fibre diameter was found to be 183 ± 112 nm and increased significantly to 305 ± 106 nm at 220% (w/v). The increase in fibre diameter is attributed to the increased concentration of the cyclodextrin solution but also the doubling of polymer flow rate from 10 $\mu\text{l/hr}$ to 20 $\mu\text{l/hr}$, which was required in order to overcome the increase in viscosity. This increase in cyclodextrin flow rate leads to the greater mass flow of polymer at the tip of the nozzle [54]. During the process of electrospinning, the electrical conductivity of the polymer solution can affect the morphology of the produced fibres [55]. The electrical conductivity is influenced by the choice of solvent, in the case of these experiments, distilled water was used, which has a very low electrical conductivity. **Table 1** shows the measured electrical conductivity of the three cyclodextrin polymer solutions, where an increase in concentration only leads to a minimal increase in electrical conductivity from 59.1 mS cm^{-1} for the 160% solution to 61.4 mS cm^{-1} for the 220% solution.

The topography of these electrospun cyclodextrin fibres also exhibits a smooth topography, with no visible surface roughness due to the use of water as a solvent. At 160% (w/v), the fibres are extensively beaded and a characteristic, bead on string morphology is observed [56]. It is proposed that the bead-on string morphology is a result of inconsistent solvent evaporation along the fibre chain [57]. Given that at a lower concentration, there is a higher ratio of water to cyclodextrin, the evaporation of cyclodextrin suffers, bringing out a bead-on-string morphology. Beaded structures could be useful in drug delivery applications where these beads can be used to embed pharmaceuticals, useful when the fibre diameter is as low as presented here [58]. This

theory is further supported when we examine the 180% (w/v) fibres where the extent of the bead frequency is reduced and then eliminated at a concentration of 220% (w/v).

When comparing the pressurised gyration spun fibres with the electrospun fibres, there are some major differences in morphology. The diameter of the fibres spun with electrospinning are significantly thinner and more uniform. In fact, the fibre diameter achieved using 160% (w/v) cyclodextrin in this work is far thinner than other studies using the same material [23, 24]. However, when we compare the productivity of the two technologies, there are also stark differences here. In order to produce these thin fibres with electrospinning, very low polymer infusion rates had to be utilised. For example, a solution flow rate of only 20 $\mu\text{l/hr}$ was used to spin the 220% (w/v) fibres, meaning that it is limited to producing a maximum of about 20 - 25 μg an hour. This value is much less than the 500 mg of fibre produced in about 15 seconds with pressurised gyration. Pressurised gyration also has greater promise in scaling up due to the lack of problems caused by electric charge interferences which hinder the scaling of electrospinning setups [59]. In an ideal scenario with perfect scaling, pressurised gyration would be capable of producing over 120 grams of cyclodextrin fibres an hour, 6 orders of magnitude higher than with electrospinning.

Given that the two manufacturing techniques produced markedly different fibre morphologies and production yield, the fibre mats of the two technologies pressurised gyration and electrospinning were combined. **Figure 3** shows images of a gyro spun cyclodextrin fibrous scaffold which was used to deposit ultrafine cyclodextrin fibres via electrospinning. Via this method, we can produce a “super-mat”, where the bulk portion is rapidly produced and adds to the structural integrity of the scaffold, but where the surface layers of the scaffold consisting of a network of cyclodextrin nanofibres which can interact with cells of all types. Using this technique and following post-processing such as crosslinking the cyclodextrin fibres, this super-mat could be used to provide filtration efficiency or act as the initial layer of rapid pharmaceutical delivery. The benefit of this novel structure and approach is that we can now leverage the strengths of different manufacturing techniques to quickly produce materials that are more personalised for use in biomedical applications such as tissue engineering where surfaces are required to have specific topography but where the inner depths of the scaffold should be large enough to support various cellular niches. As cells only interact with the surface of materials, this super-mat could be used as a tissue

engineering scaffold where bioactive ingredients can be loaded to attract cells into the centre of the scaffold where they are protected against outside danger [60].

The produced cyclodextrin fibres from both electrospinning and pressurised gyration however showed poor mechanical performance. Both of these fibre types were incredibly brittle and did not allow mechanical testing to be performed on them. Without post-processing, these fibres are not suitable as tissue engineering or filtration applications. Cross-linking can be a beneficial post-processing step to ensure that the fibres become more durable and attractive to cells. The fibres also showed gradual solubility within the environment, indicating extremely high water-solubility. As cyclodextrins have excellent solubility in aqueous environments, the dissolution rate can be controlled by producing one fibrous mat with different layers of fibres, the outer layer formed of ultrathin nanofibres which can demonstrate rapid release and the inner layer formed of thicker fibres which should provide a more sustained release profile. A follow-up study which investigates the ability of cyclodextrins to improve the drug-dissolution characteristics of existing polymers will be carried out.

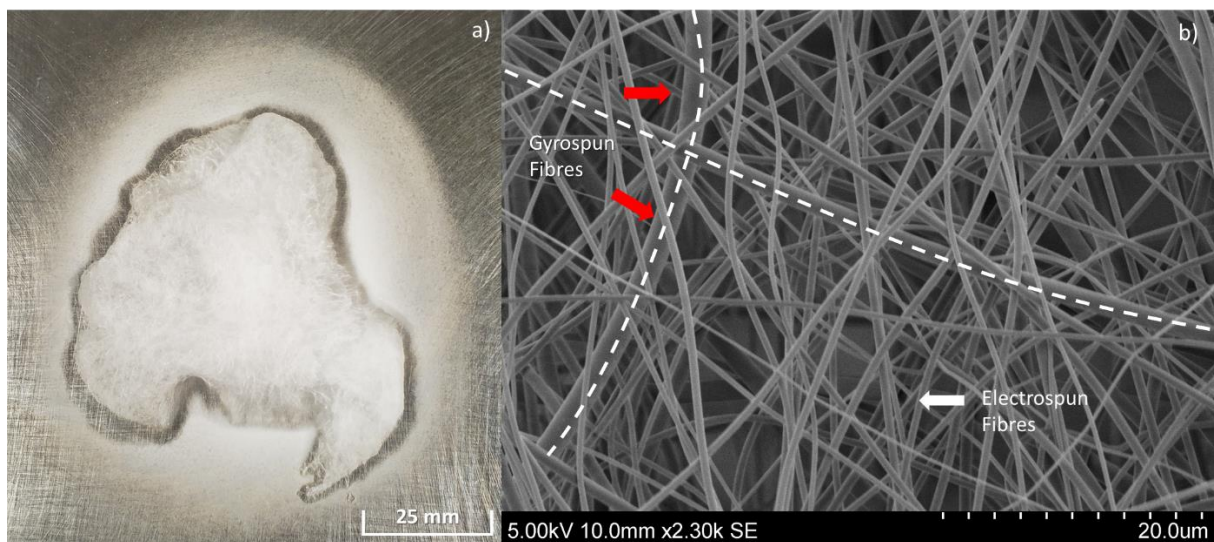


Figure 3: a) image of the cyclodextrin gyro spun and electrospun “super-mat” consisting of a gyro spun cyclodextrin base and electrospun exterior, b) scanning electron micrograph of the “super-mat” under high magnification showing the interface between the electrospun and the gyro spun cyclodextrin fibres, thicker gyration fibres have been highlighted with dotted lines.

Conclusions

In summary, the work presented here has shown that we have achieved fibres spun via electrospinning and also pressurised gyration of pure cyclodextrin ((2-Hydroxypropyl)- β -cyclodextrin)) without the use of a carrier polymer matrix and whilst using a “green” solvent such as water. We have shown that very fine fibres as small as 180 nm can be achieved by optimised spinning parameters with electrospinning and that a very high productivity of 2 grams per minute, can be gained by using a single pressurised gyration setup for carrier fibres with diameters in the micrometre range. The fibre morphology from the different techniques suggests different strengths and weaknesses and potential suitability for applications such as drug delivery and food science. The use of biocompatible materials without traditional polymers and solvents is driving forward the field of green chemistry and redecorating the landscape of polymer chemistry. The use of cyclodextrin in a fibrous form allows it to be used in more aspects of functional technologies. By leveraging the positives of both electrospinning and pressurised gyration, we were able to produce cyclodextrin “super-mats” where the surface consists of an ultrafine network of nanofibres, but the bulk material is a coarser fibrous construction.

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Conflict of interest

The authors all agree that there is no conflict of interest between them.

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