Thermosensitivity of coaxial electrospun PEG-HPMC/tricaprin fibers

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***Abstract*— In this paper we introduce thermosensitive coaxial electrospun fibers. The fibers were electrospun by using PEG-HPMC polymer blend as a shell material and tricaprin as a core material. Ethanol was used as a solvent for both the core and shell materials. For the shell material, some water was added to help HPMC to dissolve. The electrospinning process was noticed to be possible only with certain values of voltage and flow rates. With fluorescein in the core, the coaxial structure of fibers was seen by using fluorescence microscopy. The flow rate ratio was found to affect the diameter ratio of fibers. Fibers were heated under microscope and their behavior was observed. The shell of the fibers melted and the core material spread on the microscopic slide. Melting temperature was determined also with DSC.**

I. INTRODUCTION

Controlling the drug release is one of the most interesting issues in the field of biomedicine. Controllable structure is possible to obtain in many different ways [1]. Lately, electrospinning has been used to produce nanoscale materials that can act as drug carriers [2][3]. There have also been several studies of fibers as scaffolds for wound dressings [4][5]. Varying the fiber properties these can be used for controlled drug release. For example, with co- or triaxial fiber, the drug can be packed into the fiber and then release the drug with rate-controlled release [1][2][6]. Also zero-order release can be obtained with triaxial fiber [7].

Electrospinning is a versatile method of producing ultrafine fibers. The diameter of these fibers is usually in nano- and micrometer scale. In electrospinning process, the polymer solution or melt is forced through metallic needle connected to a high voltage. Because of the high electrostatic field present, the solution is charged by induction. When the electrostatic forces toward the collector are greater than the surface tension of the solution, the solution will travel down to the collector.

The diameter of fibers can be controlled by varying the electrospinning parameters. Increasing the voltage has been shown to decrease the diameter of fibers [8]. Also, with varying the flow rate of solution the diameter can be varied [9]. In coaxial setup, to the best of our knowledge there is currently no study of how core and shell diameters are affected by the solution flow rates. When controlling the release of the core material, it is important to know what the diameter ratio of the fibers is. It is assumed that the thickness of the shell determines how slowly or rapidly the core material is released. In this paper,

it is shown that core and shell materials' flow rate ratio influences the diameter ratio of the fibers.

II. Materials and methods

A. Electrospinning

The setup consisted of two syringe pumps (New Era Pump System Inc.), high voltage source (EMCO) and a coaxial spinneret. The spinneret was constructed of two metallic capillaries with inner diameters of 0.125 mm and 1.00 mm for the inner and outer pipe, respectively. Fibers were collected on to an aluminum foil with a distance of 18 cm from the spinneret. The process was controlled with in-house made LabVIEW program. The parameters were selected in such a way that the process was stable. After optimization the used voltage was 8 kV. The flow rates for outer and inner solutions were varied between Q_o = 0.5 – 0.6 ml/h (outer) and Q_i = 0.05 – 0.2 ml/h (inner).

B. Materials

The shell material was a polymer blend composed of PEG (polyethylene glycol, M = 950 – 1050 g/mol) and HPMC (hydroxypropyl methylcellulose, 28 – 30 % methoxyl, 7 – 12 % hydroxypropyl). Both of the shell polymers were purchased from Alfa Aesar. At first, the HPMC was dissolved in water (1.5 % w/v) and PEG in ethanol (60 % w/v). After the polymers were dissolved, they were mixed in a volume ratio of 1:2.

The core material was fatty acid (Tricaprin, Fluka AG) dissolved in ethanol (20 % w/v). In order to examine the coaxial structure of fibers, some fluorescein (Fluorescein sodium salt, Sigma-Aldrich) was added to tricaprin solution.

C. Characterization

In order to examine the diameter ratio as a function of the flow rate ratio, images of the fibers were taken with both fluorescence (Leitz Wetzlar) and optical microscope (BH2, Olympus). As only the core material was fluorescent, the difference between diameters was observed. The diameter ratio of the fibers d_i/d_o was determined by dividing the core diameter d_i by the diameter of the whole fiber d_o. The flow rate ratio Q_i/Q_o was determined by dividing the core's flow rate Q_i by that one of the shell material Q_o. With image processing (ImageJ, Wayne Rasband, NIH) and known scale, the diameters of the fibers were calculated. Also, with optical microscope and a hot stage (FP82, Mettler) the fibers were melted under observation. The melting process was captured with a video camera. Heating rate was 5 °C/min and the temperature range 25 – 45 °C.

Differential scanning calorimetry (DSC, Pyris Diamond DSC, Perkin Elmer) was used to determine the melting point (onset temperature) of the fibers. Approximately 4 mg of fibers were placed into aluminum pans with pierced lids. The heating rate was 10 °C/min and the used temperature range was 10 – 100 °C. Nitrogen was used as a purge gas with a flow rate of 40 ml/min. The DSC was calibrated with indium.

III. Results and discussion

A. Fiber diameter

Fluorescence microscope was used to confirm the coaxial structure of fibers. The mi-

croscope images were taken with fluorescence and optical microscopes. By overlaying these two images it was seen that fibers in the fluorescence microscope image were thinner than those in the optical microscope image (Fig. 1), confirming that fluorescein was only in the core, and that the fibers' structure was coaxial.

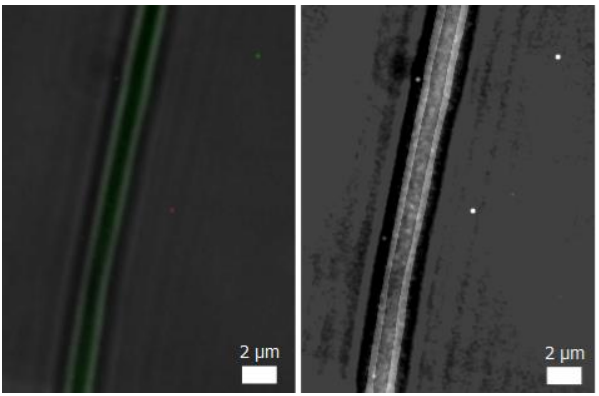

Fig. 1. The coaxial structure was observed from the overlay of the fluorescence and optical microscope images. Image color balance has been altered to enhance the core (right) compared to the original (left). The fibers were spun with flow rates 0.2 ml/h and 0.5 ml/h for core and shell material, respectively.

The diameter ratio of fibers was observed to increase when increasing the flow rate ratio (Fig. 2). If a thick shell layer is required, the shell material's flow rate should be much higher than that one of the core material.

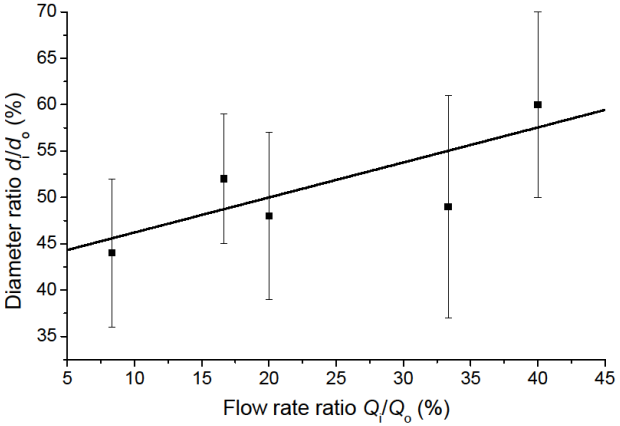

Fig. 2. The diameter ratio d_i/d_o of coaxial fibers as a function of the flow rate ratio Q_i/Q_o.

B. Polymers' effects on the melting point

Because the shell material was a polymer blend, it was crucial to know if the composition had some effect on the melting point of the fiber. In order to get information of HPMC's effects on the melting point of PEG the different compositions were studied. Compositions were made by mixing the HPMC-water- and PEG-ethanol-solutions. The

volume ratios (PEG:HPMC) of these compositions were 1:4 and 2:1. The blends were incubated for two weeks in order to evaporate the solvents.

The effect of HPMC on the melting point of PEG was studied. The DSC curves of measurements are presented in Fig. 3. The shape of the melting peak is presumably due to the large molar mass range of PEG, which was confirmed by studying only PEG. Starting points of the melting were determined from the onsets of the curves. For the first composition (1:4) the temperature was 28.0 °C and for the second one (2:1) 27.6 °C. For pure PEG the corresponding value was 28.9 °C.

No clear difference between the melting onsets was observed. HPMC had only a little effect on the melting point when dissolved to the PEG-ethanol solution. It is supposed that HPMC acted as impurity in PEG and might have decreased the melting point of PEG. Different melting points for the fibers could be realized by choosing a PEG polymer of different molecular weight.

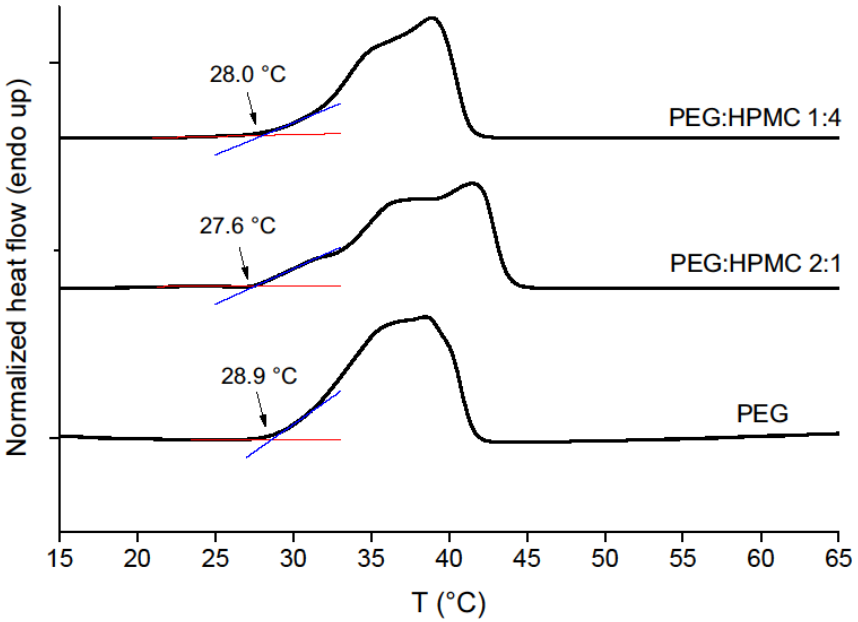

Fig. 3. DSC melting curves of the polymer blends.

C. Controlled melting of fibers

The coaxial fibers were heated on a hot stage and their behavior was observed. Studied fibers were electrospun with flow rates Q_i = 0.2 ml/h and Q_o = 0.6 ml/h. Fig. 3 presents the fibers at different temperatures. Most of the fibers melted around 40 °C. Some melting was also observed before this temperature. At 45 °C almost all the fibers had melted.

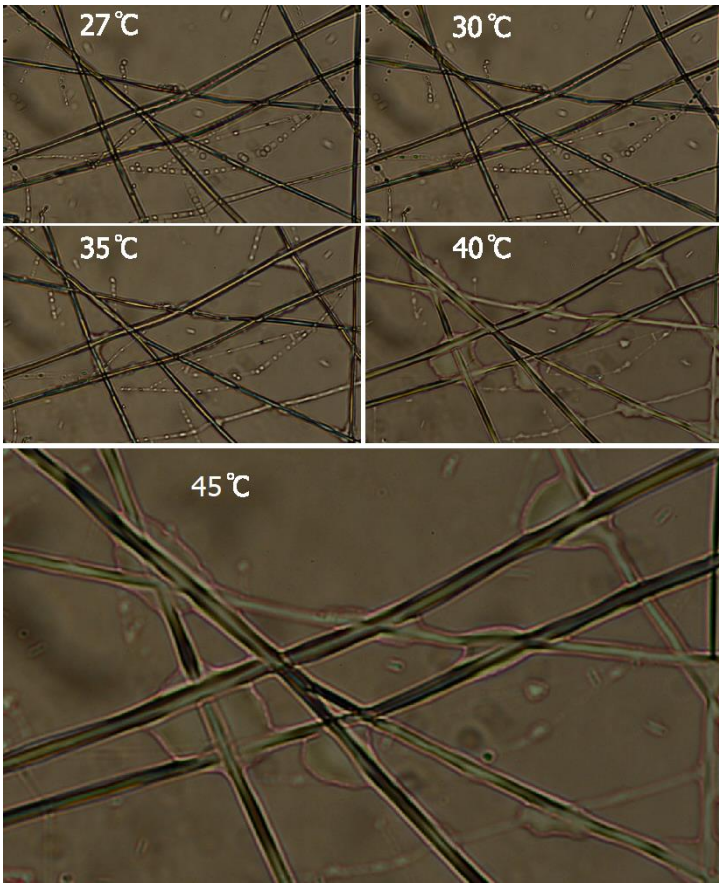

Fig. 4. Pictures of fibers in different temperatures upon heating. The fibers melted around 35 – 40 °C.

D. DSC curves of fibers

The DSC runs were made for four different coaxial fibers. At first, the fibers were electrospun for about 45 minutes using flow rates mentioned in Table 1.

TABLE 1: USED FLOW RATES FOR DSC STUDIES AND THE DETERMINED MELTING ONSETS

#	Q_i [ml/h]	Q_o [ml/h]	T_{m1} [°C]	T_{m2} [°C]
1	0.2	0.6	30.9	34.5
2	0.1	0.6	31.6	33.8
3	0.05	0.6	31.1	34.2
4	0.1	0.5	30.5	34.0

For all the coaxial fibers there were two endothermic processes seen in DSC run. Determined melting onsets are presented in Table 1. One of these DSC curves is presented in Fig. 4. The melting of the fibers started at 30.9 °C. The other melting peak was observed at 34.5 °C. The lower value might be the core material's melting temperature

because of the intense melting peak of tricaprin seen in Fig. 4. The peak at 34.5 °C is supposedly the shell material's melting peak. This value is slightly higher compared to the non-spinned shell polymer blend. A reason for the difference might be the electrospinning process. For certain conclusions more studies are needed.

Because of the HPMC present in the shell, the shell did not completely break down upon heating but still released the core material outside. Also, the core material's melting had no significant effect to the shell's melting behavior which was found from the microscope video. This means that the core material was not released until the shell material had at least partially melted.

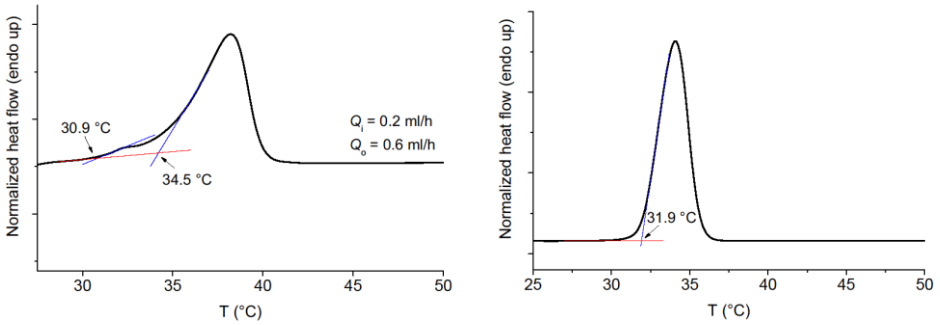

Fig. 4. DSC melting curves of coaxial fibers (left) and tricaprin (right).

IV. Conclusion

In this work it was shown that temperature-controlled release is achievable, and that it is possible to control the release of the core material with the proper choice of the shell material. The polymer blend (PEG and HPMC) acted well as a thermosensitive shell. Also, it was observed that HPMC had no significant effect on the melting point of PEG. For coaxial fibers, increasing the flow rate ratio was shown to increase the diameter ratio as well. It is of great interest to electrospin coaxial fibers where drug is in the core. Authors' next step is to electrospin antimicrobial fibers with the coaxial setup. These fibers can then be used as drug carriers for wound healing or as a controllable drug delivery system.

Acknowledgments

Turun Yliopistosäätiö (Turku University Foundation) is acknowledged for financial support.

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