The Influence of DMAc Ratio in Sheath Fluid on the Diameters of Medicated Cellulose Acetate Nanofibers

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Abstract: Accurate manipulation of electrospun nanofibers' diameter is highly sought after for realizing their functional performances. Different with traditional methods in reducing nanofiers' size, the present job demonstrated that the compositions of sheath mixed solvent were able to exert a significant influence on the modified coaxial processes and correspondingly the final solid medicated nanofibers' diameter. Scanning electron microscopic images showed that all the prepared ibuprofen-loaded cellulose acetate nanofibers had a linear morphology with few beads or spindles on them although they were prepared under a variable volume ratio of *N*, *N*-dimethylacetamide (DMAc) in the sheath mixture with acetone. The linear relationship between the medicated CA nanofibers' diameter (D) and the volume ratio of DMAc in the sheath fluid (*r*) was D= 1013-685r, with a correlated coefficient of R^2=0.9835. The strategy reported should also be useful for other electrohydrodynamic atomization methods for generating high quality micro-/nano-products in a controllable manner.

1. Introduction

The preparation of nanofibers by electrospinning is one of the most important academic and technological activities in the field of materials science and technology in the world in recent decades [1-4]. Electrospinning is becoming one of the main ways to effectively create nanofibers due to its advantages of simple manufacturing device, low spinning cost, various kinds of spinnable materials and controllable process [5-8]. In literature, electrospinning has been explored to generate a variety of nanofibers, including organic, organic/inorganic composite and inorganic nanofibers [9-12]. However, there are still some problems to be solved in the preparation of nanofibers by electrospinning, such as preparation on a large scale, accurate manipulation of the nanofibers' diameter, and preventing air pollution from the evaporation of organic solvents.

In an electrospinning process, the parameters that can exert significant influences on it and also the resultant nanofibers' quality include three categories: experimental conditions from the working fluids, the operational variables, and also the environmental factors [13-15]. To be more concrete, these parameters include 1) molecular weight, molecular weight distribution and molecular structure of polymers (branch, linearity, etc.); 2) solution properties (concentration, viscosity, conductivity, surface tension, liquid flow rate, etc.); 3) electrodynamic potential; 4) distance between capillary and collector; 5) environmental parameters (temperature, humidity and indoor air velocity); 6) motion law of collection device; and 7) shape of spinneret needle. Thus, it is often very difficult to manipulate the nanofibers' size in an accurate manner when the traditional single-fluid electrospinning is exploited [16].

Coaxial electrospinning is popular owing to its capability of creating core-sheath nanostructures. It is a common sense that the sheath working fluid must be electrospinnable for a successful coaxial preparation procedure [17]. However, this concept was broken by Yu and his co-worker, who have developed a modified coaxial electrospinning. In the modified coaxial process, the fluids without electrospinnability can also be utilized as the sheath fluids [17-19]. Because the spinnable polymers

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are extremely limited, whereas the number of unspinnable is unlimited. Thus, on one hand, the modified coaxial electrospinning can greatly expand the capability of electrospinning in developing new kinds of nanostructures. On the other hand, the modified coaxial electrospinning can be explored to generate monolithic nanofibers with higher quality [20, 21] provided solvent was utilized as the sheath fluid. Compared with the traditional blending electrospinning, there are more parameters that can be exploited to manipulate the nanofibers' diameter in a precise way, e.g. the core-to-sheath fluid flow rate ratio and the components and composition of sheath solvents. Based on the above-mentioned knowledge, here, we investigate the influence of *N*, *N*-dimethylacetamide (DMAc) ratio in sheath fluid on the diameters of medicated cellulose acetate nanofibers using a modified coaxial electrospinning.

2. Materials and methods

2.1 Materials

This Cellulose acetate (CA, white powder; M_w = 80,000 Da) was purchased from Acros (NJ, USA). Ibuprofen (IBU) was purchased from Shanghai Haosheng Chemical Co., Ltd. (Shanghai, China). *N*, *N*-dimethylacetamide (DMAc), acetone, and anhydrous ethanol were purchased from Wuhan Chemical Reagent Co., Ltd. (Wuhan, China).

2.2 Modified coaxial electrospinning

The core CA solution was prepared by dissolving 12 g of CA and 3 g of IBU, in 100 mL of a solvent mixture consisting of acetone, DMAc, and ethanol in a volume ratio of 4:1:1. The sheath fluids were prepared with a variable ratio of DMAc and acetone, which is concluded in Table 1.

Table 1. Parameters of the modified coaxial processes and their products

No.	Sheath-to-core flow rate 0.2-1.0 (mL/h)		Morphology [b]	Diameter (nm)
	Sheath fluid (content of DMAc%)	Core fluid [a]		
F1	Mixed DMAc & acetone (100%)	1.0	Linear	330±80
F2	Mixed DMAc & acetone (80%)	1.0	Linear	440±70
F3	Mixed DMAc & acetone (60%)	1.0	Linear	620±60
F4	Mixed DMAc & acetone (40%)	1.0	Linear	710±110

[a] Core fluid consists of 12% (w/v) CA and 3% (w/v) IBU in a mixture of acetone, DMAc, and ethanol at a volume ratio of 4:1:1

[b] ''Linear'' morphology refers to nanofibers with few beads or spindles on them

Two KDS100 syringe pumps (Cole-Parmer®, IL, USA), a power supply (ZGF 60 kV/2 mA, Shanghai Sute Corp., Shanghai, China), a home-made concentric spinneret, and a fiber-deposited collector were arranged together for carrying out the modified electrospinning.

Following some optimization, the applied voltage was fixed at 17 kV and the fibres were deposited on an aluminium foil collector at a distance of 20 cm. All electrospinning processes were carried out under ambient conditions (21 °C ±4 °C with relative humidity of 51% ± 4%). Electrospinning was recorded using a digital video recorder (PowerShot A490, Canon, Tokyo, Japan).

2.3 Characterization

The morphology of the electrospun products was evaluated using a field emission scanning electron microscope (FE-SEM) (S-4800, Hitachi, Tokyo, Japan). Prior to the examination, the samples were sputter-coated with platinum. The average diameter of nanofibers was determined by measuring their diameters from FE-SEM images at over 100 different places using ImageJ software (NIH, MD, USA).

3. Results and discussion

3.1. The modified coaxial processes

Electrospinning is a special form of electrostatic atomization of polymer fluids. During the working process, the substances separated by atomization are not small droplets, but polymer micro-jet, which can run for a long distance and finally solidify into fibers. Under the action of electric field, the droplets at the needle will change from spherical to conical (i.e. "Taylor cone"), and the filaments will be extended from the tip of the cone. In this way, nano diameter polymer filaments can be produced.

Similarly, coaxial electrospinning can treat two working fluids in a core-sheath manner simultaneously, resulting solid core-sheath nanofibers, nanocoating, or monolithic nanoproducts. A typical organization of coaxial electrospinning is shown in Figure 1. This system can be utilized to conduct both coaxial and modified coaxial processes, with the only difference of the spinnability of treated sheath liquids. Here, although two fluids were treated and the Taylor cone was a compound structural one, the resultant products were homogeneous medicated nanofibers, with the drug IBU uniformly distributed all over the CA matrices.

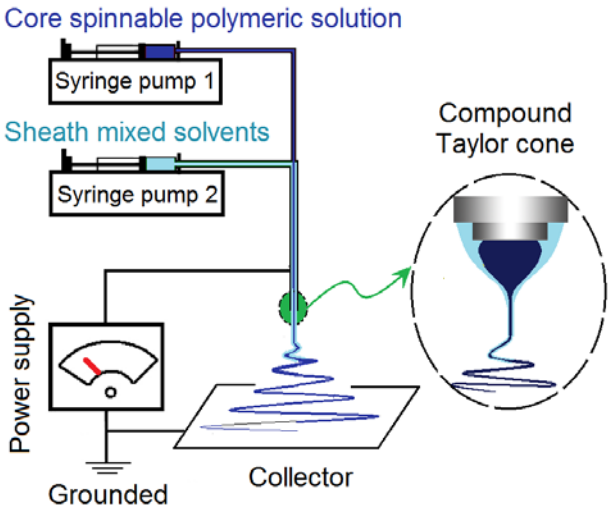

Figure 1. A diagram of the coaxial electrospinning

In the coaxial electrospinning system, the most important element is the spinneret, which is a standpoint for naming the working process. Shown in Figure 2A is the concentric spinneret utilized in the present investigation. An inner smaller stainless- steel capillary was nested into a larger metal capillary to form a concentric nozzle, which was exploited to lead the sheath and core working fluids into the electrical fields. This structural spinneret can also be explored to conduct coaxial electrospraying for creating core-shell nanoparticles [21-24] and modified coaxial electrospraying process for generating high quality nanoparticles [25-29]. In Figure 2B, the conveying of high voltage energy can be realized simply through an alligator clip. The whole systems guiding the working fluids and providing the electrical potential are very light, which should do favor to the implementation of coaxial electrospinning.

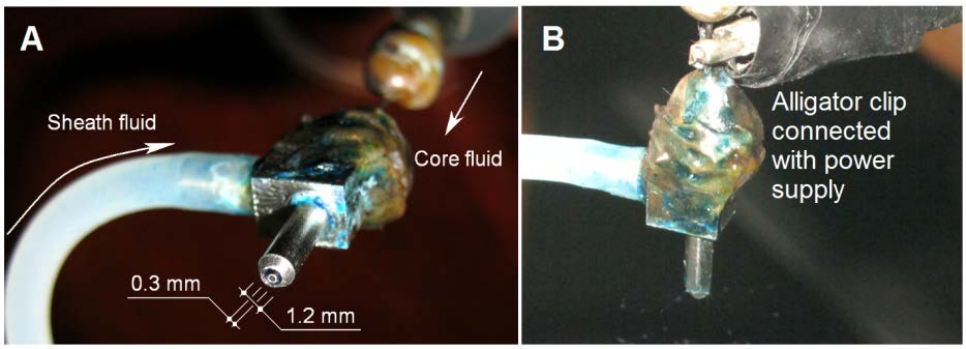

Figure 2. Implementation of the coaxial process: (A) the homemade spinneret; (B)the connection of the spinneret with the power supply through an alligator clip

Shown in Figure 3 are digital images of the real working processes with different DMAc volume ratios in the sheath mixed solvents. Corresponding to the ratios of 100% (Figure 3A), 80% (Figure 3B), 60% (Figure 3C), and 40% (Figure 3D), the as-prepared medicated nanofibers are termed as F1, F2, F3 and F4, respectively. It is clear from that images that all the processes consisted of typical three stages, i.e. the Taylor core, the straight fluid jet, and the instable region with numerous bending and whipping loops. As the decrease of DMAc contents in the sheath fluids, or as the increase of acetone concentrations, the straight fluid jets became shorter and shorter, which should have a close relationship with the easy evaporation of acetone.

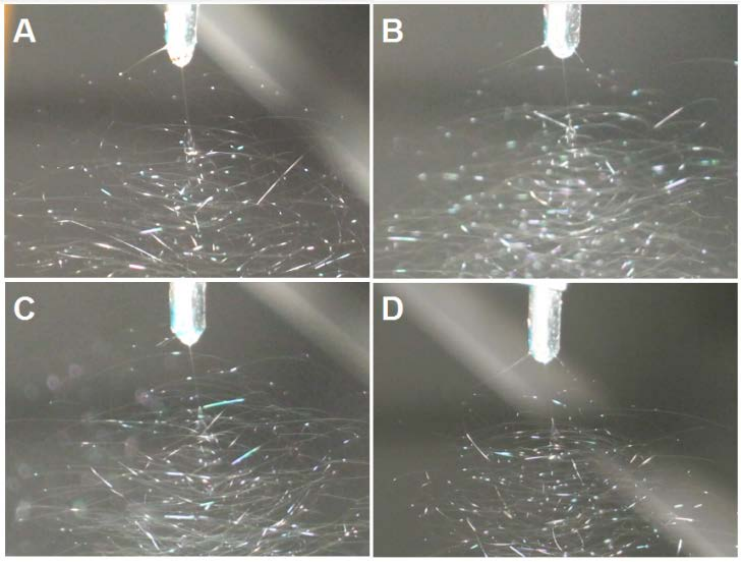

Figure 3. Digital images about the real working processes with different DMAc volume ratios in the sheath mixed solvents: (A)100%; (B)80%; (C) 60%; (D)40%

3.2. The electrospun nanofibers

The SEM images of the four types of IBU-loaded CA nanofibers were shown in Figure 4. All the medicated nanofibers generated under the selected experimental conditions have fine linear morphology with smooth surface. Few beads-on-a-string or spindles-on-a-string morphology can be found in them, reflecting the fine electrospinnability of IBU-loaded CA core working fluids and the suitable components and compositions of solvents in the mixed sheath working fluids.

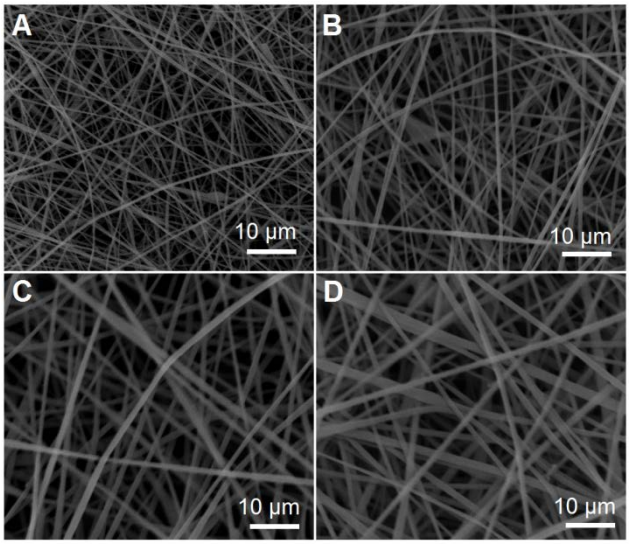

Figure 4. The FE-SEM images of the medicated nanofibers: (A) F1; (B) F2; (C) F3; (D) F4

By estimation, the medicated nanofibers F1, F2, F3 and F4 have an average diameter of 330 ± 80, 440 ± 70, 620 ± 60, 710 ± 110 nm, respectively. As the increase of acetone ration in the sheath liquid, the resultant nanofibers' diameter increased correspondingly. The reasons should be that DMAc has a high boiling point of 166 ^{o}C, whereas acetone has a low boiling point of 57 ^{o}C. A lower boiling means that the sheath solvent clung on the surface of core polymeric solution for a shorter time period, and correspondingly a shorter drawing effect by the electrical forces, thus in turn, a larger diameter of the final solid nanofibers.

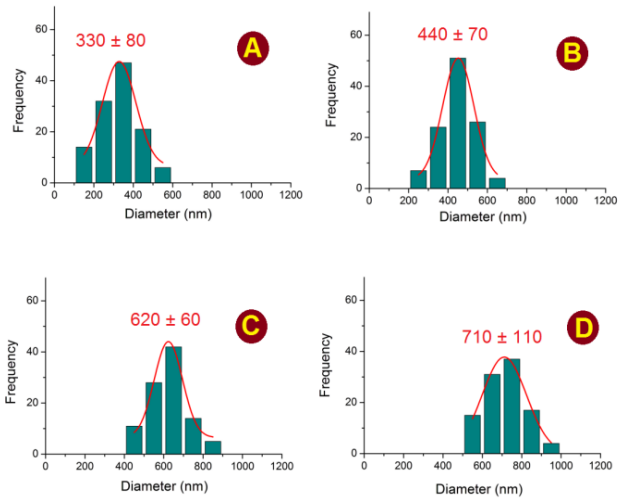

Figure 5. The estimated diameter values of the fibers: (A) F1; (B) F2; (C) F3; (D) F4

3.3. The influence of DMAc ratio on the diameters of medicated CA nanofibers

Based on the change trend of the medicated CA nanofibers' diameter (D) with the volume ratio of DMAc in the sheath fluid (*r*), a linear relationship between them can be achieved as D= 1013-685r (Figure 6). This equation has a correlated coefficient of R^2=0.9835, reflecting a good linear relationship. This relationship should be very useful for manipulating the nanofibers' size, simply through adjusting the volume ratio of DMAc in the sheath mixture, which is impossible for the traditional blending electrospinning.

Along the present job, a series of new investigations can be further conducted. For example, the in vitro controlled release profiles of the nanofibers on the encapsulated drug IBU, the in vivo experiments on the potential drug sustained release, the cell cytotoxology and biocompatibility, the

cell and even clinical effects for therapeutics. Certainly, based on the strategy here, modified coaxial electrospraying processes can also be adjusted through the compositions and components in their sheath working fluids.

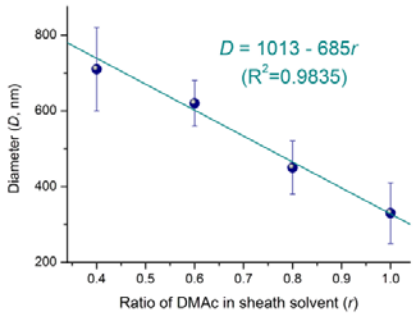

Figure 6. The influence of DMAc ratio on the diameters of medicated CA nanofibers

4. Conclusion

A series of modified coaxial electrospinning processes were successfully carried out under variable ratios of DMAc in the sheath mixture with acetone. Observations using camera demonstrated that all the working processes were smooth, continuous and robust regardless of the decrease of DMAc volume ration in the sheath fluid. However, the characteristic parameter of the electrospinning processes such as the length of straight fluid jet changed gradually with the DMAc ratio. FE-SEM images demonstrated that all the prepared ibuprofen-loaded cellulose acetate nanofibers had a linear morphology with few beads or spindles on them. A concrete linear relationship between the medicated CA nanofibers' diameter (*D*) and the volume ratio of DMAc in the sheath fluid (*r*) was achieved as D= 1013-685r with a correlated coefficient of R^2=0.9835.

Acknowledgments

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