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An Alternative Solvent System for Blend Electrospinning of Polycaprolactone/Chitosan Nanofibres

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Summary: PCL/chitosan blend nanofibres could provide an excellent nanostructured material for biomedical use since their beneficial properties are combined into one material. This paper focuses on the solvent use in the production of PCL/chitosan nanofibres by solution electrospinning, since this is a crucial parameter in the electrospinning process. It was established that an acetic acid/formic acid shows great potential for the stable electrospinning of the blend. Additionally, the fibre morphology using this solvent system was analysed.

Keywords: blends; chitosan; electrospinning; polycaprolactone

Introduction

Polymer nanofibres have taken a prominent role in the area of materials research and nanotechnology because of their promising results in numerous applications such as filtration, tissue engineering, drug delivery systems, etc.[1,2] This is due to their unique characteristics, being high specific surface area, small pore size and high porosity. There are several methods of producing nanofibres such as drawing, template synthesis, phase separation, self-assembly and electrospinning. At present, electrospinning is the only well-established technique able to produce continuous nanofibres in a convenient and upscalable process.[3] Most of the effort in electrospinning has been spent on the spinning of various single polymer-solvent systems. Recently cautious attempts towards polymer blends are noticed to meet the demand for nanofibres in which the favourable characteristics of two polymers are combined.[4]

Chitosan, a natural polysaccharide derived from chitin, is a very promising material for biomedical use due to its inherent properties. Chitosan shows biocompatibility, biodegradability, hydrophilicity, non-toxicity and antimicrobial activity.[5] Moreover, there are several structural possibilities for chemical modifications of chitosan, making it possible to introduce new functionalities for specific applications.[6–8] Chitosan nanofibrous structures may be ideal materials for tissue engineering, wound dressings, etc. since it is well-known that nanofibres promote tissue healing and cell growth by mimicking the native extracellular matrix.[9] However, chitosan has a rigid D-glucosamine structure, high crystallinity, polycationic behaviour in solution and the capacity to form intermolecular hydrogen bonds.[10] This leads to poor solubility in common organic solvents and poor processability in the electrospinning process, both causing numerous difficulties in the production of pure chitosan nanofibres. Moreover, the practical use of chitosan nanofibres is limited by their poor mechanical properties.[11] Both the electrospinnability and the mechanical properties can be improved by blending chitosan with an appropriate synthetic polymer.[12,13] Polycaprolactone

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(PCL) is a biocompatible, biodegradable, non-toxic polyester widely used in the biomedical sector. It is an ideal candidate for blend electrospinning because of its good processability, mechanical properties and exceptional blend-compatibility.[14] Moreover, using a PCL/chitosan blend compensates for the disadvantageous characteristics of PCL, such as hydrophobicity and lack of interaction with native cells, since chitosan supplies both hydrophilic and cell-recognition sites.[13] PCL/chitosan blend nanofibres could thus provide an excellent nanostructured material for biomedical use.

This study aims to investigate the solvent use in the production of PCL/chitosan blend nanofibres by solution electrospinning. An in-depth literature study and coupled practical trials were performed to identify the most promising solvent system. Subsequently, this solvent system is studied in more detail.

Materials and Methods

Materials

Medium molecular weight chitosan and PCL (Mn 70,000–90,000) were supplied by Sigma–Aldrich. Also the solvents 98 v% formic acid (FA) and 99.8 v% acetic acid (AA) were obtained from Sigma–Aldrich.

Preparation and Characterization of the Electrospinning Solutions

The solutions were magnetically stirred at room temperature for three-and-a-half hours, time needed for complete dissolution. The viscosity of the solutions obtained was measured using a Brook- field viscometer LVDV-II.

The Electrospinning Process

During the electrospinning process, the polymer solution was pumped from a 20 mL syringe into a 15.24 cm long needle with an inner diameter of 1.024 mm. A KD Scientific Syringe Pump Series 100 regulated the flow rate of the solution. The voltage was adjusted using a Glassman High Voltage Series EH 30P3 source (voltage range 0–30 kV). Electrospinning was carried out at room temperature (22 ± 2 ○C) and a relative humidity of 35 ± 5%. All the solutions were electrospun at their optimal process conditions, meaning that the tip to collector distance, the flow rate and the voltage were adjusted to obtain a stable electrospinning process. For the electrospinning of the PCL/chitosan blend, the tip to collector distance was set at 12.5 cm and the flow rate was set at 0.6 mL/h, while the voltage was adjusted to obtain the best result.

Results and Discussion

Electrospinning of Pure PCL and Pure Chitosan

The electrospinning process of pure PCL has already been researched extensively.[15–22] Our previous study indicates that an acetic acid/formic acid (AA/FA) solvent system is preferable for the electrospinning of PCL, as the production of very fine beadless nanofibres is realised in a stable way.[22] Also the electrospinning of pure chitosan nanofibres has been reported in literature.[4,5,12,23–29] Although it was generally possible to produce nanofibres, most studies indicate that there are numerous difficulties encountered when attempting to electrospin pure chitosan and very few report on the stability of the process.

There are essentially two solvent systems reported in literature that facilitate the electrospinning of pure chitosan. The first is trifluoroacetic acid (TFA), which can destroy the strong interactions between the chitosan molecules by salt formation. Further, to obtain a stable process, often dichloromethane (DCM) is added to the solvent system. These solvents are, however, toxic and thus less suitable for the envisioned biomedical applications. Secondly, aqueous acetic acid (aqAA) is frequently used, but with many difficulties that are linked to the high viscosity of chitosan in solution. It has been stated that the appropriate polymer concentration to form defect-free nanofibres by electrospinning is 2 to 2.5 times the entanglement concentration.[30] The latter is the boundary between the semidilute unentangled regime and the semidilute entangled regime of a polymer solution. However, at these concentrations chitosan solutions have a very high viscosity, often impeding the electrospinning process.[12] It is thus very difficult to find a viscosity window in which chitosan solutions are electrospinnable. In order to evaluate the aqAA solvent system, a series of experiments was carried out using medium molecular weight chitosan. None of the produced solutions could combine sufficient solubility, appropriate viscosity and electrospinnability, confirming the conclusions from literature.

Solvent Systems for Blend Electrospinning of PCL/Chitosan

As the interest in blend electrospinning is growing rapidly, also the electrospinning of PCL/chitosan blends has recently been reported in literature.[13,31–33] Several solvent systems are used, namely 1,1,1,3,3,3-hexafluoro-2-propanol (HFIP), HFIP/TFA/DCM, dimethyl formamide/methylene chloride (DMF/MC) and acetone/formic acid (Ac/FA). Because of the toxicity of most of these solvents, only the Ac/FA solvent system will be considered. However, a second solvent system may show great potential for the blend electrospinning of PCL/chitosan, namely AA/FA, since it facilitates the stable electrospinning of pure PCL[22] and the dissolution of chitosan. Both the Ac/FA solvent system suggested in literature and the novel AA/FA system were evaluated and compared.

Two blend solutions containing 8 wt% PCL and 0.8 wt% chitosan were prepared, one using 50/50 AA/FA and the other using 50/50 Ac/FA. Both solutions were electrospun at optimal process conditions and facilitated the production of nanofibres (Figure 1). As can be seen from SEM analysis, there is no significant difference in fibre morphology between both cases. However, using the Ac/FA solvent system no stable electrospinning process could be obtained because of fast solidification at the tip of the needle, probably due to the high volatility of acetone. This resulted in an interruption of the process after several seconds. Therefore, only the AA/FA solvent system was considered for further research.

Analysis of the AA/FA Solvent Ratio

The optimal AA/FA solvent ratio for the electrospinning of PCL/chitosan was determined by a series of electrospinning trials, using a polymer blend containing 8 wt% PCL and 0.8 wt% Chitosan as Representative Sample. Pure PCL can be electrospun using an AA/FA ratio from 10/90 up to 70/30. Therefore, several solvent ratios within this window were tested for blend electrospinning. Multiple solutions facilitated the production of nanofibres, but only the solutions having an AA/FA ratio of 30/70

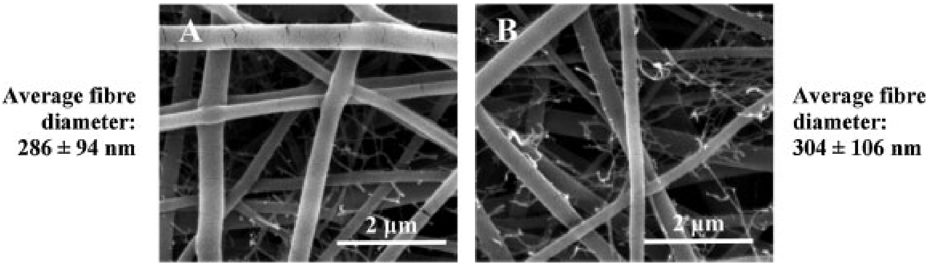


Figure 1.
SEM images of PCL/chitosan blend nanofibres produced using (A) an AA/FA solvent system and (B) an Ac/FA solvent system.

up to 50/50 resulted in a stable process. It has been proven that finer fibres can be produced when the solution conductivity is increased.[22] The AA/FA solvent ratio directly influences the solution conductivity (0.57 and 0.32 mS/cm for 30/70 and 50/50 AA/FA resp.). In line with this, lowering the AA fraction in the solvent system produced finer nanofibres (203 ± 44 nm and 367 ± 1 18 nm when using 30/70 and 50/50 AA/FA resp.). Therefore, a solvent ratio of 30/70 AA/FA was selected for further investigation.

Practical Application of the 30/70 AA/FA Solvent System

Both PCL and chitosan have to be stable in 30/70 AA/FA to guarantee that the solvent system is applicable in the blend electrospinning process. This was verified by viscosity measurements. Van der Schueren et al. determined that PCL remains stable in the AA/FA solvent system for up to 3 h after dissolving. This is considered to be a suitable time frame for electrospinning.[22] Complementary, the stability of chitosan in the solvent system was tested in a similar way. The measurements indicated that also chitosan is stable in the solvent system for a minimum of 3 h after dissolution (Figure 2), confirming the practical applicability of 30/70 AA/FA for the blend electrospinning of PCL/chitosan.

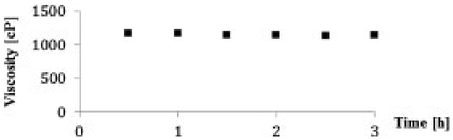
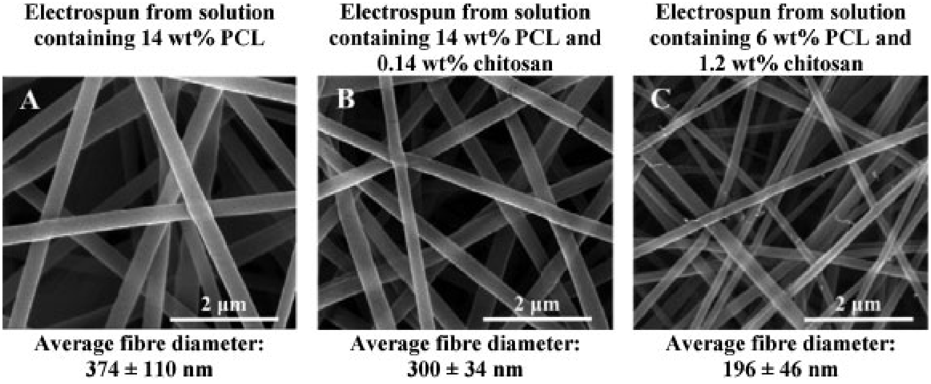


Figure 2.
Viscosity of a 1.25 wt% chitosan solution in 30/70 AA/FA as a function of time after dissolution.

Morphology of the Resulting PCL/chitosan Blend Nanofibres

Using a fixed AA/FA solvent ratio allows for the analysis of the influence of the polymer concentrations on the nanofibre morphology. By varying both polymer concentrations, it was established that chitosan has a major effect on the fibre morphology. There is namely a clear decrease in fibre diameter when the chitosan content is increased. Even the addition of a very small amount of chitosan, only 1% of the PCL concentration, leads to finer fibres with smaller deviations (Figure 3A vs. Figure 3B). By increasing the chitosan amount further to 20% of the PCL concentration, the effect becomes larger (Figure 3C). This can be ascribed to the changes in solution properties due to chitosan. The chitosan addition causes a strong increase in viscosity and charge density of the solutions. Therefore, solu-



Electrospun from solution containing 14 wt% PCL — Average fibre diameter: 374 ± 110 nm

Electrospun from solution containing 14 wt% PCL and 0.14 wt% chitosan — Average fibre diameter: 300 ± 34 nm

Electrospun from solution containing 6 wt% PCL and 1.2 wt% chitosan — Average fibre diameter: 196 ± 46 nm

Figure 3.
SEM images of PCL/chitosan blend nanofibres produced from electrospinning solutions having different PCL and chitosan concentrations in 30/70 AA/FA.

tions with a lower total polymer concentration can be electrospun and higher elongation forces are imposed during the spinning process, both leading to finer fibres.[34]

Conclusion

In this paper, the solvent use in the solution electrospinning process of a PCL/chitosan polymer blend was studied. The potential of the AA/FA solvent system has been proven and an optimal solvent ratio was established. AA fractions of 30 v% up to 50 v% resulted in a stable electrospinning process and beadless, uniform nanofibres. Decreasing the AA fractions leads to finer blend nanofibres. Additionally, both PCL and chitosan are stable in the solvent system up to 3 h after dissolution, providing an acceptable time frame for electrospinning. Also the fibre morphology was studied using the AA/FA solvent system and it was established that an increase in chitosan content decreases the average fibre diameter and deviations. In conclusion, the newly developed solvent system AA/FA shows major potential for the solution electrospinning of a PCL/chitosan polymer blend.

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[1] N. Bhardwaj, S. C. Kundu, *Biotechnol. Adv.* **2010**, *28*, 325.

[2] J. Fang, H. Niu, T. Lin, X. Wang, *Chin. Sci. Bull.* **2008**, *53*, 2265.

[3] S. Ramakrishna, K. Fujihara, W.-E. Teo, T.-C. Lim, Z. Ma, "*An introduction to electrospinning and nanofibers*", (11th ed.), World Scientific Publishing, Singapore **2005**, p. 7.

[4] J. D. Schiffman, C. L. Schauer, *Polym. Rev.* **2008**, *48*, 317.

[5] R. Jayakumar, M. Prabaharan, H. Tamura, *Biotechnol. Adv.* **2010**, *28*, 142.

[6] K. Kurita, *Mar. Biotechnol.* **2006**, *8*, 203.

[7] K. V. Harish Prashanth, R. N. Tharanthan, *Trends Food Sci. Technol.* **2007**, *18*, 117.

[8] R. Jayakumar, M. Prabaharan, S. V. Nair, S. Tokura, H. Tamura, N. Selvamurugan, *Prog. Mater. Sci.* **2010**, *55*, 675.

[9] A. Greiner, J. H. Wendorff, *Angew. Chem. Int. Ed.* **2007**, *46*, 5670.

[10] L. Li, Y.-L. Hsieh, *Carbohydr. Res.* **2006**, *341*, 374.

[11] L. Wu, H. Li, S. Li, X. Li, X. Yuan, X. Li, *J. Biomed. Mater. Res. Part A* **2010**, *92A*, 563.

[12] R. R. Klossner, H. A. Queen, A. J. Coughlin, W. E. Krause, *Biomacromolecules* **2008**, *9*, 2947.

[13] M. P. Prabhakaran, J. R. Venugopal, T. T. Chyan, L. B. Hai, C. K. Chan, A. Y. Lim, S. Ramakrishna, *Tissue Eng. Part A* **2008**, *14*, 1787.

[14] M. A. Woodruff, D. W. Hutmacher, *Prog. Polym. Sci.* **2010**, *35*, 1217.

[15] H. Yoshimoto, Y. M. Shin, H. Terai, J. P. Vacanti, *Biomaterials* **2003**, *24*, 2077.

[16] C. M. Vaz, S. van Tuijl, C. V. C. Bouten, F. P. T. Baaijens, *Acta Biomater.* **2005**, *1*, 575.

[17] F. Chen, C. N. Lee, S. H. Teoh, *Mater. Sci. Eng. C* **2007**, *27*, 325.

[18] N. Bölgen, Y. Z. Menceloglu, K. Acatay, I. Vargel, E. Piskin, *J. Biomater. Sci., Polym. Ed.* **2005**, *16*, 1537.

[19] S.-C. Wong, A. Baji, S. Leng, *Polymer* **2008**, *49*, 4713.

[20] K. Ohkawa, H. Kim, K. Lee, H. Yamamoto, *Macromol. Symp.* **2004**, *216*, 301.

[21] A. K. Moghe, R. Hufenus, S. M. Hudson, B. S. Gupta, *Polymer* **2009**, *50*, 3311.

[22] L. Van der Schueren, B. De Schoenmaker, O. Kalaoglu, K. De Clerck, *Eur. Polym. J.* **2011**, *47*, 1256.

[23] V. Sencadas, D. M. Correia, A. Areias, G. Botelho, A. M. Fonseca, I. C. Neves, J. L. Gomez Ribelles, S. Lanceros Mendez, *Carbohydr. Polym.* **2012**, *87*, 1295.

[24] K. Ohkawa, D. Cha, H. Kim, A. Nishida, H. Yamamoto, *Macromol. Rapid Commun.* **2004**, *25*, 1600.

[25] S. De Vrieze, P. Westbroek, T. Van Camp, L. Van Langenhove, *J. Mater. Sci.* **2007**, *42*, 8029.

[26] X. Geng, O.-H. Kwon, J. Jang, *Biomaterials* **2005**, *26*, 5427.

[27] H. Homayoni, S. A. H. Ravandi, M. Valizadeh, *Carbohydr. Polym.* **2009**, *77*, 656.

[28] R. Jayakumar, D. Menon, K. Manzoor, S. V. Nair, H. Tamura, *Carbohydr. Polym.* **2010**, *82*, 227.

[29] R. Nirmala, B. W. Il, R. Navamathavan, M. H. El-Newehy, H. Y. Kim, *Macromol. Res.* **2011**, *19*, 345.

[30] M. G. McKee, G. L. Wilkes, R. H. Colby, T. E. Long, *Macromolecules* **2004**, *37*, 1760.

[31] H. Yang, X. Chen, H. Wang, *Biomacromolecules* **2009**, *10*, 2772.

[32] S. Hong, G. Kim, *Carbohydr. Polym.* **2011**, *83*, 940.

[33] K. T. Shalumon, K. H. Anulekha, C. M. Girish, R. Prasanth, S. V. Nair, R. Jayakumar, *Carbohydr. Polym.* **2010**, *80*, 413.

[34] L. Van der Schueren, I. Steyaert, B. De Schoenmaker, K. De Clerck, *Carbohydr. Polym.* **2012**, *88*, 1221.