Cellulose Acetate Microstructured Particles obtained by electrospraying

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Abstract: The polymeric concentration and solvent/co-solvent characteristics used in preparing polymer solutions are fundamental in achieving particles with desired properties. Cellulose acetate (CA) films were obtained by electrospinning/electrospraying using a concentration range between 4-8 % of the polymer in acetone/ethyl acetate as the binary solvent mix. Both the solvent and co-solvent had similar characteristics except acetone, which is a better solvent for the polymer and also has a higher dielectric constant with a lower boiling point and slightly faster evaporation rate. Ethyl acetate as a co-solvent results in lower viscosity, leading to jet break up into smaller particles. The microparticles obtained showed a mean diameter of 9.52 μm +/- 2.99 μm SD at 6 % wt CA solution in a 3:2 acetone/ethyl acetate solvent mix. The resulting polygonal porous microparticles from the 4% cellulose acetate solution were anticipated, due to the physicochemical characteristics and solubility parameters of solvents and the amount of polymer near its critical concentration, showing the importance of these parameters in obtaining nanofibers or microparticles with the desired aspects.

Keywords: *microparticle, electrospinning, electrospraying, solvent selection, cellulose acetate*

Introduction

Electrospinning and electrospraying are used for making polymeric nano-microfibers and nano-microparticles, respectively, for a variety of applications. The solvent used in preparing polymer solutions has a significant influence on its spinnability and is fundamental in obtaining nanofibers or micro/nanoparticles with desired properties [1, 2, 3]. Solvents should have some properties such as good volatility, vapor pressure and boiling point. Thus, for successful electrospinning the selection of an appropriate solvent system is indispensable. The intermolecular interaction in a polymer–solvent system is either attractive or repulsive depending solely on the type of solvent [4]. A common solvent for electrospun cellulose acetate is acetone. A limitation of using acetone as a pure solvent is that its use results in clogging of the needle because of its high volatility. Liu and Hsieh [5] studied the effect of solvent on the spinnability for formation of smooth nanofibers, using cellulose acetate (CA) solutions and found that, while CA solutions in pure solvents of acetone, acetic acid, and N,N-dimethylacetamide (DMAc) do not provide the formation of continuous fibers, blending of DMAc with either acetone or acetic acid produces suitable spinnable systems. Water was also used as co-solvent at 10–15 wt% to acetone [6] and a mixed solvent of

chloroform/methanol has been shown to produce thin beaded CA fibers. Even ternary mixtures of acetone, dimethylformamide (DMF) and trifluoroethylene were reported as solvents for CA [2].

On the basis of Hansen's solubility theory, composition of binary solvent mixtures were optimized by Haas et al. (2010) [2] with respect to the control of fiber morphology.

As in electrospinning, electrospraying also involves the use of high voltages to induce the formation of a liquid jet using a relatively low polymer concentration (below or near a critical polymer concentration), which results in particles rather than fibers. The solvent/co-solvent characteristics are fundamental to produce different types or shapes of particles or fibers.

In the present study, CA microparticles were obtained from a 4 % polymer solution (w/v) in acetone/ethyl acetate as a binary solvent mix.

Materials and methods

A custom made electrospinning machine with a 60 kV HV supply was used. The syringe pump consisted of 3 ml syringes and a rotary aluminum collector adjusted to about 60 rpm. Cellulose acetate with a molecular weight of 50.000 of (Mw) was purchased from Sigma-Aldrich Co. Acetone and ethyl acetate were purchased from Labsynth Ltda. Acetone was chosen because it is a common solvent for cellulose acetate, while ethyl acetate (ETAC) was selected as the co-solvent. To test the effects of different concentrations on microparticles, 4, 6 and 8 % (w/v) of CA (between the critical polymer and entanglement concentrations) in acetone and ETAC were used. The solution of CA dissolved in the binary solvent mix was homogenized in a magnetic stirrer overnight. The solution was fed in to the electrospinning machine with a syringe pump at a rate of 0.053 ml/min using a 3 ml syringe with a blunt ended needle (BD Precision Glide 22G). A 1.81 kV/ cm voltage difference was applied between the needle and collector where the nanofiber film was deposited.

The films were analyzed in scanning electron microscopy (SEM) (JEOL JSM 6060) equipment in three different regions, selecting 30 random microparticles, which were analyzed with the ImageJ software package. The samples were deposited directly onto an aluminum support (stub). The samples which were settled in the aluminum blocks were metalized with gold and visualized in the microscope at 10kv. Each microparticle was evaluated in its maximum and minimum diameter in order to get an average size of the irregular polygonal shape.

Results and discussion

For solvent selection, Hansen three-dimensional solubility parameters were used [7]. By these means, the quality of the solvent (denoted by the R_{ij} value listed in Table 1) was estimated. The R_{ij}

value is defined as $R_{ij} = \sqrt{4(\delta_{d1} - \delta_{d2})^2 + (\delta_{p1} - \delta_{p2})^2 + (\delta_{h1} - \delta_{h2})^2}$ (where δ_{d1}, δ_{p1}, and δ_{h1} are the three-dimensional solubility parameter values for the solvent; and δ_{d2}, δ_{p2}, and δ_{h2} are those for the polymer). The smaller the R_{ij} value, the better the solvent is for the polymer. The R_{ij} of acetone is 7.73 MPa (Table 1). The lower sphere radius for the case of CA ($R_{ij} \leq 7.6$) according to Liu et al [7]) predicts that the solvent will dissolve the polymer, while ETAC will not ($R_{ij}=10.03$). Therefore, increasing the ethyl acetate content is expected to worsen the binary solvent mix effect. The use of acetone as a pure solvent is limited because it clogs the needle due to its high volatility.

Table 1. Hansen solubility parameters of polymer and solvents used [a]

Polymer/ Solvent	V (cm^3/mol)	Solubility parameter [(MPa)$^{1/2}$]				R_{ij}*
		δ_d	δ_p	δ_h	δ_t	
Cellulose Acetate		18.6	12.7	11	25.1	
Acetone	74	15.5	10.4	7	20.1	7.73
Ethyl acetate	98.5	15.8	5.3	7.2	18.2	10.03

a. Adapted from Brandrup 2000 [8]. * R_{ij} calculated by the authors

Acetone was chosen because it is a common solvent for electrospinning [5], while ETAC could lead to particle formation, as discussed below. Liu and colleagues (2008) [7] divided polymer-particle formation conditions by means of solvent characteristics. The solvents were divided into poor and good solvents. The evaporation rates of the solvents were divided into three categories: fast, medium, and slow. The physicochemical characteristics of solvents used are shown in Tab. 2.

Table 2: Physicochemical characteristics of solvents used [8].

	Surface tension (mN/m)	Evaporation rate (Ether=1)	Boiling point ^{o}C	Dipole moment	Dielectric Constant
Acetone	23	2.1	56	2.88	20.7
Ethyl acetate	23.75	2.9	78	1.78	6.02

Both the solvent and co-solvent have similar values for surface tension and medium evaporation rates, while acetone has a higher dielectric constant, lower boiling point and slightly faster evaporation rate. As the acetone is a better solvent for CA compared to ETAC, it is expected to give a higher viscosity solution. Poor solvents result in a lower viscosity, thereby allowing for jet break up into smaller particles [7], leading to an electrospray of the particles and particle formation. Because of this, ethyl acetate was chosen.

Both the solvent and co-solvent have similar characteristics except acetone, which is a better solvent for the polymer and also has a higher dielectric constant with a lower boiling point and slightly faster evaporation rate.

Due to the fact that concentration plays an important role in the shape of particles or fibers, a concentration of 4% CA was selected, corresponding to the critical polymer concentration (c*) [2]. Electrospraying is achieved at a concentration similar or lower to this.

Porous polygonal microparticles resulted from the experiment with a mean diameter of 9.52 μm 2.99 μm SD (standard deviation) and a median of 9.60 μm at 6 % wt CA solution in a 3:2 acetone/ethyl acetate solvent mix. The diameter range was between 5.94 and 10.36 μm. See figure 1 below
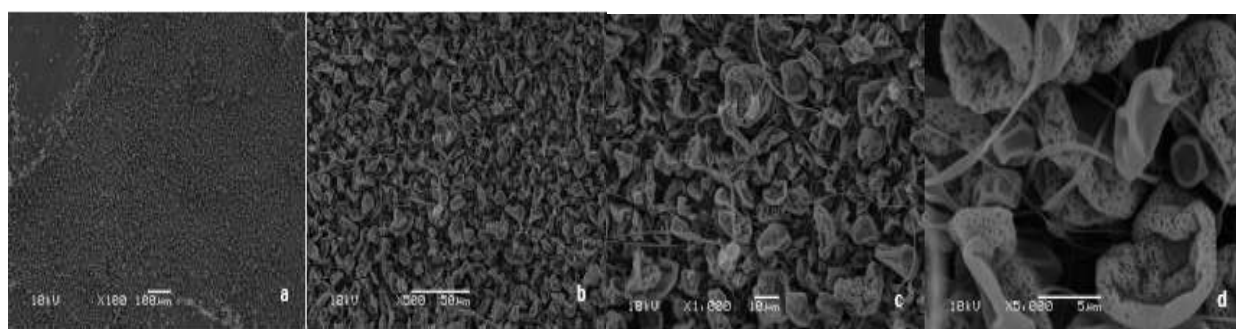

Figure 1. SEM analysis of the polygonal porous microparticles with some microparticles. Sample of a 4 % (w/v) cellulose acetate in a acetone:ethyl acetate (3:2) binary solvent mix (a, b, c e d). The scale bars corresponding to 100 μm, 50 μm, 10 μm and 5 μm, respectively (a, b, c and d).

Effect of polymer concentration: Above the critical polymer concentration (c*), 4% in the case of CA, the polymer chains can overlap, but do not entangle each other, leading to electrospray, as can be seen in Fig. 2.a and Fig. 2.b. At high concentration, above entanglement concentration (c_e), overlapping of the polymer chains favors entanglement, which gives rise to a much stronger interaction and so leads to smooth fibers [2].
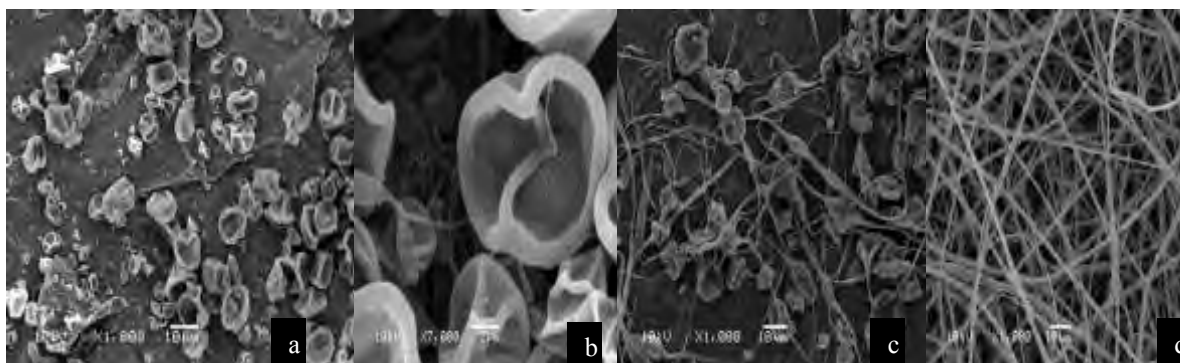

Figure 2. SEM images of CA at 4 % wt. concentration at 1,000x (a) and 7,000x (b) magnification. CA at of 6 % wt concentration (c) and 8% wt (d). Acetone: ethyl acetate (3:2) was used as binary solvent mix.

Haas and colleagues 2009 [2] showed that for the CA with molecular weight of 30,000 g/mol, the boundary concentrations were found at $c^* \approx 4$wt% and $c_e \approx 12$ wt%, while in this work beads-on-string were found at an intermediate concentration (Fig. 2.c) and smooth nanofibers without beads with a concentration lower (Fig. 2.d) than the c_e were found by Haas and colleagues. This difference could be explained by the higher molecular weight and voltage applied in this study.

Shape morphology.

According to Liu and colleagues [7], when a poor solvent with a fast evaporation rate is used, porous hollow spheres are produced. For a solvent with a medium evaporation rate, hollow spheres with open mouths are processed. For a poor solvent with a slow evaporation rate, cups are obtained, as shown in the examples (Fig. 3) [7]. Most of the studies focused on the solvent to obtain microparticles using electrospraying.
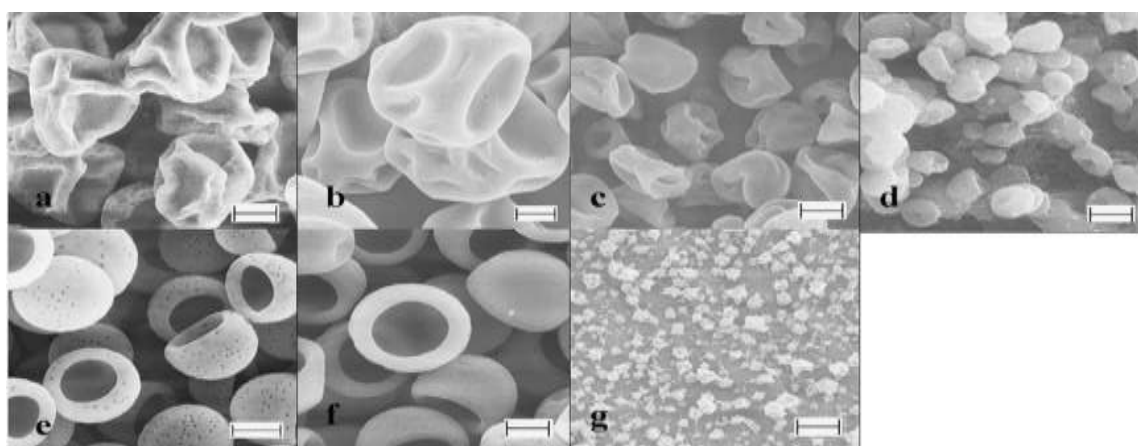

Figure 3. Electrospun particles from PMMA solution (8 wt.-%) in different solvents: (a) methylene chloride, (b) THF, (c) acetone, (d) DMF, (e) nitromethane, (f) acrylonitrile, (g) formic acid. The scale bars of (a) and (b) are 10 μm, (c) to (g) are 2 μm. From Liu and colleagues [7]

These considerations explain the shape of the microparticles produced. The mix of microparticles and rare nanofibers was expected because the shape changes from particles to beads-on-string and then to smooth nanofibers as the concentration rises and better solvents are used

Conclusion

In this study, polygonal porous microparticles were produced from a 4 % cellulose acetate solution using a binary solvent mix of acetone: ethyl acetate. The shapes of the microparticles achieved were expected by the physicochemical characteristics and solubility parameters of the solvents and also a polymer solution approximate to the critical polymer concentration.

Acknowledgments

References:

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

[2] D. Haas, S. Heinrich, P. Greil. J Mater Sci. 2010, *45*, 1299.

[3] S. Tungprapa, T. Puangparn, M. Weerasombut, I. Jangchud, P. Fakum, S. Semongkhol, C. Meechaisue, P. Supaphol. Cellulose. 2007, *14,* 563.

[4] Y. Zhang, J. Qian, Z. Ke, X. Zhu, H. Bi, K. Nie. Eur Polym J. 2002, *38,* 333.

[5] H. Liu, Y.L. Hsieh. J Polym Sci Part. B: Polym Phys. 2002, *40*, 2119.

[6] W.K. Son, J.H. Youk, T.S. Lee, Y.H. Park. J Polym Sci—Polym Phys. 2004, *42*, 5.

[7] J. Liu, A. Rasheed, H. Dong, W. W. Carr, M. D. Dadmun, S. Kumar. Chem. Phys. 2008, *209*, 2390.

[8] J. Brandrup, E. H. Immergut, and E. A. Grulke, Polymer Handbook, 4th edition, John Wiley & Sons, New York. 2000.