Electrospinning of collagen with nanocapsules of PLGA for delivery of paclitaxel in drug -eluting stents

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ABSTRACT

This work develops a new delivery system trying to understand better, the factors that influences the drug release. This system use nanofiber produced by electrospinning technic and bioabsorbable polymeric nanocapsules produced by the nanoprecipitation processes in a recirculated system develop in the research group. For this work, we used an electrospinning equipment built at the university, in which you can control the process parameters such as voltage, deposition rate, collector distance, speed and direction of rotation of the collector, to control the morphology and diameter of the nanofibers. The final electrospinning condition to obtain nanofiber of collagen (Sigma-Aldrich) with 99 ± 26 nm was 18 V, collector distance of 14cm, flow rate of 0.1mL/h and polymer concentration was 25% W/V in acetic acid and distilled water 9:1. On the other hand, we encapsulated Paclitaxel in bioabsorbible polymeric nanocapsules of PLGA (Resomer 752 H, Evonik) produced in a recirculated system design in the university. The conditions used to encapsulate the paclitaxel was 4mg/mL of polymer concertation, 20% of drug respect to dry polymer, 162 mL/min of flow rate in the recirculating system, 0.25% of Pluronic F-127 (Sigma-Aldrich) as surfactant in the aqueous phase and 2:1 ratio between aqueous phase and organic phase.

Keywords: nanpresipitation, electrospining, stents, drug delivery

INTRODUCTION

Drug-eluting stents can facilitate a drug's release directly to the specific site, but the main difficulty with drug-eluting stents is that the initial burst of drug release can extremely affect the pharmacological action and this is the biggest drawback that worries physicians and researchers in this field (1,2). Therefore, the drug release rate has become an important standard in evaluating Drug-eluting stents (2). The factors affecting the drug release rate include the drug, drug carrier, coating methods, drug storage, direction of elution, coating thickness, pore size in the coating, and release conditions like pH, temperature, release medium and hemodynamics after the stent implantation. This work develops a new delivery system trying to understand better, the factors that influences the drug release. This system use nanofiber produced by electrospinning technic and bioabsorbable polymeric nanocapsules produced by the nanoprecipitation processes in a recirculated system develop in the research group.

On the other hand, we encapsulated Paclitaxel in bioabsorbable polymeric nanocapsules of PLGA (Resomer 752 H, donated by Evonik) produced in a continuous recirculated system by nanoprecipitation technic, according to previous works (3,4). The nanocapsules were lyophilized and added to the collagen solution for electrospinning of the samples. The nanostructured delivery system and his individual components was characterized using TEM, SEM, AFM, contact angle and DLS for the nanocapsules. The released of paclitaxel was measure
ment using the HPLC method.

MATERIALS

We used PLGA (Resomer 752 H) donated by Evonik. Collagen, acetic acid, Pluronic F127, aceton and solvents for caracterization in HPLC were purchased from Sigma-Aldrich. The Paclitaxel was purchased from LC Laboratories.

3 METHODS

3.1 Syntesis of nanocapsules

To prepare the nanocapsules was necessary to use two phases. First, the organic phase was made with the polymer, solvent and the paclitaxel. Second phase or water phase was made with deionized water and the surfactant according to previous works (3). In Figure 1, it is shown the diagram of the recirculating system used for this work.

The conditions used to encapsulate the paclitaxel was 4mg/mL of polymer concertation, 20% of drug respect to dry polymer, 162 mL/min of flow rate in the recirculating system, 0.25% of Pluronic F-127 (Sigma-Aldrich) as surfactant in the aqueous phase and 2:1 ratio between aqueous phase and organic phase.

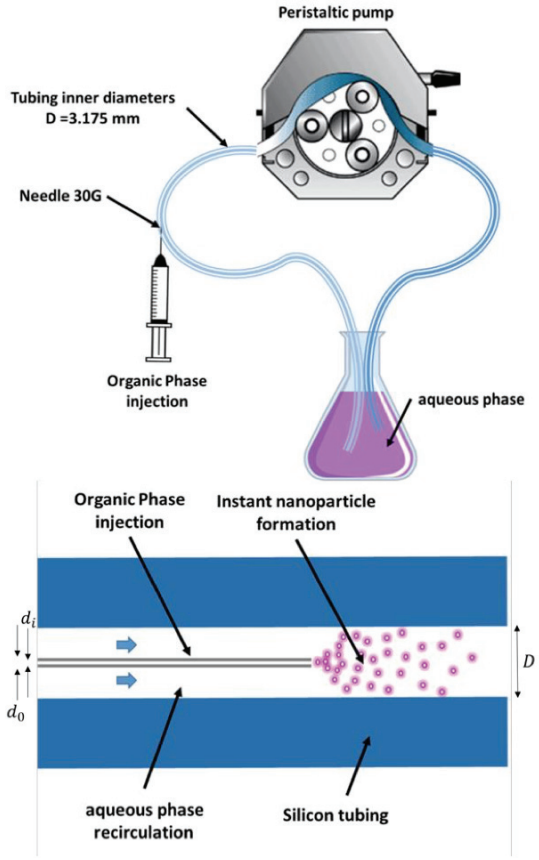

Figure 1. Description of the recirculating system(3)

3.2 Electrospinning

The electrospinning process may be considered the most promising of all nanotechnologies, due to versatility and cost to produce nanofibers, with large surface area, porosity, orientation, and dimensions in a controlled manner with excellent mechanical and easy functionalization properties for multiple applications (5–9). The collagen solutions used to electrospun the nanofibers of this work was prepared at concentrations of 25% of the polymer in a solution of acetic acid and water 9:1, the nanocapsules were added to the solution in the water portion. Each solution was taken to the electrospinning equipment to 18 kV, an injection rate of 0.1 mL/h and the collector was positioned to 14 cm.

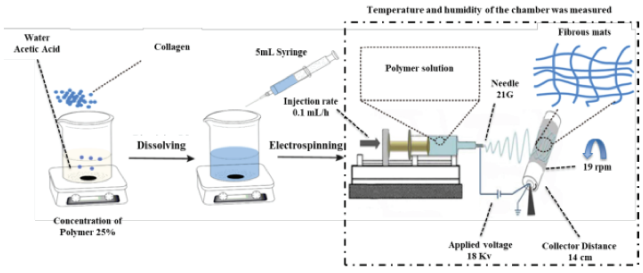

Figure 2. Description of the electrospinning process

4 RESULTS

4.1 Nanocapsules

Was possible to produce nanoparticles with good morphological characteristics, particle size distributions in the nano range, and with a low polydispersity using the recirculation system that was development in the research group. In the Figure 3 was shown the TEM images of PLGA nanocapsules with 20% of Paclitaxel used in this work.

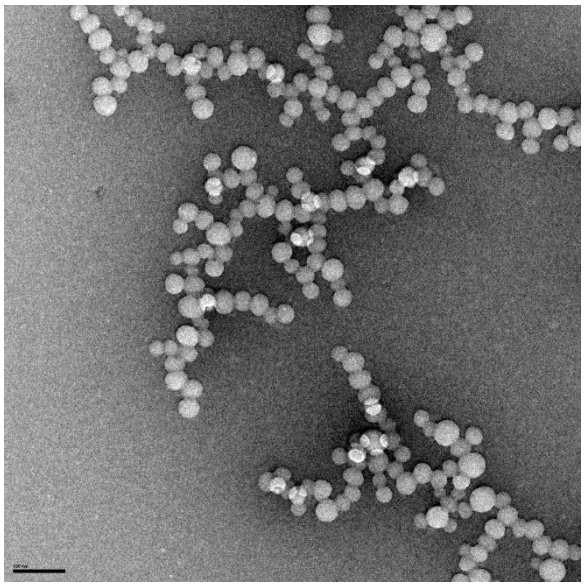

Figure 3. TEM image of PLGA nanocapsules with 20% of Paclitaxel

4.2 Electrospinning

It was also possible to obtain collagen fibers with and without PLGA nanocapsules with a good morphology and a size distribution in the nano range, as seen in Figures 4 and 5.

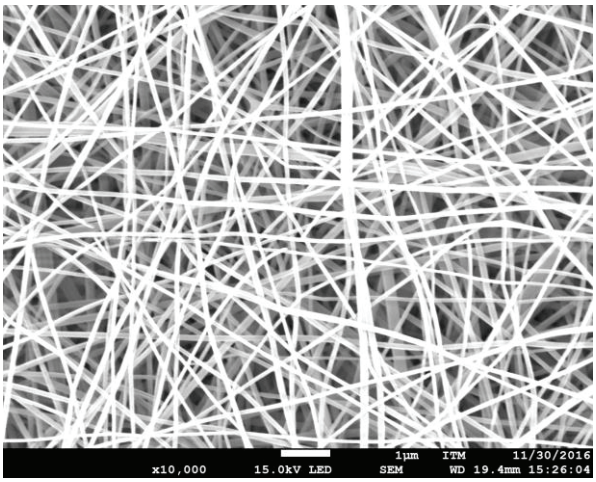

Figure 4. SEM image of nanofiber of collagen

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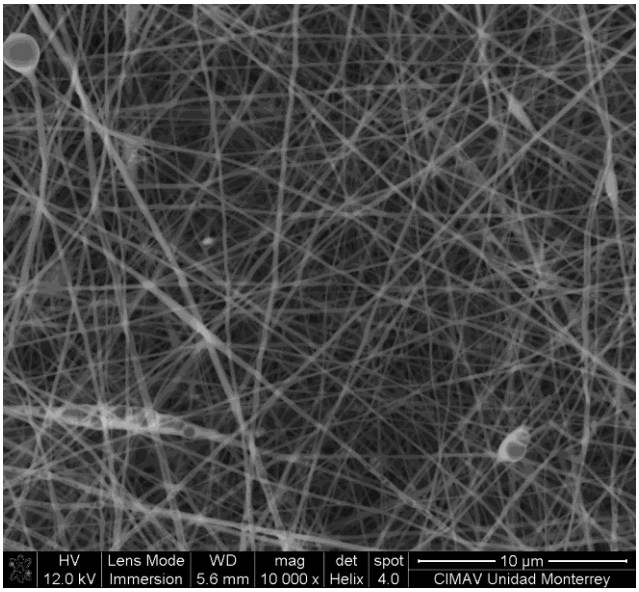

Figure 5. FESEM image of nanofiber of collagen with PLGA nanocapsules inside

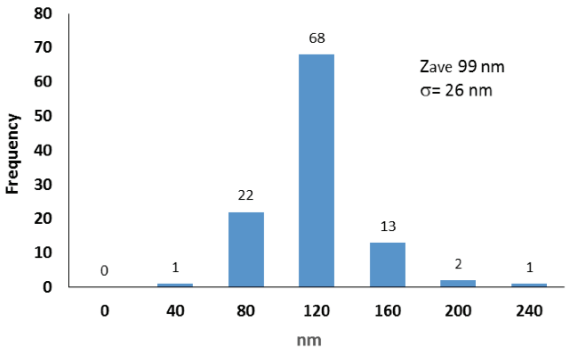

Figure 6. Distribution diameter of the nanofiber of collagen

CONCLUSION

With this work it was possible to develop a nanostructured coating obtained by the electrospinning technique using collagen and PLGA nanocapsules that carry Paclitaxel to be released slowly. Nanocapsules with low polydispersity and a particle size around 60 nm were obtained. The morphology observed in the TEM images showed that the casulas were very uniform. On the other hand, the obtained fibers reached an average diameter around 99nm, with a uniform morphology.

REFERENCES

[1] Hohenforst-Schmidt W, Zarogoulidis P, Pitsiou G, Linsmeier B, Tsavlis D, Kioumis I, et al. Drug eluting stents for malignant airway obstruction: A critical review of the literature. J Cancer. 2016;7(4):377–90.

[2] Hu T, Yang J, Cui K, Rao Q, Yin T, Tan L, et al. Controlled Slow-Release Drug-Eluting Stents for the Prevention of Coronary Restenosis: Recent Progress and Future Prospects. ACS Appl Mater Interfaces [Internet]. 2015;7(22):11695–11712. Available from: http://pubs.acs.org/doi/abs/10.1021/acsami.5b01993

[3] Colmenares Roldán GJ, Agudelo Gomez LM, Carlos Cornelio JA, Rodriguez LF, Pinal R, Hoyos Palacio LM. Production of polycaprolactone nanoparticles with low polydispersity index in a tubular recirculating system by using a multifactorial design of experiments. J Nanoparticle Res [Internet]. Journal of Nanoparticle Research; 2018 Mar 9;20(3):68. Available from: http://link.springer.com/10.1007/s11051-018-4168-8

[4] Colmenares G, Agudelo L, Pinal R, Hoyos L. Production of Bioabsorbible Nanoparticles of Polycaprolactone by Using a Recirculating System. In: TechConnect World Innovation Conferences [Internet]. TechConnect; 2017. p. 395–8. Available from: https://briefs.techconnect.org/wp-content/volumes/TCB2017v1/pdf/178.pdf

[5] Paaver U, Heinämäki J, Laidmäe I, Lust A, Kozlova J, Sillaste E, et al. Electrospun nanofibers as a potential controlled-release solid dispersion system for poorly water-soluble drugs. Int J Pharm [Internet]. Elsevier B.V.; 2015;479(1):252–60. Available from: http://linkinghub.elsevier.com/retrieve/pii/S0378517314009211

[6] Sridhar R, Venugopal JR, Sundarrajan S, Ravichandran R, Ramalingam B, Ramakrishna S. Electrospun nanofibers for pharmaceutical and medical applications. J Drug Deliv Sci Technol. 2011;21(6):451–68.

[7] Hu X, Liu S, Zhou G, Huang Y, Xie Z, Jing X. Electrospinning of polymeric nano fi bers for drug delivery applications. J Control Release [Internet]. 2014;185:12–21. Available from: http://dx.doi.org/10.1016/j.jconrel.2014.04.018

[8] Ershuai Z, Chuanshun Z, Jun Y, Hong S, Xiaomin Z, Suhua L, et al. Electrospun PDLLA / PLGA composite membranes for potential application in guided tissue regeneration. Mater Sci Eng C. 2016;58:278–85.

[9] Colmenares GJ, Quintero Y, Rodriguez LF, Agudelo LM, Hoyos LM. Influence of the molecular weight of polymer, solvents and operational condition in the electrospinning of polycaprolactone. Rev Fac Ing Univ Antioquia. 2017;(84):35–45.