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Functionalized nanofibers with anticoagulant activity for postoperative adhesions prevention: Plasma grafting or Coaxial electrospinning

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ABSTRACT

During intra-abdominal operations, postoperative adhesions, resulting in pain, occur in more than 50% of cases¹. This phenomenon consists in the formation of a fibrin matrix between organs and peritoneum 5 to 7 days following the surgery and is induced by the coagulation cascade. So, it is necessary to produce a long-term anti-coagulant active implant to limit these post-operative adhesions. Nowadays, a large variety of processes is used to design biomedical textile implants. Among them, electrospinning offers advantages in this field especially due to the nanoscale diameter range of electrospun fibers and their high porosity and surface area. In addition, cold plasma process can be used to activate and/or functionalize electrospun fibers. In the literature, cold plasma is indeed mainly used to enhance hydrophilicity or to graft polymers at the nanofibers surface². In this context, our strategy is to develop polypropylene (PP) implants, coated with polycaprolactone (PCL) electrospun nanofibers and functionalized by 2-acrylamido-2-methylpropane sulfonic acid (AMPS) (monomer with heparin-like groups). Two pathways were investigated: graft-copolymerization of AMPS onto PCL nanofibers by cold plasma treatment and coaxial electrospinning in order to obtain core-sheath (PCL-PolyAMPS) nanofibers.

First, the electrospinning conditions of PCL or AMPS simple solutions were optimized in terms of concentration, voltage, flow, tip-to-collector distance. The graft-copolymerization of AMPS onto PCL nanofibers was optimized to obtain cytocompatible nanofibers rich in SO₃H groups at the surface. Adequate physico-chemical characterizations were performed (FTIR, SEM, TGA...) at each step of the process. SEM images revealed an increase in the nanofibers diameter after the plasma induced graft-copolymerization, and mapping confirmed the presence of AMPS onto nanofibers obtained by the two pathways. Biological *in vitro* assays revealed promising results for anti-adhesive applications of these membranes for both pathways.

We have successfully optimized the electrospinning of PolyAMPS, PCL as well as AMPS grafting onto PCL mats by cold plasma, and we highlighted the presence of sulfonate groups onto the surface of the nanofibers. The cytocompatibility, haemocompatibility and anti-coagulant activities of the functionalized implants were demonstrated. Future work will focus on coaxial electrospinning of PCL and polyAMPS and the comparison of these two strategies in terms of bioactivity and industrial scale up costs. Grafting of other bioactive monomers was also consider in order to extend the field of potential biomedical applications.

<u>References :</u> [1] D. Menzies et al., Ann. R. Coll. Surg. Engl. (1993) 75 : 147-153

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