Novel Conductive Polymer-based Biomaterials for Pro-Vascularization under Electrical Stimulation

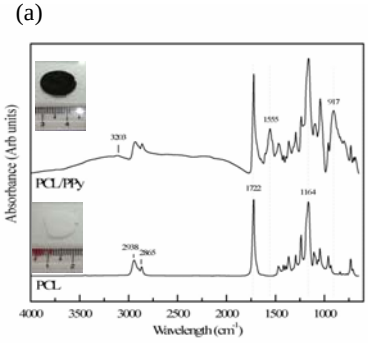
Gordon Xiong, Cleo Choong
Nanyang Technological University, Singapore

Introduction: Currently, large-volume tissue-engineered scaffolds suffer from inadequate vascularization. Although tissue-engineered scaffolds have shown some promise *in vitro* and in small animal models, large tissue grafts lose patency due to the lack of a functioning vasculature [1]. Recently, electrical stimulation has been reported to be able to promote endothelial cell proliferation and facilitate directional migration [2]. In order to explore this under-utilized mode of stimuli, we have fabricated a conductive composite scaffold consisting of polycaprolactone (PCL) and heparin-doped polypyrrole (PPy). The electrical and mechanical properties of the composite biomaterial, comprising of PCL nanofibers with a coating of PPy-heparin, was characterized for electrical and mechanical properties.

Methods: PCL nanofibrous scaffolds were obtained by electrospinning 10% (w/v) PCL dissolved in hexafluoro-2-propanol (HFP). The scaffolds were then immersed in a polymerization bath of pyrrole mononers and dopants (heparin, hydrochloric acid or camphorsulfonic acid) in diH_2O. Oxidative polymerization was initiated by the addition of ammonium persulfate (APS) and carried out for 16 h. The resulting PCL/doped-PPy scaffolds were characterized by SEM morphological examination, and resistivity and tensile readings were taken by a 4-point probe station and the Instron machine, respectively. The toluidine blue assay was also conducted on PCL/heparin-doped PPy to verify the presence of heparin on the material surface.

Results: The successful coating of PPy on the electrospun PCL fibers was verified using ATR-FTIR (Fig. 1a), while EDX analysis detected the presence of different PPy dopants (Fig. 1b).

(a)



(b)

	At% [S]	At% [Cl]	At% [C]
PCL/PPy	0.69	0.61	71.22
PCL/PPy-Hep	**2.31**	0.30	70.11
PCL/PPy-CSA	**1.25**	0.10	74.84
PCL/PPy-Cl	0.42	**4.21**	74.75

Fig. 1. (a) FTIR spectra of PCL and PCL/PPy showing characteristic peaks. (b) Atomic % of different elements in EDX spectra of different PCL/doped-PPy samples.

Resistivity measurements of the PCL/PPy scaffolds demonstrated, surprisingly, lowest resistivity in macromolecular dopant heparin (Fig. 2).

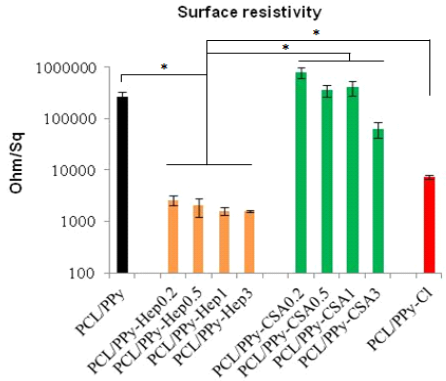


Fig. 2. Surface resistivity measurements of undoped PCL/PPy scaffolds, PCL/PPy doped with varying pyrrole-heparin weight ratios (Hep), varying pyrrole-camphorsulfonic acid molar ratios (CSA) or 1M HCl.

The toluidine blue assay also confirmed the presence of heparin entrapped within PCL/PPy-heparin scaffolds. Tensile testing revealed significant differences between the Young moduli of uncoated PCL meshes and PCL/heparin-doped PPy meshes. The nanofibers of the electronspun PCL scaffolds could be observed under SEM examination, and the coating of PPy-heparin on the PCL fibers could be seen at certain segments of the PCL/PPy-heparin scaffolds (Fig. 3)

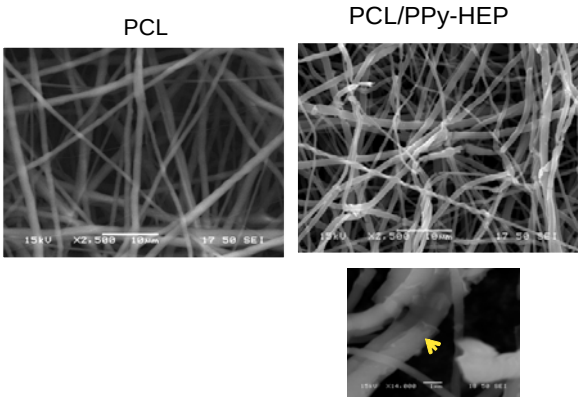


Fig. 3. Morphology of electrospun PCL scaffolds and PCL/PPy-heparin scaffolds. Higher magnification of the PCL/PPy-heparin scaffolds reveals the coat of heparin-doped PPy (yellow arrow)

Conclusion: Conductive heparin-doped PPy was successfully polymerized on PCL fibers and 3D porous collagen via oxidative polymerization and demonstrated lower resistivity and better mechanical properties than using other dopants. The novel heparin-based biomaterials could be used for endothelial cell culture, conjugation of growth factors and electrical stimulation.

References: [1] Novosel EC et al. 2011; Adv. Drug Deliv. Rev. **63:**4–5 [2] Zhao M. et al. 2004; J Cell Sci. **117**:3