Development of Conducting Polymer Composites for Peripheral Nerve Regeneration

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Introduction: The benenfits of electrical stimulation on tissue regeneration is well-documented in the scientific literature. Because of this, electrically conductive polymers have received significant interest for tissue engineering applications[1,2]. Polypyrrole (PPy) has received the most attention over other conducting polymers, such as polythiophene, for incorporation into biomatarials because of its stability, conductivity, and biocompatibility. However, polypyrrole is not suitable as a biomaterial because it has poor mechanical properties. Because PPy has poor mechanical properties, various approaches to blending PPy with other polymers that have more suitable mechanical properties are necessary. We recently developed polycaprolactone fumarate (PCLF) for applications in peripheral nerve regeneration[3, 4]. PCLF is a cross-linkable, biodegradable, flexible, and suturable material, which makes it suitable for use in nerve guidance tubes. We now extend this PCLF material to include a PPy-PCLF polymer composite that is conducting while maintaining the physical properties of the PCLF.

Methods: PCLF (M_n: 18,000 PDI: 1.96) was synthesized and molded into the desired scaffold shape by previously published procedures[3,4]. PCLF scaffolds were submerged in a solution of benzoyl peroxide (0.1-2.0 g) in methylene choride (20 mL) for various times (10-300 sec). The scaffold was removed and methylene chloride was removed under vacuum. The scaffolds were submerged in a 0 ºC aqueous 20 mL solution of pyrrole (0.56 g). and naphthalene sulfonic acid sodium salt (0.4 g) overnight. The scaffolds were removed and subsequently washed with distilled deionized water, acetone and the swelled with methylene chloride to remove residual impurities.

Results: The synthesis of PCLF-PPy scaffolds by polymerizing pyrrole in a preformed PCLF scaffold is a robust approach for incorporating PPy into complex three-dimensional architectures. PCLF scaffolds are composed of a cross-linked polycaprolactone derivative that swells, but does not dissolve, in organic solvents. This allows benzoyl peroxide to be occluded within the preformed PCLF scaffold by immersing the scaffold in a benzoyl peroxide/methylene chloride solution and then removing the solvent under vacuum. The scaffold is then submerged in an aqueous pyrrole/dopant solution. The pyrrole diffuses into the scaffold and is polymerized. This results in an interpenetrating network of PCLF-PPy. This novel technique enables the incorporation of polypyrrole into complex architectures (Figure 1) that are challenging or impossible to fabricate by other methods.

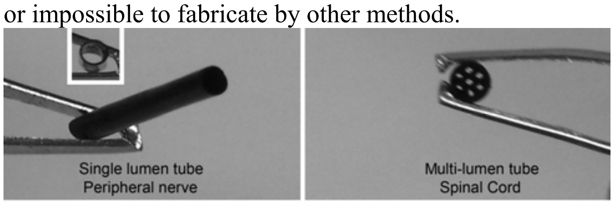

Figure 1. PCLF-PPy scaffolds of various architectures

The PCLF-PPy scaffolds were characterized by ATR-FTIR, DSC, TGA, SEM, and conductivity measurements. The conductivity of PCLF-PPy scaffolds can be manipulated by the amount of PPy incorporated into PCLF. The conductivity is affected by anion used to dope the PPy. Currently, different anions are being screened with PC 12 cells for an optimal chemical composition for cell attachment and proliferation. The presence of PPy in the scaffold is confirmed by ATR-FTIR. Figure 2 clearly shows the addition of a strong band from 1310-1610 cm^{-1} in the PPy-PCLF spectrum that is absent in the PCLF spectrum. This band is the skeletal C-C stretches characteristic of the pyrrole ring. Other bands at 1030-1070 cm^{-1} and 1150-1250 cm^{-1} are characteristic of the sulfonate group from the naphthalene sulphonic acid used to dope polypyrrole.

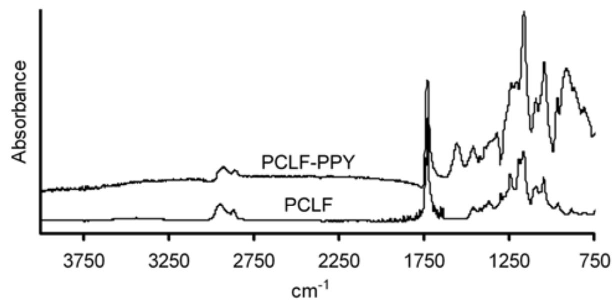

Figure 2. ATR-FTIR showing incorporation of PPy

Characterization of the PCLF-PPy thermal transitions was investigated by DSC. DSC shows a decrease in both T_m and T_c of the corresponding scaffolds. Higher percentages of PPy show larger decreases in both T_c and T_m. The T_c occurs below and T_m above the 37 ºC body temperature. The decrease in both transitions with the incorporation of PPy into the scaffold deters crystallization of the PCLF-PPy scaffold. This results in PCLF-PPy scaffolds that are more flexible than scaffolds composed solely of PCLF.

Conclusions: PCLF scaffolds that are currently being studied for applications as nerve guidance channels have been extended to include a conductive PCLF-PPy composite material. The technique reported here to incorporate PPy into the PCLF scaffolds is robust and necessary for applications that have complex three-dimensional architectures. Because PPy comprises less than twenty percent of the PCLF-PPy scaffold, the PCLF-PPy scaffold maintains the good physical properties of PCLF that are necessary for biomaterial applications.

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