Alginate/collagen porous scaffolds coated with conductive poly(3,4-ethylenedioxythiophene) nanoparticles for small-diameter tissue-engineered blood vessels

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Abstract

Cardiovascular disease (CVD) involving narrowing or obstruction of blood vessels remains the leading cause of morbidity and mortality today, despite advances made in the development of artificial vascular grafts. Although large-diameter tissue-engineered blood vessels (TEBVs) emerged some years ago as a successful alternative therapy to autologous vascular grafts to treat CVD, functional small-diameter TEBVs (∅ ≤ 6 mm) have not yet been achieved [1].

Using a triple coaxial nozzle, alginate, collagen and a sacrificial polymer were directly extruded obtaining the scaffold of a TEBV mimicking the microarchitecture of native blood vessels [2], with an outer diameter of 1599 ± 21 µm and a wall thickness of 265 ± 23 µm. After extrusion, the samples were first immersed in an aqueous solution of ammonium persulfate (APS) and secondly in a hexane solution, establishing a coating of different molar concentrations of conductive poly(3,4-ethyldenedioxythiophene) (PEDOT) nanoparticles (average diameter of 50 nm) on the outer layer of the scaffolds to promote cell adhesion and stimulation [4,5].

Double-layered conduits developed by direct extrusion showed high homogeneity and reproducibility. Moreover, it was found that liophylization of samples was not necessary after extrusion as it was not favorable for acquiring good conduit properties. The two best molar concentration ratios of PEDOT to APS were found to be 4:2 and 8:2, which proved to increase the swelling rates of pure Alg/Col scaffolds while significantly decreasing their degradation process and increasing the mechanical properties.

The improved surface roughness caused by these nanoparticles increased the hydrophilicity of the scaffolds (the higher the PEDOT molar concentration ratio, the lower the water contact angle), which favored cell adhesion in both concentrations of PEDOT/Alg/Col scaffolds. The conductive polymer increased the mechanical properties (burst pressure increased from 1.13 ± 0.05 bar in pure Alg/Col scaffolds to 3.38 ± 0.08 bar in 4PEDOT/Alg/Col scaffolds) and the electrical conductivity (PEDOT/Alg/Col hydrogels with a molar concentration ratio of 4 presented the highest electrical conductivity, 122.18 ± 1.32 µS/cm) of the scaffolds, allowing cell survival. The obtained structures were seeded with human aortic smooth muscle cells (hASMC) on the outermost layer. The PEDOT layer on the surface of the scaffolds induced a rough topography that allowed hASMCs to adhere and proliferate on the outer layer of the samples.

In summary, conductive porous conduits were developed by uniformly assembling PEDOT on the surface of Alg/Col scaffolds through in situ interfacial polymerization. The hydrophilic hydrogel was then characterized, sterilized and hASMCs were seeded. The combination of the natural polymers together with these conductive nanoparticles encompassed the advantages of both, obtaining a potentially exceptional scaffold for vascular regeneration [6]. These results suggest that this method might be suitable for stimulating smooth muscle cells (SMCs) with this small-diameter TEBV in the future. Being able to bioengineer this type of functional artificial arteries would not only represent an advance as small-diameter vascular substitutes for grafts, but also for vascularizing artificial organs.

References

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Figures

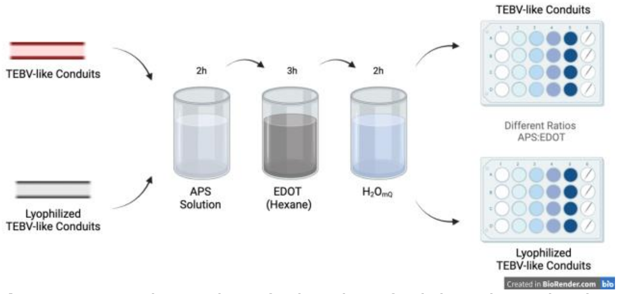

Figure 1. Schematic of the interfacial polymerization procedure to obtain conductive PEDOT/Alginate/Collagen scaffolds. Image created using BioRender.

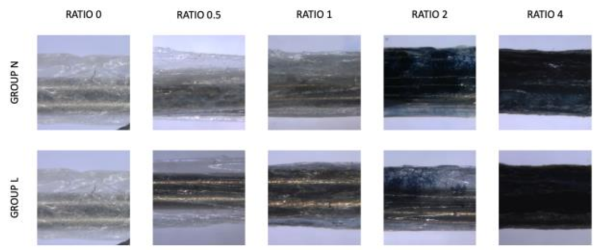

Figure 2. Optical images of the two groups of polymerized PEDOT/Alg/Col conductive scaffolds at different molar concentration ratios of APS to EDOT. Group N, lyophilized exclusively after the interfacial polymerization in situ, and Group L, lyophilized before and after the incorporation of nanoparticles.

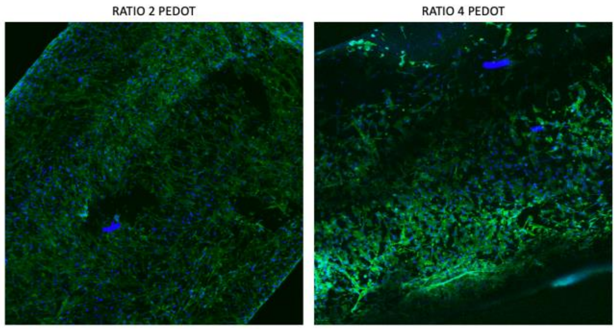

Figure 3. Confocal microscopy images of hASMCs seeded in the conduits with two different PEDOT ratios (2 and 4). Actin filaments stained in green (Phalloidin), and the nucleus stained in blue (DAPI).