PEGDA-Gelatin/PEDOT:PSS hydrogels as electroconductive and 3D-printable scaffolds for cardiac tissue engineering

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INTRODUCTION

Hydrogels are hydrophilic polymeric networks, able to mimic the microenvironment of human tissues and therefore they are widely studied in tissue engineering (TE). Electroactive tissues, such as cardiac, neural and muscle, strictly depends on electrochemical signaling between cells. Therefore, TE scaffolds interacting with those tissues should be designed with electroconductive properties [1]. Electroconductive hydrogels (ECHs), are a class of smart biomaterials that merge the electrical properties of intrinsically conductive materials with hydrogel networks. In recent studies, the *in vivo* application of conductive hydrogels demonstrated their ability to re-synchronize heart contraction, after myocardial infarction [2]. Nevertheless, a hydrogel-based scaffold with highly tunable electrical and mechanical properties, showing also bioactivity, biocompatibility and biodegradability, is still missing [1]. Furthermore, the heart tissue has an highly hierarchical and anisotropic microstructure [3]. In cardiac TE, scaffolds able to support alignment of contractile cells, are demanded. Bioprinting methods are promising as they can print oriented constructs. Furthermore, the application of bioprinting to photo-crosslinkable hydrogels may allow high spatiotemporal control of scaffold structure [3]. The aims of this work, were: (i) the development of photo-curable ECHs based on polyethylene glycol diacrylate (PEGDA), gelatin and poly(3,4-ethylenedioxythiophene):poly(styrene sulfonate) PEDOT:PSS, with tunable electrical, mechanical and bioactive properties for cardiac tissue engineering application; (ii) to investigate the suitability of PEGDA-Gelatin/PEDOT:PSS hydrogels as inks for prospective biofabrication of engineered cardiac tissues.

MATERIALS AND METHODS

Following previous studies by the authors, photo-cured PEGDA-gelatin hydrogels were optimized. Herein, Riboflavin was used as a biocompatible photoinitiator and different PEGDA/gelatin hydrogels were tested. PEDOT:PSS was added to hydrogels to impart electrical conductivity. Photopolymerization was analyzed by photorheology. Mechanical compression properties were studied, while electrical properties were evaluated by sheet resistance and dielectric spectroscopy. *In vitro* degradation properties of hydrogels were also evaluated. As a proof of concept for cardiac tissue engineering use, *in vitro* biocompatibility and adhesion tests with human cardiac fibroblasts (HCFs) were performed on hydrogels. Finally, printability of hydrogels was also preliminarily assessed.

RESULTS AND DISCUSSION

Hydrogel gelation time, final cross-linking density, microstructure, swelling and degradation properties were finely modulated by PEGDA/gelatin ratio. By its increase, hydrogels with increasing stiffness were obtained, with elastic moduli close to that of healthy native cardiac tissue. The addition of PEDOT:PSS into the hydrogels reduced gelation time and increased surface and bulk electrical properties. As a bioactive component, gelatin was successfully integrated into the hydrogel network. Hydrogels were also cytocompatible and promoted the adhesion of HCFs up to 5 days.
Finally, PEGDA-Gelatin/PEDOT:PSS hydrogels were micro-extruded into grid-shaped scaffolds.

CONCLUSIONS

Electroconductive photo-curable PEGDA-gelatin/PEDOT:PSS hydrogels were developed as promising for future bioprinting of cardiac tissues.

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