PLA/HAP MICROFIBERS INCORPORATED GRAPHENE-LOADED HYDROGELS FOR TISSUE ENGINEERING

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Introduction

In tissue engineering, it is especially important to design scaffolds which mimic the complex, multi-scale structure of natural tissues. In recent years, polymer hydrogels (polymer matrices able to absorb a large amount of water) have gained a lot of research interest [1-3] due to their similarity to the extracellular matrix (ECM).
The applicability of chitosan-based hydrogels, despite their superior biological properties, is limited by poor mechanical properties and stability. A multi-scale scaffold based on chitosan (CS) hydrogel with incorporated microfibers was proposed in this study as a solution to this issue. The advanced electrospinning (ES) method was chosen for the fabrication of poly(lactic acid)/hydroxyapatite (PLA/HAp) nonwoven. In addition, to enhance the hydrogel properties, graphene-based materials (GO or rGO) and tannic acid (cross-linker, TAc) were introduced to the polymer matrix.

Materials and Methods

CS (High Mw, DD >90%) and sodium tripolyphosphate (TPP) were obtained from Acros Organics, USA. Lactic acid (LAc, 88%), TAc, NaOH, NaCl, N,N-dimethylformamide (DMF) and dichloromethane (DCM) were purchased from Avantor Performance Materials Poland S.A. PLA was obtained from NatureWorks LLC, USA. HAp was obtained from Chema-Elektromet, Poland. Graphene oxide (GO) and reduced graphene oxide (rGO) were prepared by ITME, Poland.
The PLA microfibers modified with bioactive particles (HAp) were fabricated by an electrospinning method (ES). Polymer solution (13% w/v) was obtained by dissolving PLA in binary solvent system of DCM and DMF (2.5:1 v/v). The concentration of inorganic particles was 6 wt%. The parameters of ES were optimized (temperature: 50°C, the gap between the tip of the needle and the collector: 4 cm, humidity: 10%, voltage: 25 kV) to obtain fibers with specified microstructure. In the next step, fibers were introduced to the hydrogel matrix (5% wt. CS in 5% LAc, with 10% wt. TAc and 0.5% wt. GO or rGO) to create three-dimensional, multi-scale scaffolds. Samples were frozen in molds for 24 h. Next, they were immersed in a gelling solution (5% NaCl and 0.5% TPP, 24 h) at 4°C [4].
FTIR-ATR, XRD, XPS and SEM methods were used to characterize graphene materials and fabricated scaffolds. Also, thermal (DSC), mechanical (compression test) and rheological properties were examined. The biocompatibility of hydrogels and fibers was evaluated by culturing MG-63 cells in direct contact with the materials.

Results and Discussion

The microstructure of the PLA/HAp microfibers and CS-based tube scaffold was observed using SEM (FIG. 1).

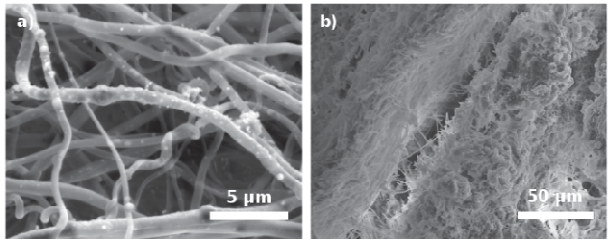

FIG. 1. SEM images of PLA/HAp microfibers (a) and CS/GO scaffold with incorporated woven (b).

The ES process allowed to successfully fabricate randomly oriented microfibers. The main aim of incorporation nonwovens into CS-based matrix was to increase the mechanical properties and degradation time of CS/GO and CS/rGO hydrogels. Also, the three-dimensional tubes exhibited unique morphology with two types of pores. Gaps between scaffolds walls can potentially improve cells penetration and transport of nutrients and metabolic wastes.
In addition, composites with microfibers exhibited improved stability during PBS immersion test (37°C, 6 weeks) and high bioactivity (SBF, 37°C, 2 and 4 weeks). *In vitro* test (MG-63) showed good cytocompatibility of all the samples.

Conclusions

A novel method was developed to fabricate three-dimensional scaffolds in the form of tubes dedicated for cartilage and bone tissue engineering. Dual porous microstructure of the samples can potentially improve cells penetration into the scaffold. Multi-scale scaffolds with hydrogel matrix were created to better mimic the complex microstructure of the ECM.

Acknowledgments

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