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Collagen modified porous pHEMA–TiO_2 composite hydrogels for tissue engineering

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Poly(2-hydroxyethyl methacrylate) (pHEMA) hydrogels are well known for their applications as vision correction devices including contact lenses and intraocular lenses. Like most other synthetic hydrogels, pHEMA is bio-inert and lacks cell binding sites for extended applications as tissue regeneration scaffolds. Collagen has been extensively used to enhance the cellular activities of biomaterials. However, modification with collagen molecules is often limited to the surface of hydrogels [1]. In this work, we report the preparation of collagen modified porous pHEMA–TiO_2 composite hydrogels through the formation of a semi-interpenetrating polymer network and the observation of significantly improved cell activities on the modified pHEMA hydrogels.

pHEMA and pHEMA–TiO_2 composite hydrogels were first produced using a reported method [2]. Collagen modification was carried out by crosslinking collagen molecules (10 mg/ml) in the presence of hydrated pHEMA and pHEMA–TiO_2, using 0.25% glutaraldehyde. The resulting hydrogels contain interconnected pores. Fibrous networks of collagen were observed on the cross-section of the modified hydrogels (Fig. 1a, b). FTIR and UV–vis spectra also demonstrated the presence of the collagen molecules in the modified hydrogel matrices (data not shown). All hydrogels were well tolerated by 3T3 mouse fibroblast cells. The growth of both 3T3 fibroblast and hMSCs was significantly enhanced and accelerated only after incorporation of the collagen into the hydrogel matrices (Fig. 1c–f). Migration and in-growth of hMSCs into the collagen bonded hydrogel scaffolds were also well demonstrated in the laser confocal images which is of significant importance for the application of any scaffolding material in the regeneration of tissues.

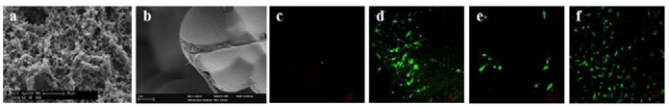

Fig. 1. SEM of a collagen modified hydrogel (a, b), showing the presence of fibrous structure of collagen; Laser confocal images showing the growth of hMSCs on collagen modified pHEMA and pHEMA–TiO_2 (d, f) and the control scaffolds containing no TiO_2 and/or collagen (c, e) at day 1.

Keywords: pHEMA, Collagen, Hydrogel, Cellular activity, Tissue scaffold

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Hierarchically designed interpenetrating network hydrogels of oxidized dextran, amino gelatin, and poly(ethylene glycol) diacrylate for tissue engineering

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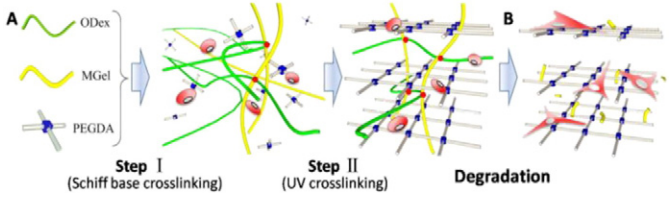
Hydrogels usually have high water content and their physical properties emulate those of the native extracellular matrix (ECM), so that they have been widely used as three-dimensional tissue engineering scaffolds to encapsulate cells [1]. Among the many factors that affect the performance of hydrogels in tissue engineering, degradation is a crucial one [2]. IPN hydrogels are one type of hybrid hydrogels composed of two or more crosslinked polymers, which can combine the properties of both the polymers. Here, we intended to combine natural materials and synthetic polymers to introduce more controllable degradation properties.

As shown in Scheme 1, a two step process was used to form amino gelatin (MGel)/oxidized dextran (ODex)/poly(ethylene glycol) diacrylate (PEGDA) IPN hydrogels for three dimensional (3D) pre-osteoblast cell (MC3T3-E1) culture. A Schiff-base reaction between ODex and MGel was used to form the primary network (Scheme 1(A). step I), then a UV light-induced secondary radical reaction of 4-arm-PEGDA was used to introduce the independent second network (Scheme 1(A). step II). Both reactions can be carried out under physiological conditions in the presence of living cells without toxicity. Compression tests demonstrated that the IPN hydrogels have an initial elastic modulus of 19.84 kPa, and a fracture stress of 76.97 kPa. Additionally, the IPN hydrogel showed controllable degradation properties. At the initial two weeks, the IPN could lose 40% to 60% of the original weight by altering the content of PEGDA from 5.5% to 4.0%, hereafter, the degradation rate decreased. The degradation mechanisms are shown in Scheme 1(B). Here, the degradation of the first network provides both the space and nutrition for encapsulated cells to spread and proliferate. Meanwhile, the presence of the second network supports cell growth in the 3D environment. MTT test demonstrated that pre-osteoblast cells could proliferate well within these IPN hydrogels. Confocal data show that cells in IPN hydrogels can spread well in a 3D environment after 4 days of culture.



Scheme 1. (A) Hydrogel formation through the Schiff-base reaction (step I) and UV crosslinking (step II) with the presence of encapsulated cells. (B) Degradation of IPN hydrogels for long-term cell culture.

Keywords: Dextran, Gelatin, Poly(ethylene glycol) diacrylate, Hydrogel, 3D culture

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Co-assembly of CdTe quantum dots and magnetic nanoparticles in imprinted matrices for magnetic separation and specific recognition of endocrine disrupting chemicals

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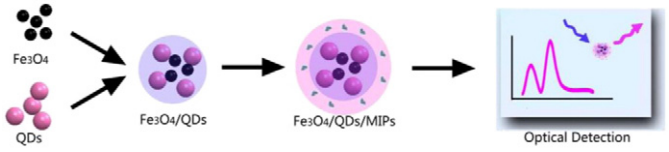
Semiconductor nanocrystals, or quantum dots (QDs), with semiconducting and size-tunable optical properties, are very attractive for use in molecular and cellular imaging, optoelectronic devices, and biosensors and bioelectronics [1]. However, one of the major drawbacks of using QDs is the nonspecific binding to cellular membranes, proteins, and complex materials. The issue of nonspecific binding causes a high level of background fluorescence that limits tagging specificity and detection sensitivity, which will be a major barrier towards the widespread use of QDs.

In this work, based on our previous work [2], we developed a general protocol for the fabrication of an imprinted matrix co-loaded with CdTe QDs and Fe_3O_4 nanoparticles for the recognition of p-nitrophenol, which is a widely used endocrine disrupting chemical (EDCs) (Scheme 1). The as-synthesized beads exhibited spherical shape (average size: 732 nm), high fluorescence intensity and superparamagnetic properties ($Ms = 1.72$ emu g^{-1}). The hybrids bind the original template p-nitrophenol with an appreciable selectivity over structurally related compounds. This advancement of magnetic fluorescent imprinting technologies may lead to exciting developments in various fields, including environmental pollutants and biochemical detection, recognition elements in biosensors and biochips.



Scheme 1. Synthesis route of magnetic fluorescent molecularly imprinted polymer beads and their application for recognition of EDCs.

Keywords: Molecularly imprinted polymer, Quantum dots, Magnetic nanoparticles, Optical detection

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Fabrication and *in vivo* test of P(LLA-CL) tubular grafts loaded with heparin

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Ideal vascular grafts should have both desirable biocompatibility and suitable mechanical properties. Despite the application of man-made polymers (Dacron, PTFE, *etc.*) in large-diameter (≥6 mm) vascular grafts, small-diameter grafts are rarely used clinically, mainly due to the acute thrombogenicity. Numerous efforts have been dedicated to tackle the problem, among them heparin loading has emerged as one of the most intensively studied antithrombotic strategies. However, the *in vivo* performance of such vascular grafts remains to be testified. In this study, we proved that the sustained release of heparin could greatly enhance the patency rate of vascular grafts in a canine model.

Heparin-loaded poly(l-Lactide-co-ε-Caprolactone) (P(LLA-CL)) tubular grafts were fabricated through coaxial electrospinning. For comparison, scaffolds from pure P(LLA-CL) solution were also electrospun as control. The *in vitro* release of heparin was measured before implantation. A bilateral implant model of dog ($n = 4$) femoral arteries was applied. After three months of implantation, digital subtraction angiography (DSA) was performed to visualize the patency of the implanted scaffolds.

As shown in Fig.1a, the heparin-loaded grafts, having an inner diameter of 4 mm and a wall thickness of 0.5 mm, were composed of core–shell structured nanofibers. The core part of the fiber was heparin, while P(LLA-CL) was selected as the shell for its superior flexibility and biocompatibility [1]. In the aqueous solution, the release of heparin was found to experience two stages: the initial burst release at day 1 and the continuous release from day 2 to day 14 (Fig.1b). The total amount of released heparin was approximately 72% after 14 days. Fig.1c showed the typical DSA image of the blood inflow into the arteries. As illustrated by the red circles, blood flow was blocked when passing through the P(LLA-CL) graft, yet was able to pass through the heparin-loaded graft smoothly. Based on the DSA results, patency rates at scheduled time points were summarized. P(LLA-CL) grafts showed a poor patency rate from the very

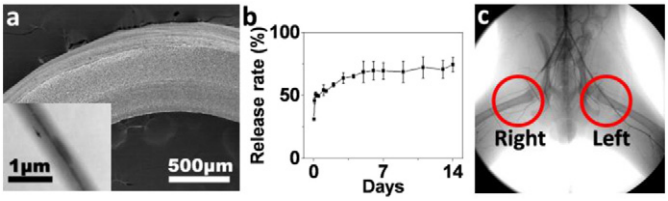

Fig. 1. a) SEM of the cross-sectional view of a heparin-loaded graft and TEM image of a single nanofiber; b) in vitro release profile of heparin from the heparin-loaded P(LLA-CL) nanofibers; c) representative DSA inspection of the implanted grafts after 3 months: the left femoral artery was replaced by heparin-loaded graft and the right one was replaced by P(LLA-CL) graft.