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Preparation and characterization of magnetic ferroscaffolds for tissue engineering

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Abstract

Magnetic-based scaffolds (ferroscaffolds) were fabricated using an in-situ synthesis of iron oxide nanoparticles in the presence of various concentration of biodegradable gelatin. The resulting ferroscaffolds show an interconnected pore structure with pore sizes ranging from 50 to 200 μm depending on gelatin concentrations. However, the yield of the iron oxide nanoparticles decreases with the increase of gelatin contents, which is due to the presence of polymeric chains that hindered the growth of iron oxide upon co-precipitation. The content of deposited magnetic nanoparticles could reach up to 9.41% and its saturation magnetization (M_s) was 23.5 emu/g. In addition, while applying a magnetic field (MF), the magnetic interparticles forces immediately formed to reduce the drug release rates in the ferroscaffolds. The ferroscaffolds which possess an excellently magnetic-sensitive behaviors can be potentially used as stimuli-responsive drug carriers and scaffolding materials for tissue engineering.

Keywords: Scaffolds; Gelatin; Magnetic nanoparticles

1. Introduction

Stimuli-responsive polymers with controlled drug-release have received great attention in the field of pharmaceutics and material science, as it provides numerous advantages over the conventional routes of drug delivery. Up to now, many stimuli-responsive polymers in response to environmental changes such as temperature, pH, external magnetic field (MF) and mechanical signal have been reported [1–3]. Recently, magnetic nanoparticles in biomedical applications have become increasingly important, due to the fact that it can be triggered via a non-contact force [4]. In our previous study, a type of magnetic sensitive hydrogels with controlled swelling-deswelling behavior has been developed for controlled drug delivery over an external MF [5]. The magnetic sensitive hydrogel can be further modified to form porous and bioactive gelatin-inorganic hybrids scaffolds, i.e., ferroscaffolds, by an in-situ co-precipitation process. It was found that the magnetic-sensitive ferroscaffolds exhibited different degrees of magnetism which can be further used to programmably control the growth factor for cells cultures. In this work, the physical properties, swelling behavior and drug-uptake of the ferroscaffolds will be investigated in terms of iron oxide content.

2. Experimental

Magnetic ferroscaffolds were fabricated by an in-situ co-precipitation process with iron oxide nanoparticles co-precipitated and deposited in the gelatin hydrogel. Firstly, gelatin was dissolved in the D.I. water for 2 h at 40 °C. an appropriate amount of $FeCl_2$ and $FeCl_3$ with molar ratio of 2:1 was added to the gelatin solution to form the hybrid sols. When completely dissolved, the hybrid sols were rapidly cooled to 4 °C for 30 min to gel the gelatin. The gels were subsequently immersed in a water solution of NH_4OH to start the formation of iron oxide. After that, the hybrid hydrogels were washed by D.I. water for several times to remove un-reacted NH_4OH solution, and then the hydrogels were kept in the freezing baths maintained at −80 °C for 1 day and finally lyophilized in a freeze-dryer for 2 days. The ferroscaffolds were formed and cured by 1-ethyl-3-[3-(dimethylammino) propyl]carbodiimide in the 9:1 acetone:water solution at 4 °C (see Fig. 1).

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3. Results and discussion

The swollen ferroscaffold presented a uniform and black color as shown in Fig. 2(a), where a porous microstructure within the ferroscaffold can be observed. The pore size in the 15ge sample was smaller than that in the 5ge, which can be attributed to a dense polymer chains in the former sample that could block the formation of pores. After the gelatin in the ferroscaffold was burned off at 350 °C for 1 h, Fig. 2(b) shows highly porous microstructure consisting of iron oxide nanoparticles. The nanoparticles were estimated about 10 nm in diameter.

The weight fraction of the iron oxide in the ferroscaffold was measured by thermo gravity analyzer (TGA) as shown in Table 1. $Fe_xO_y{}^T$ and $Fe_xO_y{}^P$ indicated the weight fraction of iron oxide nanoparticles formed without and with the existence of gelatin, respectively. It was found that when the ferroscaffolds contain higher gelatin, the yield of the $Fe_xO_y{}^P$ is lower. This is because that the growth of the nanoparticles can be hindered by strong interactions between dense polymeric chains. A comparison between 5gex1 and 5gex5 suggests that the precursor concentration apparently affects the $Fe_xO_y{}^P$ as well. Consequently, $Fe_xO_y{}^P/Fe_xO_y{}^T$ would be lower in high concentration of iron oxide precursor because the high load precursors restrained the formation of iron oxide nanoparticles. Ferroscaffolds with higher load precursors such as 5gex5 and 15gex5 would produce higher fraction of iron oxide nanoparticles in the final scaffold and showed better magnetic performance, for example, a higher saturation magnetization (M_s) of 23.5 emu/g can be obtained for 5gex5 sample.

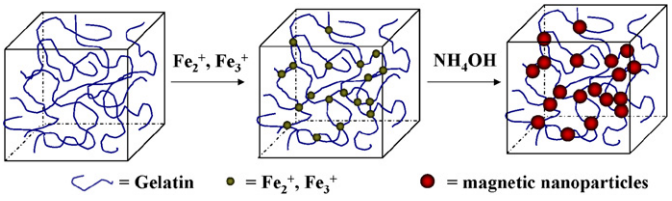

Fig. 1. Schematic illustration of the preparation of ferroscaffolds [6].

The magnetic-sensitive behavior of drug release for ferroscaffold was shown in Fig. 3. The released amount of model drug (vitamin B12) from ferroscaffolds can be determined at 361 nm using a UV spectrophotometer. As indicated in Fig. 3, the drug release rates of ferroscaffolds were strongly affected by an external MF at an electromagnet of ~400 Oe under switching "on" and "off". For a "MF on" mode, the release rate was obviously reduced. It was believed that the drug molecules were blocked in the ferroscaffolds due to the formation of magnetic interparticles forces. On the other hand, while MF was removed (i.e., MF off mode), the release rates was rapidly increased. These above results suggested that the magnetic nanoparticles play an important role in controlling drug release under applying a MF. Therefore, with the ferroscaffolds, a controllable growth factors release for cells cultures can be programmably designed for stepwise release.

4. Conclusion

Inorganic/organic hybrid ferroscaffolds with various magnetic nanoparticle contents were prepared by an in-situ co-precipitation process. The magnetic nano-parti-

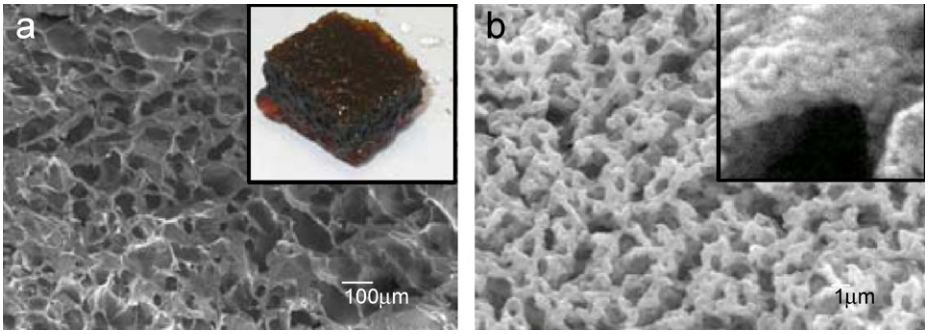

Fig. 2. (a) An SEM image and photo of the ferroscaffold. (b) Magnified view of the gelatin-removed ferroscaffold.

Table 1
Reagents used for the synthesis of composite ferro-scaffolds and properties of ferroscaffolds

Sample	Gelatin (g)	$FeCl_2$ (g)	$FeCl_3$ (g)	$Fe_xO_y{}^T$ (wt%)	$Fe_xO_y{}^P$ (wt%)	$Fe_xO_y{}^P/Fe_xO_y{}^T$
5gex1	5	1	2.7	3.7	3.4	92
5gex3	5	3	7.1	8.2	6.5	72
5gex5	5	5	13.5	15.2	9.4	62
15gex1	15	1	2.7	3.7	2.7	73
15gex3	15	3	7.1	8.2	5.3	65
15gex5	15	5	13.5	15.2	7.1	47

$Fe_xO_y{}^T$ and $Fe_xO_y{}^P$: formed without the existence of gelatin and practical weight fractions of iron oxide nanoparticles, respectively.

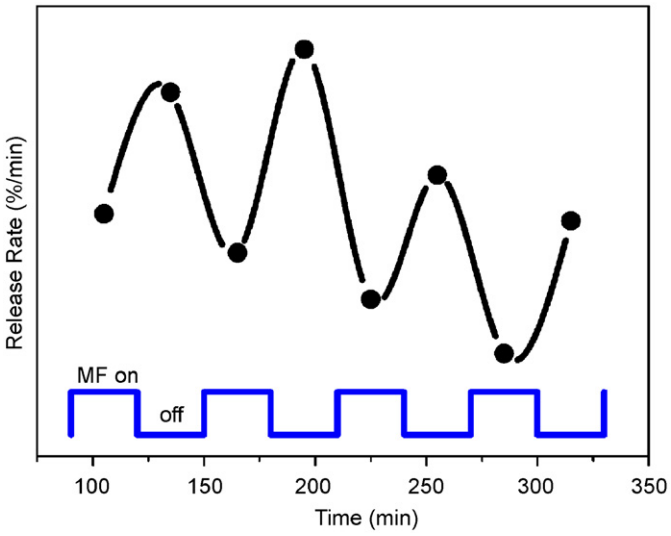

Fig. 3. The drug release rates of ferroscaffolds could be controllable under a magnetic field (MF) of switching "on" and "off".

cles can be in-situ synthesized and well dispersed in the resulting ferroscaffolds. With increasing the concentration of iron oxide nanoparticle, it revealed good performance on magnetism. Furthermore, the ferroscaffolds via applying external MF showed an outstanding controllable drug release behaviors, which could be potentially used as stimuli-responsive drug carriers and applied for tissue engineering.

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References

[1] K.Y. Lee, M.C. Peter, D.J. Mooney, Adv. Mater. 13 (2001) 837.
[2] J. Zhang, N.A. Peppas, Macromolecules 33 (2000) 102.
[3] S.C. Chena, Y.C. Wua, F.L. Mib, Y.H. Lina, L.C. Yua, H.W. Sung, J. Control. Release 96 (2004) 285.
[4] H.T. Song, J.S. Choi, Y.M. Huh, S. Kim, Y.W. Jun, J.S. Suh, J. Cheon, J. Am. Chem. Soc. 127 (2005) 9992.
[5] T.Y. Liu, S.H. Hu, K.H. Liu, D.M. Liu, S.Y. Chen, J. Magn. Magn. Mater 304 (2006) e397.
[6] R. Tannenebaum, M. Zurbis, E.P. Goldberg, S. Reich, N. Dan, Macromolecules 28 (2005) 4254.