Chemical Engineering Journal 339 (2018) 7–13

Contents lists available at ScienceDirect

Chemical Engineering Journal

journal homepage: www.elsevier.com/locate/cej

Biomimetic fluoridated hydroxyapatite coating with micron/nano-topography on magnesium alloy for orthopaedic application

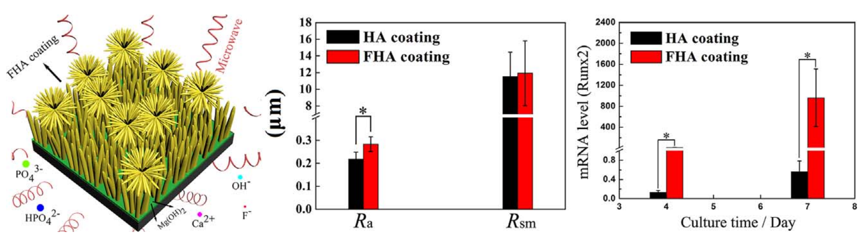
Sibo Shen[a,b], Shu Cai[a,*], Xiaogang Bao[c], Peng Xu[c], Yue Li[a], Song Jiang[a], Guohua Xu[c,*]

[a] Key Laboratory for Advanced Ceramics and Machining Technology of Ministry of Education, Tianjin University, Tianjin 300072, People's Republic of China
[b] Center for Electron Microscopy, Institute for New Energy Materials & Low-Carbon Technologies, Tianjin University of Technology, Tianjin 300384, People's Republic of China
[c] Department of Orthopedic Surgery, The Spine Surgical Center, Changzheng Hospital, Second Military Medical University, Shanghai 200003, People's Republic of China

HIGHLIGHTS

- Biomimetic FHA coating with micron/nano-topography was prepared on Mg alloy surface.
- FHA coating possesses micron/submicron-scale roughness to mimic resorption lacunae.
- Nanoneedles exhibit similar size and shape to sharp-tipped collagen fibrils.
- FHA coating presented robust osteogenic differentiation capacity.
- FHA coating and the formed HA mineralized layer retarded Mg alloy degradation.

GRAPHICAL ABSTRACT



ARTICLE INFO

Keywords:
Biomimicry
Microwave aqueous approach
Fluoridated hydroxyapatite nanoneedles
Micron/nano-topography
Osteogenic differentiation
Corrosion resistance

ABSTRACT

Biomimicry strategies, inspired by nature, are being widely used in the design of advanced biomaterials. Learning from the topographic landscape of natural bone resorption surface, which consists of micron/submicron-scale resorption lacunae and nano-scale sharp-tipped collagen fibrils, herein, a biomimetic fluoridated hydroxyapatite (FHA) coating composed of bilayer arrays of nanoneedles with micron/nano-topography was constructed on magnesium alloy surface via a microwave aqueous approach. The FHA coating possesses micron/submicron-scale roughness so as to mimic resorption lacunae. In parallel, the nanoneedles exhibit similar size and shape to collagen fibrils, especially their sharp tips. The surface topography, growth mechanism, osteogenic differentiation capacity and protection performance of this FHA coating were investigated. *In vitro* biological test showed that FHA coating significantly enhanced osteogenic differentiation capacity comprared with hydroxyapatite (HA) coating. Moreover, simulated body fluid immersion test demonstrated that FHA coating combined with formed HA mineralized layer together offered favorable long-term protection for magnesium alloy. This work may provide a new avenue of biomimetic surface topography design for orthopaedic implants with superior osteogenic differentiation capacity and corrosion resistance for long-term osseointegration of implants and fast bone regeneration.

1. Introduction

Biomimicry strategies, inspired by nature, are being widely used in the design of advanced biomaterials [1,2]. Most natural paradigms, *e.g.* bone and nacre, demonstrate sophisticated and hierarchical structures to obtain specific functionalities [3,4]. In orthopaedic applications,

* Corresponding authors.
E-mail addresses: caishu@tju.edu.cn (S. Cai), xuguohuamail@smmu.edu.cn (G. Xu).

https://doi.org/10.1016/j.cej.2018.01.083
Received 13 October 2017; Received in revised form 8 January 2018; Accepted 16 January 2018
1385-8947/

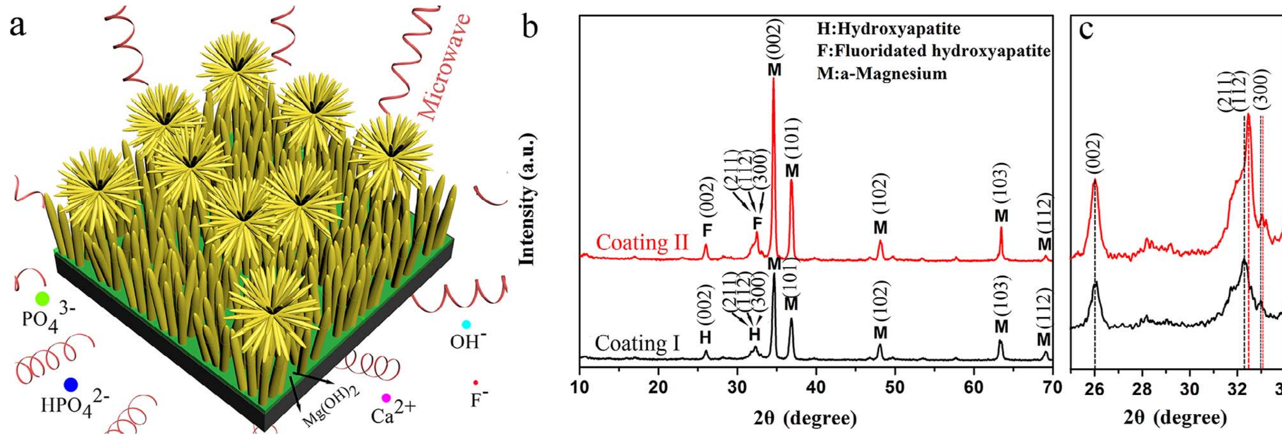


Fig. 1. (a) Schematic illustration of the designed biomimetic FHA coating. (b) XRD patterns of the prepared Coating I and Coating II. (c) Enlarged view of the XRD patterns at 2θ from 25° to 34°.

stem cell niche is an example structure which is often imitated on implants surface [5]. Stem cell niche contains highly dynamic and intricate biochemical and biophysical cues, in which the surrounding topography, ranging from scale values of 10 nm to 100 μm, can be recognized by cells via cell membrane receptors, contributing to determining cell fate [5–7]. Thus, tailoring implant surface features to mimic the surface topography of stem cell niche allows regulation of cell behaviors, *e.g.* osteogenic differentiation.

Robust osteogenic differentiation is indispensable to ensure long-term osseointegration of implants and successful bone regeneration [8,9]. During bone remodeling, natural bone resorption surface is produced by osteoclasts through acid dissolution of inorganics and enzymatic degradation of organics of the previously formed bones [10]. Specifically, natural bone resorption surface consists of micron/submicron-scale resorption lacunae and sharp-tipped collagen fibrils with the diameter of 10–300 nm quasi-vertically exposed on bone resorption surface, demonstrating distinct hierarchical micron/nano-topography [9,11,12]. This surface topography is believed to provide certain biophysical cues for initiating osteogenic differentiation. Therefore, to date, different material systems and considerable synthetic strategies were exploited to construct various biomimetic topographies on implants surface to optimize osteogenic differentiation capacity [6,13–24]. These biomimetic surface topographies possessed various nanostructures and/or micron/submicron-scale roughnesses. These nanostructures mainly covered hydroxyapatite nanorods, titanium nanotubes, calcium silicate nanoleaves, rutile nanoprotuberances and strontium substituted hardystonite nanograins, etc. These roughnesses were expressed mainly by average roughness (R_a) with values of submicron to several microns and mean distance between peaks (R_{sm}) with values of dozens of microns. Indeed, all these biomimetic surface topographies displayed some kind of similarities to the micron/submicron-scale resorption lacunae and/or nano-scale sharp-tipped collagen fibrils, thus exerting profound effects on osteogenic differentiation of stem cells or osteogenic cells. While, simultaneous mimicking the resorption lacunae and collagen fibrils still remains a great challenge. Hence, new biomimetic surface topography and synthetic strategy need to be developed. Furthermore, we deemed that selecting a material with good biocompatibility to construct this biomimetic surface topography is beneficial.

Hydroxyapatite ($Ca_{10}(PO_4)_6(OH)_2$, HA) with good biocompatibility and biodegradability, has been extensively investigated as coatings to modify orthopaedic implants for improved biological properties and corrosion resistance. Importantly, the size and shape of HA crystals can be regulated through ion doping and/or adjusting the chemical driving force for crystallization. Ion doping is able to change the lattice parameters of HA. For example, fluorine doping is substituting OH^- in HA lattice with F^- to form fluoridated hydroxyapatite ($Ca_{10}(PO_4)_6(OH)_{2-x}F_x$, FHA), leading to smaller crystals, for F^- had smaller ionic diameter than OH^- [25,26]. However, the chemical driving force for crystallization could affect the growth model of HA. The chemical driving force for HA crystallization was expressed either as supersaturation or as the Gibbs free energy difference (ΔG_{HA}) between the supersaturated coating solution containing Ca^{2+} and PO_4^{3-} and equilibrium one [27]. According to Cahn's theory, at high chemical driving forces, the growing interface can move normal to itself leading to spiral one-dimensional (1-D) growth, while at low chemical driving forces, the interface can move only laterally resulting in 2-D growth [28]. Among all kinds of HA crystals, 1-D nanocrystals are highly desirable due to their similarity to collagen fibril's size and shape. So far, the desire for 1-D HA nanocrystals drives many synthetic strategies, *e.g.* precipitation, hydrothermal and electrodeposition, *etc* [29,30]. Both the high temperature in hydrothermal method and applied electric energy in electrodeposition method could improve the chemical driving force. For example, Zhou et al. prepared a biomimetic strontium substituted HA (SrHA) coating by hydrothermal method [14]. The coating composed of SrHA nanorods with average diameter of 67.6 nm and with submicron-scale surface roughness showed excellent osteogenic differentiation capacity. Exactly, these nanorods have relative plane tips. However, collagen fibrils have sharp tips [12]. So we think that using apatite nanoneedle to mimic collagen fibril is more appropriate.

Based on the above analysis, in order to perfectly mimic the topography of natural bone resorption surface, a new type of biomimetic micron/nano-topography was rationally designed and illustrated in Fig. 1a. The biomimetic topography is constructed by a FHA coating composed of bilayer arrays of nanoneedles. The nanoneedles can mimic collagen fibrils. In parallel, FHA coating possesses proper roughness so as to mimic resorption lacunae. Herein, we developed a microwave aqueous approach to construct this biomimetic FHA coating. Currently, magnesium and magnesium alloys, as one type of the most important potential biodegradable metallic implants, attract immense attention by virtue of their good biocompatibility and mechanical compatibility [31]. However, their intrinsic drawback of rapid degradation in physiological environment limits the large-scale clinical application. To date, numerous attempts have been made to improve their corrosion resistance. Although some encouraging results of preliminary clinical trials were reported lately [32], their corrosion resistance performance needs to be further improved to fulfil the clinical requirements. Therefore, in this work, the biomimetic FHA coating was constructed on magnesium alloy surface and its enhancements for osteogenic differentiation and corrosion resistance were investigated.