Fabrication and in vitro release research on a novel antibacterial coating containing halogenated furanone compound loaded poly(L-lactic acid) nanoparticles on microarc-oxidized titanium

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ABSTRACT SUMMARY
A novel antibacterial coating containing halogenated furanone compound, (Z)-4-Bromo-5-(bromomethylene)-2(5H)-furanone (BBF) loaded poly(L-lactic acid) (PLLA) nanoparticles on microarc-oxidized titanium was developed and its release behavior was evaluated in vitro. The release study indicated that the novel antibacterial coating is a potential and promising method to prevent early peri-implant infection.

INTRODUCTION
Peri-implant infection is reported to be one of the most important causes of dental implant failure. Bacteria adhering to the surface of implant and forming biofilm play a pivotal role in early peri-implant infection. It is imperative to explore effective ways to prevent the bacterial invasion. Fabrication antibacterial coating on titanium is an important strategy to prevent early peri-implant infection, which inhibits initial bacterial adhesion.

In recent years, halogenated furanones, a class of secondary metabolites originally extracted from the red alga Delisea pulchra, have been proven to show antimicrobial properties that inhibit microbial colonization on its surface. The novel nature of their mechanisms of action would allow these new antimicrobials to be effective against bacteria that are currently antibiotic-resistant. However, there have been few relevant reports on how to apply halogenated furanones compounds on implants till now.

Developing controlled release system for several drugs (anaesthetics, antibiotics, anti-tumoural drug, proteins, etc.) from biodegradable polymers such as poly(L-lactic acid) (PLLA) has been widely developed as microsphere/nanoparticles carrier due to its desirable biocompatible and biodegradable properties.

Micro-arc oxidation (MAO) is a commonly used surface modification technique in producing inorganic glass-ceramic-like coating onto titanium surface, and the MAO coating exhibits a porous surface with pores 1-5 µm in diameter at regular intervals, which provides the space for the adhesion of nanoparticles.

The current study was to fabricate a new antibacterial coating containing BBF loaded PLLA nanoparticles (BBF-PLLA-NPs) on MAO treated titanium and evaluate its release behavior in vitro, in order to provide a new method to prevent early peri-implant infection.

EXPERIMENTAL METHODS
BBF-PLLA-NPs were performed by the classical oil-in-water (O/W) emulsion solvent-evaporation method. The simple procedure is as follows: the oil phase containing 15 mg of BBF added to 2 ml dichloromethane (DCM) in which was dissolved 100 mg of PLLA (5% w/v). This oil phase was added to 40 ml of 1% (w/v) PVA aqueous solution, and the mixture solution was then probe sonicated in an ice bath to produce O/W emulsion. The resulting emulsion was stirred for 6 h at 25 °C under reduced pressure to evaporate DCM completely. After preparation, the nanoparticles were collected and then washed in an ultrasonic bath at 37 °C, isolated by centrifugation and finally freeze-dried. The mean particle size, size distribution and polydispersity index of nanoparticles were assessed by dynamic light scattering (DLS) with a particle size analyzer.

The titanium specimens were then MAO treated. And the antibacterial coating was fabricated by cross-linking BBF-PLLA-NPs with gelatin on MAO-Ti. After oscillating, the MAO-Ti specimen was dried at 4 °C, followed by immersing in 2.5% (w/v) glutaraldehyde solution for 30 min to cross-link the gelatin. Finally, the MAO-Ti specimen was washed with...
ethanol to remove the remaining glutaraldehyde and freeze-dried. The surface morphology of antibacterial coating containing BBF-PLLA-NPs on MAO-Ti was observed by scanning electron microscopy.

The release of BBF from the antibacterial coating was performed by placing one BBF-PLLA-NPs-coated MAO-Ti specimen with 5 ml PBS in a dialysis bag.

RESULTS AND DISCUSSION

The BBF-PLLA-NPs exhibited small particle size (408 ± 14 nm), low polydispersity index (0.140 ± 0.008), high encapsulation efficiency (72.44 ± 1.27 %) and fine spherical shape with smooth surface (Figure 1).

Figure 1. SEM images of BBF loaded PLLA nanoparticles. (A) BBF-PLLA-NPs at low magnification. (B) BBF-PLLA-NPs at high magnification.

The morphology of the novel fabricated antibacterial coating showed that the BBF-PLLA-NPs were well-distributed in the pores of microarc oxidation coating, and cross-linked with each other and the wall of pores by gelatin (Figure 2).

Figure 2. SEM images of the antibacterial coating containing BBF-PLLA-NPs on MAO-Ti. (A) low magnification. (B) high magnification.

The morphological study of the degradation process of antibacterial coating was showed in Figure 3. After 15-day degradation process, some of the BBF-PLLA-NPs in the coating deformed from the spherical shape. After 60 days degradation, there were only a few degraded nanoparticles and fragments remaining in the pores on the coating. These findings were consistent with the release curves of BBF from antibacterial coating (Figure 4).

Figure 3. SEM of the degradation process of the novel coating containing BBF-PLLA-NPs. (A) 15 d. (B) 30 d. (C) 45 d. (D) 60 d.

Figure 4. In vitro release curves of BBF from the novel coating containing BBF-PLLA-NPs (A) Experimental points over the complete time assay. (B) Only the first 24 h in the release study.

CONCLUSION

A novel antibacterial coating containing BBF-PLLA-NPs was fabricated on MAO-Ti. The release study indicated that the antibacterial coating could sustain release the BBF for 60 day, with a slight initial burst release during the first 4 hour. Therefore, the novel antibacterial coating fabricated in this study is a promising method to prevent early peri-implant infection.

REFERENCES


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