Antibacterial property and biological performance of a novel antibacterial coating containing a halogenated furanone compound loaded poly(L-lactic acid) nanoparticles on microarc-oxidized titanium

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ABSTRACT SUMMARY
A novel antibacterial coating containing a new antibacterial agent, (Z-)-4-Bromo-5-(bromomethylene)-2(5H)-furanone (BBF) loaded poly(L-lactic acid) (PLLA) nanoparticles (BBF-PLLA-NPs) was fabricated on microarc-oxidized titanium (MAO-Ti). The antibacterial coating provided relatively long-term antibacterial ability and good biological performance which could be a potential and promising method to prevent implant associated infection.

INTRODUCTION
Titanium (Ti) implants play an essential role in the replacement of bony tissues that have become diseased or damaged, particularly in load-bearing applications. However, one of the most common and intractable complications of this process is implant associated infections. Therefore, a mass of antibacterial coatings have been explored and evaluated the effect. However, the emergence of drug resistant bacterium has critically challenged the use of conventional antibacteria. Besides, most of these attempts fail to deliver long-term antibacterial effects1.

Natural brominated furanones have been proven to show potent antimicrobial activity and inhibit biofilm formation2. In our study, a halogenated furanone compound, BBF loaded PLLA nanoparticles (BBF/PLLA-Nps) was prepared and a novel antibacterial coating was fabricated by cross-linking the BBF/PLLA-Nps on MAO-Ti surface. Therefore, the current study was to investigate the actual antibacterial capability in a long period and the biological performance of the fabricated antibacterial coating.

EXPERIMENT METHODS
BBF-PLLA-NPs were prepared using the classical oil-in-water emulsion solvent-evaporation method. And the antibacterial coating was fabricated by cross-linking BBF-PLLA-NPs with gelatin on MAO treated Ti surface. In brief, 20 mg of BBF-PLLA-NPs was sonicated for 20 min to disperse in 5 ml 0.2% gelatin solution (w/v), from which 400 µl suspensions was dropped onto the quadrate MAO-Ti specimen. Then the specimens were oscillated and the specimens were dried at 4 °C. Finally, the specimens were washed with ethanol thrice to remove the remaining glutaraldehyde and freeze-dried.

The surface roughness and water contact angles of the different groups: BBF/PLLA-MAO-Ti, PLLA-MAO-Ti, MAO-Ti and polished cp-Ti were measured.

The antibacterial assay was evaluated by inhibition zone, antibacterial rate and bacterial viability. And Staphylococcus aureus (S. aureus, ATCC 25923)
cultivated in nutrient agar medium at 37 °C for 24 hours was used in this antibacterial assay. For the in vitro test of the biological performance, osteoblast cell was cultured with 4 different groups. 3-(4,5-Dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay was performed to evaluate cell attachment and proliferation. Scanning electron microscope (SEM) was performed to observe the morphological appearance of the osteoblasts in contact with the specimens.

RESULTS AND DISCUSSION
The pores on the surface of MAO-Ti were almost overlaid by the cross-linked nanospheres/gelatin composite coating (Figure 1). The in vitro release profile of BBF from the antibacterial coating exhibited a biphasic release phenomenon about 60 days. The roughness of the specimens from high to low were MAO-Ti > BBF/PLLA-MAO-Ti > polished cp-Ti (p<0.05). The hydrophilicity of the specimens followed the order of BBF/PLLA-MAO-Ti > MAO-Ti > polished cp-Ti (p<0.05).

Figure 1. SEM images of the antibacterial coating: (A) ×10,000, (B) ×50,000 magnification.

For antibacterial assay, BBF/PLLA-MAO-Ti specimens gave unique antibacterial activity against *S. aureus* from 1 d to 60 d (Figure 2). In vitro biological test, statistical analysis showed that the viable cells attachment and proliferation on BBF/PLLA-MAO-Ti were higher than that on the polished surface (p<0.05). And well-flattened cells were observed on the surface of BBF/PLLA-MAO-Ti.

CONCLUSION
A novel antibacterial coatings containing BBF-PLLA-NPs was fabricated on MAO-Ti. The coating could achieve sustained release of BBF for 60 days and showed the excellent antibacterial and biological ability, which is a potential and promising method to prevent implant associated infection.

REFERENCES

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