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## ACCEPTED MANUSCRIPT

# Fabrication of hyaluronidase-responsive biocompatible multilayers on BMP2 loaded titanium nanotube for the bacterial infection prevention

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#### ABSTRACT

Infection associated with orthopedic implants is the chief cause of implant failure. An important consideration to prevent the infection at implants is to inhibit the biofilm formation for the initial 6 h. Therefore, we fabricated hyaluronidase-sensitive multilayers of chitosan (Chi)/sodium hyaluronate-lauric acid (SL) onto the surface of bone morphogenetic protein 2 (BMP2) loaded titanium nanotube (TNT) via spin-assisted layer-by-layer technique. The results of both Fourier transform infrared spectroscopy (FTIR) and nuclear magnetic resonance (<sup>1</sup>H NMR) confirmed the successful synthesis of SL. The multilayer structure on BMP2 loaded TNT was characterized by field-emission scanning electron microscopy (FE-SEM), atomic force microscopy (AFM) and water contact angle, respectively. The release profiles confirmed that hyaluronidase could trigger the release of lauric acid (LA) from the SL multilayer and accelerate the release of BMP2 in the system. The hyaluronidase-sensitive-multilayer-coated BMP2-loaded TNT (TNT/BMP2/(Chi/SL/Chi/Gel)<sub>4</sub>) not only demonstrated good antibacterial capability, but also showed good biocompatibility in *in vitro* usage, which was supported by the efficient growth inhibition of both Staphylococcus aureus and Escherichia coli, as well as higher cell viability, alkaline phosphatase activity, mineralization capability, and higher gene expression of osteoblasts on TNT/BMP2/(Chi/SL/Chi/Gel)<sub>4</sub>. This study developed an alternative approach to fabricate effective antibacterial implants for orthopedic implantation.

Keywords: titanium nanotube; sodium hyaluronate; lauric acid; antibacterial; cytocompatibility.

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