



## A Two-Phase and Long-Lasting Multi-Antibacterial to Prevent Implants-Related Infections

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### Abstract

In clinical practise, bacterial infection and aseptic loosening pose the biggest obstacles to titanium implant placement and significantly lower the survival rate of implants. The infection peak period for implants is the first four weeks following surgery. For an implant to be successful, it is crucial to prevent bacterial adhesion and growth during the initial stages as well as to encourage subsequently occurring osteointegration. Here, using a modified layer-by-layer method and dopamine polymerization, we created a quaternary ammonium carboxymethyl chitosan, collagen, and hydroxyapatite multilayer coating on Ti substrates. HAP coating demonstrated a two-phase function and several antibacterial properties. The covalently bound QCMC showed both contact-killing and release-killing properties during the infection peak phase at the first four weeks postoperatively; the second stage involves osteogenesis [1].

**Keywords:** Implant coating; Multi-antibacterial property; Osteogenicity; Modified layer-by-layer self-assembly; Dopamine polymerization

### Introduction

HAP improved the ability to promote osteointegration when the infection was effectively controlled. The multiform coating showed high biocompatibility in vivo and in vitro, and was destroyed by collagenase I for more than 45 days [2]. Most notably, the coating demonstrated persistent antibacterial efficacy against the primary pathogenic microorganisms responsible for peri-implant infections for over 3 months [3]. Ti-CCH demonstrated a favourable osteogenic differentiation potential in both in vitro and in vivo animal models. Because of this, our study reports a two-phase, long-lasting multi-antibacterial coating on Ti-CCH and suggests potential orthopaedic applications for the modified LBL strategy, which is instructive for creating useful implant and scaffold materials. Creating useful implant and scaffold materials [4]. Because of its exceptional erosion resistance, great mechanical qualities, and good biocompatibility, titanium and its alloy have been widely employed as orthopaedic implants [5]. Since more than 600 bacterial species may be found in the oral cavity, it is challenging to maintain a completely sterile environment during tooth implant surgery [6]. During the screwing procedure or after the operation, planktonic bacteria may stick to the Ti surface [7]. Once a structured biofilm has developed on the implant surface, it uses a variety of techniques to shield adherent bacteria from the host defence system and external therapeutic treatments, ultimately causing implant failure. Although structural alterations like sandblasting and acid etching have been extensively employed in clinical settings to increase the bioactivity of pure Ti, they are only partially effective in giving the implant a desired antibacterial property [8]. Performs its tasks. Additionally, it was noted that around 10% of Ti implants had infection, and roughly two-thirds of infected implants failed prior to functional loading [9]. The creation of biological coatings on Ti is therefore motivated by the drawbacks of structural changes [10]. In order to stop implant infection and failure, recent advancements have been achieved in the reduction of bacterial adherence and biofilm development using a variety of bioactive coatings [11]. However, Ti coatings that used non-covalent bonding, such electrostatic contact and hydrogen bonds, were unstable and quickly deteriorated in the first few weeks following implantation [12]. However, Ti coatings with conventional covalent bonding may release antibacterial chemicals in a burst and then only keep a low concentration for subsequent bacterial

death [13]. Peak of the illness phase of the implant lasts for four weeks following surgery, whereas overall implant stability achieves a steady state around the eighth week and is fully stable for three months [14]. Therefore, none of the aforementioned techniques could guarantee that the implant surface would retain its stable and efficient antibacterial qualities throughout time [15]. Different techniques, including plasma spraying, anodization, and layer-by-layer approach, have been thoroughly researched to manufacture bioactive coatings to provide the implant suitable qualities. Since Decher first described it, LBL has emerged as one of the most efficient ways to immobilise several extracellular matrix (ECM) components on biomaterials.

### Discussion

However, the majority of the contacts that led to the LBL multiform were electrostatic, and these connections were unstable under physiological conditions. The development of multiform structures with amido bond crosslinking was recently proposed by A using a modified LBL approach. EDC/sulfo-NHS crosslinker stimulated the interaction between carboxyl and amino groups to create the LBL multifilm structure. The modified LBL multifilm was stable in tris-buffer and disintegrated gradually when exposed to collagenase solution, in contrast to the standard LBL approach, which relied on electrostatic contact and physical crosslinking. As a result, it was clear that the modified LBL approach may be used to create antibacterial coatings with long-lasting, release-killing, and contact-killing capabilities. Numerous antibacterial agents have been used to provide implants good antibacterial action, including antibiotics, graphene oxide, nano-silver, chitosan, Due to its biocompatibility, biodegradability, and availability, chitosan is a natural polymer

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that is frequently utilised in tissue engineering and drug delivery systems. Both bioactivity and bioadhesivity. Quaternary ammonium carboxymethyl chitosan, a chitosan derivative, is a perfect water-soluble antibacterial agent. Its abundance of carboxyl and amino groups has been thought to be advantageous for the creation of covalently bound multifilm Infection linked to implants frequently develops in the first four weeks following surgery. Desirable antibacterial compounds are required in this period for the prevention and management of infection. Additionally, near the conclusion of this period, the second stability of implants begins to develop, which is crucial for improving overall implant stability and ensuring ultimate implant success. Therefore, following the first four weeks of implantation, it's necessary to have both a strong osteointegration-promotion capability and appropriate antimicrobial activity. Putting cytokines, enzymes, or major ECM components on Biomaterial surfaces have demonstrated a significant effect in eliciting specific cell responses and fortifying the tissue-implant contact. Collagen and hydroxyapatite were used in this work to replicate the ECM of natural bone and to promote osteointegration. Chemical crosslinking was used to bind HAP to QCMC and COL and to crosslink QCMC and COL as well. The implant may have a two-phase function and a long-lasting, multi-antibacterial characteristic thanks to the QCMC/COL/HAP multilayer coating. The covalently attached QCMC was susceptible to gradual degradation during the first four weeks following surgery. During the peak period of infection, the degraded QCMC displayed release-killing activity, and the residual QCMC in coatings might obtain contact-killing property. Then, during the second phase, osteogenesis and osteointegration may have been aided by HAP's osteoinductivity. Tested were the null hypotheses. It is not possible to build QCMC/COL/HAP multilayer structures using the modified LBL methodology and polydopamine binding techniques. Long-term gradual degradation of QCMC from the multilayer structure is not possible. 3) The QCMC/COL/HAP multilayer structure has a two-phase function and no long-lasting, multi-antibacterial effects. At various stages of the coating fabrication process, the samples' characterizations were carried out. In order to examine the surface morphology of the Ti coating at each stage of fabrication and the thickness of the finished coating, scanning electron microscopy (Merlin, Zeiss, Germany) was used. The elemental makeup and valence states of the Ti surface were then examined using X-ray photoelectron spectroscopy (XPS; Escalab 250, Thermo-VG Scientific, USA). Germany's confocal laser scanning microscope and water contact angle measurement were used. To assess several Ti substrates' hydrophilicity and surface roundness.

## Conclusion

The Derjaguin-Muller-Toporov model was used to investigate the Young's modulus of Ti-CCH, which was determined by atomic force microscopy Dimension fastscan bio, Bruker, Germany in the peak force quantitative Nano mechanics mode. Scratch test and SEM were used to assess the mechanical stability of the QCMC/COL/HAP coating on Ti-CCH in order to further assess its mechanical stability. Utilizing the CCK-8 test, the proliferation rate of MC3T3 E1 osteoblastic cells was assessed following co-cultivation with Ti-OH and Ti-CCH samples for 1, 3, and 7 days. To assess the strength of the cell adherence to the surfaces of Ti-OH and Ti-CCH, a fluorescent actin staining experiment was performed. Using glucose as a reference, the anthrone-sulfuric acid reaction was used to identify the release of QCMC. In a nutshell, Ti-CCH substrates were each submerged into a solution of 2 mL collagenase and 50 mmol/L trisHCL for 45 days at 37 C. After the anthrone-sulfuric acid detection, the solutions were collected and refreshed every two days. Sprague Dawley rats that were 20 weeks old were used to construct femur implant models for

testing Ti-biocompatibility. CCH's Ten SD rats were split into two groups at random. Each experimental section's grouping information may be found in the intercondylar fossa and distal femur of the rats was then exposed after a brief anaesthesia. The intercondylar fossa was punctured with a dental drill to create a hole that was 1 mm in diameter and 10 mm deep. A rod infected or not, was then inserted into the hole. The wound was stitched up in layers. Each group of rats had a body weight of monitored weekly, venous blood samples were taken 3 and 6 weeks following surgery, and the blood samples' neutrophil and haemoglobin levels were assessed. Rats were slaughtered using cervical vertebrae after being implanted for many weeks. Femurs were collected, removed, and immersed in paraformaldehyde in PBS. QCMC received a lot of interest as a novel, promising chitosan derivative and was later shown to be a functional polymer with a significant amount of bioactive groups. Chitosan was given carboxymethyl and quaternary ammonium groups to increase its water solubility and antibacterial properties in order to create QCMC. It is well known that the ECM of natural bone contains significant amounts of COL I, which serves as the organic matrix's structural scaffold. To replicate the organic bone micro-environment and provide According to earlier studies, QCMC and COL I were synthesised to create an implant coating that has a promising antibacterial property.

## Acknowledgement

None

## Conflict of Interest

None

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