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Smart controlled release of chlorhexidine from chitosan-capped mesoporous silica/titanium composite material for infection prevention in dental implant applications

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Even though dental implants generally show high success rates, their increased use concomitantly raises the incidence of infections. These infections arise due to the formation of biofilms in the periodontal pocket around the implant and can lead to the occurrence of peri-implant mucositis and, in severe cases, peri-implantitis. Current treatment options, comprising systemic antibiotics intake and surgical interventions, cannot guarantee a successful arrest of the inflammatory lesion and represent also an additional burden for both patients and health services. An upcoming anti-infective strategy is the localized release of antimicrobial agents at the infection site. As such, we have previously developed a titanium/silica composite material, consisting of a macroporous titanium matrix with a mesoporous silica diffusion barrier incorporated in the open pores, which allowed the continuous elution of therapeutic concentrations of chlorhexidine (CHX) to effectively prevent biofilm formation on the material surface. However, cytotoxicity to the host cells due to a continuous drug release remains an important concern. Therefore, in this study, the potential of an additional pH-responsive chitosan (CS) capping agent was investigated in order to further confine the CHX release to the presence of acidic bacterial biofilms. To this end, a solution of CS crosslinked with (3-glycidyloxipropyl) trimethoxy-silane (GPTMS) was dropcoated on the Ti/SiO_2 and the influence of different CS

and GPTMS concentrations was investigated. Scanning electron microscopy (SEM) and 3-D optical profilometry were used to visualize the CS coated Ti/SiO_2 and the thickness of the coating respectively. The presence of the coating was also confirmed using Fourier transform infrared spectroscopy. For samples coated with 1 wt% CS solution and 15 vol% GPTMS (CS-Ti/SiO_2), the daily CHX release rate measured using ultraviolet visible spectroscopy was ~33% lower than for prisitine Ti/SiO_2 substrates, yet absence of pH response, which could possibly be due to extra crosslinking of CS as it takes place through the same amine bonds which are also responsible for protonation in acidic medium. Still, an antimicrobial effect could be observed for CHX-releasing CS-Ti/SiO_2 substrates using co-cultures of one cariogenic, *Streptococcus sobrinus*, and one periopathogenic species, *Fusobacterium nucleatum*. Biofilm quantification by viability quantitative PCR indicated an almost 100% reduction in biofilm formation for CHX-releasing CS-Ti/SiO_2 as compared to pristine Ti/SiO_2, a result which was corroborated by biofilm visualization using SEM.