

Controlled Release of Simvastatin from Anodized Ti Granules for Improving its Antibacterial Effects

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Statement of Purpose: Prevention of bacterial colonization and formation of a bacterial biofilm on implant surfaces has been a challenge in orthopedic surgery. The treatment of implant-associated infections with conventional antibiotics has become more complicated by the emergence of multi-drug resistant bacteria. simvastatin as a lipid lowering agent has been demonstrated to have osteoanabolic effects. It also has antibacterial activity. These properties suggesting the benefit of loading simvastatin on the bone graft substitute in dental implantology. This study was designed to measure the possible effect of nanowire arrays fabricating and simvastatin loading on implant-associated infections.

Methods: Nanowire arrays on medical titanium surfaces were fabricated by anodization method and its potential for storage and release of antimicrobial substances was evaluated. The treatment of the Ti granules in fluoride containing electrolytes on ethylene glycol basis with the aim of TiO₂ nanowires formation was done. Then the anodized (AG) and non-anodized Ti granules (G) were immersed in a solution of simvastatin with a molar concentration of 1.196×10^{-4} and the solution was dried after the preincubation. Scanning electron microscopy (SEM) and energy dispersive X-ray spectroscopy (EDS) were used to characterize the granules. BET was used to characterize the granules specific surface area and attenuated total reflectance Fourier transform infrared spectroscopy (ATR-FTIR) was applied before and after simvastatin loading. Simvastatin release in PBS was investigated to examine the capability of the simvastatin loaded granules as a drug delivery system. In order to evaluate their antibacterial properties microbroth dilution assay was used.

Results: SEM images confirm the formation of nano-wires on the surface of AG samples. BET assay confirms the existence of mesopore in both samples which increases the chance of using them as a drug carrier. This assay also confirms the increasing of specific surface area of Ti granules after anodizing about 93%. Loading of simvastatin on the G and AG samples is approved by ATR-FTIR and the obtained release profile. Drug release experiments with the simvastatin showed that the increased surface area of the AG samples enabled them to have a sustain

release of simvastatin which is not monitored for the untreated Ti granules (G samples). The release profile shows that about 52% of initial loaded simvastatin released after 24 h of PBS incubation while this amount was 24% for AG samples (Fig. 1). Hence significant surface-dependent difference in the release kinetics of simvastatin is proved. As Fig. 2 shows, the bacterial proliferation on samples was significantly inhibited (about 50% and 25% for G and AG samples respectively) after simvastatin loading.

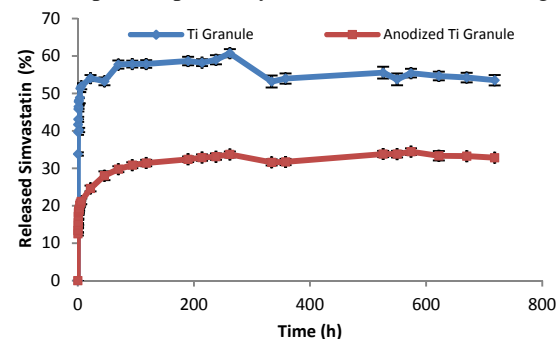


Fig. 1. Simvastatin release profile.

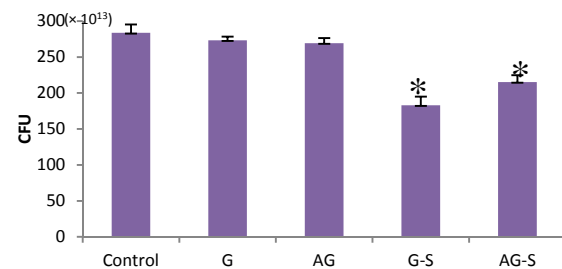


Fig. 2. Graphical representation of CFU of E. Coli in the antibacterial activity test

Conclusion: Therefore loading simvastatin on Ti granules through physical adsorption give a valuable opportunity for improving antibacterial properties of granules. It was concluded that nanowire arrays on favored medical implant materials have a high potential for loading with antimicrobial agents. Although simvastatin loading improve antibacterial properties of G samples more than AG ones but the sustain release of simvastatin in AG samples could result in improving other properties of the granules such as donating osteoanabolic effects which should be investigated in future studies.