Functionalization of Titania Nanotube Arrays for Therapeutic Drug Delivery

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Statement of Purpose: In a previous study, the cytocompatibility of anodized titania nanotube arrays was characterized and showed enhanced osteoblast (bone-forming cell) functions on such anodized titanium compared to untreated titanium[1]. Besides mimicking nanofeatures of bone, these titania nanotube arrays could potentially be a matrix for various therapeutic induction and thus lead to their controlled release. However, to facilitate loading of drugs of different hydrophobicity, the nanotube arrays need specific surface modifications. In the present study, chemical functionalizations were carried out to form either hydrophilic ($-NH_2$) groups or hydrophobic ($-CH_3$) groups on these anodized Ti nanotube arrays. The loading and release behavior of several model drugs (like penicillin/streptomycin and dexamethasone) on these surfaces were compared to test the possibility of using such functionalized titania nanotube arrays for therapeutic drug delivery.

Methods: Titania nanotube arrays were synthesized on commercially obtained titanium by anodization in dilute 1.5 wt% hydrofluoric acid. The resulting surface was then soaked in Piranha solution (1:1 sulfuric acid and 30% hydrogen peroxide) for 5 min. To achieve a $-NH_2$ functional group on the surface, the samples were cleaned with hexane and react with a 5 vol.% 3-aminopropyltriethoxysilane hexane solution. The reaction was allowed to occur for 4 h with constant stirring. To achieve $-CH_3$ functional groups, some of the samples described above underwent another step, reacting with acetic anhydride for 30 min with stirring. After chemical modification, all samples were cleaned with 70% ethanol for further characterization. An antibiotic (penicillin/streptomycin, Invitrogen) drug and an anti-inflammatory (dexamethasone, Sigma) drug were used in the present study. A drop (120µl)of drug-dissolving solution was added onto each sample (including unanodized titanium, anodized titanium, anodized titanium with $–NH_2$ groups and anodized titanium with $–CH_3$ groups) and air-dried. The surfaces were then observed under field-emission scanning electron microscopy (LEO). To achieve drug release curves, each substrate was soaked in 1 ml (10000 units penicillin/ml and 10000 µg streptomycin/ml; 200 µg/ml dexamethasone) drug solutions overnight and then transferred to 1ml fresh buffer solution. The buffer solution was collected and changed everyday. After 4 days, the amount of released drugs at each day was measured using a micro-BCA assay (PIERCE).

Results/Discussion: Micrographs of the functionalized titania nanotube arrays showed that the morphology of the nanotubes arrays remained after either the 1-step or 2-step chemical functionalization steps, only with some coarsening of the tube walls (Fig.

1). Experiments also showed that penicillin/streptomycin and dexamethasone both preferred to adsorb on $-CH_3$ group functionalized titania nanotube arrays compared to $-NH_2$ group samples (Fig. 2).

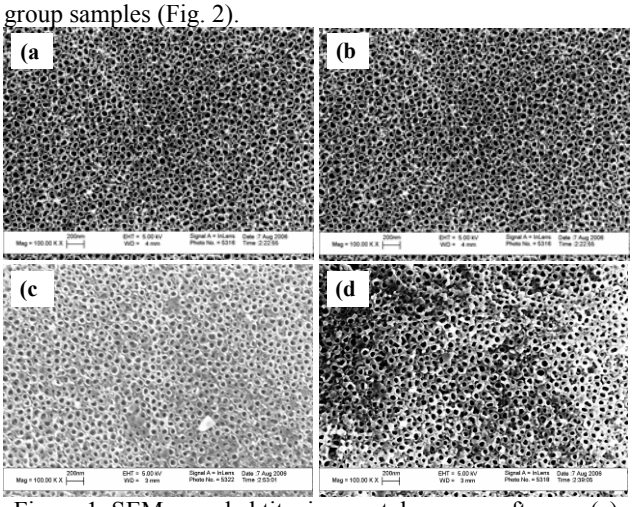

Figure 1. SEM revealed titania nanotube arrays after (a) anodization, (b) Piranha solution treatment, (c) $-CH_2$ group functionalization, and (d) $-CH_3$ group functionalization. Scale bars = 200 nm.

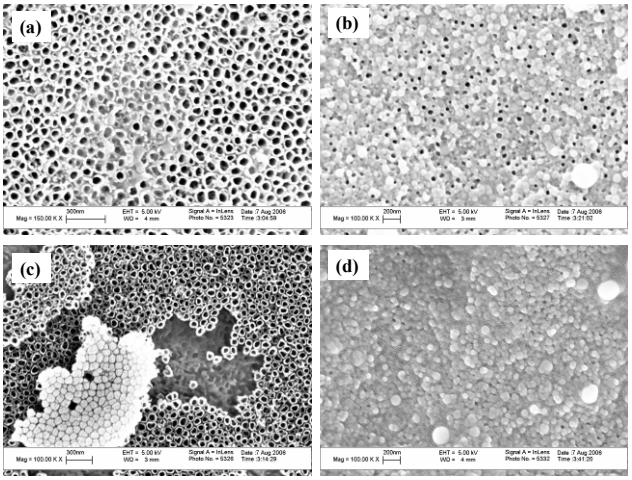

Figure 2. Penicilin/streptomycin adsorption onto (a) $-NH_2$ and (b) $-CH_3$ samples; dexamethasone adsorption onto (c) $-NH_2$ and (d) $-CH_3$ samples. Scale bars = 300 nm in (a)(c), 200 nm in (b)(d).

The release curves showed a quick release of both drugs into buffer solution after one day (data not shown).

Conclusions: Functionalization of anodized titania nanotube arrays enable these nanostructures to serve as well for later release of specific therapeutic drugs. Future studies will focus on how to achieve a zero-order or prolonged release behavior to improve the efficacy of drug delivery on antimicrobial, anti-inflammatory, and bone growth.

References

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