Effect of Titanium Dioxide Nanotubes Dimensions on Prolonged Release of Drug Molecules

Azhang Hamlekhan[1], Suman Sinha-Ray[2], Christos Takoudis[3], Mathew T. Mathew[4], Cortino Sukotjo[5], Alexander L. Yarin[2,6,*], Tolou Shokuhfar[1,2,5,7,*]

[1] Mechanical Engineering, Multi-Scale Technologies Institute, Michigan Technological University,
[2] Department of Mechanical and Industrial Engineering, University of Illinois at Chicago,
[3] Department of Bioengineering, University of Illinois at Chicago,
[4] Department of Orthopedics, Rush University Medical Center, Chicago,
[5] Department of Restorative Dentistry, College of Dentistry, University of Illinois at Chicago,
[6] College of Engineering, Korea University, Seoul, S. Korea,
[7] Department of Physics, University of Illinois at Chicago
* Corresponding authors: ayarin@uic.edu, tshokuhf@mtu.edu

Statement of Purpose: Formation of titanium dioxide nanotubes (TNTs) on titanium surface holds great potential for promoting desirable cellular response. In our previous work TNTs were successfully loaded with drug. Drug-loaded nanotubes have promoted osteoblast adhesion, proliferation [1] and differentiation [2] compared with conventional nano-tubular surfaces. However, prolongation of drug release from these nano-reservoirs remains to be a challenge. In this study the effect of TNTs dimensions on prolongation of drug release was quantified aiming the introducing of a simple novel technique which overcomes complications of previously introduced methods.

Methods: Ti6Al4V alloy disks were polished and anodized in order to fabricate TNTs. Mixture of ethylene glycol (Fisher), 0.3 wt% NH4F (Fisher) and 2 vol.% DI water was used as anodization electrolyte. In order to obtain TNTs with different aspect ratios, anodization was conducted at different voltages of 60 V, 70 V, 90 V and 120 V. At each voltage, anodization was performed for 15 min, 30 min and 2 h. Structural characterization of the prepared TNTs was performed using a field emission scanning electron microscope (FESEM), JEOL JSM-6320F. To intercalate drug into TNTs, the method of self-sustained diffusion was used. Naproxen sodium, an anti-inflamatory drug, was used in this study as a model drug. A drug solution was prepared and pipetted on nano-tubular surface during 20 times of pipetting to load substantial amount of drug. After last loading cycle, surface was wiped and quickly rinsed in PBS. Drug-loaded disks were immersed in pure PBS to release the drug. At specific time instants, a sample solution was pipetted out to measure the amount of released drug using UV-Vis photospectroscopy (Thermo Scientific, Nanodrop 1000 UV/Vis Spectrophotometer).

Results: FESEM images show that the nano-tubular structure is formed on all anodized surfaces. Using the images, length and diameter of nanotubes versus voltage were measured and, accordingly, the aspect ratio and the external volume of TNTs versus voltage were calculated. Length and diameter of TNTs increase as either the anodization voltage or anodization duration is increased. However, the aspect ratio does not seem to follow the same trend. External volume of TNTs increases as the anodization voltage or duration is increased.

Figure 1 shows the release profile of all TNT groups.

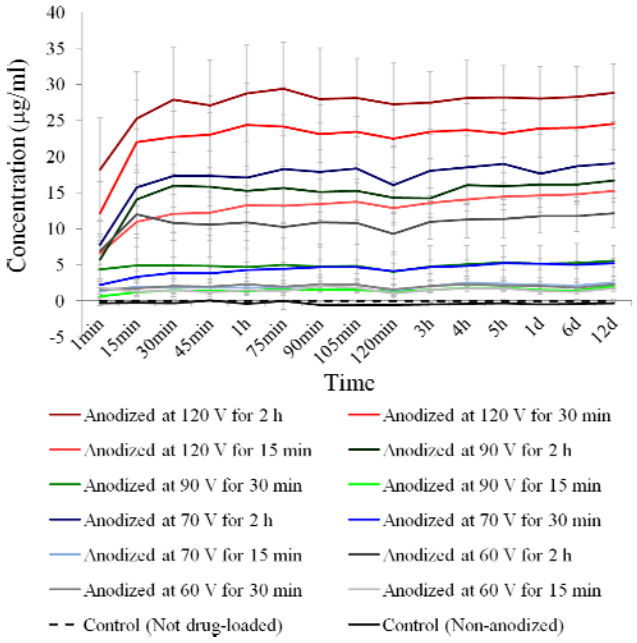

Figure 1. Release profiles of TNTs

Comparing the profiles with the TNT dimensions, it can be concluded that larger nanotubes with larger volume release larger amount of drug. The amount of loaded drug increases as the anodization duration is increased. Nanotubes with higher aspect ratio release their intercalated drug molecules at slower rate.

Our results show that some groups of TNTs release loaded drug in less than 1 h, while the other groups prolong release to more than 1 h. A correlation is observed between rate of drug release and aspect ratio. For the groups of TNTs with the highest aspect ratio, the release process was the slowest.

Conclusions: Our results suggest that drug release duration from titania nanotubes is strongly affected by the TNTs aspect ratio. Considering that increasing TNTs length is harmless for cells, increasing TNTs aspect ratio via enhancing TNTs length can be a promising technique for prolonging drug release while bioactivity of loaded drugs is protected as well.

References:

1- Gulati K. Acta Biomaterialia. 2012; 8(1): 449-456.
2- Popat KC. Biomaterials. 2007; 28(32): 4880-4888.