Titanium nanotube surface loaded with novel antibiotics for implant local action.

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Abstract

Biomaterials has improved life quality alongside its evolutions throughout society development. Titanium and its alloys are in the mainstream of structural implants. However, their lack of bioactivity requires superficial modifications in order to present some bioactivity. Nanotube surface is a modification that has been widely explored and features osteointegration and reduces bacterial contamination. Bacterium resistance, caused by misuse of antibiotics, has created a challenging problem to overcome. New antibiotics arises from studies and with them new forms of administration to avoid bacteria selection. In order to bypass this issue, this work studies two new compounds developed in the Organic Synthesis Laboratory at Universidade Federal de Itajubá, which were loaded in TiO_2 nanotube layer on titanium commercially pure (cp) to act against infections in implant surrounding. The electrolyte composition to anodization is a solution of 1:1 glycerol and deionized water plus 0.24 %wt ammonium fluoride (NH4F). After the anodization, the samples were calcinated in oven with temperature rampage at 530°C. The loading compounds were 5-[1-(3′-chlorophenyl)-3-methyl-1H-pyrazole-4-yl)]-1H-tetrazole (JVS 02) and 5-[1-(3′,4′-dichlorophenyl)-3-methyl-1H-pyrazole-4-yl)]-1H-tetrazole (JVS 05). Which 50 µl of each solution at 1 $mg.ml^{-1}$ were dropped in the surface and taken to oven with vacuum pump. The biological test growing biofilm tested the effects of the drug over *Staphylococcus aureus* from a resistant strain identified as HU25. The test of drug liberation was analyzed by spectroscopy. The results compared four distinct treatments (being titanium cp as group 1, titanium with nanotube layer as group 2, nanotubes loaded with JVS02 as group 3, and nanotubes loaded with JVS05 as group 4). The compound loaded samples successfully inhibited the forming colony units by reducing contamination in 15% for JVS02 and 20% for JVS05. The results of liberation show that the compound JVS02 presented faster liberation than JVS05, reaching equilibrium state of liberation at 1500 minutes and 3000 minutes respectively. The difference of compounds is slight, given by adding a chlorine ion, however compelling enough to present such different result. The JVS02 and JVS05 compounds improved the efficiency of TiO_2 against *S. aureus* HU25. The drug JVS05 is more effective than JVS02 even presenting slower liberation. The chlorine ion modifies the compound polarity, so it is higher in JVS05 than in JVS02. Group 4 is the best option for local dispersion among treatments, once prevents the misuse of antibiotics by local delivery, long-lasting effect and efficiency against the tested pathogen.

Keywords: Antibiotic Loaded Titanium Nanotubes; Drug Delivery; Staphylococcus aureus; Biofilm.