Sol gel Ag-doped TiO_2 coatings showing antibacterial activity

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Statement of Purpose: One of the main complication related to the use of implanted materials is represented by the infection of clinical devices [1]. The development of new surface treatments, to prevent bacterial adhesion and reduce the risk of infection, represents one of the primary goals in biomaterials research.

Sol-gel is a surface modification technology allowing the production of homogeneous ceramic coatings in mild processing conditions; In recent years, research has been focused on the possibility of incorporating anti-infective agents, such as silver, in metal oxide coatings using this technique. Silver has a broad-spectrum bactericidal activity, effective even at low concentration on antibiotic-resistant bacteria and lacks of toxic effects on cells [2]. The aim of this research was to develop and characterize new Ag-doped TiO_2 sol-gel coatings on titanium and stainless steel, designed to produce antibacterial surfaces.

Methods:

Sols preparation. TiO_2 sols were prepared by hydrolysis of titanium isopropoxide (TTIP) in acidic ambient: a solution of TTIP and acetic acid (chelating agent) was mixed with water and either nitric or acetic acid as peptizers. The resulting solutions were refluxed at 120°C for 2 hours. These control solutions were then modified by adding either $AgNO_3$ or $C_2H_3AgO_2$ ($[Ag^+/TTIP]$= 0.5÷5%).

Samples preparation. ISO 5832-2 grade 2 titanium and stainless steel disks (Φ = 12 mm, thickness 0.5 mm) were submitted to a decontamination procedure (acetone, ethanol and deionized water subsequent rinsings) before any further treatments. Dip-coatings were carried out at different extraction rates (50÷300mm/min). After dipping, coatings were subjected to different heat treatments (120÷300°C), to stabilize the obtained films.

Physico-chemical characterizations of sols and samples were performed by XRD, SEM-EDS, ICP-OES, Light Scattering, laser profilometry and contact angle measurements. A preliminary biological *in vitro* characterization was performed evaluating the *inhibition-zone* of Ag-doped TiO_2 disks in TSA (*Trypton Soya Agar*) plates and cultured for 48h with Streptococcus mutans (NCTC 10449). Optical microscopy was used to evaluate agar portions containing *Streptococcus mutans* colonies to assess the effect of silver release on bacterial proliferation.

Results: All the developed solutions were stable and characterized by the presence of Ag ions as quantified with ICP-OES spectroscopy. Light scattering revealed a significant increase in the average size of particles in solution after reflux process (from 34 to 352 nm). XRD spectra of powders revealed the presence of TiO_2 anatase crystalline phase (2θ =25°) both before and after reflux although in this case there is an increase in the degree of crystallinity characterized by sharper profile than powders before reflux (Figure 1).

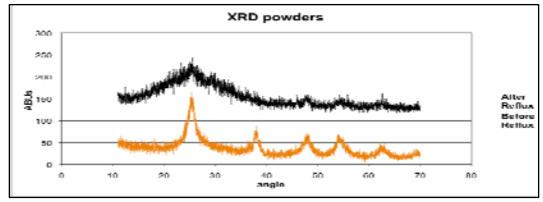

Figure 1. XRD spectra of the powder in solution containing 0.15M TTIP, Acetic Acid (1%v/v), Nitric Acid (1%v/v) and $AgNO_3$ $[Ag^+/TTIP]$= 1%

SEM pictures of the samples showed a silver incorporation, homogeneous and uniform on Ti (Figure 2B) and Steel surfaces. No decrease in the average roughness Ra has been observed.

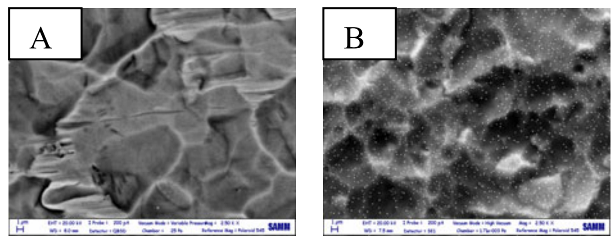

Figure 2. SEM micrographs of Titanium surface specimens A) before and B) after the dip coating in a solution containing 0.15M TTIP, Acetic Acid (1%v/v), Nitric Acid (1%v/v) and $AgNO_3$ $[Ag^+/TTIP]$= 1%

Moreover, EDS analysis showed the effective incorporation of silver in the TiO_2 films onto all samples.

XRD analysis showed the presence of a nano-structured TiO_2 anatase (2θ = 25°) on all coated samples, regardless the presence of Silver (Figure 2).

The results obtained by bacteriological studies on inhibition zone showed that the presence of silver resulted in a significant decrease of *Streptococcus* mutans CFUs in all the agar portions close to the Ag-doped surfaces (Figure 3)

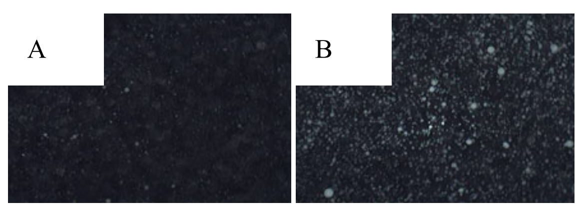

Figure 3. Light Microscopy pictures of Inhibition zone results respective in the portion A)close to the Ag-doped sample surface and B) in the outer zone of agar.

Conclusions: Although extended biological tests are necessary, the Ag-doped TiO_2 sol-gel treatments proposed in this work represent a class of promising antibacterial surface treatments for several medical devices (*e.g* temporary transcutaneous devices).

References: 1) Gottenbos B, J. Mat. Science 13,2002 (717-722) ; 2) Stobiea N, Biomaterials 29,2008 (963-969)