



The Electrochemical Behavior of Titanium Improved by Nanotubular Oxide Formed by Anodization for Biomaterial Applications: A Review

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ABSTRACT

Titanium oxide nanotube is gaining prominence in many applications like solar energy, sensors, catalyst and biomaterials. In this paper, we briefly review the electrochemical behavior of titanium oxide nanotube prepared by anodization in simulated body fluids. The electrochemical behavior of TiO_2 nanotube depends on its morphology and surface properties. When titanium oxide nanotube formed by anodization, these surface properties are depending strongly on two factors, the parameters of anodization process and the conditions of employed electrolyte. These factors must be chosen in correct manner to optimized titanium oxide nanotube with desired properties for specific application.

Keywords : Titanium oxide nanotube, anodization, biomaterials, corrosion.

INTRODUCTION

General

Titanium and its alloys are exploited in several technological fields ranging from aerospace and chemical industries to bone implant materials, because of their excellent properties and efficient performance in widespread applications^{1,2}. They are used in photo catalysis³, self-cleaning processes, solar cells, fuel cells, catalysis, gas sensing devices, semiconductors doping, biomedical, interference coatings, and manufacturing optical devices¹.

The variety of the applications of Ti is attributed to its excellent corrosion resistant, light weight⁴, low elastic modulus and biocompatibility¹. The high and remarkable corrosion resistance is attributed to a very stable passive oxide film formed on its surface when exposed to the air or water^{2,5}. The self-healing nature and compactness of the titanium oxide film make it suitable for many hostile environments¹.

Titanium in biomaterials

In biomedical devices, selecting materials for different components depends especially on

several factors. First, the implant materials must possess an excellent biocompatibility, excellent corrosion resistance and appropriate mechanical properties⁶. Low elastic modulus is required to be close to that of a human bone, in order to transfer the adequate mechanical stress to the surrounding bone⁷.

Moreover, the surface of biomaterials play an extremely important role in the response of artificial medical devices to the biological environment. When they have been implanted into the human body, a series of interactions occur between the surface of biomaterials and the biological environment. Thus, their surface characteristics such as surface morphology, microstructure, composition, and properties can determine the efficiency of artificial implants⁸.

In the field of medicine, titanium is well established as a biomaterial for bone anchorage and in soft tissues, e.g. in pacemakers, neurological implants, and metabolic sensors⁹⁻¹¹ (fig.1). The biological, mechanical and physical properties of titanium and its alloys play significant roles in the longevity of the prostheses and implants¹³.

The layer of titanium dioxide (TiO₂) covered titanium surface is believed contribute to its overall biocompatibility¹⁴⁻¹⁶. This layer with approximately 5 nm thickness forms spontaneously in air or water and exhibits favorable thermodynamic properties, and low ion formation and electrical conductivity in the physiological environment⁵. The stability of the titanium oxide film depends strongly on its composition, structure and thickness¹⁷.

Moreover, titanium oxide exhibits unique semiconductor-like properties that allow for the surface to change from Ti⁴⁺ to Ti³⁺, which make it ability to inhibit reactive oxygen species involved in the inflammatory response¹⁸⁻²⁰. Due to the semiconductor-like properties of TiO₂, it can acts as an electron donor or acceptor, and thereby actively participate in catalytic reactions with biologically relevant radicals⁴.

Importance of titanium oxide nanostructure

As bone is alive, and in order to prevent loosening and inflammation when an implant inserted

close to it, an implant must be accepted by the bone cells, and must be able to bond to and grow on it. The surface of an implant can be modified to optimize its properties and to maximize its bioactivity when interfacing with natural tissue. The surface treatments or modifications methods can enhance the biological characteristics of implants by adding material with desired properties, changing the composition or removing unwanted material from the implant surface. These methods can be classified into four categories:

- (a) Mechanical surface modifications like machining, grinding, polishing and blasting.
- (b) Physical surface treatments include thermal spraying, physical vapor deposition, ion implantation and deposition, and glow discharge plasma treatment.
- (c) Chemical surface modifications include chemical treatment (acid, hydrogen peroxide, alkaline), anodic oxidation, the sol-gel process and chemical vapour deposition.
- (d) Biochemical surface modifications.

A number of techniques have been specifically introduced for titanium and titanium alloys, such as silanized titania, photochemistry, self-assembled monolayers, protein resistance and protein immobilization²¹⁻²⁴.

Another suggestion to improve the biocompatibility of titanium and its alloys, is to use two scale surface modification, the first is nano-scale for bioactivity of the implant, and the second is micro-scale for osteoblast adhesion²⁵.

A nanometre (nm) is defined as the millionth part of a millimetre (10⁻⁹ m). The nanotechnology based on the fact that new functionalities or properties result from the nanoscale character of the components. New properties and/or functionalities can be related to scratch resistance, colourfulness, transparency, conductivity, strength etc, which result from the altered ratio of surface atoms to volume atoms and from the quantum-mechanical behaviour²⁶.

Recently, many researchers found that the formation of nanotube oxide surfaces on the native oxide resulted in very strong reinforcement of the bone response^{25,27-31}. When titanium oxide surface

tubes with nanoscale dimensions formed, the bioactivity of the implant improved and enhanced osteoblast adhesion on the surface³². The high surface area of titanium oxide nanotube and its ability for cell interlocking promote bonding to bone^{21,33,34}.

Nanotubes fabricated on implant material surfaces not only provide great potential in promoting cell adhesion, but also in proliferation and differentiation. Moreover, nanotubes can offer the possibility of bacterial infection control by loading the tubes with antibacterial agents. However, studies were conducted to establish the optimum nanotopography for favourable cell response, and the optimum sizes of nanotubes for recognition and adherence by the sensing element of a bone cell²¹.

In vitro studies on the titanium oxide nanotube showed that nanotubular surface provides a favorable template for the growth of bone cells. Moreover, the cells cultured tests on the nanotubular surfaces showed higher adhesion, proliferation, alkaline phosphate activity and bone matrix deposition compared to those grown on smooth titanium surfaces. From in vivo studies, the biocompatibility results suggested that nanotubular titania does not cause chronic inflammation or fibrosis³⁵.

Titanium oxide nanotube have attracted extensive attention due to their large surface area, low electron recombination and charge-transport properties, and are considered to be superior chemical materials because they form one-dimensional channels for carrier transport. They are of considerable interest for applications in the field of photocatalysis³⁶, water photolysis³⁷, remediation of organic pollutants³⁸, gas sensors³⁹, solar energy cells⁴⁰, a promising role for biomaterials² and corrosion resistance⁴¹.

Anodization as preferred method to forming nanostructure

There are a variety of preparation methods that have been used to fabricate titanium oxide nanotubes such as template synthesis⁴², sol-gel methods⁴³, hydrothermal synthesis⁴⁴, evaporation⁴⁵, ion-beam synthesis⁴⁶ and anodic oxidation⁴⁷.

Among these, electrochemical anodization is widely used, due to its simplicity, cost effective technique, controllable and reproducible. It is also possible to control the size and the shape of nanotubes to the desired dimensions. In addition, titanium oxide nanotubes layer prepared by this method is strongly adherent on the substrate, which is very important for many practical applications^{2,48}.

A comparison of three methods, the assisted-template method, electrochemical anodic oxidation and hydrothermal treatment, along with their advantages and disadvantages was made in previous review¹². Titanium oxide nanotubes with ordered alignment and high aspect ratio had been produced by using anodization^{12,21,49}.

In anodization process, the self-organized nanotubular titanium oxide can be produced by using electrolytes containing fluoride, such as HF electrolytes, chromic acid-HF mixtures, $(\text{NH}_4)_2\text{SO}_4$ - NH_4F mixtures, H_2SO_4 -HF mixtures and H_3PO_4 -NaF mixtures^{27,28,31,32,50,51}.

The anodization process can be conducted by using an electrochemical cell consisting of two electrodes, one is platinum (or graphite) as a counter electrode and the second is the working electrode representing the anode of the cell, as shown in fig. 2. A DC power source was employed for the purpose. Before anodization, the sample surface must be prepared by appropriate methods, i.e. employing polishing papers of different grades and ultrasonic cleaning. The anodization was performed by increasing the potential of the sample from 0 V to the desired potential with a suitable scan rate, followed by holding the sample in the potential for specific time at chosen temperature^{27,51,52}. For example, fig.3 presented titanium oxide nanotubes formed on titanium metal by anodization in 1M Na_2SO_4 + 0.5 wt.% NaF at 20 V for 30 min⁵³.

It should be possible to control the nanotube size and morphology for the desired application by controlling the electrochemical conditions, i.e. applied voltage, anodization time, and the solution conditions, i.e. composition of the electrolyte and fluoride ions concentration, pH, water content in the electrolyte and its temperature^{12,51-57}.

The first time of the titanium oxide nanotube arrays generation was grown in HF electrolytes or acidic HF mixtures⁵⁸⁻⁶⁰. These layers have a limited thickness about 500–600 nm. By taking into account the importance of the pH gradient within the tube⁷, and using buffered neutral electrolytes that containing NaF or NH₄F instead of HF, the thickness of the self-organized nanotube titanium oxide layers will increase more than 2 micrometer⁶¹⁻⁶⁴. The third generation of the nanotubes were grown in (almost) water free electrolytes. In glycerol electrolytes, the grown tubes have extremely smooth walls and a tube length exceeding 7 micrometer⁶⁵. When the anodization applied using CH₃COOH electrolytes remarkably small tube diameters could be obtained⁶⁶.

Over the past few years, the application of anodization allow the tube diameters to be adjusted over a wide range from 10 to 250 nm, and the length of nanotube from 100 nm to several hundred nm can be grown^{67,68}. In aqueous electrolytes, applying anodic potentials in the range of 1–20 V will produce tubes with diameters between 15 and 100 nm^{67,69}. However, the thickness of the nanotube layers can be influenced by varying the anodization time and the pH of the electrolyte^{52,62}.

Some studies on the titanium oxide nanotube

Titanium oxide nanotube grown from a Ti metal and its alloys have attracted wide scientific and technological interest. The electrochemical growth of titanium oxide nanotubes on titanium and its alloys has a history of about 14 years⁷⁰.

Zwilling *et al*⁷² first produced nanotubular titanium dioxide on titanium, and the fabrication of titanium oxide nanotube arrays via anodic oxidation of titanium foil in a fluoride-based solution were first reported in 2001 by Grimes and co-workers⁵⁹. After that, many workers applied anodization process to fabrication titanium oxide nanotube in several electrolytes, and characterized the microstructure of the surface by many techniques, such as scanning electron microscopy (SEM), X-ray diffraction (XRD) patterns, and Transmission electron microscope (TEM)^{1,13,40,48}. Further studies were focused on the effect of the anodization process parameters on the formation and the properties of titanium oxide nanotubes, and how to control and optimize the

desired dimension of the oxide nanotube for the desired applications^{2,56,57,71-75}. The mechanism of titanium oxide nanotube formation by anodization was discussed by many researchers^{30,76-78}.

For biomaterial applications, the electrochemical behavior of titanium covered with titanium oxide nanotube was investigated in simulated body solutions⁷⁹⁻⁸³. Also, the effects of nanotopographical on the bioactivity of titanium were studied *in vitro*^{55,70,84-88} and *in vivo*^{4,89,90}. Moreover, the growth of nanotube oxide was conducted on binary titanium alloys such as: Ti–Zr^{91,92}, Ti–Nb⁹³, NiTi⁹⁴, ternary alloys such as: Ti–6Al–4V⁵¹, Ti–6Al–7Nb⁶¹ and Ti–13Nb–13Zr⁷, and quaternary alloys like Ti–35Nb–xZr^{7,98}, Ti–29Nb–xZr⁷ and Ti–35Nb–5Ta–7Zr alloy⁵.

In the literature, there are many reviews available about titanium nanotubes formation and properties^{21,56,77,99}, and its special properties for implant applications^{12,21,100,101}. But the information about how nanotube oxide can improve the electrochemical properties of titanium as biomaterial is very little, and there are fluctuations in the research results about it. Hence, this project will focus on the titanium oxide nanotube layer prepared by anodization and its role in the change of titanium behavior for biomaterial applications.

The electrochemical behavior of titanium oxide nanotube

The conditions used to study the electrochemical behavior

The electrochemical corrosion behavior of metals is governed by the interaction between the materials surface and the electrolyte¹⁰². In the case of nanotube oxide, the effective surface area, determined by the nanotube size¹⁰³, is expected to play an important role in the electrochemical performance of nanotubular titanium and its alloys⁷⁴.

To explain the role of nanotube oxide in changing the electrochemical behavior of titanium, the studies were also conducted in titanium without nanotube oxide, which has a stable, dense oxide layers, consists mainly of TiO₂¹⁰⁴, thin (about 3–8 nm in thickness), amorphous, and stoichiometrically defective⁹³.

The electrochemical behavior of titanium oxide nanotube in simulated biological environment was studied using many electrochemical techniques, like open-circuit potential (OCP), electrochemical impedance spectroscopy (EIS), potentiodynamic (PD) and potentiostatic polarization (PS) tests.

The open circuit potential (or corrosion potential (E_{corr})) reflects the composite results of the electrochemical reactions taking place at the electrode and solution interface. Therefore, the variation in the OCP with immersion time can be employed to study the electrochemical processes⁹⁴. From potentiodynamic polarization measurements, the corrosion potential (E_{corr}) and current (I_{corr}) can be determined, as well as the passivation current (I_{pass}). The electrochemical impedance spectroscopy (EIS) is a powerful technique to study the corrosion of metals or alloys. It can provide quantitative evaluation of the corrosion properties of the studied system, which may be difficult to assess using conventional electrochemical measurements such as potentiostatic or potentiodynamic techniques. By appropriate interpretation of the EIS data in conjunction with an equivalent circuit (EC), detailed information on the electrochemical process at the film/solution interface can be disclosed^{94,53}.

The simulated biological environments employed in electrochemical studies were involve artificial saliva⁷⁴, 0.9% NaCl^{93,96}, Ringer's solution^{27,51}, Hank's solution¹⁰⁵ or phosphate buffered saline (PBS)¹⁰⁶.

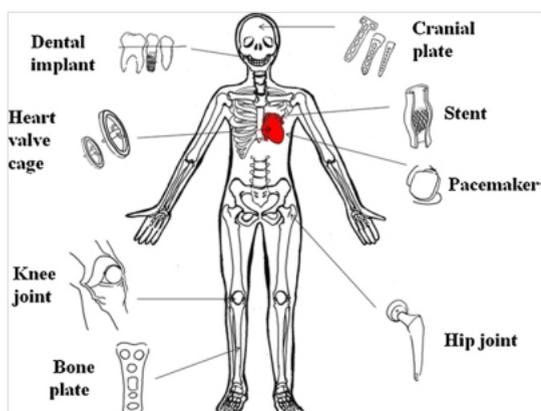


Fig. 1: Biomedical application of titanium and its alloys¹²

Results about electrochemical behavior of titanium oxide nanotube

Table 1. summaries some recently studies on the electrochemical behavior of titanium and some of its alloys with titanium oxide nanotube prepared by anodization. From the table, the results of most studies indicate that titanium materials with titanium oxide nanotube have a better corrosion resistance in simulated body fluid solutions than that of bare titanium. A smaller current density and higher OCP was observed for titanium oxide nanotube, which means an increase in the stability of titanium surface.

On the other hand, three studies found that the titanium with titanium oxide nanotube exhibited significantly higher corrosion current density and lower corrosion resistance than that of the bare titanium, meaning a lower corrosion resistance than that of titanium.

Discussion of the results

The difference in the results of the corrosion behavior of titanium oxide nanotube in simulated body fluid solutions can be attributed to the differences in the microstructure of the surface oxide layer, which are affected by several factors.

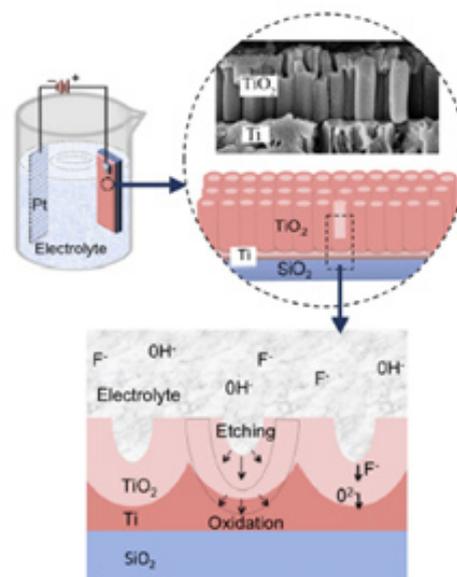


Fig. 2 : The electrochemical cell used for anodization process³⁰

The diameter and length of the nanotubes and the thickness of the barrier layer can strongly change the electrochemical corrosion behavior of nanotubular titanium^{52,74}. The differences in the methods used for preparation of the sample surface before anodization may have some effects on the properties of the oxide nanotube formed. Moreover, an important factor is the properties of the electrolyte employed in the anodization process^{1,54,96}.

The EIS of titanium oxide nanotubes indicate the presence of two time constants corresponding to the presence of two interfaces, a

highly corrosion resistant barrier layer and the outer nanotubular layer. When Ti exposed to air, a thin and stable oxide several nanometers thick is formed on its surface¹¹³. In contrast, the anodization process in fluoride solutions results in the growth of uniform arrays atop the titanium surface and a barrier layer separating the nanotubes from the conducting titanium. While the diameter and length of TiO_2 nanotube depends on the anodization voltage^{52,69}, the thickness of the barrier layer increases with anodizing voltages and approximately equal to the pore radius¹². In previous work, researchers found that a higher anodizing voltage leads to not only

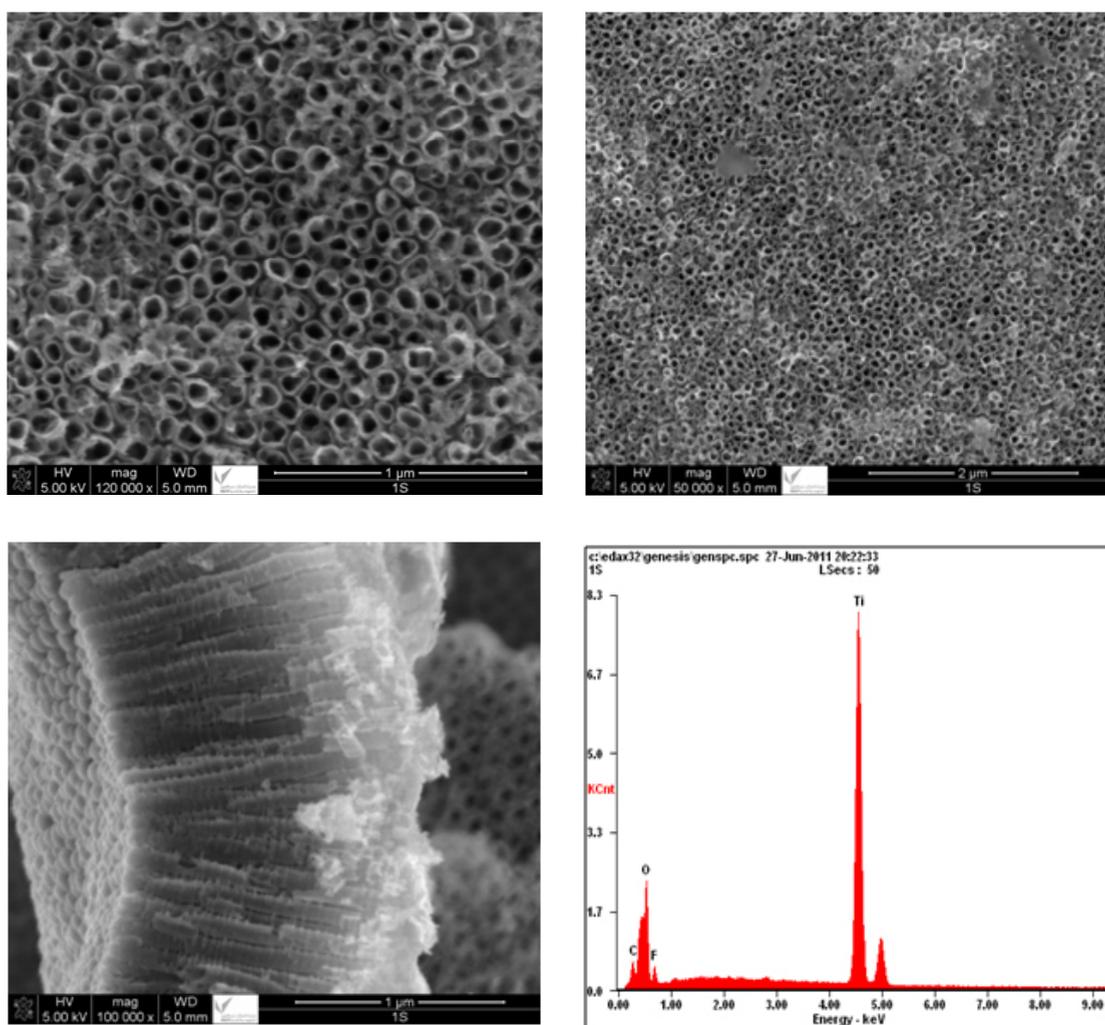


Fig. 3: The SEM images and EDX of titanium oxide nanotubes formed on titanium by anodization in 1M Na_2SO_4 + 0.5 wt.% NaF at 20 V for 30 min⁵³

Table 1: The conditions of anodization process employed to produce titanium oxide nanotube on the surface of titanium and some of its alloys and its electrochemical behavior in simulated body fluids

Ref.	Material	The conditions of anodization process				Nanotube diameter (nm)	Nanotube thickness (nm)	Other treatment	Brief results of the electrochemical behavior of
		Electrolyte	Applied potential (V)	Time (min)					
[105]	Ti	0.5 wt% HF	20	60	80	400	sintered at 450°C for 3h	TiO ₂ nanotube layers on Ti showed a better corrosion resistance than that of smooth-Ti	
[93]	Ti-xNb	1.0 M H ₃ PO ₄ + 0.8 wt.% NaF	10	120	55-220	730-2000	-	TiO ₂ nanotube surface have lower corrosion resistance compared to titanium oxides surfaces on the bare alloy	
[51]	Ti-35Nb-5Ta-7Zr	1 M H ₃ PO ₄ + 0.5 wt.% NaF	15-20	90-180	30-80	-	heat treatment at 550 °C for 180 min in Ar	The surface after nanotube formation seemed to favor an immediate and effective Passivation	
[27]	Ti-13Nb-13Zr	1 M H ₃ PO ₄ + 0.5 wt.% NaF	10-30	180	30-110	200-6000	heat treatment at 150 °C	A lower corrosion resistance of nanotubular alloy than the bare alloy. A heat treatment enhanced corrosion resistance property	
[55]	Ti-30Ta-xZr Ti-30Nb-xZr	1.0 M H ₃ PO ₄ + 0.8 wt.% NaF	10	120	150	20	-	nanotubular surface with highly ordered small and large tubes was high corrosion resistant	

[96]	Ti6Al7Nb	a. inorganic solution (NH ₄) ₂ SO ₄ + NH ₄ F (0.5 wt%) b. hybrid inorganic + organic components as glycerol + 4% H ₂ O + NH ₄ F 0.36 wt% NH ₄ F:H ₂ O:glycerol at a ratio of 1:20:79 wt. %	20	120	53-92	-	the nano structure obtained in hybrid inorganic + organic components leads to more performance corrosion potential of heat-treated sample had a novel value
[82]	Ti		20 , 30	60	5085	heat treatment for 2 h at 500 °C	
[74]	Ti	05 wt.% hydrofluoric acid	5-20	30	22-86at 5 V,39 at 10 V 59.3 at 15 V, and 86.1 at 20 V	-	when the diameter of TiO ₂ nanotube lower than 86 nm, it shows a better corrosion resistance than that of the mechanically polished Ti. The electrochemical stability of Ti nanotubes 22 to 59 nm in diameter is improved but that of Ti nanotubes larger than 86 nm decreases
[7]	Ti-29Nb-xZr	1 M H ₃ PO ₄ + 0.8 wt% NaF.	10	120	96-112	-	nanotube oxides on the alloy showed lower corrosion current density compared to non-treated sample
[106]	Ti	1MH ₃ PO ₄ + 0.5wt% HF	5 , 15	180	30-70	-	the nanotubes had higher OCP, higher resistance of the inter barrier layer, and lower I _{pass} compared to the smooth Ti annealed samples are more stable with regard to corrosion
[107]	TiTi6Al7Nb	mixture of 1:7 volumetric ratio	10	60	45	annealing at 550 °C for different times (2h or 1.5 h)	
[108]	Ti	CH ₃ COOH + 0.5 wt.% HF in water mixture of 0.14M HF and 0.2M glycerol	30	60		heat treated at 450 °C for 3h	the anodized heat treated titanium after 7 day immersion in Hank's solution showed

[53]	Ti	a. 1M Na ₂ SO ₄ + 0.5 wt.% NaF; b. 1.0 M H ₃ PO ₄ + 0.8 wt.% NaF; c. 0.5 (wt) % HF	20	30	52-93	250-1200	-	nobler shift in corrosion potential compared to untreated and anodized titanium electrochemical stability of Ti nanotubes is enhanced, and depended on the dimensions of the TiO ₂ nanotube which was controlled by optimizing the anodization electrolyte composition TiO ₂ nanotube formed at 20 V has the best stability, the duration of anodization process up to 2 hour can change the stability of TiO ₂ nanotubes.
[52]	Ti	1M H ₃ PO ₄ + 0.8 wt.% NaF	10-40	10-120	31-93	280-480	-	the titanium oxide nanotubes obtained in hybrid organic + inorganic components leads to more performances. the nanotubes exhibit worse corrosion resistance and more Ni release compared to the polished sample
[54]	Ti	a. inorganic solution (1M (NH ₄) ₂ SO ₄ + 0.5 wt.% NH ₄ F); b. organic solution as Glycerol + NH ₄ F (0.5 wt.%) c. a mixture of glycerol and water + 0.5 wt.% NH ₄ F.	20	30	22-75	200-830	-	the titanium oxide nanotubes obtained in hybrid organic + inorganic components leads to more performances. the nanotubes exhibit worse corrosion resistance and more Ni release compared to the polished sample
[109]	NiTi	ethylene glycol containing 0.2 wt.% NH ₄ F and 0.5 vol% H ₂ O	5-35	1.5-12h	23-50	100-780	annealed at 450°C for 2 h	the titanium oxide nanotubes obtained in hybrid organic + inorganic components leads to more performances. the nanotubes exhibit worse corrosion resistance and more Ni release compared to the polished sample
[57]	Ti-6Al-7Nb	a. 0.5% NaF in a 90:10 EG and water b. 0.5wt% NaF in a 90:10 G and water	60 V	5 h	160 -167nm	15-21 nm	Annealed at 450 and 600 °C	The surface modification of alloy with a nanotubular TiO ₂ layer was effective

[110]	Ti-6Al-7Nb	50 ml of 0.08 M HF in 50ml of 1 M sulfuric acid	10-30	1h	35-125 nm	-	Annealing at 450, 600, 700, 800, 850 °C for 3h	in enhancing the passive layer resistance and reducing the corrosion current density compared to the substrate anodized samples have better passivation behavior, comparable with that of the substrate
[111]	Ti-6Al-4V	50 ml of 0.08 M HF in 50 ml of 1 M sulfuric acid	20 V		80 nm	250 nm	annealing at 450 and 600 °C for 3h	anodized samples have good corrosion resistance with better passivation behavior the annealed nanotubes showed higher impedance and lower passive current density than the as-formed nanotubes
[78]	Ti	0.1 M citric acid with 0.5 wt.% NaF	20 V	0.5-3h	85-105	301-623	heat treated at 600 °C for 3 h	Samples both anodized and thermally oxidized exhibited shifts of OCP and E_{corr} in the noble direction, and lower I_{corr} than the smooth one
[112]	Ti-6Al-4V	4.0 vol.% DI-water, 0.2 wt.% NH_4F , and ethylene glycol	60 V	2h	-	-	thermal oxidation at 600°C for 3h	

larger diameter of TiO₂ nanotubes, but also thicker barrier layers^{12,91}. The thicker inner barrier layer of nanotubes may play a more important role in corrosion resistance of titanium which agrees with the result of EIS¹⁰⁵.

Many previous studies have shown that the size of titanium oxide nanotube is a key factor to determine its corrosion behavior. When a small diameter TiO₂ nanotube grows on pure Ti, a lower corrosion rate is reported, but large nanotubes have an opposite effect¹⁰⁶. When the diameter of the nanotube is increased, the electrochemical stability increases first and then diminishes when its diameter more than 86 nm⁷⁴. Improved corrosion resistance of pure titanium when a small nanotube covered it may be ascribed to relatively thick oxide layer formed during anodization at the substrate/nanotube interface. However, the large oxide nanotubes possess a high specific surface area to contact with electrolyte thus beneficial to the diffusion of corrosive ions and corrosion products. The larger nanotubes provide more channels for the electrolyte to reach the barrier layer consequently increasing the chance of the reaction between corrosive ions and titanium oxide^{91,102}. This phenomenon was reported by many workers who used nanotubes approximately 150-220 nm in size in the corrosion tests^{74,91,93}.

Some studies reported that the corrosion attack of the nanotubular Ti is attributed to the collapse of TiO₂ nanotubue layer⁷⁴. There is a suggestion that the nanotubes may act as effective channels for the electrolyte to reach the interface. Moreover, Saji and Choe suggested that the lower corrosion resistance of the nanotubular alloy can be associated with the distinctly separated barrier oxide/concave shaped tube bottom interface²⁷.

Another important factor, is the wall between TiO₂ nanotubes, which may be influencing its electrochemical stability. The morphology of the corroded titanium oxide nanotubes after the potentiodynamic polarization test showing that the nanotubular structure collapses at the localized corrosion site¹¹⁴. The nanotubes forming by anodizing titanium oxide have a dual-layer wall. The inner layer is composed from titanium oxide whereas the outer layer is composed of some form of titanium hydroxide

with a relatively low density. Between adjacent nanotubes there is a space, and when corrosive ions in the artificial saliva penetrate, the quick dissolution of the outer layer of TiO₂ nanotubes will leading to deposition of phosphate compounds¹¹⁵. When the phosphate compounds present in the solution, it will block the small space and retard diffusion of oxygen and/or other dissolved products to and away from the surface of the outer layer, respectively. With reduced oxygen, rebuilding of titanium oxide is slowed, causing further dissolution of the wall between adjacent nanotubes and eventually collapse of the wall⁷⁴.

Thus, optimized parameters of the anodization process to form nanotube oxide, such as anodization potential, nature of the electrolyte, concentration of the electrolyte, duration of anodization, temperature and the potential sweep rate is critical in achieving the desirable size and shape of the self-ordered nanotubes^{27, 51,55}.

For more improvement in the electrochemical corrosion behavior of titanium oxide nanotube, many workers suggested that suitable heat treatment processes of oxide nanotube can provide the required bioactivity and chemical stability which is important in biocompatibility point of view for potential implant applications^{27, 82}.

The structure of the grown oxide nanotube can be amorphous or crystalline, strongly dependent on the electrochemical parameters of the anodization process, such as the applied potential, the time of anodization, or the sweep rate of the potential. For example, at low voltages (below 20 V), the structure of the oxide films on Ti has typically been reported to be amorphous, and crystallization to take place at higher voltages¹¹⁶. Moreover, depending on the anodizing conditions the crystal structure can be anatase, a mixture of anatase and rutile, or rutile¹¹⁷.

Many of the studies confirm that the thermal treatments resulting in an improvement of the adhesion of nanotubes to the titanium substrate require temperatures above 400 °C^{118,119}. At such temperatures, structural changes lead to a crystalline titanium dioxide¹¹⁸. These structural

changes can enhance the mechanical stability of the porous anodic layers without changing the diameter of the oxide nanotubes. Thus, an appropriate heat treatment can render titanium oxide nanotubes .

After nanotubes were annealed, there was a significant decrease in the passive current density and corrosion current density^{27,120,121}, because the anatase nanotubes had a stable phase compared to the amorphous nanotubes^{120,121}. Furthermore, the standard potential E° of anatase nanotubes was lower than that of amorphous one, which can be attributed to the surface area decrease because the pores became smaller or were closed after annealing¹²⁰.

The role of titanium oxide nanotube on the improve the osseointegration of biomaterials

Recently, many of the researches focus on the biomaterials surface, aimed to understanding the fundamental processes at the interface between the implant surfaces and surrounding living tissues, that the human biology and nature should be considered in the design of functionalized biomaterials¹²².

When the biomaterial implanted in soft tissue, it induces a cell-mediated inflammatory response and fibrotic encapsulation¹²³, which means an inflammatory processes immediately following the implantation, that are inherently present at biomaterials surfaces during wound healing events¹⁸.

During early stage wound healing produce nitric oxide (NO), which is a key indicator of pro-inflammatory signal transduction in the inflammatory response and antimicrobial defense¹²⁴. The inflammatory cells generate superoxide anion and reactive oxygen intermediates¹²⁵. Further degradation may yield hydroxyl radicals, singlet oxygen, and hydrogen peroxide. Thus, the ability of a biomaterial to interact with inflammatory cells, and reactive oxygen and nitrogen species may be relevant for the host response. Results of titanium oxide nanotubes were shown to reduce the levels of the pro-inflammatory compared with a planar TiO_2 control surface, which suggests that the titanium oxide nanotubes elicit a favorable response in soft tissues. This may be due to the increased catalytic oxide surface area of the TiO_2 nanotubes^{4,48}. The

TiO_2 nanotubes possess an empty volume for filling with bioactivating species and provide an interface suitable for anchoring connective tissue⁸⁴.

The results of many studies conducted to evaluate the nanomaterials chemistry suggest that increased bone cell functions may be independent of the bulk materials chemistry but rather rely on the degree of the nanostructured surface roughness¹²⁶⁻¹²⁸.

Titanium oxide nanotubes offer an empty volume that can be filled with bioactive species and provide an interface suitable for anchoring connective tissue. Results indicated that the TiO_2 nanotubes enhance the process of apatite formation as compared to that on a common native oxide layer on titanium^{84,129}, which considered to be an essential step for the bone-binding ability of biomaterials to the living bone. The incorporating of calcium phosphate crystals into the nanotubes can result in better adhesion of the coating to the substrate, and more osseointegration¹⁷.

To further improve the bioactivity and biocompatibility of titanium, various types of surface modification methods have been explored to enhance hydroxyapatite formation¹³⁰. The nanotubular structure increased the surface area and also more 'in-between-nanotube path-ways for fluid'¹²⁹. The faster and better nucleation on the nanotubes might be caused by the fact that the ions have better access to the surface when it is nanotubular, they can diffuse into the channels and form nuclei very homogeneously all over the walls, whereas the apatite growth on flat TiO_2 proceeds in a more heterogeneous, mushroom-like manner⁹⁰. Thus, the increased surface area of the titanium oxide nanotubes is useful for accelerated bone growth in orthopedic/dental applications¹²⁹. Balasundaram and Webster suggest that nanophase has ability to mimic the dimensions of the constituents and components in natural bone-like proteins and hydroxyapatite⁸.

The annealing of the amorphous nanotube layers to anatase or a mixture of anatase and rutile will enhance the apatite formation⁸⁴. The proper heat treatment introduction of anatase phase form of titanium oxide in the nanotubes can further improve the biological activity¹³⁰.

CONCLUSION

When titanium and its alloys subject to anodization in suitable manner, the formation of TiO₂ nanotube will occur. The electrochemical behavior of titanium oxide nanotube in simulated body fluids depends on its morphology and surface properties. When titanium oxide nanotube formed by anodization, these surface properties are depending

strongly on two factors, The first is the parameters of anodization process, i.e. applied potential, duration of anodization and the method employed to prepare the sample surface. The second is the conditions of the electrolyte employed in the anodization cell, i.e. composition, fluoride ion concentration, temperature, pH and water content in the electrolyte. Thus, all these factors must be taken into account to produce titanium oxide nanotube with desired properties that needed for special application.

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