ELECTROCHEMICAL MODIFICATIONS OF TITANIUM AND TITANIUM ALLOYS SURFACE FOR BIOMEDICAL APPLICATIONS – A REVIEW

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ABSTRACT

The field of biomaterials requires the input of knowledge from very different areas such as biology, medicine and engineering so that the implanted material in a living body to not induce any adverse impacts. The paper focuses its attention mainly on titanium and titanium alloys, even though there are biomaterials manufactured from other metals, ceramics, polymers and composite materials. Both electrodeposition and anodic oxidation surface modification methods are discussed with several examples and a brief description of underlying theory, in order to improve the mechanical, chemical and biological properties of these materials.

KEYWORDS: titanium, titanium alloys, electrodeposition, anodic oxidation

1. Introduction

A biomaterial can be defined as any substance or combination of substances synthetic or biological in origin, used in the treatment of disease or lesion, to resolve pathology that cannot be straightened either by the natural healing process or conventional surgical intervention, using a multidisciplinary approach that requires involvement of science such as biology, medicine, and engineering. Biological biomaterials can be classified into soft (skin, tendon) and hard (bone, dentine,) tissue types. In the case of synthetic biomaterials, it is further classified into: metallic, polymeric, ceramic and composite [1-2]. The fundamental requirement of a biomaterial is that the material and the tissue environment of the body should coexist without having any undesirable or inappropriate effect on each other. The implanted material should not induce any adverse impacts like allergy, inflammation and toxicity either immediately after surgery or under post operative circumstances [3].

The necessity for biomaterials stems from an inability to treat many diseases, injuries and conditions with other therapies or procedures and biomaterials serve to replacement of body part that has lost function, correct abnormalities improve function and assist in healing.

The most important medical applications for biomaterials include orthopedic applications, dental implants, cardiovascular applications, skin repair devices, contact lenses, cochlear replacements, bone plates, bone cement, heart valves, artificial ligaments and tendons.

Metallic biomaterials represent the most highly used class of biomaterials and generally have attributes over other biomaterials in terms of strength, stiffness, toughness, impact resistance, and good processability [4]. The demand for metallic biomaterials is greatly increasing because of aging populations worldwide at a rapid rate and growing demand for a higher quality of life [5].

2. The most essential properties of a metallic biomaterial

In order to be used successfully, metallic biomaterials must have special properties that can be afforded to fulfill the requirements for their intended function, such as mechanical properties, biocompatibility, corrosion resistance, high fatigue and wear resistance.

However, depending on the application, differing requirements may appear. Sometimes these requirements can be completely reverse.

2.1. Mechanical properties

Mechanical properties of a biomaterial must be adjusted to its intended applications otherwise the implant is likely to fail. The mechanical properties such as hardness, tensile strength, modulus, elongation (strain), fracture resistance and fatigue strength or life play an important role in material selection for application in the human body [6].

The most common metals and metals alloys used for implants are fabricated from stainless steel, cobalt alloy and titanium and until nowadays have been used successfully [4-5]. These materials have the requisite strength characteristics but typically have not been resilient or flexible enough to form an optimum implant material. Also many alloys contain elements such as aluminum, vanadium, cobalt, nickel, molybdenum, and chromium which recent studies have suggested might have some long term adverse affects on human patients.

Strength of materials from which the implants are made has an influence on them, so that inadequate strength can cause fractures the implant. When the bone implant interface starts to fail, develops at the interface a soft fibrous tissue by releasing tiny particles of the implant and causes pain to the patient [5,7].

For major applications such as total joint replacement a low Young’s modulus equivalent to that of human bone is basically essential in order to prevent bone absorption [8]. These metals typically used for traditional implants have elastic modules much higher than that of bone, for example, cortical bone has a modulus between 15 and 30GPa depending on the type of the bone and measurement direction – while 316 stainless steel has an elastic modulus of about 190GPa and that of cast heat-treated Co-Cr-Mo alloy is about 210GPa. Of these the alloy with the lowest elastic modulus is Ti-6Al-4V with an elastic modulus of about 110GPa [9-10].

Fatigue strength is defined as the highest periodic stress that does not initiate a failure of the material after a given number of cycles. Metal alloys are used for load bearing applications and must have sufficient fatigue strength to endure the rigors of daily activity (walking, chewing etc).

The comparison of mechanical properties of metallic biomaterials with bone is given in table 1 [11].

Table 1. *Comparison of mechanical properties of metallic biomaterials with bone**

Material/ Parameter	Stainless steel	Co-Cr alloy	Pure Ti	Ti-6Al-4V	Cortical bone
Elastic modulus (GPa)	190	210-253	110	116	15-30
Yield Strength (Gpa)	221-1213	448-1606	485	896-1034	30-70
Tensile Strength (Mpa)	586-1351	655-1896	760	965-1103	70-150
Fatigue Limit (Mpa)	241-820	207-950	300	620	-
Density (g/cm^3)	7.9	8.4-9.2	4.5	4.5	-
Elongation (%)	12-40	5-30	15-24	10	1-2

**Adapted from J.B. Brunski. Metals, pp. 37–50 in B.D. Ratner, A.S. Hoffman, F.J. Shoen, and J.E. Lemons (eds.), Biomaterials Science: An Introduction to Materials in Medicine, Academic Press, San Diego (1996).*

2.2. Biocompatibility

There are several characteristics which influence implant biocompatibility. The first is that they should not be toxic to cells.

Toxicology deals with the substances that migrate out of biomaterials. It is convenient to say that a biomaterial should not give off anything from its mass unless specifically designed to do so. If a medical implant is fixed and it kills the surrounding cells, this would clearly cause difficulties for the patient. After a certain period the pain becomes insupportable and the implant must be substituted, a method that is called as a revision [7].

Another important factor is the compatibility of synthetic materials with blood and tissue. Interactions at the tissue-material interface may determine whether a material is tissue compatible and can coexist with the physiological environment.

A common problem with medical implants is rejection, because every biomaterial has the potential to induce biological dysfunctions such as inflammation and infection in the surrounding tissues after implantation [12]. The immune system identifies the substances from the implant as foreign and attempts to fight them and to remove them and so consequently the foreign materials to be extruded or walled off, in case they can not be removed from the body.

The degree of the tissue responses varies according to both physical and chemical nature of the implants. Pure metals tend to evoke a severe tissue reaction, due to the high-energy state or large free energy of them, which tends to lower the metal’s free energy by oxidation or corrosion.

2.3. Corrosion

Corrosion, the graded degradation of materials by electrochemical attack, is of concern particularly when metallic biomaterials are placed in the hostile electrolytic environment provided by the human body. The body environment is very aggressive and contains water, complex organic compounds, dissolved oxygen, proteins, and ions such as hydroxide, sodium and chloride, small amounts of potassium, calcium, magnesium, phosphate, sulphate and amino acids [13-14]. These ions react electrochemically with the surface of metallic biomaterials to cause corrosion. The metallic components of the alloy are oxidized to their ionic forms and the dissolved oxygen is reduced to hydroxyl ions. During corrosion process, the total rates of oxidation and reduction reactions that are termed as electron production and electron consumption respectively, must be equal [13]. The corrosion of biomaterials depends on geometric, metallurgical, mechanical and solution chemistry parameters [15].

The nature of the passive oxide films formed, and the mechanical properties of the materials form some of the essential criteria for selection of alternative or development of new materials.

Resistance to corrosion is extremely important for a metallic material because corrosion can lead to rough surface, lower recovery, and release of elements from the metal or alloy. Release of elements can produce discoloration of adjacent soft tissues and allergic reactions in patients [16]. Corrosion products may be involved in causing local pain, tissue reactions and tumefactions in the region of the implant, in the lack of infection [17].

2.4. Wear properties

Wear properties of an implant material are important, especially for various joint replacements because wear of artificial joints releases particles into the body. Wear cannot be discussed without some understanding of friction between two materials. When metallic implant is subjected to wear, the passive layer can be removed allowing active corrosion to occur while the alloy is repassivates [18]. A fatigue wear process involving fretting causes the generation of wear debris which can produce acute host–tissue reactions and tend to aggravate the fatigue problems of the biomaterial by producing enzymes and chemicals (including fast multiplication of local fibroblast-like cells and activated macrophages) that are highly corrosive and finally implant loosening, a major cause of joint implant failure [19].

2.5. Tribocorrosion synergism

Tribocorrosion is a material degradation process which results from simultaneous mechanical (wear) and chemical or electrochemical (corrosion) effects [20]. It is well known in tribology that a corrosive environment can accelerate the wear rate [20-21]. The results obtained are not just a simply summation of the electrochemical and mechanical effects but represents a complex synergy between wear and corrosion [22]. Tribocorrosion behavior cannot be predicted from wear and corrosion taken separately [23]. If for the titanium and its alloys have been conducted and reported several results on their tribocorrosion behavior, the literature reveals the need for more robust testing techniques, in particular the need for analyze the tribocorrosion behavior of the coatings on their surfaces [24-27].

2.6. Osseointegration

Osseointegration is a recently introduced term that indicates a direct biochemical bond between a non-natural substance and a bony tissue [28]. Osseointegration has made possible the development of a number of clinical applications in the field of hand surgery and orthopedics: finger joint prostheses, thumb amputations, amputation of lower limb etc.

The initial observations of osseointegration were made in the 1952 by Professor Per-Ingva Brånemark of Sweden, in an experiment where embedded titanium device into rabbits' leg bones to study bone healing. At the conclusion of the experiment, after a few months he tried to remove these titanium devices and when he discovered that the bone had integrated so completely with the implant that could not be removed [29-30]. Since Branemark made first observations, osseointegration has been intensively studied and the research is ongoing. Osseointegration is a promising technique for providing function and quality of life.

3. Metallic implant materials

Metallic biomaterials are the most suitable for replacing failed hard tissue up to now. Metals and alloys have been widely used in various forms as implants materials in the medical and dental fields such as devices for bone fixation, partial and total joint replacement, external splints, and traction apparatus as well as dental amalgams, crowns, bridges, and dentures, which provide biocompatibility, the required mechanical strength, high corrosion and wear resistance. The commonly used metallic biomaterials are stainless steels, Co-based alloys, and titanium and its alloys.

3.1. The austenitic stainless steels

The austenitic stainless steels especially types 304, 316 and 316L – are used for implants fabrication because of a favorable combination of mechanical properties, good corrosion resistance, low cost, availability and easy processing when compared to other metallic implant materials [4-5].

The austenitic class of stainless steels is nonmagnetic and offers the most resistance to corrosion in the stainless group, owing to its substantial nickel 8% content and higher levels of chromium 18%.

Types 316 and 316L stainless steels exhibit better corrosion resistance than type 304 or good elevated temperature strength. The "L" grades are used to provide extra corrosion resistance after welding. The only difference in composition between 316 and 316L stainless steel is the amount of carbon that is in the material, 316 has 0.08% maximum carbon content while 316L has a 0.03% maximum carbon content. The carbon is kept to 0.03% or under to avoid carbide precipitation. Carbon in steel when heated to temperatures in what is called the critical range (800 degrees F to 1600 degrees F) precipitates out, combines with the chromium and gathers on the grain boundaries. This deprives the steel of the chromium in solution and promotes corrosion adjacent to the grain boundaries. By controlling the amount of carbon, this is minimized.

Chromium is alloying element that is the essential stainless steel material for conferring corrosion resistance. Chromium has a great affinity for oxygen which allows the formation of a strongly adherent, self-healing and corrosion resistant film of chromium oxide on the surface of the steel Cr_2O_3, film that is too thin to be visible, and the metal remains lustrous [4, 7, 31]. A film that naturally forms on the surface of stainless steel self-repairs in the presence of oxygen if the steel is damaged mechanically or chemically, and thus prevents corrosion from occurring. Molybdenum in the presence of chromium enhances the corrosion resistance of stainless steel. The inclusion of molybdenum enhances resistance to pitting corrosion in salt water. Nickel is another alloying element used as a raw material for certain classes of stainless steel. Nickel provides high degrees of ductility (ability to change shape without fracture) as well as resistance to corrosion. The presence of nickel improves considerably the corrosion resistance when compared to the martensitic and ferritic grades.

Surgical implant application for stainless steel include: wire for surgical sutures, fractures plates, pins, screws hip nails and neurosurgical and microvascular clips [12]. Thus, stainless steels are suitable to use only in temporary implant devices because its fatigue strength that is less than other alloys. The wear resistance of austenitic stainless steel is relatively poor and therefore their use in orthopaedic joint prosthesis as metal-on-metal is limited because of high friction and large number of wear debris particles that occurring, resulting rapid loss of the implant [31]. In order to improve corrosion resistance, wear resistance and fatigue strength of these group of stainless steel, can be used surface modification methods such as anodization, passivation, hard coatings, bioceramics, ion-implantation, biomimetic coatings and glow-discharge.

3.2. Co-base alloys

Co-base alloys are generally used in applications which require wear resistance, corrosion resistance and/or thermal resistance. There are basically two types: one is the castable Co-Cr-Mo alloy, which usually has been used for many decades in dentistry and recently, in making joints, and the other is the wrought Co-Ni-Cr-Mo alloy which is a reletive newcomer now used for making the stems of prostheses for heavily loaded joints such as the knee and hip [4, 7].

Co-Cr alloys have an excellent corrosion resistance (better than that of stainless steel), which is provided by a thin adherent layer and passive of chromium-based oxides with additions of Mo on the surface even in chloride environments [7, 31-33]. Ly et al. [34] in their study they report the identification of different Cr and Co species in the passive films formed under different potentiostatic conditions, which play important roles in alloy passivation. Furthermore, they found that Mo is only present in the oxide layer if the film is air formed, but that it readily dissolves upon exposure to the solution [35]. The dissolution rate of Mo was too low to be measured, indicating that the passive film protected further oxidation of underlying Mo in the alloy [34, 36]. The modulus of elasticity for the Co-Cr alloys does not change with the changes in their ultimate tensile strength. These materials have a high elastic modulus (200–220 GPa) higher to that of stainless steel (approx. 200 GPa), and an order of magnitude higher than that of cortical bone (20–30 GPa) [4,7,32]. This may have some implications of different load transfer modes to the bone in artificial joint replacements, on contact with bone, the metallic devices will take most of the load due to their high modulus, producing stress shielding in the adjacent bone. The lack of mechanical stimuli on the bone may induce its resorption that will lead to the eventual failure and loosening of the implant [31,37].

Carbon additions between 0.1 and 0.3 wt% have been shown to favor the formation of carbides which increase wear resistance.

The Co-Ni-Cr-Mo alloy has a high degree of corrosion resistance to seawater under stres than Co-based alloys. The superior fatigue and ultimate tensile strength of the Co-Ni-Cr-Mo alloy make it very suitable for applications that require a long service life without fracture or stress fatigue.

3.3. Titanium and its alloys

Titanium and its alloys are used extensively for implant materials in the medical and dental fields, and offer many advantages such as superior biocompatibility, corrosion resistance, specific strength, relatively low modulus and strong osseointegration tendency compared with other metallic implant materials [38-39]. Among various titanium alloys, pure titanium and Ti-6Al-4V alloy have been and are still most widely used for biomedical applications. These groups of alloys, as those mentioned above are mainly used for substituting materials for hard tissues.

The greater *corrosion resistance* for titanium and its alloys derives from the spontaneous formation of a titanium oxide film on their surface as long as oxygen is present, its thickness has been evaluated to be approximately 5 nm and which possesses a low level of electronic conductivity [40-44]. This natural oxide layer for commercially pure titanium is composed of titanium oxide in different oxidation states (mainly consists of TiO_2, Ti_2O_3 and TiO), while for the alloys, aluminum, niobium, molybdenum or vanadium are additionally present in oxidized form (Al_2O_3, Nb_2O_5, MoO_2, MoO_3 or V-oxides) oxides which are thermodynamically stable at physiological pH values. The stable oxides are very insoluble in biological fluids and this lead to the excellent localized biocompatibility observed for these classes of alloys [42,45]. This film acts as an electrochemically passive film and inhibits negative ions from invading the matrix of the titanium or its alloys and in this way prevents the ion release or dissolution of titanium and alloyed elements into the body fluids. This high corrosion resistance of titanium alloys can be strongly decreased by damage of the passive film when the bending stress is loaded on the sample, even if the sample itself is not fractured [5,38,40].

The *modulus of elasticity* of these materials is about 100-110 GPa, which is half the value of Co-based alloy and is known that a lowest Young's modulus is favorable for homogeneous stress transfer between implant and bone and it was proved that an implanted Ti reduced biomechanical tissue problems, and the fatigue fracture rate following continuous physiological load-bearing is also far lower than it is with other known metals [12]. Niinomi [8] in his study reported that the level of Young's modulus is effective in inhibiting bone absorption after implantation and on the other hand a lowest Young's modulus, even similar to that of bone present some disadvantages because causes large amounts of shear motion between stem and bone, leading to the formation of fibrous tissue and finally failure.

Strong osseointegration tendency. After implantation, the oxygen atoms in the body fluid naturally react with Ti atoms and form the oxidized layer of titanium oxide (TiO_2), and the newly formed and fully mineralized bone is deposited directly upon the metal surface without any interposition [12].

4. Structure, properties and applications of titanium and Ti-6Al-4V titanium alloy

Depending on their microstructure after processing, titanium alloys may be classified into one of five classes: α, near-α, α+β, metastable β or stable β [46].

Alloying elements in Ti are classified into α, β and neutrals stabilizers on the basis of their effects on the α/β transformation temperature or on their differing solubility's in the α or β phases. Pure titanium exists in form of α-phase at temperatures above 882,5^{o}C and in form of β-phase at temperature below 882,5^{o}C [47]. The temperature of allotropic transformation of α-titanium to β-titanium is called Beta Transus Temperature. The α-stabilizing elements extend the α phase field to higher temperatures, while β-stabilizing elements shift the β phase field to lower temperatures. Neutral elements have only minor influence on the β-transus temperature. In crystallographic form of α-titanium atoms are arranged in hexagonal close packed structure (hcp), and in β-titanium atoms are arranged in body centered cubic structure (bcc) [9,46].

The substitutional element Al and the interstitial elements O, N, and C are all strong α stabilizers and increase the transus temperature with increasing solute content. Among the α stabilizers, aluminum is far the most important alloying element of titanium, because it is the only common metal raising the transition temperature and having large solubilities in both α and β phases. Other α stabilizers include B, Ga, Ge, and the rare earth elements but their solid solubilities are much lower as compared to Al or O and none of these elements is used commonly as an alloying element. The β stabilizing elements are divided into β isomorphous elements (V, Mo, Nb, Ta, Re) and β eutectoid forming elements (Cr, Fe, Si, Ni, Cu, Mn, W, Pd, Bi) depending on the details of the resulting binary phase diagrams. Sufficient concentrations of V, Mo, and Nb elements make it possible to stabilize the β phase at room temperature. The elements Zr and Sn that are found in some Ti alloys are considered to be 'neutral' alloying elements [46].

The α and near-α titanium alloys exhibit superior corrosion resistance but have limited low temperature strength. The β alloys also offer the unique characteristic of low elastic modulus and superior corrosion resistance. The alloys belonging to the α+β system contain one or more α stabilizing element with one or more β stabilizing element.

These alloys retain more β phase after solution treatment than do near-α alloys, the specific amont depending on the quantity of β stabilizers present and on heat treatment. The alpha-beta alloys, when properly treated have an excellent combination of higher strength, ductility and good hot formability. They are stronger than the alpha or the beta alloys due to the presence of both the α and β phases. Ti-6Al-4V is one of the most widely used titanium alloys for biomedical application and in generally is used in the (α+β)-annealed condition. Its total production is about half of all Ti alloys. It is an alpha-beta type containing 6 wt% Al and 4 wt% V. Aluminum is added to the alloys as α-phase stabilizer and hardener due its solution strengthening effect. Vanadium stabilizes ductile β-phase, providing hot workability of the alloy [47].

Applications of Ti-6Al-4V. Titanium is one material which receives equal attentions and interest from both the engineering and medical/dental fields. Because of their lightweight, high specific strength, low modulus of elasticity, and excellent corrosion resistance, titanium materials (both unalloyed and alloyed) have become important materials for the aerospace industry, automotive, surgery and medicine, chemical plant, power generation, oil and gas extraction, sports, and other major industries.

In aerospace industry since the early 1950s, was initially used for compressor blades in gas turbine engines. Today, wrought Ti-6Al-4V is used extensively for turbine engine and air frame applications. Engine components include blades, discs, and wheels. Ti-6Al-4V is used in a variety of airframe applications, including cargo – handling equipment, flow diverters, torque tubes for brakes, and helicopter rotor hubs. In missile and space applications, they are used for wings, missile bodies, optical sensor housings, and ordnance. Also, Ti-6Al-4V castings are used to attach the main external fuel tanks to the Space Shuttle and the boosters to the external tanks. In the automotive industry, wrought Ti-6Al-4V is used in special applications in high – performance and racing cars where is critical , usually in reciprocating and rotating parts, such as valves, valve springs, connecting rods, and rocker arms. It also has been used for drive shafts and suspension springs. Marine applications of wrought Ti-6Al-4V include armaments, sonar equipment, deep – submergence applications, hydrofoils, and capsules for telephone – cable repeater stations. Casting applications include water – jet inducers for hydrofoil propulsion and seawater ball valves for nuclear submarines. Major medical applications of this alloy are: dental applications, orthopedic applications, cardiovascular applications, cochlear implant, implantable cardiovascular devices, extracorporeal artificial organs, biomedical sensor and biosensors, bioelectodes – electrical stimulation and diagnostic devices. The popularity of titanium and its alloys in surgical implants fields can be recognized by counting the manuscripts published in literature reports. Thousands of experimental reports have addressed the excellent biocompatibility of titanium and titanium alloy.

5. Surface modification of Ti-6Al-4V for biomedical applications by electrochemical methods

Surface engineering can play a significant role in extending the performance of medical devices made of titanium and its alloys. Surface properties such composition, roughness and topography are the most important factors that depend on cellular interactions on surface engineering [48]. Surface modification is a process that changes a material's surface composition, structure, and morphology, leaving the mechanical properties intact [49].

Titanium and titanium alloys can not meet all of the clinical requirements because of its poor tribological properties such as poor wear resistance and a high co-efficient of friction which can cause problems [50]. In addition, it is dangerous for Ti-6Al-4V to stay in the human body for a long time because undergoes electrochemical exchange releasing metallic ions in the physiological environment and is known that aluminum element has strong neurotoxicity and vanadium is a strong cytotoxin, and over time, the alloy produced adverse reactions in the body tissues. The release of these elements, even in small amounts, may cause local irritation of the tissues surrounding the implant and sometimes can cause the implant failure [51-53]. Therefore, implants of titanium and titanium alloys are not used without some type of surface modification designed to provide a greater wear resistance and to add biofunction, because biofunction cannot be added during manufacturing processes [49]. Various surface modifications have been used for improving the wear, corrosion behaviour and bioactivity of Ti alloys.

The surface modification recently becomes active in the field of implants. In the biomedical domain, coatings have been used to modify the surface of implants, and sometimes to create an entirely new surface which gives the implant properties which are quite different from the uncoated device. There are a number of methods reported in the literature to modify titanium and titanium alloys for biomedical implants such thermal oxidation [54-56], plasma spraying [57-59], sol–gel method [60-62], biomimetic deposition [63-65], anodic oxidation [66-68], electrophoresis deposition [69-70] and electrochemical deposition [71-74].

5.1. Electrodeposition

Among these techniques which have been developed to deposit bioactive film on titanium and its alloys used for surface modification electrodeposition offers a number of combined advantages such as availability and inexpensive equipment, simple process, rigid control of coatings thickness, complex shapes and low process temperature [71-72, 74]. Electrodeposition parameters include bath composition, pH, temperature, overpotential, additives type, etc., while important microstructural features of the substrate are grain size, crystallographic texture, dislocation, density, and internal stress [75].

***Table 2.** Various compositions of electrolytes used for electrodeposition of calcium phosphates*

Composition	pH	Ref
- 1.46 M $CaCl_2$ - 0.87 M NaH_2PO_4	3.89	[71]
- 0.1 M $Ca(NO_3)_2$ - 0.06 M $NH_4H_2PO_4$ - H_2O_2 10 mL/L	4.3	[79]
- 0.042 mol/L $Ca(NO_3)_2$ - 0.025 mol/L $(NH_4)_2HPO_4$	4.4 adjusted by dilute HNO_3 and NH_4OH	[80]
- 0.042 M $Ca_2(NO_3)_2$ x $4H_2O$ - 0.125 M $NH_4(H_2PO_4)$	4.4	[81]
- 0.04 mol/L $Ca(NO_3)_2$ - 0.027 mol/L $(NH_4)_2HPO_4$ - 0.1 mol/L $NaNO_3$	4.5	[82]
- 0.021 M $CaCl_2$ - 0.0225 M $NH_4H_2PO_4$	4.5	[83]
- 0.61 mM $Ca(NO_3)_2$ - 0.36 mM $NH_4H_2PO_4$	6	[84]
- 137.8 mmol/L NaCl - 1.7 mmol/L K_2HPO_4 x $3H_2O$ - 2.5 mmol/L $CaCl_2$	7.2 Adjusted with tris-hydroxymethylaminomethane [$(CH_2OH)_3CNH_2$] and hydrochloric acid	[85]
- 1.67 mM phosphate containing salt, in the form of either $NH_4H_2PO_4$ or K_2HPO_4 - 2.5 mM calcium containing salt in the form of either $CaCl_2$ or $Ca(NO_3)_2$	7.2 by addition of tris(hydroxyl aminomethane), (hereafter referred as Tris) and hydrochloric acid	[72]

In order to prevent adverse tissue reactions resulting from hard tissue replacements, a bioinert material, which is stable in the human body and is immune at the interaction with body fluids and tissues, is preferred. Some bioactive materials, such as hydroxyapatite, bioactive glasses and glass ceramics are increasingly used as hard tissue replacements due to their ability to induce bone regeneration and bone in growth at the tissue–implant interface without the intermediate fibrous tissue layer by creating a bone-like apatite layer on their surface after implantation. Apatite formation is currently believed to be the main demand for the bone-bonding ability of materials [46, 76].

Hydroxyapatite $Ca_{10}(PO_4)_6(OH)_2$ (HA) is one of the first materials considered for coating metallic implants due to its close similarity of chemical composition and high biocompatibility with natural bone tissue [71-72]. Calcium phosphates are present in bone, teeth and tendons to give these organs stability, hardness, and function [77]. Hydroxyapatite has been widely used for many years as a coating material on titanium and titanium alloys as implant devices in dental and orthopedic fields, and the most important reason for that was selected is its ability to accelerate bone in growth onto the surface of implant during the early stages after implantation. There are a number of additional benefits with this coating: faster adaptation of implant and surrounding tissue with reduced healing time, firmer implant bone attachment and the reduction of metallic ion release.

Several compositions of solutions indicated in Table 2, have been used as electrolytes in order to coat calcium phosphates using the electrodeposition method: acidic solution (pH≤4); basic solution (pH>9) and nearly neutral modified simulated body fluid (SBF) (pH=7.2–7.6) [78].

Today electrodeposition is much more than just a coatings technology. Recent literature on the electrodeposition of metallic and nonmetallic coatings containing nanosized particles is intensely investigated. The incorporation of nanosized particles can give an increased microhardness and corrosion resistance, modified growth to form a nanocrystalline deposit and a shift in the reduction potential of a metal ion [75].

Due to the rapid development of nanotechnology, the potential of nano-calcium phosphates has received considerable attention. Recent developments in biomineralization and biomaterials have demonstrated that nano-calcium phosphate particles play an important role in the formation of hard tissues [77]. Literature reports indicate that cumulative adsorption of proteins from body fluids is significantly higher on smaller nanometer grain size materials compared with conventional scale size [77].

In the past decades extensive research on hydroxyapatite coated implants have focused on the tissue–implant interface and also on the problems associated with the coating process and optimization of coating parameters to enhance tissue response [76]. Hydroxyapatite coating of Ti substrate by electrodeposition has been investigated by many research groups [69, 72, 86-87]. Electrochemical deposition of hydroxyapatite coating on titanium surface is an attractive process because irregular surfaces (porous, complex shape of substrate) can be coated relatively quickly at low temperatures and therefore unwanted phase changes could be avoided [72, 82]. Additionally, the thickness, chemical composition and microstructure of the deposit can be well controlled through adequate parameters of the electrodeposition process. Several recent studies have focused on the introduction of intermediate layers, as examples of controlled anodic TiO_2 film, between bioactive HA coating and metal substrate.

5.2. Anodic oxidation

Electrochemical anodizing is one of the simplest among the different techniques employed to form rough, porous and uniform films (generally oxide/hydroxide combination) across which oxygen ions can diffuse and oxidize the substrate, increasing the thickness of the film and in this way decreases ion release, modify and enhances the in vitro corrosion resistance and biocompatibility of Ti and its alloys [88]. Recently, anodic oxidation has become an attractive method for preparing oxide films on titanium, because the porous oxide films insure apatite formation in physiological environment in order to improve implant bioactivity for biomedical applications [66, 88-90]. It is generally accepted that rough and porous surfaces have a more pronounced and beneficial influence on cellular activity than smooth ones [68]. Porous implants layer have lower density than respective bulk and good mechanical strength is provided by bulk substrate [91].

Electrochemical anodic oxidation is an electrochemical process, which after application of direct-current voltages to electrodes immersed in electrolyte leads to oxidation of metal anode that forms a solid oxide layer on the surface [92]. The type, concentration and pH of electrolyte solution as well as the electrochemical parameters such as the applied current density, the voltage, the time of oxidation can affect the surface morphology, the chemical composition and the crystalline structure of the oxide films formed by anodic oxidation [93-95].

The electrolytes most commonly used to anodize Ti and its alloys are sulphuric and phosphoric acids at different degrees of dilution and Ca-P based solutions [93, 96]. An important condition which the electrolyte solution must meet is that should not chemically attack the growth of oxide, to prevent its dissolution during the anodization process, or at least it should be guarantee that the oxide growth percentage is higher than the dissolution one [93]. The rate of anodic film formation is much higher than its dissolution rate in acidic electrolytes like sulfuric acid, acetic acid, and phosphoric acid compared to alkaline electrolytes [97-98].

The electrical potential difference imposed between cathode and anode and the current density imposed to reach that value of potential difference can vary within a wide range of values. In fact, low potentials (1–130V) causes the formation of a smooth, amorphous oxide, about 3–300 nm thick, whose color changes as a function of thickness and, consequently, of applied voltage (interference color) [93, 99]. On the contrary high potentials (100–500 V), combined with high current densities, are the parameters used in anodic spark deposition (ASD) processes, which lead to a crystalline or semi-crystalline oxide that can range from few tens to hundreds micrometers thick [93, 99]. The crystal structures of the titanium oxide have revealed different oxide structures at different thickness: TiO_2 with anatase structure was observed at 90 V [91, 100], mixture of anatase and rutile structure was formed at 155V and a single rutile phase was produced at 180V, respectively [91, 100].

The properties of anodic oxide films strongly depend on their composition, structure, and thickness. As the voltage increases, the thickness of the layer also increases and particular colors will arise at specific voltage rates. The transition from one color to another is not evident defined, but rather by nuances gradually through a limited spectrum. The apparent color transmitted to the metal is induced by interference between specific wavelengths of light reflecting off the metal and oxide coated surface [101]. Light which crosses through the oxide layer, then reflecting off of the metal, must pass farther than light reflecting directly off the surface of the oxide. If one wave type is not synchronized with the other, they will annul each other out, making that color "darker" or invisible. If through the thickness of the oxide layer is obtained a wave pattern whose path is similar to the path of a certain wavelength of light and it closely follows its path, then the wave amplitude will be increased, and this color would appear brighter. When the wave patterns cancel each other, the process it is called destructive interference, and when they match, it is constructive interference. Sometimes it is possible that the thickness of the oxide layer to create a combination of effects at the same time.

The main reactions leading to oxidation at the anode are as follows [46]:

At the Ti/Ti oxide interfaces:

$Ti \leftrightarrow Ti^{2+} + 2e^-$

At the Ti oxide/electrolyte interface:

$2H_2O \leftrightarrow 2O^{2-} + 4H^+$ (oxygen ions react with Ti to form oxide),

$2H_2O \leftrightarrow O_2$ (gas) $+ 4H^+ + 4e^-$ (O_2 gas evolves or stick at electrode surface).

At both interfaces:

$Ti^{2+} + 2O^{2-} \leftrightarrow TiO_2 + 2e^-$

The titanium and oxygen ions resulted from these redox reactions are actuated through the oxide by the externally applied electric field thus achieving the oxide film. Is know that titanium oxides obtained by anodic processes have a high resistivity relative to the electrolyte solution and the metallic components of the electrical circuit and therefore the applied voltage drop will mainly occurs across the oxide film of the anode.

As long as the electric field is high enough to lead the ions through the oxide, a current will flow and the oxide will continue to grow [46].

6. Conclusions

In this review, an overview of metallic implant application especially Ti and its alloy and the need of electrochemical surface modification methods used to improve the mechanical, chemical and biological properties of these have been given. The properties of titanium and its alloys can be upgraded to some extent after their surfaces are modified by electrochemical anodic oxidation and electrodeposition of HA.

Electrodeposition of HA to the titanium substrate is of utmost importance for the implant to function properly in physiological conditions. The application and prospective use of nano-calcium phosphate in the biological repair of bone and enamel are promising work. It is suggested that nano-HA may be the ideal biomaterial due to its good biocompatibility and bone/enamel integration.

One possible solution to improve the adhesion is to form an intermediate bonding layer between the titanium substrate and the HA coating, by anodic oxidation method. As a result of this anodic treatment, the surface of the Ti substrate is much rougher and porous. In summary, researches performed until now suggested that the anodic oxidation method followed by electrodeposition of HA is an effective way to prepare bioactive titanium surfaces.

With the development of the surface engineering, more new surface modification technologies will be introduced to improve the properties of titanium and its alloys for meeting the clinical needs.

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