Biomaterial: Concepts and Basics Properties

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ABSTRACT
Biomaterials encompass extensive tissue engineering technology that allows the development of materials to restore or replace parts of the living system. Demand has grown quickly in recent decades due to the worldwide phenomenon of population aging, being that the risk of hard tissue failure is greater for the elderly. The main objective is to obtain a longer lifespan of the biomaterial implanted or that the same lasts until the end of the life without flaws or need of revision surgery, helping to enhance the quality of life of the patients. Thus, is required of the biomaterial to satisfy several properties compliant to specific application, such as adequate mechanical strength, high corrosion and biocompatibility, high wear resistance, low friction and mechanical compatibility. The present work has as purpose to describe the main properties for the choice and development of biomaterials, with greater attention for metal biomaterials in the replacement of hard tissues, especially titanium and titanium alloys.

Keywords: biomaterial, hard tissue, biocompatibility, titanium.

1. INTRODUCTION

A biomaterial can be defined as a material which is used on a form or specific structure in order to manufacture prostheses and biomedical devices intended to replace or restore impaired body function in order to save or improve the quality of life [1]. They are materials used for the manufacture of devices that can interact with biological systems to coexist for a long time of service with minimal failures [2].

Although several definitions are employed to describe them, biomaterials are natural or synthetic materials that are useful for the repair of damaged body parts, through interaction with living systems [3,4]. Biomaterials used to maintain or replace functions in the human body consist primarily of metals, ceramics, or polymers [5,6]. Historically in relation to metal biomaterials, stainless steel was first used in the surgical field, and success was achieved when aseptic surgery was established. After vitalium, alloys based on cobalt and titanium and their alloys were put into practice (Figure 1), with titanium and its alloys becoming the most popular and attractive class of metal alloys [7-9]. This is due to excellent corrosion resistance to biological environments and mechanical properties, higher strength / weight ratio, higher adhesion to bone tissue, low density and high toughness of Ti and its alloys compared to several other metal biomaterials [7-11]. However, the metallic materials may be made of stainless steel, titanium or titanium, cobalt-chromium, magnesium, tantalum or niobium alloys, for example [12].

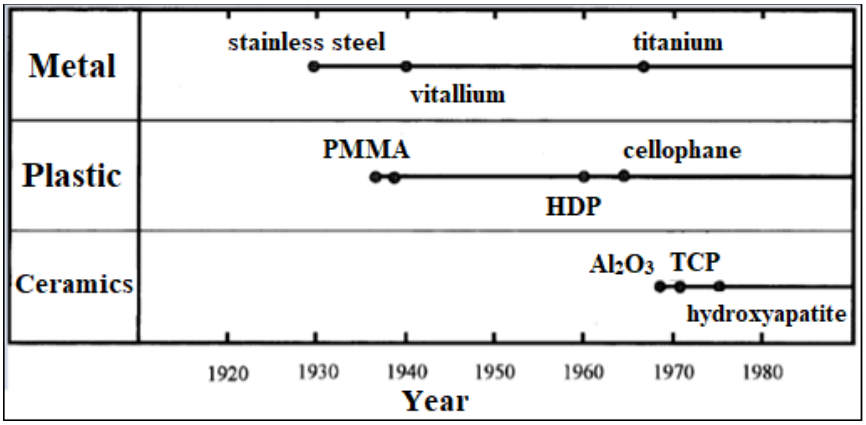


Figure 1. History of metals, plastics and ceramics for biomedical applications [8 - adapted].

These materials are used to replace a component of the human body or to support physiological functions. As such, biomaterials interact with human cells, tissues or organs and sometimes even perform their biological functions [3]. Functional repair engineering uses biomaterials to recompose different tissues with the aim of improving patients' health and quality of life [3,13]. We also find the term "nano biomaterial" that comes from the combination of biomaterial and nanotechnology[14].

The ability to exist in contact with the tissues of the human body without causing an unacceptable degree of damage to that body is the most important factor that distinguishes a biomaterial from any other material. The way in which mutually acceptable coexistence of biomaterials and tissues is developed and sustained has been of interest to biomaterial scientists and users of medical devices for many years [15].Thus, when considering a biomaterial for implantation or medical use, the first and most important requirement is non-toxic, non-immunogenic, chemically inert and acceptable to the human body [16].

Over the past fifty years, biomaterials science has investigated different types of biomaterials and their applications to replace or restore the function of compromised or degenerate tissues or organs [3]. Every year, more than 13 million prosthetics / medical devices are implanted in the US alone [3,16]. Biomaterials are used in different parts of the human body such as artificial heart valves, stents in blood vessels, replacement implants in the shoulders, knees, hips, elbows, ears and orthodontic structures. It is stated that around 70-80% of the implant materials are made of metal biomaterials, these being of great importance in the restructuring of tissues that have suffered some type of damage, especially the hard tissues [9]. A schematic illustration of a human body of hard tissues is shown in Figure 2.

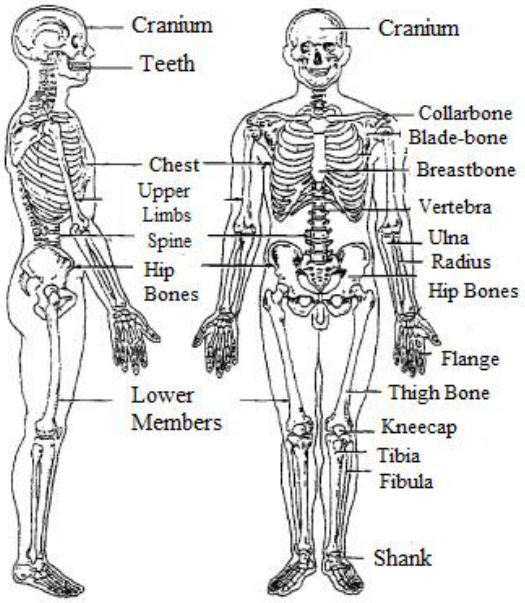
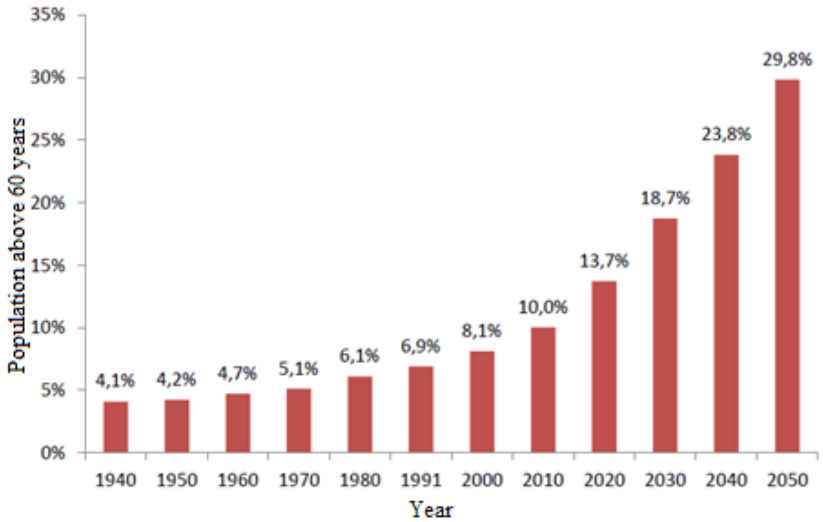


Figure 2. A schematic illustration of a human body of hard tissues [17 - adapted].

The main required property of a biomaterial is that it does not trigger an adverse reaction when put into service, which means to be a biocompatible material. In addition, good mechanical properties, osseo integration, high corrosion resistance and excellent resistance to wear, ductility and high hardness are required [5,18,19].However, the properties of an ideal biomaterial may change depending on the exact location of your implantation and even the medical history of patients. They should take into account the structure and function of the surrounding tissues and organs so that it does not disturb or interfere with their functioning.

An acceptable reason for the increase in the number of revision surgeries is due to the longer life expectancy [19,20]. In this context, the life expectancy of Brazilians, following the world trend, has also increased. IBGE data indicate that by 2050 Brazil will have approximately 30% of the population over 60 years old (Figure 3a) [21]. The proportion of elderly people in representative countries is growing rapidly, as shown in Figure 3b [8].

a)



b)

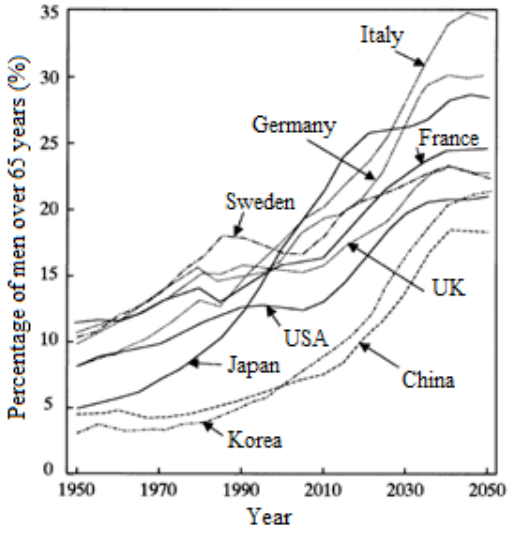


Figure 3. a) Percentage of the Brazilian population over 60 years from 1940 and a forecast up to 2050 [21]; b) change in the population of old people in each country [8 - adapted].

Consequently, the scenario has changed now, due to advances in medical technology, people live longer and moreover, the prognosis should be better for those who are physically traumatized due to sports or incorrect or exaggerated exercise habits or due to traffic road accidents and other accidents [18]. Thus, implants are expected to act much longer or to the end of life without flaws or revision surgeries, which is not inexpensive and has a lower success rate than the first implantation surgery[18]. Consequently, the development of suitable material with high longevity and excellent biocompatibility is highly essential. Although various materials are currently in use as biomaterials, titanium alloys are rapidly emerging as the first choice for most applications [9,18,19,22].

1.1 Aspects to be considered for a biomaterial selection

1.1.1. Biological compatibility or biocompatibility:

Biomaterials must be biocompatible, i.e. safe for the host organism. This means that they cannot cause harmful effects locally, in the area of implantation, nor for other tissues or organs [23]. There can be no adverse effects on the implant or host organism. Biocompatibility has traditionally been related to implantable devices that were intended to remain within a person for a long time. For those who were developing and using the first generation of implantable devices during the years between 1940 and 1980, it became increasingly obvious that the best biological performance would be achieved with materials that were the least chemically reactive [15]. Biocompatibility is defined as the ability or capacity of the material to be used in close connection with living tissue without causing adverse effects to them[24,25]. The materials used as implants are expected to be highly non-toxic and should not cause any inflammatory or allergic reactions in the human body. The rejection of an orthopedic implant due to the toxic release of metallic ions, for example, will lead to the final failure [26]. The patient body parts or tissue of who comes into contact with the implants should avoid any physical irritation, inflammation, toxicity, carcinogenic or mutagenic action [27,28].

The "fibrous capsule" surrounding the implant is also the basis of the biocompatibility of the biomaterials, and the final stage of the implantation process is represented by this capsule, which begins when the plasma proteins come into contact or are adhered to the repair [29, 80].

The biomaterials success depends mainly on the reaction of the human body to the implant and this measures the biocompatibility of a material [15]. When implants are exposed to human tissues and fluids, various reactions occur between the host and the implant material and these reactions determine the acceptability of these materials by our system. Problems related to biocompatibility are (1) thrombosis, which involves blood clotting and adhesion of blood platelets to the surface of the biomaterial, and (2) encapsulation of fibrous tissue from implanted soft tissue biomaterials [18].

However, the biocompatibility of implants also depends greatly on their corrosion behavior [5,30]. Therefore, the greater the corrosion of the implants, the more toxic ion rates are released into the body routinely and higher risk of adverse effects can be expected [5,18,31,80].

The human body consists of a significant number of natural elements with water (H_2O), comprising about 65 to 75% of the total composition in weight. Consequently, most of the mass of a human body contains oxygen and carbon [26, 32]. Table 1 shows a list of elements found in the human body. Where, about 96% of the available elements are oxygen, hydrogen, carbon and nitrogen, which are the building blocks of water and proteins. Additional ~ 4% of body mass comes in the form of bone minerals and blood composed of Ca, P, Mg and extracellular fluids comprising Na, Cl and K. As such, any implant developed on the basis of these elements would be compatible with the human body [5]. However, there are few trace elements that are toxic at high levels. Therefore, the appropriate composition required for the metal implant cannot be toxic [5]. Therefore, the implant will not release toxic metal ions, which causes inflammatory or allergic reactions in the human body [5,9,18].

Table1. Human body elements [26,32].

Element	**O**	**C**	**H**	**N**	**Ca**	**P**	**K**	**S**	**Na**	**Cl**	**Mg**	**Trace element**
Wt%	**65,0**	**18,5**	**9,5**	**3,3**	**1,5**	**1,0**	**0,4**	**0,3**	**0,2**	**0,2**	**0,1**	**<0,01**

1.1.1.1 Biocompatibility of titanium binder element

Titanium is not found in the human body, and plays no known biological role in the human body [33], and is nontoxic even in large doses [26].When humans ingested quantities of 0.8 mg of titanium daily, most of titanium was eliminated without being digested or absorbed [34].

Titanium implants are usually not rejected by the body and generally make good physical connections with the host bone. *In vitro* assays have shown that titanium can, however, inhibit osteogenic differentiation of mesenchymal stem cells [35]and may cause genetic changes in connective tissue [36].

1.1.1.2 Biocompatibility of titanium alloys

Compared with stainless steel and cobalt alloys, titanium alloys have proved to be superior in terms of biocompatibility due to their excellent corrosion resistance [26,37]. In general, 316L stainless steel shows a relatively good biocompatibility, but at a less satisfactory level than CoCrMo and titanium alloys, due to the higher corrosion rates, as outlined below [26,38].

The first generation of titanium alloys, represented by the Ti-6Al-4V alloy, has been reported to cause allergic reactions to the human body [9,39]. The second generation of titanium alloys (titanium alloys β) has been developed and investigated with great interest. Some stabilizing elements of the fase phase, such as niobium, tantalum and zirconium, are used as alloying elements and are considered relatively safe when compared to vanadium and aluminum [8,40,80,81].

The increased use of titanium and its alloys as biomaterials comes from its superior biocompatibility and excellent corrosion resistance because of the thin layer of surface oxide and good mechanical properties such as a certain modulus of elasticity and low density that make these metals present a behavior mechanic similar to the bones [9,19]. Lightweight, strong and fully biocompatible, titanium is one of the few materials that naturally combine the implantation requirements in the human body. As titanium and its alloys, commercially pure titanium (cpTi, grade 2) and Ti-6Al-4V (grade 5) are widely used as replacements for hard tissue in artificial bones, joints and dental implants [19]. In replacing hard-bone tissue, as the smallest modulus of elasticity fits in the direction of reducing the effect of voltage shielding, the low modulus of commercially pure titanium and its alloys is generally seen as a biomechanical advantage.

Viteri and Fluentes[19]also point out that another property that makes titanium and its alloys the most promising biomaterials for implants is that titanium-based materials generally have the formation of an extremely thin and adherent protective titanium oxide film. The presence of this spontaneous oxide film in the passivation or repassivation process is an important criterion for the excellent biocompatibility and corrosion resistance of titanium and its alloys.

Regarding the medical applications of these materials, the use of cp (commercially pure) titanium is more limited to dental implants due to their limited mechanical properties [19]. In cases where good mechanical characteristics are required, such as in hip or knee implants, screws and plates, the Ti-6Al-4V alloy is widely used [41,42]. One of the most common applications of titanium alloys are artificial hip joints which consist of a joint (head and femoral cup) and stem bearing, where the metal cup and hip stem components are made of titanium. In addition, they are also often used in knee joint replacements, which consist of a femoral and tibial component made of titanium and a polyethylene joint surface. Titanium and its alloys have also been used in cardiovascular devices in recent years, such as heart valves, heart pumps and vascular stents. However, titanium is a thrombogenic material [43]. A large amount of research was conducted on titanium surface-induced coagulation and several methods were applied to improve *in vitro* biocompatibility. A harder and thicker protective oxide layer was obtained with the incandescent discharge treatment and air-furnace processing performed on Ti and Ti-6Al-4V alloy, thus presenting better biocompatibility HUVECs (human umbilical vein endothelial cells) [44]. ToKumari*et al.*[45] diamond-like

carbon-coated titanium (DLC) may improve cytocompatibility*in vitro* for HUVECs. HUVEC cells were cultured and a native extracellular matrix (ECM) was obtained on the surface of pure titanium, demonstrating that this ECM produced by HUVECs not only can improve the adhesion and proliferation capacity of endothelial cells, but also inhibit the adhesion and activation of the HUVECs. platelets, which provides a basis for the preparation of modified surfaces in the application of cardiovascular implants [43].

1.1.2. Mechanical Compatibility

In addition to the biological biocompatibility discussed above, mechanical biocompatibility is vital for long-term implantation. Mechanical compatibility refers to the appropriate mechanical properties according to the function to be performed and the site to be implanted [39]. Furthermore, bio-implants must have suitable mechanical strength to withstand all the forces and related charges. Primarily, the material selected for a specific application must have the ability to withstand the load, therefore, they will not be susceptible to fracture [5].

For a specific function, purpose or application, the mechanical properties determine the type of biomaterial to be chosen. Tensile strength, hardness, osseo integration, modulus of elasticity, wear resistance to corrosion are some of the properties that are of fundamental importance. Thus, if during the application the biomaterial will be subject to repeated cyclic loads, success over the use of the implant subjected to this type of loading is determined by the fatigue strength of the material. The cyclic load is applied to orthopedic implants during body movement, resulting in alternating plastic deformation of microscopically small areas of stress concentration produced by grooves or microstructural heterogeneities [20]. Fatigue resistance of the alloys is related to the composition of the alloy and the previous history of thermomechanical processing. Fatigue resistance is also highly affected by surface processing, finishing and thermal treatments. Thus, the alloys have such a wide range of mechanical properties and can be controlled with suitable processing and thermal treatments. It is well known that the higher the fatigue strength of an alloy, the longer the life of an implant made from it[20]. Therefore, the long life of the implant, which is related to its resistance to fatigue, is a crucial property of the implant materials.

Generally, Co-Cr alloys and Ti alloys of $\alpha + \beta$ type have high fatigue strength when compared to other metallic biomaterials. The titanium alloy of type β TNTZ (Ti-29Nb-13Ta-4,6Zr) presented high resistance to fatigue with appropriate thermomechanical treatments [46].

The biomaterial that will replace the bone must have a modulus of elasticity equivalent to that of the substituted bone. The bone modulus varies in magnitude from 4 to 30 GPa depending on the type of bone and the measurement direction [47,48]. Current implant materials that have greater stiffness than bone prevent the necessary stress from being transferred to the adjacent bone, resulting in bone resorption around the implant and, consequently, to the implant loosening. This biomechanical incompatibility that leads to the death of bone cells is called the "stress shielding" [9,47,49]. Al-Tamimi*et al.*[47]describe the bone fixation implants commercially available (i.e., external fixators, internal fasteners intramedullary pin) are constructed with metallic biomaterials such as stainless steel, titanium, cobalt and their alloys (e.g., Ti6Al4V and CoCrMo), indicating that in In a large

number of cases, these implants are permanently left in the body, leading to long-term problems such as possible release of metal ions, inflammatory reactions, risk of infection, loosening of screws and, mainly, bone resorption due to the effects of the shield of tension or stress shielding.

The production of low elastic modulus biomaterials is greatly stimulated by the development of β-titanium alloys [9,40]. Thus, a material with excellent combination of high strength and low modulus closer to the bone should be used for implantation to avoid implant loosening and longer service period, avoiding revision surgery [18]. For Ti and its alloys the modulus of elasticity varies from 110 to 55 GPa compared to 316 L stainless steel (210 GPa) and chromium-cobalt alloys (240 GPa). The modulus of elasticity of various biomedical alloys is compared to the bone and shown in Figure 4.

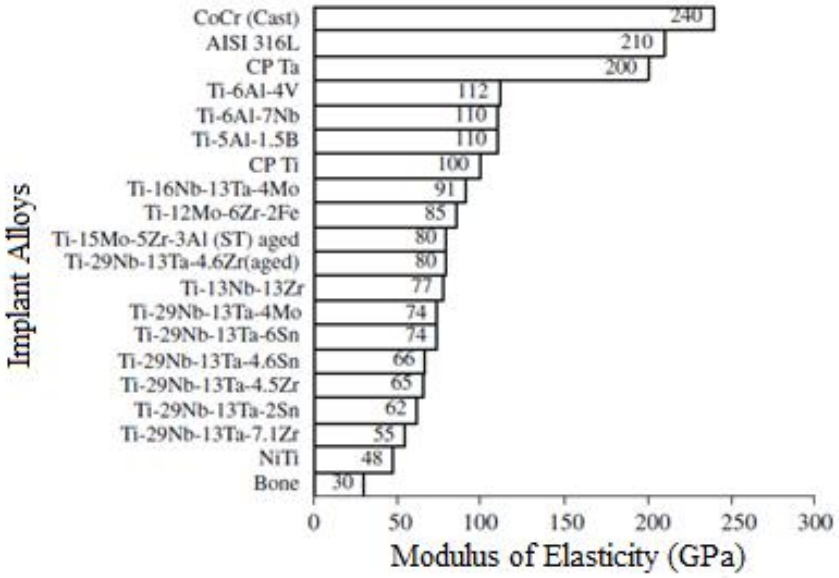


Figure 4: Modulus of elasticity of biomedical alloys [18 - adapted].

If an implant fractures due to inadequate resistance or divergence in mechanical properties between the bone and the implant, this is referred to as biomechanical incompatibility [18].

1.1.3 High corrosion resistance

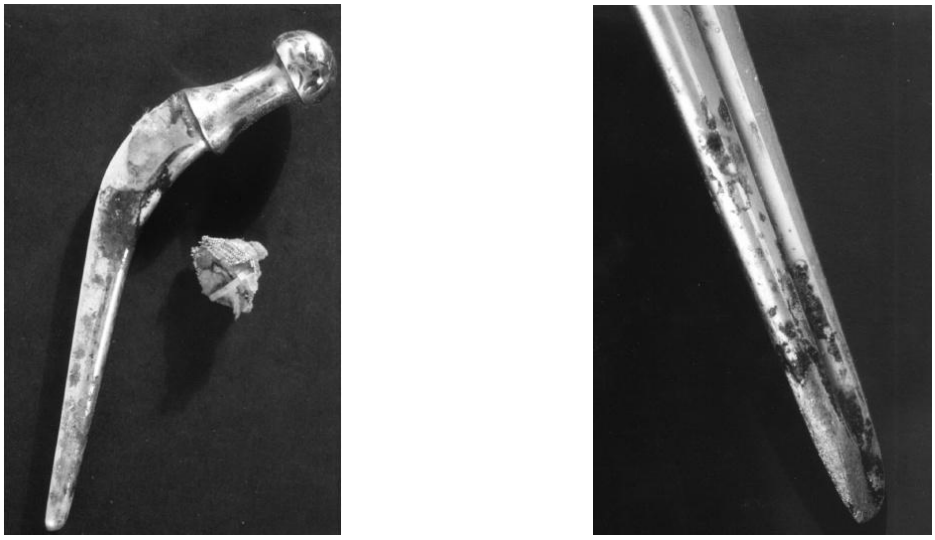
Biomaterials must be resistant to corrosion. This is a problem especially in the context of metal implants. The presence of body fluids allows metal implants to release metallic ions that may accumulate in nearby tissues or be transported to other parts of the body. Corrosion is one of the major processes that affect the life and service of orthopedic appliances made of metals and alloys used as implants in the body [2].Biomaterials are usually exposed to the critical level of humidity and in an environment with high percentage of localized corrosion [5]. The low corrosion resistance of implants in body fluid results in the release of metal ions not compatible with implants in the body[18]. It has been found that released ions cause allergic and toxic reactions[18,50]. Corroded implants in the human body cause excess of harmful and toxic metal ions such as Fe, Cr, Ni, Co, and Ti released into the body fluid [5,51].

Initially, these main trace elements in metallic implants would not be harmful by the released ions. However, when implants begin to corrode, these trace elements aggressively diffuse into the body. Excessive release of these harmful metal ions may cause adverse effects to the human body [5,80].

When the oxide layer on the metal is broken, corrosion occurs and a metal ion is released. The outer layer is then repassivated in a process known as regeneration. The regeneration time or repassivation time of the surface oxide layer is different for various applied materials [26]. The rate of corrosion and the release of some metal ions are highly dependent on the regeneration time [52].

From the observation of the regeneration time based on the formation of surface oxide layers, it was found that the regeneration time for the 316L SS alloy is longer compared to the CoCrMo and Ti-6Al-4V alloys [52].Thin layer formation through surface modification improves the biocompatibility performance with wear resistance and corrosion resistance [5].

Among the metal biomaterials, because of the properties of insufficient corrosion resistance in the living organism 316L stainless steels are not suitable for use as hip joint biomaterials for a long period [5]. Through the failure analysis it was shown that in the surface layer of both rods there was corrosion after 9-21 years of service of the implant manufactured with the specification AISI 316L [53](Figure 5). Moreover, as a result of the release of Ni in the body, 316L steel is not only susceptible to pitting corrosion but can also lead to allergic reactions in the human body [54].



(a) **(b)**

Figure 5. (a) Corrosion scale on a Charnley stainless steel rod; (b) Pitting and corrosion on a Müller stainless steel rod after removal of the implant [53].

Hatem *et al.*[55]state that one of the major disadvantages observed in the use of titanium alloy implants is premature failure due to excessive wear and corrosion. They add that these often lead to a total revision arthroplasty caused by a variety of diagnoses, with increased recurrence of infection, mechanical loosening, breaks, and dislocation. They describe that the process of tribo-corrosion, which involves sliding corrosion and fretting under body fluids, generates wear debris from the implant that leads the surrounding tissue to

inflammatory reactions, bone resorption and low osseo integration of the implant, which may result in a complete revision.

The tribo-corrosion process can expose the human body to harmful elements when they are present in the alloy composition of the implant. In the case of Ti-6Al-4V, a titanium alloy widely used in biomedical applications, the vanadium ions released from the implant can generate cytotoxic reactions and neurological disorders in the patient [56].Modifications in the surfaces of the implants to improve the tribo-corrosion behavior can be very promising to overcome the causes of mechanical loosening, especially in Ti-6Al-4V alloy implants [55]. Nevertheless, because titanium and its alloys have low tribological performance, such surface modifications are required for these alloys when the implant will be subjected to this type of stress as described in the requirement for high wear resistance.

In general, in the *in vitro* studies, the general conclusion is that the presence of metal ions in the body leads to biological responses [51]. Although the release of metal by corrosion and wear may be considered in principle to be very limited, long-term metal ions accumulation and particles in the human body is of great concern. Studies show that corrosion occurs slowly due to the electrochemical reaction, once a metal has been implanted in the human body [52,2].The presence of metallic ions in the tissues around implants has been reported to cause carcinogenicity, hypersensitivity, allergy, local tissue toxicity, inflammation and genotoxicity [51].

Notably, corrosion is not only dependent on the metal chemical properties, but is also influenced by mechanical forces. During the time of use, the friction between the implant and other tissues may increase the release of ions [23]. Remarkably, some biomaterials use an opposing approach and are designed to undergo degradation within the host organism. However, even so, it is important for the compounds that the released degradation product is biocompatible with the living organism.

Thus, the development of implants with high resistance to corrosion and wear is of prime importance for the longevity of the material in the human system [18].The prevention of biomaterials corrosion has become crucial, particularly to overcome the inflammation and allergic reactions caused by the implants of the biomaterials towards the human body [5]. Ions resulting from a corrosive process can have adverse effects on host health, which makes the materials non-biocompatible. Its release from the implant can also reduce implant life, thus requiring revision surgery.

1.1.4 High wear resistance

The low wear resistance leads to the release of wear debris from the implant into the surrounding tissue which can produce an adverse cellular response leading to the release of harmful enzymes, inflammation, osteolysis, infection, pain and bone resorption [18,57]. In general, wear occurs in the articulation of artificial joints as a result of the mixed lubrication regime.

The wear resistance of the material plays a significant role in the biomaterial proper functioning, avoiding loosening of the implant and reactions in the tissue in which it is deposited, improving the quality of life of the patient [58].

Although titanium and its alloys have excellent mechanical and physical properties, such as high corrosion resistance, high strength / weight ratio and excellent biocompatibility, they present poor tribological properties with a high coefficient of friction and wear [10,11,59,60]. This fact limits its applications in wear situations involving wear and many works have been carried out by researchers in order to solve the low tribological behavior associated with titanium alloys. The adequate surface treatment expands the use of titanium and its alloys in the biomedical areas, being one of the most effective methods to improve the wear resistance of titanium alloys[17,39].

The plasma nitriding of titanium and its alloys has been used for wear protection [61-63]. The treatment produces high hardness and a chemically inert layer that overcomes the poor wear resistance of titanium alloys [64]. Nitrogen has a high solubility in α-Ti, so that it significantly strengthens the surface layer [61]. The titanium plasma nitriding process based on the thermal diffusion mechanism can produce a composite layer formed by TiN at the top and Ti2N below, with a hardness that can reach 1500 to 3000 HV [61-63]. [61-63]. In short, several researches[62,65-68] report plasma nitriding as a very effective method that improved the tribological properties of titanium and its alloys.

Coating with thin films allows a considerable increase in wear resistance and enables a significant increase in the component life. In these techniques, coatings can be produced by physical vapor deposition (PVD), chemical vapor deposition (CVD), electrodeposition, ion implantation, among others. For example, coatings such as diamond-like carbon (DLC) and titanium nitride (TiN) are used in joint implants because of their excellent tribological properties [69]. TiN offers advantages such as high hardness and wear resistant, low price, corrosion resistant and biocompatible [69-71]; DLC has the advantages of high hardness, high resistance to corrosion and wear, biocompatibility and is a solid lubricant, chemical inertia; however, disadvantage as fragile, presents poor adhesion and high internal residual stress [55,69,72]. It has recently been shown that graphite-type carbon (GLC) and tantalum (Ta) have good potential as a coating because they have mechanical properties similar to bone - high hardness and high flexibility [69].

High wear resistance avoids loosening of the implant and reactions in the tissue in which it is deposited, improving the patient quality of life. A description of the importance of metal biomaterials wear performance was carried out in previous work by the present authors [58].

1.1.5 Osseo integration

Osseo integration refers to a phenomenon where an implant becomes so fused to the bone that it cannotbe separated without a fracture, and when an implant is osseo integrated there is no progressive relative movement between it and the bone, with which it has direct contact, meaning that osseo integration is necessary for the long-term stability of the prosthesis [73].

It is defined as the direct anchoring of an implant by the formation of bone tissue around the implant without fibrous tissue growth at the bone-implant interface [74,75].

The inability of an implant surface to integrate with adjacent bone and other tissues due to micro motions results in loosening of the implant. A fibrous tissue is formed between the bone and the implant if the implant is not well integrated with the bone. Thus, materials with

a suitable surface are highly essential for the implant to integrate well with the adjacent bone. Surface chemistry, surface roughness and surface topography play an important role in the development of good osseo integration [18].

Osseo integration is the stable and functional union between the bone and an implanted surface. This phenomenon occurs after the device insertion into the bone and bone's cells migration to the bone surface [76]. Among other factors, roughness and wettability are very important in osseo integration, and the implant needs to have adequate nano and micrometric morphological characteristics [77].The final efficacy of osseo integration depends on the topography of the surface of an implant. The implant surface properties are crucial for the adhesion and differentiation of osteoblasts during the initial phase of osseo integration, as well as for long-term bone remodeling [78].

The implant design is one of the significant parameters for the performance of osseointegration, however, so far, the ideal design for the stability of the timeless bone implant has yet to be determined [79].

The osseo integration of a bone fixation is defined as the intimate apposition of newly formed bone and reformed in congruence with the fixations, including surface irregularities, so that, with the analysis by light microscopy, there is no interposition of connective or fibrous tissue and is established a direct structural and functional connection, able to withstand normal physiological loads without excessive deformation and without initiating a rejection mechanism [54].

The presence of toxic elements in alloys can also affect osseo integration. For example, vanadium ions of the Ti-6Al-4V alloy subjected to a tribo-corrosion process are related to the problems of cytotoxic reactions and neurological disorders [56], and these toxicity reactions of vanadium ions may be detrimental to local cellular regeneration and contribute to poor osseo integration [55,80].

2. FINAL CONSIDERATIONS

Biomaterials are primarily used to replace a defective tissue in order to improve the patient's quality of life. Regarding the use of biomaterials in the long term, the following factors are paramount: biological biocompatibility and mechanical biocompatibility, resistance to corrosion and wear and osseo integration. The host's response to the implantation and presence of the biomaterial cannot have adverse effects on the implant or host organism. Therefore, biological biocompatibility is the primary point of choice, and titanium alloys are superior in terms of compatibility compared to stainless steel and cobalt alloys. The nature of passive oxide films formed on the surface and the mechanical properties of the materials form some of the essential criteria for the selection or development of new biomaterials. The high corrosion resistance avoids the degradation process and consequently a reduction of the structural integrity of the implant and the release of degradation products, which may react unfavorably with the host organism. High wear resistance avoids the generation of wear particles, which can stimulate an adverse cellular response leading to implant loosening and revision surgery. It is expected that the biomaterial used to replace the bone has mechanical properties similar to this, as an example, having a modulus of elasticity equivalent to that of bone, avoiding the effect of stress shielding and its consequences.

3. REFERENCES

[1] Tathe, A., Ghodke, M., Nikalje, A.P., "A Brief Review: Biomaterials And Their Application". International Journal Of Pharmacy And Pharmaceutical Sciences , V.2, Pp.19-23, 2010.

[2] Kamachimudali, U., Sridhar, T.M., Raj, B., "Corrosion Of Bio Implants", Sadhana, V.28, Pp.601–637, 2003.

[3] Bose, S., Ke, D., Sahasrabudhe, H., Bandyopadhyay, A., "Additive Manufacturing Of Biomaterials". Progress In Materials Science, V.93, Pp.45-111.

[4] Ebrahimi, M., "Biomaterials Application In Therapeutic And Regenerative Medicine From The Perspective Of Patients' Faith", Biomedical Journal Scientific & Technical Research, V.1, N.7, 2018.

[5] Asri, R.I., Harun, W.S., Lah, N.A., Et Al., "Corrosion And Surface Modification On Biocompatible Metals: A Review", Materials Science And Engineering: C, V.77, Pp.1261-1274, 2017.

[6] Markhoff, J., Krogull, M., Schulze, C., Et Al., "Biocompatibility And Inflammatory Potential Of Titanium Alloys Cultivated With Human Osteoblasts, Fibroblasts And Macrophages, Materials, V.10, 2017.

[7] Shi, L., Shi, L., Wang, L., Et Al., "The Improved Biological Performance Of A Novel Low Elastic Modulus Implant", Plosone, V.8, N.2, 2013.

[8] Niinomi, M., "Recent Metallic Materials For Biomedical Applications", Metallurgical And Materials Transactions A, V.33a, Pp.477- 486, 2002.

[9] Niinomi, M., Nakai, M., Hieda, J. "Development Of New Metallic Alloys For Biomedical Applications", ActaBiomaterialia, V.8, Pp.3888–3903, 2012.

[10] Zhang, C., Tang, Y., Li, Y., Et Al., "Adhesion Enhancement Of Diamond-Like Carbon Thin Films On Ti Alloys By Incorporation Of Nanodiamond Particles", Thin Solid Films, V.528, Pp.111–115, 2013.

[11] He, D., Zheng, S., Pu, J., Et Al., "Improving Tribological Properties Of Titanium Alloys By Combining Laser Surface Texturing And Diamond-Like Carbon Film", Tribology International, V.82, Pp.20–27, 2015.

[12] Niinomi, M., Liu, Y., Nakai, M., Et Al., "Biomedical Titanium Alloys With Young's Moduli Close To That Of Cortical Bone", Regenerative Biomaterials, Pp.173–185, 2016.

[13] De Sousa, W.J.B., Barbosa, R.C., Fook, M.V.L., Et Al., " Membranas De Polihidroxibutirato Com Hidroxiapatita Para Utilização Como Biomaterial", RevistaMatéria, V.22, N.4, 2016.

[14] Moryan, K., "Application OfNanobiomaterials In Endodontics", Biomedical Journal Scientific & Technical Research, V.1, N.7, 2017.

[15] Williams, D. F. "On The Mechanisms Of Biocompatibility". Biomaterials, V.29, Pp.2941–2953, 2008.

[16] Wang, X., "Overview On Biocompatibilities Of Implantable Biomaterials", Advances In Biomaterials Science And Biomedical Applications, Pp.111-155, 2013.

[17] Liu, X., Chu, P. K., Ding, C., "Surface Modification Of Titanium, Titanium Alloys, And Related Materials For Biomedical Applications", Materials Science And Engineering, V.47, Pp.49-121, 2004.

[18] Geetha, M., Singh, A. K., Asokamani, R., Et Al., "Ti Based Biomaterials, The Ultimate Choice For Orthopaedic Implants – A Review", Progress In Materials Science, V.54, Pp.397–425, 2009.

[19] Viteri, V. S., Fuentes, H., "Titanium And Titanium Alloys As Biomaterials", Tribology - Fundamentals And Advancements, Pp.155-181, 2013.

[20] Gepreel, M. A., Niinomi, M., "Biocompatibility OfTi-Alloys For Long-Term Implantation", Journal Of The Mechanical Behavior Of Biomedical Materials, V.20, Pp.407-415, 2013.

[21] 21.Silva, L.M., "Influência Da Dopagem Com OxigênioNasPropriedadesAnelásticas E Biocompatibilidade De Ligas Ti-5%Pnb E Ti-10%Pnb". In: Dissertação De MestradoEmCiência E Tecnologia De Materiais)-Bauru-Sp, Unesp, 121p, 2010.

[22] Lili, Z., Yonghai, Z., Wengang, C., "Study On The Tribological Properties Of Titanium Alloy Modified By Surface Texture Composite Dlc Film". In: 4th International Conference On Sensors, Measurement And Intelligent Materials, Pp.590-595, 2015.

[23] Patel, N.R., Gohil, P.P., "A Review On Biomaterials: Scope, Applications & Human Anatomy Significance". International Journal Of Emerging Technology And Advanced Engineering, V.2, N.4, 2012.

[24] Hedberg, Y., Qian, B., Shen, Z., Et Al., "In Vitro Biocompatibility OfCocrmo Dental Alloysfabricated By Selective Laser Melting", Dental Materials, 2014.

[25] Plummer, D.R., Berger, R.A., Paprosky, W.G., Et Al., "Diagnosis And Management Of Adverse Local Tissue Reactions Secondary To Corrosion At The Head-Neck Junction In Patients With Metal On Polyethylene Bearings". The Journal Of Arthroplasty, V.31, N.1, Pp. 264-268, 2016.

[26] Chen, Q., Thouas, G. A. "Metallic Implant Biomaterials", Materials Science And Engineering R, V.87, 2015.

[27] Freire, W.P., Fook, M.V., Barbosa, E.F., Et Al., "Biocompatibility Of Dental Restorative Materials", Materials Science Forum, V.805, Pp.19-25, 2015.

[28] Fathi, M. H., Salehi, M., Saatchi, A., Et Al., "In Vitro Corrosion Behavior OfBioceramic, Metallic, And Bioceramic–Metallic Coated Stainless Steel Dental Implants", Dental Materials, V.19, N.3, Pp.188–198, 2003.

[29] Gottfried, L., "Biocompatibility Of Injectable Microspheres", Biomedical Journal Scientific & Technical Research, V.2, N.1, 2018.

[30] Agarwal, S., Curtin, J., Duffy, B. Et Al., "Biodegradable Magnesium Alloys For Orthopaedic Applications: A Review On Corrosion, Biocompatibility And Surface Modifications", Materials Science And Engineering: C, V.68, Pp.948-963, 2016.

[31] Dorozhkin, S.V., "Calcium Orthophosphate Coatings On Magnesium And Its Biodegradable Alloys", ActaBiomaterialia, V.10, N.7, Pp.2919–2934, 2014.

[32] Underwood, E. Trace Elements In Human And Animal Nutrition, Elsevier, 2012.

[33] Pais, I., Feher, M., Farkas, Et Al., "Titanium As A New Trace Element", Communications In Soil Science And Plant Analysis, V.8, N.5, Pp 407-410, 1977.

[34] Yaghoubi, S., Schwietert, C. W., Mccue, J. P., "Biological Roles Of Titanium", Biological Trace Element Research, V.78, Pp.205–217, 2000.

[35] Wang, M.L., Tuli, R., Maner, P. A., Et Al., "Direct And Indirect Induction Of Apoptosis In Human Mesenchymal Stem Cells In Response To Titanium Particles", Journal Of Orthopaedic Research, V.21, Pp.697-707, 2003.

[36] Coen, N., Kadhim, M.A., Wright, E.G., Et Al. "Particulate Debris From A Titanium Metal Prosthesis Induces Genomic Instability In Primary Human Fibroblast Cells", British Journal Of Cancer, V.88, Pp.548-552, 2003.

[37] Lemons, J. E., Niemann, K. M., Weiss, A. B., "Biocompatibility Studies On Surgical-Grade Titanium-, Cobalt-, And Iron-Base Alloys", Journal Of Biomedical Materials Research, V.10, Pp.549-553, 1976.

[38] Davies, J. R., "Metaliic Materials. Handbook Of Materials For Medical Devices", Asm International, Materials Park, Ohio, P.21–50, 2003.

[39] Niinomi, M., "Mechanical Biocompatibilities Of Titanium Alloys For Biomedical Applications" Journal Of The Mechanical Behavior Of Biomedical Materials I, P.30-42, 2008.

[40] Taddei, E.B, Henriques, V.A.R, Silva, C.R.M., "Ensaio De Citotoxicidade E Influência Do Tratamento De Solubilização Na Microestrutura Da Liga Ti-35nb-7zr-5ta Para PotenciaisAplicaçõesOrtopédicas" RevistaMatéria, V.12, N.1, Pp.120 – 127, 2007.

[41] Stadlinger, B., Ferguson, S. J., Eckelt, U., Et Al., "Biomechanical Evaluation Of A Titanium Implant Surface Conditioned By A Hydroxide Ion Solution", British Journal Of Oral And Maxillofacial Surgery, V.50, Pp.74-79, 2012.

[42] Subramani, K., Mathew, R., "Titanium Surface Modification Techniques For Dental Implants - From Microscale To Nanoscale", Emerging Nanotechnologies In Dentistry, Pp.85-102, 2012.

[43] Xue, X., Ang, J., Zhu, Y., Et Al., "Biocompatibility Of Pure Titanium Modified By Human Endothelial Cell-Derived Extracellular Matrix", Applied Surface Science, V.256, Pp.3866–3873, 2010.

[44] Bruni, S., Martinesi, M., Stio, M., Et Al., "Effects Of Surface Treatment Of Ti–6al–4v Titanium Alloy On Biocompatibility In Cultured Human Umbilical Vein Endothelial Cell", Acta Mater, V.1, Pp.23–234, 2005.

[45] Kumari, T.V., Kumar, P.R., Muraleedharan, C.V., Et Al., "In Vitro Cytocompatibility Studies Of Diamond Like Carbon Coatings On Titanium", Bio-Med. Mater. Eng., V.12, Pp.329–338, 2002.

[46] Nakai, M., Niinomi, M., Zhao, X., Et Al., "Self-Adjustment Of Young's Modulus In Biomedical Titanium Alloys During Orthopaedic Operation", Materials Letters, V.65, Pp.688–690, 2011.

[47] Al-Tamimi, A.A., Peach, C., Fernandes, P.R., Et Al., "Topology Optimization To Reduce The Stress Shielding Effect For Orthopedic Applications", Procedia Cirp, V.65, Pp. 202-206, 2017.

[48] Murr, L.E., "Open-Cellular Metal Implant Design And Fabrication For Biomechanical Compatibility With Bone Using Electron Beam Melting", Journal Of The Mechanical Behavior Of Biomedical Materials, V. 76, Pp.164-177, 2017.

[49] Yamako, G., Chosa, E., Totoribe, K., Et Al., "Trade-Off Between Stress Shielding And Initial Stability On An Anatomical Cementless Stem Shortening: In-Vitro Biomechanical Study", Medical Engineering And Physics, V.37, P.820–825, 2015.

[50] Hallab, N. J., Anderson, S., Stafford, T. G., Et Al., "Lymphocyte Responses In Patients With Total Hip Arthroplasty", Journal Of Orthopaedic Research, V. 23, Pp. 384-391, 2005.

[51] Espallargas, N., Torres, C., Muñoz, A. L., "A Metal Ion Release Study Of Cocrmo Exposed To Corrosion And Tribocorrosion Conditions In Simulated Body Fluids", Wear, V.332–333, Pp.669-678, 2015.

[52] Hanawa, T., "In Vivo Metallic Biomaterials And Surface Modification", Materials Science And Engineering , V. A267, Pp.260–266, 1999.

[53] Walczak, J., Shahgaldi, F., Heatley, F., "In Vivo Corrosion Of 316l Stainless-Steel Hip Implants: Morphology And Elemental Compositions Of Corrosion Products", Biomaterials, V.19, Pp.229-237, 1998.

[54] Subramanian, B., Maruthamuthu, S., Rajan, S.T., "Biocompatibility Evaluation Of Sputtered Zirconium-Based Thin Film Metallic Glass-Coated Steels", International Journal Of Nanomedicine, Pp.17-29, 2015.

[55] Hatem, A., Lin, J., Wei, R., Et Al., "Tribocorrosion Behavior OfDlc-Coated Ti-6al-4v Alloy Deposited By Piid And Pems + Piid Techniques For Biomedical Applications", Surface Coatings Technology, V.332, Pp.223-232, 2017.

[56] Paszenda, Z., Walke, W., Jadacka, S., "Electrochemical Investigations Of Ti6al4v And Ti6al7nb Alloys Used On Implants In Bone Surgery", J. Achiev. Mater. Manuf. Eng., V.38, Pp.24–32, 2010.

[57] Li, S.J., Yang, R., Li, S., Et Al. "Wear Characteristics OfTi–Nb–Ta–Zr And Ti–6al–4v Alloys For Biomedical Applications", Wear, V. 257, Pp.869-876, 2004.

[58] Gobbi, S.J., Gobbi, V.J., "Wear Resistance Of Metallic Orthopedic Implants - Mini Review", Biomedical Journal Scientific & Technical Research, V.12, N.3, 2018.

[59] Falcade, T., Shmitzhaus, T. E., Reis, G. D., Et Al., "Electrodeposition Of Diamond-Like Carbon Films On Titanium Alloy Using Organic Liquids: Corrosion And Wear Resistance", Applied Surface Science, V.263, Pp. 18–24, 2012.

[60] Wang, J., Ma, J., Huang, W., Et Al., "The Investigation Of The Structures And Tribological Properties Of F-Dlc Coatings Deposited On Ti-6al-4v Alloys", Surface And Coatings Technology, V.316, Pp. 22-29, 2017.

[61] Zhecheva, A., Sha, W., Malinov, S., Et Al., "Enhancing The Microstructure And Properties Of Titanium Alloys Through Nitriding And Other Surface Engineering Methods", Surface Coatings Technology, V.200, Pp.2192– 2207, 2005.

[62] El-Hossary, S.M., Negm, N.Z., Abd El-Rahman, A.M., Et Al., "Tribo-Mechanical And Electrochemical Properties Of Plasma Nitriding Titanium", Surface & Coatings Technology, V.276, Pp.658–667, 2015.

[63] She, D., Yue, W., Fu, Z., Et Al., "Effects OfNitriding Temperature On Microstructures And Vacuum Tribological Properties Of Plasma-Nitrided Titanium", Surface & Coatings Technology, V.264, Pp.32–40, 2015.

[64] Mohseni, H., Nandwana, P., Tsoi, A., "In Situ Nitrided Titanium Alloys: Microstructural Evolution During Solidification And Wear", ActaMaterialia, V.83, Pp.61–74, 2015.

[65] Bansal, D.G., Eryilmaz, O.L., Blau, P.J. "Surface Engineering To Improve The Durability And Lubricity Of Ti–6al–4v Alloy", Wear, V.271, Pp.2006– 2015, 2011.

[66] Cassar, G., Wilson, A.B., Banfield, S., Et Al., "A Study Of The Reciprocating-Sliding Wear Performance Of Plasma Surface Treated Titanium Alloy", Wear , V.269, Pp.60-70, 2010.

[67] Yetim, A.F., Yildiz, F., Vangolu, Y., Et Al., "Several Plasma Diffusion Processes For Improving Wear Properties Of Ti6al4v Alloy", Wear, V.267, Pp.2179–2185, 2009.

[68] Nolan, D., Huang, S.W., Leskovsek, V., Et Al., "Sliding Wear Of Titanium Nitride Thin Films Deposited On Ti–6al–4v Alloy By Pvd And Plasma Nitriding Processes", Surface & Coatings Technology, V.200, Pp.5698–5705, 2006.

[69] Ching, H. A., Choudhury, D., Nine, M. J., Et Al., "Effects Of Surface Coating On Reducing Friction And Wear Of Orthopedic Implants" Science And Technology Of Advanced Materials, V. 15, 2014.

[70] Serro, A.P., Completo, C., Colaço, R., Et Al., "A Comparative Study Of Titanium Nitrides, Tin, Tinbn And Ticn, As Coatings For Biomedical Applications", Surface And Coatings Technology, V.203, Pp.3701–7, 2009.

[71] Manhabosco, T., Muller, I. L., "Electrodeposition Of Diamond-Like Carbon (Dlc) Films On Ti", Applied Surface Science, V.255, Pp.4082–4086, 2009.

[72] Fox, V., Jones, A., Renevier, N.M., Et Al., "Hard Lubricating Coatings For Cutting And Forming Tools And Mechanical Components", Surface And Coatings Technology, V.125, Pp.347-353, 2000.

[73] Rigo, E.C.S., Boschi, A.O., Yoshimoto. M., Et Al., "Evaluation In Vitro And In Vivo Of Biomimetic Hydroxyapatite Coated On Titanium Dental Implants" Materials Science And Engineering: C, V.24, Pp.647–51, 2004.

[74] Albrektsson, T., Branemark, P.I., Et Al., "Osseointegrated Titanium Implants. Requirements For Ensuring A Long-Lasting, Direct Bone-To-Implant Anchorage In Man", ActaOrthopaedicaScandinavica, V.52, Pp.155–170, 1981.

[75] Carlsson, L, Rostlund, T., Et Al. "OsseointegrationOf Titanium Implants", ActaOrthopaedicaScandinavica, V.57, N.4, Pp.285-289, 1986.

[76] Nasab, M.B., Hassan, M. R., Sahari, B.B., "Metallic Biomaterials Of Knee And Hip - A Review", Trends Biomater. Artif. Organs, V.24, N.2, Pp.69-82, 2010.

[77] Maximo, F.S., Elias, C.N., Fernandes, D.J., Et Al., "Análise Da Superfície E Osseointegração De ImplantesDentários Com SuperfíciesBiomiméticasContendo Ca, Mg E F", RevistaMatéria, V.21,N.1, Pp.196-203, 2016.

[78] Junker, R., Dimakis, A., Thoneick, M. Et Al., "Jansen Ja. Effects Of Implant Surface Coatings And Composition On Bone Integration: A Systematic Review", Clin Oral Implants Res, V.20, Pp.185-206, 2009.

[79] Coelho, P.G., Jimbo, R., Tovar, N., Et Al., "Osseointegration: Hierarchical Designing Encompassing The Macrometer, Micrometer, And Nanometer Length Scales", Dental Materials, V.31, Pp. 37-52, 2015.

[80] Gobbi, S.J., Gobbi, V.J., Rocha, Y., "Requirements For Selection/Development Of A Biomaterial," Biomed J Sci& Tech Res, 14(3), 2019.

[81] Gobbi, S.J., Gobbi, V.J., Reinke, G., Rocha, Y., OrthopedicImplants: CoatingWithTin,"Biomed J Sci& Tech Res, 16(1), 2019.