

# Titanium Corrosion: Implications For Dental Implants

## Keywords

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## Authors

Dr Rucha Shah <sup>§</sup>  
(M.D.S.)

Dr Deepika Shree Lakshmi Penmetsa <sup>\*</sup>  
(B.D.S.)

Prof. Raison Thomas <sup>†</sup>  
(M.D.S)

Prof. Dhoom Singh Mehta <sup>^</sup>  
(DS, M.D.S., FICD, FADI, FISOI.)

## Address for Correspondence

Dr Deepika Shree Lakshmi Penmetsa <sup>\*</sup>

Email: [deepika276@gmail.com](mailto:deepika276@gmail.com)

<sup>\*</sup> Post Graduate resident, Department of Periodontics, Bapuji Dental College and Hospital, Davangere-577004, Karnataka, India.

<sup>§</sup> Senior Lecturer, Department of Periodontics, Bapuji Dental College and Hospital, Davangere-577004, Karnataka, India.

<sup>†</sup> Professor, Department of Periodontics, Bapuji Dental College and Hospital, Davangere-577004, Karnataka, India.

<sup>^</sup> Professor and Head of the Department, Department of Periodontics, Bapuji Dental College and Hospital, Davangere-577004, Karnataka, India.

## ABSTRACT

*Titanium has been considered as one of the most biocompatible metals. Studies testing its corrosion resistance have proposed that the titanium oxide layer formed on the metal surface is lost under certain unavoidable conditions to which it is exposed in the oral environment. This questions its property of corrosion resistance in the oral cavity. Hence, there is a need to understand the mechanisms of corrosion, which can help in the long-term stability and function of implants. Here, we review the possible pathways of corrosion of titanium in the oral cavity, its implications and proposed methods of prevention of corrosion.*

## INTRODUCTION

In the current practice of dentistry, the treatment of both complete and partial edentulism using dental implants has become one of the fundamental treatment modalities. Historically, several materials have been tried as implants for tooth replacement such as ivory & gold.<sup>1</sup> In the search for the ideal implant biomaterial, the introduction of titanium (Ti) as a potential biomaterial was a major milestone. The pioneer studies by Branemark introduced titanium in the dental scenario as a potential implant material.<sup>2</sup> Over the next few decades, this material was increasingly used, studied and accepted as a dental implant material. Its adequate mechanical properties, inertness, high biocompatibility and corrosion resistant nature are the main characteristics which make it an excellent material for dental implant.<sup>3</sup>

In lieu of the increasing acceptance of implants, the scientific literature concerning dental implant techniques & survival is extensive and continuously increasing. Recently, in several studies concerning titanium dental implants, it was noted that titanium particles were observed in cytologic analysis of peri implant tissues.<sup>4,5</sup> Similar observations have been made for titanium implants in extra oral sites such as hip implants.<sup>6</sup> These reports mark a question on the inertness of titanium implants and prove that under various conditions, titanium may corrode and leach into the surrounding tissues.<sup>13</sup> This review was written with the aim to summarise the current evidence on corrosion of titanium surface from dental implants and its possible effects in oral cavity.

## TITANIUM AS AN INERT BIOMATERIAL

Titanium was first discovered in 1791 by the geologist Reverend William Gregor.<sup>2</sup> It is a silvery-white metal with atomic weight of 47.87, density 4.50 gm/cm<sup>3</sup>, melting point 1668°C and boiling point 3287°C.<sup>2</sup> Bothe, Beaton, and

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Davenport in 1940, were the first to observe osseointegration by implanting titanium in an animal and noticed that it had a tendency to fuse with the bone.<sup>7</sup> Later in 1951, Gottlieb Leventhal described osseointegration by placing titanium screws in rat femurs and observed that the femur fractured when an attempt was made to remove the screws.<sup>8</sup> Later in 1952, the term "Osseointegration" was given by Per-Ingvar Brånemark when he implanted titanium in rabbit tibia to study the blood flow.<sup>2</sup> He noticed that the metal was completely integrated with the bone and saw the possibilities for human use.

Titanium is the most widely used dental implant material. It is considered as the most biocompatible metal available to be used as intra-oral or extra-oral implants in human body.<sup>3</sup> Commercially pure titanium comes in four grades based on their iron and oxygen content. Currently, the most widely used titanium for biomedical purposes is Ti-6Al-4V.

Pure titanium metal, when exposed to the environment or any source of minute amounts of oxygen or nitrogen, immediately reacts to form a dense and an even oxide layer (TiO<sub>2</sub>). The process is called passivation. This oxide layer is around 5 to 10 nm in thickness. It is composed of three layers i.e. one layer in contact with the metal, an intermediary layer and one facing the oral cavity. It is the most superficial layer which aids in osseointegration and has good corrosion resistant capabilities.<sup>9</sup> It has low electrical conductivity and ideally, is insoluble at physiological pH.<sup>10</sup> At physiological pH, and normal body temperature & in the absence of interfacial motion or adverse environmental conditions, it shows minimum bio-corrosion.<sup>11</sup> The passivity can be stable (self healing after disruption) or unstable (which does not heal after being disrupted) depending on the conditions of the environment. When the passivity is unstable, the titanium surface is directly exposed to the varying conditions of the surrounding biologic fluids and tissue.<sup>12</sup>

In the confined closures of extra oral implants, the titanium implant follows the expected behaviour of an inert biomaterial. However, in the oral cavity, implants are exposed to hostile conditions such as the plaque biofilm and its by-products, variations in temperature & pH, functional micromotion, salivary variations, plasma, a variety of ions including sodium, chlorine, potassium, oxygen, bicarbonate, proteins and different kinds of edibles.<sup>13</sup> Such environment may disrupt the oxide layer irreversibly and stimulate corrosion of titanium implants. In a recent review on titanium as a biomaterial, it was concluded that the main source of titanium exposure in humans was dental and medical implants. Also, despite being considered highly biocompatible, the most likely cause of release of Ti was in the presence of biological fluids and tissue, especially in the case of dental implants.<sup>14</sup>

## TITANIUM CORROSION

Corrosion is the graded degradation of materials by electrochemical or chemical process.<sup>15</sup> The protective oxide layer of titanium is not completely inert to corrosive attack. Vijayaraghavan *et al* in 2012 have reported that, in its fully passive form, the corrosion rates of titanium are quite low and within the maximum acceptable corrosion rate for ideal biomaterial design at 0.13 mm/year.<sup>16</sup> However, titanium can become as corrosive as other base metals if the oxide layer is lost irreversibly.<sup>17</sup> The corrosion of titanium begins after its implantation when it comes in contact with the biologic tissues. Olmedo *et al.* in 2013 performed cytologic analysis of peri-implant tissues in patients with and without peri-implantitis and concluded that regardless of presence of inflammatory response, titanium is released in ion or particle form into the surrounding tissues.<sup>5</sup> Such studies on peri-implant soft tissues to detect signs of metal corrosion and tissue reactions were first done on extra-oral implants where they found metal-protein complexes and chronic inflammation in the soft tissues.<sup>18</sup>

### MECHANISMS OF CORROSION:

Titanium corrosion seems to be a multifactorial process. Many factors have been proposed that may directly or indirectly influence the same.<sup>19</sup> These are a combination of mainly mechanical and electrochemical factors. Different ways by which corrosion of titanium implant may occur in the oral cavity are as follows:

### MICROBIOLOGICALLY INFLUENCED CORROSION (MIC)/ BIO-CORROSION

This is the deterioration of a metal or metal alloy due to the metabolic reaction and products from micro-organisms in a biofilm. Biofilm formation on the surface of dental implants is unavoidable as the oral cavity is the portal of entry for microorganisms and harbours large number of microorganisms. Species that colonize dental implants include the same species that are found in healthy gingiva and in gingivitis sites.<sup>20</sup> Mombelli *et al* in 2011, assessed the characteristics of biofilm in peri-implant disease and found that they are similar to that of the biofilms in chronic periodontitis.<sup>21</sup> Subramani *et al* in 2009, reported that streptococci were predominant initial colonizing microbes.<sup>22</sup> The factors that affect biofilm formation on the surface of an implant include the composition of the biofilm, the speed of biofilm formation, the surface energy, roughness, chemical characteristics of the implant, the abutment materials, and the prosthetic components.<sup>22</sup> The bacterial products including enzymes, exo-polymers, organic and inorganic acids, volatile compounds including ammonia or hydrogen sulphide are frequently central in assisting titanium corrosion. These products when accumulate may affect the cathodic/anodic reactions at the metal interface.<sup>23</sup> One or more of these products are present in plaque biofilm.<sup>24</sup> MIC occurs in one or more of the following ways:

Role of organic compounds: Bacteria form and release various organic compounds during glycolysis pathways which reduce the pH.<sup>25</sup> These include products such as lipopolysaccharide, lactate, formate and succinate. Souza *et al.* in 2013 demonstrated that presence of bacterial colonies, such as *S. mutans*, have a negative impact on the biocompatibility and corrosion resistance of titanium.<sup>26</sup> Barao *et al.* in 2014 performed a study on the attachment of *Porphyromonas gingivalis* to corroded titanium surfaces, and concluded that corrosion of titanium significantly increased the attachment of pathogenic bacteria to the implant surface.<sup>27</sup> Gil *et al.* in 2012 evaluated the effect of bacteria on mechanical properties of titanium and found that they cause pitting type of corrosion and significantly deteriorate the properties of the implant which may reduce the life of implant.<sup>28</sup>

Yu *et al.* in 2015 found that in presence of bacterial lipopolysaccharides at a pH of 4-7, the dissolution of titanium was significant. However, in a pH of 2 the release was inhibited. The authors concluded by saying that at the commonly encountered body conditions, bacterial LPS increases titanium corrosion.<sup>29</sup> As a result to all the above factors, the oxide layer in corresponding areas on the implant is lost and the surface of the implant is thus exposed. This exposed surface comes in contact with different concentrations of oxygen in its micro-environment. The areas with less concentration of oxygen act as anode and those with more concentration act as cathode. As a result of this, the corrosion process begins with the liberation of metal particles from anode zones into the saliva.<sup>30</sup>

Role of inorganic compounds: In the plaque biofilm several inorganic components are present which may directly or indirectly affect titanium corrosion. Various oxidizing bacteria produce inorganic by-products as a result of various interactions. Some of the inorganic products that can be found as by products include  $MnCl_2$ ,  $FeCl_3$ ,  $FeO$ ,  $Fe_2O_3$  and sulphuric acid. These compounds along with the released metal ions and chloride ions in the saliva form other corrosive products which pre-dispose the implant to increased corrosion.<sup>10,31</sup> In the presence of albumin (a physiological component) along with hydrogen peroxide (an inflammatory compound), the rate of metal release from titanium alloy is much higher than both of them alone.<sup>32</sup>

Also, the passage of titanium ions to the bacteria, especially to the sulphur found in bacteria, caused by corrosion may create weak points and initiate fatigue cracks which propagate further causing fracture of implant.<sup>28</sup> As the corrosion of metal takes place, it may lead to increased attachment of bacterial pathogens to the implant surface. This forms a vicious circle where the biofilm formation leads to corrosion of titanium surface which in turn favours attachment of pathogenic bacteria to the surface.

## GALVANISM

When dissimilar alloys of prosthesis or restorations having different corrosion potentials, contact each other in the presence of an electrolyte (saliva), it results in the generation of electric current between them.<sup>33</sup> One of the metal acts as cathode and the other as anode and in the presence of the current, leaching of the anodic ions takes place. It has been seen that titanium in contact with other restorative materials such as gold alloys, Ni-Cr, Ag-Pd and Co-Cr alloys leads to galvanism and subsequently, causes break in the protective oxide layer leading to corrosion.<sup>13</sup> A study which evaluated the susceptibility of titanium coupled with different restorative materials to galvanic corrosion concluded by stating that Ni-Cr-Be alloy when coupled to titanium resulted in higher galvanic corrosion when compared to Co-Cr-Mo, Ni-Cr and Fe-based alloys. Noble restorative (Au-, Ag-, and Pd-based) alloys were least susceptible to galvanic corrosion when coupled with titanium.<sup>34</sup> It has been varyingly reported to be the most common/least likely cause of corrosion of dental implants.<sup>12</sup> Also, it has been proposed that galvanic corrosion may enhance the corrosion initiated by other mechanisms.

## MECHANICALLY ASSISTED CREVICE CORROSION/ TRIBOCORROSION

This is an umbrella term used which includes a complex interactions at the crevice initiated or assisted by mechanical micromotions. This can include but is not limited to fretting corrosion, pitting corrosion, crevice corrosion and stress corrosion. It is the combined effect of material wear and chemical corrosion. Each masticatory cycle is a small tribocorrosion cycle where wear is happening because of occlusal load in presence of a chemical i.e. saliva.<sup>35</sup> The combination of high magnitudes of applied mechanical stress plus simultaneous exposure to corrosive environment can result in failure of metallic materials by cracking.<sup>12</sup> In a study, Riberio & co-workers in 2005 assessed the tribocorrosion behaviour of grade 2 titanium in contact with artificial saliva and additives under varying motion and found that titanium showed highest weight loss in presence of citric acid.<sup>36</sup> Also, in another study by Addison & co-workers in 2012, it was found that even in absence of obvious macroscopic wear, implant corrosion may occur due to micromotion and localized corrosion in crevices.<sup>37</sup>

Fretting corrosion is caused due to the micromotion of an implant in function. The micromotion induces titanium particle release in two ways. First, the repeated motion of separate metallic components (implant and abutment) against each other may disrupt the continuity of the passivating layer on the contact surfaces and hence, the implant gets exposed. For re-passivation solution dissolved oxygen is consumed. This results in a deficiency of oxygen and excess of ions such as chlorides. These then react with the titanium to form titanium chlorides. These chlorides are highly unstable and hydrolyze to form hydrochloric acid and titanium corrosion products.

Second, this may also lead to some amount of microscopic mechanical wear from the two surfaces in contact.<sup>12</sup>

Pitting corrosion is an extremely localized form of corrosion that occurs in the presence of ions like chlorides & sulphides. Exposure to these cause localized breakdown of the passivating layer and causes dissolution of the underlying metal. This causes formation of localized pits where corrosion takes place. This is not a very commonly seen mechanism of corrosion in dental implants.<sup>38</sup> Surface irregularities in forms of pits and/or crevices on the implant may also lead to pit corrosion. It has been proposed that it may lead to some implant failures because of high concentration of forces at abutment-implant body interface.<sup>39</sup>

## ENVIRONMENTAL FACTORS

### Effects of fluorides

The acidic nature of fluoride ions may disrupt the protective TiO<sub>2</sub> layer formed on the metal surface. This may inhibit osseointegration of the metal to the bone. A study done by Probst *et al.* in 2008, on effect of fluoride prophylactic agents including gels and fluoride mouthrinse on titanium surface concluded that these agents have effects comparable to that of hydrofluoric acid in causing severe surface changes.<sup>40</sup> Siiril & Knnen in 1992, performed a study on the application of fluoride on commercially pure titanium and stated that, repeated application of topical fluorides should be avoided on titanium surfaces.<sup>41</sup> Oral hygiene practices like tooth brushing with a medium bristled brush along with fluoridated toothpastes can also alter the surface roughness of implants. A soft bristled brush would be less detrimental to the surface of titanium. However, case specific consideration is required while choosing the toothbrush for the patients with implants.<sup>42</sup>

### Corrosion due to pH variations

Change in the pH of the environment might significantly alter the corrosion resistance of titanium. Apart from the microbial by-products several other factors such as the pH of saliva, variations due to food and beverages may cause the pH of oral cavity to wide pH (2-11) changes. Hence, an ideal biomaterial to be placed in the oral cavity should have the properties to resist decomposition in oral environment. Titanium was found to dissolve in corrosive solutions of pH 2.4, 5.6 and 10.8. This dissolution may lead to reduction in fracture resistance leading to failure of implant.<sup>43</sup> In another study, it was demonstrated that titanium lost its corrosion resistance at pH less than 6.2.<sup>44</sup> According to a study titanium exhibited poorest corrosion resistance at a pH of 7.5. Scanning electron microscopy results showed that pH levels of 6.5, 7.5, and 9.0 led to substantial surface corrosion.<sup>45</sup> Such pH fluctuations may influence the corrosion resistance of titanium.

## SYSTEMIC FACTORS

Apart from the above mentioned local factors, systemic factors may also have the potential to affect titanium corrosion. The influence of hyperglycemia and acidic pH on implant corrosion was studied and the results showed that implants in dextrose containing solution were more prone to corrosion, and the acidic pH further increased the corrosion rate.<sup>46</sup> Another study which was done to determine the corrosion resistance of titanium alloy at various dilutions of dextrose and lipopolysaccharide concluded that titanium dental implants are at a higher risk of corrosion in diabetic patients.<sup>47</sup> Hence, uncontrolled diabetics may be more prone to corrosion of titanium implants.

## MISCELLANEOUS

A study done by Assuncao *et al.* in 2014 stated that hydrogen peroxide is contraindicated post-operatively after implant placement owing to the enhanced titanium corrosion demonstrated by it. Cetylpyridinium chloride and chlorhexidine digluconate can be the mouthwashes of choice in patients with dental implants.<sup>48</sup>

## CONSEQUENCES OF TITANIUM CORROSION

Several studies have attributed various clinical findings to the loss of titanium from the surface of dental implants. However, a direct cause response relationship between titanium corrosion and any clinical outcome has not been established. The following responses at macro & micro physiological level have been observed as a consequence to titanium corrosion.

Cellular consequences: Corrosion by-products released into the surrounding tissues initiate certain cellular response depending on the size, shape, composition, charge and number of particles.<sup>49</sup> Titanium has shown to have a cytotoxic effect in concentration dependent manner.<sup>35</sup> Voggenreiter *et al.* in 2007 demonstrated that macrophages phagocytize these titanium particles and get activated.<sup>50</sup>

Titanium ions released may also increase the production of cytokines which may lead to release of pro-inflammatory and pro-osteoclastogenic cytokines which may clinically lead to peri-implant mucositis or periimplantitis.<sup>37</sup> Nishimura *et al.* in 2003 examined the effect of titanium ions on the LPS (Lipopolysaccharide) stimulated murine splenocytes and found significant increase in the levels of pro-inflammatory and pro-osteoclastogenic cytokines including interleukin 1 $\beta$ , interleukin 6, interleukin 10, interferon- $\gamma$ , tumor necrosis factor- $\alpha$ , and granulocyte macrophage-colony stimulating factor.<sup>51</sup> In a study assessing the effect of Ti particles on peri-implant cells including osteoblasts, fibroblasts, and lymphocytes it was found that the corrosion products released from Ti-based alloys are most likely to mediate toxicity to peri-implant cells.<sup>52</sup> Also, in another study it was seen that, Ti particles may cause initiation of apoptosis, elevated the products of lipid peroxi-

dation and may oxidatively damage cell DNA.<sup>53</sup> Another study demonstrated that Ti- particles may be endocytosed by human mesenchymal stem cells and cause reduced rates of cell adhesion and proliferation, reduced differentiation to osteogenic lineages and increased apoptosis. This may result in impairment of the innate healing capacity of the peri-implant tissues.<sup>54</sup>

These findings were corroborated by other studies which evaluated peri-implantitis by collecting samples of peri-implant mucosa and crevicular fluid and examining cytokine levels. Duarte & co-workers in 2006 assessed the gene expression of IL-12, IL-4, IL-10 and TNF-alpha in peri-implant disease and concluded that these factors play an important role in initiation and progression of peri-implant disease.<sup>55</sup> Haynes and co-workers showed that titanium-aluminum-vanadium particles induced significantly higher release of pro-inflammatory cytokines including prostaglandin E2, TNF, IL-1 and IL-6. These pro-inflammatory cytokines in turn have the capacity to tilt the balance of the tissue towards the pro-inflammatory side which is followed by sequelae such as peri-implant tissue destruction and bone loss.<sup>56</sup>

Bone loss: RANK/RANKL is the main axis that regulates bone loss.<sup>49</sup> Titanium causes activation of kinases and transcription factors including tyrosine kinase c-src, mitogen-activated protein kinases, and the nuclear factor- $\kappa$ B (NF- $\kappa$ B) cascade.<sup>57</sup> This results in release of large quantities of proinflammatory osteoclastogenic factors such as TNF, IL-1 $\alpha$  and IL-1 $\beta$ , IL-6, RANKL and PGE2. These may eventually lead to osteoclastogenesis, subsequent osteolysis and bone loss.<sup>49</sup> In a study assessing the titanium uptake by human T-lymphocytes after bio-corrosion, it was found that Ti significantly increased expression of CD69+ and CCR4+ cells and the production of RANKL which may lead to local inhibition of osteoblast function and activation of osteoclastogenesis leading to bone loss.<sup>58</sup>

The corrosion products may also inhibit osseointegration of the implants by hampering the growth of hydroxyapatite crystals. Olmedo *et al.* in 2010 studied peri-implant soft tissue sections and concluded that the presence of macrophages in these tissues as a result of corrosion process plays a vital role in failure of implants as these particles inhibit mineralisation of bone leading to local osteolysis and loss of stability of the implant.<sup>59</sup>

Clinical manifestations: Clinically, several consequences have been attributed to titanium corrosion. The soft tissues surrounding implants may become pigmented because of discharge of metal particles (metallosis).<sup>17</sup> Pain and swelling in the region of implant in the absence of any infection may result.<sup>13</sup> Corrosion may cause leaching of metal which in turn leads to dimensional changes between prosthetic crown and abutment or between abutment and implant. These dimensional changes may influence the direction of mechanical load, thus causing failure of implant.<sup>30</sup>

Fracture of the implant is one of the possible complications affecting dental implants. The fissures and cracks developed on the implant due to leaching of metal may decrease its resistance to fatigue leading to fracture of implant.<sup>13</sup> Implant fractures is a multifactorial phenomenon. Due to a combined effect of stress and dissolution (tensocorrosion), the fatigue strength of the implant is reduced (corrosion fatigue) and the implant may become more prone to fractures.<sup>60</sup> The corrosion products can cause inflammation, bone resorption and subsequent aseptic loosening of the implant.<sup>35</sup>

Titanium allergy: According to Schramm & Pitto in 2010, titanium ions released due to corrosion may cause hypersensitivity reaction by binding to the host proteins and forming haptens or by initiating degranulation of leukocytes.<sup>61,62</sup> Different cases with various clinical findings such as glottis edema, spontaneous exfoliation of implants, eczema in response to titanium implants have been reported.<sup>63</sup>

Dissemination of titanium to other biological compartments: The corrosion products which may be released, are not localised to the tissues around implants, but may disseminate to different sites in the body.<sup>64</sup> Studies done on titanium implants in the field of orthopaedics have shown that the titanium ions released into the surrounding tissues also circulate to other regions in the body and are excreted through urine.<sup>65</sup> Traces of metals were found in different organs of the body.<sup>66</sup> An experimental study in animals demonstrated highest concentration of titanium particles in lungs and lower concentrations in kidneys and livers.<sup>67</sup> Also during the implant placement, titanium particles were deposited on the bone bed as a result of abrasion during placement; which were missing five months after the placement of implants.<sup>68</sup>

A study evaluated the genotoxic potential of the corrosion products of dental implants on osteoblasts and fibroblasts *in vitro* and concluded that they do not cause any damage to the DNA of these cells.<sup>69</sup> However, in some reports, the disseminated titanium particles have been demonstrated to be associated with neoplasia such as squamous cell carcinoma, osteosarcoma and plasmacytoma of mandible.<sup>70,71,72</sup> Titanium dioxide (TiO<sub>2</sub>) has now categorized as a possible carcinogenic agent to humans (Group 2B of carcinogens) by the International Agency for Research on Cancer (IARC).<sup>73</sup> The literature on the carcinogenic potential of titanium is limited to weak and largely uncorroborated evidence such as case reports. The evidence they provide is of association type and not causal. Considering the widespread use of dental implants, it is improbable that such sequelae, if frequent, remain unreported. The actual carcinogenic potential of dental implants remains questionable, if at all.

## PREVENTION OF CORROSION:

With the development of the concepts of titanium corrosion and dissemination, research is now being conducted to develop methods of minimizing the titanium corrosion. Surface

Figure: Diverse pathways of corrosion and its consequences in the oral cavity

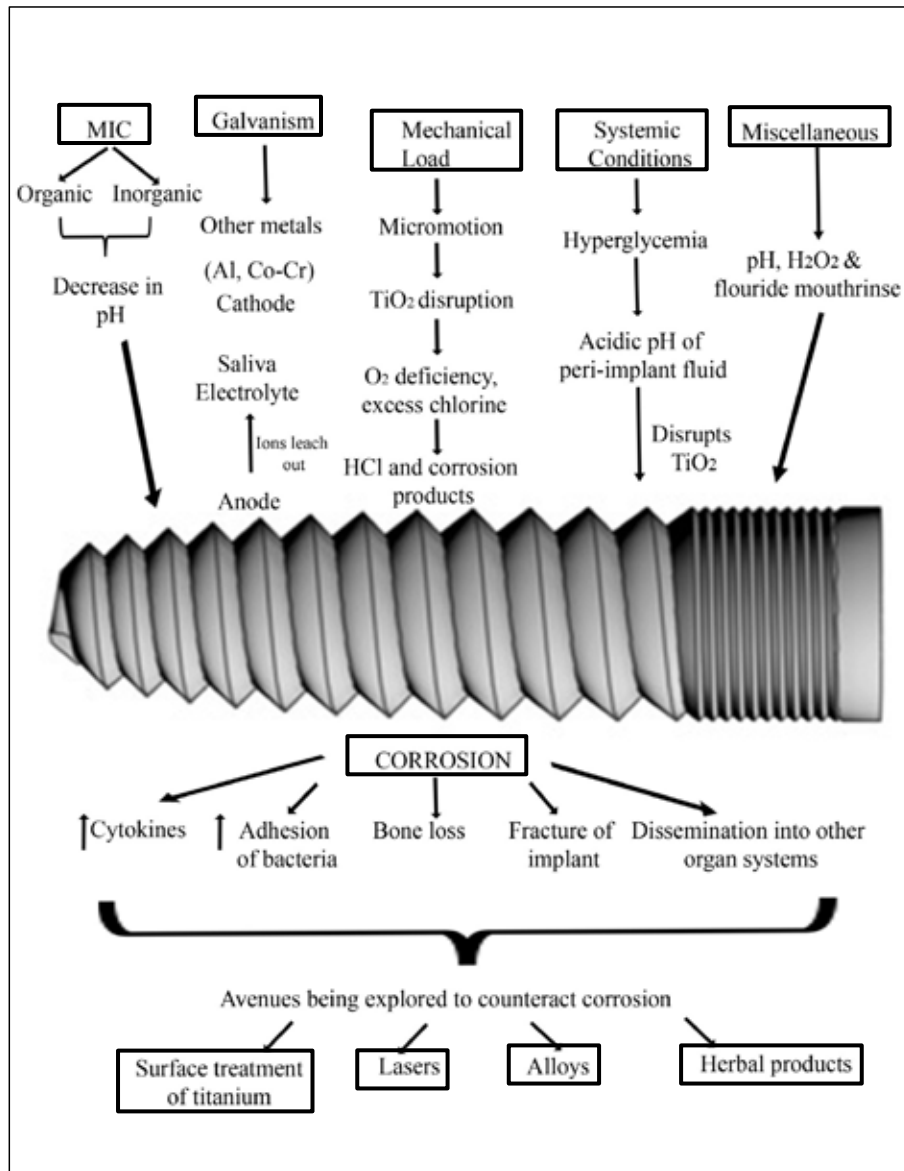


Figure 1: Current concepts in relation to titanium corrosion. MIC: Microbiologically influenced corrosion.

characteristics of implants are one of the important factors in their successful osseointegration. Surface modifications including acid etching, sandblasting, machining, electropolishing, anodic oxidation, plasma-spraying and biocompatible/biodegradable coatings have been suggested to affect the properties of osseointegration and may improve the corrosion resistance of metals.<sup>45</sup> Detailed discussion of the newer alloys and surface modifications has been done elsewhere.<sup>74</sup> One of the first modalities to be assessed to minimize titanium corrosion was glow-discharge treatment of the surface of implants. Improved corrosion resistance by formation of oxide layer which has greater passivity was observed.<sup>75</sup>

Currently, the methods of preventing titanium corrosion are broadly divided into introduction of newer alloys with chemical modifications or surface modifications to prevent corrosion or enhance resistance to corrosion. One of the methods

to reduce corrosion of titanium is the introduction of  $\beta$  phase Titanium alloys. This occurs when titanium is alloyed with  $\beta$  stabilizing elements which include copper, vanadium, nickel, molybdenum, niobium, chromium, vanadium, tantalum etc. Several such modifications have been studied and varying corrosion resistance have been found. Also, the corrosion resistance appeared to be affected by the manufacturing process. Several novel titanium alloy compositions are being assessed for decreased corrosion resistance. Among them Ti-24Nb-4Zr-7.9Sn and Ti-24Nb-4Zr-8Sn are the most recent ones.<sup>76</sup> The modification of titanium with bulk metallic glasses (BMG) is another method used to produce titanium resistant to corrosion. For biomedical applications, the most commonly assessed modifications are those of Ti-Zr-Cu-Pd. In various *in vitro* studies it has been seen that these Ti based BMG alloys have superior corrosion resistance.<sup>74,77</sup>

Also, several surface modifications have been assessed in the same context. A study assessing the effect of titanium surface coated with diamond-like carbon (DLC) showed better and stable electrochemical properties and concluded that it acts as a barrier for galvanic corrosion.<sup>78</sup> Lasers have also been successfully used in surface modification of implants which improved the hardness and corrosion resistance of the material.<sup>79</sup> Yue *et al.* in their study on the effect of excimer laser on titanium found a seven fold increase in corrosion resistance.<sup>80</sup>

Another study by Ye & Tang in 2002 assessed the coupling asynchronous acoustoelectric effects (CAAE) of the high-energy electropulsing treatment (EPT) on titanium alloys, and demonstrated that it is high-efficiency and energy-saving method to obtain superior anti-corrosion performance, micro-hardness and biocompatibility.<sup>81</sup> Bio-inspired citrate-functionalized apatite films coated on Ti-6Al-4V implants have shown to minimize corrosion of titanium.<sup>82</sup> It has also been shown that self-assembled monolayers (SAM) on titanium alloys are superior in their surface properties and also exhibit better corrosion resistance by obstruction of electron transfer.<sup>83</sup> Jindal *et al.* in 2014 proposed that the process of ultrasonic shot peening and stress relieving may result in increased proliferation of osteoblasts and enhance the resistance of titanium to corrosion.<sup>84</sup> These alloys have shown to have more corrosion resistance than titanium. However, the research in this area is still in its infancy. Recently, the effect of a natural plant extract, Myricetin, on titanium particle-induced osteolysis was assessed and was found that it inhibits periprosthetic osteolysis and osteoclastogenesis.<sup>85</sup>

The above mentioned surface treatments need to be substantiated with further research with long term follow up. More controlled studies are required to create a clinically effective solution for the issue of titanium corrosion.

## CLINICAL IMPLICATIONS

Even though the literature on the occurrence of titanium corrosion and leaching is increasing, the clinical implications are not clear. The oral cavity is an open cavity with constant communication from the environment. Several factors like routine oral hygiene procedures such as use of mouthwash, tooth brushing, fluoride application, changes in pH and systemically compromised patients like diabetics affect the corrosion of titanium.<sup>13,22,39,63</sup> A lack of knowledge and understanding of titanium corrosion related implant complications or failures might have led to a gross under-reporting of such cases. Hence, it is safe to assume that all titanium implants undergo corrosion after being placed in the oral cavity. The question that can be raised here is that whether the corrosion products participate in any potentially harmful immune response. Unfortunately, the answer is not clear. The implications of the leaching of Ti into the peri-implant tissues and other compartments of the body may be immense. A sum-

mary of current concepts in relation to titanium corrosion are demonstrated in Figure 1.

The role of titanium corrosion in implant survival or failure is not clear. The mere presence of titanium particles in peri-implant tissues is not sufficient to implicate it as a factor in peri-implant disease. It may just be an inert phenomenon with no major implications in the progression of peri-implant diseases. However, the mounting evidence indicates otherwise. Until recently, the corrosion aspects of dental implants were not given much importance and the studies done just revealed the presence of metal particles in the peri-implant tissues. Of late, the researchers have thrown light on molecular aspects of host tissue response to the metal particles released from implants. The evidence for osteoclast formation in response to titanium corrosion products points towards the possible role of titanium corrosion in inducing or exaggerating pre-existing peri-implant disease. Also, by increasing the cytokine production, it may indirectly contribute to peri-implant inflammation and bone loss.

Several surface modification techniques and alterations in titanium alloy composition have been used to improve corrosion resistance of titanium. However, most of them are in research stage. More controlled studies should be carried out to evaluate the clinical feasibility of these modifications.

## CONCLUSION

Corrosion of titanium implants when placed in the oral cavity, at-least in microscopic amount, currently, seems inevitable. To improve the understanding of the host response to the corrosion at molecular level & its clinical implications more long term studies are required. This will help to lay a foundation on which relevant biomaterial research & therapeutic interventions can be established to avoid the corrosion and its consequences.

## REFERENCES

1. Abraham CM. A brief historical perspective on dental implants, their surface coatings and treatments. *Open Dent J.*, 2014; **16**:50.55.
2. Jorge JR, Barão VA, Delben JA, Faverani LP, Queiroz TP, Assunção WG. Titanium in dentistry: historical development, state of the art and future perspectives. *J Indian Prosthodont Soc.*, 2013; **13**:71.77.
3. Guo CY, Matinlinna JP, Tang AT. Effects of surface charges on dental implants: past, present, and future. *Int J Biomater.*, 2012; **2012**:381535.
4. Lucchese A, Scivetti M, Giuliani M, Lajolo C, Serpico R, Favia G. Cellular populations of periimplant tissues: cytological analysis with sulcular microbrushing. *Implant Dent.*, 2014; **23**:98.102.
5. Olmedo DG, Nalli G, Verdú S, Paparella ML, Cabrini RL. Exfoliative cytology and titanium dental implants: a pilot study. *J Periodontol.*, 2013; **84**:78.83.
6. Lombardi AV Jr, Mallory TH, Vaughn BK, Drouillard P. Aseptic loosening in total hip arthroplasty secondary to osteolysis induced by wear debris from titanium-alloy modular femoral heads. *J Bone Joint Surg Am.*, 1989; **71**:1337.1342.

7. Rudy RJ, Levi PA, Bonacci FJ, Weisgold AS, Engler-Hamm D. Intraosseous anchorage of dental prostheses: an early 20th century contribution. *Compend Contin Educ Dent.*, 2008; **29**: 220-222, 224, 226-228
8. Leventhal GS. Titanium, a metal for surgery. *J Bone Joint Surg Am* 1951; **33**:473.474.
9. Gemelli E, Camargo N.H.A. Oxidation kinetics of commercially pure titanium. *Matéria (Rio de Janeiro)* 2007;12,525.31.
10. Kim K, Lee BA, Piao XH, Chung HJ, Kim YJ. Surface characteristics and bioactivity of an anodized titanium surface. *J Periodontal Implant Sci.*, 2013; **43**:198.205.
11. Lemons JE, Misch- Diets F. Biomaterials for dental implants. In Misch CE. (Eds): Contemporary implant dentistry. St. Louis: Mosby Elsevier, 2008: 511.542.
12. Gittens RA, Olivares-Navarrete R, Tannenbaum R, Boyan BD, Schwartz Z. Electrical implications of corrosion for osseointegration of titanium implants. *J Dent Res* 2011;**90**:1389.97.
13. Chaturvedi TP. An overview of the corrosion aspect of dental implants (titanium and its alloys). *Indian J Dent Res.*, 2009; **20**:91.98.
14. Fage SW, Muris J, Jakobsen SS, Thyssen JP. Titanium: a review on exposure, release, penetration, allergy, epidemiology, and clinical reactivity. *Contact Dermatitis* 2016;**74**:323.45.
15. Rawls H R. Physical and chemical properties of solids. In Kenneth J. Anusavice, Chiayi Shen and H. Ralph Rawls. (Eds): Phillips' Science of Dental Materials. India: WB Saunders, 2013;**30**:47.
16. Vijayaraghavan V, Sabane AV, Tejas K. Hypersensitivity to titanium: a less explored area of research. *J Indian Prosthodont Soc.*, 2012; **12**:201.207
17. Tschernitschek H, Borchers L, Geurtsen W. Nonalloyed titanium as a bioinert metal: A review. *Quintessence Int.*, 2005; **36**:523.530.
18. Zaitseva KK, Gritsanov AI. [Tissue metallosis of the implant bed as a late complication of metal osteosynthesis]. *Arkh Patol.*, 1984; **46**:37.45.
19. Agarwal A, Tyagi A, Ahuja A, Kumar N, De N, Bhutani H. Corrosion aspect of dental implants—An overview and literature review. *Open J Stomatol* 2014;**4**:56.60.
20. Leonhardt A, Olsson J, Dahlén G. Bacterial colonization on titanium, hydroxyapatite, and amalgam surfaces in vivo. *J Dent Res.*, 1995; **74**:1607.1612.
21. Mombelli A, Décaillot F. The characteristics of biofilms in peri-implant disease. *J Clin Periodontol.*, 2011; **38**:203.213.
22. Subramani K, Jung RE, Molenberg A, Hammerle CH. Biofilm on dental implants: a review of the literature. *Int J Oral Maxillofac Implants.*, 2009; **24**:616.626.
23. Beech, Iwona B, Gaylarde, Christine C. Recent advances in the study of biocorrosion: an overview. *Revista de Microbiologia* 1999;**30**:117.190.
24. Michael Newman. Carranza's Clinical Periodontology, 12th Edition. Elsevier Health Sciences; 2015.
25. Petersen RC. Titanium Implant Osseointegration Problems with Alternating Solutions Using Epoxy/Carbon-Fiber-Reinforced Composite. *Metals (Basel).*, 2014; **4**:549.569.
26. Souza JC, Ponthiaux P, Henriques M, et al. Corrosion behaviour of titanium in the presence of *Streptococcus mutans*. *J Dent.*, 2013; **41**:528.534.
27. Barão VA, Yoon CJ, Mathew MT, Yuan JC, Wu CD, Sukotjo C. Attachment of *Porphyromonas gingivalis* to corroded commercially pure titanium and titanium-aluminum-vanadium alloy. *J Periodontol.*, 2014; **85**:1275.1282.
28. Gil FJ, Rodriguez A, Espinar E, Llamas JM, Padullés E, Juárez A. Effect of oral bacteria on the mechanical behavior of titanium dental implants. *Int J Oral Maxillofac Implants.*, 2012; **27**:64.68.
29. Yu F, Addison O, Baker SJ, Davenport AJ. Lipopolysaccharide inhibits or accelerates biomedical titanium corrosion depending on environmental acidity. *Int J Oral Sci* 2015;**7**:179.86.
30. Chang JC, Oshida Y, Gregory RL, Andres CJ, Barco TM, Brown DT. Electrochemical study on microbiology-related corrosion of metallic dental materials. *Biomed Mater Eng.*, 2003; **13**:281.295.
31. Maruthamuthu S, Rajasekar A, Sathiyarayanan S, Muthukumar N, Palaniswamy N. Electrochemical behaviour of microbes on orthodontic wires. *Current Science* 2005;**89**:988.96.
32. Yu F, Addison O, Davenport AJ. A synergistic effect of albumin and H<sub>2</sub>O<sub>2</sub> accelerates corrosion of Ti6Al4V. *Acta Biomater.*, 2015;**26**:355.65.
33. Cortada M, Giner L, Costa S, Gil FJ, Rodríguez D, Planell JA. Galvanic corrosion behavior of titanium implants coupled to dental alloys. *J Mater Sci Mater Med.*, 2000; **11**:287.293.
34. Venugopalan R, Lucas LC. Evaluation of restorative and implant alloys galvanically coupled to titanium. *Dent Mater.*, 1998; **14**:165.172.
35. Mathew MT, Kerwell S, Lundberg HJ, Sukotjo C, Mercuri LG. Tribocorrosion and oral and maxillofacial surgical devices. *Br J Oral Maxillofac Surg.*, 2014; **52**:396.400.
36. Ribeiro A R L, Rocha L A, Ariza E, Gomes J R, Celis J P. Tribocorrosion behaviour of titanium grade 2 in alternative linear regime of sliding in artificial saliva solutions. in Proceedings of the European Corrosion Congress (EUROCORR '05), pp. 1–10, Lisbon, Portugal, September 2005.
37. Addison O, Davenport AJ, Newport RJ, Kalra S, Monir M, Moslemans JF, Proops D, Martin RA. Do 'passive' medical titanium surfaces deteriorate in service in the absence of wear? *J R Soc Interface.* 2012;**9**:3161-4.
38. M T, Pai P S, Pourzal R, Fischer A, Wimmer M A. Significance of Tribocorrosion in Biomedical Applications: Overview and Current Status. *Advances in Tribology*, 2009:250986.
39. Bhola R, Bhola S M, Mishra B, Olson D L. Corrosion in titanium dental implants/prostheses - A review. *Trends Biomater Artif Organs* 2011;**25**:34.46.
40. Jack E. Lemons, Francine Misch-Dietsh. Biomaterials for dental implants. In Carl E.Misch. (Eds): Contemporary Implant Dentistry. India: Mosby, 2008: 511.542.
41. Pröbster L, Lin W, Hüttemann H. Effect of fluoride prophylactic agents on titanium surfaces. *Int J Oral Maxillofac Implants.*, 1992; **7**:390.394.
42. Siirilä HS, Könönen M. The effect of oral topical fluorides on the surface of commercially pure titanium. *Int J Oral Maxillofac Implants.*, 1991; **6**:50.54.
43. Acharya BL, Nadiger R, Shetty B, Gururaj G, Kumar KN, Darshan DD. Brushing-induced surface roughness of two nickel based alloys and a titanium based alloy: a comparative study - in vitro study. *J Int Oral Health.*, 2014; **6**:36.49.
44. Bayramoğlu G, Alemdaroğlu T, Kedici S, Aksüt AA. The effect of pH on the corrosion of dental metal alloys. *J Oral Rehabil.*, 2000; **27**:563.575.

45. Nakagawa M, Matsuya S, Shiraishi T, Ohta M. Effect of fluoride concentration and pH on corrosion behavior of titanium for dental use. *J Dent Res.*, 1999; **78**:1568.1572.
46. Abey S, Mathew MT, Lee DJ, Knoernschild KL, Wimmer MA, Sukotjo C. Electrochemical behavior of titanium in artificial saliva: influence of pH. *J Oral Implantol.*, 2014; **40**:3.10.
47. Tamam E, Turkyilmaz I. Effects of pH and elevated glucose levels on the electrochemical behavior of dental implants. *J Oral Implantol.*, 2014; **40**:153.159.
48. Faverani LP, Assunção WG, de Carvalho PS, et al. Effects of dextrose and lipopolysaccharide on the corrosion behavior of a Ti-6Al-4V alloy with a smooth surface or treated with double-acid-etching. *PLoS One.*, 2014; **26**:e93377.
49. Faverani LP, Barao VA, Pires MF, et al. Corrosion kinetics and topography analysis of Ti-6Al-4V alloy subjected to different mouthwash solutions. *Mater Sci Eng C Mater Biol Appl.*, 2014; **43**:1.10.
50. Abu-Amer Y, Darweh I, Clohisy JC. Aseptic loosening of total joint replacements: mechanisms underlying osteolysis and potential therapies. *Arthritis Res Ther.*, 2007; **9**:S6.
51. Voggenreiter G, Leiting S, Brauer H, et al. Immuno-inflammatory tissue reaction to stainless-steel and titanium plates used for internal fixation of long bones. *Biomaterials.*, 2003; **24**:247.254.
52. Nishimura K, Kato T, Ito T, et al. Influence of titanium ions on cytokine levels of murine splenocytes stimulated with periodontopathic bacterial lipopolysaccharide. *Int J Oral Maxillofac Implants.*, 2014; **29**:472.477
53. Hallab NJ, Anderson S, Caicedo M, Brasher A, Mikecz K, Jacobs JJ. Effects of soluble metals on human peri-implant cells. *J Biomed Mater Res A.* 2005;**74**:124.40.
54. Møller P, Jacobsen NR, Folkmann JK, Danielsen PH, Mikkelsen L, Hemmingsen JG, Vesterdal LK, Forchhammer L, Wallin H, Loft S. Role of oxidative damage in toxicity of particulates. *Free Radic Res.* 2010;**44**:1.46.
55. Okafor CC, Haleem-Smith H, Laqueriere P, Manner PA, Tuan RS. Particulate endocytosis mediates biological responses of human mesenchymal stem cells to titanium wear debris. *J Orthop Res.* 2006;**24**:461.73.
56. Duarte PM, de Mendonça AC, Máximo MB, Santos VR, Bastos MF, Nociti Júnior FH. Differential cytokine expressions affect the severity of peri-implant disease. *Clin Oral Implants Res.*, 2009;**20**:514.20.
57. Haynes DR, Rogers SD, Hay S, Percy MJ, Howie DW. The differences in toxicity and release of bone-resorbing mediators induced by titanium and cobalt-chromium-alloy wear particles. *J Bone Joint Surg Am.* 1993;**75**:825.34.
58. Abu-Amer Y. Advances in osteoclast differentiation and function. *Curr Drug Targets Immune Endocr Metabol Disord.*, 2005; **5**:347.355.
59. Cadosch D, Sutanto M, Chan E, Mhawi A, Gautschi OP, von Katterfeld B, Simmen HP, Filgueira L. Titanium uptake, induction of RANK-L expression, and enhanced proliferation of human T-lymphocytes. *J Orthop Res.* 2010;**28**:341.347.
60. Olmedo D, Fernández MM, Guglielmotti MB, Cabrini RL. Macrophages related to dental implant failure. *Implant Dent.*, 2003;**12**:75.80.
61. Sbordone L, Traini T, Caputi S, Scarano A, Bortolaia C, Piattelli A. Scanning electron microscopy fractography analysis of fractured hollow implants. *J Oral Implantol.*, 2010; **36**:105.111.
62. Schramm M, Pitto RP. Clinical relevance of allergological tests in total hip joint replacement. In Willmann G, Zweymuller K. (Eds): *Bioceramics in Hip joint replacement.* New York, USA: Thieme, 2000: 101.106.
63. Goutam M, Giriya pura C, Mishra SK, Gupta S. Titanium allergy: a literature review. *Indian J Dermatol.*, 2014; **59**:630.
64. Sicilia A, Cuesta S, Coma G, et al. Titanium allergy in dental implant patients. *Clin Oral Impl Res.*, 2008; **19**:823.835
65. Smith DC. Biomaterials in dentistry. *J Dent Res.*, 1975; **54**:B146.152.
66. Jacobs JJ, Skipor AK, Patterson LM, et al. Metal release in patients who have had a primary total hip arthroplasty. A prospective, controlled, longitudinal study. *J Bone Joint Surg Am.*, 1998; **80**:1447.1458.
67. Smith DC, Lugowski S, McHugh A, Deporter D, Watson PA, Chipman M. Systemic metal ion levels in dental implant patients. *Int J Oral Maxillofac Implants.*, 1997; **12**:828.834.
68. Sarmiento-González A, Encinar JR, Marchante-Gayón JM, Sanz-Medel A. Titanium levels in the organs and blood of rats with a titanium implant, in the absence of wear, as determined by double-focusing ICP-MS. *Anal Bioanal Chem.*, 2009; **393**:335.343.
69. Schliephake H, Reiss G, Urban R, Neukam FW, Guckel S. Metal release from titanium fixtures during placement in the mandible: an experimental study. *Int J Oral Maxillofac Implants.*, 1993; **8**:502.511.
70. Matsumoto M, Filho HN, Ferrari R, Fernandes K, Renno AC, Ribeiro D. Genotoxicity of endosseous implants using two cellular lineages in vitro. *J Oral Implantol.*, 2014; **40**:25.29.
71. Gallego L, Junquera L, Baladrón J, Villarreal P. Oral squamous cell carcinoma associated with symphyseal dental implants: an unusual case report. *J Am Dent Assoc.*, 2008; **139**:1061.1065.
72. McGuff HS, Heim-Hall J, Holsinger FC, Jones AA, O'Dell DS, Hafemeister AC. Maxillary osteosarcoma associated with a dental implant: report of a case and review of the literature regarding implant-related sarcomas. *J Am Dent Assoc.*, 2008; **139**:1052.1059.
73. Poggio CE. Plasmacytoma of the mandible associated with a dental implant failure: a clinical report. *Clin Oral Implants Res.*, 2007; **18**:540.543.
74. Baan R, Straif K, Grosse Y, Secretan B, El Ghissassi F, Coglianò V; WHO International Agency for Research on Cancer Monograph Working Group. *Carcinogenicity of carbon black, titanium dioxide, and talc.* *Lancet Oncol.*, 2006; **7**:295.296.
75. Fornell J, Pellicer E, Van Steenberghe N., et al. Improved plasticity and corrosion behavior in Ti-Zr-Cu-Pd metallic glass with minor additions of Nb: an alloy composition intended for biomedical applications. *Materials Science and Engineering A.* 2013;**559**:159.164.
76. Vargas E, Baier RE, Meyer AE. Reduced corrosion of CP Ti and Ti-6Al-4V alloy endosseous dental implants after glow-discharge treatment: a preliminary report. *Int J Oral Maxillofac Implants.*, 1992; **7**:338.344.
77. Cheng Y, Hu J, Zhang C, Wang Z, Hao Y, Gao B. Corrosion behavior of novel Ti-24Nb-4Zr-7.9Sn alloy for dental implant applications in vitro. *J Biomed Mater Res B Appl Biomater.*, 2013; **101**:287.294.
78. C. L., Oak J. J., Ohtsu N., Asami K., Inoue A. XPS study on the surface films of a newly designed Ni-free Ti-based bulk metallic glass. *Acta Materialia.* 2007;**55**:2057.2063.
79. Ozkomur A, Erbil M, Akova T. Diamond like carbon coating as a galvanic corrosion barrier between dental implant abutments and nickel-chromium superstructures. *Int J Oral Maxillofac Implants.*, 2013; **28**:1037.1047.

80. Hsu SH, Liu BS, Lin WH, Chiang HC, Huang SC, Cheng SS. Characterization and biocompatibility of a titanium dental implant with a laser irradiated and dual-acid etched surface. *Biomed Mater Eng.*, 2007; **17**:53.68.
81. Yue TM, Yu JK, Mei Z, Man HC. Excimer laser surface treatment of Ti-6Al-4V alloy for corrosion resistance enhancement. *Mater Lett* 2002;**52**: 206.212.
82. Ye X, Tang G. Effect of coupling asynchronous acoustoelectric effects on the corrosion behavior, microhardness and biocompatibility of biomedical titanium alloy strips. *J Mater Sci Mater Med.*, 2015; **26**:5371.
83. Delgado-López JM, Iafisco M, Rodríguez-Ruiz I, Gómez-Morales J. Bio-inspired citrate-functionalized apatite thin films crystallized on Ti-6Al-4V implants pre-coated with corrosion resistant layers. *J Inorg Biochem.*, 2013; **127**:261.268.
84. Metoki N, Liu L, Beilis E, Eliaz N, Mandler D. Preparation and characterization of alkylphosphonic acid self-assembled monolayers on titanium alloy by chemisorption and electrochemical deposition. *Langmuir.*, 2014; **30**:6791.6799.
85. Jindal S, Bansal R, Singh BP, et al. Enhanced osteoblast proliferation and corrosion resistance of commercially pure titanium through surface nanostructuring by ultrasonic shot peening and stress relieving. *J Oral Implantol.*, 2014; **40**:347.355.
86. Wu C, Wang W, Tian B, et al. Myricetin prevents titanium particle-induced osteolysis in vivo and inhibits RANKL-induced osteoclastogenesis in vitro. *Biochem Pharmacol.*, 2015; **93**:59.71.