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Biomimetic Implant Coatings – A Perspective

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Abstract

Titanium-based materials have been used for dental implants due to their excellent biological compatibility, superior mechanical strength and high corrosion resistance. In an attempt to increase the success rate of implants the surface of implant is modified to enhance the properties by physical methods like acid etching , mechanical blasting, anodization , laser treatment or by addition of bioactive coatings on the implant surface.˙ As the topic is vast this article is limited only to the overview of Bio-active or bio-mimeticimplant coatings and their applications . Clinical advantages attributed to these surface coatings discussed in this article are osseo-integration, antimicrobial activity , wear and corrosion resistance .

Keywords: Surface coatings, Osseo-integration , Antimicrobial , Corrosion resistance & Wear resistance .

Introduction

Pure titanium and titanium alloys are well established standard materials in dental implants because of their favorable combination of mechanical strength, chemical stability, and biocompatibility (Brunette *et al.*, 2001) [1]. Dental implants are bio-inert and do not bond chemically to bone therefore the main objective for coating the implant surface is to promote osseointegration, with faster and stronger bone formation .

An ideal implant coating must fulfil three main requirements. First, it must be easily processable to be applied on implants of any shape and size. Second, it must be strongly adhered to the implant surface in order to survive the harsh implantation conditions and daily wear. Third, the coating should facilitate early osseointegration by encouraging bone deposition on the implant surface and stabilizing the bone implant interface [2].

Transforming an implant into a biomimetic implant requires adding a coating of growth factor or pharmacological agent of choice. This coated layer should preferably be thin enough not to alter the underlying surface topography [3]. Essential requirements of the coatings include good adherence to the implant, fixation to the bone, fine gradient and thickness control with programmed dissolution rate in body fluids, and therapeutic capabilities. The addition of such coatings may require pre-coating of the implant with an appropriate delivery vehicle for attachment and release of the active agent [4] .

Coatings for Osseointegration

Osseointegration is defined as a direct structural and functional connection between ordered, living bone and the surface of a load-carrying implant, is critical for implant stability, and is considered a prerequisite for implant loading and long-term clinical success of endosseous dental implants [5]. Titanium is a bio inert metal that would not bond or integrate with tissues. However, its instantaneous surface oxidation creates a passivation layer of titanium oxides, which have ceramic-like properties, making it very compatible with tissues.

Bioactive coatings are applied to orthopedic & dental implants to facilitate implant fixation and bone growth [6]. The bone tissue-coating event is a biochemical bonding between the coating material, which is "bioactive therefore, in strict biological term, bone attachment to surface coatings is referred to as biochemical integration or "Bio-integration" . The coating has the potential to undergo deterioration as a result of wear and corrosion as well as foreign body reaction. Coating detachment and deterioration lead to implant failure.

The most prevalent bioactive materials that help in osseo-integration are calcium phosphates (CP), such as hydroxyapatite (HA) or tricalcium phosphate (TCP), and bioactive glasses. When implanted, these bioactive ceramics form a carbonated apatite (HCA) layer on their surfaces through dissolution and precipitation. Animal studies have shown that, compared with uncoated implants, implants with a thin layer of CP have markedly enhanced interfacial attachment of bone tissue over a period of several months [7]. Also, numerous histological studies provide evidence that coated implants yield a more reliable interface with bone than mechanical osseointegration of Ti [8] .

a .Calcium phosphate (Ca-P) coatings : Calcium phosphate (CaP) coatings on the surfaces of titanium implants increase the surface area and gives implant a porous surface that the bone can penetrate more readily achieving faster osseointegration and long-term integrity. Benefits arise during healing and subsequent bone-remodeling processes , including faster healing time , enhanced bone formation , firmer implant-bone attachment [9] and reduced metallic ion release [10] .

b.Hydroxyapatite coatings (HA) coatings : Hydroxyapatite (HA) coatings are frequently applied to orthopedic implants to stimulate osseointegration and accelerate bone formation. Some biological advantages of hydroxyapatite coating are enhancement of bone formation, accelerated bonding between the implant surfaces and surrounding tissue and reduction of potentially harmful metallic ion release [11].

c. Bisphosphate : loaded implant surfaces have been reported to improve implant osseointegration. Bisphosphates are antiresorptive agents that have beneficial effects for the patients on preventing further bone loss, and their effects on increasing the bone mass is modest [12]. It has been shown that bisphosphonate incorporated on to titanium implants increased bone density locally in the peri-implant region [13] .

d. Fluoride : Addition of fluoride to implant surface improves the biocompatibility of titanium and promote osteogenesis. This process is based on the formation of fluorapatite from interaction of fluoride and HA present in bone tissue, followed by promotion of osteoblast proliferation and stimulation of alkaline phosphatise activity. Currently, the implants treated with fluoride as a biomimetic agent are commercially available for clinical use [14].

e. Other bioactive surface coatings: Several growth factor coatings like Transforming growth factor (TGF), Platelet derived growth factor (PDGF) , Insulin-like growth factor (IGF) and Bone morphogenetic proteins (BMPs), act as bone stimulating agents [15]. Also, incorporation of bone anti resorptive drugs such as bisphonates , statins like simvastatin [16], antibacterial coatings including gentamycin or tetracycline have demonstrated impressive potential for improving the nature of osseointegration.[23]

Antibiotic Coatings

Bacterial colonization and subsequent biofilm formation are primary causes of implant-associated infections. Once a biofilm is formed, it is difficult to remove, as it protects the bacterial colonies from host defence systems and from bactericidal agents [17]. Antibiotics have difficulty to penetrate the bio film and reach the bacteria [18] . In addition to this, altered metabolism of the bacteria in the bio film diminishes the efficacy of many antibiotics. Hence, local application of antibiotics on the implant surface may be more efficient because the bacteria are killed locally directly upon binding, before the biofilm can be formed.

A variety of antibiotics were co-precipitated on titanium surfaces, resulting in drug-releasing surface coatings. It was found that the antibiotics that have the best calcium chelating properties showed the most optimal release kinetics and thus the best and longest lasting antimicrobial properties. The antibiotics that did not bind well to calcium, were washed rapidly out of the coating and the antimicrobial activity on the surface was quickly lost [19]. The principal function of these adhesion-resistant coatings is to prevent adhesion of bacteria around the implant .The simplest example of this technology is the application of antibiotic coatings by spraying the metal implant with a methanol solution containing antibiotics, which is then allowed to air dry, leaving a coat of pure antibiotic powder on the device surface.[20]

Gentamicin along with the layer of HA can be coated onto the implant surface which may act as a local prophylactic agent along with the systemic antibiotics in dental implant surgery [21].

Tetracycline-HCl coating functions as an antimicrobial agent capable of killing micro-organisms present on the contaminated implant surface. It also effectively removes the smear layer as well as endotoxins from the implant surface. Further, it inhibits collagenase activity, increases cell proliferation as well as attachment and bone healing [22].Tetracycline also enhances blood\clot attachment and retention on the implant surface during the initial phaseof the healing process and thus promotes osseointegration [23]

Doxycycline-coated implant surface has been shown to enhance bone formation both in vitro and in vivo. Biofilm formation on the Doxy-coated surface was significantly inhibited . This is important because steady-state biofilm is difficult to eradicate after formation as it is more resistant to antibiotics than planktonic bacteria [24] and requires up to 250 times greater concentration of an antibiotic agent to inhibit the growth compared to the same strains grown planktonically[25]. As a tetracycline analogue, Doxy inhibits ribosomal protein synthesis after being translocated into the cytoplasm of bacteria [26]. Studies indicate that cephalothin, carbenicillin, amoxicillin, tobramycin and vancomycin have been used in coatings on bone implants [27].

Silver : The application of silver nanoparticles on the surface of implants has been used to prevent bacterial adhesion and subsequent biofilm formation. The silver is slowly released from the surface, thereby killing the bacteria present near the surface. In contrast to antibiotics, silver (Ag) is a non-specific bactericide that acts against a broad spectrum of bacterial and fungal species. Ag is attractive on account of the good stability in the physiological environment and the difficulty to develop resistant strains [28]. The antibacterial action of Ag may be explained that silver nano particles get attached to the bacteria resulting in bacterial wall pitting , deactivating cellular enzymes, disrupting membrane permeability, and finally leading to bacteria lysis and death [29.] In vitro studies have demonstrated that silver coatings possess excellent biocompatibility without genotoxicity or cytotoxicity[30] and in vivo studies have indicated that silver coatings have no local or systemic side-effects.[31]

Chitosan : Similarly, chitosan, a biopolymer derived from the shells of crustaceans or fungi, is a biodegradable, biocompatible material that has bacteriostatic and osteo conductive properties; some success has been reported when used as a coating on metal implants [32].

B. Groessner-Schreiber et al. [33] showed that TiN and ZrN coatings possessed antibacterial performance to the oral microflora and Streptococcus. **Chen et al.** [34] had cosputtered Ag and hydroxyapatite (HA) to make an antibacterial-bioactive coating, which inhibited bacterial attachment without cytotoxic effects. Traditional metal implants coated with a thin layer of antibiotic-loaded biocompatible, biodegradable polymer, such as polylactic-co-glycolic acid [35], poly (D,L-lactide) [36], successfully decreased the amount of bacteria.

Lee et al employed a double layer of polylactic-co-glycolic acid encapsulation on antibiotic Cefuroxime-coated titanium disks that extended antibiotic releasing time without burst release for up to 10 days [37]. This coating technique was found to be effective against infection and was associated with less bone damage.**Nelson et al** used erythromycin impregnated strontium-doped calcium polyphosphate (SCPP) to completely inhibit bacterial growth for up to 14 days [38].

Non antibiotic Antimicrobial Coatings

Regarding the risk of antibiotic resistance non antibiotic organic antimicrobial agents such as chlorhexidine, chloroxylenol, and poly(hexamethylenebiguanide)[39] may be good alternatives. They are widely used in daily life for their broad spectrum of antimicrobial action and lower risk of drug resistance, especially chlorhexidine [40]. Studies have shown that chlorhexidine can adsorb to the TiO_2 layer on the titanium surface and desorb gradually over a period of several days [41].

Coatings for wear resistance

Dental implants made of pure commercial titanium are prone to wear and abrasion . Corrosion is accelerated in the presence of wear and also simultaneous corrosion and wear are often encountered in biomedical implants .Among the surface modifications aiming at improving abrasion resistance, titanium nitride (TiN) coatings were successfully proposed [42] . One approach is to compensate the wear resistance by applying a hard ceramic coating onto the titanium parts. This novel biocompatible hard-coating could enhance the wear resistivity of titanium implants that are free from Co, Cr and Ni [43] .

Generally, nitride coatings, by a factor of approximately 10, increase the surface hardness , wear resistance , and corrosion resistance of implant materials [44]. After 1 year of clinical use, TiN coated attachment systems appeared unchanged while extensive wear was evident in uncoated systems [45]. The adherence of Streptococcus mutans and Streptococcus sanguis was significantly reduced on TiN surfaces compared to polished ones [46].Though Ti-6Al-4V alloy has a lower wear resistance it has higher elastic modulus than bone which leads to ‘‘stress shielding effect’’ [47].

Coatings for Corrosion resistance

According to material science the excellent corrosion resistance of titanium and its alloys used for implants is due the formation of a thermodynamically stable, continuous, highly adherent, and protective surface oxide film formed spontaneously and instantly when fresh metal surface is exposed to air and/or moisture about 100´ thick within a minute. Indeed, oxidative processes can thicken and condense the TiO_2 layer on the surface, improving the corrosion stability of the underlying Ti . Although the oxide coating is thermodynamically stable, any form of chemical, electrochemical and mechanical trauma can lead to release of alloying elements through passive dissolution process.

Corrosion of metallic implants may jeopardize the mechanical stability of the implant and the integrity of the surrounding tissue . The implants face severe corrosion environment which includes blood and other constituents of the body fluid which encompass several constituents like water, sodium, chlorine, proteins, plasma, amino acids along with mucin in the case of saliva . Implant failure in the form of aseptic loosening, or osteolysis, may result from metal release in the form of wear debris or electrochemical products generated during corrosion events. Increasing evidence is found that titanium and various substitutional alloying elements leach into the crevicular space around the implant [48] . The leached ions may induce potentially osteolytic cytokines into tissues leading to implant loosening and may even cause severe allergic reactions or hypersensitivity [49.] In the case of Ti-6Al-4V alloy, vanadium oxide in the passive film dissolves and results in the generation and diffusion of vacancies in the oxide layer [50]. Although it has got several positive n features, detailed studies have shown that they lead to long term ill effects such as peripheral neuropathy, osteomalacia and Alzheimer disease due to the release of aluminum and vanadium ions from the alloy [51] .

In recent years, researchers' attentions have focused on the use of Niobium (Nb) and Tantalum (Ta) as implant materials because of their outstanding biocompatibility, superior corrosion resistance and excellent fatigue resistance . It has been mentioned that deposition of Nb on a titanium surface is one possible way of improving corrosion resistance in special environments [52] . However, the addition of alloying element such as Nb enhances the passivation by the formation of Nb rich pentoxide which is highly stable in the body environment leading to high corrosion resistance [53]. Tantalum is gaining considerable attention for designing a novel type of dental implant, due to its biocompatibility, corrosion resistance and elastic modulus (1.3–10 GPa) close to that of cortical bone (12–18 GPa). Tantalum promotes bone ingrowth by establishing osseoincorporation that will enhance the secondary stability of implants in bone tissue and is more osteoconductive than titanium or cobalt-chromium alloys [54] . A comparative study on the corrosion behavior between Ti-Ta and Ti-6Al-4V alloys showed that the addition of Ta greatly reduces the concentration of metal release from the surface oxide layer because of the formation of highly stable Ta2O5 oxides [55]. In addition, Ta alloys are known to have excellent biocompatibility which makes TaN an excellent protective coatings in biomedical applications [56].Other oxides, such as SiO_2 also been tested as alternatives to TiO2 to improve the properties of dental implants, reduce the bacterial adhesion , improve the biocompatibility [57] or protect from the corrosion exerted by the body fluids [58] .

Ferguson et al [59] first documented the elevated titanium levels locally around the implant periphery. **Cortada et al**[60] used the ICP-AES (inductively coupled plasma-atomic emission spectroscopy) technique to confirm the release of metallic ions during titanium implant galvanism.

Richard et al. observed that corrosion resistance and fretting wear of Cp Ti increased several fold when coated with nano Al2O3-TiO2 [61].

Fluoride ions are one of the few media that have the ability to provide a corrosive effect to a titanium surface. When titanium is exposed to fluoride, its oxide layer is damaged, and titanium is then e asily degraded. This is due to the incorporation of fluoride ions in the oxide layer, considerably decreasing its protective properties [62].

Medicaments with fluoride content like pastes, gels and mouthwashes to be used with caution.

Conclusion

By altering the implant surface or adding a coating to improve the osseo - integration of the implant could improve stability in the short-term and ultimately reduce failures and revision surgeries in the long-term The surface - charge modification of titanium implant seems to be a promising new direction for improving the osseo-integration . Selecting the appropriate surface texture , developing efficient carrier vehicles for antibiotics and smart coatings which can deliver bactericidal agents only when bacteria invasion occurs may be a good research direction. [63] To avoid ion release, it is necessary to develop new titanium alloy processing or increase the mechanical properties of cp Ti by coating with nano-crystalline materials, which can offer very high strength, toughness, and fatigue resistance [64]. Implant geometry, chemistry ,bioactivity and the interactions between these factors is the key to future improvements in implant design and to ensuring progress in this exciting and rewarding field of dentistry.

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