IMPACT OF TITANIUM AND IT'S ALLOYS IN THE FIELD OF BIOMATERIAL: A REVIEW

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Abstract: Some of the selective materials which are present in earth or synthetically produced, by its alluring properties show excellent compatibility with bone, tissues, body fluids etc. Hence it provides us different types of bio-material that comes out as benediction for human being. In this review paper an attempt has been made to cover up an eminent biomaterial titanium. This review gives a brief knowledge about its benefits and drawbacks with further improvements and some idea about how one can improvise biomaterial against bacterial effect.

I. INTRODUCTION

Definition of biomaterial

A biomaterial is defined as a synthetic material used to make devices to replace part of a living system or to function in intimate contact with living tissue without any adverse effect on the biological system [1]. For e.g., medical implants, contact lenses, drug delivery systems, scaffolding for tissue regeneration, etc. all fall under the broad category of biomaterials.

Criterion of Biomaterial

The performance of biomaterial depends upon their chemical, physical and biological properties [2], their shape and material tissue attraction. Important consideration is the effect that the material has on the living tissue along with the effect of the living tissue on the material. The most important criterion for a material to be considered as a biomaterial is- it must be biocompatible, non-toxic, non-carcinogenic, non-allergic, non-inflammatory and bio functional over substantial period of time. The degraded products must also be non-toxic, should either have ease of renal removal or be absorbed by the body.

Types of Biomaterial

Biomedical materials play an important and critical role in manufacturing a variety of prosthetic devices in a modern world [3]. Depending on their use biomaterials are mainly categorized into four types of biomaterials. They are polymer, ceramic, composite and metal.

Polymers

Many polymers came into picture as potential biomaterial due to its less stiffness, high fatigue strength and radiolucency [4] such as polyether ether ketone (PEEK) [5], [4], [6], [7], [8], [9], [10], [11], [12] poly (L-lactide) (PLLA) [13-19] etc. Poly (1,8-octanediol-co-citrate) (POC), biodegradable elastomer is also used as biomaterial [20,21]. In early days epoxy resins compression plates were used which had a harmful influence on human body and it was soon replaced by PEEK [22].Orthopedic, cranio-facial, and oral-maxillofacial surgeons often use tissue fixation devices such as pins, plates, and screws that are made from poly (L-lactide) (PLLA), a biodegradable polymer [13-19]. Polydimethylsiloxane (PDMS) based elastomer have been used in blood pumps, cardiac pacemaker leads, artificial skin, contact lenses, finger joints, maxillofacial reconstruction and drug delivery systems from past three decades due to its inertness, low toxicity, good blood compatibility and low modulus etc. [23]. Poly methyl methacrylate (PMMA) and poly 2-hydroxy-ethyl methacrylate (PHEMA) are mainly used as hard (a term usually denoting glassy polymeric films) and soft (term usually denoting rubbery amorphous or semi-crystalline polymeric membranes) contact lenses respectively [24]. Apart from polymers polyethylene, polypropylene and polytetrafluoroethylene are also used as biomaterials. Polymer has a drawback of low mechanical strength. Main applications of polymer are in arteries, veins, ears, nose, heart valves, lenses breast implants and sutures [25,1].

Ceramics

Hydroxyapatite [$Ca_{10}(PO_4)_6(OH)_2$] is a ceramic material which is brittle but having very high bonding ability with bone, good wear resistance, high biocompatibility [26]. Although HA has spontaneous osteointegration property, it cannot be used as bone substitutes under highly loaded condition because of their low fracture toughness which is not as high as human cortical bone [27]. Hence HA is not used as an individual implant but applied as coating material on metallic biomaterials (SS, Co-Cr-Mo, Ti metal and its alloys) done by plasma spray method [28], so that it can form bond with the bone tissue. It also forms composite with polymer materials such as PEEK-HA suitable for load bearing functions [12], POC-HA composite [20] which is widely used as bone screws and in orthopedic implants. Researchers have enlightened that under certain conditions, addition of HA particles can increase the mechanical properties of the PLLA component when applied in a composite blend [29-31]. Alumina is another ceramic biomaterial which is used in hip joint socket components and dental root implants. Tricalcium phosphate, zinc calcium phosphate and aluminum calcium phosphate are used to substitute or augment bony structures and deliver drugs. During 1990s stabilized zirconia was used as ceramic femoral heads due to its high fracture toughness but hydrothermal effect in-vivo condition leads to transform it to monoclinic phase which has low hardness and low resistance to crack formation. In 2001 high fracture rates of femoral heads based on zirconia limited is use as biomaterial. Zirconia Toughened Alumina (ZTA) are reported to have superior mechanical properties than alumina but still not in use extensively due to low temperature degradation which has undesirable effect on hip bearing performance. In vivo, if monoclinic phase is formed at bearing surface of zirconia, it increases the surface roughness and further increase wear rate and may leads to fracture. ZTA is more fracture resistant than monolithic Alumina or stabilized Zirconia, exhibiting properties superior to both, in terms of strength, toughness, wear resistance and low temperature degradation. Studies has shown ATZ to be a viable substrate for the growth of osteoblasts in rats [32,33]. Bioglass and ceravital can form chemical bonds with hard and soft tissues. Silicon alloyed pyrolytic carbon deposited onto a substrate at low temperature with isotropic crystal morphology which has high compatibility with blood and used for cardiovascular implant fabrication [1]. Apart from brittleness ceramic biomaterials are difficult to reproduce and has difficulties in processing and fabrication [25].

Composites

Composite can also be used potentially in the field of bio material as they have different physical and chemical properties which allows us to incorporate tailor-made properties. Composite is a material which is made of two or more constituents and when they are combined it gives a characteristic property different from individual components. It can also introduce anisotropic properties that is different properties in different directions with the use of laminates. One of the most important examples is the use of carbon fibers in polyether ether ketone and polyether sulphone (PES) which are used for construction of hip stems [34]. Carbon fiber polyether ether ketone (CF-PEEK) is currently used as load bearing orthopedic implant [35-43] due to its bone like stiffness, modulus of elasticity, good chemical properties, fatigue resistance, high temperature durability, good wear properties and easy fabricability [12]. Moreover, it is nontoxic, radiolucent (helps in radiographic assessment) MRI (magnetic resonance imaging) compatibility [42,44]. Other attracting uses of composite are as a combination of hydroxyapatite with different polymers like polyethylene, polymethylmethacrylate (PMMA), polyethylmethacrylate (PEMA), polysulphone, poly L-lactide (PLLA). Development of PEEK-HA composite having upto 40 vol% hydroxyapatite is a promising composite which can be applied for high load-bearing application in medical implant, devices and structure scaffolds [12]. One major problem of composite is difficulty in fabrication.

Metals

Metals having good combination of high mechanical strength and fracture toughness are suitable for load bearing applications compared with polymeric or ceramic materials [45,46]. Conventionally, metallic materials are essential for orthopedic implants, bone fixators, artificial joints, external fixators etc. since they can substitute the function of hard tissues in orthopedic. Tenable use of metals in biomedical field is caused because of their toughness, elasticity, inertness, biocompatibility. Traditionally Co-Cr alloy and Ti to which V and Al are added, are used for stem implant. These metals have a major drawback due to its elastic moduli which is 10-20 times greater than that of bone [47].

Specially, stainless steels and Co based alloys, Mg based alloys, pure titanium and titanium alloys are widely used as orthopedic implant materials in clinical practice.

Stainless steel is widely used as orthopedic implant due to its low cost but one of the associated disadvantages is due to intergranular corrosion caused by precipitation of Cr-carbides at the grain boundaries [3], called sensitization. 316 type stainless steel was used in early days but in 1950s the carbon content in 316 type stainless steel was reduced to 0.8% to 0.3% to minimize sensitization and it is known as 316L stainless steel. It has better corrosion resistance and Ni (12-14%) and Cr (17-20%) are added to stabilize the austenitic phase at room temperature and enhances corrosion resistance. 316L stainless steels may also corrode inside the body under certain circumstances in a highly stressed and oxygen depleted region. Thus, these stainless steels are suitable for use only in temporary implant devices like fracture plates,screws, and hip nails [1].

CoCr is another highly used metallic biomaterial and divided in two types. They are castable CoCrMo alloy and CoNiCrMo alloy which is wrought by forging. They are used in dentistry, making of artificial joints and for making stem of prostheses [1]. Up to 65% Co is used to form solid solution and addition of Mo is to produce finer grains which increases strength [48]. Wear, corrosion and fretting can deteriorate the organ and local tissues due to release of metallic products as Co is toxic to human osteoblast [1]. Toxicity of Co and Cr can be minimized by surface treatment. Plasma nitriding of CoCrMo alloys can improve mechanical properties [48].

Mg based materials are very much compatible to human bone due to its mechanical and physical properties and it has density and elastic modulus fairly close to each other. Moreover, Mg is an ingredient present in the natural composition of bone and is an important element required in metabolism of the body. But it has a problem of low corrosion resistance [49].

Titanium and its alloys are potential biomaterial. From 1930s attempt were taken to use it as biomaterials and the main feature which makes it a biomaterial is its lightness [1].

This review paper mainly focuses on titanium metal and its alloys as biomaterial, their further development and also gives a very brief idea on bacterial effects and its remedies.

II. TITANIUM AND ITS ALLOYS

Applications

Titanium covers a huge application field from dental implants, parts of orthodontic surgery, joint replacement parts for hips, knee, shoulder, spine, elbow and wrist, bone fixation materials like nails, screws, nuts, plates, housing device for the pacemaker, artificial heart valves, surgical instruments to components in high speed blood centrifuges [50]. Hence titanium is very beneficial in the field of bio-material as it holds wide range of applications such as osteosythesis, oral implantology, joint prosthetics etc. [51]. Applications of titanium alloys in artificial hip joints that consist of an articulating bearing (femoral head and cup) and stem, where metallic cup and hip stem components are made of titanium, is highly recognized. They are also often used in knee joint replacements, which consist of a femoral and tibial component made of titanium and a polyethylene articulating surface [52].

Fig.1 schematic diagram of artificial hip joint (left) and knee implant (right) [53]

Properties

Titanium based materials is selected as a biomaterial because of its certain favorable properties like corrosion resistance, mechanical resistance, low modulus of elasticity, density, bio-compatibility, [51, 52] bio-inertness, high resistance to fatigue and non-toxicity [55-59], capacity of joining with bone and other tissue (osteointegration) [60,61]. One of the main reasons for its acceptance as implant material is because of its low elastic modulus [around 110 GPa] which reduce bone resorption (stress shielding) as compared to other metallic bio-material. Reports based on several studies [62] shows that titanium supports cell growth as it readily absorbs proteins like albumin [63,64], laminin [65], glycosaminoglycans [66], collagenase [67], fibronectin [56], complement proteins [68] and fibrogen [69] from biological fluids. Density of titanium and its alloy is 4.5 g/cm^3 which is less than stainless steel (7.9 g/cm^3), CoCrMo (8.3 g/cm^3) and CoNiCrMo (9.2 g/cm^3) [1]. Another property that makes titanium and its alloy the most promising biomaterial for implant is the ability to form extremely thin, adherent, protective titanium oxide layer which is biocompatible and corrosion resistance [52]. The depth of this oxide layer is around 10 nm [1]. The oxide layer helps to provide osteointegration.

Types

Titanium as a biomaterial is broadly categorized into two types commercially pure Ti (Cp) and Ti-6Al-4V [50]. This two are actually biologically inert and when it is incorporated in human body, human body tries to isolate it by encasing it in fibrous tissue but it does not show any adverse effect and very much tolerated by in vivo atmosphere. Ti (Cp) is 98.9 - 99.6 % pure due to presence of other interstitial elements such as C and N. Nitrogen has greater hardening effect than carbon and oxygen. These interstitial elements strengthen the metal through interstitial solid solution strengthening mechanism [70]. There are four grades of unalloyed commercially pure (Cp) titanium for surgical implant applications according to the presence of oxygen, iron and other elements shown in the Table 1. Table 2 gives the tensile strength, yield strength, elongation etc. of commercially pure (Cp). Pure titanium gives two allotropes i.e. hexagonal alpha and cubic beta which is later described elaborately.

Ti-6Al-4V is widely applied to manufacture implants and its chemical requirements are given in Table 2. Titanium alloys can be strengthened and mechanical properties can be varied by controlled composition and thermomechanical processing techniques [1]. Requisite amount of aluminium is used to stabilize the alpha phase and controlled amount vanadium is needed to stabilize the beta phase. Using of two above said elements that is aluminium and vanadium gives a mixture of properties which promotes good weldability as well as excellent strength due to presence of both phases. Aging heat treatment gives rise to precipitation of beta phase which produces local strain field and capable of absorbing deformation energy hence crack is arrested. It is reported to have elastic modulus of 110 GPa which is less than stainless steel (210 GPa) and Co based alloys (240 GPa) [70]. Table 2 given below also shows the mechanical properties of Ti-6Al-4V [1].

Table 1. chemical compositions of Ti and its alloy [American Society of Testing and Materials, F-67-89,p.39;F136-84,p.55,1992]

Element	Grade 1	Grade 2	Grade 3	Grade 4	Ti6Al4V[a]
Nitrogen	0.03	0.03	0.05	0.05	0.05
Carbon	0.10	0.10	0.10	0.10	0.08
Hydrogen	0.015	0.015	0.015	0.015	0.0125
Iron	0.20	0.30	0.30	0.50	0.25
Oxygen	0.18	0.25	0.35	0.40	0.13
Titanium			Balance		

Table 2. mechanical properties of Ti and its alloy (ASTM F136) [American Society of Testing and Materials, F-67-89, p.39; F136-84, p.55, 1992 and Davidson et al., 1994]

Property	Grade 1	Grade 2	Grade 3	Grade 4	Ti6Al4V	Ti13Nb13Zr
Tensile strength (M Pa)	240	345	450	550	860	1030
Yield strength (0.2% offset) (M Pa)	170	275	380	485	795	900
Elongation (%)	24	20	18	15	10	15
Reduction of area (%)	30	30	30	25	25	45

Production Process

Fabrication processes of titanium alloys is somewhat difficult because most beta titanium alloys contain considerable amounts of refractory elements with high melting temperatures which results in difficulty in melting, solidification processing, low plastic deformability and high materials costs. The molten metal and the hot casting are susceptible to atmospheric contamination.

Being very reactive in oxygen and other atmospheric gases, the melting and casting processes of titanium alloy implies high temperature fusion and casting under vacuum or protective neutral atmospheres. Powder metallurgy (P/M) is also used to fabrication titanium alloys in which metal powders are utilized by compacting and sintering to get the final product. This method is employed primarily to produce simple shapes with good dimensional stability, to form shapes with material of extremely high melting temperatures and to produce parts not feasible by other means. Production of cast titanium requires 16 times more energy per tonne than the production of steel. Instead of conventional melting, milling and machining, P/M techniques implies powders that remain in solid form during the entire procedure. This process saves a tremendous amount of processing energy [71].

Problem with Ti-6Al-4V

Long term use of Ti-6Al-4V alloy causes Alzheimer, Parkinson disease. In addition vanadium is also toxic both in element state and oxides V_2O_5 , which are present at the surface [50]. V free titanium alloys like Ti-6Al-7Nb and Ti-5Al-2.5Fe have been developed because toxicity of V has been reported. The cytotoxicity of pure metals and the relationship between biocompatibility and polarization resistance of surgical implant materials have been reported by Steinemann. Kawahara has reported that metals Al, V and Fe has high cytotoxic [54]. Therefore, in this study, new β type titanium alloys composed of non-toxic elements such as Nb, Ta, Zr, Mo and Sn were made with lower moduli of elasticity, greater strength and greater corrosion resistance.

Phases of Titanium and its Alloys

Depending on titanium allotropes there are 3 classes of titanium alloys 'alpha', 'alpha-beta' and 'beta'. Hexagonal closed packed crystal structure (hcp) i.e. α phase exists at room temperature and transform into bcc or beta phase when titanium solidified from liquid or when solid titanium is heated to above 883˚C. α-titanium exhibit good elevated temperature creep properties and do not shows ductile brittle transition temperature, that's why it is beneficial for cryogenic application [62]. The alloy has a single-phase microstructure which gives good weldability. These alloys give excellent strength characteristics and oxidation resistance at high temperature (300~600˚C) due to the stabilizing effect of the high aluminum content. As they are single-phased, these alloys cannot be heat treated for precipitation hardening [1]. Moreover, α-alloys are extensively used in application that requires high corrosion resistance of titanium [72]. β type of titanium alloy shows lower modulus of elasticity increased corrosion resistance and improve tissue response [54]. It also offers high strength with adequate toughness and fatigue resistance and mostly satisfy requirement for being biomaterial [72]. Aluminium, tin and oxygen are used to stabilize α phase and niobium, molybdenum, tantalum, chromium, iron, vanadium are used to stabilize β phase [62]. Stabilizing element for β phase is more bio compatible than α phase stabilizing element hence, it makes β phase more bio compatible than α phase. Moreover, recent biomaterial research is mainly based on β titanium alloy because processing variables can be controlled to produce selected results. [73]. The addition of controlled amounts of β-stabilizers produces the higher strength -phase to persist below the transformation temperature which leads to two-phase system. The precipitates of β-phase will generate by heat treatment in the solid solution temperature and subsequent quenching, followed by aging at a somewhat lower temperature [52]. Another Ti alloy (Ti13Nb13Zr) with 13% Nb and 13% Zr showed martensite structure after water quenching followed by aging, which showed high corrosion resistance with low modulus (E= 79 MPa) [1]

α-β Ti alloy has balanced amount of α and β stabilizer and exhibit good mechanical properties [62] such as strength, toughness with high temperature resistance [72]. Another titanium alloy Ti- 35Nb-7Zr-5Ta which has elastic modulus (554 Pa) close to bone, does not show any short term or long-term potential adverse effect. This type of alloys can be manufactured by mixing corresponding hydride powder from a sequence of uniaxial and cold iso-static pressing with subsequent densification by sintering between 900-1700˚C [51]. X-ray diffraction reveals with increasing temperature upto 1500ºC, stabilization of β phase occurs due to the increase of the dissolution of Nb and Ta particles whereas low sintering (900-1100˚C) temperature forms intermediary widman-statten (α+β) phase. Tantalum dissolution starts from 1300ºC and sintering temperature of 1700˚C shows almost low amount of α phase due to high dissolution of β stabilizers i.e. Nb and Ta [51]. Micro segregation is observed with increasing beta stabilizer content and on examination of partition coefficient shows that Nb and Mo are the most likely to segregate. Addition of β stabilizing element shows metastable transformation to hexagonal or orthorhombic martensite i.e the omega phase and also shows α phase separation reaction [72].

Titanium can form alloy with excellent biocompatibility, corrosion, resistance and mechanical properties to contribute in orthopedics. Electronic structures are calculated for bcc. Ti alloyed with a variety of elements and two alloying parameters are determined theoretically by employing a molecular orbital method. One is the bond order (hereafter referred to as B_o) which is the measurement of the covalent bond strength between Ti and an alloying element. The other is the metal d-orbital energy level (M_d) which correlates with the electronegativity and the metallic radius of elements [54]. For alloys, the average values of B_o and M_d are defined by taking the compositional averages of the parameters and denote them $\overline{B_o}$ and $\overline{M_d}$, respectively. $\overline{B_o}$ and $\overline{M_d}$ values, and the chemical compositions of the designed alloys in this study are given in Table 3.

Table 3 values of $\overline{B_o}$ and $\overline{M_d}$ in designed alloys

Alloy Number	Chemical Composition (mass%)	$\overline{B_o}$	$\overline{M_d}$
1	Ti-29Nb-13Ta-4.6Zr	2.878	2.462
2	Ti-16Nb-13Ta-4Mo	2.843	2.436
3	Ti-29Nb-13Ta	2.866	2.446
4	Ti-29Nb-13Ta-4Mo	2.815	2.413
5	Ti-29Nb-13Ta-2Sn	2.856	2.438
6	Ti-29Nb-13Ta-6Sn	2.853	2.434

Areas of alpha, alpha beta and beta type alloys are separated clearly in the phase stability map (Fig.2) called the $\overline{B_o\text{-}M_d}$ map. Higher $\overline{B_o}$ and the lower $\overline{M_d}$ region gives stability to beta type alloys. Positions of titanium and titanium alloys are given by the numbers surrounded by the open circles in Fig. 3 where the values of moduli of elasticity are also shown. The values of moduli of elasticity for these alloys are decreased with increasing $\overline{B_o}$ and $\overline{M_d}$ values in beta type alloys region on the $\overline{B_o}$-$\overline{M_d}$ map. With varying alloy composition alloy position moves in $\overline{M_d}$ map as shown in Fig.4. Once a specific $\overline{B_o}$-$\overline{M_d}$ region and a specific alloy system is set in the map, the vector sum can be used to determine corresponding alloy composition. B_o-M_d diagram use to define the boundaries of the martensite and omega transformations in relation to the modulus of the beta phase using experimental data from a wide variety of alloying system [72].

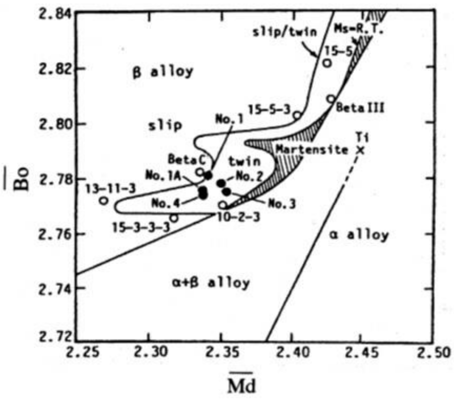

Fig.2 phase stability index diagram based on $\overline{B_o}$ and $\overline{M_d}$ parameters [54].

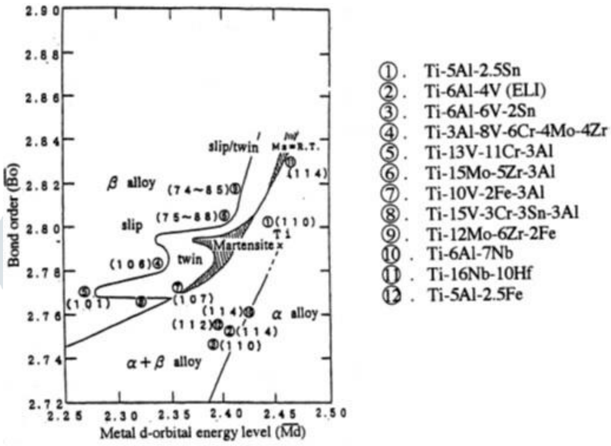

Fig.3 phase stability index diagram based on $\overline{B_o}$ and $\overline{M_d}$ parameters. Modulus (GPa) in each alloy is shown in the parenthesis [54].

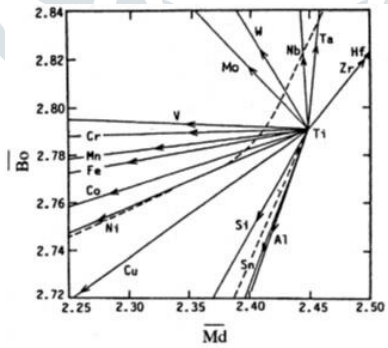

Fig.4 B_o–M_d lines drawn for various Ti–M binary alloys. M indicates an alloying element [54].

Kuroda et al. [54] also reported a research work based upon design of a type of alloy by choosing 2 alloying parameters B_o (bond order) and M_d (metal d orbital energy level), where the average values of B_o and M_d are defined by taking the compositional averages of the parameters and denoted by $\overline{B_o}$ and $\overline{M_d}$ (shown in the fig). Ti-29Nb-13Ta-4.6Zr, Ti-16Nb-13Ta-4Mo, Ti-29Nb-13Ta, Ti-29Nb-13Ta-2Sn, Ti-29Nb-13Ta-6Sn, Ti-16Nb-13Ta-4Mo system alloys were designed by melting appropriate mixture of sponge Ti and alloying elements then cold rolling to 75% reduction then they are solutionized at 1117K for 1.8Ks after homogenization, then they are aged at 673,723,773K for 10.8 hours. Thorough investigation revealed that tensile strength of Ti-29Nb-13Ta-4.6Zr is equivalent to or greater than conventional titanium alloy and Ti-16Nb-13Ta-4Mo shows greatest tensile strength. Tensile strength is found to increase with increasing ω phase, which precipitate at lower temperature aging in β-alloys with a lower equivalent percentage of Mo. The moduli of elasticity of as-solutionized designed alloys are lower as compared with those of conventional titanium alloys for medical implant, so they are expected to have greater performances as implant material. Fig.5 and 6 gives the comparison of elastic modulus and mechanical properties of different alloys respectively [54].

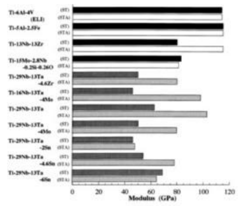

Fig.5 comparison of elastic modulus of different alloys

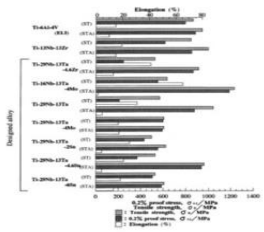

Fig.6 comparison of mechanical properties of different alloys

Surface Treatment

Surface treatment can extend the performance of orthopedic devices made of titanium. It can improve the tribological behavior, corrosion resistance, and osteointegration. Many surface modification techniques such as oxidation, physical deposition methods like ion implantation, plasma spray coating as well as thermo-chemical surface treatments like nitriding, carburizing, boriding are effective to enhance wear resistance, surface hardness, corrosion resistance [52,74,75].

Efforts are also made to increase surface oxide layer on titanium to have good biological response [52]. Oxidation is the most popular technique for the surface modification of Ti alloys; these oxide layers on titanium are commonly occurred by either heat treatment [76-78] or electrolytic anodizing [79]. 15-30 μm thick titanium dioxide layer of the rutile phase can be formed by thermal oxidation [51].

"Diamond-Like Carbon" (DLC) coating i.e. an amorphous carbon [mixture of diamond (sp^3) and graphite (sp^2)] films deposited by either Physical Vapor Deposition (PVD) or Plasma-Enhanced Chemical Vapor Deposition (PECVD) on titanium which has high hardness, low friction coefficient, owing to the solid lubricant because of its graphite and amorphous carbon contents, good chemical stability and excellent bio and hemocompatibility [80-82].

Hydroxyapatite is brittle and weak but highly bioactive. Hydroxyapatite is added to Ti alloy as second phase by powder metallurgy techniques which can improve bone interaction and further improves load bearing properties of Ti alloys. The manufacturing process of this composite is difficult because Ti is stable in vacuum or reducing atmosphere and HA is stable in oxidizing atmosphere [83]. Literature reported the formation of $CaTiO_3$, $CaTi_2O_5$ by reaction between Ti alloy and HA. If TiO_2 is not added intentionally then also calcium titanate is formed [84].

Although there is difficulty in formation of composite, to improve osteoblast ingrowth titanium is coated with HA by plasma spray coating. In this process basically, molten material is sprayed on a surface at very high velocity. Cook et al. [85] reported a comparative study of matte finish commercially pure titanium with HA coated Ti-6Al-4V and showed coated surface had greater interfacial strength than uncoated one. Osteoconductive HA surface may provide a method of accelerated tissue adaptation and attachment which reflected by increase in shear strength [85]. Hydroxyapatite powder is heated above 1000˚C to become partially molten and decompose. Structure and composition of coated layer is different from hydroxyapatite in its structure. An amorphous sodium titanate layer generates on the surfaces of titanium metal and its alloys when they are subjected to NaOH and heat treatment which can spontaneously bond to the living bone through an apatite layer [27,86].

III. POROUS TITANIUM

Production of implant with a certain amount of controlled porosity is advantageous for a good osteointegration. Moreover, Stiffness of titanium which is up to 10 times greater than surrounding bones, causes a stress-shielding effect, bone resorption and it sequentially leads to implant loosening. Lifetime of implant shortens as in case of bulk titanium due to formation of an interface between bone and implant. Use of porous titanium as implant material is reported which can build bone ingrowth into the porous structure [87].

Several studies were conducted to see the efficiency of porous titanium prostheses whereas porous ceramic implants lose its tensile strength, fatigue resistance and impact strengths. Powder metallurgical techniques have been applied to prepare stellite alloy implant which is not always yield inferior product compared to casting and forging. Porosity required to provide osteoblastic ingrowth (20-40%) results in decrease of the tensile strength from between 62000 and 70000 psi for the stellites to approximately 10000 psi at 65% of theoretical density and to about 30000 psi at 75% of theoretical density. Adherence to the bone is thus obtained at considerable sacrifice in mechanical strength [88].

For metallic implant's durability and successful implantation one of the key issues is strong bone implant interface [89]. Smooth implant might get loosen caused by encapsulation [90]. A porous coating or material can promote partial to complete bone ingrowth which enhances the strength of the interface and reduces the capsule formation around the implant. As metals implants being stiffer than bone carries inordinate number of loads which causes stress shielding to the surrounding bone and loosening of implants [91]. Porous coating on the implant can curtail the shielding effect by bone ingrowth within the implant. There are various methods to fabricate porous Ti based alloys such as investment casting [92], sintering loose titanium powder or fiber [93], slurry sintering [94], rapid prototyping [95] etc. Shen et al. [87] investigated novel porous commercially pure (Cp) Ti and Ti-6Al-4V which was super plastically expand by compressed argon bubbles up to 50% porosity. Tensile load can be applied during the process to further elongate the pores. Morphology can be controlled by suitable choice of powder [96]. A significant amount of open pore can cause substantial bone ingrowth which improves bone implant interface as well as minimizes stress shielding by reducing the stiffness of Ti metal implant. Microstructure of porosity, pore size, morphology, spatial distribution are very important factors as incorporation of porosity dramatically changes mechanical properties, strength, fatigue resistance.

Improvement of Porous Titanium

Sometimes obtaining of bone ingrowth into porous surface is problematic and this can be solved by incorporating bioactive materials such as calcium phosphate coatings, by the use of electrical stimulation and osteoconductive agents. Nishiguchi et al. [97] have developed a new method to enhance bone-bonding strength of smooth titanium implant (measured by tensile and shear test method) by soaking in alkali solution and subsequent heating [98,99]. Nakashima et al. [100] showed that conventional HA plasma spraying obstructed the opening of porous surfaces which leads to reduction in pore volume available for bone ingrowth. Alkali heat treatment of porous titanium do not reduce pore space available for bone ingrowth also shows significantly higher bonding shear strength in the canine femoral push out model at 4 weeks after implantation [97]. Yamanuro et al. [101] studied the effect of AW-GC (glass ceramic) coating on porous titanium as AW-GC has superior bioactivity and higher fracture toughness. On comparison with fully coated or uncoated implants, plasma coated AW-GC coating on the bottom of porous surface shows increased bonding strength of titanium plasma sprayed implants under loading condition at 4,8 and 24 weeks after implantation. They named this coating technique “AW bottom coating”.

IV. LIMITATION

Some unavoidable problems are; processing energy, melting and casting difficulties make it costly, it has higher elastic modulus compared to bone, although its inertness is a good property but bone attachment is difficult because it does not react with the human tissues [70]. Fundamental drawbacks such as poor fretting fatigue resistance and poor tribological properties are caused by low hardness and high coefficient of friction. Titanium has also some drawbacks like corrosion due to potential metal ion release, allergenicity, limit of fabrication, inconsistency in material supply [8]. Its poor shear strength makes it less desirable for bone screws, plates etc. Titanium also suffers from several wears when it is rubbed between itself or between other metals. Galling and seizing are most common for moving or sliding parts of titanium [52]. Titanium alloys that have a high coefficient of friction can cause to the formation of wear debris that result in inflammatory reaction causing pain and loosening of implants due to osteolysis [102].

Despite of continuous attempt to improve the life span of prosthesis it remains finite because of mechanical wear, aseptic loosening, infection, instability and periprosthetic fractures [10]. Most importantly failures occurring due to microbiological infection is an indubitable problem of concern. The infecting organisms either are introduced during implantation of a prosthesis or are carried to the biomaterial surface by a temporary bacteremia where they adhere and grow to from a biofilm [103]. Biomaterial associated infection can be influenced by many factors such as asepsis, preparation of patient, preparation of antibiotics, length and time of surgery, type of procedure followed to apply the device or the implant, apart from all these it also depends on the age and health condition of the patient. Infection due to bacteria mainly based on adhesion, if bacteria cannot adhere to solid surface there will be no possibility of colonization [104].

Further Improvement

The problem of wear due to presence of stress can be ameliorated by nitride (titanium nitride) coating on titanium. Ion implantation is used to place a nitrogen enriched layer on the surface of the orthopedic implant devices. Plasma nitriding of the outer surface of the orthopedic implant device occurs at temperature preferably between approximately 600-700°C approximately which can give nitrogen rich coating of good wear resistance and also high strength. This process improves adhesion between bone cement and orthopedic implant. Nitrogen is introduced to the reaction vessels after sputter cleaning operation of the outer surface of the implant [105]. It is basically ejection of solid particles from solid target material due to bombardment of the target by energetic particles.

TiO_2 is widely used as biomaterial surface coating. It has an additional benefit of self-defecting properties [106] which is caused by its photo chemical activity. Co-Sputtering of Ag-HA on titanium surface showed lower invitro bacterial adhesion of S. Aureus and S. Epidermidis [107]. Using Ag is beneficial as it has bactericidal properties. Nano structured materials are also effective in limiting bacterial adhesion by lowering surface area or creating superhydrophobic surface [104].

In vitro studies have suggested nano-dimentional TiO_2-coated Ti-based implants with a moderate surface energy at 38.79 mJ/m^2 prevents colonization of a wide range of bacteria. Gram positive strain, S. Aureus, both methicillin resistant and normal strain along with gram negative type E. Coli gave satisfactory outcome upon addition of TiO_2 coating without the use of any antibiotics [108]. Studies conducted by Boniyadi et al. [109] and Peiris et al. [110] showed TiO_2 as a potential antimicrobial agent effective on a large range of hospital bacteria comprising of both gram positive and gram-negative type. TiO_2 is hypothesized to degrade bacteria by producing hydroxyl radical that increases the oxidative stress resulting in bactericidal activity. In another set of study conducted by Haghighi and group, antifungal effect of TiO_2 nanoparticles were established [111].

Invention of orthopedic implant with therapeutic active agents for example anti-inflammatory agents, analgesic agents, anti-microbial or anti-viral agents which can cause proper healing after surgical implantation is a zone of attraction [112]. Polymethylmethacrylate loaded bone cement is also a potential material to prevent and cure orthopedic implant infection [113]. Combination of different properties such as, osteoconductive, chondroconductive and bacteriophobic effect, tantalum is attracting the attraction as an eminent orthopedic implant [114]. Nablo et al. [115] reported another process to reduce orthopedic infection in which he used nitric oxide (NO) releasing sol-gel antibacterial coating on stainless steel. Use of composite material of poly octanediol citrate (POC) and zinc oxide (ZnO) is also reported, synthesized by sol-gel method releases controlled rate of ZnO having antibacterial properties against Escherichia Coli. [2]. A broad range of substances like Hamamelitannin, [117,118] Proteinase R, [117] EDTA, [119] Trypsin [120] etc. actually been identified that possess antibiofilm activity and can be either grafted on biomaterial surfaces or released appropriate coating [121].

V. CONCLUSION

Biomaterials play a pivotal role in benediction of living beings and are integral part of health and development sectors. Different biomaterials either individually or in combination serve different purpose. Among the broadly classified biomaterials (metallic, polymer, ceramics), metallic biomaterials are mainly chosen for their load bearing capacities where titanium and its composites (e.g. Hap coated Ti etc.) have attracted much recognition for their superior properties. Alpha and beta phases of titanium shows variation of properties where the former is used mostly for cryogenic application and the latter is more bio compatible. Further development of these biomaterials is continuing with technological advancements. Special attention is also given towards the bacterial infection associated with these biomaterials in order to obliterate the harmful effects of microorganisms.

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