SCHOOL OF MATERIALS AND MINERAL RESOURCES ENGINEERING UNIVERSITI SAINS MALAYSIA

BIOACTIVE SURFACE MODIFICATION OF TI-NB ALLOY BY ALKALINE TREATMENT IN POTASSIUM HYDROXIDE SOLUTION

By

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Dissertation submitted in fulfilment of the requirements for the degree of Master of Science (Material Engineering)

Universiti Sains Malaysia

SEPTEMBER 2020

DECLARATION

I hereby declare that I have conducted, completed the research work and written the dissertation entitled "Bioactive Surface Modification of Ti-Nb Alloy by Alkaline Treatment in Potassium Hydroxide Solution". I also declare that it has not been previously submitted for the award of any degree or diploma or other similar title of this for any other examining body or university.

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ACKNOWLEDGMENT

First and foremost, I would like to thank Allah as I could finish this paper writing in a given time. Thanks to the School of Materials and Minerals Resources Engineering, University Sains Malaysia for allowing me to utilize their laboratories and providing necessary apparatus, chemicals, and services required to complete my research project. Special thanks to my supervisor Prof. Ir. Dr. Zuhailawati Hussain for her guidance, patience, motivation, enthusiasm, immense knowledge, and advice throughout this research project has helped me accomplished my research project. Hereby, I also would like to thank my co-supervisor, Dr. Khairul Anuar Shariff for his willingness to provide some useful information. A special thanks to the technical assistant for their cooperation and guidance during this research. A special thanks to the lecturers and friends for their contribution and support throughout this research project. Last but not least, a special thank for my family, Basry Bin Jaafar, Siti Khalizah Binti Yusoff and Minah Binti Noor for their support and motivation throughout my master's degree.

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LIST OF SYMBOLS

C	Celsius
G	Gram
ml	Millilitre
M	Molarity
Θ	Theta

LIST OF ABBREVIATION

BCC	Body centred cubic
C	Carbon
Co	Cobalt
Cr	Chromium
Cu	Copper
EDX	Energy Dispersive Electron Probe X-ray Analyzer
Fe	Iron
GPa	Gigapascal
H	Hydrogen
HCP	Hexagonal close pack
$HTiO_3{}^{-}nH_2O$	Titanate Hydrate
K	Potassium
KOH	Potassium Hydroxide
M	Molar
Mn	Manganese
MPa	Megapascal
N	Nitrogen

Na	Sodium
NaOH	Sodium Hydroxide
Nb	Niobium
Ni	Nickel
O	Oxygen
OH	Hydroxyl Group
SEM	Scanning electron microscope
Si	Silicon
Sn	Tin
Ti	Titanium
TiO_2	Titanium Dioxide
XRD	X-ray diffraction
Zr	Zirconium
β	Beta
α	Alpha

PENGUBAHSUAIAN BIOAKTIF PERMUKAAN ALOI TI-NB OLEH RAWATAN ALKALI DALAM KALIUM HIDROXIDE

ABSTRAK

Rawatan beralkali terhadap struktur β Ti aloi implant yang serasi dan tidak bertoksik didalam kalium hidroxide untuk mengubahsuai bioaktiviti aloi telah dikaji. Ti-40wt%Nb telah dihasilkan menggunakan kaedah metalurgi serbuk dengan mengisar campuran Ti-Nb, mengenakan tekanan pada 550MPa dan disinter pada suhu 1200°C selama 2 jam. Rawatan beralkali terhadap aloi ini telah dikaji dalam cecair akueus kalium hidroxide (KOH) pada suhu 60°C selama 24 jam pada kepekatan yang berbeza (iaitu 0.5M dan 5.0M). Aloi beralkali menjalani proses penyepuhlindapan pada suhu 600°C selama 2 jam untuk mengkaji kesan daripada rawatan haba terhadap aloi beralkali. Kesan tindak balas aloi yang dirawat menggunakan alkali dibandingkan dengan Ti dan Nb tulen. X-ray analisis pembelauan menunjukkan kehadiran lapisan amorf alkali titanate hydrogel seperti titanium terhidrat, kalium hydrogen titanium oksida dan niobium oksida untuk rawatan 0.5M. Untuk 5.0M, fasa baru di kesan iaitu titanium oksida dan dikalium dititanium oksida. Analisis FTIR menunjukkan dua band penting OH pada 3223 cm^{-1} dan 1633 cm^{-1} di permukaan Ti-40Nb selepas rawatan alkali dan selepas penyepuhlindapan. Pemerhatian dibawah pengibasan elektron mikroskop dan analisis unsur menunjukkan pemendapan lapisan titanate dengan kehadiran komposisi tinggi kalium dan oksigen. Kajian bioaktiviti di dalam cecair Hanks selama 24 jam mendapati unsur Ca dan P wujud di permukaan aloi yang dirawat pada kepekatan yang berbeza selepas rawatan alkali dan penyepuhlindapan. Penemuan ini mencadangkan bahawa aloi baru β Ti dengan 40wt% Nb sesuai untuk rawatan alkali di dalam cecair KOH untuk membentuk lapisan kalium titanate yang penting untuk pemendapan mineral apatite.

BIOACTIVE SURFACE MODIFICATION OF Ti-Nb ALLOY BY ALKALINE TREATMENT IN POTASSIUM HYDROXIDE SOLUTION

ABSTRACT

Alkaline treatment of biocompatible and non-toxic new β structure Ti alloy implant in potassium hydroxide for modifying bioactivity of the alloy was investigated. Ti-40wt%Nb was fabricated by powder metallurgy method by milling of Ti-Nb mixture, pressing at 550MPa and -sintering at 1200°C for 2 hours. Alkaline treatment of the alloy was studied in the potassium hydroxide (KOH) aqueous solution at 60°C for 24 hours at different concentration of (i.e., 0.5 and 5M). The effect of post heat was investigating by annealed alkaline treated alloy at 600°C for 2 hours. The responsive behavior of the alloy alkaline treated alloy was compared to pure Ti and Nb. X-ray diffraction analysis showed the presence of amorphous alkaline titanate hydrogel layer such as titanium hydrate, potassium hydrogen titanium oxide, and niobium oxide for 0.5M treatment. For 5M, new phases are noticed (potassium titanium oxide and dipotassium dititanium oxide). The FTIR analysis show two significant band of OH at 3223 cm^{-1} and 1633 cm^{-1} on the Ti-40wt%Nb surface after alkaline and post heat treatment. Morphology observation under scanning electron microscope and elemental analysis indicate the deposition of titanate layer with the presence of high composition of potassium and oxygen. Bioactivity study in Hanks solution for 1 day discovered the trace of Ca and P elements on alloy surfaces treated in different concentration after alkaline as well as annealing treatment. These findings suggest that the new β-Ti alloy with 40wt% Nb were feasible for alkaline treatment in KOH solution forming potassium based titanate layer that were prerequisite for bone mineral apatite deposition.

CHAPTER 1

INTRODUCTION

1.1 Introduction

Titanium alloy is commonly used as implant material application because of their biocompatibility and the existence of natural oxide layer that can improve its corrosion resistance. The commercially used Ti alloy such as Ti-6Al-4V (grade 5) alloy with Young modulus 110 GPa are widely used in hard tissue replacement, dental implants and joint (Viteri and Fuentes, 2012). Lai *et al.*, (2015) reported on cortical bone Young modulus is in the range 17 to 20 GPa. Whereas for pure Ti metal is 120 GPa. In order to be used in the implant, the artificial bone must have Young modulus almost in the similar range as cortical bone. However, the Ti-6Al-4V alloy have high young modulus that result in the stress shielding effect thus not suitable to be used for bone replacement. One way to solve this problem is by introducing β-type structure to the Ti alloy. β-type structure Ti alloy with β-stabilizer like vanadium and niobium has decreased the great differences of Young modulus in bone and replacement implant. For example, Ahmad et al, (2018) reported that Ti-40wt% Nb alloy showed Young Modulus of 26 GPa that is in range with bone's as well as high compressive strength (2123 MPa). Elastic modulus in the range of the bone has been proposed can reduce the stress shielding effect.

However, the properties for a new type of alloy such as biocompatibility may differ with other type of Ti alloy. In order to make sure the new alloy is compatible to be an implant material that can support the healing of the broken bone, surface modification should be done to make sure it able to form a bonding with the bone part that can assist healing. Therefor, biomaterial fields mainly focus on developing new alloy that have specialized mechanical properties which similar with human bone. While biocompatibility of the biomaterial is closely related to their corrosion behavior in biological environment.

Biocompatibility of the new biomaterial can be enhanced by surface modification techniques enhancing their surface bioactivity. The surface modification technique used to improve the properties of titanium-based surfaces such as physical and chemical vapor deposition, thermal and chemical oxidation, thermal spraying, ion implantation, bio ceramic or biopolymer coating deposition and alkaline treatment. Among this surface modification technique alkaline treatment has received attention including surface modification of Ti alloys (Da Silva *et al.*, 2019).

Alkaline treatment is the chemical treatment in which the alloy of interest are immersed in a known concentration of aqueous sodium hydroxide for given temperature and period time (Ouarhim *et al.*, 2018). has studied the surface modification for Ti-6Al-2Nb-Ta using alkaline treatment with sodium hydroxide solution (NaOH). The surface modification using alkaline treatment produces strong bonding of apatite layer to the substrate and uniform gradient of stress transfer to be used in bone replacement. Many different parameters has been studied using alkaline treatment including soaking time of the alloy, concentration of the alkaline solution and temperature used during alkaline treatment . Du *et al.* (2014) has studied the influence of alkaline treatment to the Ti-6Al-4V and hydroxyapatite coating, whereas Zhao *et al.*, (2015) has studied the effect of concentration of alkaline treatment to the Ti alloy surface and Hanib *et al.*, (2016) has studied the effect of temperature used for alkaline treatment to the Ti-6Al-4V.

Even though many research have investigated modifying Ti and alloys surface by alkaline treatment for improving bioactivity properties, treatment in KOH is still less reported. Investigation on phase formation and the developed microstructure under the variation of treatment variables such as concentration of KOH and post heat treatment, are still lacking. In addition, alkali-heat treatment on new Ti alloy has not been explored and reported to date. Research on simple alkaline treatment of new alloy such as Ti-Nb is necessary to determine the feasibility of Ti-Nb undergo alkali-heat treatment considering it has potential as non-toxic and biocompatible implant alloy.

The present study was aimed to investigate the feasibility of surface modification of a new alloy of β-Ti alloy with Ti-40wt% Nb in KOH solution towards the formation of alkali titanate layer. Phase, surface morphology and chemical composition of the deposited materials was compared to treated pure Ti and Nb in order to understand the behaviour of the new alloy under KOH treatment.

1.2 Problem statement

A new biocompatible and non-toxic β-Ti alloy has been reported to solve the problem of great difference in elastic modulus of human bone and commercial Ti and Ti-Al-V alloy implants. Surface treatment in alkaline solution has been reported to be success on the enhancement of bioactivities commercial pure titanium and titanium alloy with low amount of alloying elements, such as Ti-6Al-2Nb-Ta. Thus, responsive of the Ti-40wt% Nb alloy towards alkaline treatment needs investigation as a comparison to pure Ti and Nb. Alkaline treatment has been done in different kind of alkaline solution. Till date sodium hydroxide (NaOH) received more attention compared to potassium hydroxide (KOH) while KOH has been claimed is more reactive than NaOH. Thus, structure and composition of the deposited material on the Ti-Nb alloy need detail investigation.

Ti metals exposed to strong alkali formed apatite on the surface when soaked in simulated body fluid due to formation of negative charge titanate hydrogel that form when Ti metal immerse in KOH. This is because absorption and accumulation of positively charge K^+ ions in KOH solution to the negative charge titanate hydrogel layer on the Ti metal surface. Concentration of the alkaline solution is one of the important variables in controlling the surface charge. While high concentration hydroxyl (OH^-) ions could excessively attack the TiO_2 passive layer as well as Ti substrate. Due to these possible reactions that occur simultaneously, morphology and type as well as surface properties of deposited material need to be identified under high and low concentration of KOH.

Combination of alkaline treatment and post heat treatment is reported increase biocompatibility and enhance bonding with living bone because alkaline treatment alone formed unstable hydrogel titanate layer with poor strength which could be damaged during preservation or implantation in human body. The post heat treatment would densify the hydrogel formation, which is accompanied with enhanced mechanical integrity, thus bone bonding ability of the titanate gel could be maintained. However, elevated temperature could cause diffusion of atoms in the hydrogel that might results in high crystallinity or phase transformation.   New characteristic of the heat treated titanate requires an investigation on the bioactivity properties.

1.3 Objectives

1. To study alkaline titanate hydrogel formation effect by KOH alkaline treatment on Ti-40wt%Nb alloys with different concentration of KOH solution.
2. To compare phase, surface morphology and chemical composition of the KOH treated surface Ti-40wt%Nb with pure Ti and Nb.
3. To investigate the effect of heat treatment on surface of alkali treated metals

1.4 Scope of study

In this work, KOH alkaline treatment was conducted on a Ti-40Nb alloy in order to enhance bioactivity of the alloy. The alloy was fabricated using powder metallurgy parameters and composition developed by previous work (Ahmad, 2020 and Ahmad and Hussain, 2018) which reported has potential for implant material. Two concentrations of KOH were selected based on literature i.e., 0.5 and 5M which reported for Ti and Nb while the other variables were kept constant. Heat treatment at 600°C was also performed after the KOH treatment to study the effect of heat on the deposited material on the metal surface. Surface structural changes of the treated and non-treated Ti-40Nb alloys were examined using X-ray diffractometer (XRD) and a scanning electron microscope (SEM) attach with energy-dispersive electron probe X-ray analyzer (EDX).Bioactivity of the alloy was investigated in Hank solution as it is necessary to investigate electrochemical and behavior of the new alloy under the simulated body fluid (Hong *et al.*, 2010).

1.5 Thesis outline

This thesis was organized into five chapter. The first chapter cover the research background, problem statement, objective, and scope of research. In the second chapter, literature review cover on the Ti-40Nb, alkaline treatment and heat-treatment. Chapter 3 explains the material used, experimental procedure, parameter conduct, and the characterization. The result and discussion are discussed in chapter 4. Finally, chapter 5 conclude the research and recommendation for future work.

CHAPTER 2

LITERATURE REVIEW

2.1 Biomaterial for implant

Biomaterial for implant nowadays has become a demand for the biomedical industry because it was a material that can be used in human body which the biocompatibility between the bone and the implant material is essential. Suitable biomaterial for implant material should be biocompatible, bioactive or surface reactive, bioinert, biodegradable, low weight, reasonable cost as well as excellent in mechanical and physical properties.

Based on Table 2.1, the used of biomaterial is depend on their specific properties which suitable for the body part of human body that would be replace or support the part of lost function due to diseases or trauma. The replacement of damage part is to assist healing and improve the performance of the body. Different biomaterial has different properties which would influence the function of the implant part.

Table 2. 1: Uses of biomaterials (Parida et al., 2012)

Problem area infected	Examples of implant part
Replacement of damaged or diseased part	kidney dialysis machine and artificial hip joint
Support in healing	Sutures, screws and bone plates
Recover the function	Intraocular lens and Cardiac pacemaker
Correct functional abnormality	pacemaker of cardiac
To diagnosis	Probes and catheters
For treatment	Catheters, drains

Total hip joint replacement as shown in Figure 2.1 gaining popularity in medical field to improve the quality of patient that suffering arthritis and replacing damaged joint. However, factor that influencing the implant is the type of material used, mechanical properties and the biocompatibility of the material that would affect the life span and performance of the implant material.

The commonly used biomaterial in medical field is metal, ceramics, glass and plastic that were used as an implant, devices, and support. Despite that, although metal alloy implant are frequently used as total hip replacement, metal ions are released due to wear which can create negative effect to the patient body as mentioned by Ghalme *et al.* (2016). In total hip replacement, the femoral head used ceramic because of its high specific strength and toughness which would reduce the risk of fracture according to Affatato et al. (2015). As stated by DiPuccio et al. (2015), the plastic used only for the socket replacement which is Plastic Liner in between acetabular component and femoral head.

Variety of implant material are produced to fulfill the need of various medical application. Biomaterial that has been improved in term of inertness and corrosion resistance which can enhance the cytotoxicity. Cytotoxicity are involving the quality of the material whether it will become toxic to cell that affected the acceptance of the body to material. Implant that is rejected by the body will cause implant failure. Preferred biomaterial should be material that biologically, functionally, and mechanically compatible with bone.

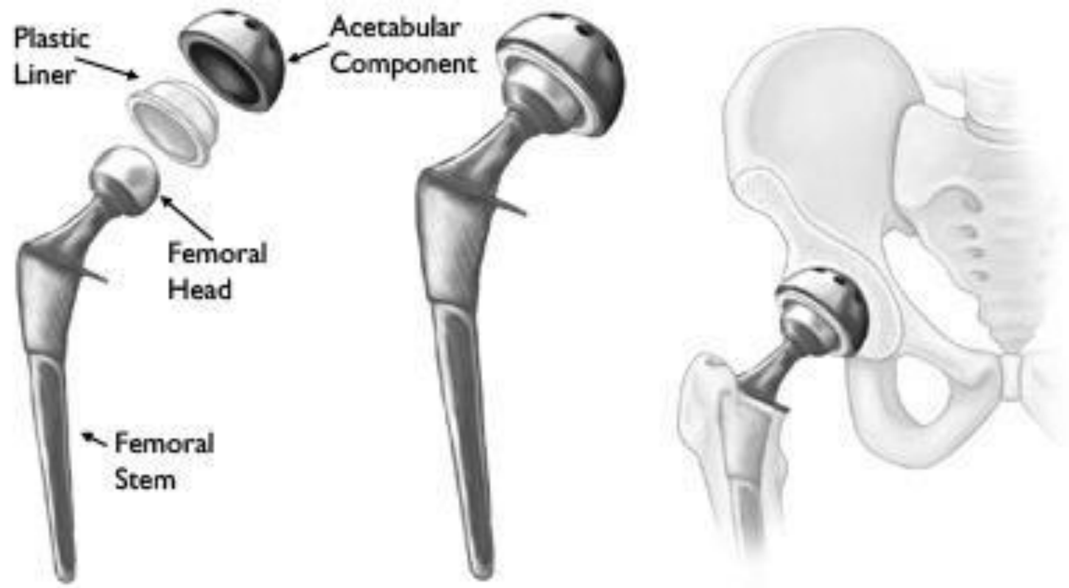

Figure 2. 1: Component of hip joint replacement (Ghalme et al., 2016)

As a biomaterial implant, an implant material must be able to produce a positive response from the organism because it was a key factor for a long-term success of the implant. A positive response from implant to human body which is a suitable implant material would optimize biologic performance. The implant material that is not suitable which is not biocompatible would give negative response that can lead to problem such as implant failure, corrosion, toxicity, infection and muscle re-attachment based on Shayesteh *et al.* (2016). The corrosion that causing the wear of the implant material can introduce toxic to human body that could infect the cell surrounding of implant material. The cell that is infected by the toxic would be infection and could cause implant failure. Inflammation may occur at the part where the implant failure happens which the patient would have severe pain and discomfort.

A suitable biomaterial implant would be able to increase cell productivity which the biomaterial that can trigger osteopath-genesis and the attachment of the implant to the connective tissue of the bone. Sivakumar et al. (2017) stated that roughness and the texture of the implant material is the important parameter for bioimplant material as they guide the growth factor of tissue on the implant surface. For implant material, growth factor is very important in bony or tissue regenerating (Sachelarie et al., 2015).

2.2 Titanium Alloy

Application that is commonly demonstrated the used of titanium is by the biomedical field. Titanium is the metallic biomaterials in both dental and medical fields which successful as biomedical devices. Titanium based material is mostly used as surgical instrument, dental implant, and prosthetic femoral component. The properties and application of the titanium are influenced by the titanium element, alloying element, mechanical processing, and chemical composition.

Pure titanium has good corrosion resistance, moderate strength, low thermal density, low density, low thermal elastic modulus and has high reactivity with variety of element. Pure titanium poses hexagonal closed pack structure (HCP) which called α titanium at low temperature. However, it poses stable structure with body centered cubic BCC called β titanium at high temperature. The basis for large variety of titanium alloy properties varies by the existence of the two different crystal structure.

Pure titanium and titanium alloy are widely used in implant applications because of their high mechanical ability, biocompatibility and existence of natural oxide layers that can enhance the corrosion resistance of the surface (Hamdi *et al.*, 2018). Titanium alloy is used in medical field as an implant material, device and medical machine which is the material used was nontoxic and would not give negative effect to patient body. In addition, biomaterial implant mostly prefer to use titanium alloy as an implant material because of the increase in mechanical properties such as high load bearing, optimize the hindrance fatigue, can withstand a high ultimate stress, good in tensile stress and yield stress compare to pure titanium. However, stress shielding effect could occur that would result in bone density reduction which can loosening the implant in long term.

A suitable metal implant that has almost the same mechanical properties as bone such as elastic modulus is preferred to avoid stress shielding effect from occur. As shown in Table 2.2, there are varieties of titanium alloy used as implant material. Ti-6Al-4V or beta phase metal material was commonly used as implant because of they have lower Young's modulus compared to other titanium alloy. However, the Young's modulus of cortical bone is 10-30 GPa which is still lower than titanium alloy's Young's modulus. Thus, stress shielding is still unavoidable regardless type of titanium alloy used. Therefore, it is necessary to remove the titanium alloy implant material after the completion of bone repair.

Nowadays, popularity of titanium alloy has increased due to new generation of titanium alloy which has promising properties for medical implant. As studied by (Tan *et al.*, 2019), Ti-23Nb-7Zr mainly formed an α phase. However, for Ti-28Nb-7Zr and Ti-33Nb-7Zr consist of both α and β phase with the increase in Nb added to the titanium alloy. In addition, Ti-33Nb-7Zr showed an increased in β phase amount than Ti-28Nb-7Zr. The increased in amount of β phase is because it was stabilized by the Nb in the solution treated condition which decreased amount of α phase.

Table 2. 2: Young's modulus of pure titanium, titanium alloy and bone (Tan *et al.*, 2019)

Pure titanium/titanium alloy/bone	Young's modulus (GPa)
Pure Ti (Cp grade 1-4) (α)	100
Ti-6Al-4V (α+β)	110-112
Ti-13Nb-13Zr (Metastable β)	78-84
Ti-12Mo-6Zr-2Fe (TMZF) (β)	74-85
Ti-35Nb-7Zr-5Ta (TNZT) (β)	55
Ti-29Nb-13Ta-4.6Zr (β)	65
Ti-35Nb-5Ta-7Zr-0.4O (TNZTO) (β)	66
Cortical bone	10-30

2.3 Physical Metallurgy of Titanium Alloy

Titanium and its alloy are relatively known as an engineering material that posses extraordinary combination of properties. Pure Ti metal posses relatively low density (4.5g/cm^3), high melting point (1668°C) and an elastic modulus of 107 GPa. Ti alloy are extremely strong, high tensile strength (1400MPa) and remarkable strength. Furthermore, Ti alloys are highly ductile and easily forged or machined (Callister et al., 2011).

Commercially pure Ti has a hexagonal closed packed (HCP) crystal structure as shown in Figure 2.2 (a) which is alpha, α, phase at room temperature. Referring to Figure 2.3, at 883°C the HCP material transform into a body centered cubic (BCC) as shown in Figure 2.2 (c) which is beta, β, phase as mentioned by Zwecke et al. (2015). Transformation temperature is strongly influenced by the presence of alloying elements.

For example, the addition of vanadium, niobium and molybdenum as an alloying elements could decrease the α to β transformation temperature and promote the formation of β-Ti phase since they are β stabilizer which cause the β-Ti may exist at room temperature. For some composition, both α and β phases co-exist at room temperature. Phases that present after processing could varied because of Ti alloy could fall into four classification which are α, β, α + β and near α.

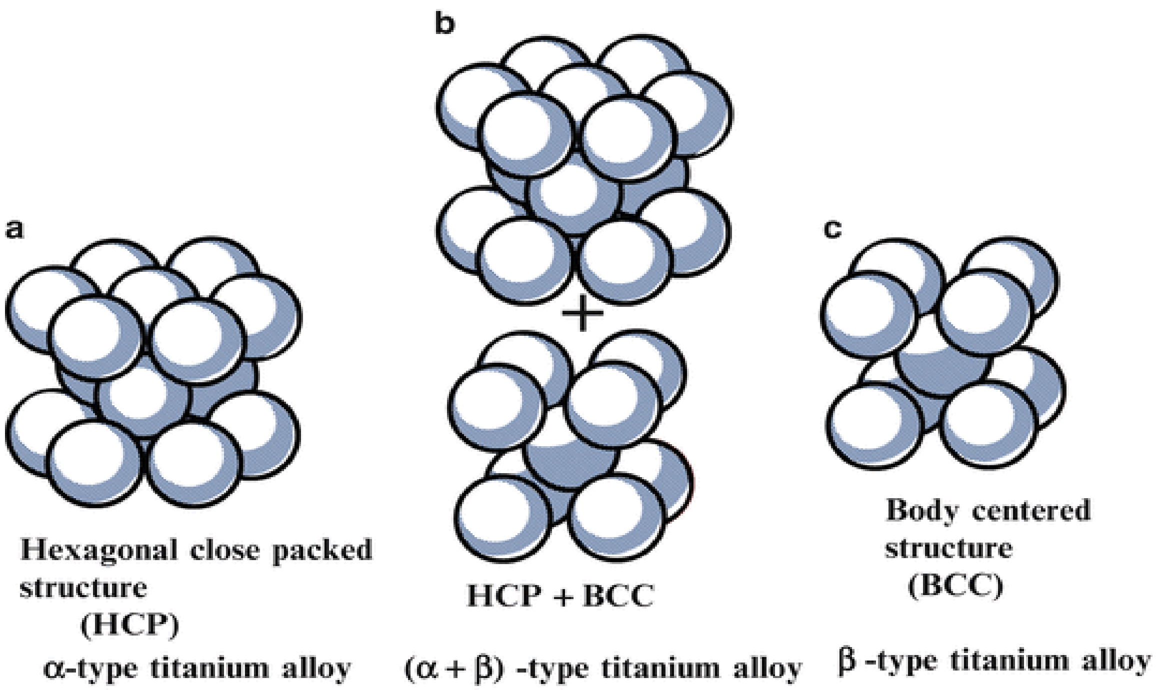

Figure 2. 2: Phase of titanium alloys a) the HCP structure of α phase type, b) the HCP + BCC structure of α + β phase type and c) the BCC structure of β type phase for Ti alloys (Niinomi et al, 2015).

2.4 Alloying elements

The solubility of α and β phases as α stabilizer, β stabilizer and neutral element classification was influenced by the alloying elements of Ti alloy as mentions in Figure 2.3. Some of the alloying element that added to Ti alloy tend to act as an α stabilizer. An α stabilizer would extend the β phase field to higher temperature that increase the transus temperature (T_{β}). Al act as a substitutional role in Ti alloy where Al is the most used alloying element in Ti alloys due to its large solubility in α and β phases and its capacity that could increase T_{β}. Furthermore, O, N and C are the most usual interstitial elements element for this β phase type.

The β stabilizer would shift the β phase field to a lower temperature that decrease T_{β}. The alloy element that act as a β stabilizer are divided into 2 which is β isomorphous and β eutectoid element. An alloying element such as V, Mo, Nb, Ta and Re are the most important β isomorphous because of their higher solubility in Ti. However, Ta and Re are rarely used due to their high density. Moreover, the β eutectoid such as Fe, Mn, Cr, Co, Ni, Cu, Si and H could lead to the formation of intermetallic compounds. In addition, Sn and Zr are the most common neutral element that give minor influence on T_{β} or on the α/β phase boundary. However, they could increase the strength of α.

The α Ti alloys commonly alloyed with aluminium or tin, they are preferred for high temperature application because of their creep characteristics. Furthermore, α is a stable phase that make α not eligible for strengthening by heat treatment. This type of Ti alloy materials are normally used in annealed or recrystallized states. In this state, strength and toughness are satisfactory where forge ability is an inferior to other Ti alloy types.

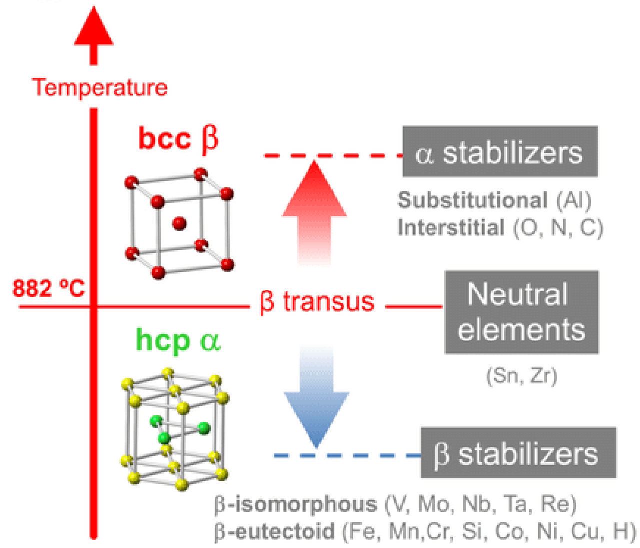

Figure 2. 3: Classification of alloying elements of titanium according to their influence on the β-transus temperature, T_β (Zwecke et al, 2015)

The β titanium alloys contain sufficient concentrations of β stabilizing elements such as V and Mo. Upon cooling at sufficient rapid rates, the β (metastable) phase is retained at room temperature as shown in Figure 2.4. These types of materials are highly forgeable and exhibit high fracture toughness.

There is also a state that α + β materials are alloyed with stabilizing element for both constituent phases. The strength of these alloy could be improved and controlled by heat treatment. A different type of alloying element in Ti alloy would give variety microstructure that may consist of an α phase and retained or transformed into β phase. Moreover, another type of phase which is near-α alloy that also composed of α and β phase. However, they only contain small proportion of β type. Thus, it contains low concentration of β stabilizer. These types of alloy material properties and fabrication characteristic are similar to those of the α alloy materials. However, the different between near-α alloy and α phase material are near-α alloy have varieties of microstructures and different properties that are possible for near-α alloys.

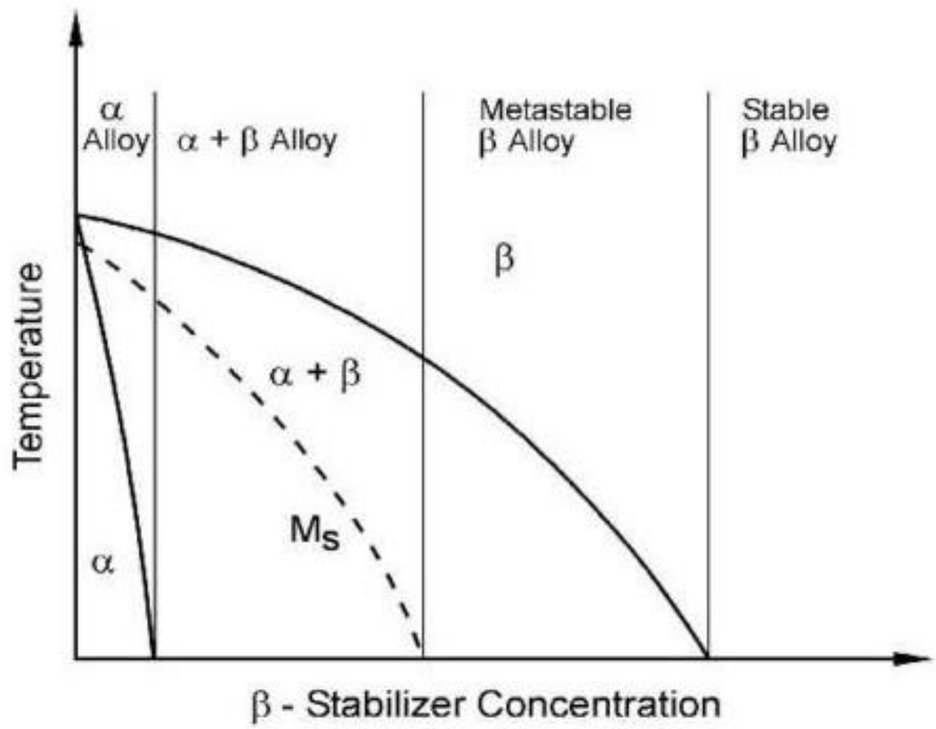

Figure 2. 4: Diagram pattern for the Ti alloy (Niinomi et al., 2015)

The phase diagram for titanium and niobium in Figure 2.5 show that the β transus temperature at 882°C for titanium metal. For new metal, for example Ti-40Nb, it can be sintered at temperature 1200°C. By referring to phase diagram for Ti-Nb alloy, it shows that β titanium would form in this alloy. The β titanium exhibit the BCC allotropic form of titanium. This occur due to there is a high amount of β stabilizer element added to the titanium alloy, which lower the β transus temperature of the Ti-40Nb alloy.

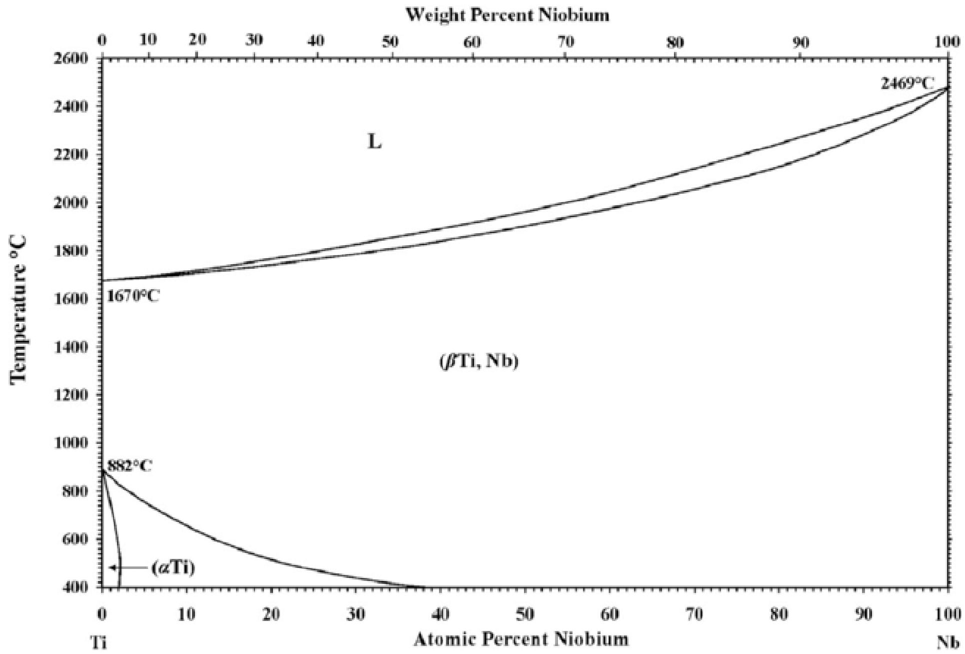

Figure 2. 5: Phase diagram for titanium and niobium (Fallah *et al.*, 2012)

2.5 Ti-Nb alloy as implant

Nowadays, Ti alloys with Nb and Ta addition have raised much attention because the addition of Nb and Ta can reduce the modulus of Ti alloy originated from the formation of β and α phase based on Chen et al. (2020). The formation of stable oxide such as Nb_2O_5 with the combination in Ti alloy can give high corrosion resistance in comparison with the standard implant metal such as Ti-6Al-4V.

For an implant material, highly inert and unreactive nature of its metallic surface which correspond to biomaterial is essential to make sure the compatibility of the metal implant and bone tissue. The compatibility between implant and bone is necessary even for the alloying element added. Implantable metallic biomaterial is focus on the metallic material to excel in corrosion resistance and higher biocompatibility. The Nb material is currently has increasing their popularity as an alloying element in medical field due to biocompatibility aspect of Nb surface. The good indicator of biocompatibility in Nb alloying element can be seen by the stability of readily form and protective oxide layer on Nb metal surface which is almost the same properties with the main element, Ti material. As studied by O’Brien, (2015), Nb alloying element does not diffused into the surrounding bone tissue demonstrated by elemental mapping technique which show no inflammatory response that indicated positive outcome of the soft tissue implant. It also mentioned that Nb surface show high resistance to oxide film breakdown in physical solution.

The Nb surface roughness also would influence the integration of the device within the surrounding bone tissue that would improve the bone to metal contact. The increased in global awareness of the biocompatibility of Nb has brought several positive advanced in recent year. The benefit of the Nb effect can be seen even when it is present within the material only as an alloying addition. The level of osteogenesis on Nb was similar to Ti and it had a performance comparable to pure titanium. The performance of Ti alloying material can be improve by Nb added that attribute to the formation of β-Ti.

2.6 Bioactivity of Titanium Alloy Implant

For biomaterial that compatible to be implant material, the cell that associated with the bioimplant material would give positive feedback. Figure 2.6 shows the classic foreign body reaction for biocompatible biomaterial. It shows that protein absorption occurs on the surface of biomaterial implant after 1 minute. Then, after one day of embedding of implant, neutrophil interrogation occurs which lead to macrophage interrogation after three day. Giant cell formation after one to two weeks would allow collagenous encapsulate the surrounding giant cell. Positive response from the cell to titanium alloy that is compatible with human body could promote bone bonding ability between the implant material and surrounding cell.

Commonly used Ti alloys such as Ti-6Al-4V, Ti-6Al-2Nb-Ta and Ti-15Mo-5Zr-3Al (Cui *et al.*, 2008) are an implant materials because they are biocompatible and provide bone bonding ability after surface modification. Surface modification include mechanical method, chemical etching, sol gel, oxidation and ion implantation. They are considered as the most attractive metallic materials for biomedical applications such as artificial knee joint, artificial hip joint, screw for fracture fixation, pacemakers, artificial hearts and cardiac valve prostheses. However, in the case of Ti alloys that contain aluminum and vanadium, they may cause a negative immunological response of organisms based on Fojt (2012).

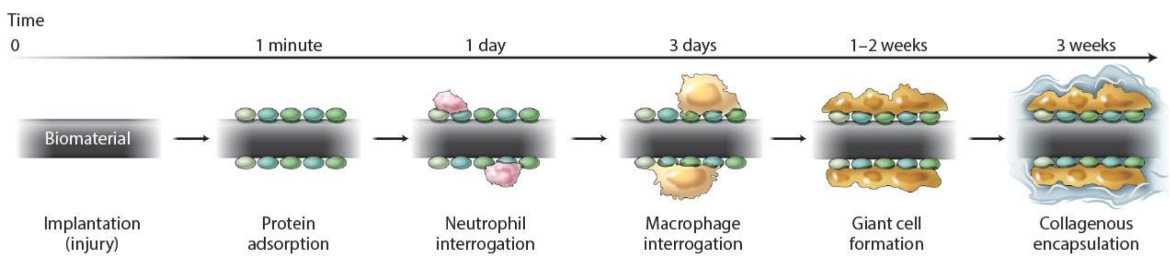

Figure 2. 6: Classic foreign body reaction for biocompatible biomaterial (Ratner, 2015)

Numerous of experimental work have been done to the Ti alloys in order to determine their significant different based on biological and physical properties. Their properties can be manipulated by their type alloying elements, composition of alloying element, processing method and surface treatment. Many researches on alloying element and processing method have been done in order to improve titanium alloy biocompatibility.

As a new developed Ti alloy that contain almost half of alloying element composition, Ti-40Nb alloy in term of biocompatibility, this type of alloy posses no cytotoxicity and give benefit to human osteoblasts based on Chen *et al.*, (2020). For Ti-40Nb alloy, high amount of Nb added will contribute to high amount of β stabilizer which promote the formation of β titanium. The buildup of β titanium alloy would improve the strength and fatigue resistance due to the strength and fatigue resistance of β titanium is higher than α titanium.

2.7 Surface treatment

Majority of metal implant including Ti alloy are unable to bond directly to the bone surface. Several studies based on the metallic materials surface has been conducted to improve the bioactivity of the metallic material. From the previous study on the Ti alloys, HA coating on the Ti alloys surface to improve the biocompatibility only give mechanically bonded HA layer that was able to peel off. HA coating tend to be thermally unstable that make it degradation of the coated HA layer is inevitable. Manipulation on their materials surface can improve the porosity, bone growth and mechanical fixation of the implant. Referring to Nishiguchi *et al.*, (2003), surface treatment of the implant can be done to enhance body integration include surface blasting to produce a rough surface and plasma spraying with metal powders, hydroxyapatite or hydroxyapatite/tricalcium phosphate.

To improve bioactivity of the metal implant, several surface modifications such as electrophoretic deposition, ion beam or radiofrequency sputtering and alkaline treatment has been done. However, alkaline treatment able to produce bioactive coating bonded chemically to the substrate, whereas the other attempt involves physical coating.

There is disagreement between in vivo and in vitro data for alkaline and alkaline heat treated Ti alloy for bond bonding strength. Alkali and heat-treated Ti metal were reported to bond to bone and was thought to be clinically applicable as an orthopaedic implant material. If alkali treatment without heat treatment could induce bone-bonding ability on Ti metal, it would be possible to prepare bioactive Ti implants by soaking pre-existing Ti implants in NaOH solution at the operating heater. As study by Nishiguchi et al., (1999) the detaching test showed that the bonding strength of alkali- and heat-treated Ti metal increased to 4.17 kgf at 16 weeks. In contrast, alkali treated titanium showed almost no bonding. Kim et al. reported that alkali treated Ti metal without heat treatment has the ability to form apatite on its surface in SBF just like alkali and heat-treated Ti metal does. They also showed that once an apatite layer is formed, the tensile strength of the apatite layer and the alkali-treated titanium is comparable to that of the alkali- and heat-treated ones. Thus, if an apatite layer is formed in vivo, there will be no difference in bone-bonding strength between alkali- and heat-treated Ti metal and that of alkali-treated Ti metal. As studied by Nishiguchi et al., however, the bone bonding strength of alkali-treated Ti metal was significantly lower than that of the alkali and heat-treated Ti metal, which indicates a discrepancy between the in vitro and in vivo data.

The discrepancy in vivo and in vitro data can be explained in a way that after soaking Ti in alkaline solution, alkaline titanate hydrogel layer would form in it surface.

However, the titanate hydrogel layer formed was unstable as it could lose its apatite forming ability during in vivo or implantation. Despite, it is not known at which stage the apatite forming ability is lost. Based on in vitro studied by Kim et al. (2013), the surface layer of alkaline treated Ti can be detached from its substrate using an adhesive tape. Thus, the surface layer is mechanically weak. They recommended that heat treatment should be added to form more stable alkaline titanate layer. Nishiguchi et al. (2003) stated that although alkaline treated Ti has the ability to formed apatite in SBF, it not suitable as a bone bonding material in practical use. However, alkaline treatment is important for the alkaline titanate layer formation that can induce the apatite layer on Ti alloy surface. Thus, both alkaline and heat treated is essential for inducing bioactivity in Ti. Alkaline and heat treatment enhanced bone formation at the interface between bone and Ti because alkaline heat treated Ti had direct contact to bone.

2.8 Alkaline Treatment and Its mechanism

Alkaline surface treatment is a rapid, environmentally friendly and highly efficient for surface modification compared to other modification method (Li *et al.*, 2014). As studied by Rastegari et al., (2019), alkaline treatment could alter and improving the wettability, apatite formation ability, corrosion resistance and biocompatibility of titanium alloy.

2.8.1 Mechanism of reaction

Mechanism for alkaline treatment of titanium has been proposed consists of few stages. There are passive oxide layers on the surface of titanium metal before alkaline treatment as shown in Figure 2.7. Then, the passive titanium oxide layer partially dissolves in alkaline solution due to corrosion attack on hydroxyl group (OH) during alkaline treatment as shown in equation 2.1. The reaction is assumed to continue and simultaneously proceed with following hydration of Ti metal as stated in equation 2.2-2.4 referring to Kim et al. (2013) and He et al. (2016). Equation 2.5 indicates further hydroxyl attack to hydrated TiO_2 that will produce negatively charge hydrated species on the titanium alloy metal surface. Then, the negatively charge species, $HTiO_3^{-}nH_2O$ would combine with the alkali ion in the aqueous solution which resulting in the formation of alkali titanate hydrogel layer.

$$TiO_2 + OH^{-} \rightarrow HTiO_3^{-} \quad (2.1)$$

$$Ti + 3OH^{-} \rightarrow Ti\,(OH)_3^{+} + 4e^{-} \quad (2.2)$$

$$Ti\,(OH)_3^{+}\ e^{-} \rightarrow TiO_2 \cdot nH_2O + 0.5H_2\uparrow \quad (2.3)$$

$$Ti\,(OH)_3^{+} + OH^{-} \rightarrow Ti\,(OH)_4 \quad (2.4)$$

$$TiO_2 \cdot nH_2O + OH^{-} \rightarrow HTiO_3^{-}nH_2O \quad (2.5)$$

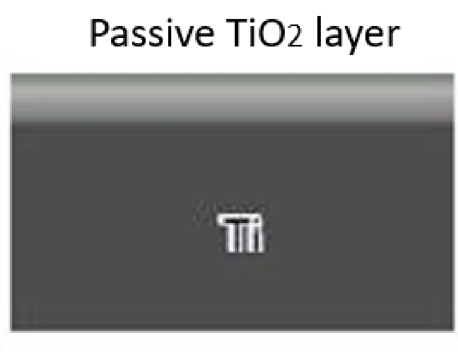

Figure 2. 7: Titanium oxide layer in titanium metal surface before alkaline treatment (Kokubo et al., 2017).

For Ti metal that soaked in the NaOH aqueous solution, the negatively charged species react with alkali ions, Na^+ in the alkaline aqueous solution as shown in Figure 2.8. The alkaline treatment by the NaOH aqueous solution resulting the formation of sodium titanate hydrogel.

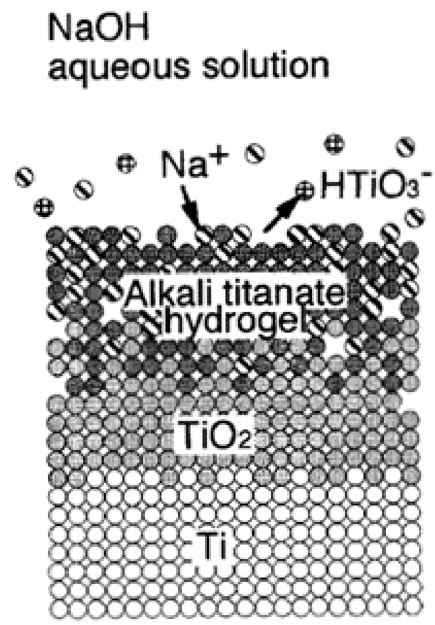

Figure 2. 8: Formation of sodium titanate hydrogel by alkali treatment (Kim *et al.*, 1996)

2.8.2 Alkaline Treatment Parameter

Alkaline treatment typically uses NaOH and KOH for surface modification of the titanium alloy. Theoretically, KOH aqueous solution is slightly reactive than NaOH aqueous solution (Hanib *et al.*, 2016). Alkaline treatment by other researchers commonly applies different temperature, concentration of alkaline aqueous solution and different soaking time. As studied by Kim *et al.*(2013), they used different temperatures of alkaline aqueous solution of NaOH and KOH for Ti metal. The Ti sample was soaked in alkaline solution at 37°C, 60°C and 90°C for 24 hours. The SEM observation for Ti coupon in