Chapter 2

LITERATURE REVIEW

This chapter briefly discusses the literature used for the present study. Firstly, the literature on biomaterial, its classification, and the essential criteria of biomaterial are briefly reviewed. The following section is reviewed conventional metallic biomaterial, focusing mainly on Ti-based metallic biomaterial used for load-bearing implant applications. Finally, the literature review of present and past studies is briefly given for a better understanding of the effect of different alloying elements on the properties of Ti alloy.

2.1 Biomaterial

Biomaterial term is a combination of two words, “Bio” and “material,” which means the material which is used for biological application is termed “Biomaterial.” The main characteristic of biomaterials is the capability to function in close proximity to a live organism (Chen & Thouas, 2015). The study of biomaterials has progressed to the point where it can now save the lives of people who are afflicted with a variety of diseases or who have lost their mobility as a result of the fracture of their joints and other body parts as a result of aging, accidents, or diseases. Thus, the biomaterial is also used to replace hard tissue and bone without adversely affecting the surrounding tissue. A biomaterial is also defined as a nondrug substance suitable for inclusion in the system which replaces the function of body tissue or organs (Ghasemi-Mobarakeh et al., 2019). The field of biomaterials has grown to save the lives of people with different diseases or who can't move because their joints or other parts have broken due to age, accidents, or diseases. In the last few decades, research and development of suitable biomaterials have saved millions of lives and made life better for many people. Researchers in this field come from many different fields, such as materials science, applied science, engineering, and medicine. As a result, this field is very multidisciplinary. From a business point of view, it has become a multibillion-dollar industry because the need for biomaterials has grown so much in recent years because people are living longer. From a scientific point of view, and mainly since nanomaterials have spread to all fields, research and development on biomaterials have taken on new forms.

Biomaterials have been utilized in several clinical applications, including orthopedics, dentistry, plastic, reconstructive surgery, ophthalmology, cardiovascular surgery, neurosurgery, immunology, histopathology, experimental surgery, veterinary medicine, and surgery. Consequently, this field necessitates knowledge and skills from numerous disciplines. The significant implants used in the fields mentioned above include intraocular lenses, contact lenses, vascular grafts, drug delivery compounds, wound healing materials, hip and knee implants, catheters, heart valves, stents, breast implants, dental implants, surgical instruments, pacemakers, renal dialyzers, and other devices (Chen & Thouas, 2015).

2.2 Basic requirement of a biomaterial

2.2.1 Biocompatibility

Alloying elements in an alloy should not provoke an immune response, inflammation, blood clotting, etc., when implanted in a human body. Corrosion and wear of alloying elements within the human body, followed by the response of the surrounding cells and tissues, are the two primary factors affecting biocompatibility (Watari et al., 2004; Williams, 2008). Because no material is completely inert when used as an implant in the living system for a reasonable amount of time, the first thought in designing and selecting a biomaterial is using elements already existing in the living system. This is done in order to avoid any adverse effects, either locally or systemically (Chen & Thouas, 2015).

2.2.2 Corrosion resistance

When a material is subjected to an aggressive environment, this process causes the material to degrade or deteriorate, which is referred to as corrosion (Eliaz, 2019). The implant's resistance to corrosion and longevity can be improved by giving the implant's surface a high-quality finish. The microstructure, grain size, and constituent elements of the alloy are the primary determinants of its corrosion resistance (Niinomi et al., 1999). The ideal metallic implant should be resistant to corrosion; as a result, the release of metal ions from a metallic biomaterial, which in turn causes toxic reactions. It should be minimized and remain at acceptable low levels under the harshest conditions and for more than 30 years (a long service) under normal physiological conditions (Chen & Thouas, 2015).

2.2.3 Mechanical properties

Any metallic implant used to replace a living body part, such as a bone, must be able to perform mechanically similarly to the original bone. Therefore, when designing and choosing a metallic implant, the mechanical characteristics of the implant, including its Young's modulus, toughness, and ultimate tensile strength (UTS), must be considered. Table 1 lists the mechanical characteristics of the three main types of metallic biomaterials: titanium-based alloys, cobalt-based alloys, and stainless steels (Long & Rack, 1998). The elastic modulus of the implant material should be near the elastic modulus of the bone; otherwise, it will cause a stress-shielding effect and finally affect the implant stability.

2.2.4 Wear resistance

The loss of material that occurs due to relative motion between two surfaces in contact with one another is called wear. Biomedical implants with lower wear resistance formed wear debris when exposed to contact with relative motion against the bone. This wear debris accumulates nearby tissues, which causes adverse health issues such as inflammation, infections, enzyme damage, and pain near the surrounding area. These adverse effects on the implant result in loosening by osteolysis. It can even lead to the implant completely dislodging (Mohammed et al., 2013). The wear between an implant and the surrounding bone is shown in Fig. 2.1.

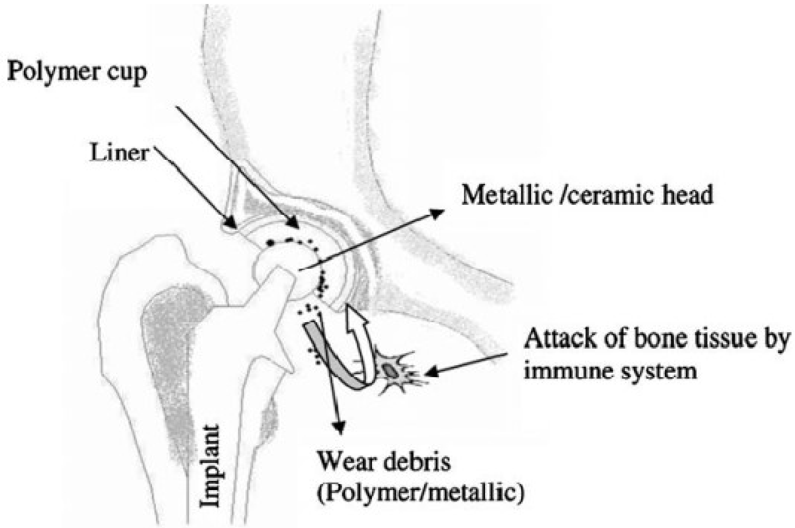

Fig. 2.1. Wear between the hip implant and human bone (Mohammed et al., 2013).

Because of this, the friction and wear characteristics of a biomedical Ti alloy play an extremely important role in determining how long an implant will last while it is being used. The surface of the alloy can be made harder, which will allow this goal to be accomplished.

2.2.5 Osseo-integration

Osseo-integration is another essential criterion for the selection of biomedical implants. It is defined as the process of new bone formation and bone healing. When an implant is inserted in the body, the surrounding tissue and cells must grow all around or inside the implant to give stability. The loosening of the prosthesis is caused by the non-integration of an implant surface into the surrounding bone and other tissue around the implant. Thus an implant should be capable of allowing the growth of new tissue and bone with proper integration inside the human body (Nasab et al., 2010). In order to achieve successful osseointegration, it is necessary to take into account a number of factors, including surface topography, surface chemistry, and surface roughness.

2.2.6 Antibacterial properties

The widespread use and success of Ti-6Al-4V and CP-Ti as implant alloys are due to their corrosion and wear resistance, low modulus, and osseointegration properties. Although titanium alloys are a strong contender for use as an implant material, none can inhibit bacterial colonization once they have been tainted. So, if contaminated materials are implanted during surgery, or if bacteria from the mouth grow on a dental implant that has already been put in, antibiotic treatments will be needed. However, these treatments might not work on bacteria that are resistant to antibiotics. As a result, in addition to using antibiotics during surgery, another option to limit the risk of infection is to design novel implants with antibacterial properties. Antibacterial rudiments (Cu^{2+}, Ag^{+}, and Zn^{2+}) have been incorporated into titanium and titanium alloys to generate antibacterial titanium alloys to improve the implants' antibacterial properties. Copper will be one of the utmost favorable elements in medical applications because of its low cost, high antibacterial efficiency, low cytotoxicity, and stable reactivity (R. Liu et al., 2018).

2.3 Conventional metallic implant material

The high reliability of metallic biomaterials in terms of mechanical performance has led to their widespread use in the fabrication of medical devices used to replace hard tissue, such as artificial hip joints, bone plates, and dental implants. With the advancement of technology from the 19th century, metals are used in biomedical applications. There are mainly three metals that are used widely as implant material to replace hard tissue and bone (i) stainless steel, (ii) cobalt-chromium alloys, and (iii) titanium and its alloys. The advantage and disadvantages of these materials are given below in brief:

2.3.1 Stainless steel

Since the 1920s, stainless steel has been used for medical implants, and among stainless steel, 316L is the most common biomaterial widely acceptable for biomedical applications. Although this alloy can passivate and form a passive oxide film that is predominately made up of chromium oxide, stainless steel tends to corrode inside the body under certain conditions, specifically in highly stressed and oxygen-depleted regions (Niinomi, 2008). Since 316L stainless steel contains an adequate amount of Ni; therefore, research has shown that Ni causes allergy inside the human body. Research is also going on to develop Ni-free stainless steel (Kuroda et al., 2007). In addition to this, 316L stainless steel also shows poor Osseo-integration when implanted into the legs of the pig and finally loosens the contact between bone and implant (Breme et al., 1988). Thus, the requirement for superior biocompatibility and more corrosion resistance alloy led to the development of new cobalt-chromium alloys for biomedical applications.

2.3.2 Cobalt-chromium alloys

The use of cobalt-chromium alloys for biomedical application is from the last 50 years, and it has been proven for better corrosion resistance than stainless-steel alloys. The high chromium contents form a strong passive layer in an aqueous solution to protect the surface from chemical attack. Furthermore, the element Co of the alloy, when released in the body, causes the toxic effect on the human osteoblast-like cell lines and inhibits the synthesis of type –I collagen, osteocalcin, and alkaline phosphatase in culture medium. Apart from this, both cobalt-chromium (240 GPa) and stainless steel (210 GPa) contain more Young's modulus than the human bone (12-30 GPa), which further causes the stress-shielding effect and finally causes bone resorption and loosening of the implant. Because stainless steel and cobalt-based alloys typically contain harmful elements such as Ni, Co, and Cr, commercially pure titanium and titanium alloys have been proposed as a replacement for stainless steel alloys (316L) and cobalt-based alloys (Chen & Thouas, 2015).

2.3.3 Titanium and its alloys

Literature survey shows that titanium and its alloys have been used as biomedical implants since the 1970s. Firstly, commercially pure titanium is used as an implant because it possesses higher corrosion resistance and can spontaneously form a passive oxide layer when exposed to a corrosive environment. CP-Ti is classified into grades 1 to 4 according to the American

Society for Testing and Materials (ASTM) (Nasab et al., 2010). Among all the four grades, grade 2 is the unalloyed or purest form used for dental implant application. However, the mechanical properties of CP-Ti are far better than the above discussed two alloys, but the high Young's modulus (110 GPa) than the bone further causes problems to the stability of the implant for long-life application. To decrease the elastic modulus of CP-Ti, 6% Aluminium and 4% Vanadium are alloyed with titanium, and grade 5 (Ti-6Al-4V) alloy with $\alpha+\beta$ phase was proposed to replace the CP-Ti (Geetha et al., 2009). Although the mechanical and chemical properties of this alloy are suitable to use as an implant but toxic element released by Al and V causes further problems for human cells (Ponader et al., 2010). To tackle this issue, many V and Al-free alloys were developed. Although these α-type and $\alpha+\beta$ type titanium alloys possess many advantages but higher elastic modulus compared to the bone causes issues for long-life application (Adell, 1981; Bombač, 2007; Sidambe et al., 2013). Now, nitinol (Ni-Ti) is also used for medical applications such as bone fracture fixtures, orthodontic wires, and dental intravascular stents (Geetha et al., 2009). The equal weight percentage of Ni and Ti gives superior properties like shape memory effect, biocompatibility, superior plasticity, and high damping capacity. The elastic modulus of porous nitinol is found near the elastic modulus of bone (Prymak et al., 2005). The porous nature of nitinol permits cells/tissues to penetrate with proper integration with the bone. However, the release of Ni element from nitinol was also reported in the study. Ni causes allergic reactions to the surrounding tissue. Based on the above developed metallic alloys, titanium alloy without Ni, Al, and V with low modulus can be the solution for present implant needs. The allotropic nature of the titanium gives the possibility to change the microstructure, physical, mechanical and chemical properties of the titanium alloys to use it as implant material according to application in the human body.

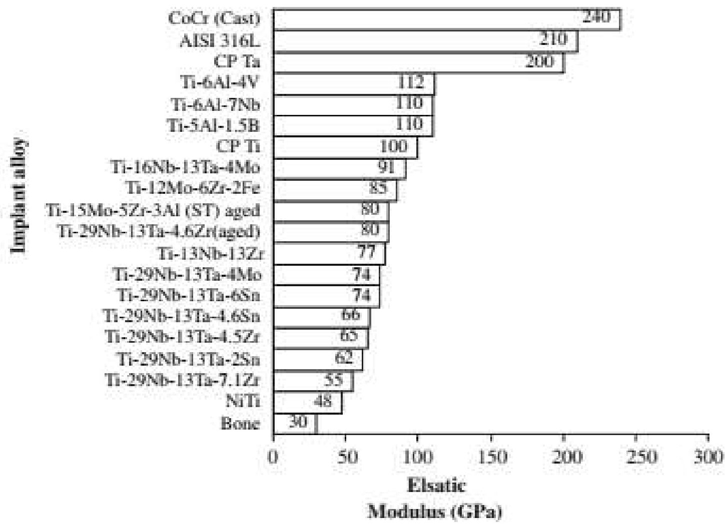

Fig. 2.2. Elastic modulus of alloy in comparison to human bone (Geetha et al., 2009).

2.4 Titanium properties and microstructure

Titanium was first founded in England by William Gregor in the year 1791 and named by Martin Heinrich Klaproth as the Titans of Greek mythology. Titanium constantly forms chemical bonds with other elements in nature, and it is the seventh most abundant metal in the world. Titanium is known for its high specific strength (strength-to-weight ratio), low density, and high ductility. Its low density compared to stainless steel and cobalt-chromium alloys make it favorable for implant application. Titanium exhibits two crystallographic structures depending on the temperature; below 882 °C, it behaves like hexagonal close pack structure (*hcp*) known as α-Ti, and above, it shows body-centered cubic structure (*bcc*) known as β- Ti. The primary effect of alloying additions to titanium is the modification of the transformation temperature and the formation of a two-phase field containing both alpha and beta phases (Akbarpour et al., 2022). The temperature at which alpha titanium transforms into beta titanium is known as the "beta transus" temperature, and it is the lowest temperature at which the alpha phase (*hcp*) completely transforms into the beta phase (*bcc*). The temperature at which this transformation occurs is significantly impacted by the addition of alloying elements for making titanium alloys. The elements like Al, B, C, O, and N are known as an alpha stabilizers because these elements increase the beta transus temperature, and Cu, Cr, Nb, Ta, Fe, V, Ni, Mo, W, and Co elements decrease the transformation temperature and regard as beta stabilizer elements. There are also some elements like Zr and Sn that do not alter the transformation temperature when alloyed with titanium. The phase diagram of Ti- alloys depends on the alloying element wt.% as shown in fig. 2.3.

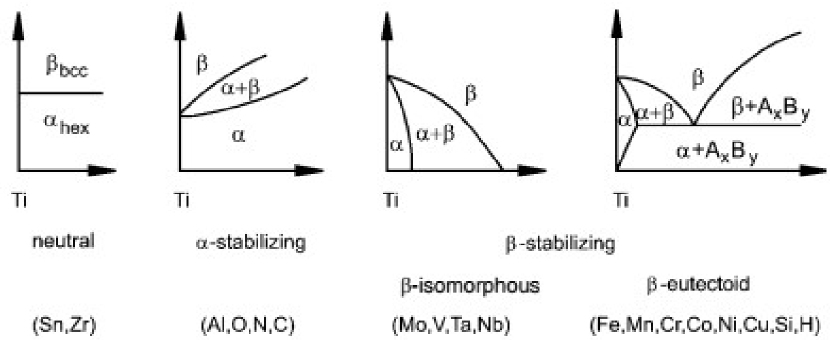

Fig. 2.3. An investigation of the effect of alloying elements on the phase diagrams of titanium alloys (C. Leyens and M. Peters, 2003).

Depending upon the crystallography and metallurgical compositions, titanium alloys are classified into four main groups (C. Leyens and M. Peters, 2003):

- Alpha and near-alpha alloys: These alloys have high corrosion resistance and contain elements that can stabilize the α-phase. The behavior of near-alpha alloys is quite comparable to that of conventional alpha alloys. This is because near-alpha alloys are analogous to alpha alloys but contain only limited amounts of β-stabilizer elements.
- Alpha+beta alloys: When α-stabilizer and β-stabilizer are both added to titanium, the resulting alloys have a microstructure that is a mixture of α+β phases even when cooled to room temperature. Ti-6Al-4V is the most well-known example of one of these alloys, as it is the most commonly used of its kind for structural applications as well as biomedical applications for its superior biocompatibility.
- Beta alloys: These alloys contain β-stabilizing elements and have a high strength up to intermediate temperature levels, are generally capable of being welded, and can be heat

treated easily. In the condition of having been treated with solution, the cold formability is typically excellent.

- Unalloyed Ti-alloys: These titanium alloys have a high resistance to corrosion but very little strength. Strength is improved through the addition of trace amounts of oxygen and iron.

2.5 Powder metallurgy technique for the development of titanium alloys:

Studies have shown that powder metallurgy, also known as PM, is an effective alternative technique for obtaining biomedical implants with controlled porosity. This method also has the advantage of allowing all steps to be performed in the solid phase. Controlling the processing parameters allows one to achieve the desired degree of powder consolidation (Manne et al., 2020). Powder metallurgy is the only route for making the tiny and complex shape of titanium alloy at a lower cost. It involves mixing metals in powder form with appropriate proportion, followed by compaction under pressure and sintering at elevated temperatures to allow diffusion to take place. It is a highly versatile process and allows to combine dissimilar materials, which any other process cannot do. Following thoroughly mixing the titanium powder with the alloying elements using an appropriate powder blender, the resulting mixture is then compacted under high pressure and sintered. This technique is known as "compaction and sintered." Sintering is a high-temperature and high-pressure treatment process that causes the powder particles to bond to each other with only a minor change to the particle shape. This process also enables the formation of porosity in the product when the temperature is properly controlled. Using this method, it is possible to produce titanium alloy parts with high performance at a low cost. The titanium alloy that is produced by powder metallurgy has several advantages over the titanium parts that are produced by other conventional melting processes. These advantages include comparable mechanical properties, near-net shape, low cost, fully dense material, minimal inner defect, nearly homogenous microstructure, good particle-to-particle bonding, and low internal stress (Ryan et al., 2006).

2.6 Peri-implantitis

Inflammatory processes in the tissues surrounding an implant are collectively known as peri-implant diseases. These diseases include peri-implant mucositis (also known as a soft-tissue inflammatory condition that affects implant sites even in the absence of signs of bone loss) and peri-implantitis (an inflammatory condition affecting implant sites that are also characterized by loss of peri-implant bone) (Albrektsson et al., 1994). Tannerella forsythia, Treponema denticola, and Porphyromonas gingivalis are some of the bacteria that have been linked to this disease (Mombelli et al., 2012). Other bacteria may also be involved. These bacteria are responsible for the loss of bone that occurs proximal to the implant, which can ultimately result in the failure of the implant. In its early stages, the disease manifests itself as gingival inflammation, which is then followed by bone resorption. Diabetes, smoking, and alcoholism have all been identified as factors that contribute to the progression of peri-implantitis (Deepak et al., 2019). Even though the rates aren't always the same, studies have shown that peri-implant diseases are common in people with dental implants. In a study that looked at people who had implants 9 to 14 years after the surgery, peri-implant mucositis was found in 48% of the implants and peri-implantitis in 6.6% of the implants (Roos-Jansåker et al., 2006). A separate study found that between 28% and 56% of implant recipients have peri-implantitis, and about 80% of implant recipients have peri-implantitis (Lindhe & Meyle, 2008). A systematic review of the literature also found that the rate of peri-implantitis is 10% for implant sites and 20% for patients in the 5 to 10 years after implantation (Mombelli et al., 2012). Figure 2.4 shows the schematic diagram of the progression of peri-implantitis in human teeth.

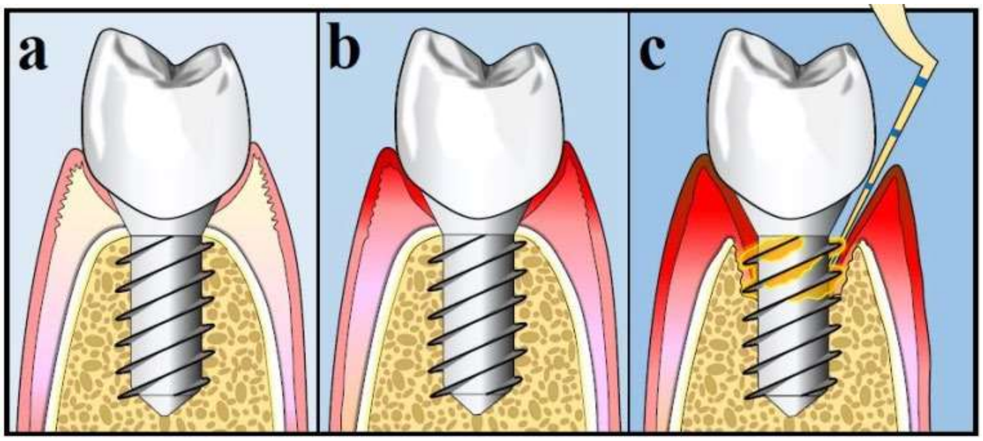

Fig. 2.4. Peri-imaplntitis in dental implant (a) healthy implant, (b) peri-implant mucositis, and (c) Peri-implantitis (Kormas et al., 2020).

2.7 Corrosion

The term "corrosion" refers to an irreversible chemical or electrochemical reaction that takes place at the interface between a metal and the surrounding environment. Corrosion is the rapid, progressive, or slow deterioration of metal properties, such as mechanical properties, surface aspect, and appearance, caused by the surrounding environment (Niinomi et al., 1999). The metal has three possible responses when placed in a corrosive environment, depending on the metal and the environment. The first state is one in which the metal is immune to corrosion. The second response occurs when the metal is in an active state, which will corrode and cause metal loss and or dissolution of one of the corrosive environment's constituents into the metal. The third state is the passive state, in which the metal can generate a passive oxide film on its surface, thereby reducing the corrosion rate.

2.7.1 Types of corrosion

Metals are susceptible to a wide variety of types of corrosion when they are placed in corrosive environments. The following is a brief overview of some of the most typical forms of corrosion:

- **Uniform corrosion** is also called “General corrosion,” in which the entire surface is attacked by the corrosion with equivalent intensity. Most surface effects caused by direct chemical attacks, such as acid, are uniform metal etching. General corrosion is visible to the naked eye and is simple to protect against by painting or coating.

- **Galvanic corrosion** is a type of corrosion that can occur when dissimilar materials come into contact with one another and are then subjected to a conductive solution. Their disparate potentials have a tendency to accelerate the rate of corrosion in the material that is more active. The galvanic cell is used to determine how well something resists oxidation and corrosion when exposed to air. In a galvanic cell, the metal with the highest potential is the anode, and its corrosion rate is lower or higher, respectively, than that of the other metals.
- **Pitting corrosion** is a type of localized corrosion that causes the formation of small cavities or holes on the surface of the metal. This type of corrosion is known as "pitting corrosion." The oxidation reaction in the pit causes the pH to drop, which in turn causes chloride ions to migrate to neutralize the metal ions' positive charge. This results in a more hostile environment locally, which speeds up the corrosion process and causes it to penetrate rapidly. Pitting corrosion is one of the most dangerous forms of corrosion, leading to equipment failure.
- **Crevice corrosion** is a type of localized corrosion that occurs when a metal surface is partially covered by the environment, for instance, in small openings, joints, or deep cracks. Anodic reactions occur preferentially in the crevice because of the difference in aeration with the bulk environment. Crevice corrosion can be reduced by optimizing a design or selecting suitable materials.
- **Fretting corrosion** occurs at the interface of contacting surfaces when there is a small amount of relative motion between them. Fretting corrosion can also be caused by moisture. Fretting corrosion can cause damage that weakens the oxide layer that protects passive metals, which can lead to increased corrosion.

- **Tribocorrosion** is the corrosion that is caused by both mechanical and chemical attacks on the surface of a metal. The protective passive layer is disrupted by the wear, and the surface is quickly attacked by the chemical reaction between the environment and the surface. This corrosion normally happens when the surface is exposed to wear and corrosion at the same time.

The metallic implant inside the body is always in contact with surrounding body fluid. The body fluid behaves like an electrolyte and causes corrosion to the surface of the implant. The different phases of titanium alloys lead to galvanic, pitting, and fretting corrosion. So, the newly developed alloys must be checked for the confrontation of the corrosion attack in suitable body fluid to use as implant material.

2.7.2 Corrosion of the titanium and its alloys

Titanium and its alloys show excellent corrosion resistance due to the presence of a passive oxide film composed of TiO_2. A good surface finish on the implant enhances its corrosion resistance and durability. The wear and corrosion resistance of an alloy is primarily determined by its microstructure, grain size, and composition (Atapour et al., 2011). The electrochemical behavior of titanium alloys is significantly influenced by the microstructure formed and the redistribution of the alloying elements during heat treatment. According to reports, the surface of +-microstructure Ti-6Al-4V alloy has good corrosion resistance due to the formation of TiO_2 and Al_2O_3 (Geetha et al., 2009). The literature survey shows that the anti-corrosive property of titanium and its alloys can be improved by the addition of alloying elements, which are incredibly stable in corrosive environments. For instance, adding Nb, Mo, Ta, and Zr would improve the corrosion response of titanium. Reports have shown that these alloying elements can stabilize the oxide layers in biological media and form a protective, stable oxide. Some examples of this oxide type include Nb_2O_5, Ta_2O_5, and ZrO_2 (Ho, 2008; MARECI et al., 2013; Y. B. Wang & Zheng, 2009; Zhou et al., 2005). It has been asserted that the corrosion resistance offered by titanium and its alloys with the aforementioned alloying elements is superior to that offered by wrought CoNiCr alloy and stainless steel 316L (Polmear et al., 2005).

According to the above review, titanium alloys should have excellent environmental stability due to the formation of a passive film on their surfaces. To have a surface with a high level of corrosion resistance, it is crucial to carefully select the alloying elements and heat treatment. From this current perspective, one of the goals of the present work was to examine the electrochemical behavior of various titanium alloys to learn how corrosion can degrade the surface of the alloy.

2.8 Tribology

Tribology is the science that deals with friction, wear, and lubrication. Consequently, tribology encompasses the physical and chemical properties of surfaces, including topography, the interactions of surfaces under load, and the modifications of these interactions when tangential motion is introduced. This section will briefly discuss friction, wear, and lubrication.

2.8.1 Friction

Friction is the resisting force that occurs during the relative motion of two objects. The asperities on the surface of mating objects resist the motion when coming in contact with each other. The response of any material to friction is determined by the structure of the material, the state of the surface of the material, and the nature of the contact, which might be corrosive, dry, or lubricated. Friction results in mechanical wear or degradation of the mating surfaces, so it is essential to control the friction to function the materials properly.

2.8.2 Wear

Wear is defined as the gradual loss of material from solid bodies in relative motion. This material loss occurs when the bodies are in contact with one another. The chemical interactions, mechanical properties of the rubbing surfaces, and testing conditions influence the wear process. During the wear process, material degradation will occur, which can ultimately result in failure. The rate of material degradation is primarily related to the surface of the two contact materials as well as the conditions of the surrounding environment. Material wear has been classified based on the operative mechanisms, with the major types of wear being (i) abrasive, (ii) adhesive, (iii) fatigue, and (iv) corrosive wear.

Adhesive wear occurs as a result of the formation of micro-junctions caused by welding between opposing asperities of two rubbing surfaces. In other words, adhesive wear occurs as a result of material transfer when two bodies slide against or press against each other. Asperities support the applied load on a body. Because the asperities have a smaller apparent area, the load on them is high enough to deform and adhere to each other, forming the micro-joints. The movement of the body causes the joints to rupture, and the rupture occurs from the non-deformed region. Material is transferred from the counter-body in this manner. Figure 2.5 shows the schematic diagram of the different types of wear mechanisms.

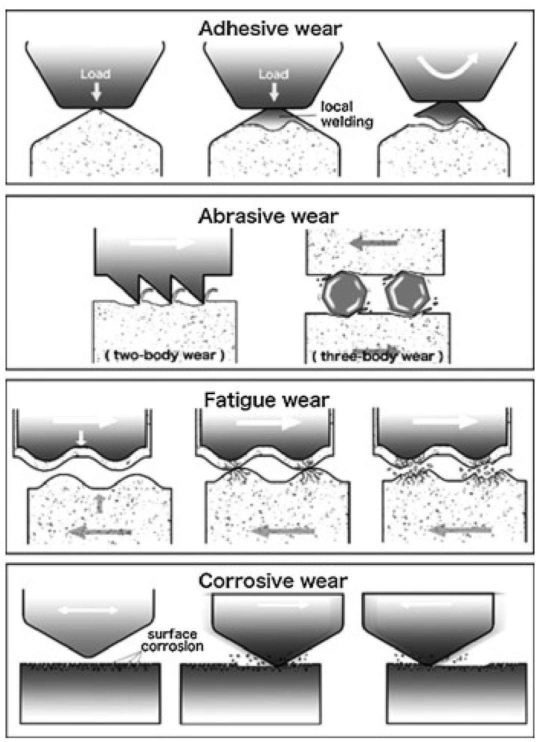

Fig. 2.5. Mechanisms of wear in general: adhesive wear; abrasive wear; fatigue wear; corrosive wear (Tsujimoto et al., 2018).

Abrasive wear happens when hard parts that stick out and hit soft parts cause the soft parts to wear away. It depends on the type of contact and where it takes place. When there are two parts that rub against each other, this is called two-body wear. In this type of abrasive wear, sharp edges on the hard body cause the soft body to lose material as it slides. When hard particles get stuck between two surfaces and wear away the material, this is called third-body abrasion.

The repeated stressing and relaxing of material cause **fatigue wear**, which can, over time, lead to the formation of micro-cracks at or below the surface. These micro-cracks increase due to the cyclic loading and finally detach from the surface, resulting in loss of material. **Corrosive wear** occurs when a corrosive medium contributes to surface deterioration through corrosion or oxidation during the sliding process. It is also possible to experience this phenomenon when dry sliding or when exposed to a gas. An overabundance of anti-wear agents or some other chemical interaction can also cause corrosive wear. This type of wear can also be caused by exposure to extreme environmental conditions, such as high heat, salt water, or a highly acidic or basic medium.

2.8.3 Tribology of titanium and its alloys

Titanium and titanium alloys have been studied extensively over the past few decades because of their unique properties, including high strength, lightweight, biocompatibility, and excellent corrosion resistance. However, research has shown that the tribological performance of titanium is inferior. Dong et al., 1999, showed in their findings that there are many factors involved in the friction component of titanium. Titanium shows a high friction coefficient, which is the primary reason for its poor wear resistance. Sathish, 2011, found that metal with low tensile and shear strength exhibits high friction coefficient than higher-strength material. Several new studies on the tribological properties of different types of titanium alloys have shown that the wear resistance and friction coefficient have been improved in different ways. Titanium alloys' tribological behavior can be significantly changed by the passivity and repassivation that happen when an oxide film forms during rubbing. The tribological behaviour of titanium alloys, as well as the influence of the passive oxide layer during rubbing, has been the subject of a number of studies (Alam & Haseeb, 2002). The authors found in this study that the $\alpha''+\beta$ microstructure of Ti-24Al-11Nb has the ability to form a protective oxide layer during rubbing, which results in improved wear resistance of the alloy. Choubey et al., 2004, studied the tribological behaviour of the CP-Ti, Ti-6Al-4V, Ti-5Al-2.5Fe, Ti-13Nb-13Zr, and Co-28Cr-6Mo materials. They found that Ti-5Al-2Fe had the lowest coefficient of friction out of all the materials they studied. The materials used in the total hip prosthesis, like AISI 316L SS and Ti-6Al-7Nb, were tested for wear study against the 100C6 chromium ball under the load of 3, 6, and 10 N. Furthermore, they discovered that friction and wear characteristics between the two alloys were comparable (Fellah et al., 2014). The coefficient of friction showed no appreciable change with the sliding speed in Ti-6Al-7Nb, but it did increase linearly with speed in AISI 316L SS.

The above literature survey shows that the wear resistance of titanium alloys can be enhanced with alloying elements under different conditions. Adding Nb to Ti alloys improves their wear resistance and increases their COF. Therefore, one objective of the present work is to investigate the impact of tribological behavior on the wear behavior of developed titanium alloys.

2.9 Effect of alloying Cu and Nb to titanium alloys on microstructure, mechanical properties, corrosion behavior, wear resistance, antibacterial property, and cytocompatibility

Copper is known for its outstanding corrosion resistance, high ductility, excellent biocompatibility, and superior antibacterial properties. Researchers have found that adding Cu to make Ti-Cu alloys, which are used in dentistry and orthopedics, lowers the liquidus temperature below the melting point of Ti and increases the hardness, strength, and wear resistance. It also improves bio-corrosion resistance, antibacterial activity, and biocompatibility by making different Ti_xCu_y intermetallic compounds with different microstructures (Akbarpour et al., 2022).

Nb is well known beta-stabilizing element known for its superior biocompatibility. It has been shown that Nb can reduce the transus temperature. Ti has a β transus temperature of 882 °C, and this temperature drops with increasing Nb content. The addition of Nb to the Ti increases the strength of the alloy by solid solution strengthening mechanism (Han et al., 2015). It was also reported that Nb reduces the elastic modulus of Ti alloys when added in the range of 10-20 mass %. If the amount of Nb in the alloy is between 14 and 34 mass%, then both α and β phases will be found in the material (Han et al., 2015). In an alloy, the proportion of the phase will increase in proportion to the amount of Nb present in the alloy. Niobium is thought to play a minor biological role in the human body; however, certain compounds containing niobium, such as niobium chloride and niobates, are toxic. Niobium's role in the human body is not well understood. Some important literature review of earlier study is given below in brief:

Chirico et al., 2022 use powder metallurgy to develop two innovative, inexpensive Ti-5Fe-25Nb and Ti-40Nb in wt.% Ti alloys with lower elastic modulus. In order to assess the improvement in wear resistance, dry sliding tests were carried out against an alumina ball while applying 10 N and 20 N loads. Ti-Nb-Fe system samples exhibit more excellent wear resistance than Ti-Nb system samples. This is explained by the fact that Ti-5Fe-25Nb alloys are stronger than Ti-40Nb, have higher hardness, and have less porosity.

Shivaram et al., 2021 prepared the porous Ti-20Nb-5Ag (wt. %) alloy by PM route and obtained up to 43% porosity after sintering in high vacuum furnace. SEM image reveals that the size of pores is in varying micrometer ranges. The tribocorrosion study of the sample was tested in SBF against the alumina ball under varying loads from 1 N to 10 N. The corrosion potential was found to be decreasing while the corrosion current density was increasing with increasing applied loads, as measured by the potentiodynamic polarisation method. According to the findings, the newly developed porous alloys of Ti-20Nb-5Ag have superior tribocorrosion properties in simulated body fluid.

Duan et al., 2021 coated the Ti-6Al-4V alloy with Ti-Si-xCu coatings (x = 5, 10 and 15 wt. %) by laser cladding method. According to the findings of XRD, new Ti_5Si_3 and TiCu phases with micro-textured morphology were formed, which ultimately led to an improvement in the surface's wettability as well as its resistance to bio-corrosion. Additionally, the corrosion resistance of coated samples was found to vary with the amount of copper present; higher corrosion resistance was achieved by reducing the amount of copper present in the coatings. All of the Ti-Si-xCu (x = 5, 10, and 15) coated samples performed well in biological tests, but the cell reactions are highly elicited varied. The TS-xC coated samples presented excellent antibacterial performance, particularly the coatings with a higher content of Cu addition. All TS-xC coated samples had significantly higher rates of cell attachment and proliferation compared to CP-Ti coated samples. Therefore, the observed biological improvements for the TS-xC coated samples were due to the change in the surface's morphology as well as its chemical composition.

Tao et al., 2020 prepared the porous Ti-3Cu alloy using Mg space holder by the microwave sintering process. In order to compare the pore size, microstructure, mechanical, corrosion, and antibacterial properties, the alloy was sintered at a varying temperature from 650 °C to 800 °C. According to the findings, the porous Ti-3Cu alloys are composed of the α-Ti phase and the Ti_2Cu phase, and when the sintering temperatures rise, the intensity of the Ti_2Cu diffraction peaks increases. The elastic modulus of the alloy was obtained very close to the human cortical bone, while the compressive strength was much higher than the human cortical bone. Ti-3Cu sintered at 800 °C showed the maximum corrosion resistance in SBF. The antibacterial property of Ti-3Cu was obtained around 100% when tested in S. aureus and E. coli bacteria.

Tan et al., 2019 observed the effect of niobium content on the microstructure and mechanical properties of new Ti alloys, including Ti-23Nb-7Zr, Ti-28Nb-7Zr, and Ti-33Nb-7Zr (wt.%) in their study. Niobium promotes the formation of α´´ and β phases of titanium. The morphologies of the α´´ phase are needle-like, while β is distributed equixially in the alloy. The hardness and Young's modulus of the alloy decrease with increasing Nb percentage in Ti-7Zr. As the Nb concentration rises, the softer "martensitic structure" volume proportion in Ti-28Nb-7Zr increases, lowering the alloys' hardness. When the Nb content is raised to 33 wt.%, as in Ti-33Nb-7Zr, where the β-phase almost completely covers the surface, the hardness is further lowered. When Nb is raised from 23 weight percent to 33 weight percent, this also contributes to a decreased level of Young's modulus from 35.6 GPa to 29.0 GPa. Young's modulus and hardness characteristics of Ti-xNb-7Zr alloys are strongly influenced by Nb concentration.

Wang et al., 2019 in their findings added 3, 5, and 7 wt.% to Ti, which were fabricated as novel biomaterials for dental application. The Ti-Cu alloy was annealed at different temperatures to get different phases and microstructure. Typical microstructures, α-Ti+Ti_2Cu, α-Ti+ transformed β-Ti, and transformed β-Ti were obtained at elevated temperatures. The results showed that the ductility was highest in the Ti-Cu alloys with the microstructure of α-Ti+Ti_2Cu, followed by the Ti-Cu alloys with the microstructures of α-Ti + transformed β-Ti, and finally, the Ti-Cu alloys with the microstructure of completely transformed β-Ti. However, the ductility decreased significantly with increasing Cu content because of the increased amount of Ti_2Cu, which strengthened both solid solution and precipitation.

E. Zhang et al., 2016 compared the mechanical, anti-corrosion, and antibacterial behavior of HIP-sintered and arc-melted Ti-5Cu and Ti-10Cu alloy. The arc melted sample further heat treated at 900 °C for varying times. The copper element showed a strong solid solution-strengthening ability; also, the Ti_2Cu enhanced the hardness and reduced the elastic modulus of the alloy. Sintered Ti10Cu sample showed the lowest corrosion current density compared to others. The antibacterial properties of Ti-Cu alloys were enhanced by their high Cu content and fine Ti_2Cu precipitate.

Pina et al., 2016 analyzed the microstructure, electrochemical, and wear behavior of different titanium-copper biomedical alloys (Ti-xCu, x= 3, 7.1, and 12 wt.%) by powder metallurgy route for dental application. The samples were compacted in an automated press using uniaxial pressure of 700 MPa and sintered at 950 °C for 4 hours under vacuum. In the alloy, copper promotes the production of Ti_2Cu intermetallic, increases the quantity of eutectoid at the grain boundary, and raises the hardness of the alloys. When compared to cPTi, EY (elastic modulus) for Ti-xCu alloys is lower, and hardness increases linearly as copper content increases in the alloy. With increasing in Ti_2Cu intermetallic, which also reduces wear volume, and the overall material loss from wear and corrosion also decreases.

Cordeiro et al., 2017) developed the Ti-5Zr and Ti-10Zr, added 35%Nb in both by arc melting process and compared the property of all four alloys with CP-Ti and Ti-6Al-4V. The mechanical properties and microstructure of the alloy changed with the addition of Nb. The Nb addition reduces the hardness and elastic modulus of Ti5Zr and Ti10Zr. However, the corrosion-resistant property of the binary Zr alloy is obtained better compared to the ternary Nb alloy. The protein absorption ability of the ternary alloy also improved with the addition of niobium.

S. Wang et al., 2015 developed titanium alloys by adding 5 wt.% copper into CP-Ti and Ti-6Al-4V and tested the friction and wear response against ZrO_2 ball in bovine serum using a ball on disk tribometer. Due to the precipitation of Ti_2Cu, the tribological results for both Ti-5Cu and Ti-6Al-4V-5Cu alloys demonstrated an improvement in friction and wear resistance. The findings also showed that when articulated with hard zirconia, both cPTi and Ti- 5Cu performed better in terms of wear resistance than Ti-6Al-4V and Ti-6Al-4V-5Cu due to differing wear mechanisms.

Zhang et al., 2015 in their research, developed Ti-15Mo-xNb (x= 0, 5, 10, and 15 mass fraction) by vacuum arc melting process. The effect of Nb addition was studied to evaluate the change in microstructure, mechanical properties, and castability of Ti-15Mo alloy. All of the alloys are composed of a single beta-phase, as shown by phase analysis and microstructure observations, and the equiaxed beta-grain becomes finer as the Nb content rises. The compressive strength and yield stress increase with the addition of Nb. Also, the hardness of the alloy decreases with Nb inclusion and the minimum value obtained for Ti-15Mo-15Nb. The castability test demonstrates that the castability of the Ti-15Mo-xNb alloys reduces following Nb addition. The highest castability is seen in the Ti-15Mo alloy, 92.01%. The castability of the Ti-15Mo-xNb alloys definitely decreases with increasing Nb content, and Ti-15Mo-15Nb has only 47.63% castability.

Han et al., 2015 in their work explored the relationship between phase/microstructure and various properties of Ti-x%Nb alloys, the effects of Nb addition (5-20 wt.%) on the microstructure, mechanical properties, corrosion behavior, and cytotoxicity of Ti-Nb alloys. According to the findings of XRD and optical microscopy, the Ti-5Nb alloy had the α and β phases. In Ti-xNb alloys (x = 10–20 wt.%) with $\alpha+\beta$ phases, the ω phase was seen, and the ω phase grew as Nb content grew. The presence of β and ω phases in the alloy also increases the Vickers hardness value. While the elastic modulus increased during the ω phase, it decreased during the β phase. In high temperatures, the cast Ti-xNb alloy demonstrated superior oxidation protection than CP-Ti.

J. Liu et al., 2014 developed four binary alloys Ti-xCu (x= 2, 5, 10, 25 wt.%) by the hot isostatic process at 580 to 1080 °C under a high vacuum environment. The peaks of the Ti_2Cu phase in XRD increase with the increasing amount of copper, and at 2 wt.% Cu, the hardness reaches a high value of 55HRC. The hardness is not appreciably altered by further increases in Cu concentration. The elastic modulus was found to be maximum for Ti-2Cu (25-28%) and lowest for another sample (15%). The author concluded in his research that a minimum of 5% copper is essential for getting excellent antibacterial properties against S. aureus and E. coli. Bacteria.

Ren et al., 2014 fabricated a series of copper-bearing titanium alloy Ti-6Al-4V-xCu (x=1, 3, and 5 wt.%) to reduce the bacterial infection using a strong antibacterial ability of Cu element by arc melting process. The lowest $i_{corr,}$ i.e., maximum anticorrosive behavior, showed by Ti-6Al-4V-3Cu, and the pitting potential of all the samples was obtained approximately similar against physical saline 0.9% NaCl solution. Moreover, all the samples showed excellent anticorrosive response compared to Ti-6Al-4V. The cell viability and cytotoxicity behavior of the Ti-6Al-4V-3Cu were similar to Ti-6Al-4V. Also, the no of colonies of the cultured bacteria obtained minimum with increasing Cu concentration in Ti-6Al-4V.

E. Zhang et al., 2013 in their research, developed the binary Ti-10Cu alloy by hot pressing at 850 - 1050 °C. The relative density of the alloys reached 99.7% of the theoretical density and compressive strength to 1707.9 MPa. The XRD and SEM report showed the presence of α- Ti and Ti_2Cu. The antibacterial property was tested in S. aureus and E. coli, and about 100 % antibacterial rate was obtained. The corrosion current density was in the range of (0.506-0.177μA/cm^{-2}) in 0.9% NaCl. Compared to cPTi, the Ti-10Cu sample showed better mechanical properties, good anticorrosive behavior, and excellent antibacterial property.

2.10 Formulation of the problem and objective of the study

This section of the thesis presented a comprehensive analysis of the published literature on the development and investigation of different properties of titanium alloys for use in the biomedical field. Till now, numerous binary and ternary titanium alloys have been developed by several researchers for biomedical applications. These studies are majorly focused on the development of alloys, microstructure, alpha and beta phase, mechanical, and corrosion properties. However, very limited literature on ternary titanium alloys is available by adding copper and other alpha or beta-stabilizer elements to use for biomedical applications.

So, in the present study, the ternary titanium alloys are developed for the complete study to use as implant application. The requirement for an antibacterial metallic implant is currently the need of the implant industry. There are very limited research works have been done so far on the development of ternary titanium alloys with alloying copper elements. Copper makes the Ti_xCu_y compound with titanium, which enhances the antibacterial property, cytocompatibility, and mechanical properties of the titanium alloys.

Also, these alloys are developed by the conventional melting process. The requirement of the beta phase of titanium is essential to make the implant corrosion and wear-resistant. So based on the exhaustive literature review, the following objectives have been decided to achieve in the present study:

- To develop a novel $\alpha + \beta$ titanium alloy with Ti_xCu_y compound for biomedical application via powder metallurgy route.
- Phase and microstructural analysis of the above aforementioned developed alloy.
- Mechanical and physical behavior testing of the alloys for:
    - Micro-hardness value,
    - Compressive strength, and
    - Density measurements
- The corrosion resistance of the developed alloy in simulated body fluid by electrochemical corrosion measurement techniques for the study of:
    - Open-circuit potential behavior
    - Electrochemical Impedance Spectroscopy analysis, and
    - Potentiodynamic polarization behavior
- Wear resistance testing by the ball on disk on bio-tribometer against zirconia ball at different loading in SBF.

- Antibacterial testing in *Staphylococcus aureus* and *Escherichia coli* bacteria.
- Cell culture, proliferation, and viability test in MG-63 (human osteosarcoma) cells.