Chapter 2

LITERATURE REVIEW

This chapter presents a literature survey on the use of biomaterials for load-bearing implants, specifically focusing on orthopedic and dental applications. It covers both historical and modern perspectives on biomaterials development. The chapter discusses the limitations of existing implant materials and highlights advancements in titanium alloys for load-bearing applications. Additionally, it summarizes the research gaps and motivations for the current study, outlining the defined objectives.

2.1 Historical perspective of biomedical implants

The history of implant materials traces back to ancient times and has evolved significantly through the centuries, reflecting advances in materials science, medicine, and technology. Evidence of early attempts at implants can be found in ancient Egyptian, Rome, and Incan civilizations, where materials like shells, metals, wood, and stones were used to replace missing teeth and bones fixation [67,68]. In recent decades, this evolution has accelerated due to advancements in materials science, medical techniques, and biocompatibility research. As the present study primarily focuses on orthopedic and dental implants, below is a detailed overview of the historical development of these implant materials.

2.1.1 Historical perspective of orthopedic implants

The history of orthopedic implants dates back to ancient times when early humans sought ways to repair fractured bones. However, modern orthopedic implants, as we know them today, have their roots in the advancements of the 19th and 20th centuries. Here’s an overview of the key developments in orthopedic implant history:

Ancient practices

The earliest evidence of orthopedic interventions comes from ancient Egypt and Rome, where primitive techniques were used to treat fractures and dislocations using materials like wood and metal. Ancient Egyptian mummies have been found with metal rods used to stabilize bones.

18^{th} to 19^{th} century

The century marked a transformative period in surgical practices with the introduction of anesthesia and antisepsis, significantly enhancing the safety of surgeries and improving recovery rates. Concurrently, this era witnessed the advent of orthopedic implants, beginning with the innovation of metal plates and screws for the internal fixation of fractures. Notable pioneers such as Sir Robert Jones and Sir William Arbuthnot Lane played crucial roles in developing these techniques, laying the foundation for modern orthopedic surgery and the effective treatment of musculoskeletal injuries.

20th century

In 1928, German surgeon Gerhard Küntscher introduced the intramedullary nail for fracture fixation, while in the 1960s, British orthopedic surgeon Sir John Charnley pioneered modern hip replacement by developing the first total hip replacement system using stainless steel and ultra-high-molecular-weight polyethylene (UHMWPE), laying the groundwork for contemporary joint replacement surgeries.

21st century

Recent advancements in materials science have facilitated the use of titanium and cobalt-chromium alloys in orthopedic implants, offering superior strength and biocompatibility compared to earlier metals. The 21st century has introduced innovative technologies, such as computer-assisted surgery and 3D printing, enabling the customization of implants tailored to individual patient anatomy. Furthermore, ongoing research into novel biomaterials and bioactive coatings aims to enhance osseointegration, reducing the risk of implant rejection and improving long-term outcomes. Current trends also focus on the development of biodegradable implants that provide temporary support during the healing process, thereby eliminating the need for subsequent removal surgeries.

2.1.2 Historical perspective of dental implants

The history of dental implants is a fascinating journey that reflects the evolution of dental practices and the relentless pursuit of solutions for tooth loss. From ancient attempts at tooth replacement to modern titanium implants, the field has undergone significant advancements driven by innovations in materials and surgical techniques.

Ancient civilizations

The origins of dental implants can be traced back thousands of years. Archaeological findings indicate that ancient civilizations, such as the Egyptians and the Mayans, made attempts to replace missing teeth. Evidence suggests that ancient Egyptians used materials like ivory and metal to create rudimentary dental implants, with some mummies discovered with these objects embedded in their jawbones. Similarly, the Mayans were known to have used seashells and other materials as substitutes for lost teeth [68].

18th to 19th century

By the 18th century, dental practices had formalized, leading to more sophisticated tooth replacement techniques. Dentists in Europe began using metals like gold to create artificial teeth, but these early dental implants faced challenges, including poor integration with surrounding bone and high rejection rates. The 19th century brought significant advancements, notably with Pierre Fauchard's publication of "Le Chirurgien

Dentiste" in 1861, which detailed various tooth restoration methods, including metal implants. Despite these innovations, the success rates of early dental implants remained low due to issues such as infection and inadequate bone integration.

20th century

The modern era of dental implants began in the 1950s when Swedish orthopedic surgeon Dr. Per-Ingvar Brånemark discovered that titanium could integrate directly with bone tissue, a process he named "osseointegration." This groundbreaking finding laid the groundwork for modern dental implants. In 1965, Brånemark placed the first successful titanium dental implant in a patient, marking a significant milestone in the field. His pioneering work demonstrated the stability and longevity of titanium implants for tooth replacement. By the 1970s, Brånemark's techniques had gained widespread acceptance, establishing titanium implants as the gold standard in dentistry.

21st century

The 21st century has seen significant advancements in dental implant technology, with a focus on customization, biocompatibility, and improved success rates. Innovations like computer-aided design (CAD) and 3D printing enable the creation of patient-specific implants tailored to individual anatomical needs, improving fit, function, and long-term outcomes. Ongoing research into biomaterials and bioactive coatings continues to enhance osseointegration, with materials like zirconia being explored for both their aesthetic properties and biocompatibility. Furthermore, advancements in biodegradable implants are gaining attention, providing temporary support during healing and reducing the need for removal surgeries, contributing to better overall success in dental implant procedures.

2.2 Conventional metallic materials for biomedical implants and their limitations

Metallic materials are preferred over ceramics and polymers for biomedical implants due to their superior mechanical strength, durability, and resistance to fatigue, which are essential for long-term stability in load-bearing applications like orthopedic and dental implants. Metals such as titanium alloys also exhibit excellent biocompatibility, corrosion resistance, and the ability to integrate with bone (osseointegration), making them ideal for implants. While ceramics offer good biocompatibility and polymers provide flexibility, their limitations in mechanical strength and wear resistance make metals the more reliable choice for critical structural implants. The major metallic materials used in present for biomedical implants are 316L stainless steel (SS 316L), cobalt chromium (Co-Cr) alloys, titanium and its alloys (cpTi and Ti-6Al-4V). These materials are widely employed due to their favorable mechanical properties, corrosion resistance, and biocompatibility. The most common existing materials with their properties are given in Table 2.1. However, each has limitations:

Titanium and its Alloys (e.g., Ti-6Al-4V)

Titanium and its alloys (e.g., Ti-6Al-4V) offer excellent biocompatibility, strong corrosion resistance, and a high strength-to-weight ratio. However, titanium alloys can release toxic aluminium (Al) and vanadium (V) ions, potentially causing long-term biological issues. Additionally, they exhibit lower wear resistance compared to certain other metals.

Stainless steel (SS 316L)

Stainless Steel 316L is cost-effective, easy to fabricate, and offers adequate mechanical properties. However, it is susceptible to long-term corrosion in chloride-rich environments, such as the human body, which may lead to metal ion release and potentially cause inflammatory reactions.

Cobalt-chromium (Co-Cr) alloys

Cobalt-chromium (Co-Cr) alloys offer excellent wear and corrosion resistance, high strength, and fatigue resistance, making them durable in biomedical applications. However, they may cause allergic reactions due to cobalt ion release, are difficult to fabricate, and their high stiffness can lead to stress shielding, potentially impacting bone health.

These limitations have led to ongoing research into newer metallic alloys, coatings, and surface modifications to enhance their performance and safety in biomedical applications.

2.3 Titanium and its alloys: An overview and advancements

Titanium was first discovered in 1791 by William Gregor in England and later named by Martin Heinrich Klaproth after the Titans of Greek mythology. It is the seventh most abundant metal in the Earth's crust and is valued for forming strong chemical bonds with other elements. Due to its high strength-to-weight ratio, low density, excellent corrosion resistance, and superior biocompatibility, titanium and its alloys are widely used in aerospace, automotive, chemical processing, and especially biomedical industries [74]. In biomedical applications, titanium is classified as a bioinert material and has shown better long-term tissue compatibility than biotolerant materials like SS 316L and Co-Cr alloys [75]. Titanium-based biomaterials such as commercially pure titanium (cpTi) and Ti-6Al-4V alloy are widely used in load-bearing implants including dental fixtures and joint replacements. cpTi is valued for its corrosion resistance and biocompatibility, while Ti-6Al-4V offers improved mechanical strength. However, Ti-6Al-4V is also associated with potential cytotoxic effects due to the release of aluminium and vanadium ions in physiological conditions [76].

Table 2.1: Conventional metallic materials and their mechanical, biological, tribological, and corrosion response

Materials	**Mechanical properties**				**Biological response**	**Tribological response**	**Corrosion resistance**	**Conclusion**	**Refer ences**
Metals and its alloys	Elastic modulus (in GPa)	Tensile strength (in MPa)	Compressive strength (in MPa)	Hard-ness (VHN)					
Stainless steel (316L)	193-200	480-1000	480-620	140-248	Cytotoxic (Ni ions)	Excellent	Inferior to titanium	Obsoleted	[69–71]
Co-Cr-Mo alloys	240	900-1540	948-1943	335-385	Cytotoxic (Cr ions)	Excellent	Excellent	Obsoleted	[71,72]
Gold	97	552	_	188-216	Good	Poor	Good	Obsoleted	[71]
Magnesium	41	87-180	40-140	45-95	Degrades	Poor	Poor	Biodegradable	[71]
cpTi	102-104	240-550	130-170	165-206	Good	Poor	Excellent	Lack in properties	[73]
Ti-6Al-4V	114	860-965	896-1172	330-380	Cytotoxic	Higher than cpTi	Excellent	Need an alternative	[71]

Additionally, titanium-based materials exhibit significantly lower elastic modulus (~105-110 GPa for cpTi and Ti-6Al-4V) compared to stainless steel (~200 GPa) and Co-Cr alloys (~220-240 GPa), which helps to reduce stress shielding in orthopedic applications. However, this modulus is still substantially higher than cortical bone (10-30 GPa), necessitating the development of novel alloys with further reduced stiffness [61]. In this context, novel titanium-based alloys and high entropy alloys (HEAs) are of particular interest due to their potential to combine low elastic modulus, high strength, enhanced corrosion resistance, and excellent biocompatibility, making them highly suitable for next-generation biomedical implants.

Titanium alloys are typically classified into three major types based on their phase composition: α-type, β-type, and α + β-type. Pure titanium exhibits a hexagonal close-packed (HCP) crystal structure (α phase) at room temperature and transforms into a body-centered cubic (BCC) structure (β phase) upon heating. The temperature at which this allotropic transformation occurs is referred to as the β-transus temperature, which is approximately 882 °C for pure titanium [77]. This transition is influenced by alloying elements: α stabilizers such as aluminium (Al), boron (B), carbon (C), oxygen (O), and nitrogen (N) increase the β-transus temperature and stabilize the α phase. In contrast, β stabilizers like molybdenum (Mo), niobium (Nb), vanadium (V), tantalum (Ta), iron (Fe), and cobalt (Co) lower the transformation temperature and stabilize the β phase. Elements such as zirconium (Zr) and tin (Sn) are considered neutral as they have minimal impact on the transformation temperature [78]. Alloys containing both α and β phases are classified as α + β-type titanium alloys [73,79].

Based on the number and type of alloying elements, titanium alloys can also be categorized as binary, ternary, quaternary, or high entropy alloys. This thesis focuses on the design and development of binary, ternary, and high entropy titanium-based alloys for biomedical applications, with particular attention to their physical, mechanical, electrochemical corrosion, wear, and tribocorrosion behavior. To establish a strong foundation for this research, the subsequent sections critically review the existing literature on these alloy systems, highlighting their current development status, key properties, and limitations to identify relevant research gaps.

2.3.1 Binary Ti alloys

Binary Ti alloys consist of titanium and a single alloying element, selected to enhance specific properties such as mechanical strength, corrosion resistance, and biocompatibility, making them well-suited for biomedical applications. Common alloying elements include aluminium (Al), vanadium (V), molybdenum (Mo), and zirconium (Zr), each contributing unique advantages. In recent years, various binary Ti alloys have been developed and extensively studied. A brief overview of each alloy is presented below, followed by a comparative summary of their key mechanical properties, as shown in Table 2.2.

Takahashi et al. (2002) investigated binary Ti-Ag alloys containing 5 to 20 wt.% silver and Ti-Cu alloys with 2 to 10 wt.% copper for dental applications, prepared using casting techniques. Compared to commercially pure titanium, which has a yield strength of approximately 380 MPa and elongation around 24%, the Ti-5Cu alloy showed improved mechanical properties, with a yield strength near 540 MPa, a tensile strength of about 650 MPa, and moderate elongation of 5.5%. Increasing the copper content to 10 wt.% further raised the yield strength to roughly 600 MPa but reduced ductility to 2.5%. In Ti-Ag alloys, yield strength increased from approximately 470 MPa at 5% silver to 570 MPa at 20%, while elongation decreased from 16% to 6%. These improvements were attributed to solid solution strengthening and the precipitation of Ti_2Cu and Ti_2Ag intermetallic phases within the α-Ti matrix. Both alloy systems also maintained good corrosion resistance and biocompatibility, indicating their suitability for dental prosthetic applications.

Zhou et al. (2004) studied binary Ti-Ta alloys with Ta content ranging from 10 to 80 wt.% percent, prepared through arc melting, solution treatment, and water quenching. The alloy microstructure varied significantly with composition, transitioning from lamellar alpha prime martensite at lower tantalum levels to orthorhombic alpha double prime at intermediate compositions, and to a fully retained metastable beta phase above 70%. The dynamic Young's modulus reached minimum values of 69 GPa at 30 percent tantalum and 67 GPa at 70%, both notably lower than conventional titanium alloys. Tensile strength ranged from 510 to 690 MPa, with yield strength between 400 and 610 MPa. Alloys with 30 and 70% tantalum provided the most favorable balance of low modulus and high strength, with strength-to-modulus ratios above 8. These combinations, along with good corrosion resistance and biocompatibility, make them promising candidates for load-bearing biomedical implants.

Hsu et al. (2009) investigated binary Ti-Sn alloys with tin contents ranging from 1 to 30 wt.%, fabricated using arc melting and dental pressure casting techniques, to assess their potential for dental applications. X-ray diffraction analysis revealed that all examined alloys maintained the alpha phase structure, with no evidence of beta or intermediate phases. Mechanical testing indicated that Ti-Sn alloys exhibited increased bending strength and modulus relative to commercially pure titanium. Among the compositions studied, the Ti-1Sn alloy showed the highest bending strength of approximately 1420 MPa and a bending modulus of 147 GPa. Additionally, this alloy demonstrated an elastic recovery angle approximately 240% greater than commercially pure titanium. Alloys containing up to 10 wt.% Sn exhibited ductile characteristics, whereas those with 20 wt.% or higher displayed increased brittleness. The Ti-1Sn, Ti-

5Sn, and Ti-10Sn alloys resisted fracture under deflections up to 8 mm. These findings suggest that small additions of Sn can significantly influence the mechanical properties of titanium alloys relevant to dental applications.

Cordeiro et al. (2018) evaluated Ti-Zr binary alloys with 5, 10, and 15 wt.% Zr for dental implant applications, comparing them to cpTi and Ti-6Al-4V. The alloys were prepared by arc melting and subjected to machined and double acid-etched surface treatments. The Ti-Zr alloys maintained a single α-phase structure and exhibited grain morphology changes, including Widmanstätten patterns at higher Zr contents. Mechanically, they exhibited increased hardness (up to ~370 HV) compared to both cpTi and Ti-6Al-4V, while elastic modulus values ranged from ~115 to 135 GPa depending on Zr content, with some compositions approaching those of Ti-6Al-4V. Electrochemical testing in SBFA indicated higher polarization resistance (up to ~12 $M\Omega \cdot cm^2$) and lower corrosion current densities (as low as ~7 nA/cm^2), suggesting improved corrosion resistance. In terms of biocompatibility, all tested alloys supported MC3T3-E1 osteoblast adhesion, with double acid-etched surfaces enhancing cell spreading and filopodia formation. The study demonstrated that Zr addition and surface treatment influenced key properties such as mechanical strength, corrosion resistance, and cytocompatibility in Ti-based materials.

Zhang et al. (2019) investigated Ti-Nb binary alloys with Nb contents ranging from 5 to 25 wt.% as potential materials for biomedical implants. The alloys were fabricated using vacuum arc melting followed by thermomechanical processing and machining into disk specimens. XRD analysis confirmed that all compositions exhibited dual-phase α + β structure, with higher Nb content promoting β-phase formation. Alloys containing 10-25 wt.% Nb showed enhanced mechanical properties, including increased yield and tensile strengths, reduced elastic modulus in the range of 69-88

GPa, and improved surface hardness. The study also reported good corrosion resistance in artificial saliva and acidic environments, along with generally favorable biocompatibility based on MC3T3-E1 osteoblast viability and differentiation. However, variations in cell response and wettability, particularly in Ti-5Nb, indicate that the relationship between composition and biological performance warrants further investigation.

Chen et al. (2020) developed Ti-xNb alloys (33, 40, 56, and 66 wt.% Nb) using a low-cost blended elemental powder metallurgy route involving uniaxial pressing and vacuum sintering at 1350 °C for 2 h. All alloys achieved ~95% relative density, though porosity and microstructural inhomogeneity increased with Nb content. XRD and SEM analyses showed increasing β-phase (from 87% to 95%) and decreasing α-phase with higher Nb. Mechanical tests revealed that yield strength decreased with Nb from 850 MPa (Ti-33Nb) to 194 MPa (Ti-66Nb), while Young's modulus also declined (from 107 GPa to 54 GPa), beneficial for reducing stress shielding. Ti-40Nb exhibited a balanced profile with 591 MPa yield strength and 76 GPa modulus, outperforming cpTi. Biocompatibility testing using hMSCs showed all alloys supported cell viability, with Ti-40Nb showing the best cell adhesion and cytoskeletal development.

Shahedi Asl et al. (2020) investigated the densification and mechanical behavior of spark plasma sintered (SPS) Ti-Mo alloys with varying Mo contents (4, 8, 12, 16, and 20 wt.%) for potential biomedical applications. The samples were sintered at 1200 °C under 50 MPa for 5 minutes. The study utilized both conventional and nanoindentation techniques to assess mechanical properties. The alloy with 16 wt.% Mo demonstrated the highest relative density (99.9%) and hardness values (372 HV30 macrohardness and 592 HV0.3 microhardness), attributed to solid solution strengthening and the presence of refined α + β colonies. However, the maximum ultimate tensile strength

(UTS) of 852 MPa at room temperature and 600 MPa at 600 °C was observed for the Ti-8 wt.% Mo sample, likely due to strain-induced transformation and the formation of metastable β-Ti phase. The highest flexural strength (~2 GPa) was recorded for the Ti-12 wt.% Mo alloy, suggesting enhanced solid solution strengthening in this composition. Nanoindentation studies revealed that β-phase exhibited the highest hardness (~5.97 GPa), while α-phase was comparatively softer. Ti-12Mo also showed superior average values of nano-hardness, elastic modulus, and stiffness compared to Ti-20Mo, indicating its better mechanical integrity.

Zhang et al. (2022) studied the tribocorrosion behavior and mechanical performance of binary Ti-Cu alloys containing 5 and 10 wt.% copper, processed via powder metallurgy and subsequent hot extrusion, for potential biomedical applications. The alloys were tested in SBF, including Hank's solution, neutral and acidic artificial saliva, and fluoride-containing media. Compared to cpTi which exhibited a hardness of approximately 160 HV and lacked significant compressive yield strength, the Ti-5Cu(S) alloy demonstrated a marked improvement in mechanical properties, with a hardness of 350 HV, compressive yield strength of 1050 MPa, and compressive strength up to 1700 MPa. The Ti-10Cu(S) alloy further increased the hardness to 425 HV and compressive strength to 1800 MPa, although ductility was slightly reduced. Extrusion processing refined the microstructure and further enhanced the mechanical properties, with Ti-10Cu(E) achieving a compressive yield strength of 1325 MPa and maintaining the same hardness (425 HV), while resisting fracture under maximum applied strain (~18.5%).

The improved properties were attributed to the formation and uniform distribution of the Ti_2Cu intermetallic phase, which contributed to both grain refinement and strengthening. In tribocorrosion tests, all Ti-Cu alloys showed superior performance compared to cpTi, with lower corrosion current densities, reduced wear rates, and more stable open circuit potentials during sliding. SEM analysis confirmed reduced surface damage and predominant abrasive wear in Ti-Cu alloys, as opposed to the adhesive and fatigue wear observed in cpTi. These enhancements, along with previously established antibacterial activity, suggest that Ti-Cu alloys, especially in extruded form, offer significant promise for dental and orthopedic applications requiring simultaneous mechanical durability and biological compatibility.

Table 2.2: Binary Ti alloys and their mechanical properties

Alloys	Processing technique	Hardness (HV)	Ultimate strength (MPa)	Elastic modulus (GPa)	Ref.
Ti-Mo	Melting	270-340	696-800	71-95	[80,81]
Ti-Ag	Melting	150-230	280-410	–	[82]
Ti-Sn	Melting	246-357	1225-2014	100-142	[83,84]
Ti-Cu	Melting	224-274	437-678	105-135	[85]
Ti-Ta	Melting	–	510-690	67-88	[86]
Ti-Nb	Melting	176.6-329.6	536.5-1014	69.2-87.9	[87]
Ti-Zr	Melting	115.4-134.9	–	350-475	[88]
Ti-Nb	Powder metallurgy	–	194-850	54-107	[89]

2.3.2 Ternary Ti alloys

Ternary titanium (Ti) alloys are composed of titanium and two additional alloying elements. These alloys are developed to tailor the properties of titanium more precisely than binary alloys, potentially offering improvements in mechanical, chemical, or biological performance. By carefully selecting and balancing the secondary elements, ternary Ti alloys can be optimized for advanced biomedical applications. A brief overview of selected ternary alloys is presented below, followed by a summary of relevant literature in Table 2.3.

Hussein et al. (2015) developed a nanostructured Ti-20Nb-13Zr alloy for biomedical applications using mechanical alloying followed by spark plasma sintering (SPS). Elemental powders of Ti, Nb, and Zr were mechanically alloyed for 10 hours and consolidated via SPS at temperatures ranging from 800 to 1200 °C, with a heating rate of 100 K/min and a holding time of 10 minutes under a uniaxial pressure of 50 MPa. The SPS process enabled near-full densification (~99.5%) at 1200 °C and preserved nanograin sizes (70-140 nm), forming a duplex microstructure with β-Ti (BCC) matrix and equiaxed α-Ti (HCP) grains.

The alloy exhibited a maximum Vickers hardness of 660 HV at 900 °C, attributed to the nanostructure and uniform elemental distribution. Compared to conventionally sintered Ti-13Nb-13Zr and Ti-6Al-4V alloys, the SPS-consolidated Ti-20Nb-13Zr demonstrated superior hardness, phase homogeneity, and refined microstructure at significantly lower sintering temperatures. The presence of non-toxic β-stabilizers (Nb and Zr) and the nanograined structure are expected to enhance mechanical performance, corrosion resistance, and biocompatibility, making this alloy a promising candidate for orthopedic and dental implants.

Yılmaz et al. (2017) investigated Ti-16Nb alloys with 0-4 wt.% Sn additions, fabricated via Powder Injection Molding (PIM), to evaluate their suitability for biomedical implants. The alloys developed showed typical Widmanstätten (α + β) microstructures, with porosity levels below 5% and relative densities reaching up to 96-97% at a sintering temperature of 1550 °C. The addition of 2 wt.% Sn significantly reduced the elastic modulus from 128 GPa (base alloy) to 77 GPa, bringing it closer to the modulus range of human cortical bone. Further Sn addition (4 wt.%) did not yield additional reduction. Hardness decreased initially with 2 wt.% Sn (4573 MPa) but increased moderately with 4 wt.% Sn (6178 MPa), likely due to solid solution strengthening and β-phase stabilization. XRD and SEM confirmed a metastable α + β phase constitution with enhanced β-phase fraction in Sn-containing alloys. These results demonstrate that Sn can effectively tailor the mechanical properties of Ti-Nb alloys for reduced stress shielding in implant applications.

Sun et al. (2018) investigated the effect of silver (Ag) addition on the microstructure and mechanical behavior of Ti-16Nb-xAg (x = 0, 0.3, 0.7, 1 at.%) alloys for biomedical applications. The alloys were fabricated via vacuum arc melting, followed by hot and cold rolling, and solution treatment at 900 °C. The addition of Ag led to a notable increase in ultimate tensile strength from 743 MPa (0% Ag) to 840 MPa (1% Ag), while the elastic modulus decreased from approximately 93 GPa to 73 GPa. The Ag-containing alloys also exhibited improved work hardening rates and enhanced shape memory effect (SME), with a maximum recoverable strain of 1.7% observed in the Ti-16Nb-0.7Ag alloy. These improvements are primarily attributed to solid solution hardening and modifications in the martensitic twin structures, underscoring the potential of the Ti-Nb-Ag system for advanced biomedical implant applications.

Quadros et al. (2019) developed and characterized a Ti-25Ta-10Zr alloy aimed at biomedical applications, particularly orthopedic implants. The alloy was synthesized through arc melting followed by homogenization heat treatment at 1000 °C for 24 h to ensure chemical homogeneity, confirmed by EDS mapping and density measurements (5.72 g/cm^3, closely matching the theoretical 5.73 g/cm^3). X-ray diffraction analysis and Rietveld refinement revealed a multi-phase structure consisting of α′ (HCP), α″ (orthorhombic), and β (BCC) phases, with the heat-treated alloy containing approximately 65% α′ and 35% β. Vickers microhardness testing showed a value of ~350 HV, which is significantly higher than cpTi (~160 HV) and Ti-6Al-4V (~290

HV), indicating effective solid solution strengthening by Ta and Zr. Additionally, indirect cytotoxicity assays using osteogenic cells demonstrated no adverse effects on cell viability or morphology, suggesting the alloy's suitability for biomedical use.

Xu et al. (2020) developed Ti-10Mo-xCu alloys (x = 0, 1, 3, 5 wt.%) using powder metallurgy to enhance the antibacterial properties of Ti-Mo alloys for biomedical applications. Alloys exhibited high relative density (~98%) and typical Widmanstätten ($\alpha + \beta$) microstructures, with Ti_2Cu precipitates forming at ≥3 wt.% Cu. Mechanical testing showed that tensile strength increased with Cu content, reaching 1162 MPa for Ti-10Mo-5Cu, while elongation decreased from 14.8% to 1.97%. Ti-10Mo-3Cu achieved a balance with UTS of 1098 MPa and 5.2% elongation. The elastic modulus remained low across all compositions (71-77 GPa), supporting load-bearing implant suitability. Cytocompatibility assays using MC3T3-E1 cells confirmed non-cytotoxic behavior for all compositions. Antibacterial testing revealed Cu-dependent inhibitory effects against S. aureus (20-60%) and E. coli (15-50%) after 24 h, attributed to Cu ion release and Ti_2Cu phase. The Ti-10Mo-3Cu alloy offered an optimal combination of mechanical strength, cytocompatibility, and bacterial resistance for potential orthopedic use.

Qi et al. (2021) investigated a novel series of ternary Ti-6Zr-xFe alloys (x = 4, 5, 6, 7 wt.%) as potential candidates for biomedical applications. The alloys were produced via vacuum arc remelting and characterized in their as-cast state. Microstructural analysis revealed dual-phase $\alpha + \beta$ structures with the β-phase fraction increasing and β grain size decreasing from 488 μm to 295 μm, as Fe content increased. A small amount of ω-phase was detected at higher Fe contents, which contributed to changes in mechanical behavior. Mechanical testing showed increasing microhardness from 264 to 348 HV and ultimate tensile strength 748 to 994 MPa with higher Fe content, attributed to solid solution strengthening, β-phase refinement, and ω-phase formation. The Young's modulus ranged from 90 to 94 GPa, lower than that of Ti-6Al-4V (112 GPa), indicating improved elastic compatibility with bone. Electrochemical analysis in 0.9% NaCl solution showed that alloys with 4-5 wt.% Fe had better corrosion resistance, with increasing Fe content leading to reduced electrochemical stability.

Li et al. (2021) fabricated novel Ti-35Nb-xMg (x = 3 and 5 wt.%) alloys using mechanical alloying (MA) followed by spark plasma sintering (SPS) for biomedical applications. The powders were milled at different ball-to-powder ratios (BPRs) of 10:1 and 20:1, and sintered at 900 °C under vacuum. The MA process under 20:1 BPR successfully produced nearly single-phase (Ti, Nb, Mg) bcc solid solutions, while 10:1 BPR led to incomplete alloying. SPS consolidation retained β-phase as the major constituent along with minor α-Ti and Mg phases, and introduced uniformly distributed nanopores, mainly due to Mg volatilization.

Mechanically, alloys processed at 20:1 BPR showed higher ductility and ultimate compressive strength (UCS), ranging from 896 to 1259 MPa, compared to their 10:1 counterpart. However, increasing Mg content from 3 wt.% to 5 wt.% reduced both strength and strain due to Mg precipitation and pore formation. The Ti-35Nb-5Mg alloy under 20:1 (TN_5M-20) exhibited good hydrophilicity and superior early-stage cell adhesion, indicating its potential for promoting osseointegration. These results suggest that the Ti-Nb-Mg system, particularly TN_5M-20, is a promising low-modulus, bioactive alloy for implant applications.

Pandey et al. (2022) developed Ti-5Cu-x%Nb (x = 0, 5, 10, 15 wt.%) alloys via powder metallurgy involving high-energy ball milling, uniaxial pressing (650 MPa), and vacuum sintering at 900 °C for 1 hour. The aim was to enhance the mechanical, corrosion, and antibacterial properties of titanium for biomedical, especially dental, applications. Microstructural analysis revealed the formation of α-Ti, Ti_2Cu, and β-Ti phases, with β-phase volume fraction increasing with Nb content, confirming β-stabilization by Nb.

Among the compositions, Ti-5Cu-5Nb (S2) showed the best mechanical performance with a microhardness of 542 HV, compressive strength of 1090 MPa, and elastic modulus of 24.7 GPa significantly superior to cpTi (186 HV, 886 MPa, 98.6 GPa). The elastic modulus for all alloys (14.7-24.7 GPa) was closer to the cortical bone (13-20 GPa), potentially reducing stress shielding. While corrosion resistance decreased with Nb addition, all samples outperformed cpTi in antibacterial activity. Notably, all sintered alloys showed ~100% antibacterial efficacy against E. coli and S. aureus, attributed to the Ti_2Cu phase. The study identified Ti-5Cu-15Nb as having the most favorable combination of mechanical properties and biological performance for implant applications

Table 2.3: Ternary Ti alloys and their mechanical properties

Alloys	**Processing technique**	**Hardness (HV)**	**Strength (MPa)**	**Elastic modulus (GPa)**	**Ref.**
Ti-Nb-Zr	Melting	416-434	–	82-137	[90]
Ti-Nb-Ag	Melting	–	743-840	73-93	[91]
Ti-Ta-Zr	Melting	407-409	–	–	[92]
Ti-Zr-Fe	Melting	264-348	748-994	90-94	[93]
Ti-Nb-Sn	Powder Injection Modeling	4573-6178 MPa	–	77-128	[94]
Ti-Mo-Cu	Powder Metallurgy	_	71-77	1098-1162	[95]
Ti-Nb-Mg	Powder Metallurgy-SPS	–	869-1259	_	[96]
Ti-Cu-Nb	Powder Metallurgy	542	1090	_	[97]

2.3.3 High entropy Ti alloys

High-entropy titanium (Ti) alloys are a class of advanced materials that consists of titanium combined with multiple alloying elements, typically five or more, in near-equal proportions. These alloys deviate from conventional alloy design, where one principal element (like titanium) is alloyed with small amounts of other elements. In high-entropy alloys (HEAs), the concept is to achieve a highly stable and balanced material by incorporating multiple elements, leading to unique and enhanced properties. Major advancements in the field of Ti based high entropy alloys with properties are detailed in Table 2.4.

Kopova et al. (2016) studied Ti-35Nb-7Zr-6Ta (TNZT) alloys with 0-2 wt.% Fe and 0-1 wt.% Si additions to enhance mechanical strength and biocompatibility. The modified alloys exhibited increased yield strength (up to >700 MPa) and UTS (>800 MPa) while maintaining a low elastic modulus (~85 GPa), suitable for load-bearing applications. Fe improved ductility through work hardening, whereas Si refined grains but reduced elongation due to silicide formation. Biologically, the alloy with 2 wt.% Fe and 0.5 wt.% Si supported superior osteoblast adhesion, proliferation, and collagen I production compared to Ti-6Al-4V, indicating improved osteogenic potential.

Popescu et al. (2018) investigated a novel TiZrNbTaFe high-entropy alloy (HEA) for biomedical applications, developed via powder metallurgy. Elemental powders of Ti, Zr, Nb, Ta, and Fe (nominal composition $Ti_{40}Zr_{20}Nb_{20}Ta_{10}Fe_{10}$ at.%) were mechanically alloyed for 20 and 40 hours in a planetary ball mill under argon atmosphere, compacted at 200 MPa, and sintered at 1000 °C for 2-3 hours. Structural analysis indicated partial alloying after 20 hours of milling, with the formation of multiphase microstructures including NbTiZr and intermetallic compounds such as Zr_2Fe and TaFe oxides.

The alloy demonstrated promising mechanical properties, with a maximum Vickers hardness of 955 HV. Using the empirical relation $\sigma = HV/3$, a tensile strength of approximately 318 MPa was estimated. Corrosion testing in Ringer's lactate solution showed superior performance of the TiZrNbTaFe alloy compared to Ti-6Al-4V, including higher corrosion potential (-71.7 mV vs. -125.5 mV), lower corrosion current density (0.22 $\mu A/cm^2$ vs. 0.31 $\mu A/cm^2$), and lower passive current density (8.46 $\mu A/cm^2$ vs. 12.35 $\mu A/cm^2$). These improvements were attributed to the formation of a stable oxide layer comprising TiO_2, Nb_2O_5, ZrO_2, and Ta_2O_5. The corrosion resistance was further enhanced by the homogeneous β-phase microstructure, which minimized galvanic effects seen in dual-phase alloys like Ti-6Al-4V.

Motallebzadeh et al. (2019) investigated two biocompatible refractory high-entropy alloys, TiZrTaHfNb and $Ti_{1.5}ZrTa_{0.5}Hf_{0.5}Nb_{0.5}$, as potential alternatives to conventional biomedical materials like 316L, CoCrMo, and Ti-6Al-4V. Both alloys exhibited single-phase BCC structures with uniform elemental distribution. Nanoindentation revealed hardness values of 3.14 GPa and 3.02 GPa, and elastic moduli of 112.74 GPa and 98.57 GPa, for TiZrTaHfNb and $Ti_{1.5}ZrTa_{0.5}Hf_{0.5}Nb_{0.5}$, respectively. Their higher H/E and H^3/E^2 ratios indicate improved wear resistance and reduced plastic deformation. The RHEAs also showed good surface wettability and enhanced corrosion resistance in PBS at 37 °C, exhibiting passive behavior without pitting up to 1800 mV and lower corrosion current densities than standard alloys. $Ti_{1.5}ZrTa_{0.5}Hf_{0.5}Nb_{0.5}$ demonstrated slightly improved performance, attributed to its lower lattice strain and higher Ti and Zr content. Based on these results, the authors proposed that such RHEAs could be promising candidates for future biomedical applications, particularly in load-bearing environments.

Yang et al. (2020) investigated the corrosion resistance and in vitro biocompatibility of an equimolar TiZrHfNbTa high-entropy alloy (HEA) designed for biomedical applications. The alloy was produced via arc melting and exhibited a homogeneous single-phase BCC structure with grain sizes between 100 and 200 μm. Electrochemical tests in Hank's solution at body temperature revealed spontaneous passivation with a low passive current density of approximately 0.01 A/m^2 and a corrosion rate of 5.6×10^{-4} mm/year, slightly lower than Ti-6Al-4V. High electrochemical impedance (up to 10^6 $\Omega \cdot cm^2$) and low ion release confirmed the formation of a stable passive film primarily composed of TiO_2, ZrO_2, HfO_2, Nb_2O_5, and Ta_2O_5. Cell culture experiments with MC3T3-E1 pre-osteoblasts showed good cell adhesion, viability, and proliferation, with no significant difference from Ti-6Al-4V. The alloy's relatively low elastic modulus (~80 GPa) and high yield strength (800-985 MPa) further support its potential for orthopedic implant use, particularly for minimizing stress shielding while maintaining mechanical integrity.

Hua et al. (2021) studied the microstructure, mechanical, corrosion, and wear properties of a series of Ti-Zr-Nb-Ta-Mo high entropy alloys (HEAs) with varying Ti contents (x = 0.5, 1.0, 1.5, and 2.0 molar ratio) for biomedical implant applications. All HEAs exhibited a dendritic microstructure with dual body-centered cubic (BCC) solid solution phases. The $Ti_{0.5}ZrNbTaMo$ alloy showed the highest hardness (~500 HV), compressive strength (up to 2600 MPa), and plastic strain (~30%), attributed to its coarse dendritic morphology enriched in high-melting Ta and Mo. Electrochemical testing in phosphate-buffered saline revealed low corrosion current densities (~10^{-3} A/m^2), spontaneous passivation, and higher corrosion potentials than Ti-6Al-4V, indicating excellent corrosion resistance. XPS analysis confirmed the formation of stable passive films comprising TiO_2, ZrO_2, Nb_2O_5, Ta_2O_5, and Mo oxides. Wear tests demonstrated that the HEAs possessed lower wear rates and higher wear resistance than Ti-6Al-4V, under both dry and wet conditions, with the $Ti_{0.5}$ alloy performing best.

Wang et al. (2022) developed novel TiZrHfNbFex (x = 0-2.0) refractory high-entropy alloys (HEAs) for biomedical applications using arc melting under an argon atmosphere, followed by multiple remelting cycles to ensure compositional homogeneity. The alloys exhibited dendritic microstructures consisting of BCC and Laves phases, with increasing Fe content promoting the formation of the brittle Laves phase. Mechanical testing revealed that hardness increased monotonically with Fe addition, reaching ~770 HV for Fe_2, while the compressive yield strength peaked at ~1500 MPa for Fe1. However, plastic strain decreased with increasing Fe, indicating a trade-off between strength and ductility. The $Fe_{0.5}$ alloy showed the most balanced mechanical behavior with a yield strength of ~1450 MPa and ~8% plastic strain. Electrochemical testing in phosphate-buffered saline (PBS) showed that the $Fe_{0.5}$ alloy also has best corrosion resistance, with a low corrosion current density (~2.8×10^{-7} Acm^{-2}) and no pitting up to 1.5 V. XPS analysis confirmed the formation of stable passive films enriched in TiO^2, ZrO^2, Nb^2O^5, and Fe_2O_3. Wear testing demonstrated that wear resistance improved with Fe content, with the $Fe_{0.5}$ alloy again offering the best performance under both dry and wet conditions. These properties, combined with the use of low-cost, biocompatible elements and a modulus (~50 GPa) close to human bone, suggest that $TiZrHfNbFe_{0.5}$ is a promising candidate for load-bearing biomedical implants.

Srivastav et al. (2023) developed a nanocrystalline Ti-$Co_{0.35}$-$Cr^{0.35}$-Nb-Zr high-entropy alloy (HEA) for biomedical applications using mechanical alloying (MA) followed by vacuum sintering at 750 °C, 850 °C, and 950 °C. The alloy powders were milled for 50 hours, achieving a single-phase BCC solid solution with an average crystallite size of ~7 nm and minor undissolved Zr. Differential scanning calorimetry indicated a phase transformation at ~821 °C, with the β (BCC) phase partially converting to α (HCP) at higher sintering temperatures. SEM and TEM confirmed homogeneous elemental distribution and nanostructured morphology.

The sintered samples showed increasing density and micro-hardness with temperature. Densities ranged from 5.39 to 5.87 g/cm^3, and micro-hardness values increased from 461 HV at 750 °C to 582 HV at 950 °C. These values exceed those of conventional biomaterials such as cpTi and Ti-6Al-4V. The high hardness, thermal stability, and uniform microstructure suggest that the Ti-$Co_{0.35}$-$Cr_{0.35}$-Nb-Zr HEA shows strong potential for use in load-bearing biomedical implants.

Srivastav et al. (2024) developed a nanocrystalline Ti-Nb-Ta-Cr-$Co_{0.5}$ HEA for biomedical applications using mechanical alloying (50 h) followed by spark plasma sintering (SPS) at 1000 °C. XRD and TEM analyses of the milled powder revealed the formation of dual BCC phases (BCC1 and BCC2) with nanocrystalline sizes of ~6 nm. Post-SPS, a third HCP phase evolved, resulting in a multi-phase microstructure. The sintered sample exhibited a high hardness of 652 ± 20 HV, compressive strength of 1418 ± 23 MPa, and a Young's modulus of 82 ± 5 GPa values favorable for load-bearing implants, with the reduced modulus minimizing stress shielding. Cytocompatibility was assessed using MG-63 osteoblast-like cells, and the alloy showed >97% cell viability after 6 days, indicating non-cytotoxic behavior. The combination of high strength, moderate stiffness, and excellent biocompatibility demonstrates significant potential for orthopedic implant applications, particularly in load-bearing environments where mechanical compatibility with bone is critical.

Table 2.4: High entropy Ti alloys and their mechanical properties

Alloys	Processing technique	Hardness (HV)	Strength (MPa)	Elastic modulus (GPa)	Ref.
Ti-Zr-Nb-Ta-Mo	Melting	420-480	1440-1580	–	[98]
Ti-Zr-Hf-Nb-Fe	Melting	400-770	750-1500	50	[99]
Ti-Zr-Hf-Nb-Ta	Melting	_	800-985	80	[100]
Ti-Nb-Zr-Ta-Fe-Si	Melting	–	800	85	[101]
Ti-Zr-Nb-Ta-Fe	Powder Metallurgy	955	318	–	[102]
Ti-Co-Cr-Nb-Zr	Powder Metallurgy	461-582	–	–	[103]
Ti-Nb-Ta-Cr-Co	Powder Metallurgy-SPS	652	1418	82	[104]
Ti-Zr-Ta-Hf-Nb	Melting	3.02-3.14 GPa	–	98.57-112.74	[105]

2.4 Processing techniques for Ti alloys

Fabrication techniques significantly influence the mechanical properties, microstructure, and biological performance of Ti and its alloys for biomedical implants. This section outlines key processing methods including casting, powder metallurgy, additive manufacturing, and hot isostatic pressing, along with their advantages, limitations, and biomedical relevance.

2.4.1 Casting

Casting is a traditional and cost-effective fabrication method for titanium and its alloys, involving melting the metal and pouring it into ceramic-coated graphite or zircon molds to form near-net-shape components [106]. This technique offers advantages such as the ability to produce complex geometries at relatively low cost, making it suitable for preliminary biomedical implant prototypes and certain non-load-bearing applications

[107]. However, casting often results in defects like microstructural inhomogeneity, uncontrolled porosity, shrinkage cavities, and surface roughness, which degrade mechanical strength, fatigue resistance, and corrosion behavior, properties critical for long-term implant performance [108]. Additionally, dimensional inaccuracies inherent to casting require further machining or polishing before biomedical use [109]. Consequently, despite its economic and manufacturing benefits, casting is generally limited in producing high-quality titanium implants that meet the stringent mechanical and biocompatibility requirements necessary for load-bearing biomedical applications. This limitation motivates the exploration of advanced fabrication methods with improved control over microstructure and material properties.

2.4.2 Additive manufacturing (3D printing)

Additive manufacturing (AM) techniques such as selective laser melting (SLM), electron beam melting (EBM), and selective laser sintering (SLS) build titanium alloy components layer-by-layer directly from computer-aided designs, enabling fabrication of complex and patient-specific geometries [110]. AM offers significant advantages including excellent design flexibility, reduced material waste, and the ability to produce porous structures that enhance osseointegration and reduce implant stiffness to better match the mechanical properties of bone, thereby improving implant performance [111]. Despite these benefits, AM processes face limitations such as residual stresses, anisotropic mechanical behavior, and the presence of defects like porosity and incomplete fusion, which can compromise fatigue life and corrosion resistance [112]. Consequently, careful optimization of process parameters and post-processing treatments are crucial to ensure biomedical-grade implant quality.

2.4.3 Hot isostatic pressing (HIP)

Hot isostatic pressing (HIP) involves applying high temperature and isostatic gas pressure to titanium components, effectively eliminating internal porosity and enhancing mechanical properties such as density, strength, and fatigue resistance [113]. The primary advantage of HIP lies in its ability to produce fully dense, high-integrity parts with improved corrosion resistance and structural reliability, which are critical for long-term performance of biomedical implants. However, the process is limited by high operational costs and the requirement for specialized, high-pressure equipment, which can increase manufacturing complexity and expenses [114]. Despite these limitations, HIP is widely employed as a post-processing technique for powder metallurgy and cast titanium implants to meet stringent biomedical standards for durability and biocompatibility.

2.4.4 Powder metallurgy

Powder metallurgy (PM) is a solid-state fabrication technique involving the blending or mechanical alloying of elemental or pre-alloyed titanium powders, followed by compaction and sintering at elevated temperatures in a vacuum or inert atmosphere, for which schematic diagram is shown in Fig. 2.1. Unlike casting, which involves complete melting and subsequent solidification, PM enables microstructural control without severe thermal gradients or segregation. It offers flexibility in tailoring alloy compositions and processing parameters to achieve desired mechanical and biological properties [115].

A key feature of PM is the ability to introduce and control porosity through variations in powder size, compaction pressure, sintering temperature, or via space-holder techniques [116]. This controlled porosity, which can be designed to be partially interconnected, significantly differs from casting-induced porosity. In casting, pores often arise from solidification shrinkage or gas entrapment, leading to random, non-uniform voids that act as stress concentrators, compromising fatigue strength and corrosion resistance. In contrast, PM-induced porosity is more uniformly distributed and can be tailored to enhance biological performance without severely degrading mechanical properties.

In the context of load-bearing biomedical implants, porous Ti-based structures fabricated via PM offer several benefits. Firstly, the presence of controlled porosity lowers the elastic modulus of the material, reducing the mismatch with natural bone and thus minimizing stress shielding effects. Secondly, pore architectures—particularly those in the range of 100–500 µm, can promote osteoconduction, vascularization, and long-term osseointegration [117,118]. Studies have shown that such porous implants enhance the anchorage of bone tissue, improving the mechanical interlock and long-term stability of orthopedic and dental implants [119]. However, PM processes may face challenges such as contamination from milling media and difficulty achieving full densification, which can be mitigated with proper process optimization [120]. Overall, PM provides a cost-effective, compositionally flexible, and biologically advantageous route for fabricating next-generation Ti-based implants with tunable porosity and mechanical properties that align with clinical requirements.

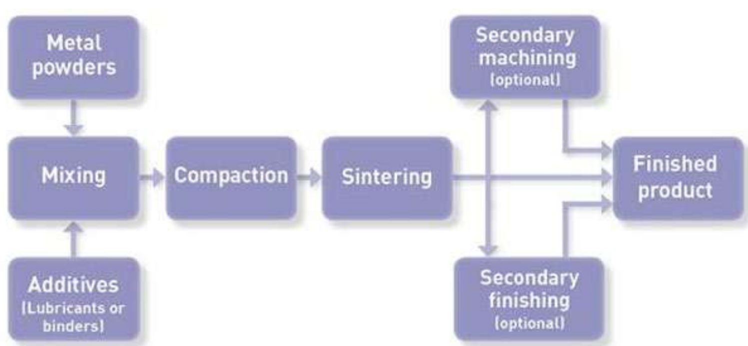

Fig. 2.1: Powder metallurgy flow chart [121]

2.5 Corrosion in titanium implants

Titanium and its alloys are widely recognized for their superior corrosion resistance in physiological environments. This resistance primarily stems from the spontaneous formation of a stable and adherent TiO_2 passive film on their surfaces. However, under certain biological and mechanical conditions, this passive film may degrade, leading to various forms of localized or synergistic corrosion [61,122].

2.5.1 Types of corrosion in titanium implants

Pitting corrosion is among the most critical forms of localized attack in chloride-containing environments, such as blood plasma or interstitial fluid. Once the passive oxide layer is locally disrupted by aggressive anions like Cl^-, pits can nucleate and propagate, especially at microstructural inhomogeneities or second-phase boundaries. These pits act as anodic sites, resulting in enhanced metal dissolution and ion release, which can undermine implant integrity and increase biological risks [123].

Crevice corrosion typically occurs in confined microenvironments with restricted oxygen access, such as at modular component interfaces, screw holes, or implant-bone junctions. In these locations, limited oxygen diffusion hinders the regeneration of the protective passive oxide film on metallic surfaces, leading to localized acidification and the accumulation of aggressive chloride ions. These changes create a highly corrosive environment that promotes the initiation and propagation of localized corrosion [124]. This phenomenon is particularly critical in implants with intricate geometries or modular designs, where fluid stagnation exacerbates crevice formation and corrosion susceptibility.

Tribocorrosion refers to the combined and often synergistic effect of mechanical wear and electrochemical corrosion, which is particularly critical in load-bearing orthopedic implants such as hip and knee prostheses. During cyclic loading and articulation, mechanical motion can disrupt the naturally formed passive oxide layer on titanium and its alloys, repeatedly exposing the underlying metal to corrosive physiological fluids. This dynamic breakdown and repassivation process not only accelerates material loss but also increases the release of metal ions into surrounding tissues. Such ion release has been associated with adverse biological responses, including inflammation, osteolysis, and eventual implant loosening or failure [125,126]. Therefore, evaluating the tribocorrosion resistance of newly developed Ti-based alloys is essential to ensure their long-term functional performance under physiological loading conditions.

Microbiologically influenced corrosion (MIC) is another potential degradation mechanism in biomedical implants, driven by bacterial adhesion and biofilm formation on metallic surfaces. The metabolic activity of microorganisms, particularly Staphylococcus aureus, a common pathogen in orthopedic and dental infections, can locally alter the pH, oxygen concentration, and redox conditions, thereby promoting corrosion through enzymatic and electrochemical reactions. These microbial interactions can compromise the passive oxide layer on titanium alloys, accelerating localized corrosion and contributing to implant failure. With the increasing incidence of implant-associated infections in clinical settings, understanding MIC is essential for evaluating the long-term corrosion resistance and biological safety of newly developed Ti-based biomaterials [127].

Although uniform and intergranular corrosion are uncommon in titanium and its alloys due to their stable passive oxide layer and homogeneous microstructure, they cannot be completely ruled out under certain conditions. Uniform corrosion may occur in highly acidic or reducing environments, which are rare but possible in the presence of persistent infection or inflammatory responses. Intergranular corrosion, while not typically observed in vivo, may arise if alloy processing introduces microstructural heterogeneities such as grain boundary segregation, second-phase particles, or residual stress concentrations. These microstructural features can create localized electrochemical differences that promote grain boundary attack, especially if the passive film is disrupted. Therefore, while not prevalent under normal physiological conditions, careful control of alloy composition and processing is essential to mitigate even low-risk corrosion modes.

2.5.2 Factors influencing corrosion in titanium implants

The long-term stability of the passive layer in Ti alloys can be compromised by several interrelated clinical and engineering variables. These factors influence the localized corrosion behavior, degradation kinetics, and electrochemical response of titanium-based implants in vivo.

Environmental factors in physiological sites

Orthopedic and dental implants operate in a chemically complex and dynamic environment that significantly influences their corrosion behavior. Under normal physiological conditions, body fluid pH is around 7.4. However, localized factors such as inflammation, infection, or surgical trauma can reduce the pH to as low as 4.0-5.5, compromising the stability of the passive oxide layer on titanium-based implants and accelerating metal ion release [128]. Additionally, chloride ions naturally present in interstitial fluids can penetrate compromised passive films, promoting localized corrosion mechanisms such as pitting and crevice corrosion [129].

Alloying Elements and Phase Stability

Corrosion resistance of titanium alloys in biomedical applications depends on the passive oxide layer and alloying elements. Niobium forms stable Nb_2O_5 that enhances oxide uniformity and reduces electronic conductivity, improving film protectiveness [130]. Molybdenum promotes repassivation and inhibits localized corrosion by forming transient Mo oxides that hinder chloride attack [131]. Zirconium contributes chemically inert ZrO_2, increasing oxide adherence and density, thus limiting ion diffusion [132]. Together, these oxides stabilize the passive film, reduce micro-galvanic corrosion, and enhance implant longevity in physiological environments [130–132].

Surface treatment and coatings

Surface treatments and biocompatible coatings are critical for enhancing the corrosion resistance of titanium-based implants. Techniques such as anodization, acid etching, and thermal oxidation promote the formation of stable and uniform oxide films, improving chemical stability and reducing surface reactivity in physiological environments [133]. These methods enhance the barrier properties of the TiO_2 layer by increasing its thickness and minimizing defects. Additional protection can be provided by ceramic or polymer-based coatings like hydroxyapatite, TiN, or DLC, which act as physical barriers to ion diffusion. To be effective, such coatings must exhibit strong adhesion, mechanical durability, and resistance to delamination under in vivo loading [134].

Mechanical stresses

Several studies have reported that mechanical stresses significantly influence the corrosion performance of titanium and its alloys under physiological conditions. Both cyclic and static loads can accelerate degradation through mechanisms such as stress corrosion cracking and corrosion fatigue, particularly in materials with microstructural heterogeneities or surface defects [135]. Surface roughness has also been identified as a critical factor, as it enhances local stress concentrations and fluid entrapment, thereby increasing susceptibility to localized corrosion [136].

Temperature and microbial activity

Physiological temperature (~37 °C) generally supports the formation and stability of the passive TiO_2 oxide layer on titanium alloys, which is essential for corrosion resistance. However, localized temperature increases due to inflammation or infection can accelerate electrochemical reactions, compromising oxide layer integrity and increasing corrosion rates [54]. Additionally, microbial colonization on implant surfaces may induce microbial-induced corrosion (MIC), where metabolic byproducts alter the local chemical environment and promote localized attack on the implant [137].

2.5.3 Impacts of corrosion on biocompatibility

Corrosion of titanium alloys leads to the release of metal ions and particulate debris into peri-implant tissues, which critically affects their biocompatibility and clinical performance. Studies report that ions released from these alloys induce localized inflammatory responses, cytotoxicity, and osteolysis, thereby impairing bone remodeling and potentially causing implant loosening [61,138]. The corrosion-induced disruption of the protective TiO_2 layer on these alloys also promotes surface roughness, favoring bacterial adhesion and biofilm formation, which are primary factors in peri-implant infections and implant failure [139]. Furthermore, microbial-induced corrosion in crevice or micro-gap regions exacerbates localized implant degradation and interferes with osseointegration by creating acidic microenvironments that are unfavorable for bone cell activity [139]. To mitigate these effects, optimizing the alloy composition, particularly the control of Nb and Zr content, and employing surface treatments such as anodization have been shown to enhance corrosion resistance, reduce ion release, and limit biofilm formation, ultimately improving the biocompatibility and longevity of titanium-based implants [140,141].

2.6 Tribology in titanium implants

Tribology, encompassing friction, wear, and lubrication, plays a critical role in the long-term success of load-bearing biomedical implants. Ti and its alloys, despite their excellent biocompatibility and corrosion resistance, face inherent tribological challenges such as relatively high coefficient of friction (COF), low hardness, and limited wear resistance under physiological loading conditions. These limitations can lead to premature implant failure [142].

2.6.1 Frictional behavior of titanium implants

Titanium alloys, especially at articulating or interfacing zones, frequently exhibit COF values exceeding 0.4 under boundary lubrication conditions [143]. The synovial fluid present in joint spaces often fails to form a stable lubricating film on Ti surfaces due to their intrinsic surface roughness and low wettability [144]. Elevated friction results in increased wear and localized heating, accelerating surface degradation and the generation of wear debris. Compared to cobalt-chrome or ceramic biomaterials, Ti alloys tend to generate higher frictional forces and more wear particles, which can induce inflammatory responses and osteolysis [145]. Alloying strategies involving β-stabilizers such as niobium (Nb), zirconium (Zr), and molybdenum (Mo) have been shown to modify surface chemistry, refine microstructure, and consequently reduce COF [146].

2.6.2 Wear in titanium implants

Wear in Ti-based biomedical implants results from the combined effects of mechanical loading, micro-motions, and chemical interactions at articulating interfaces or modular junctions in the presence of biological fluids:

Adhesive wear occurs due to localized bonding between surface asperities of the implant and the counter face (e.g., bone or metal components). Titanium’s high chemical reactivity, especially in the presence of proteins and body fluids, promotes strong adhesion and material transfer under load [147].

Abrasive wear results from contact with harder surfaces or entrapped third-body particles such as bone fragments, hydroxyapatite debris, or metal particulates. These particles can plough or cut the softer Ti surface, leading to material loss [147].

Fretting wear arises at modular junctions (e.g., head-neck or stem-socket interfaces) or bone-implant contacts where micro-movements occur. This repeated disruption of the protective oxide layer increases susceptibility to wear and facilitates crevice corrosion [148].

Tribocorrosion is a synergistic phenomenon involving simultaneous mechanical wear and electrochemical corrosion. The breakdown of the passive TiO_2 layer during articulation exposes fresh metal, accelerating corrosion and ion release, which can contribute to inflammation and cytotoxicity [149].

2.6.3 Strategies for wear reduction

Recent studies emphasize alloying and advanced processing as effective routes to enhance tribological performance. Incorporation of β-stabilizing elements such as Nb and Mo, as well as solid solution strengtheners like Zr, has been shown to improve hardness, wear resistance, and corrosion behavior under simulated physiological conditions [150,151]. Tin (Sn) and copper (Cu) additions contribute to oxidative stability and antibacterial activity, respectively, which can further reduce friction and wear [150]. Processing techniques such as mechanical alloying and spark plasma sintering (SPS) enable homogeneous element dispersion, ultrafine grain sizes, and dense microstructures, which collectively enhance wear resistance [61]. Although surface engineering approaches like anodization and hard coatings (e.g., TiN, DLC) can synergistically improve tribological properties, these are beyond the scope of the present study [151].

2.7 Tribo-corrosion in titanium implants

Tribo-corrosion, the synergistic interaction between mechanical wear and electrochemical corrosion, is a critical issue in metallic implants, particularly those used in load-bearing applications such as orthopedic and dental implants [152]. Although titanium forms a stable TiO_2 passive layer that offers excellent corrosion resistance, fretting, micromotion, and mechanical abrasion under physiological conditions can disrupt this oxide layer [153]. The removal of this protective film leads to direct exposure of the reactive titanium surface to body fluids, accelerating localized corrosion, such as pitting and crevice attack, especially in modular implant junctions [154]. The interaction of wear and corrosion leads to accelerated material loss and a higher rate of metal ion release, which can result in adverse biological responses such as inflammation, osteolysis, and implant loosening [155]. Moreover, alloy composition and microstructure play crucial roles in modulating tribo-corrosion behavior. Elements like Nb, Zr, and Mo have been reported to enhance passivation and mechanical integrity, thereby mitigating the severity of tribo-corrosive degradation [156].

2.8 Summary of research gaps and research objectives

2.8.1 Summary of research progress and available research gap

The materials used in orthopedic and dental implants have significantly evolved from rudimentary substances to advanced high-performance biomaterials, driven by progress in materials science, biomechanics, and clinical surgical techniques. Early implants, made of wood, ivory, or unalloyed metals, have now been replaced by advanced metallic, ceramic, and polymeric biomaterials with enhanced biocompatibility, strength, and longevity [67,68,157]. Among these, titanium (Ti) and its alloys have emerged as the most promising candidates for load-bearing biomedical implants due to their favorable combination of mechanical properties, corrosion resistance, and biocompatibility [1,158,159]. Despite the clinical success of metallic biomaterials like stainless steel (SS 316L), cobalt-chromium (Co-Cr) alloys, and Ti-based alloys (e.g., Ti-6Al-4V), each system poses certain limitations. Stainless steel, although cost-effective and widely used, exhibits relatively poor corrosion resistance and can lead to the release of nickel and chromium ions over time, potentially causing allergic or inflammatory responses [160]. Co-Cr alloys offer excellent strength and wear resistance but may also release Co and Cr ions, raising biocompatibility concerns [161]. Ti-based alloys, particularly Ti-6Al-4V, are preferred due to their high strength-to-weight ratio and corrosion resistance; however, concerns remain about the long-term biological effects of vanadium and aluminium [162], and the significant mismatch in elastic modulus leads to stress shielding and implant loosening [163].

To address these concerns, biocompatible and non-toxic elements such as niobium (Nb), molybdenum (Mo), tin (Sn), and tantalum (Ta), which act as β-phase stabilizers, along with neutral zirconium (Zr), have been investigated as alloying additions in titanium-based alloys to improve corrosion resistance, reduce elastic modulus, and enhance biocompatibility [164]. For instance, Nb effectively stabilizes the β-phase and lowers elastic modulus, Zr enhances corrosion resistance and cell compatibility, while Mo and Sn contribute to phase stabilization and solid solution strengthening [165]. In addition, a small amount of copper (Cu) enhances the antibacterial properties of Ti alloys [82].

However, the literature review reveals that most Ti-based alloys have been developed through conventional melting or casting routes, which typically result in dense microstructures and a high elastic modulus. Moreover, casting methods often lead to inhomogeneous element distribution, segregation, and the formation of unwanted intermetallic phases, which can adversely affect the mechanical properties and biocompatibility of the implant material. In contrast, powder metallurgy (PM) offers a superior alternative for the development of biomedical Ti alloys. PM is a solid-state processing route that allows precise control over microstructure and porosity [117]. By varying sintering conditions, compaction pressure, process control agents, and alloying elements, it is possible to fabricate porous Ti alloys with tunable elastic modulus and mechanical properties closer to those of natural bone [118]. PM also facilitates near-net shape fabrication, homogenous microstructure distribution, and better dimensional control compared to casting routes [166]. These attributes make PM an effective method for producing high-performance implant materials with tailored properties [167].

In this context, several attempts have been made to develop a new Ti alloy with biocompatible alloying elements through powder metallurgy. The literature studies on these alloys are discussed in more detail in Section 2.4. Specifically, the previous study on Ti-Nb development through powder metallurgy is limited to the mechanical and biological evaluation. However, the study of friction, wear, corrosion, and tribocorrosion behavior is crucial for biomedical implant materials, which is not considered in the previous studies of Ti-Nb alloys and are still to be explored. Similarly, to the best of the author’s knowledge, there has been no prior study examining the tribological, electrochemical corrosion, and tribocorrosion behavior of Ti-Zr alloys developed through powder metallurgy utilizing the vacuum sealing assisted sintering. However, the study of friction, wear, corrosion, and tribocorrosion behavior is crucial for biomedical implant materials, which is not considered in the previous studies of Ti-Nb and Ti-Zr alloys and are still to be explored. In addition, a few studies have reported the synthesis of Ti-Zr-Nb alloys via powder metallurgy, comprehensive investigations on their tribological, electrochemical performance, and tribocorrosion particularly in simulated body environments, remain largely unexplored. Furthermore, the emerging class of titanium-based high entropy alloys (HEAs), which consist of five or more principal elements, has garnered significant attention for biomedical applications. This interest is primarily due to their exceptional combination of mechanical strength, corrosion resistance, and biocompatibility. In the previous studies on Ti-based high entropy alloys (HEAs), as discussed in Section 2.4, most of the alloys have been developed either through melting techniques or spark plasma sintering. The fabrication of HEAs using conventional powder metallurgy sintering remains largely unexplored. Moreover, to the best of the author's knowledge, HEAs comprising the elemental combinations of Ti-Nb-Mo-Zr-Cu and Ti-Nb-Mo-Zr-Sn have not been developed using any synthesis technique to date. In addition, the tribological, corrosion, and tribocorrosion behaviors of these novel HEAs have not been systematically investigated yet. Therefore, based on these identified research gaps, the objectives of the present study are outlined in the subsequent section.

2.8.2 Research objectives of the present study

The present study aims to develop and evaluate novel titanium-based alloys for biomedical implant applications using the powder metallurgy processing route. The specific objectives of the study are:

- To design and synthesize three categories of Ti-based alloys, namely:
  - Binary Ti-xNb and Ti-xZr alloys with varying concentrations to investigate the influence of individual alloying elements.
  - Ternary Ti-10Zr-xNb alloys to understand the combined effect of Zr and Nb on alloy performance.
  - High Entropy Alloys (HEAs), $TiNb_{1.5}Mo_{1.1}Zr_{1.15}Cu_{0.25}$ and $TiNbZr_{0.8}Mo_{0.92}Sn_{0.28}$, to explore the potential of multicomponent systems for improved biomedical properties.

- To characterize the phase composition and microstructure of all developed alloys using X-ray diffraction (XRD), scanning electron microscopy (SEM), and energy-dispersive X-ray spectroscopy (EDS), in order to establish correlations with processing and composition.
- To evaluate the physical properties such as theoretical and sintered density, and porosity, to assess the quality and integrity of sintered alloys.
- To investigate the mechanical properties of the alloys through microhardness and elastic modulus measurements, relevant to load-bearing biomedical applications.
- To examine the corrosion resistance of the alloys in SBF through electrochemical techniques including open-circuit potential, electrochemical impedance spectroscopy, and potentiodynamic polarization, along with post-corrosion surface analysis.
- To assess the tribological behaviour under SBF using ball-on-disc reciprocating wear tests, evaluating friction, wear rate, and wear mechanisms.
- To study the tribocorrosion performance of the developed alloys in SBF, considering the synergistic effects of simultaneous mechanical wear and electrochemical corrosion.
- To compare the developed alloys with commercially pure titanium (cpTi) and Ti-6Al-4V, benchmarking their suitability and potential for biomedical implant applications.