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REVIEWS

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A review—metastable β titanium alloy for biomedical applications

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Abstract

Titanium and its alloys have already been widely used as implant materials due to their outstanding mechanical characteristics and biocompatibility. Notwithstanding this, researchers and businesses alike have continued to actively pursue superior alloys since there are still problems which need urgent consideration. One of these is a noteworthy difference in the implant material's elastics modulus and that of natural bone, which result into an issue of stress shielding. With prolonged use Ti alloys releases dangerous ions. The Ti alloy surface has a low bioactivity, which prolongs the healing process. β-Ti alloys could be used as viable alternatives when creating dental implants. Additionally, β-Ti alloys characteristics, such as low Young modulus, increased strength, appropriate biocompatibility, and strong abrasion and corrosion resistance, serve as the necessary evidence. Ti alloys when altered structurally, chemically, and by thermomechanical treatment thereby enabling the creation of material which can match the requirements of a various clinical practise scenarios. Additional research is needed which can focused on identifying next century Ti alloys consisting of some more compatible phase and transforming the Ti alloys surface from intrinsically bioinert to bioactive to prevent different issues. In order to give scientific support for adopting β-Ti-based alloys as an alternative to cpTi, this paper evaluates the information currently available on the chemical, mechanical, biological, and electrochemical properties of key β-titanium alloys designed from the past few years. This article is also focusing on β-titanium alloy, its properties and performance over other type of titanium alloy such as α titanium alloys. However, in-vivo research is needed to evaluate novel β titanium alloys to support their use as cpTi alternatives.

Keywords: Titanium, Biomaterials, β-titanium, Titanium alloy, Osseointegrations, Biocompatibility, Low elastic modulus titanium alloy, β-stabilizers, Stress shielding

Introduction

Because of its great strength and low density, titanium has been used in technical disciplines such as the automotive, aviation industries and biomedical field. Menachanite is the first titanium mineral that was found, but production did not begin until 1910. Since then, alloying elements have further enhanced titanium characteristics. Ever since 1960 various biomedical treatments, including craniofacial, orthopaedic, dental, prosthetic, and joint replacement surgery have routinely used titanium (Ti) and its alloys as metallic biomaterials [1, 2]. The first report on plates for internal fixing dates back to 1895 [3].

Since then, the use of medical stainless steel (316 L), cobalt-chromium (Co-Cr), and titanium alloys in angioplasty and bone fracture fixing has increased significantly [4]. These materials have outstanding mechanical qualities, long-term stability, and strong biocompatibility. Because of their great osseointegration, higher biocompatibility, outstanding corrosion performance, mechanical stability, and excellent physicochemical stability, biomedical implants, in particular bone implants, have been made using titanium and its alloys [4]. However, not all titanium alloys are compatible with the human body.

The preferred material for creating dental implants is commercially pure titanium (cpTi) [5]. However, its application is not permitted in locations with high levels of wear, tensile strength, and fatigue [5–7]. Particularly when used in small-diameter implants, which must adhere to stringent mechanical stability specifications to prevent overloading and implant breakage [8], pure titanium is a rather soft metal [9], making it prone to fatigue. Additional factors that restrict the applications of cpTi as a material for dental implant are its higher Young's modulus and without sacrificing biocompatibility, it is difficult to increase the material's mechanical characteristics [10]. Another option is to use titanium alloy, which is made by combining titanium with other metals, to obtain superior mechanical properties [9]. Ti is a versatile element that may be combined with a variety of other elements to produce alloys with distinctive characteristics and designs for dental implants that are most closely resemble the ideal. Ti6Al4V alloy has various applications because of its superior mechanical performance [7]. The discharge of Al and V from this alloy however, had a negative effect on cells viability and severely reduced implants biocompatibility [11]. Al has in fact been associated to serious neurotoxic consequences, particularly in light of research linking it to bone brittleness [12], Alzheimer's disease [13], and possible local inflammatory triggers. The usage of Ti6Al4V has been discouraged as a result of these studies, which have also sparked the creation of alloys devoid of harmful substances that are inert in the oral cavity. β titanium alloys do not have above drawbacks. Experimental alloys must have adequate mechanical properties, be strong and stable in corrosive environments, and be safe for usage in-vivo to expand their clinical applicability [14]. They must also be biocompatible. Due to their exceptional strength and outstanding biocompatibility [15] as well as characteristics including higher strength, better corrosion resistance [16], and Young modulus near to natural human tissues [17, 18] titanium alloys have demonstrated to be highly desirable for biomedical field. These exceptional qualities have made titanium alloys attractive candidates to replace cpTi in the production of dental implant and other applications, and in many circumstances to serve as the initial line of therapy [19]. Despite the fact that several alloys are made for biomedical purposes, numerous research on the viability of using these novel materials as alternatives to cpTi have come up empty. Additionally, few studies have put experimental alloys to the test in living organisms to support their application.

Metastable β-titanium alloys are extremely adaptable materials with substantial usage in the medical and other engineering fields. These alloys provide excellent structural materials for use in aircraft because of their low density and high strength, which may be obtained through precipitation hardening. Because they can be created with non-toxic components and have high strength, low modulus, and low porosity, β-Ti alloys are desired biomedical materials. β-titanium structure is helpful in biomedical and other technical applications because it has the ability for shape memory and has super elastic properties [20]. The selection of alloy components and desired properties in titanium alloys is controlled by application-specific design criteria. For instance, β-Ti alloy's non-toxicity is a key prerequisite for its usage in biomedicine. The alloying additions should not, however, cause the density of aerospace β-Ti alloys to increase. Due to the prevalence and variety of β-Ti alloys, current article emphases on β-Ti alloys of the biomedical grade. Most β-Ti alloys used in biomedicine can be categorized into two groups. The first group consists of structural alloys used in orthopaedic applications to sustain loads, while the second group consists of functional alloys used in orthodontic and cardiovascular applications. The design goals for these two groups of applications also differ significantly. Orthopedic alloys, for example, need higher strength and lower modulus, while functional alloys must have super elasticity or shape memory qualities [20]. Reviewing β-Ti alloys as biomedical materials for dental and orthopedic applications is the main objective of this study.

Current biomedical alloys have inherent toxicity brought on by discharge of metal ions and stress shielding effects that could only be avoided by developing new material [21, 22]. The design of metastable β-titanium alloys for orthopaedic use is dependent on solutions to above problems. The innocuous elements Mo, Nb, Fe, Zr, Ta, and Sn are among those found in newer compositions of titanium alloys [23]. Furthermore, compared to existing metallic biomaterials Ti-6Al-4 V, Co-Cr–Mo alloys, and 316L stainless steel β-Ti alloys have a lower modulus [24]. Research on the production of β-Ti alloys focuses on three factors: alloy composition design, thermo-mechanical processing, and performance assessment. Low elastic modulus is the goal in the creation of alloy compositions. Thermo-mechanical processing is used on β-Ti alloys to raise their strength while keeping their modulus of elasticity at lower value. The performance metrics that need to be determined are biocompatibility, corrosion, fatigue, and wear. Only a short description of β-Ti alloys has been made in studies that have tracked developments in the field of metallic biomaterials as a whole [23, 25]. Despite the significant advancements in this field, an inclusive topical study of β-Ti alloys for biomedical usage is not yet accessible. We present an overview of numerous important Ti alloys for various implants-related aspects in this article. To support the use of titanium alloys as substitute to cpTi and its alloys in clinical backgrounds, the existing knowledge regarding the mechanical, electrochemical, biological, and chemical characteristics of the principal alloys generated during the recent years is thoroughly studied. This article provides a comprehensive examination of methods for designing alloy compositions, thermo-mechanical processing methods, and how these factors affect the performance of these alloys.

Classification of titanium alloys

A transition metal called titanium can combine with substances that have atoms of a comparable size to generate solid solutions. Up to 882.5 °C, it displays a hexagonal close-packed (HCP) geometry termed as the α structure. Solid titanium above this temperature develops a BCC crystal structure and form a common β structure before melting at 1688 °C [26]. There are numerous varieties of titanium alloys that are either pure α or pure β, or blends of the two [27]. Either α-stabilizers, like oxygen, aluminum, or β-stabilizers, like vanadium, iron, nickel, and cobalt are used to alloy titanium [28].

Table 1 Titanium alloy stabiliser with its effects and different properties [11]

Stabilizing elements	Impacts on transition temperature	Effects on properties of Ti
α stabilizers: O, C, Al, N	Increase	Hardening
β stabilizers: Cr, Mo, Co, V, Fe, Ni, Nb	Decrease	Grain refiners
Neutral: Zr and Sn	No noticeable impact	Hardening

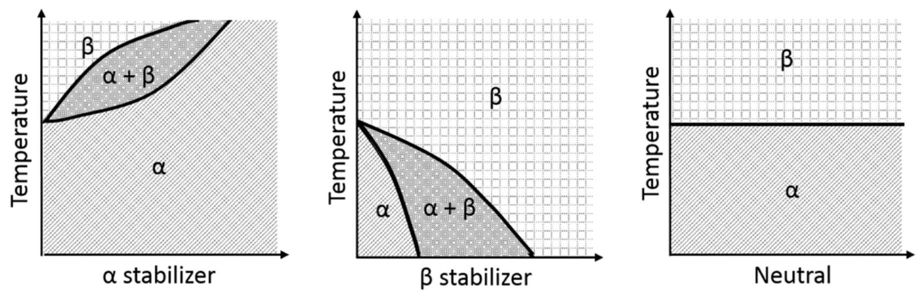

Fig. 1 Titanium phase diagram as per stabilizer's compositions [11]

Some metallic substances, such as zirconium also have no impact on the stability of any phase. Titanium alloys are predominantly recommended for implant fabrication due to their exceptional corrosion performance. The α micro-structure can be favored during processing, and this has an impact on the mechanical characteristics (fatigue resistance, strength, fracture toughness, ductility, etc.). Table 1 shows the different stabilizing elements added to titanium alloy to stabilize particular structure and improve properties of titanium alloys.

It is necessary to characterize the room temperature crystalline phase, the concentration, the kind of alloying components, and the microstructure of Ti alloys [29, 30]. There are three categories of elements that could be used to create titanium alloys: N, Al, O, and C are examples of α-stabilizer which try to stabilise the α-phase due to increase in transition temperature; Fe, Mo, Ni, V, Cr, Nb, and Co are examples of β-stabilizers that try to stabilise the β structure by lowering the transition temperature; and Zr and Sn are regarded as neutral elements which have no impacts on the stability of α or β structure. For ease of understanding, Table 1 provides a summary of these data. Figure 1 demonstrations impacts of stabilising elements on the titanium phase diagram to understand their mechanism. It is easy to see how adding atoms has an impact on the α and β phases and at their transition temperature.

Based on the proportional amounts of each phase, titanium may be further split into the near α, α, α + β, near β, and β phases [31]. Near α-alloys contain 1–2% of β-stabilizers and 5–10% of β phases; α + β alloys however have higher amounts of β-stabilizers in their constitutions and typically contain 10–0% of β phase in their microstructures [19]. Near-β and α + β alloys are mostly having α, β phases and have larger concentrations of β-stabilizers. It is well understood that the volume percentage, form, size, and distribution of the phase precipitates within the matrix substantially influence the structure, which has a significant impact on the material's chemical and physical characteristics [32, 33]. The alloying components that can affect the microstructure of titanium are known to researchers. To create implants with superior performance than those created with cpTi, they added elements to pure titanium. For example, the combination of Ti and Al to generate Ti6Al4V was thought to develop a biphasic microstructure (α + β) due to stabilising impact of α and β, V and Al. Alloys which shows the α + β microstructure include characteristics such as high strength, ductility, and lower-cyclic fatigue [19]. Ti6Al4V is a popular Ti alloy that is utilised in biomedical applications where high strength is required [34]. The titanium matrix hardens quickly in solid solution when alloys with Al are used [35].

Additionally, the effects of solid solution hardening have been produced using Bi and Zr, like Al [36, 37]. Alloys can be created in a range of ratios when titanium is cast entirely with Zr, which often increases Ti's mechanical strength as well as its potential for corrosion and resistance to wear [31]. In contrast, β-stabilisers that also serve as grain refiners are present in β-titanium alloys [14]. Nb, Mo, and Ta have gotten the most attention for creating β-titanium alloys that combine better mechanical qualities with great biocompatibility [32, 37]. They are among the most effective alloys for making implants as a result of these properties [29, 32].

α-Ti and near-α Ti alloys

Only the α-phase is present in α-type Ti alloys, which are composed of cp-Ti and Ti alloys in various grades. In general, cp-Ti comes in four grades that range from 0.18 to 0.40 wt% O and 0.20–0.50 wt% Fe [38]. Compared to α-Ti alloys, near α-Ti alloys principally comprise α-phase and a negligible percentage of β-phase, that are the result of the adding a smaller number of β-stabilisers (1–2 weight %) [39]. Similar characteristics, for example outstanding corrosion performance, superior weldability, and strong creep performance, are shared by both α-Ti alloys and near α-Ti alloys. This makes them appropriate for applications involving high temperatures. However, due to the far more solid HCP structure, their strength is noticeably lower at room temperature and typically could not be increased by heating process.

β-titanium alloys

In comparison to (α + β)-titanium alloys, β-titanium alloys have lower percentage of α-stabilizers (like O, C, N, Al) and larger percentage of β-stabilizer (like Mo, Ta, and Zr), with no intermetallic phases forming [40]. Because there is no micro-galvanic activity between the different phases, β-type titanium alloys are projected to have superior corrosion resistance in human tissue than (α + β)-titanium alloys and are also comparably stronger and more biocompatible [41]. Because of this, β-type Ti alloys may be able to overcome challenges in the development of biomedical implant. For biomedical applications, numerous newer β-titanium alloys [42] and gum metal, a class of β-titanium alloys with particular alloying elements which seemed to undergo a dislocation-free method of deformation, have been created in the previous two decades. These alloys often have comparable or improved properties. As a result, recent research has concentrated on creating novel, inexpensive β-titanium alloys that have advantageous mechanical characteristics for biomedical field and are composed of inexpensive alloying elements including Fe, Mn, Sn, and Cr [43]. Some of the important β-titanium alloys are Ti12Mo6Zr2Fe, Ti(10 – 80), Ti15Mo5Zr3Al, Ti16Nb10Hf, Ti15Mo2.8Nb3Al, Ti13Nb13Zr, Ti15Mo, Ti24Nb0.5O, Ti24Nb0.5N, Ti29Nb13Ta4.6Zr, Ti23Nb0.7Ta2Zr, TI36Nb2Ta3Zr0.3O, Ti23Nb0.7Ta2Zr1.2O, Ti35Nb5Ta7Zr. Table 2 shows different properties of above mention β-titanium alloys.

(α + β)-titanium alloys

More β-stabilisers are present in (α + β)-type titanium alloys than in near α-type titanium alloys. Therefore, (α + β)-titanium alloys have a high percentage of the β-phase (between 5 and 30 volume%) [50]. (α + β)-titanium alloys have better fabrication ability, and moderate high temperature strength [51]. In contrast to α-titanium alloys, (α + β)-titanium alloys can heat treated, allowing for the optimization of their mechanical properties. The volume fractions and properties of the α and β phases can alter depending on the alloy chemistry, heat treatment temperature, and cooling rate [52]. In addition to CP-Ti, Ti6Al4V (Ti64) is the most widely used (+ α + β)-titanium alloy for use in biomedical field, accounting for 50% of total Ti production [39]. By reducing the number of interstitial impurities (for examples H, O, C, and N), Ti-6Al-4 V also recognized as Ti6Al4V ELI, which has been further enhanced and is now frequently utilised for plates for bone fixation and the stem of prosthetic hip joints [53]. Ti6Al4V has been replaced with Ti6Al7Nb and Ti5Al2.5Fe

Table 2 Mechanical characteristics of human bones and different titanium alloys are compared

	Materials	Yield Strength (MPa)	UTS (MPa)	E (GPa)	Ref
Human Bone	Cortical bone	30 – 70	194 – 195	5 – 23	[44]
	Cancellous bone	–	0.9 – 8.80	0.01 – 1.57	[44–46]
α microstructure	Cp Ti (grade 1)	170	240	115	45
	Cp Ti (grade 2)	275	344	105	46
	Cp Ti (grade 3)	380	450	115	47
	Cp Ti (grade 4)	480	550	105	[2, 47]
α + *β* microstructure	Ti-3Al-2.5 V	585	690	100	25
	Ti-6Al-7Nb	921	1024	105	[25, 48]
	Ti-5Al-2.5Fe	914	1033	110	45
	Ti-6Al-4 V (annealed)	825–869	895–930	110–114	[25, 45]
β microstructure	Ti-12Mo-6Zr-2Fe	1000–1060	1060–1100	74–85	[48, 49]
	Ti-(10–80) Nb	760–930	900–1030	65–93	25
	Ti-15Mo-5Zr-3Al 870	870–968	882–975	75	45
	Ti-16Nb-10Hf	730–740	740–850	81	[2, 25]
	Ti-15Mo-2.8Nb-3Al	771	812	82	[48, 49]
	Ti-13Nb-13Zr	900	1030	79	45
	Ti-15Mo	544	874	78	[2, 45]
	Ti-24Nb-0.5O	665	810	54	2
	Ti-24Nb-0.5N	665	665	43	2
	Ti-29Nb-13Ta-4.6Zr	368	593	65	46
	Ti-23Nb-0.7Ta-2Zr	280	400	55	2
	TI-36Nb-2Ta-3Zr-0.3O	670–1150	835–1180	32	2
	Ti-23Nb-0.7Ta-2Zr-1.2O	830	880	60	2
	Ti-35Nb-5Ta-7Zr 530 590 55 [18]	530	590	55	45

because Ti6Al4V contains poisonous V [53, 54]. Ti6Al7Nb has been utilised in biomedical devices like plates for fracture fixation, femoral hip stems, fastenings, wires, and screws because it has better wear resistance than T6Al-4 V [55]. Because Ti5Al2.5Fe is metallurgically analogous to Ti6Al4V, it has been used to make hip prostheses and hip prosthesis heads. Despite the fact that Ti6Al7Nb and Ti5Al2.5Fe both can remove harmful V from Ti6Al4V, Al yet present in both alloys and could potentially cause a certain sickness (such as Alzheimer) [56]. Ti alloys of the $(\alpha + \beta)$ class are not the best option for biomedical implants because of this. Between 1950 and 1990, the very first generation of biomaterials, which included cp-Ti, Ti6Al4V, Ti6Al4V ELI, Ti6Al7Nb, and Ti5Al2.5Fe, were developed [57]. Evidently, the moduli of $(\alpha + \beta)$-titanium alloys are still considerably greater as compared to bones, that could lead to implant loosening and bone resorption. These factors result into creation of β-titanium alloys, which have reduced elastic moduli and improved biocompatibility as well as non-toxic β-stabilizers (like Ta, Zr, and Mo) [58].

Shape memory alloys based on titanium

Ti-based shape-memory alloys, such as TiNi, TiZr, TiNiAg, and TiNbSn, are often used as biomedical materials due to their exceptional mechanical characteristics [59, 60]. A reversible martensitic transformation is the basis for the near equiatomic TiNi alloy's original discovery of superelasticity and shape-memory properties, they have a low elastic modulus, high recover strain, and high strength [61]. Due to these benefits, TiNi alloy is suitable for a variety of applications. Nonetheless, the principal uses for Ti-Ni and other shape-memory alloys based on titanium continue to be biomedical and aerospace. For biomedical applications, TiNi alloy exhibits superior biocompatibility to stainless steel and other titanium implant [62].

In artificial saliva, corrosion resistance of TiNi alloy is also marginally greater as compared to Co-Cr-based alloys. Thierry et al. [62] examined the thrombogenicity of Ti-Ni vs. SS stents in an in vivo shunt porcine model. The findings revealed that while SS stents undoubtedly shows higher thrombus, TiNi stents only represent a small percentage of thrombus, with most of it concentrated at the intersections of the struts. Several more investigations into the biological performance of TiNi alloy have also been made, and it is generally agreed that both in vitro and in vivo testing of TiNi alloy demonstrates biocompatible behavior [63]. TiNi alloy can be used for a variety of bone implants, including stents, bone tissue engineering, and spine fracture repair, cervical and joint replacements, thanks to its high strength and comparatively low stiffness [64]. The shape-recovery property in particular makes it possible for the TiNi alloy implant within the host tissue to maintain mechanical integrity. Walking and running can achieve the recoverable strains in a superelastic TiNi implant, which encourages the formation of bone cells around and/or inside Ti-Ni implants [65]. The ability of implant strain to drive cell development has been extensively studied in vivo utilizing guinea pig models [66]. When compared to TiNi alloy, other metallic implants consistently show lower stresses and are stiffer. As a result, implants made of TiNi alloy and other Ti-based shape-memory alloys have an advantage in terms of osseointegration.

Titanium alloy production methods for use in biomedical applications

Casting, cold, and hot working, powder metallurgy, machining, and additive manufacturing are some of the production methods for Ti alloys used in biomedical field. Three different types of Ti alloys, including, α, β, and (α + β) are produced. Certain alloying elements, for example Al, O, Si, Sn, and Zr dissolve preferentially in the α-phase, elevating the (α + β)-phase [67]. These elements are added to alloys to change their characteristics, such as hardening and increased tensile strength. The range of strength of various classes, collectively known as cp-Ti, is mostly controlled by oxygen. Due to their lower elastic modulus (that is lower as compared to α-phase and (α + β)-phase and close to that of the human bone) and higher specific strength, titanium alloys stabilized by the β-phase transformation are appropriate for biomedical applications [68]. The cpTi and Ti6Al4V are produced using the conventional methods, using materials that are graded 1–5 by the ASTM standard, such as bars, sheets, billets, strips, plates, wires and forgings. Unalloyed cpTi is existing in grades 1–4, and alloyed Ti-64 is available in grade 5 [39].

Due to its advantages of low cost, resource efficiency, suitable time, and customized fabrication parameters, the powder-based additive manufacturing method of titanium and its alloys, one of the AM approaches, has gained considerable attention for biomedical applications [69]. The chosen additive manufacturing method, as well as the quality Ti and its alloy powder, has a substantial effect on the quality of implants made via additive manufacturing. The biomaterials are produced using additive manufacturing techniques such as directed energy deposition [70], laser-based powder bed fusion of metals (PBF-LB/M) [71], powder fed system of binder jetting [72], electron beam powder bed fusion of metals (PBF-EB/M) [73], plasma atomization [74], gas atomization [75], and plasma rotating electrode process [76].

Design improvements have been made possible by advancements in porous titanium structures for biomaterial applications. Using additive printing techniques, porous surface surfaces with predetermined, predictable unit cells for biomedical implants can be created, which have the requisite properties like encouraging cell growth and osseointegration. By having compressive strength and elastic modulus that are comparable to those of human bone, biomedical implants might avoid difficulties after implantation such as stress shielding effects [77, 78]. Biomedical implants need to have an exact design of porosities and pores in order to replicate the various mechanical qualities and features of the two main types of bones, cortical bone and trabecular bone [79]. While exhibiting comparable composition in respect of porosity and the proportion of organic and inorganic components, these two bone types are different from one another. These two types of bone are mixed and arranged differently depending on the mechanical loading that is being applied as well as the skeletal region. Cell differentiation and proliferation are impacted by the size, porosity, and quantity of pores, which affect their form [80].

The two primary categories of cellular structures are stochastic and non-stochastic. In contrast to stochastic structures, which have cells with randomly changing shapes and sizes, non-stochastic structures can be represented by the periodic recurrence of a lattice structure. On the basis of production via powder bed technologies, which produces superior mechanical characteristics and the ease of eliminating unfused powder, non-stochastic metal structures are favoured over stochastic metal foams [81, 82].

This is due to the fact that their cell sizes and shapes do not vary at random. Changes in non-stochastic structures, such as pore size and shape, permeability, and porosity, have been assessed in terms of how they affect the mechanical properties of Ti6Al4V scaffolds made by selective laser melting as well as in vitro biological findings (SLM). The amount of cells adhered to the Ti-6Al-4 V scaffold was affected by the different pore shapes' effects on cell permeability. Further research demonstrated that the hexagonal pore shape experiences higher pore occlusion than rectangular or triangular pores, which mostly explains why the circular cell growth pattern was irrespective of pore size and shape [83].

Furthermore, research on titanium hip implants has been done to reduce the effects of stress shielding without compromising mechanical strength. This was achieved by incorporating fabrication methods including finite element analysis (FEA) and electron beam melting (EBM) into the design process. To accomplish the necessary reduction in implant stiffness, the solid stems were altered using a periodic lattice structure. The comparisons between the built model and the simulated model showed that it is possible to create non-stochastic lattice architectures using EBM. Lattice strut orientation was important for the fabrication process as well. The EBM-fabricated model and the FEA-simulated model had different strut surfaces; therefore, safety considerations had to be built into the implant design [67].

In contrast to the FEA model's constant cross-section and smooth surface, the manufactured struts had slight fluctuations in their cross sections and textured surfaces. The three model configurations used in the study were complete solid, hole, and mesh forms. At the proximal part of the femur, it was discovered that the mesh arrangement built into the Ti-6Al-4 V stem had improved stress distribution characteristics [84, 85]. Another investigation was done to ascertain the internal geometry, pore size, and pore density of porous structures made of Ti-6Al-4 V using pulsed and continuous laser melting deposition (LMD). Although different densities were obtained in both cases when the parameters, such as laser power and powder mass flow rate, were changed, it was demonstrated that both manufacturing techniques produced different internal porous architectures. On the substrate, Ti6Al4V powder was employed as the deposition medium, and parameter tuning led to the creation of pores that were appropriate for osseointegration. Discovering analytical models of the Wolfram Mathematica-created processes is required in order to find interacting, transient heat, temperature, and mass flow models [86]. Compared to a continuous beam, a more regulated porosity might be achieved by using a pulsed manufacturing technique. To prevent early failure, a regular structure was essential [87].

Titanium alloys' characteristics

Mechanical characteristics

The mechanical properties and biocompatibility of a novel alloy are its primary design considerations [15]. Dental implants must have robust mechanical properties due to the stresses and fatigue cycles they encounter during use [88, 89]. By using methods including solid solution strengthening by substitutional and interstitial atoms, precipitation, grain refinement, dispersion strengthening, and work hardening, including lamellar and dispersed phases, titanium and its alloys' mechanical characteristics can be enhanced

[90]. It is expected that biomaterials will combine higher strength and lower elastic modulus [91]. For solid materials, particularly metals and alloys these qualities appear to be mutually exclusive [18]. Strength and elastic modulus of titanium alloy are typically increased by adding elements like Mo, Nb, Ta, and Zr [36]. To make implants operate better than those manufactured with cpTi, it is crucial to find a balance between strength and elastic modulus. As a result, it is important to comprehend the characteristics of biomaterials and forecast how they will behave when anchored to bone [92]. The mechanical characteristics of Ti alloys created for biomedical purposes are displayed in Table 2. Because Table 2 summarizes multiple studies whose procedures were not standardized, it is important to proceed with caution when drawing conclusions from the analyses there.

Ductility and strength

The alloy's strength ought to be sufficient to support the load placed on an implant [15, 93], which may include bending, torsion, compression, and tension [32]. Materials that are employed as substitutes for hard tissue must have certain qualities, including tensile strength and fracture toughness for protecting the implant integrity and avoiding plastic deformation at the time of implantation in order to maintain stability between prosthetic components and implant [10]. Contrarily, ductility makes a number of manufacturing process easier [91], which is crucial because implants have complicated geometries. The structure and grain size of the alloy can be changed to increase its strength and ductility.

The solid solution alloy is altered by the addition of V and Al, resulting in particle precipitation and a transformation in the phase from α to the $\alpha + \beta$ [10] which make the tensile strength of Ti6Al4V is much stronger than that of cpTi. Similar results were obtained by adding Al to TiNb and Si to TiNbZrTa, which strengthened the solid solution and refined the grain [94, 95]. Because silicide intermetallic particles supported the grain boundaries, grain development was suppressed when Si was added [94]. In comparison to pure Ti, the yield strength and tensile strength of Ti grains refined by adding Nb are improved by 1.5–1.6 times [49]. Additionally, there is evidence that the presence of Ta to Ti-Nb-Zr, which features an elastic and completely plastic material increases the alloy's ultimate tensile strength and elongation [96]. High-pressure torsion proved successful in improving the microstructure and enhancing the tensile strength of an alloy with a comparable composition by increasing the density of dislocations [16]. However, Ta was the reason for a reduction in Ti-Fe alloy strength [97], despite the alloy's increased hardness and compressive yield strength. It is not always the case that the mechanical qualities of the alloy will be improved by adding alloying components.

Increased Sn additions to the β phase of an alloy in the instance of TiNbSn tend to reduce alloy's ductility and tensile strength [91]. According to research by Datta et al. [15], a higher concentration of β-stabilisers may be able to lower the material's resistance. This was first noted in a prediction model, and then confirmed by producing a Ti–Al-Zr-Mo-Nb–Ta-Sn-Cr alloy that shown lesser strength as compared to Ti6Al4V whereas other two types of alloys with smaller concentrations of β stabilizers displayed high resistance level. A thermomechanical alloy process must be consolidated in order to provide a microstructure with reduced levels of β stabilizers.

Strength and ductility of Ti alloys are both directly correlated with interstitial content of materials [10, 98]. Although interstitial solutes reduce the cpTi hardness and enhance the material's strength, they also have a negative impact on the material's elongation values [10]. Similar behaviour in alloys is caused by intermetallic phases produced by substitution elements like Fe, Ni, and Cu. One sort of research which investigated two alloys with varying CuNi levels found that reducing the amount of these elements enhanced the alloy's ductility and raised the tensile strength to 1050 MPa [98]. The qualities of an alloy are also influenced by the manufacturing process. The Ti alloy is made stronger and more ductile by cold rolling, aging, annealing, and small-scale incorporation of ceramic particles into the matrix [16, 32, 94]. Since dental implants are subjected to continual pressures or cyclic stresses, long-term longevity of the material depends on assuring its biomechanical compatibility with bone [19]. Ti alloys made using various processes range in tensile strength from 360 to 3267 MPa (Table 2). Alloys of the ($\alpha + \beta$) type were found to have high yield and ultimate tensile strength values in general. It is clear that the presence of Zr, Ta, Si, Fe, Al, and Mo tends to increase alloy strength. This feature is not greatly affected by the presence of Nb, Sn, or Bi. The alloy strength is also influenced by the processing method, with SPS yielding has the greatest values.

Elastic modulus and hardness

Hardness is the capacity of a substance to withstand persistent deformation by indentation [37, 99]. It should be modest while making implants to ensure optimal machinability, but it should also have enough stiffness for protecting the bone from stresses [10]. Young modulus is a crucial property for the biomechanical interface of the bone and implant. Lessening the elastic modulus reduces bone atrophy while improving stress distribution at the implant-bone interface [10]. The elastic modulus has to be as near the bone as possible and feasible because "stress shielding" has been associated with osteoporosis and bone resorption near to implant site [7, 100].

The metallic implant would move in small ways if the Young's modulus were too low, hence this should be avoided, which can result in the prosthesis failing and the implant coming loose [49]. Although the existence of a α phase is associated with greater alloy hardness values, the elastic modulus may not prefer its presence. Because α-stabilizers function as a substitutional solute that reduces the material's atomic mobility [31] or whenever the alloys are aged at low temperature, it promotes the phase's precipitation [19], they increase the hardness of the specimen. The elastic modulus should first rise with increasing β content then fall abruptly at higher concentrations [15].

Usually, β-stabilizers having lower concentrations lead to $\alpha + \beta$ alloys, which have greater elastic modulus values because the α phase is present. The reduction of the α structure in an alloy structure by a rise in β stabilisers can lead to low hardness [37, 91] and as a result, the elastic modulus is decreased. When Zr and Bi were added to Ti, the hardness values improved in comparison to cpTi [31, 36, 101]; however, when Zr concentration grew, the hardness somewhat decreased [21, 88]. For the elastic modulus, Zr behaves differently. Zr was added in mass amounts ranging from 5 to 10%, which initially resulted in a fall in values; however, the value of this feature was increased beyond that of cpTi [31] at concentrations higher than 15%. The difference was due to Zr's greater atomic radius than Ti, which the scientists related to a change in distances between the atoms of an alloy's compositions. As a result, the atomic-level force that controls modulus of elasticity is altered. Addition of Nb to a TiZr alloy produced a biphasic $\alpha+\beta$ microstructure as well as increase in hardness, that was then further improved with aging heat treatments [35]. However, this process typically raises the Young modulus to levels more than 100 GPa [94]. The addition of Sn to the Ti-30Nb resulted in an alloy with a high level of β structure, which, aside from lowering the elastic modulus, had no influence on the material's hardness [102]. This was caused by the distribution of Nb throughout the titanium matrix. A Ti33Nb4Sn alloy produced by cold-rolling and then annealing methods had one of the lowest elastic moduli (36 MPa) ever recorded in the history of titanium as a biomaterial [18]. This was made likely by the creation of a β structure with little β-stabilizer content.

Even while cpTi and its alloys have lower elastic moduli than SS and Co-Cr alloy [7, 16], they nevertheless have reasonably high elastic moduli when compared to human bones (10–30 GPa) [10, 103]. In comparisons to cpTi, α and $\alpha+\beta$ alloys, β alloys have demonstrated more favourable results in terms of Young's modulus [92, 104]. This might be because of the BCC structure and lower atom lattice density of the β phase are different from the α phase's HCP structure [16]. This guarantees that the alloy has a higher plastic deformability [100]. These diverse architectures' atom spacing result in variations in the atomic-bonding force and, as a result, variations to elastic modulus [31]. With thermomechanical processing, alloy elastic modulus might vary greatly [15, 16]. For example, samples quenched in water had lower values for Young's modulus [15, 32], which is consistent with Table 2. Fast cooling prevents the creation of the α structure, that inhibits the conversion of α phase to the β phase and causes decrease in elastic modulus [32]. According to the literature, titanium alloys' elastic moduli range from 35 to 175 GPa, with focus on the β alloys whose values are equivalent to those of bone, Ti-36Nb-4Sn and Ti-23.72Nb-4.83Zr-1.74Ta(-Si) alloys which exhibited lower elastic modulus values are notably mentioned by the researchers [11]. The hardness value of cpTi, which is among the lowest, dramatically increases by adding of Fe, Zr, Mo, and Al. Ti-Fe(-Ta), TiAlV, and TiZr are the three hardest metals [11].

Fatigue behaviors

Unlike pure monotonic loading, it simulates a much more practical circumstance, cyclic loading must be used to assess the fatigue behaviour of materials used for dental implants [89, 105]. Additionally, the environment in which implants are placed might affect their ability to withstand fatigue by hastening the onset of surface imperfection and its growth to a critical size, which causes the implants to fracture [106–108]. Despite this, there are not many research that examine how Ti alloys perform in human-like media in this situation. Ti24Nb-Zr7.6Sn in 0.9% NaCl solution withstood more fatigue cycles before failing than it did in air because of the cooling action of this medium, which can prevent materials from softening due to an increase in temperature at the time of the fatigue test [109].

Moreover, the NaCl solution's oxide layer may strengthen the alloy's corrosion and wear resistance. In the strain-controlled fatigue test, Ti-24Nb4Zr7.6Sn showed a significantly greater fatigue resistance than Ti-6Al-4 V ELI [109]. In Eagle's solution, a corrosion fatigue test involving Ti alloys was conducted. At 108 cycles, TiZrNbTaPdON and

TiSnNbTaPdO had fatigue strengths of around 600 MPa, whereas Ti–Al-Nb–Ta had a fatigue strength of about 700 MPa. At 107 cycles, the Ti-Mo-Zr-Al alloy displayed lower performance than earlier alloys [110]. When compared to Ti-Grade IV, Ti-15Zr discs and dental implant performed much better under fatigue. The alloy's and cpTi's upper limits for fatigue endurance were 560 MPa and 435 MPa respectively [111].

The fatigue strengths of Ti-7.5Mo and Ti-13Nb-13Zr were lower than those of Ti-6Al-4 V and cpTi. However, when strain controlled fatigue resistance is taken into account, Ti-7.5Mo exhibited the best fatigue performance [112]. Combining material qualities, surface properties, and design optimization of implants can improve fatigue behavior [111]. In this context, the employment of various heat treatments, the deposition of hard thin coatings, and mechanical processing process all have an important effect on how well Ti alloys handle fatigue [106]. By creating considerably smaller microstructures, cold rolling increases fatigue resistance [109]. Alloy fatigue cracks may primarily be caused by surface porosity created during the casting process [112]. Similar to this, surface treatments like SLA that induce roughness have been shown to have a negative impact on a material's fatigue behaviour and increase fracture initiation susceptibility [111]. In general, more research is advised on the fatigue performance of titanium alloys with cyclic load in media that are similar to those found in humans, such as synthetic saliva and SBF. Which is necessary because dental implant materials are more susceptible to the combined impact of cyclic mechanical loads and a corrosive environment than to any factor acting alone [105]. Improvements must also be made to thermomechanical processes and surface treatments to prevent manufacturing flaws that could act as stress concentration sites and cause failure initiation or propagation.

Surface properties

Surface qualities like composition and topography have an important effect on the outcome of implants therapy. Implants need a surface that encourages appropriate mineralization and osteogenic differentiation during the first phase of integration [113]. Cell adherence to bone apatite is influenced either indirectly or directly by surface characteristics of the implant's components, such as surface roughness, surface energy, and substrate compositions [114, 115]. It is ideal for dental implant that the alloy maintains hydrophilic surface simultaneously preserving the topographic micro-roughness [116].

Implant surface roughness is compatible with micrometre (0.11–100 μm) and nanoscale (1–100 nm) [117], and surface morphology is likewise compatible with these scales (Fig. 2). There are signs that bone response is influenced by micrometre and nanoscale levels [118], resulting in appropriate cells attachment, increased contact of implant/bone, and higher resistance to torque release [113, 119]. It was observed that easily ingestible, physiologically significant nanometric proteins will influence cellular responses favorably [120]. It was discovered that rough topographies were linked to osteoblast differentiation, whereas a smooth surface was linked to cell proliferation. According to theory when cells come into touch with a rough surface, the autophagic process may be triggered physically which may cause cells to differentiate [121]. To enhance and hasten osseointegration, a surface that promotes cell maturation is essential. As shown in Fig. 2, the topography at the nanoscale exhibits a reduction in the water contact angle and an accompanying rise in hydrophilicity and surface energy.

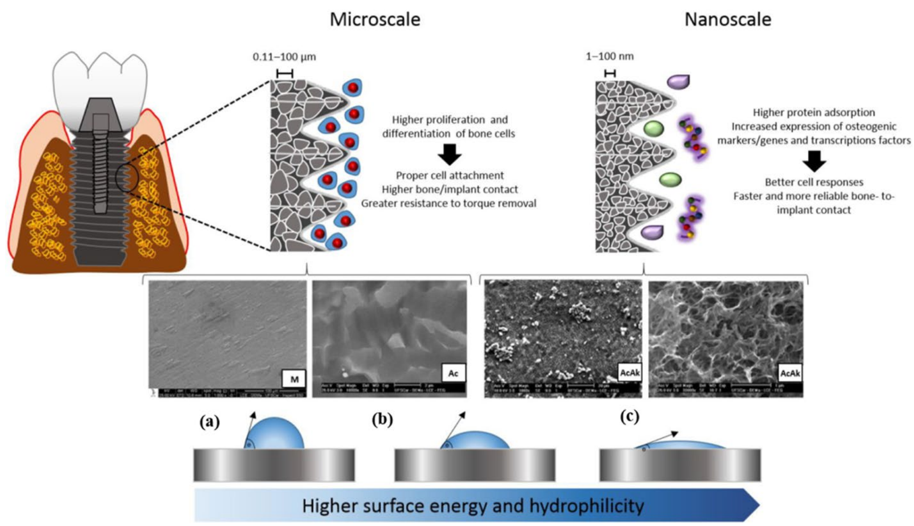

Fig. 2 Impact of topographic features at the micro- and nanoscales on implants. **a** Machined Ti6Al4V sample. **b** Acid etched sample. **c** Acid etched combined with alkaline treatment sample, adapted from [11]

In earlier research [117], a Ti6Al4V alloy with various surface roughness level was produced. Higher rough surface led to better results. Cell adhesion and proliferation were responsive to variations in topographies. A rough surface was also found to have a higher overall protein adhesion rate, fibronectin may bind to a rough surface up to ten times more than it can to a smooth one. There is still room for improvement in the explanation of how minor variations in surface roughness (Ra < 0.50 µm) affect cellular responsiveness and protein adsorption [115]. Increased wettability is also necessary for improved cell proliferation and adhesion on Ti alloy implant surfaces [122].

Surface physical and chemical characteristics can affect how wettable the alloy is. A surface is referred to as “hydrophilic” or “hydrophobic” if the water contact angle is less than 90°, and vice versa [123]. Having a narrower contact angle (81.75°) than cpTi (96.46°), Ti45Nb was found to have better hydrophilicity [49]. However, the Ti50Zr alloy had a greater surface energy and lower surface roughness (37 mN/m, 0.17 µm) than cpTi (34 mN/m, 0.20 µm) and the Ti50Nb alloy (32 mN/m, 0.46 µm) [115]. These characteristics of the substrate composition ensured that the Ti-Zr alloy had a good in-vitro biological profile (cell adherence and proliferation). The alloy’s surface area was greater, but Ti had a coarser topography than Ti-Ta-Nb-Zr. The outcomes of surface changes using different treatment techniques have likewise been outstanding. On the Ti25Nb3Mo3Zr2Sn alloy, treatment by mechanical friction resulted in various grain sizes [124].

The nano-grained alloy (7.0 nm; 50.4°) had the lowest surface roughness and the best wettability when compared to the finest-grain (7.4 nm; 64.1°) and coarser-grain alloys (7.1 nm; 67.8°). Nanoscale grains (30 nm) displayed improved cells response and absorb more protein when comparing to particle sizes of 90 µm and 180 nm [124]. The surface micro-roughness (0.14–0.48 µm), improvement in wettability (from 70 to 35°), and surface structure of Ti6Al4V-ELI were obtained by combining two acid-etched surfaces with an alkaline treatment [125]. It is clear that the morphology of the treated samples has changed among an acid etching (Ac) and machined surface with the alkaline solution-treated samples displaying an efficient osteoconductive behaviour (AcAk).

In a prior work [122], an electrochemical anodization process on a Ti-6Al-7Nb alloy produced a nanotopography. From 61.4° (machined surface), the contact angle was drastically reduced to 14.8° (treated surface). But when compared to a machined surface's (123 nm; 59°) roughness and contact angle, the anodized Ti-25Nb-25Zr alloy's nanoporous surface (with pores smaller than 15 nm) remained unchanged as well [126]. Despite this, the surface composition and altered morphology were able to dramatically enhance mesenchymal cells' proliferation, adhesion, mineralization, and migration.

The biomechanical qualities of porous and rough surfaces are strengthened as a response to microscale bonding strength, facilitating interactions between the implant and the surrounding cells [113]. This is because implant surface created by these surfaces has a wider area of contact with newly developed bone. Enhancing cells feasibility and differentiation on the surface of Ti13Nb13Zr with a hydrothermal process that uses an alkaline solution having Ca and a straightforward post-heat treatment appears to be a successful technique without dramatically changing surface morphology [127]. This is because it increases surface hydrophilicity and perhaps increases surface area at the nanoscale and forms anatase structures [128]. The anatase phase's presence was found to be crucial in boosting surface reactivity and energy [123].

Cell differentiation and maturation with osteogenic potential have already been found on a cpTi surface with submicron roughness and considerable hydrophilicity [128, 129]. Additionally, there are not much research that compare how different metals' surfaces affect material qualities and tissue response. Most studies only examine surface attributes in connection with surface treatments. From this perspective, more investigation is required to thoroughly analyze how the makeup of various alloy surfaces that can impacts wettability, roughness, and biological aspects [130].

Corrosion behavior

The creation of a stable passive layer, primarily made of TiO_2 is widely recognised to be the reason why titanium and related alloys shows better corrosion resistance in a different condition [2, 131, 132]. Despite any degradation to the passive coating on the Ti samples, it is possible to rebuild it relatively quickly. Ti alloys of α-type and $\alpha+\beta$ type are frequently used in early biomedical applications. The application environment, alloy compositions, and microstructure are typically important determinants of how corrosion behaves in metallic materials [133–135]. The environment inside the human body, for instance during inflammation and allergies, is typically steady, despite the fact that human temperature, environmental chemistry, and pH might occasionally change. According to Alves et al. [136], for cpTi and Ti6Al4V, 25 °C offers higher corrosion resistance compared to 37 °C.'s analysis of the corrosion resistance of the materials in simulated body fluid at the two various temperatures. As a result, cpTi and Ti-6Al-4 V exhibit different corrosion behaviours depending on the temperature. Like this, Ti-6Al-4 V corrosion behavior is similarly influenced by the pH value [137]. Although its passive range is limited at pH = 8, high corrosion resistance is demonstrated by Ti6Al4V in the neutral Ringer's solution [137].

Because there is more oxygen and acidic food available, Ti-6Al-4 V pitting corrosion frequently occurs in the oral environment [19]. In Ringer's solution, the alloys Ti15Mo, cpTi, and Ti6Al4V all have better corrosion resistance, but only Ti15Mo demonstrates a steady passive coating [138]. The environment of a human body, such as when brushing teeth will inevitably have a higher fluoride solution [139, 140]. As a result, in situations like these, α titanium and (α + β) Ti alloy shows lower corrosion resistance than β Ti alloys. For metal orthopaedic implants, fretting corrosion must also be taken into consideration [140]. The creation of a protective oxide layer reduces fretting corrosion, which typically manifests at modular connections [140]. Therefore, it is essential to utilise Ti alloys that are appropriate for biomedical field and have strong corrosion resistance. The development of β-type Ti alloys makes them prospective users in biological applications [141].

The chemical homogeneity of the underlying substrate, however, has a considerable impact on the passive film's quality. Generally, heterogeneous microstructures with individual Nb grains are formed when SLM is used to create Ti-35Nb using mixed powder. According to a study by Wang et al., heating SLM-manufactured Ti35Nb to 1000 °C for 24 h in Ar environment considerably improves the substrate's chemical homogeneity. Therefore, when compared to Ti-35Nb produced using SLM, the heat-treated version has a corrosion potential that is greater, measuring − 0.46 V. (− 0.55 V versus SCE). Additionally, Alves et al. [142] showed that the stability of passive coatings affects the corrosion resistance of β-type Ti alloys. After heat treatment, they discovered that Ti-10Mo alloy exhibits extremely lower passive current densities. With the aim of developing Ti alloys that are better suited for biomedical use, there are surely much comparative research on the corrosion rate of three distinct types of titanium alloys.

In the Ringer's solution, Kumar et al. [138] investigated corrosion behaviour of cpTi, Ti6Al4V, and Ti15Mo alloys. They found that Ti15Mo alloy has a wider passivation range than cpTi (145–1522 mV vs SCE) and Ti6Al4V. (155–1460 mV versus SCE). The corrosion behaviour of as-cast TiZrNbMo alloys with various Mo concentrations was studied by one of the researchers. The findings demonstrated that constitutional undercooling caused by Mo leads the TiZrNbMo alloy's grain size to shrink with increasing Mo concentration, and the least passivation current density is found in the TiZrNbMo alloy, which has a Mo adding of 15 weight percent and a value of 2.31 ± 0.03 A cm^{-2}. Zareidoost et al. [143] found that the alloy with the addition of Ag demonstrated excellent corrosion resistance in the Ringer's solution when Fe, Sn, and Ag were individually added to Ti25Zr10Nb10Ta. The passive film that is produced on Ti25Zr10Nb10Ta is more stable because Ag's standard electrode potential is higher (0.799 V) than Ti's (0.98 V). In Ringer's solution, Ti25Zr10Nb10Ta1.5Ag exhibits higher corrosion resistance. Ti40Ta22Hf11.7Zr's microstructure was altered by Lin et al. [144] through the application of various solution treatments and age treatments techniques. The findings demonstrated that the solution-treated Ti40Ta22Hf11.7Zr exhibits a β + ω structure as-cast, that changes to a monolithic β phase after heated to 900 °C for 1 h. The β-phase slowly changes into the β + α", β + α" + α', β + α + ω phases after aging at 300 °C for 15 min, 1.5 h, 12 h, and 24 h respectively [145]. Ti-40Ta-22Hf-11.7Zr alloys with such diverse microstructures exhibit various electrochemical behaviours in Hank's solution. The sample that has been subjected to solution treatment and has a singular β microstructure exhibits the lowest current density (0.49 0.03 A cm^{-2}). In comparison to their conventionally made counterparts, Ti-6Al-4 V alloys made using SLM are more susceptible to pitting corrosion in 3.5 weight percent NaCl solution, while Ti-6Al-4 V alloys made using EBM exhibit better corrosion resistance in phosphate-buffered saline than their wrought counterparts [94, 106]. Hence, the following unanswered query is posed: do Ti alloys made by various preparation techniques exhibit differential corrosion behavior? To solve this problem, Suwanpreecha C et al. and Qin et al. [146, 147] looked at the corrosion behaviour of Ti-24Nb-4Zr-8Sn alloys produced using SLM and conventional monolithic methods. These two alloys are identical in terms of their chemical makeup and monolithic phase, but they have different structures. These alloys have essentially identical potentiodynamic polarization curves and Nyquist plots, as shown in Fig. 3 [145, 147]. It follows that differences in Ti-6Al-4 V alloy corrosion behaviour resulting from different production processes are connected to the creation of various phase composition in the structure.

Biocompatibility

Materials for implants must have great biocompatibility in addition to mechanical and corrosion resistance [145, 148]. Long-lasting implants made of ideal materials can be placed in human without requiring additional surgery [149, 150]. Following implantation, the materials would cause a sizable number of interactions with bodily fluid, proteins, and cells in the human body. Conventional α + β titanium alloys include potentially hazardous components. As a result, β titanium alloys have been created recently, and an examination of their biocompatibility has also been carried out. When McMahon et al. [151] examined the cytotoxicity of Ni49.2Ti and Ti26Nb, they discovered that Ti26Nb is less cytotoxic. According to Xue et al. [152], the Ti19Zr10Nb1Fe alloy shows greater hemocompatibility as compared to the Ni–Ti alloy but equivalent cytocompatibility. The absence of harmful alloying components is the cause of the better biocompatibility of β-type Ti alloys [153]. There is an immediate need for more study of β-type titanium alloys. Fibrous tissue capsules are far more likely to form on the implant's surface

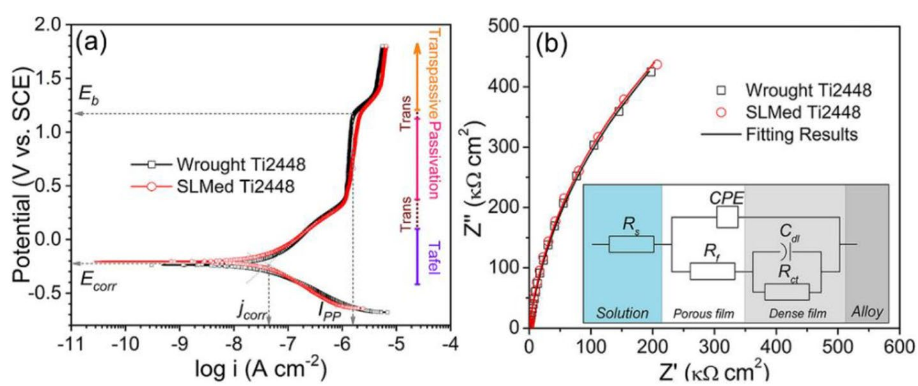

Fig. 3 **a** Potentiodynamic polarisation curves and **b** Nyquist plots show electrochemical measurements of Ti-24Nb-4Zr-8Sn that has been selectively laser melted and wrought Ti-24Nb-4Zr-8Sn was denoted by Ti-2448 [145]

because of the biological resistance of titanium alloys [2]. All varieties of Ti alloys will eventually experience this behaviour. Because of their biological inertness, alloys of the β-type Ti are safe but not bioactive. So, even though β-type Ti alloys do not include any possibly harmful alloying components, osseointegration should be further improved. In general, surface modification with the goal of enhancing Ti alloys' bioactivity has drawn a lot of attention. Takematsu et al. [154] used electrochemical, hydrothermal, or combined techniques to apply alkali solution treatments to Ti29Nb13Ta4.6Zr over a variety of durations. The findings shown that the surface of Ti29Nb13Ta4.6Zr evolves into a mesh-like structure and has a potent capability to promote the development of apatite regardless of the techniques or variables used.

Dikici et al. [155] developed composite coatings on Ti29Nb13Ta4.6Zr with calcium phosphate/TiO_2 by using the sol–gel technique. They discovered that because calcium phosphate and titanium dioxide are both highly bioactive to bone cells, the coating can significantly boost the material's bioactivity. Fibrous tissue capsules are far more likely to form on the implant's surface due to the biological inertia of titanium alloys [2]. Organic coatings have also drawn a lot of attention in addition to inorganic coatings. Extracellular matrix (ECM) proteins have been successfully immobilised on titanium implants surface over the last few decades by research on cpTi and Ti6Al4V [156]. For example, human mesenchymal cells respond more favourably to cpTi coated with collagen [156]. Other coatings provide similar outcomes as well [157]. For instance, human mesenchymal cells respond more favourably to cpTi coated with collagen [156]. Other coatings provide similar outcomes as well [157]. Unfortunately, information on the organic coatings on β-type Ti alloys is currently scarce in the literature. In contrast, it is anticipated that β-type Ti alloys with bioactive coatings will emerge as a future trend for biomedical Ti alloys given the noteworthy accomplishment of organic coating on other types of titanium alloys.

Osseointegration

The capacity of implants to osseointegrate and their success depend on optimising their surface topography and chemistry to encourage cell proliferation, adhesion, and differentiation. A prior literature study found that cpTi and Ti6Al4V exhibit equivalent osseointegration and biomechanical anchoring [11, 158]. In contrast, cpTi and a few alloys including Ti15Mo1Bi, Ti15Zr, and Ti24Nb4Zr7.9Sn have surpassed Ti6Al4V in animal tests (Table 3). It is evident that when alloys are fastened to animal bones, they behave biologically similarly to cpTi in the majority of investigations. In one investigation, Ti-Zr implants outperformed cpTi implants in terms of new bone volume creation and removal torque value [9]. The alloys TiCu, TiNb, and TiNbTaZr are also noteworthy since they demonstrated bone tissue biocompatibility without impairing the development of new bone [49, 159, 160]. Without altering cpTi implants, the Ti-Nb–Ta-Zr alloy implant's surrounding bone volume increased with time [161, 162]. Human studies with titanium alloys is very rare and is limited to TiZr, that is available commercially.

Studies employing tiny diameter Ti-Zr implants in humans in vivo [5, 163, 164] shown that these materials display osseointegration similar to that of cpTi. This study found that both the success rates and implant life were satisfactory. Despite the findings, the majority of studies only provide a maximum 1-year follow-up which suggests that more

Table 3 Survey of titanium alloys applications with its properties and animal model observations

Materials	Animal studies	Parameters	Follow-up period	Results	Ref
Ti-10.1Ta-1.7Nb-1.6Zr	38 screws-shaped implants were placed in each group of 38 male Sprague–Dawley rats	Bone-implant contact (BIC) and bone area ratio (BA) evaluations, gene expression, and removal torque evaluation	4 weeks	The RT among the TiTaNbZr and Ti implants did not differ significantly; the BA (41.2%) for the cpTi implant was greater than Ti-Ta-Nb-Zr implant ($p = 0.012$); the BIC percentage did not differ significantly; and the gene expression of an implants attached cells exhibited that the TiTaNbZr implants had roughly 3-, 6-, and two-fold lesser countenance of the proinflammatory, bone development	164
Ti-24Nb-4Zr-7.9Sn	White female rabbits; each group has cylindrical implants	Pull-out force; BV; Tissue Mineral Density (TMD);	12 weeks	At 12 weeks, the Ti-Nb-Zr-Sn group had higher pull-out strength than the Ti6Al4V group (p 0.05), and the experimental group's BV and TMD were significantly higher as compared to the control group's at the same time (p 0.05)	170
Ti-45Nb	12 cylindrical implants in each group; rabbits; Beagle tibia implant model	BIC and BA, bone integration, irritation of the oral mucosa, and the ratio of bone tissue to total tissue volume (BV/TV)	12 weeks	Both groups had similar peri-implant bone volume and tissue volume; Ti-Nb alloy and pure titanium demonstrated comparable effects on osseointegration; bone area and bone contact of the TiNb alloy improved quickly up to 12 weeks, without discernible change from titanium; both groups did not report oral damage or discomfort	46
Ti-15Mo-1Bi	White female rabbits; each group contains 24 cylindrical implants	New bone development	26 weeks	There had not been any noticeable differences between the groups at 6 or 12 weeks. post-implantation; at 26 weeks, the bone areas of the Ti15Mo1Bi implant were bigger Ti6Al4V implant (p 0.001); and the total bone areas of the Ti15Mo1Bi implant were approximately 249% of those of the Ti-6Al-4 V implant	171
Ti-35Nb-2Ta-3Zr	White male rabbits with 48 implants per group	Surface bone apposition ratio(BAR), pull-out force, and new BA	12 weeks	Pull-out force, BAR, and BA did not significantly differ across groups at any point	161

Table 3 (continued)

Materials	Animal studies	Parameters	Follow-up period	Results	Ref
Ti24Nb4Zr7.9Sn and nanotube-Ti-24Nb-4Zr-7.9Sn	White female rabbits; each group contains 8 cylindrical implants	BV/TV, BIC, BA, and ratios; Average trabecular thickness (Tb.Th); Average trabecular number (Tb.N); Trabecular mean separation (Tb.Sp)	Up to 12 weeks	At 6 weeks, the nanotube implants' BIC and in comparison, to the other two categories, BA ratios were considerably greater ($p < 0.05$), while at 12 weeks, in comparison to the other three categories, the nanotube-Ti-Nb-Zr-Sn implants' bone area ratio was considerably higher ($p < 0.05$). At both 6 and 12 weeks, for the nanotube, the greatest values were BV/TV, Tb.N, and Tb.Th. Ti-Nb-Zr-Sn	172
Ti-10Cu	White rabbits; each set contains 96 implants	Mean optical density (MOD), Mineral addition rate (MAR), and BIC in the expression of TGF-b1 and BMP-2	Up to 12 weeks	At any point in time, there was not any differences in bone density among groups, BIC, or MAR; At weeks 1 and 4, the Ti-10Cu group's Mean optical density value for BMP-2 was considerably greater than that of the cp-Ti category. At any time period, there was no difference in TGF-b1 expression across groups	162
Ti-Zr, SLActive® Straumann Roxolid®	13 screw-type implants were placed in each group of 13 female Bama minipigs (younger and older groups)	Rate of implant success and survival; assessment of RT	8 weeks	Ti-Zr implants had a survival rate of 85.7%, which was the same as titanium implant in the elderly category; The mean value for peak RT of titanium implant in the younger group was greater than TiZr implant ($p = 0.219$); Ti-Zr implants outperformed titanium implant in the aged group in terms of mean peak RT ($p = 0.250$);	174

extensive long-term research is required to establish the therapeutic effectiveness of the treatment. Long-term studies examining osseointegration in people are typically only conducted in a small number of cases in part because it is challenging to eliminate biases that the population being studied is subject to, such as biological variations, gender and age differences, and patient health conditions [165, 166]. Since in vivo investigations are difficult and contain a risk of patient injury, before doing such studies using Ti alloys it is essential that the chemical, mechanical, biological, and electrochemical characteristics of such alloys should be extensively confirmed from previous research. The advancement of in vivo investigations may also be hampered by ethical concerns and expenses. But it is important to promote human and animal research since they are essential for confirming the effectiveness and security of alloys before they are used in clinical settings.

Surface modification of Ti alloys

The surface layer of titanium implants produced using standard production methods is frequently oxidised, contaminated, regularly stretched and plastically deformed, non-uniform, and terribly weakly defined, which required surface modification to suit for biomedical applications [167]. Moreover, titanium requires surface treatment because it is bioinert and obviously unsuitable for biomedical applications. The need for specific surface properties that are different from those in the bulk Ti for many medical devices is a key additional justification for surface modification [4, 168]. For instance, having high bone formability is essential to achieving biological integration. For devices that come into contact with blood, like mechanical heart valves, blood compatibility is essential. In other applications, it is also essential to have good wear and corrosion resistance. Surface modification is critical for overcoming these challenges. The ideal surface modification technique boosts specific surface qualities required for certain therapeutic applications while also keeping the superior bulk properties of titanium and its alloys [169]. Figure 4 provides a schematic representation of several surface modification techniques that have been presented in response to various therapeutic demands. The following characteristics could be attained through surface modifications of the titanium

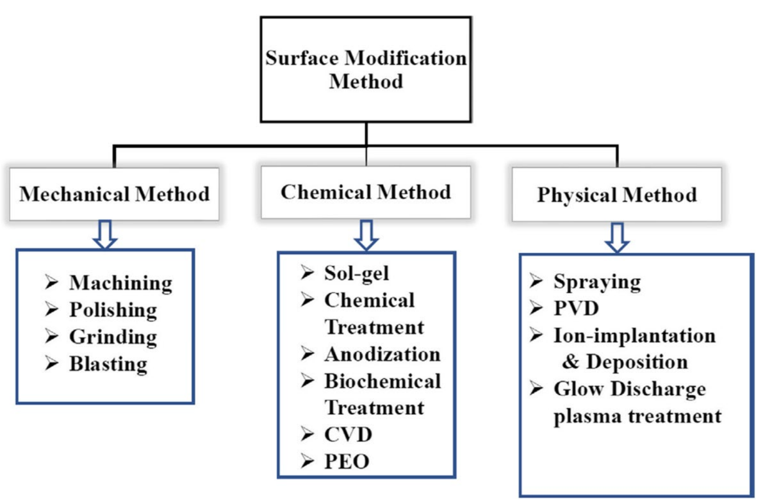

Fig. 4 Diagram displaying the various methods for surface alteration [4]

implant: increased bonding at implant/bone, increased inductivity and conductivity of bone, increased wear and corrosion resistance, increased bioactivity, and biocompatibility, and accelerated post-implantation healing [169]. Surface modifications techniques are divided into physical, chemical, and mechanical categories based on how the altered layer develops on the material surface [167, 170]. For example, it was observed that the surface treated dental implants have higher survival rates than machined implants [171, 172]. Achieving an osteoconductive surface that resembles bone, promoting cell adhesion, enhancing corrosion resistance, and preventing ion escape into the environment are the main objectives of the surface treatments. Several methods, including mechanical friction [124], isothermal oxidation [173], and hydrothermal synthesis [174], can be used to alter the surface of Ti alloys.

The sandblasting of particles followed by acid etching (SLA) of an implant is one of the Ti surfaces techniques that has been implemented in a medical context with the greatest degree of success [175]. SLA implant have revealed enhanced cell differentiation and bone apposition in the primary phases of osseointegration, along with strong contact between implants and bone [176, 177]. This kind of SLActive® (Straumann) treatment, which has been proven to be an excellent choice for enhancing the material's qualities, can be used to alter the TiZr alloy. In-vitro investigations have shown that the high-voltage anodic oxidation technique known as micro arc oxidation (MAO) in electrolytic solutions works well for different titanium alloys including β titanium alloys [178, 179]. With this technique, a coating is produced that is substantial, porous, rough, and corrosion-resistant, as well as having improved biocompatibility and a large surface area where the implant and bone can contact [4, 178, 180]. Moreover, the coating is made of hydroxyapatite, which improves the stability and interaction between the implant and the bone and improve the mineralization and osteoblastic growth processes. The electrochemical anodizing technique creates a nanoporous oxide layer on the surface of biomaterials, which enhances adhesion and cellular proliferation similar to polished surfaces of Ti6Al7Nb and Ti25Nb25Zr alloys [10, 181].

The environment for the process of cellular migration is improved by the growth of pores and nanotubes on a material's surface [181]. Unite (Nobel Biocare) Ti implants are now readily available for this kind of treatment. They have been shown to have higher in vivo osteoconductive activity and survival rates than milled Ti [182]. With a tendency to increase the surface's wettability, femtosecond (FS) laser-produced nanostructured thin films have shown significant cellular growth and dissemination [183, 184]. Similar outcomes were obtained using glow-discharge plasma, which raised Ti surface energy to enhance cellular adhesion [113]. Plasma treatments are now highly popular because they produce excellent electrochemical stability and protein adsorption outcomes, both of which are connected to the specimen chemical and physical surface modifications [185, 186]. Niobium pentoxide and another monolayer of graphene were combined to enhance the mechanical properties of Ti6Al4V alloy, including toughness and wear resistance to shield implant's surface from the corrosion process [187]. Surface toughness and corrosion resistance were strengthened by the addition of Nb-based coatings to stainless steel substrates there by improving the material's biocompatibility [88]. In order to change the biological, mechanical, physical, and chemical characteristics of dental implants, surface treatments can be used with a range of goals. With the aid of modern technology, materials with cytotoxic properties such as stainless steel and Ti–Al-V alloy can have their surfaces altered making them more attractive choices for rehabilitation therapies. More research is required on commercially available surface treatments for titanium implants in order to treat Ti-based alloys without degrading their properties. The sections that follow explain several methods for surface modification, including mechanical, physical, and chemical methods.

Mechanical surface modification

Ti surface morphology can be altered using mechanical surface modification techniques to affect osteoblast cell adhesion, cell proliferation, and cell differentiation. Fundamental surface modification methods including grinding, blasting, micromachining, and polishing physically alter or remove the surface of the implant material. Mechanical surface treatments' goals are to provide the proper surface features and surface roughness, eliminate surface impurities, and maybe improve implant-tissue adhesion during later bonding operations [188, 189].

Physical surface modification

Chemical reactions do not happen when using physical surface modification approaches. Basic physical surface modification techniques include heat spraying and physical vapour deposition (PVD). For the growth of a coating, layer, or film on a Ti surface, these procedures use electrical, thermal, and kinetic energy [189–191]. The coating substance in the thermal spraying process melted into a liquid, microscopic droplet, and was then placed on the substrate with a lot of kinetic energy. Coating material is supplied to the substrate in the form of ions, molecules, and atoms, which condense in reaction with the substrate atoms to form a film during the physical surface modification process. This film growth is caused by the reaction between the implant surface and the adjacent vapor. Electron beam, resistive heating, laser, or electric discharge in vacuum produce the ions, molecules, and atoms that make up coating materials. Techniques for physically altering the surface of a surface include ion implantation and discharge plasma therapy [188].

Chemical surface modification

Sol–gel processes, anodic oxidations, chemical vapour deposition (CVD), and chemical treatment are examples of chemical surface modification methods. During chemical surface modification, electrochemical, chemical, or biological activities may take place at the contact of a Ti implant surface and a solution. Chemical interactions that occur in the gaseous phase of chemicals and the implant surface during the CVD process coat the implant surface with non-volatile compounds [192]. The sol–gel approach allows the connection of mineral phases with biological or organic systems by inducing a modest inorganic polymerization reaction. When adopting the sol–gel method, chemical reactions take place in the solution phase as opposed to at the implant surface-solution or gel interface [188, 193].

ListParagraph4ListParagraph Surface modification of Ti alloys for antimicrobial properties

The degree of bacterial adhesion to an implant surface can be influenced by its topography. The most suitable method for maintaining a strategy to prevent both the growth of bacteria and material decay is the counteraction of biofilm formation by antimicrobial surfaces [194]. Antibacterial macromolecules, antimicrobial peptides, and other inorganic antibacterial metal components (silver, copper, zinc, etc.) can all be used to immobilise antimicrobial particles onto implant surfaces. Many micro- and nanoparticles, including Ag, Cu, and others, can be utilized as antibacterial agents [195, 196]. These antibacterial elements prevent infection on implant surfaces via oxidatively stress-induced membrane destruction of bacteria. The PEO technique on titanium and its alloy can be used to improve the coating's antibacterial characteristics [197].

The antibacterial properties of a Ti6Al4V alloy made by Ren et al. [198] were established by increasing the Cu content. Cu ions released into the environment appear to inhibit biofilm development and cause bacterial death. Copper is still regarded as the alloy that shown excellent cytocompatibility and corrosion resistance despite being a heavy metal with a moderate level of toxicity. In a manner similar to this, a Ti-Cu alloy showed powerful antibacterial activity without compromising the alloy's mechanical properties or corrosion resistance [199]. When added to an electrolyte solution, Cu nanoparticles can fuse into the oxide layer. It has been noted that the Cu-incorporated coating was quite compact in nature and adhered to the implant surface effectively. Bacteria have been seen to absorb copper ions, which caused their cell walls to develop holes as a result of their contact with the copper ions [196]. Another investigation revealed that there was a considerable connection between Cu nanoparticles and the bacterium surface, indicating that the bactericidal process is linked to the contact killing of bacteria. To S. aureus and E. coli bacteria, the Cu-incorporated TiO2 coating shown extraordinary bactericidal capabilities [196, 200].

By sputtering Cu onto Ti-6Al-4 V, TiCuO coatings have been created with promising in vitro antibacterial activities and biocompatibility, in addition to its inclusion into Ti to form alloys [194, 201]. Investigations on the antibacterial qualities of Ti-Ag alloys have also been conducted [194, 202, 203]. With an increase in Ag content, the alloy's antibacterial activity and corrosion resistance dramatically enhanced while maintaining biocompatibility [202–204]. Following surgery when the tissue is vulnerable to pathogenic bacteria, antibacterial capabilities are essential as well as shortly after osseointegration, whenever biofilms and the start of peri-implantitis may develop [160]. According to Chen et al. [202], for a substance to have a long-lasting and potent antibacterial action on Streptococcus aureus, amount of Ag must be minimum 3% by mass. The capability of the specimen to discharge Ag ions in solution may be connected to their antimicrobial activities [205]. This could make bacterium's cell membrane more permeable and cause depolarization of the cells and phosphate efflux, which would cause cell contents to leak out and DNA replication to stop [203, 206]. With a considerable decrease in bacteria compared to untreated surfaces, the integration of Ag (nm) on the surface of materials by the surface modifications was equally advantageous in improving antibacterial activities without reducing the biocompatibility of the materials [178, 205, 207]. According to a prior work [208], Ti-Ag coatings still produce a modest amount of antibacterial activity 75 days after immersion, showing a sustained bactericidal potential. The development of a tantalum nitrate coating was another process utilised for antibacterial objectives [209]. Ag particle doped coating showed remarkable antibacterial properties against S. aureus and E. coli bacteria. Additionally, the antibacterial activity of the coating surface improved with a rise in the percentage of AgNP in the electrolyte. Effective bactericidal outcomes were attained as a result of the interaction between contact killing and the release of A + from AgNP [194, 195]. The antibacterial capacity of coatings with added silver is typically dependent on the concentrations of delivered silver particles, which can effectively impede the development of microscopic organisms through reactions with thiol groups in proteins, subsequently shortening DNA, and finally stopping replication capacity [195]. The process also considerably enhanced the material's resistance to bacterial corrosion [201].

Antibacterial coatings must have accurate substrate decay, be biocompatible, thinner, denser, and rigid in order to be effective. They also need to be physically inert, not affect the material's physical properties, and have the least potential effect on the final price of an implants [201]. The ideal scenario, notwithstanding the encouraging results would be for the materials to directly display bactericidal activity through their components without obstructing bone formation and osseointegration, as was the case for Ti-Cu and TiAg alloys. However, the creation of surfaces that can lessen bacterial adherence and kill germs locally by contact without releasing any material is a promising method to get around toxicity issues [210, 211].

Current challenges and recommendations in developing new Ti-based implant materials

The most important factor for any implant is its ability to remain in human body for longer time without creating any adverse side effects, especially metallic implants made of Ti alloy. The management of the grain size of different titanium phases, as well as their shape, orientation, and distribution, are always difficult problems in the manufacturing of titanium alloys. Although other metallic biomaterials like SS and Co-Cr alloys have higher Young's moduli than titanium alloys do, this attribute of titanium alloys may be the cause of the stress shielding effect because of a considerable difference with human bone [1, 212]. This still poses the biggest issue and obstacle for the development of implants made of titanium alloy. A porous Ti-based alloy is regarded as a novel invention for the foreseeable future since it has been shown to encourage tissue regeneration and firmly secure implant by regulating the degree of sintering [148, 213]. Moreover, the traditional powder metallurgy process can be enhanced using the self-propagating higher temperature synthesis (SHS) method of sintering [214, 215]. Surface treatment with the intention of stimulating surface to create a bind to the implantation sites presents a substantial difficulty in the development of titanium alloy implants.

Surface modification techniques include deposition, anodization, electrophoretic, ion implantation, sol–gel, MAO, acid, and alkaline treatment. To make a novel and remarkable finding, more research into their propensity to develop a more bioresponsive surface layer is required. It is obvious that superior surface oxide nanotubes on Ti alloy are a top priority for advanced surface modification techniques with additional benefits to come [188].

Future research on titanium alloys for orthopaedics can be improved in the key areas listed below: (1) creating novel alloys for use in biomedical field requires computational materials science. Modeling the evolution of the microstructure during processing and how it affects the mechanical characteristics can be done using sophisticated approaches like phase field modelling. For example, phase field modelling could be utilised to simulate the build-up precipitate at the time of anti-aging treatment. A starting point for predicting mechanical characteristics can be found in the subsequent developing microstructure. Designing novel compositions of β Ti alloys can make greater use of first-principles calculations.

(2) The development of thermomechanical processes that can give alloys superior fatigue and wear resistance should be encouraged. By creating high throughput methods to filter potential microstructures could be facilitated. The lack of information on these alloys' performance parameters hinders their use in therapeutic settings. AM should be investigated with the goal of creating both new materials and custom-designed implants. (3) Large animal models must be used to determine long-term biocompatibility. Investigating leached metal ion concentrations and its cytotoxic impact, rates of corrosion, debris formation due to wear and the accompanying inflammatory responses, rate of osseointegration, and stress shielding effects could be the main focus of these investigations. In addition to in vivo testing, the effectiveness of such materials must be assessed using commercially available medical device simulators.

Use of cpTi is limited to harsh environments with high tensile and fatigue strengths. The release of Al and V from the Ti6Al4V alloy had a detrimental impact on cell viability, which in turn had a negative impact on implant biocompatibility [216, 217]. Al has been associated with serious neurotoxic effects, particularly when taking into account reports of its connection to Alzheimer's disease. By releasing V iron into the body, vanadium (V) has detrimental effects on cell viability, which have a negative impact on implant biocompatibility [216, 217]. As Ti and its alloys are bio-inert and cannot immediately connect to natural human bone after implantation into a human body, they are still insufficient for long-term therapeutic use. Materials' surfaces must be changed in order for them to satisfy clinical requirements [188, 192].

Due to the bio-inert nature of titanium (Ti) and its alloys, they cannot quickly bond to living bone after being implanted in a human body [218]. Ti does not solidly connect with both soft and hard tissue since it lacks antibacterial qualities and is bioinert, that effect the usage of such materials in the field of biomedical field. Implant-associated infection (IAI) starts with bacterial attachment on surface of an implants. Once the bacteria start to colonize the implant surface to a greater extent, the biofilm is created. Whenever a biofilm has developed on an implant surface and it will be highly difficult to eliminate it using any other procedures or methods, expulsion of the prosthesis and re-implantation are the only options left [219]. Moreover, titanium is often more expensive when compared to metals like steel, iron, and aluminum. Titanium have drawbacks that must be mitigated when machining; the appropriate cutting tools, speeds, and feeds must be employed. The methods used to extract titanium ores have been plagued by problems. The trees are typically cut down in order to reach the rock, depending on the region. If not properly treated, titanium may contribute to soil degradation and lead to the release of heavy metals into the soil, which poses a substantial danger of contaminating drinking water.

Conclusions

1. Some of the current biomedical alloys have inherent toxicity, also some of the biomaterials undergoes stress shielding effects when implanted into human body because of imbalance among bone and modulus of elasticity of an implant material. The design of metastable β-titanium alloys for biomedical use including orthopedic and dental use is dependent on solutions to above two problems. The non-toxic and bioactive elements Mo, Nb, Fe, Zr, Ta, and Sn can be used to design β titanium alloy to solve above problems. Furthermore, compared to existing metallic biomaterials Ti-6Al-4 V (110 GPa), 316 L stainless steel (200 GPa), and Co-Cr–Mo alloys (200–230 GPa), β-Ti alloys have a lower modulus.
2. It was observed that strength and ductility of Ti alloys are both directly correlated with interstitial content of materials. Although interstitial solutes reduce the cpTi hardness and enhance the material's strength, they also have a negative impact on the material's elongation values, for examples intermetallic phases produced by substitution elements like Fe, Ni, and Cu reduces the ductility of titanium alloy. The alloy's ductility was enhanced, and the tensile strength was raised to 1050 MPa by reducing the concentration of these components. Additionally, it was found that the production process had an impact on an alloy's characteristics. The Ti alloy is made stronger and more ductile by cold rolling, ageing, annealing, and small-scale incorporation of ceramic particles into the matrix.
3. It was noticed that lesser the elastic modulus reduces bone atrophy while improving stress distribution at the interface of bone-implant. It is necessary for the Young's modulus to be as closer to the bone as feasible, as "stress shielding" has been associated with osteoporosis and bone resorption near to implant site. It was seen that metallic implant would move in small ways if the Young's modulus were too low, which would made the implants to become loose and perhaps it will result into failure of the prosthesis; hence, this should be avoided. It was observed that α titanium alloy have greater hardness values and elastic modulus because α-stabilizers function as a substitutional solute that reduces the material's atomic mobility or whenever the alloys are aged at low temperature, it promotes the phase's precipitation and that will increase the hardness of the material. As compared α titanium alloy β titanium alloys have lesser elastic modulus. A Ti-33Nb-4Sn alloy made by cold-rolling and then annealing methods had one of the lowest elastic modulus values ever recorded in the literature (36 MPa).
4. In the strain-controlled fatigue test, Ti-24Nb4Zr7.6Sn shown a significantly greater fatigue resistance than Ti-6Al-4 V ELI. When compared to Ti-Grade IV, Ti-15Zr discs and dental implant performed much better under fatigue. The alloy's and cpTi's upper limits for fatigue endurance were 560 MPa and 435 MPa respectively. The strength and Young's modulus of titanium alloys are improved by the inclusion of metals like Mo, Nb, Ta, and Zr. It was found that the titanium alloys with the highest tensile strengths were Ti12Mo6Zr2Fe and TI36Nb2Ta3Zr0.3O.
5. Ti45Nb has a narrower contact angle (81.75°) than cpTi (96.46°), which result into better hydrophilicity. However, the Ti50Zr alloy had a greater surface energy and lower surface roughness (37 mN/m, 0.17 μm) than cpTi (34 mN/m, 0.20 μm) and the

Ti50Nb alloy (32 mN/m, 0.46 μm). These characteristics of the substrate composition ensured that the Ti-Zr alloy had a good in- vitro biological profile (cell adherence and proliferation). The alloy's surface area was greater, but Ti had a coarser topography than Ti-Ta-Nb-Zr.

6. Researchers have examined the cytotoxicity of Ni49.2Ti and Ti26Nb and they have discovered that Ti26Nb is less cytotoxic. It was observed that Ti19Zr10Nb1Fe alloy shows greater hemocompatibility as compared to the Ni–Ti alloy but equivalent cytocompatibility. The absence of harmful alloying components is the cause of the better biocompatibility of β-type Ti alloys but there is urgent need for more in-vitro study on β-type titanium alloys. It was observed that the alloys TiCu, TiNb, and TiNbTaZr are also noteworthy since they demonstrated bone tissue biocompatibility without impairing the development of new bone.

Abbreviations

Ti	Titanium
cpTi	Commercial pure titanium
SPS	Spark Plasma Sintering
BCC	Body-centered cubic
HCP	Hexagonal close packed
MPa	Megapascal
GPa	Gigapascals
SLA	Sand blasted and acid etched
SLM	Selective laser melting
ECM	Extracellular matrix
MAO	Micro arc oxidation
SS	Stainless steel
SHS	Self-propagating high-temperature synthesis
AM	Additive manufacturing
SBF	Simulated body fluid

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Declarations

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"Not applicable." For the current work, the authors have not conducted any animal or human trials.

Consent for publication
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