

# Effect of Alloying Elements on the Compressive Mechanical Properties of Biomedical Titanium Alloys: A Systematic Review

Syed Faraz Jawed,\* Chirag Dhirajlal Rabadia, Muhammad Ahmed Khan, and Saad Jawaid Khan

Cite This: *ACS Omega* 2022, 7, 29526–29542

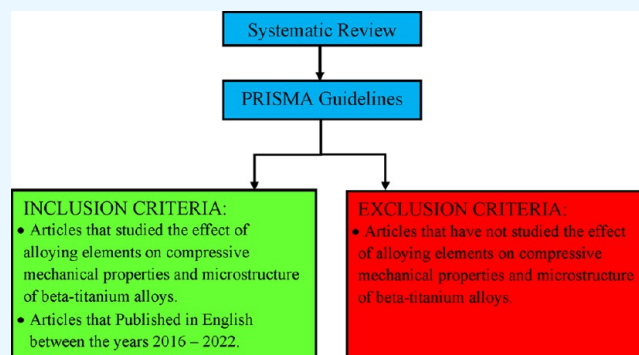
Read Online

ACCESS |

Metrics & More

Article Recommendations

**ABSTRACT:** Due to problems such as the stress-shielding effect, strength–ductility trade-off dilemma, and use of rare-earth, expensive elements with high melting points in Ti alloys, the need for the design of new Ti alloys for biomedical applications has emerged. This article reports the effect of various alloying elements on the compressive mechanical performance of Ti alloys for biomedical applications for the first time as a systematic review following the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines on this subject. The search strategy in this systematic review used Scopus, Web of Science, and PubMed databases and searched the articles using (Beta-type OR  $\beta$ ) AND Titanium AND (Mechanical property OR Microstructure) AND Alloying element keywords. Original articles from 2016 to 2022 published in English have been selected for this study as per the inclusion criteria. The results have shown that Nb can be used as the primary alloying element with Ti as it is a strong  $\beta$ -stabilizer element which also reduces the elastic modulus of Ti alloys. The  $\beta$ -eutectic elements (Fe, Cr, and Mn) have also emerged as cost-effective alloying elements that could improve the mechanical performance of Ti alloys. Ti–Nb–Zr–Ta alloyed with Si has shown potential to withstand the strength–ductility trade-off dilemma. The combination of a Ti–Nb binary alloy has emerged as an attractive material for designing low elastic modulus Ti alloys. The mechanical performance of the Ti–Nb alloy can be further improved using the  $\beta$ -eutectic (Fe, Cr, and Mn) and neutral (Zr, Sn) elements to be alloyed with a Ti–Nb binary alloy. The strength–ductility trade-off issue can be overcome using Si as an alloying element in Ti–Nb–Zr–Ta alloys.



## 1. INTRODUCTION

The exponential increase in the demand of lightweight alloys for different structural engineering applications such as biomedical, automotive, and aerospace has urged material scientists to explore light-density materials.<sup>1,2</sup> The materials research fraternity has witnessed titanium (Ti) and its alloys to be the most preferred materials among other lightweight metallic materials for industrial applications.<sup>3,4</sup> Ti and its alloys possess this distinguished position because of their excellent traits, e.g., high specific strength, low density, excellent strain hardening abilities, high corrosion and wear resistance, and good superelastic and fatigue behavior.<sup>3</sup> Typically, combining large plasticity and high strength is difficult to attain simultaneously in metallic materials and alloys.<sup>5,6</sup> However, Ti alloys display a superior combination of plasticity and strength.<sup>7</sup>

Ti alloys were initially applied as a structural material in the aerospace sector. Afterward, Ti alloys were used in orthodontic implants during the 1950s.<sup>8</sup> Ti alloys were later identified as a possible biomaterial for application in orthopedic implants.<sup>8</sup> Ti alloys have a low density of 4.8 g/cm<sup>3</sup>, which permits them to have high specific strength (i.e., strength to density ratio), greater biocompatibility, and high affinity for osseointegration.

When compared to 316 SS and Co–Cr alloys, Ti alloy has a lower elastic modulus as demonstrated in Figure 1.<sup>8</sup> Notably, Ti alloys also possess good corrosion resistance due to the production of chemically inert, active, stable, and self-protecting TiO<sub>2</sub> layers on their surface.<sup>9</sup> Ti and its alloys have greater biocompatibility when compared to 316 SS and Co–Cr alloys as a biomaterial for implant applications. Pure Ti also has low fatigue and mechanical strength.<sup>8</sup> Different alloying elements, such as Al, V, Mo, Zr, and Nb, can be added to pure Ti to improve its mechanical properties. The commercially available biomedical Ti alloys, such as Ti–6Al–4V (Ti64) and commercially pure Ti (CP-Ti), exhibit low biocompatibility and poor corrosion resistance for implant applications.<sup>10,11</sup> It has been well documented that the release of aluminum (Al) and

Received: April 5, 2022

Accepted: July 27, 2022

Published: August 15, 2022



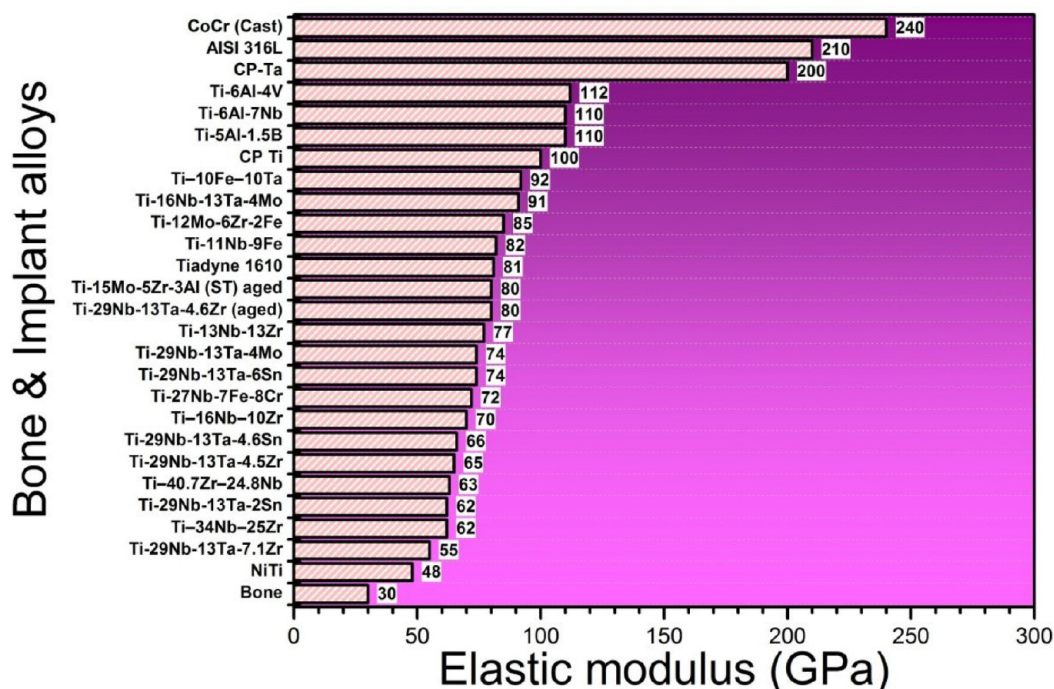


Figure 1. Comparison of elastic modulus values of different biomaterials with that of human bone.<sup>3,30–34</sup>

vanadium(V) ions into the human body induces cytotoxic effects which can lead to long-term diseases such as Alzheimer's.<sup>12</sup> Therefore, many scientists are continuously striving in developing new Ti alloys. However, Ti alloys developed in the past decades are struggling due to the problem of stress shielding.<sup>13,14</sup> Stress shielding is a medical condition due to a mismatch in the elastic modulus of the implant material and specific bone.<sup>10</sup>

Furthermore, the poor osseointegration of conventional Ti alloys has also caused the development of novel Ti alloys with high strength, large plasticity, and low stiffness for orthopedic implant applications.<sup>16,17</sup> Furthermore, martensitic nitinol (Ti-rich Ni–Ti) and austenitic nitinol (Ni-rich Ni–Ti) alloys have been widely used as superelastic and shape memory biomedical alloys, respectively.<sup>15–17</sup> Ni-free superelastic and shape memory biomedical alloys are needed because of the hypersensitive and carcinogenic effects of Ni in the human body.<sup>18,19</sup> In 1971, Ni-free Ti–35 wt % Nb was created for the first time as a biological shape memory alloy.<sup>20,21</sup> However, because of their low critical stress for slip deformation, Ti–Nb binary alloys have a moderate recoverable strain.<sup>21,22</sup> The superelastic behavior of Ti–Nb binary alloys can be enhanced by lowering the quantity of Nb in Ti–35 wt % Nb and adding other  $\beta$ -stabilized ternary or quaternary alloying elements.<sup>23,24</sup> Notably, the majority of newly produced biomedical Ti alloys are made up of costly and rare-earth metals (i.e., Ta, Mo, Hf, Nb).<sup>25</sup> Therefore, while designing new Ti alloys for biomedical applications, low-cost, nontoxic, and plentiful metals (i.e., Cr, Mn, and Fe) with compressive properties similar to those of bones and hard tissues should be considered. The compressive mechanical properties of bone are presented in Table 1.

**1.1. Effect of Alloying Elements on Microstructures and Deformation of Ti Alloys.** Ti exhibits two allotropic phases with an allotropic transformation temperature of 883 °C.<sup>30</sup> Pure Ti has an  $\alpha$  phase that consists of an hcp crystal

Table 1. Compressive Mechanical Properties of Bone

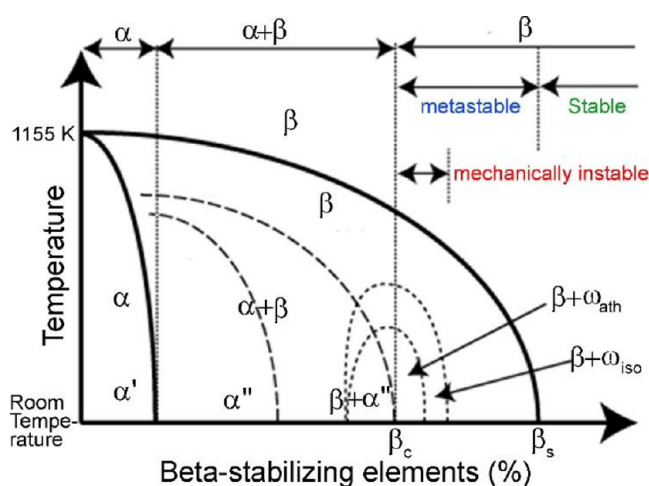
properties	cancellous bone	cortical bone	refs
density	1.99 g/cm <sup>3</sup>	0.05–10 g/cm <sup>3</sup>	26,27
porosity	5–30%	30–90%	28
compressive strength	106–224 MPa	2–5 MPa	26
elastic modulus	16–30 GPa	0.76–4 GPa	9,29

structure, which transforms into a bcc structure known as the  $\beta$  phase of Ti above a  $\beta$ -transformation temperature of 883 °C.<sup>1,35</sup>

On the basis of the volume proportion of  $\alpha$  and  $\beta$  microstructures in Ti alloys, there are four types of Ti alloys: (1)  $\alpha$  alloys are those that contain just  $\alpha$  stabilizers and are completely composed of  $\alpha$  microstructure, (2) near  $\alpha$  alloys contain 1–2%  $\beta$ -stabilizer elements, resulting in 5–10%  $\beta$  phase in microstructures of near  $\alpha$  Ti alloys, (3)  $\alpha + \beta$  alloys which have a higher amount of  $\beta$ -stabilizer elements than near  $\alpha$  Ti alloys, causing the microstructures of Ti alloys to contain 10–40%  $\beta$  phase, and (4)  $\beta$ -type alloys that contain practically all  $\beta$  stabilizers and are rapidly cooled to produce a  $\beta$  microstructure.<sup>1,36,37</sup> The microstructures of Ti alloys vary with the addition of different alloying elements; some elements, such as N, Al, and O, raise the  $\beta$ -transformation temperature and stabilize the  $\alpha$  microstructure, while others, such as Ta, Nb, Mo, W, V, Cr, Ni, Fe, Mn, and Cu, lower the  $\beta$ -transformation temperature to stabilize the  $\beta$  microstructure.<sup>38</sup> Furthermore, some of them, such as Sn and Zr, are classified as neutral alloying elements because they do not affect the  $\beta$ -transformation temperature.<sup>39</sup>

In comparison to ( $\alpha + \beta$ )-type Ti alloys,  $\beta$ -type Ti alloys have a higher number of  $\beta$ -stabilizing elements.<sup>40,41</sup> Metastable and stable  $\beta$ -type Ti alloys can be obtained, without the formation of intermetallic phases, based on the proportion of  $\beta$ -stabilizing elements (i.e., Nb, Mo, Ta, W, Cr, Mn, Fe, etc.).<sup>40–42</sup> Because  $\beta$ -type Ti alloys are heat treatable, their strength can be increased by solution treatment followed by aging at temperatures ranging from 450 to 650 °C.<sup>43</sup> In particular, increasing the quantity of  $\beta$

phase in Ti alloys improves the toughness, hardenability, and plasticity while lowering the elastic moduli of Ti alloys.<sup>44</sup> Ti alloys have a lower elastic modulus than other types of Ti alloys, which inhibits the problem of stress shielding. In comparison to ( $\alpha + \beta$ )-type Ti alloys,  $\beta$ -type Ti alloys also display superior biocompatibility, strength, and corrosion resistance in the human body.<sup>43,45</sup> As a result,  $\beta$ -type Ti alloys have emerged as a more viable biomaterial to be used in orthopedic implants. Furthermore, when  $\beta$ -stabilizer elements are added in excess as alloying elements with Ti, the temperature of the allotropic transition begins to lower accordingly.<sup>46</sup> A sufficient amount of  $\beta$  stabilizers should be added to Ti alloys to prevent phase precipitation. Therefore, the metastable  $\beta$  phase can be preserved as depicted in Figure 2.<sup>47</sup>



**Figure 2.** Effect of  $\beta$ -stabilizer content with temperature on the phase of the titanium alloys. Reprinted with permission from ref 47. Copyright 1998 Elsevier.

Furthermore, metastable  $\omega$  phase precipitate formation is susceptible to aging, which is undesirable because it reduces the plasticity and may cause severe brittleness and fatigue resistance.<sup>48</sup> A limited amount of  $\omega$  phase forms due to the high-temperature  $\beta$  phase after quenching, which leads to the formation of a thermal  $\omega$  phase.<sup>49</sup> There is the possibility of forming a  $\omega$  phase at room temperature also after quick quenching, which forms an isothermal  $\omega$  phase later.<sup>49</sup> The precipitation of both  $\alpha$  and  $\omega$  phases is undesirable because it leads to an increase in the elastic modulus and strength, which leads to the problem of stress shielding.<sup>50</sup> Hence, adding a sufficient amount of  $\beta$ -stabilizer elements to Ti alloy can improve its  $\beta$ -phase stability. Most of the  $\beta$ -stabilizer elements that are used in Ti alloys are rare earth with high melting temperatures which leads to issues, such as expensive raw material costs and segregation during preparation.<sup>51,52</sup> Therefore, new low-cost  $\beta$ -eutectic elements with low melting points such as Cr, Mn, and Fe have been receiving a lot of attention in the development of novel Ti alloys.

The deformability among different types of Ti alloys follows the trend  $\beta > \alpha + \beta > \alpha$ . This is because the  $\beta$ -type Ti alloys exhibit a greater number of slip systems than other types of Ti alloys.<sup>7</sup> The fraction of the  $\beta$  phase significantly influences the mechanical and corrosion properties of Ti alloys.<sup>53</sup> As mentioned earlier, the percentage of  $\beta$ -stabilizer elements (i.e., Ta, Mo, Nb, Mn, Fe, and Cr) impacts the fraction of the  $\beta$  phase in Ti alloys.<sup>54,55</sup> Therefore, the choice of  $\beta$ -stabilizing elements

is of vital importance when developing new groups of Ti alloys. Moreover, some electronic parameters including the valence atom to electron ratio ( $e/a$ ), atomic radius ( $\Delta r$ ), molybdenum equivalency ( $Mo_{eq}$ ), bond order (Bo), d-orbital energy level (Md), and bonding force (BF) also play an important role for predicting the  $\beta$ -stabilization, mechanical, superelastic, and deformation behaviors of Ti alloys.<sup>23,56–58</sup>

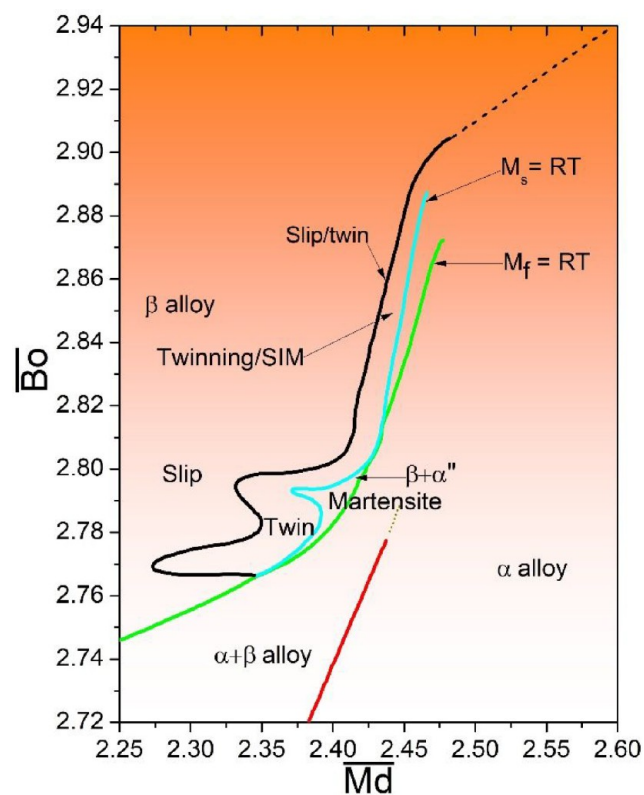
**1.2. Theoretical Approaches Rationale of Ti Alloys.** The initial design of new Ti alloys is based on the well-known theoretical approach developed by Morinaga et al.,<sup>59</sup> which is called the DV- $X\alpha$  cluster approach. The theoretical approach is very effective for predicting the  $\beta$ -phase stability and various deformation mechanisms for newly designed Ti alloys using two electronic parameters.<sup>60</sup> The mean values of  $\overline{Bo}$  and  $\overline{Md}$  for the investigated Ti alloys were evaluated using eqs 1 and 2, respectively

$$\overline{Bo} = \sum X_i(Bo)_i \quad (1)$$

$$\overline{Md} = \sum X_i(Md)_i \quad (2)$$

where  $X_i$  is the atomic fraction.

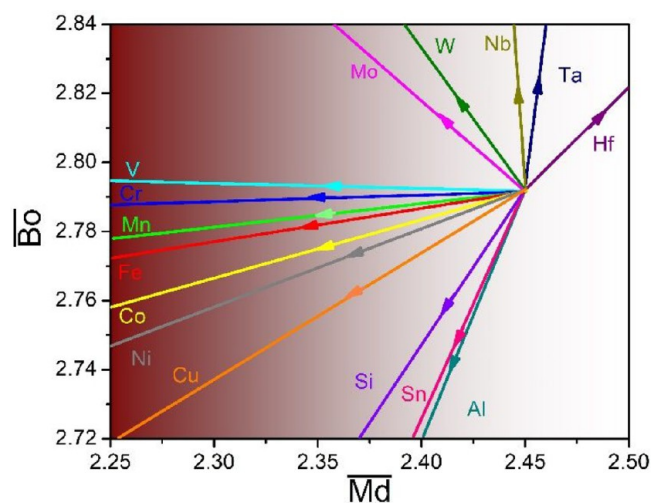
The aforementioned  $\overline{Bo}$ – $\overline{Md}$  map presented in Figure 3 has been used by many researchers to design new metastable  $\beta$  Ti



**Figure 3.**  $\overline{Bo}$ – $\overline{Md}$  map for designing Ti alloys. Reprinted with permission from ref 58. Copyright 2006 Elsevier.

alloys with simultaneous twinning and stress-induced martensite (SIM) deformation mechanisms.<sup>61</sup> The values of Bo and Md for various elements are depicted in Figure 4. Notably, various newly designed  $\beta$  Ti alloys have been in line with their theoretical prediction using a  $\overline{Bo}$ – $\overline{Md}$  map and the actual deformation mechanism.<sup>57</sup> Nonetheless, some newly designed alloys show discrepancies between the theoretical deformation mechanism using the  $\overline{Bo}$ – $\overline{Md}$  map and the actual deformation





**Figure 4.** Vector diagram for individual elements in Ti on a  $\overline{Bo}$ – $\overline{Md}$  map. Reprinted with permission from ref 43. Copyright 1998 Elsevier.

mechanism.<sup>57</sup> A new semiempirical approach has been recently designed for the theoretical prediction of various deformation mechanisms for newly designed  $\beta$ -Ti alloys using the average electron–atom ratio ( $\overline{e/a}$ ) and the atomic radius difference ( $\overline{\Delta r}$ ).<sup>10,57</sup> The approach suggested by Wang et al. shows that the twinning/SIM region has lower values of  $\overline{e/a}$  in comparison to the slip region, which actually occurs when  $\overline{e/a} < 4$  and  $\overline{\Delta r} > -2.5$ . Further, the value of  $\overline{e/a}$  are at its peak for the twinning/SIM region when  $\overline{\Delta r}$  is approximately 0 and decreases as the value of  $\overline{\Delta r}$  increases. Hence, the  $\overline{e/a}$  and  $\overline{\Delta r}$  also influence the prediction of various deformation behaviors for newly  $\beta$ -type Ti alloys through controlling the lattice shear difficulty. However, recently, a revised semiempirical approach based on  $\overline{e/a}$  and  $\overline{\Delta r}$  has been proposed by Rabadia et al. for prediction of the deformation mechanism of newly designed Ti alloys as presented in Figure 5.<sup>62</sup>

$Mo_{eq}$  is another key parameter in predicting the deformation behavior of a Ti alloy. According to one study, an alloy will undergo a martensitic transformation during fast cooling if  $Mo_{eq}$  is less than 10%, while if its value is greater than 10%, it can retain in a metastable  $\beta$  state.<sup>63,64</sup> It has been reported that the increase in the value of  $Mo_{eq}$  enhances the  $\beta$ -phase stability of an alloy.  $Mo_{eq}$  can be evaluated using eq 3<sup>56</sup>

$$\begin{aligned}
 [Mo]_{eq} = & [Mo] + \frac{[Ta]}{5} + \frac{[Nb]}{3.6} + \frac{[W]}{2.5} + \frac{[V]}{1.5} \\
 & + 1.25[Cr] + 1.25[Ni] + 1.7[Mn] + 1.7[Co] \\
 & + 2.5[Fe]
 \end{aligned} \quad (3)$$

Notably, a newly introduced bonding force (BF)–d-electron superelasticity theoretical approach was developed from the compositional averages of the effective charge experienced by the valence electron, bond order, and metal d-orbital energy level to predict the superelastic behavior of Ti alloys.<sup>23</sup> By combining Coulomb's law and d-electron theory, the interatomic bonding force (BF) of newly designed Ti alloys can be calculated using eq 4<sup>23</sup>

$$BF \propto \frac{\overline{Z_{eff}} \overline{Bo}}{\overline{Md}} \quad (4)$$

where  $\overline{Z_{eff}}$ ,  $\overline{Bo}$ , and  $\overline{Md}$  are the compositional averages of the effective charge experienced by the valence electron, bond order, and metal d-orbital energy level, respectively.

Notably, for the last two decades, material scientists have been working hard to design a biomaterial for implant applications that could meet the compressive mechanical properties of human bone using various theoretical parameters. A literature review shows that there are a lot of narrative reviews that have been presented for Ti alloys in biomedical applications, but very few studies are available based on a systematic review.

Therefore, in this work, a systematic review of the compressive mechanical properties of Ti alloys for biomedical applications is presented using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) search strategy for the first time. Scopus, Web of Science, and PubMed have been used as search databases for original articles from 2016 to 2022 that are reporting the effect of various elements on the compressive mechanical properties of Ti alloys.

## 2. METHODS

The Web of Science, Scopus, and PubMed were electronically searched for keywords (Beta-type OR  $\beta$ ) AND Titanium AND (Mechanical property OR Microstructure) AND Alloying element.

The inclusion criteria are the articles that studied the effect of different alloying elements on the microstructure and compressive mechanical properties of newly designed Ti alloys for biomedical applications between 2016 and 2022 and published in English.

The exclusion criteria are the articles that did not study Ti alloys with the effect of different alloying elements on their compressive mechanical properties and microstructure.

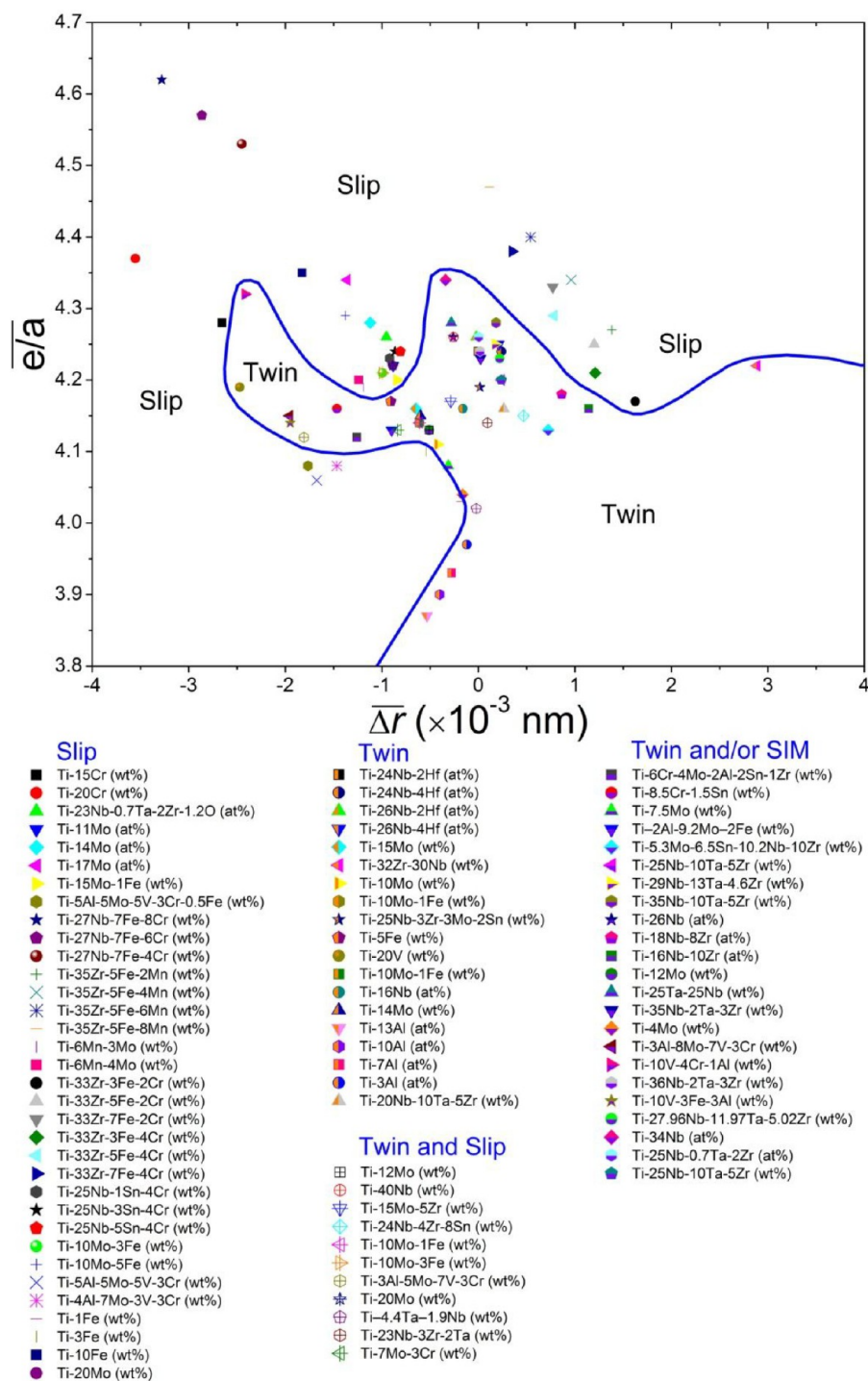
Notably, it has been reported in the literature that the human body experiences compressive loads during daily living activities (DLA).<sup>65</sup> Therefore, the influence of alloying elements on the compressive mechanical properties of alloys is of crucial importance for assessment of the alloy's performance for implant applications. Hence, in this work, research articles are included that studied the compressive mechanical properties of alloys, whereas research articles that studied the tensile mechanical properties were excluded from the systematic review.

The PRISMA flowchart is presented in Figure 6. Initially, 322 articles popped up using the previously mentioned keywords and databases. Furthermore, 4 articles were added from other sources. Among them 25 were duplicates, and 219 articles were excluded after reading the title and abstract. By applying the inclusion criteria, 45 articles were selected for full-text reading; among them, 17 articles were excluded because of not fulfilling the inclusion criteria in their entirety. Finally, 28 articles were included in the study.

## 3. RESULTS

The studies<sup>66–80</sup> used the casting method for the fabrication of dense alloys as presented in Table 2. By contrast, some of the included studies<sup>81–86</sup> investigated the compressive mechanical properties of porous metals and metal foam for biomedical applications. The main objectives and major findings for each type of alloy included in this study are summarized in Table 2.

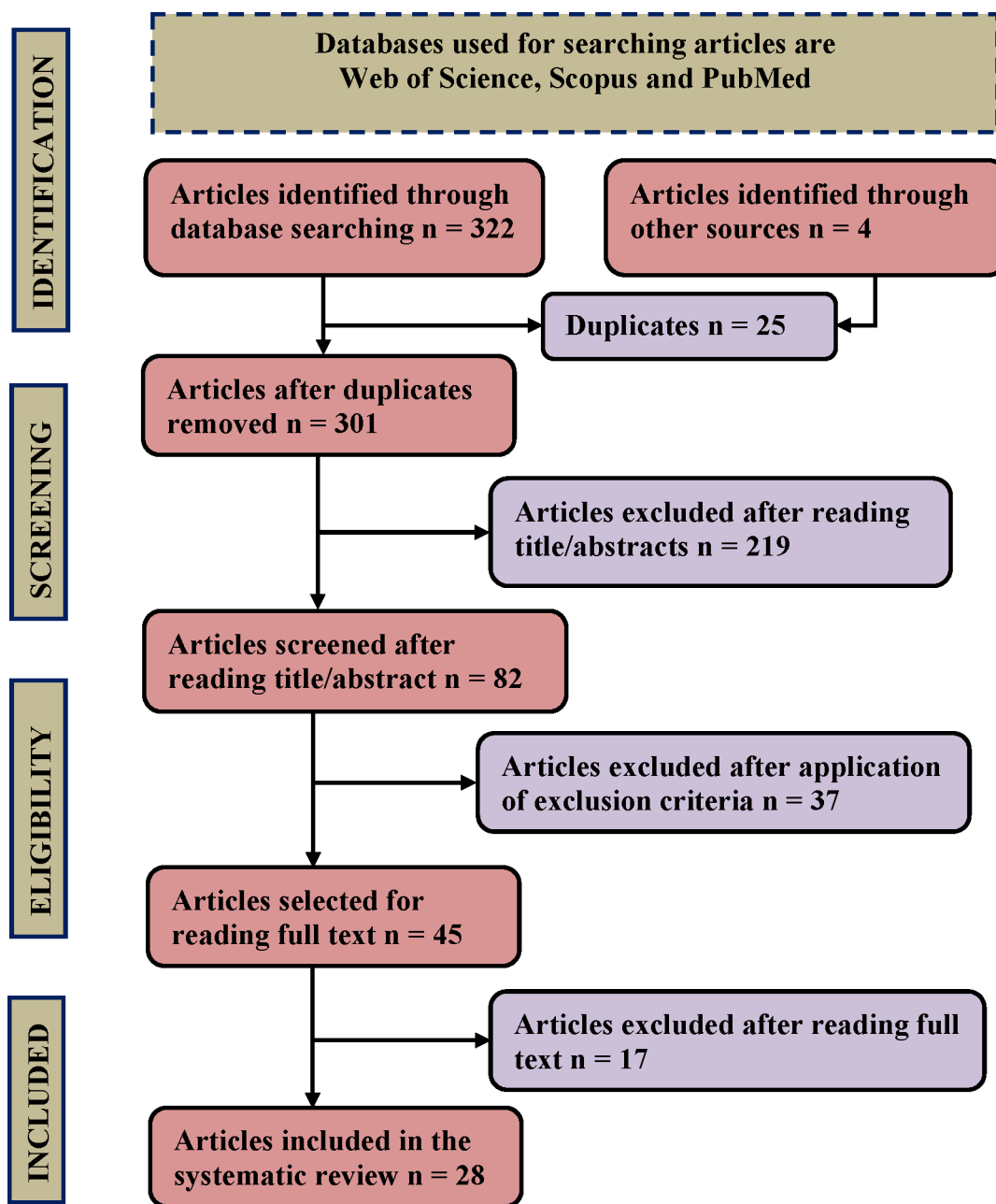
All of the incorporated studies<sup>24,66–85,87,88</sup> in this systematic review evaluated the microstructures and compressive mechanical properties of the investigated alloys. The biocompatibility



**Figure 5.**  $\overline{e/a}-\overline{\Delta r}$  diagram developed to distinguish the Slip and Twinning/SIM regions based on the reviews of published works. Reprinted with permission from ref 62. Copyright 2021 ACS Publications.

and electrochemical properties have also been evaluated by the studies<sup>81–84,86–88</sup> for the investigated alloys. These are the studies<sup>24,66,67,69,70,72–74,78,81,83,84,87</sup> that analyze the effect of a series of alloying elements on their compressive mechanical properties. The authors of some studies suggested the best alloy among the investigated alloys based on their optimum characteristics for biomedical applications. Therefore, the best alloy suggested by the author among the series of alloys has been considered in this systematic review.

Table 3 presents a comparative analysis of the quantitative compressive mechanical features, including elastic modulus, yield strength, ultimate compressive strength, hardness, and elongation of alloys, in the incorporated studies. It can be noted from Table 3 that each included study does not evaluate all of the selected compressive mechanical features for the investigated alloys. Among the dense materials, a study<sup>70</sup> reported an outstanding lowest elastic modulus of 14.72 GPa for Ti–2Zr–0.1Nb–0.1Sn alloy, whereas studies<sup>67,68,78</sup> reported a low elastic modulus of around 65 GPa for Ti–10Nb–5Sn, Ti–20Nb–1Ru,



**Figure 6.** Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flowchart for the screening and selection strategy.

and Ti–25Zr–10Nb–10Ta–1.5Ag alloys in comparison to other investigated alloys. Among the porous materials, a study<sup>83</sup> reported the lowest elastic modulus of 9.04 GPa for Ti–5Mo alloy, and the highest elastic modulus was reported for Ti–5W foam, which is 25 GPa.<sup>85</sup> It can be observed from Table 3 that the highest compressive and yield strength for dense Ti–5Mo–5Ag alloy are reported<sup>88</sup> to be 2100 and 1694 MPa, respectively. The maximum elongation and hardness for dense alloys are reported<sup>79</sup> to be 35.72% and 433.4 HV, respectively, for Ti–38.3Ta–22Zr–8.1Nb alloys. Notably, addition of Si in a Ti–Nb–Zr–Ta alloy is shown to be a suitable solution for the strength–ductility trade-off dilemma.<sup>89–91</sup> Ti–35Nb–7Zr–5Ta–3Si, Ti–34.5Nb–6.9Zr–5Ta–1.4Si, and Ti–23.33Nb–5Zr–1.67Ta–5Si have high yield strengths of 1151, 1286, and 1569 MPa with low elastic moduli of  $48.7 \pm 1$ ,  $79 \pm 3$ , and  $53 \pm 6$  GPa, respectively.<sup>89–91</sup>

The included studies in this systematic review developed and characterized the alloys that are to be used in biomedical applications. Therefore, it can be noted from Table 3 that the primary phase in all of the investigated alloys is the bcc  $\beta$  phase with or without the existence of  $\alpha$ ,  $\alpha'$ ,  $\alpha''$ , and  $\omega$  phases in their microstructures. Each mechanical features for the investigated alloys will be discussed individually in the subsequent section.

#### 4. DISCUSSION

The individual trends of compressive mechanical features including the elastic modulus (GPa), yield strength (MPa), ultimate compressive strength (MPa), elongation (%), and hardness (HV) of the investigated alloys from the incorporated studies in this systematic review are presented in Figures 7, 8, 9, 10, and 11, respectively.

Table 2. Summary of Included Studies in the Systematic Review

S. no.	author <sup>[ref]</sup>	title	keywords	objectives	fabrication technique/structure	major findings
1	Yolun et al. <sup>86</sup>	Fabrication, characterization, and in vivo biocompatibility evaluation of titanium–niobium implants	Powder metallurgy, Ti–Nb alloys, biomaterial, biocompatibility, implant	objective of this paper is to examine the effect of Nb (5.4, 18 wt %) concentration with different sintering temperatures and pressing pressures on the microstructural and mechanical properties along with in vivo biocompatibility of Ti alloys	powder sintering metallurgy/porous	(1) this study reveals the inverse relationship between the phase transformation temperatures and the niobium content; (2) strength and elastic modulus of Ti–Nb alloys increased due to a decrease in porosity which happened because the dimensions of the Nb particles (5 μm) are smaller than those of the Ti particles (45 μm); (3) pressing pressure enhances the interaction between the powder particles and makes diffusion easier
2	Santos et al. <sup>66</sup>	Oxygen addition in biomedical Ti–Nb alloys with low Nb contents: Effect on the microstructure and mechanical properties	Titanium alloys, Interstitial, Hardness, Compressive strength, Young's modulus	this paper reports the effect of Nb (15, 17.5, 20, 22.5 wt %) and O (0.15, 0.25, 0.40 wt %) with heat-treatment procedures (hot rolled, solution treated at 1200 °C for 1 h, and furnace cooled) on phase transformation and mechanical characterization of titanium alloys	arc melting/dense	(1) thickness of α plates is increased with O addition, whereas it is impaired with Nb addition; (2) β transformation temperature is directly proportional to O, whereas it is inversely proportional to Nb; (3) hardness and yield strength increase with simultaneous addition of O and Nb; (4) Young's modulus increases moderately with addition of Nb
3	Li et al. <sup>81</sup>	Characteristics of Ti–Nb–Mg alloy by powder metallurgy for biomedical applications	Mechanical alloying, Spark plasma sintering, Ti–Nb–Mg alloy, Mechanical properties, Biocompatibility	this paper investigates the microstructure, mechanical, and biological properties of Ti–35 wt % Nb alloy with the addition of different (3, 5 wt %) Mg concentrations and varying ball to powder ratios (10:1, 20:1)	mechanical alloying followed by spark plasma/porous	(1) 20:1 ball to powder ratio exhibits a single β phase, whereas a 10:1 ball to powder ratio does not exhibit a monolithic β phase for both Ti–35Nb–(3.5)Mg alloys; (2) addition of Mg from 3 to 5 wt % at a similar condition in Ti–Nb–Mg alloys decreases the mechanical properties (i.e., strength and plasticity)
4	Kalita et al. <sup>87</sup>	Effect of Mo and Ta on the Mechanical and Superelastic Properties of Ti–Nb Alloys Prepared by Mechanical Alloying	titanium alloys; superelastic alloys; Ti–Nb alloys; twinning; deformation mechanisms; mechanical properties; powder metallurgy	(1) this work aims to systematically investigate the mechanical and superelastic behavior of binary Ti–14 atom % Nb alloys upon addition of 2 atom % Mo and Ta individually in ternary Ti alloys; (2) further, slight subtraction of Nb in Ti–Nb–(Mo, Ta) alloys, i.e., Ti–8Nb–2Mo (atom %) and Ti–12Nb–2Ta (atom %) were also analyzed	mechanical alloying followed by spark plasma sintering/dense	(1) 2 atom % addition of Mo and Ta reduces the yield strength, whereas increasing the plasticity of binary Ti–14 atom % Nb alloy; (2) addition of Mo in the Ti–Nb binary alloy demonstrates an obvious β-phase stability effect because only twinning was observed during deformation, while Ta addition demonstrates twinning along with the stress-induced martensitic transformation
5	Zareidoost et al. <sup>67</sup>	A study on the mechanical properties and corrosion behavior of the new as-cast TZNT alloys for biomedical applications	TZNT alloy, Mechanical properties, Biomaterials, Corrosion behavior	this study focuses on the development of quaternary Ti–25Zr–10Nb–10Ta (atom %) and analyzes the effect of small addition Fe (0.5 atom %), Sn (2 atom %), and Ag (1.5 atom %) on the microstructure, mechanical properties, and corrosion resistance of TZNT alloy	as cast/dense	(1) all of the tested alloys show large plasticity with a monolithic β phase; (2) addition of 1.5 atom % Ag in Ti–25Zr–10Nb–10Ta (atom %) demonstrates the lowest Young's modulus and compressive yield stress and highest elastic admissible strain; (3) addition of 0.5 atom % Fe improves the hardness of Ti–25Zr–10Nb–10Ta (atom %)
6	Torres-Sánchez et al. <sup>68</sup>	Addition of Sn to Ti–Nb alloys to improve mechanical performance and surface properties conducive to enhanced cell activity	Titanium, Niobium, Tin, Bulk properties, Surface properties, Preosteoblasts	this work characterizes the physicochemical properties and bioactivity of newly designed Ti–40Nb, Ti–10Sn, and Ti–10Nb–5Sn (atom %) alloy	as cast/dense	(1) all three investigated alloys possess dual phases in their microstructure; (2) ternary Ti–Nb–Sn demonstrates the lowest elastic modulus and yield strength in comparison to binary Ti–Nb and Ti–Sn alloys; (3) ternary Ti–Nb–Sn alloy exhibits the highest elastic admissible strain among the investigated alloys and positioned it as a promising biomedical implant material
7	Sjaifrizal et al. <sup>82</sup>	Effect of Fe addition on properties of Ti–6Al–xFe manufactured by blended elemental process	Titanium alloy; Phase stability; Microstructure; Mechanical properties; Powder metallurgy	objective of this work is to estimate the ideal content of Fe (1, 3, 5 wt %) in Ti–6Al (wt %) alloy to attain an enhanced sintering effect and its optimized microstructure and mechanical properties	press and sintering/porous	(1) β stability and strength of ternary Ti–6Al–(1, 3, 5) wt % Fe increases with increasing amount of Fe; (2) Ti–6Al–3Fe (wt %) demonstrates the highest elastic admissible strain among the investigated alloys
8	Jawed et al. <sup>69</sup>	Strengthening mechanism and corrosion resistance of beta-type Ti–Nb–Zr–Mn alloys	Titanium alloy, Microstructure, Strengthening mechanism,	purpose of this study is to achieve an effective balance between strength and plasticity in newly designed biomedical Ti–26Nb–(4, 7, 10)Zr–(3, 5)Mn wt % alloys and characterize the	cold crucible levitation melting/dense	(1) designed alloys demonstrate monolithic β phase; (2) addition of Mn improves the strength and corrosion resistance of Ti–Nb–Zr–Mn, alloys whereas addition of Zr decreases the strength of investigated alloys



Table 2. continued

S. no.	author <sup>[ref]</sup>	title	keywords	objectives	fabrication technique/structure	major findings
9	Jawed et al. <sup>24</sup>	Tailoring deformation and superelastic behaviors of beta-type Ti–Nb–Mn–Sn alloys	Strain hardening index, Corrosion resistance	effect of Zr and Mn on the mechanical and electrochemical behavior of quaternary Ti–Nb–Zr–Mn alloys	cold crucible levitation melting/dense	(1) all investigated alloys demonstrate a single $\beta$ phase except Ti–25Nb–2Mn–1Sn alloy which exhibits a dual $\alpha''$ + $\beta$ phase; (2) addition of Mn in Ti–Nb–Mn–Sn alloys improves its mechanical and superelastic properties, whereas addition of Sn decreases its strength
10	Dang et al. <sup>70</sup>	Development and characterization of $\beta$ -type Ti–Zr–Nb–Sn dental implant materials	Ti–Zr alloys/ $\beta$ -type, biomedical materials, dental implant, mechanical behavior	in this work, quaternary Ti–2Zr–(0.1,0.2,0.3)Nb–(0.1,0.2,0.3)Sn and Ti–2Zr–(0.1,0.2,0.3)Nb–(0.1,0.2,0.3)Mo were designed for optimizing the mechanical performance of Ti alloys for dental applications	as cast/dense	(1) addition of Nb, Mo, and Sn in quaternary Ti–Zr–Nb–Mn and Ti–Zr–Nb–Sn alloys improves its $\beta$ -phase stability; (2) addition of Nb and Mo improves the yield strength and plasticity of Ti–Zr–Nb–Mo alloys, whereas addition of Nb and Sn improves the mechanical properties in comparison to Ti–2Zr alloy
11	Pengfei et al. <sup>71</sup>	Mechanical properties and corrosion behavior of $\beta$ -type Ti–Zr–Nb–Mo alloys for biomedical application	Ti–Zr–Nb–Mo alloy; Microstructure; Mechanical properties; Corrosion behavior; Biomedical materials	objective of this study is to assess the microstructure, mechanical, and electrochemical properties of the new series designed $\beta$ -type (Ti–Zr)/77–Nb15–Mo8, (Ti–Zr)/75–Nb15–Mo10, (Ti–Zr)/72–Nb15–Mo13, and (Ti–Zr)/70–Nb15–Mo15 (atom %)	as cast/dense	(1) all of the investigated alloys display a monolithic $\beta$ phase in Ti–Zr–Nb–Mo alloys; (2) strength, hardness, elastic energy, and corrosion resistance of Ti–Zr–Nb–Mo alloys increased with addition of Mo
12	Xu et al. <sup>83</sup>	Effects of Mo contents on the microstructure, properties and Cytocompatibility of the microwave sintered porous Ti–Mo alloys	Porous Ti–Mo alloy, Microwave sintering, Mo content, Mechanical properties, Cytocompatibility	this work focuses on characterizing the effect of Mo (5, 10, 15, 20 wt %) on the microstructure and mechanical properties of porous Ti–Mo alloys	microwave sintering/porous	(1) addition of Mo in porous Ti–Mo alloys increases the $\beta$ -phase stability and porosity but decreases the compressive strength, bending strength, and elastic modulus; (2) upon increasing Mo content, porous Ti–Mo alloys do not display a significant effect on corrosion resistance and cytocompatibility
13	Wu et al. <sup>84</sup>	High Recoverable Strain Tailoring by Zr adjustment of sintered Ti–13Nb–(0–6)Zr biomedical alloys	Sintered titanium-based alloy; Martensitic transformation; Recoverable strain; Biomedical alloy	this work focuses on investigating the effect of Zr (0, 2, 4, 6 atom %) on the microstructure, mechanical properties, and martensite transformation temperature on sintered Ti–13Nb alloy	sintering/porous	(1) major finding of this work is that the highest recoverable strain for SMA can be obtained by adjusting its martensite transformation temperature close to room temperature and reducing the percentage of $\alpha$ phase by regulating the Zr/Nb ratio.
14	Salvador et al. <sup>72</sup>	Solute lean Ti–Nb–Fe alloys: an exploratory study	Titanium alloys; Alloy design; Quenching; Phase transformations; Mechanical properties	objective of this work is to design and characterize the cost-effective alloy with low elastic modulus and low Nb addition; amount of Nb is gradually replaced with Fe	casting/dense	(1) it has been noted in this work that the athermal $\omega$ phase has been found in all of the investigated alloys after water quenching from the $\beta$ field; (2) it has also been observed that the strength and elastic modulus of the investigated alloys increases with the addition of Fe in Ti–Nb–Fe alloys
15	Lu et al. <sup>73</sup>	Electrochemical corrosion behavior and elasticity properties of Ti–6Al–xFe alloys for biomedical applications	Ti–6Al–xFe alloys, Microstructure, Corrosion resistance, Elasticity, Biomaterial application	this work characterizes the effect of Fe (1, 2, 4 wt %) addition on the microstructure, corrosion resistance, and elasticity properties of Ti–6Al alloys	casting/dense	(1) this work reported that the gradual addition of Fe in Ti–6Al increases its $\beta$ -phase stability, lowers the elastic modulus, and improves the elastic admissible strain of investigated alloys
16	Shima et al. <sup>74</sup>	Influence of Nb on the $\beta \rightarrow \alpha''$ Martensitic phase transformation and properties of the newly designed Ti–Fe–Nb alloys	Titanium alloy, Phase stability, Microstructure, Mechanical properties, Shear bands	this study assesses the effect of Nb (0, 1, 4, 6, 9, 11 wt %) on the phase stability, microstructure, and mechanical properties of Ti–7Fe alloy	as cast/dense	(1) this study found that addition of Nb in Ti–7Fe alloy increases its $\beta$ -phase stability and plastic strain while decreasing the strength, hardness, and elastic modulus of the investigated alloys
17	Biesiekierski et al. <sup>75</sup>	Investigations into Ti–(Nb,Ta)–Fe alloys for biomedical applications	Titanium, Orthopedic biomaterials, Admissible strain,	this study shows Fe is a cheap and plentiful $\beta$ -stabilizer element and develops three combinations of Ti–Fe alloys with different concentrations of Ta and Nb that are Ti–5Fe–12Nb and	as cast/dense	(1) investigated alloys display elastic moduli in the range of 90–120 GPa and demonstrate a comparable strength to Ti–6Al–4V and Ti–6Al–7Nb commercially available alloys



Table 2. continued

S. no.	author <sup>[ref]</sup>	title	keywords	objectives	fabrication technique/structure	major findings
18	Zhang et al. <sup>88</sup>	Fabrication of high strength, antibacterial and biocompatible Ti–5Mo–5Ag alloy for medical and surgical implant applications	Microstructure, High strength, Spark plasma sintering, Titanium alloy, Microstructure, Antibacterial activity	Ti–(7,10)Ta–(5,4)Fe and performs its mechanical, thermal, corrosion, and biological analyses for implant applications this work characterizes the mechanical properties, corrosion resistance, antibacterial activity, and in vitro cytocompatibility of the newly designed Ti–5Mo–5Ag alloy	sintered at 900 °C/dense	(1) Ti–5Mo–5Ag displays better $\beta$ -phase stability and improved mechanical properties at 900 °C sintered temperature in comparison to being sintered at 800 °C
19	Wang et al. <sup>76</sup>	Microstructure and mechanical properties of a newly developed low Young's modulus Ti–15Zr–5Cr–2Al biomedical alloy	Titanium alloy, Microstructure, Mechanical properties, Young's modulus, Biomedical applications	in this work, a new Ti–15Zr–5Cr–2Al alloy has been developed and characterized the effect of aluminum and different cooling conditions on its mechanical and microstructural properties	as cast	(1) addition of Al (2 wt %) in Ti–15Zr–5Cr (wt %) improves the ductility and compressive strength where the hardness and elastic modulus have decreased; (2) addition of Al with water-quenched conditions demonstrates the ideal mechanical properties to be used as implant biomaterials
20	Choi et al. <sup>85</sup>	Study of the compression and wear-resistance properties of freeze-cast Ti and Ti–5W alloy foams for biomedical applications	Implant, Ti alloy foam, Compressive strain, Wear	objective of this work is to investigate the mechanical and microstructural behavior of Ti alloys with addition of 5 wt % W and various percentages of porosities	freeze casting/foam	(1) addition of W in Ti demonstrates the Widmanstätten $\alpha/\beta$ structure with segregation of W in $\beta$ phase; (2) 2 wt % of W addition in Ti foam improves its strength, hardness, and wear resistance
21	Lin et al. <sup>77</sup>	Novel Ti–Ta–Hf–Zr alloys with promising mechanical properties for prospective stent applications	Novel Ti–Ta–Hf–Zr alloys	different compositions of Ta, Hf, and Zr have been alloyed with Ti including Ti–37Ta–26Hf–13Zr, Ti–40Ta–22Hf–11.7Zr, and Ti–45Ta–18.4Hf–10Zr (wt %) to optimize the microstructural, mechanical, and biocompatible characteristics of Ti alloys	cold crucible levitation melting/dense	(1) all of the investigated THZT alloys mainly exhibit $\beta$ phase with $\omega$ nanoparticles; (2) investigated THZT alloys demonstrate low Young's modulus and high hardness, strength, and elastic admissible strain in comparison to commercially available Ti alloys for biomedical application
22	Biesiekierski et al. <sup>78</sup>	Impact of ruthenium on mechanical properties, biological response, and thermal processing of $\beta$ -type Ti–Nb–Ru alloys	$\beta$ -Titanium alloys, Biomaterials, Mechanical testing, Thermal analysis	objective of this work is to assess the impact of Ru addition on the mechanical properties, biological response, and thermal properties of newly designed Ti–20Nb–(0, 0.5%, 1%, and 1.5%)Ru for implant applications	cold crucible levitation melting	(1) addition of Ru in Ti–20Nb alloys increases the strength up to 1% and decreases upon addition of 1.5% Ru and vice versa happening to the elastic modulus; (2) among the investigated alloys Ti–20Nb–1Ru demonstrates the ideal mechanical properties for their application as an implant material
23	Ozan et al. <sup>80</sup>	New Ti–Ta–Zr–Nb alloys with ultrahigh strength and elastic strain for potential orthopedic implant applications	TTZT (Ti–Ta–Zr–Nb) alloys, orthopedic implants, mechanical properties, elastic strain, cytocompatibility.	in this work, three new combinations of Ti–Ta–Zr–Nb have been developed that are Ti–38.3Ta–22Zr–8.1Nb, Ti–38.9Ta–25Zr5Nb, and Ti–39.5Ta–28Zr–2.5Nb which were analyze for their microstructure and mechanical properties	cold crucible levitation melting/dense	(1) all of the investigated alloys demonstrate mainly the $\beta$ phase along with the small $\omega$ phase; (2) mechanical properties of investigated alloys were found to be better than commercially available Ti alloys; (3) among the investigated alloys Ti–38.3Ta–22Zr–8.1Nb demonstrates the lowest compressive strength and elastic modulus but the highest plastic strain
24	Weng et al. <sup>79</sup>	Impact of the rare earth elements scandium and yttrium on beta-type Ti–24Nb–38Zr–2Mo-base alloys for orthopedic applications	Beta-type, Ti alloy, Rare earth element, Mechanical properties, Microstructure, Cytocompatibility	this work investigates the effect of rare-earth metals, Sc and Yr, on the microstructure and mechanical properties of Ti–24Nb–38Zr–2Mo alloy	cold crucible levitation melting/dense	(1) all of the investigated alloys exhibit monolithic $\beta$ phase in their microstructure; (2) this work found that addition of Sc and Yr does not cause a significant improvement in the mechanical properties of the Ti–24Nb–38Zr–2Mo alloy
25	Luo et al. <sup>89</sup>	Effect of silicon content on the microstructure evolution, mechanical properties, and biocompatibility of $\beta$ -type TiNbZrTa alloys fabricated by laser powder bed fusion	$\beta$ -Type titanium alloys, Laser powder bed fusion, Microstructure, Mechanical properties, Biocompatibility	in this study (3, 5 atom %) Si has been added to a biomedical Ti–35Nb–7Zr–5Ta (wt %) alloy to improve its yield strength; further, the microstructure and cytocompatibility of newly designed alloys were also assessed	laser powder bed fusion	(1) LPBF-fabricated TNZT alloy exhibits a $\beta$ phase and twins along with a $\omega$ phase; addition of 5 atom % Si to TNZT transforms the thin shell-shaped S1 phase of TNZT–3 atom %Si into a thin shell-shaped S2 phase; TNZT–3 atom %Si was found to possess the most suitable mechanical and biocompatible properties and can be a potential candidate for biomedical applications
26	Luo et al. <sup>90</sup>	Achieving ultrahigh-strength in beta-type titanium alloy by controlling the melt pool	Beta-type titanium alloys, Selective laser melting	objective of this study is to determine the pattern of the keyhole mechanism and development of high-strength dense Ti–Nb–Zr–Ta alloys; this study also characterizes the micro-	selective laser melting	(1) in this study, $\beta$ grains are surrounded by a thin shell-shaped S2 phase along with the dotted S1 phase in both the keyhole and the conduction mode; SLMed Ti–Nb–Zr–Ta–Si alloy exhibits superior mechanical

Table 2. continued

S. no.	author <sup>[ref]</sup>	title	keywords	objectives	fabrication technique/structure	major findings
27	Yang et al. <sup>91</sup>	Nonisothermal and isothermal crystallization kinetics and their effect on the microstructure of sintered and crystallized TiNbZrTa-Si bulk alloys	Single track, Microstructure Metallic glass, Crystallization mechanism, Microstructure, Mechanical property, Powder metallurgy	structure, mechanical property, and strengthening mechanism of the newly designed Ti-Nb-Zr-Ta-Si alloy  this study focuses on a comparison of the isothermal and nonisothermal crystallization kinetics of mechanically alloyed Ti-23.33Nb-5Zr-1.67Ta-5Si alloy	spark plasma sintering	properties; moreover, it has been noted that coherent S2 and semicoherent S1 phases impede the dislocation motion and dislocation initiation which correspondingly increases the strength of the alloy  (1) crystallization of metallic glass powder possesses two separate steps because of the consequent two different phases cubic $\beta$ -Ti and hexagonal (Ti, Zr) <sub>2</sub> Si phase; different sintering processing parameters were attributed to different microstructure properties in bulk and crystallized samples
28	Liu et al. <sup>13</sup>	Compressive and fatigue behavior of beta-type titanium porous structures fabricated by electron beam melting	Electron beam melting, Titanium alloys, Mechanical properties, Heat treatment, Porous structures, Superelasticity	objective of this study is to produce porous Ti-24Nb-4Zr-7.9Sn alloys through electron beam melting and characterize their macrostructure and mechanical properties	electron beam melting	(1) mechanical properties of Ti alloys can be improved by increasing the porosity of a porous sample; Ti-24Nb-4Zr-7.9Sn possesses better fatigue strength and larger plastic zones compared to the Ti-6Al-4V porous sample

Figure 7 displays the elastic modulus of the studied alloys; the highest elastic modulus was found to be 121 GPa for Ti-10Ta-4Fe alloy.<sup>75</sup> Ti-10Ta-4Fe exhibits such a high elastic modulus value due to the presence of the  $\omega$  phase in its microstructure. Notably, the dense Ti-2Zr-0.1Nb-0.1Sn alloy exhibits a remarkably low elastic modulus of 14.72 GPa despite containing intermetallic phases, i.e., TiZr in its microstructure which is not reported for the dense alloys.<sup>83</sup> However, the study does not mention the use of a strain gauge or extensometer for estimation of the precise elastic modulus. Studies<sup>67,68,78</sup> have shown a moderately low elastic modulus of around 65 GPa for Ti-10Nb-5Sn, Ti-20Nb-1Ru, and Ti-25Zr-10Nb-10Ta-1.5Ag alloys in comparison to other investigated alloys. These alloys are alloyed with 10–20 wt % of Nb, which is a strong  $\beta$ -stabilizer element.<sup>54</sup> Therefore, Ti-20Nb-1Ru and Ti-25Zr-10Nb-10Ta-1.5Ag demonstrate a monolithic  $\beta$  phase in their microstructure, whereas Ti-10Nb-5Sn exhibits a  $\beta + \alpha'$  phase in its microstructure.<sup>67,68,78</sup> Increasing the Nb content leads to a lower elastic modulus; Ti-10Nb-5Sn, Ti-20Nb-1Ru, and Ti-25Zr-10Nb-10Ta-1.5Ag alloys demonstrated a low elastic modulus.<sup>92</sup> It can be noted from this trend that most of the Fe-containing alloys demonstrate a higher elastic modulus. However, Fe is a strong  $\beta$  stabilizer, but it increases the elastic modulus of Ti alloys.<sup>72,73,93</sup>

Figure 8 demonstrates the trends of the yield strength of the studied alloys. Among the studied alloys, dense Ti-5Mo-5Ag alloy displays the highest yield strength of 1694 MPa, whereas the lowest yield strength of 477 MPa was shown for a dense Ti-31Nb-1.0Fe alloy.<sup>72</sup> Among the porous materials, Ti-6Al-3Fe demonstrates the highest yield strength of 1067 MPa whereas Ti-5Mo displays the lowest yield strength of 320 MPa.<sup>82,83</sup> Alloys containing a single  $\beta$  phase have a low yield strength compared to alloys containing a dual  $\alpha + \beta$  phase.

The ultimate compressive strength and elongation results of the studied alloys are displayed in Figures 9 and 10. Ti-25Nb-4Mn-1Sn and Ti-26Nb-5Mn-4Zr have extremely high values of the ultimate compressive strength and plasticity.<sup>24,69</sup> However, these high values have no significant impact because none of the Ti-25Nb-4Mn-1Sn and Ti-26Nb-5Mn-4Zr alloys fail during the compression test until the maximum load capacity, i.e., 100 KN of the universal testing machine.<sup>24,69</sup> Ti-5Mo-5Ag has the highest ultimate compressive strength of 2100 MPa, and Ti-38.3Ta-22Zr-8.1Nb has a large plasticity of 35.72%.<sup>88,94</sup> It has been reported in the literature that plasticity is directly proportional to  $\beta$ -phase stability. It can be noted from Table 3 that those alloys that have a dominant  $\beta$  phase demonstrate a large plasticity.

Figure 11 demonstrates the hardness of the studied alloys. It can be noticed that Ti-38.3Ta-22Zr-8.1Nb demonstrates the maximum hardness of 433.4 HV among the dense alloys, whereas Ti-25Nb-4Mn-1Sn demonstrates the lowest hardness of 228.4 HV among the studied alloys.<sup>24,79</sup> None of the porous materials have estimated the value of hardness. However, Ti-5W foam demonstrates a hardness of 271 HV.<sup>85</sup>

It can be observed from the included studies that 17 out of 24 studies contain Nb as an alloying element in Ti alloys. This shows that combination of a binary Ti-Nb alloy has received more attention among the materials research community for biomedical applications. This is because Nb is a strong  $\beta$  stabilizer and reduces the elastic modulus and strength of Ti alloys.<sup>92</sup> However, Nb is a rare-earth and expensive material having a high melting point.<sup>54,62</sup> Therefore, it is very important for material scientists to bear in mind the four important factors

Table 3. Microstructure and Compressive Mechanical Properties of Alloys Included in the Systematic Review

S. no.	author <sup>[ref]</sup>	alloy compositions	microstructure	elastic modulus (GPa)/ testing method	yield strength (MPa)	ultimate compressive strength (MPa)	hardness (HV)	elongation (%)
1	Yolun et al. <sup>86</sup>	Ti-5.4Nb Ti-18Nb Ti-20Nb-0.025O	$\alpha + \beta + \alpha''$ $\alpha + \beta + \alpha''$ $\alpha + \beta$	35/compression test 40/compression test 87 ± 1.9/pulse-echo acoustic emission technique	818 ± 51	850 900	273 ± 3	31 ± 4
3	Li et al. <sup>81</sup>	Ti-35Nb-3Mg	$\alpha + \beta$			1259		
4	Kalita et al. <sup>87</sup>	Ti-14Nb Ti-14Nb-2Mo Ti-14Nb-2Ta	$\beta + \alpha''$ $\beta + \alpha''$ $\beta + \alpha''$		790 ± 58 682 ± 15 766 ± 32	1429 ± 81 1312 ± 80 1440 ± 88		20 ± 2 29 ± 2 25 ± 4
5	Zareidoost et al. <sup>67</sup>	Ti-25Zr-10Nb-10Ta Ti-25Zr-10Nb-10Ta-0.5Fe Ti-25Zr-10Nb-10Ta-2Sn Ti-25Zr-10Nb-10Ta-1.5Ag Ti-40Nb	$\beta$ $\beta$ $\beta$ $\beta$ $\beta$ (minor $\alpha'$ )	78.56 ± 3.46/nanoindentation technique 71.6 ± 3.72/nanoindentation technique 76.01 ± 2.37/nanoindentation technique 65.54 ± 1.7/nanoindentation technique 80.75 ± 1.77/compression testing	727 ± 26 750 ± 34 738 ± 40 711 ± 23 994.37 ± 40.01		350.8 ± 7.13	
6	Torres-Sánchez et al. <sup>68</sup>	Ti-10Sn Ti-10Nb-5Sn Ti-6Al-3Fe	$\alpha' + \text{Ti3Sn IMCs}$ $\beta + \alpha''$ $\alpha + \beta$	78.68 ± 2.12/compression testing 65.19 ± 1.97/compression testing 97/compression testing	922.64 ± 37.79 1283.38 ± 52.31 1067		403.8 ± 15.3 390.5 ± 41.8	
7	Sjafrizal et al. <sup>82</sup>	Ti-26Nb-5Mn-4Zr	$\beta$		609 ± 18	4917 ± 109	241.7 ± 5.098	78.9 ± 0.7
8	Jawed et al. <sup>69</sup>	Ti-25Nb-4Mn-1Sn	$\beta$		490 ± 30	4524 ± 173	228.4 ± 2.039	80.0 ± 0.42
9	Jawed et al. <sup>24</sup>	Ti-2Zr-0.1Nb-0.1Sn	$\beta + \text{TiZr}$	14.72/compression testing	1525	1494		27.1
10	Dang et al. <sup>70</sup>	TiZr-15Nb-8Mo	$\beta$	96/nanoindentation technique	545			
11	Pengfei et al. <sup>71</sup>	TiZr-15Nb-15Mo	$\beta$	105/nanoindentation technique	834			
12	Xu et al. <sup>83</sup>	Ti-5Mo (porous)	$\alpha + \beta$	9.08/compression testing	320			
13	Wu et al. <sup>84</sup>	Ti-13Nb-2Zr	$\beta + \alpha''$		1376			
14	Salvador et al. <sup>72</sup>	Ti-3INb-1.0Fe Ti-11Nb-3.5Fe	$\beta + \omega$ $\beta$	81 ± 3/pulse-echo panametrics 97 ± 1/pulse-echo panametrics	477 ± 79 715 ± 44		230 ± 11 382 ± 3	
15	Lu et al. <sup>73</sup>	Ti-6Al-2Fe	$\alpha + \beta$	110/static extensometer	925			12
16	Shima et al. <sup>74</sup>	Ti-7Fe-11Nb	$\beta$	84/clip-on extensometer	985		325	38
17	Biesiekierski et al. <sup>75</sup>	Ti-10Ta-4Fe	$\beta + \omega$	121 ± 2/strain gauge	1360 ± 20	1450 ± 20	410 ± 10	
18	Zhang et al. <sup>88</sup>	Ti-5Mo-5Ag	$\alpha + \beta$		1694 ± 8.4	2100 ± 33.8		22.3 ± 1.2
19	Wang et al. <sup>76</sup>	Ti-15Zr-5Cr-2Al	$\alpha + \beta$	96.1 ± 3.2 strain gauge	1147.6 ± 36.2	1689.5 ± 44.5	385 ± 20	24.0 ± 0.7
20	Choi et al. <sup>85</sup>	Ti-5W (foam)	$\alpha + \beta$	25.4/compression testing	322.6		271 ± 37.7	
21	Lin et al. <sup>77</sup>	Ti-40Ta-22HF-11.7Zr	$\beta$	71.7 ± 2.3/compression testing	1154.0 ± 31.2		374.7 ± 5.8	
22	Biesiekierski et al. <sup>78</sup>	Ti-20Nb-1Ru	$\beta$	65 ± 3/strain gauge	920 ± 60	960 ± 50		22
23	Ozan et al. <sup>80</sup>	Ti-38.3Ta-22Zr-8.1Nb	$\beta + \omega$		1317.42 ± 7.24	1787.19 ± 49.37	433.4 ± 7.9	35.72 ± 1.97
24	Weng et al. <sup>79</sup>	Ti-24Nb-38Zr-2Mo	$\beta$		691 ± 63		270 ± 6	
25	Luo et al. <sup>89</sup>	Ti-35Nb-7Zr-5Ta Ti-35Nb-7Zr-5Ta-3Si Ti-35Nb-7Zr-5Ta-5Si	$\beta$ -Ti $\beta$ -Ti + S1 $\beta$ -Ti + S1 + S2	41.4 ± 0.5/compression testing 48.7 ± 1/compression testing 60.6 ± 2.3/compression testing	802 ± 5 1151 ± 17 1228 ± 23	2451 ± 32 2341 ± 53	321 ± 8.1 355.3 ± 8.4	46.7 ± 1.1 39.6 ± 1.6
26	Luo et al. <sup>90</sup>	Ti-34.5Nb-6.9Zr-5Ta-1.4Si	$\beta$ -Ti + S1	79 ± 3/compression testing	1286 ± 16	2375 ± 8		42.5 ± 1.3
27	Yang et al. <sup>91</sup>	Ti-23.33Nb-5Zr-1.67Ta-5Si	$\beta$ -Ti + S2	53 ± 6/strain gauge	1569 ± 2	2563 ± 45		40 ± 2
28	Liu et al. <sup>13</sup>	Ti-24Nb-4Zr-7.9Sn (porous)	$\beta$	1.44 ± 0.2/compression testing		38		



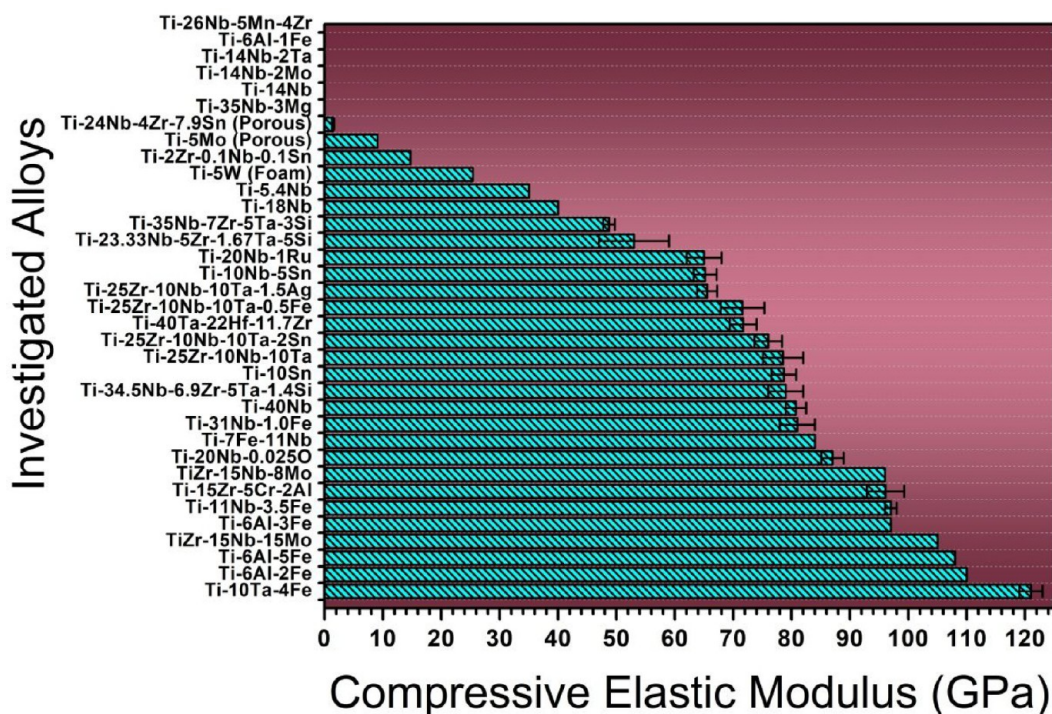


Figure 7. Compressive elastic modulus of the alloys included in this systematic review.<sup>13,24,66–91</sup>

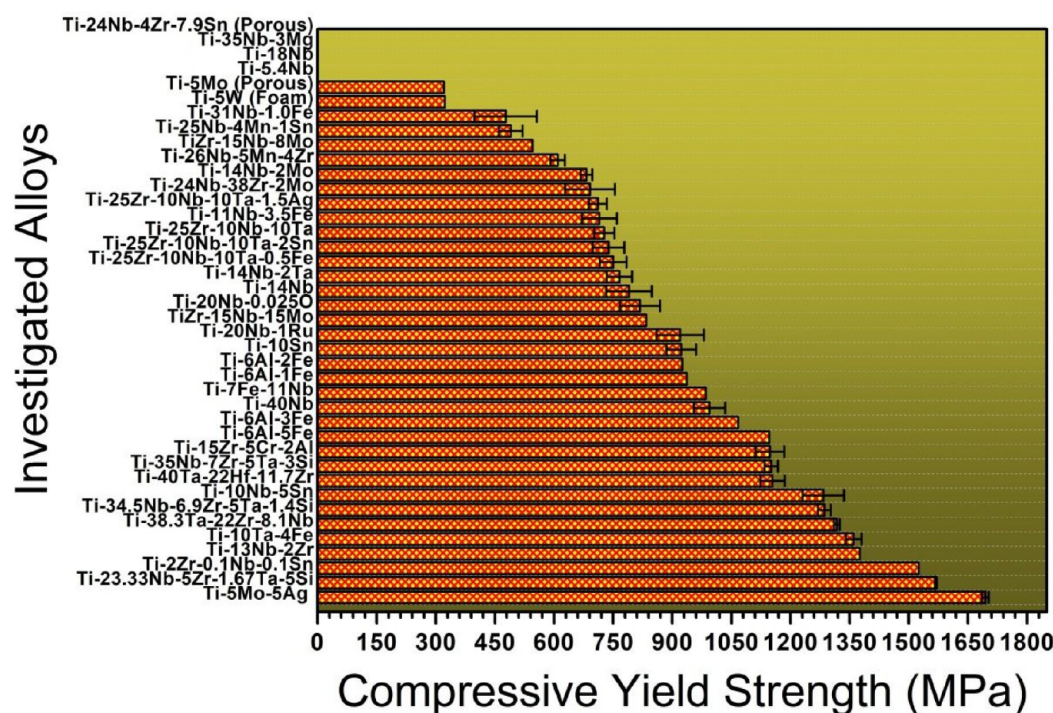


Figure 8. Compressive yield strength of the alloys included in this systematic review.<sup>13,24,66–91</sup>

when designing new Ti alloys for biomedical applications: (i) reducing the stress-shielding effect, (ii) controlling the strength–ductility trade-off dilemma, (iii) application of low-cost and abundantly available materials having low melting points, and (iv) use of nontoxic elements.<sup>94–97</sup> It has been observed from the included studies that when scientists tried to reduce the stress-shielding effect, which is an elastic modulus mismatch between a bone and an implant material, the strength was compromised to some extent. It is very important to keep

the balance between plasticity and strength to achieve optimum functionality of the implant material.<sup>98</sup> Luo et al. found that the strength–ductility trade-off can be overcome by addition of Si to Ti–Nb–Zr–Ta alloys due to formation of the globular S2 phase in Ti alloys.<sup>99,100</sup> Notably, addition of Si to Ti–Nb–Zr–Ta alloy forms high-strength Ti–Nb–Zr–Ta–Si alloy microstructures with a bcc  $\beta$ -Ti matrix and hexagonal S2 reinforced phase when fabricated by spark plasma sintering of the nanocomposite powders, whereas the Ti–Nb–Zr–Ta–Si alloys

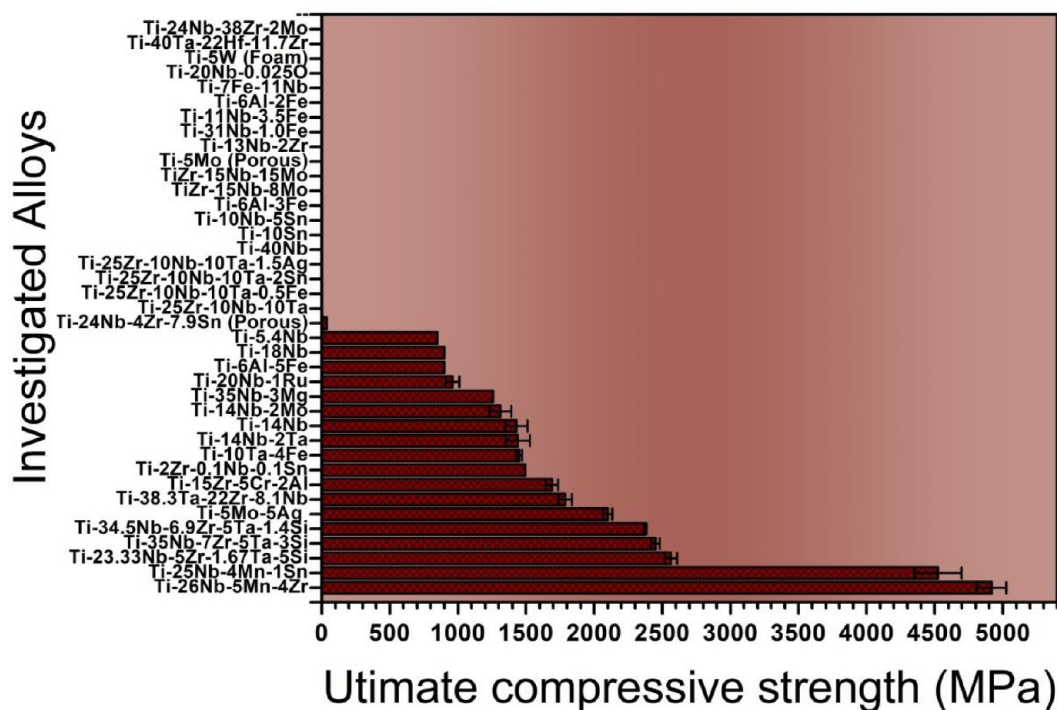


Figure 9. Ultimate compressive strength of the alloys included in this systematic review.<sup>13,24,66–91</sup>

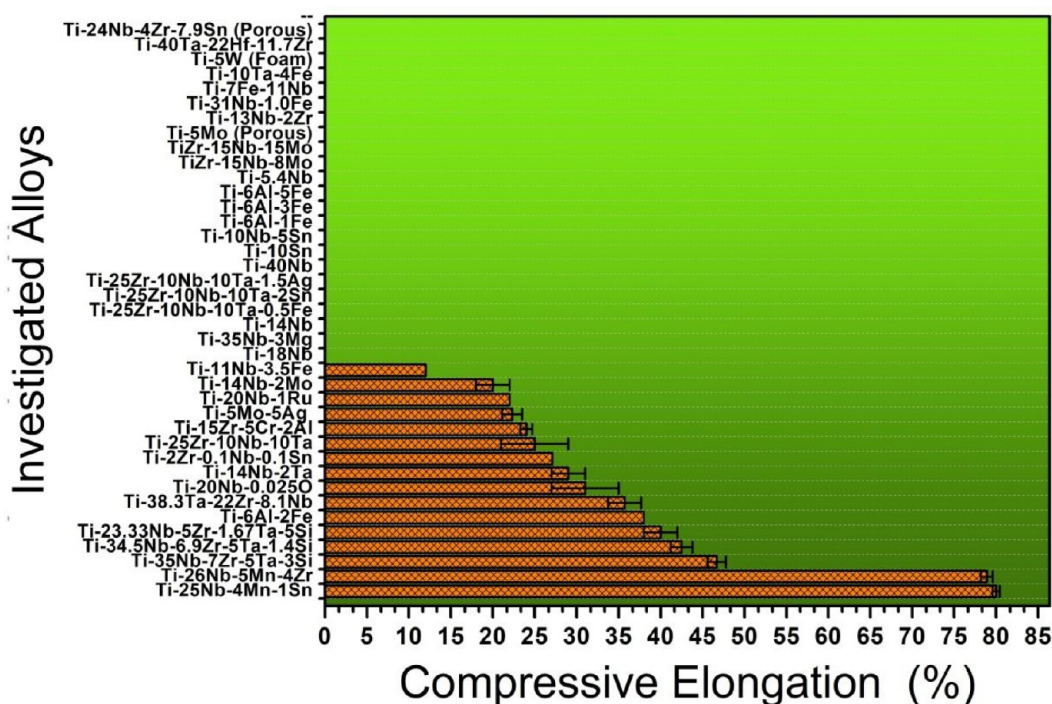


Figure 10. Compressive elongation of the alloys included in this systematic review.<sup>13,24,66–91</sup>

produced by additive manufacturing show a different microstructure (thin shell-shaped metastable S1 phase surrounding the columnar  $\beta$ -Ti grain) and mechanical properties. However, a comparison of the processing technologies is not the scope of this work, but both processing technologies show a moderate balance between high strength and low modulus due to the addition of Si in Ti–Nb–Zr–Ta alloys, which makes them an ideal candidates for biomedical applications.<sup>89–91</sup> It has been reported in the literature that alloying elements have different

types of phase-stabilizing effects on Ti alloys.  $\beta$ -Phase stabilizers are divided into two categories: (i)  $\beta$ -eutectic (Fe, Mn, Cr) and (ii)  $\beta$ -isomorphous (Nb, Mo, Ta, W). It has also been reported that neutral elements such as Zr and Sn have no effect on the phase stability of Ti alloys, but when alloyed with  $\beta$ -stabilizer elements, they also stabilize the  $\beta$  phase along with them.<sup>101</sup> Although the combination of a Ti–Nb binary alloy is effective for biomedical applications, its percentage should be reduced with other alloying elements. The balanced combination of



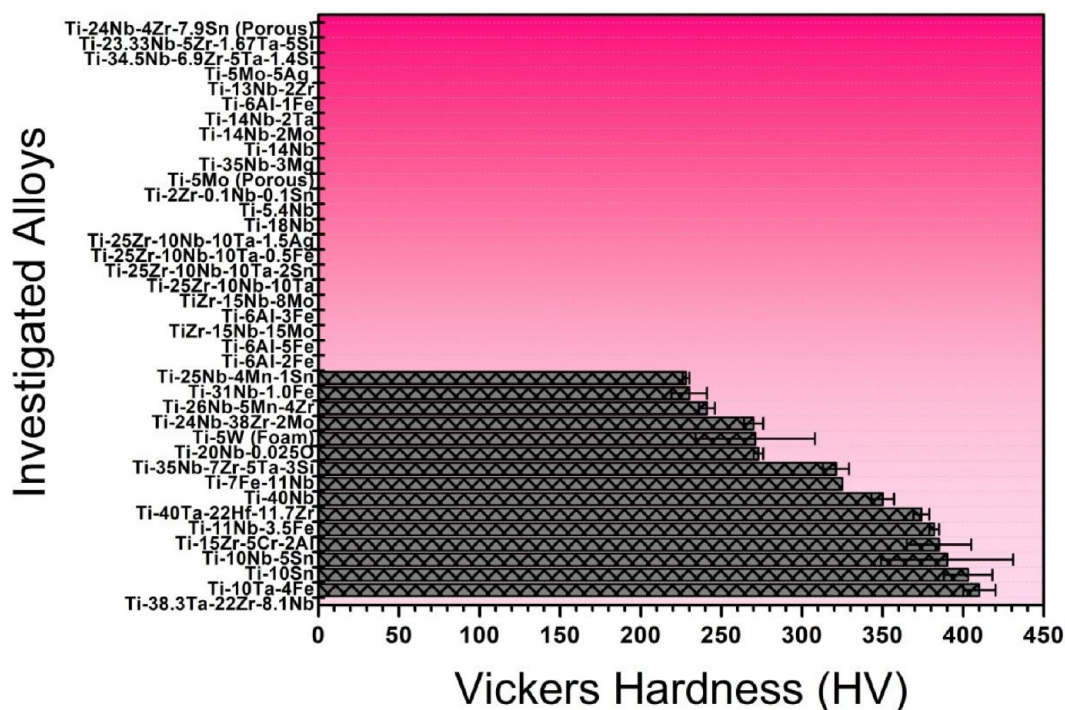


Figure 11. Vickers hardness of the alloys included in this systematic review.<sup>13,24,66–91</sup>

alloying elements that are alloying one element from the  $\beta$ -isomorphous category, one element from the  $\beta$ -eutectic category, and one element from the neutral category in Ti alloys would display a balanced mechanical performance as reported by some studies as well.<sup>10,54</sup>

Therefore, in the author's opinion, when designing low modulus, moderate strength, and low-cost Ti alloys for biomedical applications, combination of a Ti–Nb binary alloy along with some  $\beta$ -eutectic elements (Fe, Cr, Mn) and neutral elements (Sn, Zr) in appropriate percentages would be an ideal material for biomedical applications. This is because the addition of Nb in Ti alloys can significantly lower the elastic modulus and stabilizes the  $\beta$  phase. However, addition of Nb lowers the compressive yield strength as well, which could be increased by the addition of  $\beta$ -eutectic elements (Fe, Cr, Mn) and neutral element (Sn, Zr) in Ti–Nb alloys. Moreover, addition of Si in Ti–Nb–Zr–Ta alloys improves its yield strength and lowers the elastic modulus. Finally, this systematic review comprehensively reported the effect of different alloying elements on the compressive mechanical performance of Ti alloys that would be very useful for the material research community in designing new  $\beta$ -type Ti alloys for biomedical applications.

## 5. CONCLUSION

The following concluding remarks of this systematic review are as follows.

- (1) Analyses of the compressive mechanical features of Ti alloys for biomedical applications are of utmost importance as human bones are primarily experiencing compressive loads during their daily living activities.
- (2) Element selection and its percentage to be alloyed with Ti for biomedical applications must be balanced, and its effect should be theoretically predicted using the various reported theoretical approaches in this systematic review.

- (3) The combination Ti–Nb binary alloy has emerged as an attractive material for designing low elastic modulus Ti alloys. To further improve the mechanical performance of Ti–Nb alloys,  $\beta$ -eutectic (Fe, Cr, and Mn) and neutral (Zr, Sn) elements should be alloyed with a Ti–Nb binary alloy.
- (4) Addition of Si to Ti–Nb–Zr–Ta alloys improves its biomechanical performance, which could be an optimum solution to overcome the strength–ductility trade-off dilemma in Ti alloys produced for biomedical applications.
- (5) This work reports the effect of alloying elements on the compressive mechanical properties. In the future, a systematic review on the effect of interstitial elements and heat treatments on the compressive mechanical performance of Ti alloys will be presented which has not been reported yet as a systematic review.

## AUTHOR INFORMATION

### Corresponding Author

Syed Faraz Jawed – Department of Biomedical Engineering, NED University of Engineering & Technology, Karachi 75270, Pakistan; [orcid.org/0000-0003-4507-6095](https://orcid.org/0000-0003-4507-6095); Email: [farazjawed@neduet.edu.pk](mailto:farazjawed@neduet.edu.pk), [farazjawed88@hotmail.com](mailto:farazjawed88@hotmail.com)

### Authors

Chirag Dhirajlal Rabadia – School of Engineering, Edith Cowan University, Joondalup, Western Australia 6027, Australia; Engineering Institute of Technology, Bentley, Western Australia 6012, Australia

Muhammad Ahmed Khan – Department of Health Technology, Technical University of Denmark, Lyngby 2800, Denmark; School of Medicine, Stanford University, Palo Alto, California 94304, United States



Saad Jawaid Khan – Department of Biomedical Engineering,  
Ziauddin University, Karachi 74600, Pakistan

Complete contact information is available at:  
<https://pubs.acs.org/10.1021/acsomega.2c02096>

## Notes

The authors declare no competing financial interest.

## REFERENCES

- (1) Geetha, M.; Singh, A.; Asokamani, R.; Gogia, A. Ti based biomaterials, the ultimate choice for orthopaedic implants—a review. *Prog. Mater. Sci.* **2009**, *54* (3), 397–425.
- (2) Chen, L.-Y.; Cui, Y.-W.; Zhang, L.-C. Recent Development in Beta Titanium Alloys for Biomedical Applications. *Metals* **2020**, *10* (9), 1139.
- (3) Rabadia, C. D.; Liu, Y. J.; Cao, G. H.; Li, Y. H.; Zhang, C. W.; Sercombe, T. B.; Sun, H.; Zhang, L. C. High-strength  $\beta$  stabilized Ti–Nb–Fe–Cr alloys with large plasticity. *Mater. Sci. Eng., A* **2018**, *732*, 368–377.
- (4) Sidhu, S. S.; Singh, H.; Gepreel, M. A.-H. A review on alloy design, biological response, and strengthening of  $\beta$ -titanium alloys as biomaterials. *Mater. Sci. Eng., C* **2021**, *121*, 111661.
- (5) Callister, W. D. *Fundamentals of materials science and engineering*; Wiley: London, 2000.
- (6) Liang, S. Review of the Design of Titanium Alloys with Low Elastic Modulus as Implant Materials. *Adv. Eng. Mater.* **2020**, *22* (11), 2000555.
- (7) Zhang, L.; Liu, Y.; Li, S.; Hao, Y. Additive manufacturing of titanium alloys by electron beam melting: A review. *Adv. Eng. Mater.* **2018**, *20* (5), 1700842.
- (8) Ibrahim, M. Z.; Sarhan, A. A.; Yusuf, F.; Hamdi, M. Biomedical materials and techniques to improve the tribological, mechanical and biomedical properties of orthopedic implants—A review article. *J. Alloys Compd.* **2017**, *714*, 636–667.
- (9) Nouri, A.; Hodgson, P. D.; Wen, C. e. Biomimetic porous titanium scaffolds for orthopedic and dental applications. In *Biomimetics learning from nature*, Mukherjee, A., Ed.; IntechOpen, 2010; pp 415–450.
- (10) Jawed, S. F.; Rabadia, C. D.; Liu, Y. J.; Wang, L. Q.; Li, Y. H.; Zhang, X. H.; Zhang, L. C. Mechanical characterization and deformation behavior of  $\beta$ -stabilized Ti–Nb–Sn–Cr alloys. *J. Alloys Compd.* **2019**, *792*, 684–693.
- (11) Yu, H.; Yan, M.; Li, J.; Godbole, A. R.; Lu, C.; Tieu, K.; Li, H.; Kong, C. Mechanical properties and microstructure of a Ti–6Al–4V alloy subjected to cold rolling, asymmetric rolling and asymmetric cryo-rolling. *Mater. Sci. Eng. A-Struct.* **2018**, *710*, 10–16.
- (12) Quadros, F. d. F.; Kuroda, P. A. B.; Sousa, K. d. S. J.; Donato, T. A. G.; Grandini, C. R. Preparation, structural and microstructural characterization of Ti–25Ta–10Zr alloy for biomedical applications. *J. Mater. Res. Technol.* **2019**, *8* (5), 4108–4114.
- (13) Liu, Y.J.; Wang, H.L.; Li, S.J.; Wang, S.G.; Wang, W.J.; Hou, W.T.; Hao, Y.L.; Yang, R.; Zhang, L.C. Compressive and fatigue behavior of beta-type titanium porous structures fabricated by electron beam melting. *Acta Mater.* **2017**, *126*, 58–66.
- (14) Soro, N.; Attar, H.; Brodie, E.; Veidt, M.; Molotnikov, A.; Dargusch, M. S. Evaluation of the mechanical compatibility of additively manufactured porous Ti–25Ta alloy for load-bearing implant applications. *J. Mech. Behav. Biomed. Mater.* **2019**, *97*, 149–158.
- (15) Wang, L.; Xie, L.; Zhang, L.-C.; Chen, L.; Ding, Z.; Lv, Y.; Zhang, W.; Lu, W.; Zhang, D. Microstructure evolution and superelasticity of layer-like NiTiNb porous metal prepared by eutectic reaction. *Acta Mater.* **2018**, *143*, 214–226.
- (16) Wang, L.; Wang, C.; Zhang, L.-C.; Chen, L.; Lu, W.; Zhang, D. Phase transformation and deformation behavior of NiTi–Nb eutectic joined NiTi wires. *Sci. Rep.* **2016**, *6* (1), 23905.
- (17) Lu, H. Z.; Yang, C.; Luo, X.; Ma, H. W.; Song, B.; Li, Y. Y.; Zhang, L.-C. Ultrahigh-performance TiNi shape memory alloy by 4D printing. *Mater. Sci. Eng., A* **2019**, *763*, 138166.
- (18) Al-Zain, Y.; Yamamoto, A.; AlAjjlouni, J. M.; Al-Abbadi, M. A.; Al-Sayyed, M. R.; Aloweidi, A. S.; Kim, H. Y.; Miyazaki, S. Corrosion behavior, in vitro and in vivo biocompatibility of a newly developed Ti–16Nb–3Mo–1Sn superelastic alloy. *Mater. Sci. Eng., C* **2019**, *104*, 109906.
- (19) Frutos, E.; Karlík, M.; Jiménez, J. A.; Langhansová, H.; Lieskovská, J.; Polcar, T. Development of new  $\beta/\alpha'$ -Ti–Nb–Zr biocompatible coating with low Young's modulus and high toughness for medical applications. *Mater. Des.* **2018**, *142*, 44–55.
- (20) Baker, C. The Shape-Memory Effect in a Titanium–35 wt.-% Niobium Alloy. *Met. Sci. J.* **1971**, *5* (1), 92–100.
- (21) Kim, H. Y.; Ikehara, Y.; Kim, J. I.; Hosoda, H.; Miyazaki, S. Martensitic transformation, shape memory effect and superelasticity of Ti–Nb binary alloys. *Acta Mater.* **2006**, *54* (9), 2419–2429.
- (22) Li, S.; Kim, Y.-w.; Choi, M.-s.; Nam, T.-h. Highly porous Ni-free Ti-based scaffolds with large recoverable strain for biomedical applications. *Intermetallics* **2020**, *116*, 106657.
- (23) Ramezannejad, A.; Xu, W.; Xiao, W. L.; Fox, K.; Liang, D.; Qian, M. New insights into nickel-free superelastic titanium alloys for biomedical applications. *Curr. Opin. Solid State Mater. Sci.* **2019**, *23* (6), 100783.
- (24) Jawed, S. F.; Liu, Y. J.; Wang, J. C.; Rabadia, C. D.; Wang, L. Q.; Li, Y. H.; Zhang, X. H.; Zhang, L. C. Tailoring deformation and superelastic behaviors of beta-type Ti–Nb–Mn–Sn alloys. *J. Mech. Behav. Biomed. Mater.* **2020**, *110*, 103867.
- (25) Niinomi, M.; Boehlert, C. J. Titanium Alloys for Biomedical Applications. In *Advances in Metallic Biomaterials: Tissues, Materials and Biological Reactions*; Niinomi, M., Narushima, T., Nakai, M., Eds.; Springer Berlin Heidelberg, 2015; pp 179–213.
- (26) Currey, J. Cortical Bone. In *Handbook of Biomaterial Properties* Murphy, W., Black, J., Hastings, G., Eds.; Springer New York, 2016; Chapter A1, pp 3–13.
- (27) Hernandez, C. J. Cancellous Bone. In *Handbook of Biomaterial Properties*; Murphy, W., Black, J., Hastings, G., Eds.; Springer New York, 2016; Chapter A2, pp 15–21.
- (28) Hall, S. J. *Basic Biomechanics*; McGraw-Hill, 2012.
- (29) Thomson, R. C.; Wake, M. C.; Yaszemski, M. J.; Mikos, A. G. Biodegradable polymer scaffolds to regenerate organs. In *Biopolymers II*; Peppas, N. A., Langer, R. S., Eds.; Springer Berlin Heidelberg, 1995; Vol. 122, pp 245–274.
- (30) Zhang, L.; Chen, L. Y. A review on biomedical titanium alloys: recent progress and prospect. *Adv. Eng. Mater.* **2019**, *21* (4), 1801215.
- (31) Zhang, L.; Wang, L. Microstructure and Mechanical Properties of Beta Type Ti–Fe Based Alloys. In *Development and Application of Biomedical Titanium Alloys*, Zhang, L.; Wang, L. Eds.; Bentham Books, 2018; pp 51–72.
- (32) Bolmaro, R.; Parau, A. C.; Pruna, V.; Surmeneva, M. A.; Constantin, L. R.; Avalos, M.; Cotrut, C. M.; Tutuianu, R.; Braic, M.; Cojocar, D. V.; Dan, I.; Croitoru, S.; Surmeneva, R. A.; Vladescu, A. Investigation of cast and annealed Ti25Nb10Zr alloy as material for orthopedic devices. *J. Mater. Res. Technol.* **2019**, *8* (4), 3399–3414.
- (33) Wang, K. The use of titanium for medical applications in the USA. *Mater. Sci. Eng., A* **1996**, *213* (1–2), 134–137.
- (34) Ozan, S.; Lin, J.; Li, Y.; Ipek, R.; Wen, C. Development of Ti–Nb–Zr alloys with high elastic admissible strain for temporary orthopedic devices. *Acta Biomater.* **2015**, *20*, 176–187.
- (35) Guillemot, F.; Prima, F.; Bareille, R.; Gordin, D.; Gloriant, T.; Porté-Durrieu, M.; Ansel, D.; Baquey, C. Design of new titanium alloys for orthopaedic applications. *Med. Biol. Eng. Comput.* **2004**, *42* (1), 137–141.
- (36) Li, Y.; Yang, C.; Zhao, H.; Qu, S.; Li, X.; Li, Y. New developments of Ti-based alloys for biomedical applications. *Mater.* **2014**, *7* (3), 1709–1800.
- (37) Biesiekierski, A.; Wang, J.; Abdel-Hady Gepreel, M.; Wen, C. A new look at biomedical Ti-based shape memory alloys. *Acta Biomater.* **2012**, *8* (5), 1661–1669.
- (38) Haghghi, S. E.; Lu, H.; Jian, G.; Cao, G.; Habibi, D.; Zhang, L. Effect of  $\alpha'$  martensite on the microstructure and mechanical properties of beta-type Ti–Fe–Ta alloys. *Mater. Des.* **2015**, *76*, 47–54.

- (39) Nnamchi, P. S.; Obayi, C.; Todd, I.; Rainforth, M. Mechanical and electrochemical characterisation of new Ti–Mo–Nb–Zr alloys for biomedical applications. *J. Mech. Behav. Biomed. Mater.* **2016**, *60*, 68–77.
- (40) Niinomi, M. Mechanical properties of biomedical titanium alloys. *Mater. Sci. Eng., A* **1998**, *243* (1), 231–236.
- (41) Lütjering, G.; Williams, J.; Gysler, A. Microstructure and mechanical properties of titanium alloys. In *Microstructure and Properties of Materials*; Li, J. C. M., Ed.; World Scientific Publishing Co., 2000; Vol. 2, pp 1–77.
- (42) Zhang, Y. S.; Hu, J. J.; Zhang, W.; Yu, S.; Yu, Z. T.; Zhao, Y. Q.; Zhang, L.-C. Discontinuous core-shell structured Ti-25Nb-3Mo-3Zr-2Sn alloy with high strength and good plasticity. *Mater. Charact.* **2019**, *147*, 127–130.
- (43) Kuroda, D.; Niinomi, M.; Morinaga, M.; Kato, Y.; Yashiro, T. Design and mechanical properties of new  $\beta$  type titanium alloys for implant materials. *Mater. Sci. Eng., A* **1998**, *243* (1–2), 244–249.
- (44) Oshida, Y. *Bioscience and Bioengineering of Titanium Materials*; Elsevier, 2012. DOI: 10.1016/C2011-0-07805-5.
- (45) Chen, J.-R.; Tsai, W.-T. In situ corrosion monitoring of Ti–6Al–4V alloy in H<sub>2</sub>SO<sub>4</sub>/HCl mixed solution using electrochemical AFM. *Electrochim. Acta* **2011**, *56* (4), 1746–1751.
- (46) Elias, C.; Lima, J.; Valiev, R.; Meyers, M. Biomedical applications of titanium and its alloys. *JOM* **2008**, *60* (3), 46–49.
- (47) Long, M.; Rack, H. J. Titanium alloys in total joint replacement—a materials science perspective. *Biomaterials* **1998**, *19* (18), 1621–1639.
- (48) Zheng, Y. *Nucleation mechanisms of refined alpha microstructure in beta titanium alloys*. The Ohio State University: Columbus, OH, 2013.
- (49) Balazic, M.; Kopac, J.; Jackson, M. J.; Ahmed, W. Titanium and titanium alloy applications in medicine. *Int. J. Nano Biomater.* **2007**, *1* (1), 3–34.
- (50) Niinomi, M.; Liu, Y.; Nakai, M.; Liu, H.; Li, H. Biomedical titanium alloys with Young's moduli close to that of cortical bone. *Regen. Biomater* **2016**, *3* (3), 173–185.
- (51) Nakai, M.; Niinomi, M.; Zhao, X.; Zhao, X. Self-adjustment of Young's modulus in biomedical titanium alloys during orthopaedic operation. *Mater. Lett.* **2011**, *65* (4), 688–690.
- (52) Fernandes Santos, P.; Niinomi, M.; Liu, H.; Cho, K.; Nakai, M.; Trenggono, A.; Champagne, S.; Hermawan, H.; Narushima, T. Improvement of microstructure, mechanical and corrosion properties of biomedical Ti–Mn alloys by Mo addition. *Mater. Des.* **2016**, *110*, 414–424.
- (53) Rabadia, C. D.; Liu, Y. J.; Wang, L.; Sun, H.; Zhang, L. C. Laves phase precipitation in Ti–Zr–Fe–Cr alloys with high strength and large plasticity. *Mater. Des.* **2018**, *154*, 228–238.
- (54) Jawed, S. F.; Rabadia, C. D.; Liu, Y. J.; Wang, L. Q.; Li, Y. H.; Zhang, X. H.; Zhang, L. C. Beta-type Ti–Nb–Zr–Cr alloys with large plasticity and significant strain hardening. *Mater. Des.* **2019**, *181*, 108064.
- (55) Rao, M. N.; Manivasagam, G. Mechanical Behaviour of Beta Titanium Alloys. *Mater. Sci. Forum* **2021**, *1016*, 964–970.
- (56) Kolli, R. P.; Joost, W. J.; Ankem, S. Phase Stability and Stress-Induced Transformations in Beta Titanium Alloys. *JOM* **2015**, *67* (6), 1273–1280.
- (57) Wang, C. H.; Russell, A. M.; Cao, G. H. A semi-empirical approach to the prediction of deformation behaviors of  $\beta$ -Ti alloys. *Scr. Mater.* **2019**, *158*, 62–65.
- (58) Abdel-Hady, M.; Hinoshita, K.; Morinaga, M. General approach to phase stability and elastic properties of  $\beta$ -type Ti-alloys using electronic parameters. *Scr. Mater.* **2006**, *55* (5), 477–480.
- (59) Morinaga, M.; Kato, M.; Kamimura, T.; Fukumoto, M.; Harada, I.; Kubo, K. Theoretical Design of  $\beta$ -type Titanium alloys. In *Titanium '92, science and technology: proceedings of the Seventh International Conference on Titanium*, San Diego, California, USA, June 29–July 2, 1992; Froes, F. H., Caplan, I. L., Eds.; Metallurgical Society of AIME: Warrendale, PA, USA, 1992; pp 276–283.
- (60) Sadeghpour, S.; Abbasi, S.; Morakabati, M.; Kisko, A.; Karjalainen, L.; Porter, D. On the compressive deformation behavior of new beta titanium alloys designed by d-electron method. *J. Alloys Compd.* **2018**, *746*, 206–217.
- (61) Sun, F.; Zhang, J. Y.; Marteleur, M.; Brozek, C.; Rauch, E. F.; Veron, M.; Vermaut, P.; Jacques, P. J.; Prima, F. A new titanium alloy with a combination of high strength, high strain hardening and improved ductility. *Scr. Mater.* **2015**, *94*, 17–20.
- (62) Rabadia, C. D.; Jawed, S. F.; Wang, J.; Siddhpura, M.; Siddhpura, A. Revised Semiempirical Approach to Predict the Occurrence of Twinning in Titanium Alloys. *ACS Omega* **2021**, *6*, 34056.
- (63) Wang, Q.; Han, C.; Choma, T.; Wei, Q.; Yan, C.; Song, B.; Shi, Y. Effect of Nb content on microstructure, property and in vitro apatite-forming capability of Ti–Nb alloys fabricated via selective laser melting. *Mater. Des.* **2017**, *126*, 268–277.
- (64) Jiang, B.; Wang, Q.; Wen, D.; Xu, F.; Chen, G.; Dong, C.; Sun, L.; Liaw, P. K. Effects of Nb and Zr on structural stabilities of Ti–Mo–Sn-based alloys with low modulus. *Mater. Sci. Eng., A* **2017**, *687*, 1–7.
- (65) Jawed, S. F.; Rabadia, C. D.; Azim, F.; Khan, S. J. Effect of Nb on  $\beta\alpha'$  Martensitic Phase Transformation and Characterization of New Biomedical Ti–xNb–3Fe–9Zr Alloys. *Scanning* **2021**, *2021*, 8173425.
- (66) Umbelino dos Santos, L.; Campo, K. N.; Caram, R.; Najjar Lopes, É. S. Oxygen addition in biomedical Ti–Nb alloys with low Nb contents: Effect on the microstructure and mechanical properties. *Mater. Sci. Eng. A* **2021**, *823*, 141750.
- (67) Zareidoost, A.; Yousefpour, M. A study on the mechanical properties and corrosion behavior of the new as-cast TZNT alloys for biomedical applications. *Mater. Sci. Eng., C* **2020**, *110*, 110725.
- (68) Torres-Sánchez, C.; Wang, J.; Norrito, M.; Zani, L.; Conway, P. P. Addition of Sn to TiNb alloys to improve mechanical performance and surface properties conducive to enhanced cell activity. *Mater. Sci. Eng. C* **2020**, *115*, 110839.
- (69) Jawed, S. F.; Rabadia, C. D.; Liu, Y. J.; Wang, L. Q.; Qin, P.; Li, Y. H.; Zhang, X. H.; Zhang, L. C. Strengthening mechanism and corrosion resistance of beta-type Ti–Nb–Zr–Mn alloys. *Mater. Sci. Eng. C* **2020**, *110*, 110728.
- (70) Dang, Z.; Zhan, Y. Development and characterization of  $\beta$ -type Ti–Zr–Nb–Sn dental implant materials. *Materialwiss. Werkstofftech.* **2020**, *51* (3), 330–337.
- (71) Chui, P. F.; Jing, R.; Zhang, F. G.; Li, J. H.; Feng, T. Mechanical properties and corrosion behavior of beta-type Ti–Zr–Nb–Mo alloys for biomedical application. *J. Alloys Compd.* **2020**, *842*, 155693.
- (72) Salvador, C. A. F.; Dal Bó, M. R.; Costa, F. H.; Taipina, M. O.; Lopes, E. S. N.; Caram, R. Solute lean Ti–Nb–Fe alloys: An exploratory study. *J. Mech. Behav. Biomed. Mater.* **2017**, *65*, 761–769.
- (73) Lu, J.; Zhao, Y.; Niu, H.; Zhang, Y.; Du, Y.; Zhang, W.; Huo, W. Electrochemical corrosion behavior and elasticity properties of Ti–6Al–xFe alloys for biomedical applications. *Mater. Sci. Eng. C* **2016**, *62*, 36–44.
- (74) Ehtemam-Haghighi, S.; Liu, Y.; Cao, G.; Zhang, L. C. Influence of Nb on the  $\beta\alpha'$  martensitic phase transformation and properties of the newly designed Ti–Fe–Nb alloys. *Mater. Sci. Eng. C* **2016**, *60*, 503–510.
- (75) Biesiekierski, A.; Lin, J.; Li, Y.; Ping, D.; Yamabe-Mitarai, Y.; Wen, C. Investigations into Ti–(Nb,Ta)–Fe alloys for biomedical applications. *Acta Biomater.* **2016**, *32*, 336–347.
- (76) Wang, P.; Wu, L.; Feng, Y.; Bai, J.; Zhang, B.; Song, J.; Guan, S. Microstructure and mechanical properties of a newly developed low Young's modulus Ti–15Zr–5Cr–2Al biomedical alloy. *Mater. Sci. Eng. C* **2017**, *72*, 536–542.
- (77) Lin, J.; Ozan, S.; Li, Y.; Ping, D.; Tong, X.; Li, G.; Wen, C. Novel Ti–Ta–Hf–Zr alloys with promising mechanical properties for prospective stent applications. *Sci. Rep.* **2016**, *6* (1), 37901.
- (78) Biesiekierski, A.; Lin, J.; Li, Y.; Ping, D.; Yamabe-Mitarai, Y.; Wen, C. Impact of ruthenium on mechanical properties, biological response and thermal processing of  $\beta$ -type Ti–Nb–Ru alloys. *Acta Biomater.* **2017**, *48*, 461–467.
- (79) Weng, W.; Biesiekierski, A.; Lin, J.; Ozan, S.; Li, Y.; Wen, C. Impact of the rare earth elements scandium and yttrium on beta-type Ti–24Nb–38Zr–2Mo-base alloys for orthopedic applications. *Materialia* **2020**, *9*, 100586.

- (80) Ozan, S.; Lin, J.; Li, Y.; Wen, C. New Ti-Ta-Zr-Nb alloys with ultrahigh strength for potential orthopedic implant applications. *J. Mech. Behav. Biomed. Mater.* **2017**, *75*, 119–127.
- (81) Li, Z.; Xu, H.; Dong, A.; Qiu, J.; He, L.; Zhang, T.; Du, D.; Xing, H.; Zhu, G.; Wang, D.; Sun, B. Characteristics of Ti-Nb-Mg alloy by powder metallurgy for biomedical applications. *Mater. Charact.* **2021**, *173*, 110953.
- (82) Sjafrizal, T.; Dehghan-Manshadi, A.; Kent, D.; Yan, M.; Dargusch, M. S. Effect of Fe addition on properties of Ti–6Al–xFe manufactured by blended elemental process. *J. Mech. Behav. Biomed. Mater.* **2020**, *102*, 103518.
- (83) Xu, J. L.; Tao, S. C.; Bao, L. Z.; Luo, J. M.; Zheng, Y. F. Effects of Mo contents on the microstructure, properties and cytocompatibility of the microwave sintered porous Ti-Mo alloys. *Mater. Sci. Eng. C* **2019**, *97*, 156–165.
- (84) Wu, J.; Li, H.; Yuan, B.; Gao, Y. High recoverable strain tailoring by Zr adjustment of sintered Ti-13Nb-(0–6) Zr biomedical alloys. *J. Mech. Behav. Biomed. Mater.* **2017**, *75*, 574–580.
- (85) Choi, H.; Shil'ko, S.; Gubicza, J.; Choe, H. Study of the compression and wear-resistance properties of freeze-cast Ti and Ti–5W alloy foams for biomedical applications. *J. Mech. Behav. Biomed. Mater.* **2017**, *72*, 66–73.
- (86) Yolun, A.; Şimşek, M.; Kaya, M.; Annaç, E. E.; Köm, M.; Çakmak, Ö. Fabrication, characterization, and in vivo biocompatibility evaluation of titanium-niobium implants. *Proceedings of the Institution of Mechanical Engineers, Part H: Journal of Engineering in Medicine* **2021**, *235* (1), 99–108.
- (87) Kalita, D.; Rogal, Ł.; Berent, K.; Góral, A.; Dutkiewicz, J. Effect of Mo and Ta on the Mechanical and Superelastic Properties of Ti-Nb Alloys Prepared by Mechanical Alloying and Spark Plasma Sintering. *Mater.* **2021**, *14* (10), 2619.
- (88) Zhang, Y.; Chu, K.; He, S.; Wang, B.; Zhu, W.; Ren, F. Fabrication of high strength, antibacterial and biocompatible Ti-5Mo-5Ag alloy for medical and surgical implant applications. *Mater. Sci. Eng., C* **2020**, *106*, 110165.
- (89) Luo, X.; Yang, C.; Li, R. Y.; Wang, H.; Lu, H. Z.; Song, T.; Ma, H. W.; Li, D. D.; Gebert, A.; Li, Y. Y. Effect of silicon content on the microstructure evolution, mechanical properties, and biocompatibility of  $\beta$ -type TiNbZrTa alloys fabricated by laser powder bed fusion. *Biomater. Adv.* **2021**, 112625.
- (90) Luo, X.; Yang, C.; Fu, Z. Q.; Liu, L. H.; Lu, H. Z.; Ma, H. W.; Wang, Z.; Li, D. D.; Zhang, L. C.; Li, Y. Y. Achieving ultrahigh-strength in beta-type titanium alloy by controlling the melt pool mode in selective laser melting. *Mater. Sci. Eng., A* **2021**, *823*, 141731.
- (91) Li, Y. H.; Yang, C.; Kang, L. M.; Zhao, H. D.; Qu, S. G.; Li, X. Q.; Zhang, W. W.; Li, Y. Y. Non-isothermal and isothermal crystallization kinetics and their effect on microstructure of sintered and crystallized TiNbZrTaSi bulk alloys. *J. Non-Cryst. Solids* **2016**, *432*, 440–452.
- (92) Ehtemam-Haghighi, S.; Liu, Y. J.; Cao, G. H.; Zhang, L. C. Influence of Nb on the  $\beta$   $\alpha$  "martensitic phase transformation and properties of the newly designed Ti–Fe–Nb alloys. *Mater. Sci. Eng., C* **2016**, *60*, 503–510.
- (93) Zou, L. M.; Li, Y. H.; Yang, C.; Qu, S. G.; Li, Y. Y. Effect of Fe content on glass-forming ability and crystallization behavior of a (Ti69.7Nb23.7Zr4.9Ta1.7)100–xFex alloy synthesized by mechanical alloying. *J. Alloys Compd.* **2013**, *553*, 40–47.
- (94) Weng, W.; Biesiekierski, A.; Li, Y.; Wen, C. Effects of selected metallic and interstitial elements on the microstructure and mechanical properties of beta titanium alloys for orthopedic applications. *Materialia* **2019**, *6*, 100323.
- (95) Ehtemam-Haghighi, S.; Prashanth, K.; Attar, H.; Chaubey, A. K.; Cao, G. H.; Zhang, L. C. Evaluation of mechanical and wear properties of Ti<sub>x</sub>Nb<sub>7</sub>Fe alloys designed for biomedical applications. *Mater. Des.* **2016**, *111*, 592–599.
- (96) Bahl, S.; Suwas, S.; Chatterjee, K. Comprehensive review on alloy design, processing, and performance of  $\beta$  Titanium alloys as biomedical materials. *Int. Mater. Rev.* **2021**, *66* (2), 114–139.
- (97) Li, Y. H.; Yang, C.; Wang, F.; Zhao, H. D.; Qu, S. G.; Li, X. Q.; Zhang, W. W.; Li, Y. Y. Biomedical TiNbZrTaSi alloys designed by d-electron alloy design theory. *Mater. Des.* **2015**, *85*, 7–13.
- (98) Rabadia, C. D.; Liu, Y. J.; Zhao, C. H.; Wang, J. C.; Jawed, S. F.; Wang, L. Q.; Chen, L. Y.; Sun, H.; Zhang, L. C. Improved trade-off between strength and plasticity in titanium based metastable beta type Ti-Zr-Fe-Sn alloys. *Mater. Sci. Eng., A* **2019**, *766*, 138340.
- (99) Luo, X.; Liu, L. H.; Yang, C.; Lu, H. Z.; Ma, H. W.; Wang, Z.; Li, D. D.; Zhang, L. C.; Li, Y. Y. Overcoming the strength–ductility trade-off by tailoring grain-boundary metastable Si-containing phase in  $\beta$ -type titanium alloy. *J. Mater. Sci. Technol.* **2021**, *68*, 112–123.
- (100) Luo, X.; Li, D. D.; Yang, C.; Gebert, A.; Lu, H. Z.; Song, T.; Ma, H. W.; Kang, L. M.; Long, Y.; Li, Y. Y. Circumventing the strength–ductility trade-off of  $\beta$ -type titanium alloys by defect engineering during laser powder bed fusion. *Addit. Manuf.* **2022**, *51*, 102640.
- (101) Kaur, M.; Singh, K. Review on titanium and titanium based alloys as biomaterials for orthopaedic applications. *Mater. Sci. Eng., C* **2019**, *102*, 844–862.