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Review

Development of Low Elastic Modulus Titanium Alloys as Implant Biomaterials

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Abstract

Biomaterials have always been the focus of material scientists and engineers. Titanium and its alloys have favorable properties, such as high strength, low density, good corrosion resistance, non-toxicity, low elastic modulus, biocompatibility, etc. Thus, Ti alloys have received much attention from scientists and engineers who work with biomaterials. Among these properties, the elastic modulus is a very important property for implant biomaterials because it avoids the "stress shielding" effect. In this study, we summarized low elastic modulus titanium alloys, which have great application potential for implant biomaterials. The major series of titanium alloys with low elastic modulus, including TiNb-based, TiMo-based, and TiZr-based series of titanium alloys, were discussed. The research status and the possible factors related to the low elastic modulus of these major titanium alloys were analyzed. Finally, the development prospects of the above series of low elastic modulus titanium alloys were compared, and the future direction of low elastic modulus Ti alloys as biomaterials was proposed.

Keywords
Biomaterials; titanium alloys; low elastic modulus

1. Introduction

The development of biomaterial science and engineering is very important for humans to enjoy a long life. Thus, biomaterials have always been the focus of material scientists and engineers and have received much attention. As hard tissue implants, biomaterials should possess high strength, a certain degree of plasticity, should be non-toxic, the elastic modulus should be close to that of the bone, and should have good biocompatibility. Research and clinical applications have shown that Ti and its alloys are the most suitable to be used as hard tissue implant biomaterials [1-3]. Long-term experiments and clinical applications have shown that a mismatch of elastic modulus between implants and surrounding bones causes a "stress shielding" effect [4-6]. The one with a low elastic modulus bears less stress when two materials with different elastic modulus are stressed together. Wolff's law [7] showed that if the bones in the human body are exposed to external pressure for a long time, the density and hardness of the bone can increase. Conversely, bones can undergo osteoporosis and resorption if they are exposed to low stress or are in a stress-free state for a long period. To decrease or avoid such an effect, researchers are committed to developing alloys with a low elastic modulus [8-10]. Ti and its alloys are the most studied and the most promising to be used as hard tissue implant materials. In recent decades, many Ti alloys have been developed, and some have been clinically applied [11, 12]. Interestingly, some porous Ti alloys show a very low elastic modulus (0.05 ~ 5.7 GPa) [13]. Some methods have also been developed to prepare the porous Ti alloys for biomaterials. The methods that are generally used consist of reverse freeze casting [14], dynamic freeze casting [15, 16], HF/HNO_3-treatment [13], powder-based additive manufacturing [17], etc.

This study reviewed the advancements in the application of low elastic modulus Ti alloys as a type of hard tissue implant biomaterial. The major series of low elastic modulus Ti alloys as implant biomaterials, including TiNb-based, TiMo-based, and TiZr-based alloys, were introduced, discussed, and compared. This study might be used as a reference for the development of low modulus metallic biomaterials.

2. Early Low Modulus Titanium Alloys for Biomaterials

In the early stage, stainless steel and Vitallium were used as the major hard tissue implant materials [18]. But The elastic modulus of stainless steel is approximately 200 GPa, and that of Vitallium is close to 220 GPa [1, 19, 20]. The elastic modulus of these alloys is very high compared to that of the bones (10 to 30 GPa) and, thus, might result in a "stress shielding" effect. Among common metals, pure Ti has a low elastic modulus of 110 GPa, and the typical commercial titanium alloy, Ti-6Al-4V (TC4), also has a similar elastic modulus and higher strength. Thus, pure Ti and the TC4 alloy are the major Ti alloys that are used in the early application stage as hard tissue implant biomaterials [11, 21]. Besides these Ti alloys, the Ti-6Al-7Nb [22], Ti-28Nb-7Al [23], and Ti-15Nb-25Zr-8Fe [24] alloys were also developed and can be used as an implanted biomaterial. However, clinical applications have shown that elements Al [25, 26] and V [27-29] have some side effects on the human body. Hence, the toxicity, negative effects, cell activity, and other biocompatibilities of alloying elements are taken seriously [30-32]. Steineman and Kawahar summarized the toxicity and biocompatibility of various metals (see Figure 1) [33, 34]. Besides Ti, elements such as Zr, Nb, Ta, Sn, Pa, Mo, etc., also have favorable biocompatibility and are suitable for being used as alloying elements for bio-Ti alloys.

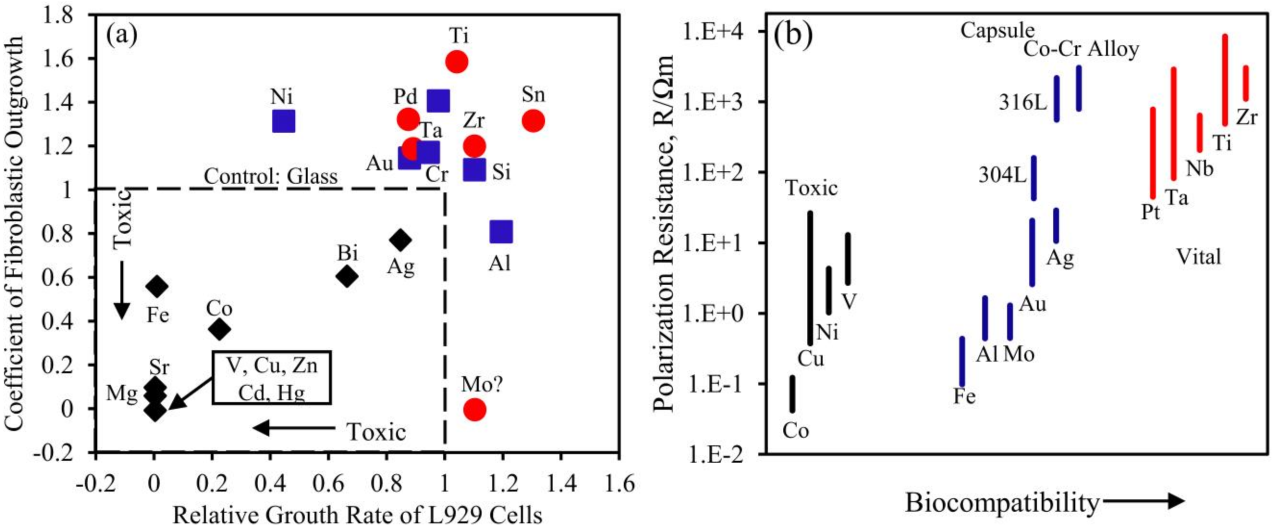

Figure 1 The biocompatibility of common metals and alloys: (a) toxicity and (b) polarization resistance vs. biocompatibility.

3. TiZr-based Low Elastic Modulus Ti Alloys for Biomaterials

Due to toxicity and negative effects, researchers have realized the importance of the development of low elastic modulus Ti alloys with compatible elements. Many studies have suggested that metastable beta Ti alloys should have a low elastic modulus [8, 35, 36]. Nb is a non-toxic and typical beta stabilizer. Thus, Nb is preferred for developing low elastic modulus Ti alloys. Many researchers have investigated low elastic modulus TiNb-based alloys for bio-applications. The main TiNb-based alloys without toxic elements and their elastic modulus are shown in Table 1 [37-41], Table 2 [12, 42-53], and Table 3 [12, 43-45, 50, 54-66] based on the number of components. Based on Table 1, the elastic modulus of bulk Ti-Nb binary alloys like Ti-38Nb, Ti-40Nb, and Ti-45Nb is over 55 GPa. However, that is low to 25 GPa for microporous Ti-35Nb binary alloy and an amazing low value to 2.6 GPa for macroporous Ti-35Nb. The addition of one more alloying element in ternary TiNb-based alloys results in an elastic modulus close to the upper limit of biological bones (~30 GPa). Especially, the elastic modulus of bulk Ti-19Nb-14Zr ternary alloy is as low as 14 GPa, which is similar to that of most bones. According to the strengthening theory, the addition of alloying element can strengthen alloys. Thus, the multi-component TiNb-based alloys could have both low elastic modulus and high strength. As shown in Table 3, the bulk multi-component TiNb-based alloys have elastic modulus close to that of the bones. The elastic modulus of porous Ti-35Nb-2Ta-3Zr alloys is as low as 3.1 GPa. Thus, the TiNb-based alloys can have an elastic modulus similar to that of bones.

These elastic moduli can be adjusted across a wide range of values to meet the different requirements. Overall, the porous TiNb-based alloys can have a lower elastic modulus than the bulk ones. However, the low strength can limit the application of porous alloys as hard tissue implants [67].

Table 1 The major low elastic modulus Ti-Nb binary alloys.

Alloys	E, GPa	Ref.
Ti-45Nb	57	[37]
Ti-38Nb	56.0	[38]
Ti-40Nb	60.0	[39]
Ti-40Nb (Porous)	33	[40]
Ti-35Nb (Microporous)	25.0	[41]
Ti-35Nb (Macroporous)	2.6	[41]

Table 2 The major low elastic modulus TiNb-based ternary alloys.

Alloys	E, GPa	Ref.	Alloys	E, GPa	Ref.
Ti-16.6Nb-10.6Sn	80.0	[43]	Ti-25Nb-25Ta	55.0	[47]
Ti-13Nb-13Zr	80.0	[43]	$Ti_{66}Nb_{26}Mo_8$(at%)	54.5	[48]
Ti-21.1Nb-10.4Sn	75.0	[12]	Ti-38.1Nb-12.1Mo	54.5	[12]
Ti-39.9Nb-3.2Mo	67.0	[12]	Ti-(18-20)Nb-(5-6)Zr	45.0	[49]
Ti-41.1Nb-7.1Zr	65.0	[44]	Ti-35Nb-4Sn	44.0	[50]
Ti-39.3Nb-6.3Mo	63.6	[12]	(Ti-35Nb)-4Sn (rolling)	42.0	[45]
Ti-29Nb-13Ta	62.0	[43]	Ti-33Nb-4Sn	36.0	[51]
(Ti-35Nb)-7Sn (solution)	62.0	[45]	Ti-23Nb-7Zr	35.9	[52]
Ti-25.4Nb-10.1Sn	62.0	[12]	Ti-28Nb-7Zr	29.1	[52]
$Ti_{75}Nb_{20}Sn_5$ (at%)	61.0	[46]	Ti-33Nb-7Zr	29.0	[52]
Ti-30.8Nb-9.8Sn	61.0	[12]	Ti-19Nb-14Zr	14.0	[42]
Ti-38.7Nb-9.2Mo	55.7	[12]	Ti-(18-20)Nb-(5-6)Zr	3.7	[49]
(Ti-35Nb)-4Sn (solution)	55.0	[45]	Ti-Nb-Zr (Porous)	0.1-2.0	[53]

Table 3 The major low elastic modulus TiNb-based multi-component (≥4) alloys.

Alloys	E, GPa	Ref.	Alloys	E, GPa	Ref.
Ti-29Nb-2Mo-6Zr	76.36	[54]	Ti-9.7Nb-9.5Zr-5Mo-6.2Sn	54.0	[58]
Ti-25Nb-2Ta-3Zr	75.2	[12]	Ti-14.6Nb-5.7Zr-9.9Sn-5.5Ta	52.2	[58]
Ti-16.6Nb-4.9Mo -2Sn-9.2Ta	73.0	[57]	Ti-35Nb-2Ta-3Zr	52.0	[12]
Ti-18.5Nb-9.1Zr-4.8Mo-5.9Sn	72.0	[58]	Ti-24Nb-4Zr-7.5Sn	52.0	[56]
Ti-35Nb-5Ta-7Zr-0.4O	66.0	[59]	Ti-29Nb-11Ta-5Zr	50.0	[43]
Ti-29Nb-7Zr-0.7O	65.0	[65]	Ti-29Nb-13Ta-4Mo	50.0	[43]

Ti-29Nb-13Ta-6Sn	65.0	[43]	Ti-20.5Nb-4.5Ta-5.1Zr	50.0	[12]
Ti-25Nb-2Mo-4Sn	65.0	[50]	Ti-29Nb-13Ta-4.6Zr	50.0	[43]
Ti-29Nb-13Ta-4.5Zr	65.0	[55]	Ti-4.9Nb-5Mo -9.5Zr-6.2Sn-	49.0	[57]
Ti-35.3Nb-5.7Ta-7.3Zr-0.25Si	65.0	[60]	Ti-23.2Nb-9.2Zr-5.7Sn	48.7	[50]
Ti-35.3Nb-7.1Zr-5.1Ta	63.0	[44]	Ti-29Nb-13Ta-2Sn	48.0	[43]
Ti-34Nb-2Ta-3Zr-0.5O	63.0	[64]	Ti-24.2Nb-2Ta-5.1Zr	48.0	[12]
Ti-35.3Nb-5.7Ta-7.3Zr	63.0	[60]	Ti-10.2Nb-10Zr-5.3Mo-6.5Sn	48.0	[58]
Ti-35Nb-7Zr-5Ta	63.0	[66]	Ti-32.5Nb-6.8Zr-2.7Sn	47.1	[12]
Ti-29Nb-13Ta-5Zr	60.0	[50]	Ti-16Nb-13Ta-4Mo	47.0	[43]
Ti-9.9Nb-4.9Zr-5.1Mo-6.3Sn	59.0	[58]	Ti-21.2Nb-4.2Zr-5.4Sn-8.2Ta	47.0	[57]
Ti-40Nb-2Ta-3Zr	57.8	[12]	Ti-29Nb-13Ta-2Sn	46.0	[50]
Ti-30Nb-2Ta-3Zr	57.1	[12]	Ti-13.5Nb-2.8Mo -4.4Zr-8Sn-	46.0	[57]
Ti-35Nb-5.7Ta-7.2Zr	57.0	[50]	Ti-31Nb-6Zr-5Mo	44.0	[62]
Ti-14.2Nb-9.3Zr-4.9Mo-6Sn	56.0	[58]	Ti-29Nb-6Ta-5Zr	43.0	[50]
Ti-17.4Nb-8.1Ta-3.4Zr	55.3	[12]	Ti-11.6Nb-11.4Zr-12.0Sn	42.4	[45]
Ti-29Nb-13Ta-7.1Zr	55.0	[50]	Ti-24Nb-4Zr-8Sn	42	[12]
Ti-35Nb-7Zr-5Ta	55.0	[12]	Ti-35Nb-7Zr-5Ta-0.35O	41	[63]
Ti-15.2Nb-5Zr-5.3Mo-6.5Sn	55.0	[58]	Ti-24Nb-4Zr-7.9Sn	33.0	[50]
Ti-29Nb-13Ta-4.6Sn	54.0	[43]	Ti-35Nb-2Ta-3Zr (Porous)	3.1	[61]

4. Major Low Elastic Modulus TiMo-based Alloys for Biomaterials

Besides Nb, Mo is another major alloying element to produce low elastic modulus Ti alloys for implant biomaterials. Mo is a typical beta stabilizer for Ti alloys. Many researchers have used the Mo equivalent to design and develop various Ti alloys containing low modulus Ti alloys for different purposes [68, 69]. The major low elastic modulus of TiMo-based alloys and their modulus are listed in Table 4 [43, 50, 55, 70-81]. The effect of Mo on biocompatibility and cell activity is controversial (Figure 1). Thus, the number of developed low elastic modulus TiMo-based alloys is considerably lesser than that of TiNb-based alloys. The elastic modulus of bulk Ti-Mo binary alloys is higher than 50 GPa, and the lowest modulus of reported bulk Ti-Mo binary alloys is 55 GPa, as shown in Table 4. Like TiNb-based alloys, the porous TiMo-based alloys also have a very low elastic modulus. The porous Ti-10Mo alloy has a very low modulus of 6.4 GPa, which is lower than that of most bones (4~30). The elastic modulus of TiMo-based alloys also can be regulated and decreased by adding other alloying elements, such as Nb, Zr, Si, Sn, etc. A series of Ti-Mo-Si-Zr alloys have an elastic modulus near the upper limit of biological bones (30 GPa). The lowest elastic modulus of the reported Ti-10Mo-1.25Si-4Zr alloy is 23.1 GPa. Compared to the composition of TiNb-based and TiMo-based alloys, the addition of Mo in low elastic modulus TiMo-based alloys is mostly below 15 wt.%, but the Nb content in low elastic modulus TiNb-based alloys can reach up to 40 wt.%. Previous studies [8, 35, 36] have shown that metastable beta Ti alloys have the lowest elastic modulus. The coefficient of Nb in the Mo equivalent formula is only 0.28 [12]. This indicates that the stabilization effect of 1 wt.% Mo to beta Ti phase is equivalent to approximately 3.5 wt.% Nb. Thus, the required Mo content is lesser than that of Nb.

Table 4 The low elastic modulus TiMo-based alloys.

Alloys	E, GPa	Ref.	Alloys	E, GPa	Ref.
Ti-12Mo-8Nb	103.0	[74]	Ti-11.1Mo-10.8Nb	56.9	[73]
Ti-6Mo-6Nb-12Sn	88.0	[71]	Ti-7.5Mo	55.0	[75]
Ti-3.2Mo	83.8	[76]	Ti-8Mo-4Nb-5Zr	52.0	[71]
Ti-8Mo	83.0	[76]	Ti-9Mo	38	[81]
Ti-15Mo-2.8Nb-0.2Si-0.26O	80.0	[43]	Ti-5.5Mo-8Al-6Zr (mol.%, 98% rolled)	36	[80]
Ti-12Mo-5Ta	74.0	[50]	Ti-8Mo-4Nb-2Zr	35.0	[71]
Ti-8Mo-6Nb-4Zr	72.0	[71]	Ti-10Mo-1.25Si-13Zr	32.6	[77]
Ti-15Mo	71.0	[55]	Ti-10Mo-1.25Si-7Zr	29.5	[77]
Ti-9.2Mo-26.7Nb	71.0	[73]	Ti-10Mo-1.25Si-10Zr	28.4	[77]
Ti-15.05Mo	70.0	[70]	Ti-10Mo-1.25Si-4Zr	23.1	[77]
Ti-8Mo-5Nb-3Zr	69.0	[71]	Ti-10Mo-5Fe (Porous)	16	[79]
Ti-12Mo-5Zr	64.0	[72]	Ti-10Mo (Porous)	6.4	[78]
Ti-10.2Mo-19.5Nb	63.0	[73]			

5. TiZr-based Low Modulus Ti Alloys for Biomaterials

The elements Zr and Ti belong to the same group in the periodic table. Hence, they have similar physical and chemical properties. Some researchers have studied the effects of Zr addition on the phase transformation, microstructure, and properties of Ti and its alloys and developed some TiZr-based alloys with high strength and toughness [82-85]. As a neutral element of Ti and its alloys, the addition of Zr has a weak stabilizing effect on the beta phase of Ti and its alloys. However, when the content of Zr exceeds 10%, it has a stabilizing effect on the beta phase of Ti alloys [86]. Zr is also an alloying element with good biocompatibility. Therefore, many researchers have studied TiZr-based biomedical alloys, and many alloys with a low elastic modulus have been obtained from this series of elements, as presented in Table 5 [50, 57, 87-102]. When only a small amount of the alloying elements is added, the elastic modulus of TiZr-based alloys does not decrease much. For example, the elastic modulus of Ti-6Zr-*x*Fe (*x* = 4 to 7) alloys exceeds 90 GPa. With an increase in the content of the alloying element, the elastic modulus of TiZr-based alloys decreases gradually. The Ti-30Zr-5Al-3V alloy has the lowest elastic modulus of 34 GPa of the reported bulk TiZr-based alloys. Similarly, when a TiZr-based alloy is prepared in a porous material, its elastic modulus can be reduced to 5 GPa. Therefore, the elastic modulus of this series of alloys can also be close to that of the bone. Thus, TiZr-based alloys have a great potential for being used as implant biomaterials.

Table 5 The major low elastic modulus TiZr-based alloys.

Alloys	E, GPa	Ref.	Alloys	E, GPa	Ref.
Ti-6Zr-7Fe	94	[87]	Ti-30Zr-5Cr	66.6	[88]
Ti-6Zr-5Fe	93	[87]	Ti-30Zr-2Cr-4Mo	64.2	[88]
Ti-6Zr-6Fe	93	[87]	Ti-30Zr-6Mo	60	[89]
Ti-6Zr-4Fe	90	[87]	Ti-15Zr-5Cr-2Al	58	[92]
Ti-15Zr	82	[90]	Ti-12Zr -5.3Mo-8.1Nb-6.5Sn	58	[57]
Ti-15Zr-10Cr	78	[91]	Ti-5.3Mo-5.1Nb-15Zr-6.5Sn	56	[57]

Ti-18.7Zr-9.6Nb-9.8Sn	77.2	[57]	TiZrNb	52	[94]
$Ti_{34}Zr_{52}Nb_{14}$	76.5	[93]	Ti-10Zr-5Ta-5Nb	51.97	[50]
Ti-13Zr-13Nb-13Ag	75	[95]	Ti-50Zr-5Al-4V	45	[98]
Ti-16.1Zr-15.3Nb-6.1Sn	72	[96]	Ti-12Zr-12Nb-12Sn	42	[96]
Ti-30Zr-4Cr	69.4	[88]	Ti-18Zr-5Nb-3Sn-2.5Mo	40	[99]
Ti-30Zr-1Cr-5Mo	69.1	[88]	Ti-38Zr-11Nb	38.8	[100]
Ti-11.6Zr-5.7Nb-11.8Sn-5.3Mo	68.8	[96]	Ti-30Zr-5Al-3V	34	[101]
Ti-30Zr-3Cr-3Mo	68.5	[88]	Ti-13Zr-13Ta-3Nb (Porous)	5	[102]
Ti-30Zr-34Nb	67.9	[97]			

Besides the above TiNb-based, TiMo-based, and TiZr-based titanium alloys, some other Ti-based alloys with a low elastic modulus have also been developed through composition design and process adjustment, such as the TiCr-based series [103-105], the TiFe-based series [106-108], the TiCu-based series [109, 110], etc. However, these alloys contain some alloying elements with toxic and negative effects. Therefore, they are not used as implanted biomaterials and are not described here.

By comparing the abovementioned series of Ti alloys with a low elastic modulus, it is evident that although all three series of Ti alloys have a very low elastic modulus showing a great application potential as implant biomaterials, the TiNb-based alloy series is the most preferred. Furthermore, the elastic modulus of all Ti alloys can be decreased dramatically to even lower than the elastic modulus of bones by producing them in porous materials using special methods like additive manufacturing [111], electron beam melting [112], and selective laser melting [113]. The properties of porous Ti alloys, including elastic modulus, are affected by parameters of pores [114] such as size, porosity, shape, etc.

6. Summary and Future

This study summarized low elastic modulus titanium with great application potential as implant biomaterials. The study mainly introduced the major series of titanium alloys with a low elastic modulus, including the TiNb-based, TiMo-based, and TiZr-based series of titanium alloys. The research status and possible factors of the low elastic modulus of these major titanium alloys were analyzed. Finally, the development prospects of the abovementioned series of low elastic modulus titanium alloys were compared. Several low elastic modulus titanium alloys have been developed to be used as implant biomaterials. However, most of these studies are still in the experimental stage. Thus, practical clinical applications need time. The development of low elastic modulus titanium alloys should mainly focus on the promotion of the clinical application of some titanium alloys with a low elastic modulus and stable performance. Especially, some advanced methods, such as additive manufacturing, electron beam melting, and selective laser melting, need to be developed for optimizing the properties and promoting the application of porous Ti alloys with a favorable low elastic modulus.

Author Contributions

Kai-Yang Liu: Writing - Original Draft, Visualization; Li-Xia Yin: Data Curation, Project Administration; Xu Lin: Check and modify the revised manuscript; Shun-Xing Liang: Funding Acquisition, Conceptualization, Writing - Review & Editing.

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Competing Interests

The authors have declared that no competing interests exist.

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