

## Review

# The Role of Bioinorganics in Improving the Mechanical Properties of Silicate Ceramics as Bone Regenerative Materials

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received October 9, 2014; received in revised form January 4, 2015; accepted January 23, 2015

## Abstract

One of the important parameters in bone regeneration is the mechanical properties. The calcium-silicate-based ceramics (Ca-Si) have shown great potential as orthopedic biomaterials, however, they are brittle. The addition of trace elements such as magnesium ( $Mg^{2+}$ ) or zinc ( $Zn^{2+}$ ) to the silicate biomaterials has been used to overcome this complication. In this review paper, we investigate the effects of adding different trace elements to improve the mechanical properties of silicate-based ceramics as bone regenerative materials.

*Keywords:* Calcium silicate, mechanical properties, trace element, bone regeneration

## I. Introduction

The demand for synthetic materials to replace and repair damaged bone tissue has increased considerably over the past ten years<sup>1</sup>. Based on the load-sharing principle, the development of synthetic bone grafts with adequate mechanical strength for bone regeneration applications is required<sup>2</sup> since mechanical properties play an important role in the clinical success of bone tissue ingrowth and vascularization<sup>3-7</sup>. This development is mostly aimed at increasing the strain to failure and decreasing the elastic modulus<sup>8</sup>. The currently used synthetic materials to repair bone damage show limited mechanical strength and stress shielding effects<sup>9,10</sup>. Some dense bioceramics are able to offer sufficient mechanical properties for load-bearing applications<sup>2,11</sup>.

Traditional ceramics such as beta-tricalcium phosphate ( $\beta$ -TCP) and hydroxyapatite (HA) do not provide mechano-compatibility with bone tissue owing to their low mechanical properties, especially their fracture toughness. As a result, they can only be used in non- or low-load-bearing applications<sup>12-14</sup>. For example, porous  $\beta$ -TCP has low compressive strength<sup>15,16</sup>. Also, the bonding strength of bioactive glass (BG) is lower than that of dense bone<sup>17</sup>. Thus, owing to the low mechanical properties of conventional ceramics and glasses, the design of bone regenerative materials with high mechanical strength is essential for bone tissue engineering purposes and is expected to improve clinical outcomes.

$CaSiO_3$  (Ca-Si) has shown great potential in bone regeneration. Some calcium silicate ceramics have shown

bending strength comparable to that of human cortical bone<sup>18</sup>, which is higher than the bending strength of HA ceramics<sup>19</sup>. However, one of the main drawbacks of Ca-Si based ceramics and scaffolds are the lack of sufficient mechanical strength, which compromises their osseointegration ability<sup>20</sup>. These materials are brittle and possess low mechanical strength, which limits their load-bearing applications. Therefore, improving the mechanical properties of these ceramics is important prior to using them in clinical applications<sup>21</sup>.

The incorporation of trace elements (bioinorganics) into the calcium silicate structure is of great importance to improve its orthopedic application. The trace elements such as magnesium ( $Mg^{2+}$ ), zinc ( $Zn^{2+}$ ), titanium ( $Ti^{4+}$ ) and zirconium ( $Zr^{4+}$ ) have been incorporated in the Ca-Si structure<sup>22,23</sup>. In a previous study, the effects of adding trace element to Ca-Si on their biological properties have been reported<sup>24</sup>. However, the investigation of their mechanical strength for load-bearing applications is also of great importance, which is the object of this review.

## II. Mechanical Strength of Silicate Bioceramics

The mechanical properties of bioactive materials have a significant effect on their osteogenesis. It was found that the mechanical strength of some bulk Ca-Si ceramics, mainly their fracture toughness, is considerably higher than that of HA ceramics (see Table 1). Most of the bulk silicate ceramics exhibit a similar bending strength and elastic modulus to human cortical bone<sup>25</sup>. Brittleness is the disadvantage of Ca-Si ceramics<sup>19,25-28</sup>.

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**Table 1:** The mechanical properties of trace-elements-incorporated CS-based ceramics.

Bioceramic	Bending strength (MPa)	Fracture toughness (MPa <sup>m</sup> <sup>1/2</sup> )	Young's modulus (GPa)	References
Cortical bone	50–150	2–12	7–30	57
Cancellous bone	10–20	-	0.2–0.5	80
Hydroxyapatite	115–200 110 107.3 115–120 107.3 ± 4.3 80–89.07	0.6–1 1.1 0.86 1.0 0.86 ± 0.12 0.75–1.0	80–120 47 67 80–110 67 ± 3	44,54,57,63,64,72,73
CaSiO <sub>3</sub>	95	<1.0	-	19,20
Bredigite	156 ± 6	1.57 ± 0.12	43.00 ± 4.53	57
Diopside	300	3.5	170	54
Akermanite	176.2 ± 9.8 141.8 ± 2.3	1.83 ± 0.10 1.53 ± 0.10	42.0 ± 5.4 56.2 ± 5.4	36,50
Monticellite	163.9 ± 3.6 159.7	1.65 ± 0.12 1.63	45.5 ± 4.1 51	50,71
Merwinite	128.4 ± 4.7 151.2 ± 5.7	1.57 ± 0.17 1.72 ± 0.11	49.3 ± 2.3 31 ± 2	44,50
Hardystonite	136.4	1.24	37	34
Strontium hardystonite	53	-	27	74

The mechanical property of Ca-Si is not adequate for load-bearing applications<sup>19</sup>. Pressureless Ca-Si ceramics possess low fracture toughness. The reason is that Ca-Si ceramics are difficult to sinter fully and their have low density affecting their mechanical strength. In other words, they cannot be simply sintered so there are micro-pores in pore walls that impair their mechanical properties<sup>28</sup>.

To overcome this problem, spark plasma sintering (SPS) has been suggested. The SPS-sintered silicate bioceramics such as CaSiO<sub>3</sub> and dicalcium silicate (Ca<sub>2</sub>SiO<sub>4</sub>) showed significantly improved mechanical properties compared to pressureless-sintered silicate ceramics<sup>29</sup>. It should be noted that at load-bearing sites, the strength of SPS-sintered CaSiO<sub>3</sub> reached the lowest limits of the strength of human bone. Furthermore, these SPS-sintered silicate ceramics possess a bending strength higher than that of human cortical bone, their fracture toughness being comparable to human cortical bone<sup>30</sup>.

Silicate biomaterials possess high melting points, and therefore their synthesis with enhanced mechanical properties is fairly difficult<sup>31</sup>, which restrict their possible implant applications<sup>28</sup>. The porogen method has been used to prepare Ca-Si scaffold. It was revealed that high compressive strength is obtained owing to the low porosity and pore interconnectivity. However, scaffolds prepared with the polyurethane-foam templating method showed comparatively low compressive strength. The compressive strength of 3D-plotted wollastonite scaffolds is 10 times that of polyurethane-foam-templated Ca-Si scaffolds<sup>32</sup>.

### III. The Effects of Trace Elements on the Mechanical Properties of Ca-Si Bioceramics

#### (1) *The mechanism of improving mechanical properties with trace elements*

There are several important factors that have an influence on the mechanical properties of ceramics including chemical composition, relative density, average crystal size, densification and the sintering time<sup>33,34</sup>, which in turn affects their osteogenesis<sup>35–37</sup>. The crystal structure also affects the mechanical properties of ceramics<sup>38,39</sup>, which in turn affect their osseointegration ability and mechanical strength<sup>25–28,40</sup>. The incorporation of elements into the biomaterial, since this changes their crystal structures<sup>41</sup>, improves their mechanical properties<sup>42,43</sup>. The addition of magnesium and zinc to the CaO-SiO<sub>2</sub> ceramics improves their mechanical properties<sup>21,44</sup>. Zinc can be used as reinforcement in calcium silicate ceramic structures; here a new crystal phase is formed as a result of a reaction with calcium, silicone and oxygen<sup>34</sup>. Strontium can be substituted with calcium, which occupies more spaces in the lattice, impeding the movement other ions owing to the atomic radius of strontium being larger than that of calcium<sup>45,46</sup>. When zinc and strontium are incorporated in the structure, increased loading may help charge compensation of zinc in the network to form a stable zinc/strontium tetrahedron<sup>47</sup>.

The mechanism by which the addition of trace elements might control the mechanical properties of silicate biomaterials is described as follows. It is suggested that when the trace elements (MgO, ZnO, SrO) are introduced, the movement of calcium atoms in the structure are inhibit-

ed and the structure is made more stable. Also, the bond energy of X-O (in which X= Mg<sup>2+</sup>, Zn<sup>2+</sup>) is higher than that of Ca-O bond, which also leads to the formation of a stable structure. It is observed that the higher stability of the structure may affect the mechanical properties<sup>48,49</sup>. Thus, it seems that introducing different kinds of trace elements into CaSiO<sub>3</sub> ceramics can result in complicated structures and various bond strengths between ions<sup>40</sup>. For instance, when the amounts of magnesium oxide (MgO) are decreased, the mechanical strength of akermanite is decreased and the mechanical properties of the calcium silicate ceramics enhanced from merwinite to akermanite and monticellite<sup>50</sup>.

## (2) Effect of trace elements (Mg,Zn,Sr) on the mechanical properties of silicate ceramics

By incorporating trace elements such as zinc, magnesium and strontium into the CaO-SiO<sub>2</sub> system (that has a triclinic crystal structure<sup>51</sup>), a series of materials with broad chemical composition and crystal structure are obtained including bredigite (Ca<sub>7</sub>MgSi<sub>4</sub>O<sub>16</sub>) with an orthorhombic<sup>52,53,54</sup>, diopside (CaMgSi<sub>2</sub>O<sub>6</sub>) with a monoclinic<sup>54,55</sup>, akermanite (Ca<sub>2</sub>MgSi<sub>2</sub>O<sub>7</sub>) with a tetragonal structure<sup>56</sup>, monticellite (CaMgSiO<sub>4</sub>) with a trimetric structure<sup>50</sup>, hardystonite (Ca<sub>2</sub>ZnSi<sub>2</sub>O<sub>7</sub>) with a tetragonal structure<sup>40</sup> and strontium-hardystonite (Sr-CaO-ZnO-SiO<sub>2</sub>) (see Table 2).

**Table 2:** The different types of trace-elements-incorporated CS-based ceramics.

Bioceramic	Crystal structure	Chemical formulation	References
Bredigite	Orthorhombic	Ca <sub>7</sub> MgSi <sub>4</sub> O <sub>16</sub>	52, 55
Diopside	Monoclinic	CaMgSi <sub>2</sub> O <sub>6</sub>	54,55
Akermanite	Tetragonal	Ca <sub>2</sub> MgSi <sub>2</sub> O <sub>7</sub>	56
Monticellite	Trimetric	CaMgSiO <sub>4</sub>	50
Hardystonite	Tetragonal	Ca <sub>2</sub> ZnSi <sub>2</sub> O <sub>7</sub>	40

Not many reports are focused on the sintering and mechanical properties of bredigite ceramics for biomedical applications. Bredigite showed improved fracture toughness, bending strength and Young's modulus<sup>57</sup>, which is close to that of cortical bone<sup>57-59</sup> and higher than that of HA<sup>60,61</sup>. A significant decrease in the Young's modulus of bredigite was found compared to sintered HA. This low Young's modulus of bredigite also leads to better matching with tissue compared to HA<sup>58</sup>. The polymer sponger method was used to prepare porous bredigite scaffolds with a biomimetic apatite layer (BTAP)<sup>55</sup>. The results showed that although the mechanical strength of BTAP scaffold is lower than that of pure a bredigite scaffold, it was still higher than that of observed for  $\beta$ -TCP scaffolds prepared with the same method.

Diopside showed improved mechanical properties compared to HA and CaSiO<sub>3</sub><sup>62</sup> which are relatively higher than that of HA<sup>54,63,64</sup>. It was revealed that diopside is unlikely to fracture and is more durable or long-standing compared to HA, which improves mechanical stabil-

ity<sup>54,65</sup> owing to the significantly different composition compared to traditional bioceramics and their various sintering properties<sup>49</sup>. It is well known that porosity has an important influence on the mechanical properties of the scaffolds (see Table 3). The diopside scaffold with a porosity of 75–80 %, showed higher compressive strength<sup>66</sup> compared to that of porous HA with 69–86 % porosity<sup>13</sup>, 45S5 bioglass with 82–89 %<sup>12</sup> and porous CaSiO<sub>3</sub> with 81 % porosity<sup>28</sup>. The compressive strength of diopside scaffold is decreased with an increase in the porosity. The results indicated the stable mechanical properties of diopside scaffold, which is in the range of spongy (cancellous) bone<sup>66</sup>. Mechanical stability is a key parameter of bioactive scaffolds in order to maintain sufficient mechanical strength during their degradation. After being soaked in simulated body fluids (SBF) solution for 14 days, the compressive strength of diopside scaffold decreased 30 % compared with 54 % and 60 % of bioglass and CaSiO<sub>3</sub>.

Akermanite possesses improved mechanical properties in comparison to HA<sup>56,67,68</sup>. The mechanical properties of akermanite showed that its bending strength and Young's modulus are close to that of cortical bone<sup>36</sup>, but it possessed lower fracture toughness than that of cortical bone<sup>69</sup>. It was observed that the bending strength and fracture toughness of akermanite is considerably lower than those of diopside ceramic. It is suggested that akermanite ceramic was not completely sintered, to some extent has an influence on their mechanical properties, which indicates the effect of densification on the mechanical properties. Thus, it is proposed that it is possible to enhance the mechanical properties by means of different consolidation and sintering techniques. Based on some previous studies, densification has influence on the mechanical strengths of the sintered glass-ceramics<sup>41,70</sup>. The polymer sponge method was used to prepare porous akermanite scaffolds. It was reported that the porosity of the scaffolds could be controlled and the compressive strength of the scaffold varies with changes in porosity, which shows the effect of porosity on the mechanical properties of scaffolds<sup>68</sup>.

Monticellite showed that the fracture toughness improved as well as a significant decrease in Young's modulus in comparison with sintered HA. However, the bending strength of monticellite was similar to that of HA<sup>71</sup>. It was observed that the monticellite may be unlikely to fracture and its fracture toughness was closer to that of cortical bone<sup>69</sup>. According to previous studies, monticellite and merwinite ceramics showed mechanical properties comparable to akermanite and bredigite<sup>26,28</sup>. However, monticellite exhibits mechanical properties that are higher than that of akermanite and merwinite<sup>50</sup>. It was shown that different mechanical properties between monticellite, akermanite and merwinite might be attributed to their different chemical composition and their average crystal size and relative density did not considerably change.

Merwinite bioceramic showed mechanical properties compared to sintered HA in that bending strength was high, fracture toughness improved and Young's modulus decreased<sup>44</sup>. Also, the mechanical properties of merwinite were close to that of cortical bone<sup>69</sup>.

**Table 3:** The mechanical properties of trace-elements-incorporated CS-based scaffolds.

Bioceramic	Porosity (%)	Compressive strength (MPa)	References
Cancellous bone	70–90	0.2–4.0	75
Hydroxyapatite	69–86	0.03–0.29	13
$\beta$ -TCP	-	$0.05 \pm 0.02$	55
45S5 Bioglass	82–89 84–89	0.42–0.6 0.42–0.6	12,28
$\text{CaSiO}_3$	90 81 81	$0.03 \pm 0.007$ 0.33 $0.32 \pm 0.11$	12,22,28
Bredigite	-	$0.233 \pm 0.014$	55
Bredigite with biomimetic apatite layer	90	$0.101 \pm 0.008$	55
Diopside	75–80	0.63–1.36	66
Porous akermanite	63.5–90.3	0.53–1.35	68
Hardystonite	87 78	$0.06 \pm 0.008$ $1.99 \pm 0.45$	22,75
$\text{CaSiO}_3$ -hardystonite	89	$0.12 \pm 0.02$	22
Strontium hardystonite	78	$2.16 \pm 0.52$	75
Strontium-hardystonite-gahnite	85 85	0.8–4.1 $4.1 \pm 3$	76,79

Hardystonite showed enhanced mechanical properties<sup>34</sup>, which is higher than that of HA<sup>72,73</sup>. The  $\text{CaSiO}_3$  scaffold with a porosity of nearly 90 % has shown lower compressive strength than that of previously reported value for  $\text{CaSiO}_3$  scaffold with a porosity of almost 80 %<sup>28</sup>. Also, the compressive strength of hardystonite scaffold was greater than that of the  $\text{CaSiO}_3$  scaffold. With the incorporation of hardystonite into the  $\text{CaSiO}_3$  scaffold, the composite scaffold showed a higher compressive strength, which is nearly four times and double that of  $\text{CaSiO}_3$  and double that of hardystonite scaffolds<sup>22</sup>.

In another study, strontium was incorporated into the hardystonite structure to prepare  $(\text{Sr}_2\text{ZnSi}_2\text{O}_7)$ <sup>74</sup> ceramics. It was found that the bending strength and Young's modulus of strontium-hardystonite reached almost that of cortical bone<sup>60</sup>. With an increase in the sintering time, the bending strength and Young's modulus can be improved, indicating that this ceramic is not sufficiently strong to be used in load-bearing applications.

With the incorporation of strontium and zinc, the compressive strength of porous hardystonite and strontium-hardystonite scaffolds with the porosity of nearly 78 %<sup>75</sup> were higher than that of  $\text{CaSiO}_3$ , HA scaffolds<sup>12,13,28</sup>.

Aluminum oxide ( $\text{Al}_2\text{O}_3$ ) was incorporated into the strontium hardystonite to design a  $(\text{Sr}_2\text{ZnSi}_2\text{O}_7\text{-gahnite})$  scaffold to be used under load. The highly porous strontium-hardystonite-gahnite scaffolds with a porosity of 85 % exhibited compressive strength comparable to that of cancellous bone, which is a mechanically strong and highly porous for load-bearing applications<sup>76</sup>. These scaffolds showed a compressive strength comparable to can-

cellous bone. A highly porous strontium-hardystonite-gahnite with a porosity of 85 % revealed a compressive strength comparable to that of cancellous bone<sup>77</sup> and higher than that of other glass, glass-ceramic, crystalline ceramic, polymer and polymer-ceramic composite scaffolds<sup>77,78</sup>. However, with an increase in the porosity to 95 %, the compressive strength decreased<sup>79</sup>.

As it can be seen, although the bending strength of  $\text{CaSiO}_3$  ceramic is near to that of cortical bone, it possesses low fracture toughness of nearly  $1 \text{ MPa}\cdot\text{m}^{1/2} (< 1.0)$ <sup>19,20</sup>, which compromises its mechanical strength. With the incorporation of trace elements into  $\text{CaSiO}_3$  structure, the fracture toughness of trace-element-incorporated Ca-Si-based ceramics is improved compared with both HA and  $\text{CaSiO}_3$  ceramics. In terms of bending strength, the presence of trace elements increased the bending strength of bredigite, diopside, akermanite, monticellite, merwinite and diopside compared to HA and  $\text{CaSiO}_3$ , indicating they are durable and fracture improbable. However, the incorporation of strontium into the hardystonite structure decreased the bending strength, which indicates that it is not a strong bioceramic. In addition, the Young's modulus of bredigite, akermanite, monticellite, merwinite, and strontium hardystonite decreased to be closer to that of cortical bone. Nevertheless, diopside showed a Young's modulus of 170 GPa, which is significantly higher than that of cortical bone. It may be suggested that diopside is likely to induce bone resorption, but further investigations are needed. The trace-element-incorporated Ca-Si-based scaffolds showed improved compressive strength compared with  $\text{CaSiO}_3$  and HA, which was close to that of



spongy bone. Collectively, the mechanical strength of Ca-Si-based ceramics and scaffolds is considerably improved with the incorporation of trace elements into their structure.

#### IV. Conclusions

Although Ca-Si-based ceramics possess bioactivity and osteoconductivity, their mechanical properties remain far from optimal for bone regeneration. The incorporation of trace elements is a promising approach to improve their mechanical properties for bone repair applications. When different trace elements are incorporated into  $\text{CaSiO}_3$  ceramics, complex structures and various bond strengths between ions are formed. In addition, the presence of trace elements forms various crystal structures, and makes the structures more stable. Thus the mechanical properties are improved to some extent, which is required for bone tissue regeneration. However, more and detailed studies, especially *in vivo*, are needed in order to develop materials with optimum mechanical strength.

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