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Magnesium-containing bioactive polycrystalline silicate-based ceramics and glass-ceramics for biomedical applications

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ABSTRACT

With improvement of orthopaedic technologies for bone replacement and regeneration, there is an increasing need for materials with superior properties. Mg-containing silicate ceramics and glass-ceramics have been shown to be bioactive and exhibit various advantages for biomedical applications. This review paper is intended to summarize and discuss the most relevant studies carried out in the field of Mg-containing bioactive silicate ceramics and glass-ceramics.

1. Introduction

Degenerative and inflammatory conditions of bone, teeth and joints are typical causes of chronic disability, while the number of people suffering from musculoskeletal conditions has increased by 25% over the past decade [1]. These problems affect several hundred millions of people worldwide, and a sharp increase of this figure is expected due to the predicted doubling in the number of people over 50 years old by the year 2020 [2,3]. Affordable measures to treat musculoskeletal conditions are continuously required, with both replacement and regeneration of damaged hard tissues being suitable therapeutic alternatives.

Ceramic materials feature prominently among established biomaterials for the replacement or regeneration of the musculoskeletal system and in dental applications [4–6]. For example, ceramics have been widely used in the repair of skull bone defects [7,8] and maxillofacial reconstruction [9], including alveolar ridge augmentation [10], periodontal pocket obliteration [11] as well as dental [12,13] and orthopaedic implants [14,15]. Bioceramics can be classified in bioinert, bioactive and bioresorbable materials, based on their chemical surface reactivity [16,17]. Bioactive materials are materials able to form a chemical bond with living tissues. In the context of bone replacement materials, the bioactivity of a material is commonly characterized by its ability to induce formation of an apatite layer on its surface upon immersion in biological fluids [18]. However, it is important to mention that some materials (e.g. β-tricalcium phosphate) have been reported not to be able to form a surface apatite layer but still be able to bond to bone tissue in vivo [19]. Alternatively, bioceramics can be classified by their primary chemical composition [20]. Silicate and phosphate ceramics and glass-ceramics are the two broadest categories and include, basically, all the bioactive and bioresorbable compositions. Oxide ceramics such as alumina and zirconia are among the bioinert ceramics and are mainly used as prosthetic devices in medicine and dentistry.

It is well-known that the composition of bioceramics is one of the key parameters affecting their properties and determining their biocompatibility, bioactivity and biodegradability [6]. Furthermore, it has been shown that release of specific elements (ions) from inorganic, bioactive materials, e.g. bioactive silicate glasses and calcium phosphates, can induce positive effects in their surrounding biological environment [21,22].

The relevance of magnesium for biomedical applications is related to its fundamental role in cellular processes and human metabolism [23,24]. Magnesium is one of the most important - mineral elements in the human body, with approximately half of the total physiological magnesium stored in bony tissues [25]. Several studies have indicated that divalent cations (e.g. Mg^{2+}) have a key role in bone remodelling and skeletal development [26,27]. It is well known that magnesium is a co-factor for many

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enzymes and stabilizes the structures of RNA and DNA [24,28]. Furthermore, research studies have consistently demonstrated that surface modification of bioceramics with Mg^{2+} substantially affects the phenotype of osteogenic cells in vivo and in vitro [29,30]. Osteoblast cells-biomaterials surface interactions are mainly mediated by cell membrane adhesion receptors (integrins), in which magnesium plays an important role [28,31]. Mg^{2+} can bond to integrins α subunits [32,33], and extracellular changes of Mg^{2+} can modulate the affinity of the cells to the biomaterial surface [34–36].

Various studies have investigated magnesium-containing polycrystalline ceramics and glass-ceramics for biomedical applications; which is the subject of the present review article [23–25,37–39]. It has been shown that these materials are promising candidates for applications in bone tissue regeneration and magnesium-based bone fillers have been approved by the FDA (Osteocrete; Bone Solutions, Inc., Dallas, TX), which confirms the potential of Mg to be used as a component of bone healing materials.

Furthermore, Mg-containing bioactive ceramics and glass-ceramics are attractive from the point of view of their mechanical properties, bioactivity and biocompatibility [40–43]. These materials have been shown to promote cell adhesion, proliferation, spreading, and differentiation [39,44,45], which make them promising candidates for tissue engineering applications. In addition, a recent study [46] has indicated the ability of a Mg-containing silicate bioceramic to induce angiogenesis in biological conditions. Although there is an increasing interest in these materials, there has not been a comprehensive overview discussing their properties and potential for biomedical purposes.

The widespread use of magnesium-containing inorganic materials in biomedical applications is at the centre of numerous research efforts and it represents an emerging area of biomaterials research. The biomedical applications of Mg-containing bioactive (amorphous) glasses were reviewed in our recent article [47]. The present review will focus on polycrystalline ceramics and glass-ceramics. In addition, several studies have investigated Mg-containing non-silicate systems, including calcium phosphate [48–50] and magnesium phosphate [51,52] systems. However, this review paper is intended to discuss the most relevant studies carried out for Mg-containing bioactive silicate ceramics and glass-ceramics.

2. Mg-containing bioactive silicate ceramics

Various Mg-containing silicate ceramics have been shown to be bioactive and attractive for biomedical applications. Table 1 presents an overview of basic characteristics of these ceramics. Moreover, Table 2 summarizes the relevant in vitro and in vivo biological properties reported in the literature.

2.1. Akermanite

2.1.1. Synthesis

Normally, the naturally occurring akermanite is associated with other minerals and accordingly is not pure. Therefore, sol–gel [37,53–58] and combustion synthesis [59] methods have been used in order to synthesize pure akermanite ceramics for biomedical applications. In 2004, Wu and Chang [53] reported the chemical synthesis of pure akermanite powders via sol–gel method. It was shown that calcification temperature is an important factor for obtaining pure akermanite ceramics, and merwinite and diopside impurities could be observed at calcification temperatures lower than 1300 °C. The optimum calcination temperature for the sol–gel synthesis of pure akermanite powders was reported to be 1300 °C, which leads to formation of porous agglomerated akermanite particles with particle size about 5–40 μm containing pores of about 1–5 μm in size [53]. In 2011, Bhatkar and Bhatkar [59] synthesized akermanite powders using a combustion synthesis method. They claimed that this technique is easier than previously used sol–gel methods [53] and it produces akermanite powders with a narrower size distribution and average agglomerate particle sizes in the range 0.5–5 μm.

2.1.2. Sintering and mechanical properties

The sintering process of akermanite ceramics highly determines the mechanical properties of the material in the bulk form. Table 3 shows density and mechanical properties values of akermanite disks prepared by uniaxial pressing (10 MPa) of sol–gel akermanite powders and subsequent sintering using different schedules [55]. It was reported that akermanite could not be obtained at 1400 °C [55].

It is important to consider that the mechanical properties of ceramics can be altered by producing porous structures. Thus, Wu et al. [57] showed an indirect relationship between the porosity and mechanical strength of akermanite porous structures. It was shown that with increase of porosity from 63.5% to 90.3%, the mechanical strength decreased from 1130 kPa to 530 kPa [57].

2.1.3. In vitro bioactivity and degradation

To the best of the authors' knowledge, diopside ceramics were the first type of Mg-containing silicate ceramics, which was reported to be bioactive [60]. This finding motivated many researchers to study bioactivity and bioactivity related applications of other Mg-containing silicate ceramics [53,61]. Various studies have evaluated the in vitro bioactivity and degradation of akermanite ceramics [53–57]. Wu and Chang [53,55] revealed the apatite-forming ability of sol–gel derived akermanite powders and disks by immersion of the samples in simulated body fluid (SBF) solution. Due to the similar composition and different structure of akermanite compared to bioactive diopside [62], it

Table 1
Overview of Mg-containing bioactive silicate ceramics.

Name	Crystal system	Chemical formula	Composition (wt.%)				Melting T (°C)
			Mg	Ca	Si	O	
Akermanite	Tetragonal	$Ca_2MgSi_2O_7$	8.92	29.40	20.6	41.08	1454
Bredigite	Orthorhombic	$Ca_7Mg(SiO_4)_4$	3.61	41.67	16.69	38.03	1372 ± 2[a]
Diopside	Monoclinic	$CaMgSi_2O_6$	11.22	18.51	25.94	44.33	1391
Forsterite	Orthorhombic	Mg_2SiO_4	34.55	0	19.96	45.49	1890
Merwinite	Monoclinic	$Ca_3Mg(SiO_4)_2$	7.39	36.58	17.09	38.94	1450
Monticellite	Orthorhombic	$CaMgSiO_4$	15.53	25.61	17.95	40.9	1454
Proto-enstatite	Orthorhombic	$MgSiO_3$	24.31	0	28.09	15.00	1557[b]

[a] Upper stability limit (decomposes to Ca_2SiO_4 and merwinite).
[b] Decomposes to forsterite.