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Microwave assisted synthesis and characterization of magnesium substituted calcium phosphate bioceramics

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ABSTRACT

Hydroxyapatite is used extensively in hard tissue repair due to its biocompatibility and similarity to biological apatite, the mineral component of bone. It differs subtly in composition from biological apatite which contains other ions such as magnesium, zinc, carbonate and silicon (believed to play biological roles). Traditional methods of hydroxyapatite synthesis are time consuming and require strict reaction parameter control. This paper outlines synthesis of magnesium substituted hydroxyapatite using simple microwave irradiation of precipitated suspensions. Microwave irradiation resulted in a drastic decrease in ageing times of amorphous apatitic phases. Time taken to synthesize hydroxyapatite (which remained stable upon heat treatment at 900 °C for 1 h) reduced twelve folds (to 2 h) as compared to traditionally required times. The effects of increasing magnesium concentration in the precursors on particle size, surface area, phase-purity, agglomeration and thermal stability, were observed using scanning electron microscopy, BET surface area analysis, X-ray diffraction and photo acoustic Fourier transform infra-red spectroscopy. Porous agglomerates were obtained after a brief heat-treatment (1 h) at 900 °C.

1. Introduction

Hydroxyapatite [HA] is a key bioceramic due to its excellent biocompatibility and its bioactivity which stems from its compositional and structural similarity to the mineral part of bone, enamel and dentine [1–4]. Although bone mineral is an apatitic phase it also contains additional ions which include magnesium, carbonate, strontium, zinc and silicate ions [5–7]. The type and amount of ionic substitution in biological apatite varies from wt% level (e.g. CO_3^{2-}) to the ppm–ppb level (Mg^{2+} or Sr^{2+}) [8–10]. These ionic substitutions affect the crystal lattice structure of HA and influence the dissolution rate and hence the resulting bioactivity of the bone mineral [11–13].

Magnesium substitution into HA is of interest due to its potential impact on the mineralization process and crystallization of apatite [14–16]. It has been reported that in calcified tissues, the amount of magnesium associated with the apatite phase is higher (5% at.) at the first stages of the bone remodeling process and decreases with increasing calcification and ageing of an individual [17–19]. Moreover, magnesium can directly stimulate osteoblast proliferation [20,21]. During synthesis magnesium ions also bind to the surface of apatite crystals inhibiting their growth resulting in smaller particles (higher bioactivity due to higher surface area) [22,23]. Decrease in content of magnesium in bone and loss of some crystallinity are associated with osteoporosis [24,25]. These adverse effects related to magnesium deficiency can impair bone growth and reduce bone quality (strength and density) and increase bone fragility [5,20].

As the magnesium ion is smaller than the a calcium ion (0.86 Å vs. 1.14 Å), the incorporation of magnesium affects the crystal structure of HA and substitution cannot occur over the full compositional range (i.e. magnesium ions cannot replace all calcium ions in HA) [26,27]. Substituting magnesium ions into HA lattice reduces crystal cell parameters and hence cell volume as expected; above a concentration limit of ~0.15Mg^{2+}/Ca^{2+} the apatite structure cannot accommodate any more magnesium resulting in the formation of additional phases (typically TCP or amorphous calcium magnesium phosphates), that act as segregating phases for this ion, is observed [28,29]. TCP phases are known to have higher solubility than that of HA [30].

Several methods can be used for preparing calcium phosphates including magnesium substituted HA (Mg–HA), such as wet chemical routes based on precipitation at low temperature [22,31–36] or solid-

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state reactions at elevated temperatures [37,38] resulting in a range of 0.3–29 wt.% magnesium substitution. Traditional co-precipitation routes often require aging times of 18 h or more in order for the Ca:P phases to reach maturation (and hence thermal stability) [39,40]. Other methods such as sol–gel syntheses [41], batch hydrothermal syntheses [5], mechanochemical-hydrothermal synthesis methods [42,43] and continuous hydrothermal flow synthesis [29] have been reported to produce phase pure materials in the range of 0.5–28 wt.% magnesium substitution. Some of these techniques require expensive starting materials, strict reaction parameter control and monitoring or require expensive equipment. Therefore, a technique that reduces the time of hydroxyapatite synthesis without compromising on its desired properties and also ensures sufficient ion substitution into hydroxyapatite would be of use.

The advantages of microwave irradiation during chemical reactions include acceleration of the reaction, smaller particle sizes with narrow particle distribution and finer nanostructures leading to improved mechanical properties when formed into dense test specimens [44–49]. Despite the benefits, ion substitutions using microwave assisted approaches have not been reported extensively in literature. Magnesium [50] and silver [51] ion substitutions in HA have been reported using microwave assisted methods. The authors previously reported on the magnesium ion substitution into the HA lattice using Continuous Hydrothermal Flow Synthesis (CHFS) Technology [29]. CHFS synthesis of Mg–HA exploited the benefits provided by near-critical water to result in rapid maturation (increase in Ca:P ratio from an initial amorphous precipitate). CHFS is a high throughput technique, however it requires an expensive setup which works at high temperature and pressure [52–54]. The authors have also previously reported on the rapid synthesis of thermally stable hydroxyapatite using microwave irradiation and its deposition on metallic substrates [55,56]. In the current work, microwave irradiation was used as a much simpler alternative method to controllably produce a range of magnesium substituted calcium phosphates with differing compositions and thermal stabilities in a rapid manner.

2. Materials and methods

2.1. Materials

Diammonium hydrogen phosphate $(NH_4)_2HPO_4$ (Applichem, Darmstadt, Germany, 96–102%), calcium nitrate tetrahydrate $Ca(NO_3)_2 \cdot 4H_2O$ (Unichem, Guangzzhou, China 99%), magnesium nitrate hexahydrate $Mg(NO_3)_2 \cdot 6H_2O$ (Pamrea quimica SA, Barcelona, Spain 98%) and ammonium hydroxide NH_4OH (Fisher Scientific, Loughborough, UK, 33%) were used. Deionized water was used in all reactions. The wet-chemical precipitation method for synthesis of HA can be expressed by the following equation:

$$xMg(NO_3)_2 + (10-x)Ca(NO_3)_2 + 6(NH_4)_2HPO_4 \rightarrow Ca_{10-x}Mg_x(PO_4)_6(OH)_2 + 12NH_4NO_3 + 8HNO_3.$$

2.2. Synthesis methodology

For a typical reaction, calcium and magnesium nitrate solutions were prepared by dissolving appropriate amounts in 100 mL deionized water such that (Ca + Mg):P molar ratio was always ~1.67. A control sample (for structural comparison based on XRD and FTIR) labeled Ca–P was prepared by the same synthesis method but without any magnesium. Sample Ids and amounts of calcium nitrate and magnesium nitrate used are given in Table 1. Amounts were selected based on the following formula for magnesium substituted HA [Mg–HA, $Ca_{10-x}Mg_x(PO_4)_6OH_2$]. Samples were denoted as follows: Ca–P corresponds to a sample without any Mg (no magnesium nitrate added), 0.5Mg–CaP corresponds to 0.5 wt.% Mg substituted in hydroxyapatite (based on theoretical 100% magnesium substitution into HA lattice). Similarly 2Mg–CaP corresponds to a sample with 2 wt.% Mg substituted into HA. Therefore x and 10 − x represent Mg:Ca molar ratio. The sample labeled as Mg–P corresponds to a powder made using magnesium nitrate and no calcium nitrate.

0.3 M diammonium hydrogen phosphate solution was prepared by dissolving 3.96 g diammonium hydrogen phosphate in 100 mL deionized water (pH adjusted to 10 by ammonium hydroxide addition). Diammonium hydrogen phosphate solution was added drop wise into the calcium nitrate (if any) and magnesium nitrate (if any) solutions. During addition, the pH of suspension (as instantaneous precipitation took place) was maintained at pH 10 by ammonium hydroxide addition and once complete, the suspension was stirred for 30 min. The suspension was put into a modified household microwave oven (600 W, 2.45 GHz) modified with a refluxing system. Microwave irradiation was performed under ambient air for 5 min (15 s on and 15 s off) [49]. The suspensions were observed to bubble at the base of the cooling condenser (due to boiling by heating due to microwave irradiation). After completion of exposure to microwave irradiation the suspension was then filtered and washed with deionized water. The precipitate was dried at 80 °C in a drying oven for 24 h and sieved (below 74 μm). The sieved powder was then heat-treated at 900 °C for 1 h.

2.3. Characterization

Powder X-ray diffraction (PXRD) data was collected on a X'Pert Pro PW3050/60 diffractometer in the 20–80° range, based on Cu K-α radiation [1.54060 Å], a step size of 0.02 and a scan time of 0.15 s per step.

Table 1
Sample IDs, corresponding x values, theoretical substitution weight percentages and amounts of reagents used.

Sample ID	x (Mg)	10 − x (Ca)	Mg:Ca molar ratio (x:10 − x)	Mg wt %	Added to 100 mL deionized water (grams)			
					Calcium nitrate		Magnesium nitrate	
					Concentration (M)	Amount (grams)	Concentration (M)	Amount (grams)
CaP	–	10	–	–	0.500	11.800	–	–
0.1Mg–CaP	0.04	9.96	0.004	0.1	0.497	11.700	0.002	0.054
0.5Mg–CaP	0.20	9.80	0.020	0.5	0.490	11.570	0.010	0.256
1Mg–CaP	0.40	9.60	0.042	1.0	0.480	11.330	0.020	0.513
1.5Mg–CaP	0.60	9.40	0.064	1.5	0.470	11.100	0.030	0.769
2Mg–CaP	0.80	9.20	0.087	2.0	0.460	10.860	0.040	1.026
4Mg–CaP	1.60	8.40	0.191	4.0	0.420	9.920	0.080	2.051
5Mg–CaP	2.00	8.00	0.250	5.0	0.400	9.447	0.100	2.564
10Mg–CaP	4.00	6.00	0.670	10.0	0.300	7.085	0.200	5.128
16Mg–CaP	6.00	4.00	1.500	16.0	0.200	4.724	0.300	7.692
22Mg–CaP	8.00	2.00	4.000	22.0	0.100	2.362	0.400	10.256
Mg–P	10.00	0.00	–	29.0	0.000	0.000	0.500	12.821