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SYNTHESIS AND CHARACTERIZATION OF MAGNESIUM DOPED CALCIUM PHOSPHATEFOR BONE IMPLANT APPLICATION

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ABSTRACT

Calcium phosphate (CaP) has been extensively studied for its excellent performance in promoting bone tissues ingrowth or osseointegration as in bone graft substitute and biomimetic coating of prosthetic implants. However poor mechanical properties of CaP has made its limited in a load bearing application and it has become an interests in research investigation for biomedical applications challenging. Here we employ an optimized mechanochemical method to synthesis calcium phosphate and Magnesium-doped Calcium Phosphate (Mg-CaP) in various weight percentages. The change of adsorption band in FTIR indicates that the Mg has been substituted into CaP. Doping by MgOH is found to effectively increase the densification and hardness of CaP when sintered at 1200 ^{o}C. Mg doping could be contributes to the improvement in artificial implant of calcium phosphate (CaP) for bone implant application in load bearing area.

Keywords: magnesium, biomaterial, calcium phosphate, mechanochemical, vickers hardness.

INTRODUCTION

In early application of artificial implants, orthopedic made use of implants fabricated from natural materials such as corals, ivory as well as human and animal bones for replacing bone tissue defects (Le Geroz, 2008). The problem of substitutes for hard tissues goes beyond stomatology, because today, like earlier, a considerable part of population suffers from diseases of skeletal bone tissues caused by pathological degradation (osteoporosis), inflammatory processes and cancer. In the developed countries, the number of patients with such chronic diseases reaches about 50% of all population above 50. According to the statistics, the number of aged people will double by the year of 2020 due to the overall increase in the life expectancy and the gain in population. Curing bone tissue diseases, especially malignant growths (osteo-sarcoma), was often associated with surgical operations that as a rule led to extended post-operative defects. The problem lies in recovery of lost functions of individual organs, parts of skeleton and the whole locomotor apparatus components (Barinov, 2010).Calcium phosphate ceramics have been successfully used in bone replacement for more than 30 years as an alternative to autografts. Calcium phosphate still considered the gold standard by many surgeons, as they eliminate painful side-effects associated with bone harvesting and the risks of employing bone allografts obtained from cadavers. The most widely employed calcium phosphate materials are hydroxyapatite (HA) [$Ca_{10}(PO_4)_6(OH)_2$] and tricalcium phosphate in both of its polymorphs (α- and β-TCP) [$Ca_3(PO_4)_2$]. HA and β-TCP, as well as their mixtures, are osteoconductive and can be used as fillers to coat the surface of metallic implants and in drug delivery devices. However, their future seems to be closely tied to the field of tissue regeneration, where these materials should play a major role in the fabrication of scaffolds for bone engineering (Franco *et al.* 2010). Current calcium phosphate bone substitutes do not give full satisfaction. Micro- and macro-porosities and their effect on biological properties are not always taken into account, which results in a large variability of physico-chemical properties among current commercial substitutes. Another strong limitation is their brittleness associated to low crack resistance which restricts their use to non-load-bearing applications, and makes them difficult to handle during surgery. For further improvement, their bioactivity should be increased in order to promote a faster and better bone reconstruction (Chevaliar & Gremillard, 2009). An ideal synthetic bone substitution material should be integrated into the physiological bone formation and remodeling process. Bone formation and remodeling include the resorption of bone and the subsequent growth of new bone. The degradation behavior of a calcium phosphate-based material in the body occurs by two mechanisms where dissolution process is due to physico-chemical solubility and resorption process by osteoclasts (typically denoted as resorption). The degradation of bone substitutes is mainly mediated by osteoclasts, macrophages and monocytes (Detsch *et al.* 2010). Magnesium is an important trace element in bone and teeth and available in low concentration between 0.5 and 1.5 wt%.Itis important in bone metabolism, in particular during the early stages of osteogenesis where it stimulates osteoblast proliferation, and its depletion causes bone fragility and bone loss. It is well known that Mg has amarked inhibitory effect on HA nucleation and growth, where as it selectively stabilizes more acidic precursor phases. Many researchers have worked on the preparation of apatite and calcium phosphate implant materials containing low levels of Mg. (Boanini *et al.* 2010). Mg

substituted calcium phosphate powders have been prepared by precipitation and hydrolysis methods indicating limited replacement of Ca^2 with Mg^2 (up to 0.3wt. %) (LeGeros, 1984). Some other studies on precipitation of Mg substituted calcium phosphate powders also showed substitution of Mg in HA (Suchanek *et al.* 2004). Mayer et al. precipitated HA powders containing up to 1.5wt.% of Mg without simultaneous carbonate substitution (Mayer *et al.* 1997). Golden and Ming managed to synthesize from aqueous solutions Mg substituted calcium phosphate powders with up to 2wt% of Mg (Golden & Ming, 1999). Bigi *et al*. synthesized Mg substituted calcium phosphate powders with up to 5wt% of Mg in HA under hydrothermal conditions at 120ºC(Bigi *et al.* 1993; Hanifi *et al.* 2010). In this study, calcium phosphate (CaP) will be doped with Mg ion from 1.0 to 2.0 wt.% through the simple method of mechanochemical synthesis. The powder propertiesand the densification behavior of sintered dense CaP and Mg-CaP will be investigated.

EXPERIMENTAL METHOD

The starting precursors for Mg-doped Calcium Phosphate (Mg-CaP) powder were commercially available Calcium Hydroxide, $Ca(OH)_2$ (96%, Q-Rec), Phosphoric Acid, H_3PO_4 (99%, Q-Rec) and Magnesium Hydroxide, $Mg(OH)_2$ (95% – 100%, Q-Rec).The reaction equation for Mg-doped CaP from the three precursors is described in Equation.(1):

$$(5\text{-}X)\ Ca\ (OH)_2 + XMg(OH)_2 + 3(H_3)PO_4 \rightarrow Ca_{5-x}Mg_x(PO_4)_3(OH)_2 + (9\text{-}X)H_2O \quad (1)$$

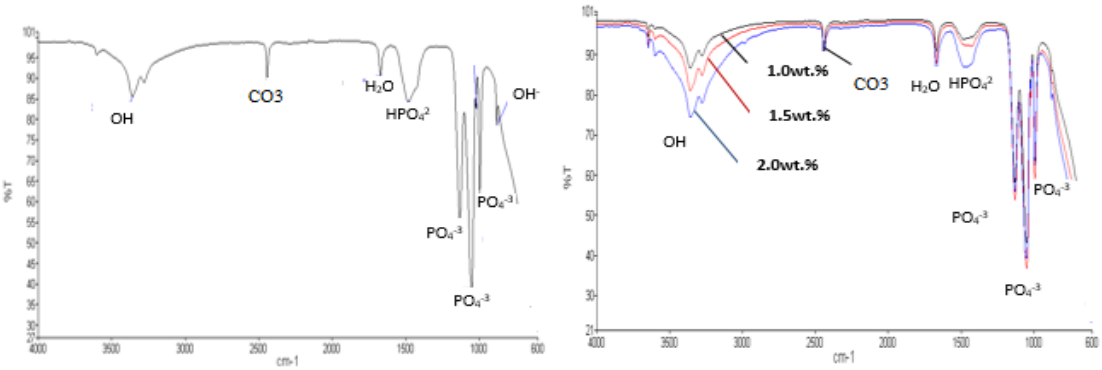
Where X = 0, 0.05, 0.75, 1.00 denoted as Mg precursor. The weight percentage for every molar concentration of Mg is 1.0 wt.% Mg-CaP, 1.5 wt.% Mg-CaP and 2.0 wt.% Mg-CaP. The milling process was carried out in in Retsch planetary ball mill. The mixed precursors were milled at 300 rpm for 10 hours where 15 minutes were set as an interval pause for every 1 hour of milling. After that, the synthesized powderwasdriedin oven at 80 ºC for 24 hours. The dried sample was crushed and sieved to get the powder.The synthesized CaP and Mg-CaP powders were analysed under Fourier Transform Infra-Red (FTIR).1g of the synthesized CaP and Mg-CaP powders were compacted at 2.5 MPa load into disc shape (10.3 mm diameter x 5.3 mm thickness) using a hardened steel mould and die set. The mould should be cleaned first by using oil (e.g. WD40) or silicon spray to remove any impurities and to remove the sample easily after compaction.The compacted samples were sintered at 1200 ºC in 2 hours with 2 ºC/min of heating and cooling rates. The bulk densities of sintered compacts were obtained by using water immersion technique based on Archimedes principle by a standard Mettler Toledo Balance Densitometer. The sintered disc samples were ground on SiC paper (600 – 1000 grit) and polished with 1µm diamond suspension (Mecapol, P260) to yield an optical reflective surface prior to Vickers hardness test. 10 indentations were made by using pyramidal diamond indenter (HMV, Shimadzu) for 10-15 seconds under 200 gf load (HV 0.2).

RESULTS AND DISCUSSION

Figure-1(a) and (b) show the combination of FTIR infrared spectra of mechanochemically synthesized CaP and Mg-CaP powders, as a function of the different peaks concentration. The graph shows that the FTIR indicates the characteristic peaks of$PO_4^{-3}$and OH^- groups which corresponding to calcium phosphate were existed in all the synthesized powders. The PO_4^{-3} bands at 1000-1200 cm^{-1} become sharper and narrow by the increase of magnesium concentration. Higher concentration of Mg also increase the OH and HPO_4^{2-}bands.HPO_4^{2-}denotes that the calcium phosphate has been changed to tricalcium phosphate (Ca_3PO_4). HPO_4^{2-} can be observed in the region 1300 – 1600cm^{-1}. The OH^- band existed at 3354cm^{-1} and in the region 660-680cm^{-1}. The H_2O band also existed in all the synthesized powders at 1660-1680cm^{-1}. According to Suchanek *et al*. (2004), the decrease of intensity and the broadening of the adsorption bands of PO_4^{3-} are attributed to the less of Ca^{2+} ion due to the replacement of Mg^{2+} ion substitution into HA structure leading to the reduction of Ca/P ratio. In constrast to this study, higher Mg concentration increased the PO_4^{3-}bands. Suchanek *et al*. (2004) found that OH^- group (630 cm-1 and 3570 cm^{-1}) decreased with the increase of Mg^{2+} concentration which occurred because of the combination of the adsorbed water and the high surface area of the MgHA powder at higher Mg^{2+} concentration. The CO_3^{-2} group existed in this synthesized powders because of all steps of the experimental procedure was carried out in air. The change of peaks intensity indicate that Mg has been substituted into CaP where tricalcium phosphate was formed by the existing of HPO_4^{2-}.

Figure-2 shows that the density of all the samples generally increase from 1000 ºC to 1100 ºC. The density of CaP increases with the increase of Mg concentration. At 1100 ºC, the maximum density is belongs to 2.0wt. % Mg-CaP at 3.46 g/cm^3. However, at 1200 ºC, the density of all samples averagely decreased where the maximum density is found in 1.5 wt. % Mg-CaP at 3.25 g/cm^3. The densities of all the samples are higher than the hydroxyapatite (HA) standard of density, 3.16 g/cm^3.The hardness of the samples sintered at 1200 ºC is plotted in a graph as shown in Figure-3.The hardness of CaP, 1.13GPa is linearly increased with Mg concentration until 1.5wt. % Mg-CaP at a maximum value of 1.31GPa. However, the hardness is decreases to 1.25 GPa at 2.0wt. % Mg-CaP. Generally, Mg has improved the hardness of CaP when sintered at 1200 ºC. The maximum hardness obtained is linearly similar with the density at 1200 ºC. It indicates that the hardness was influenced by densification. This relationship could also be affected by particle size where smaller particle size generally increases the specific surface area as well as the driving force for densification leading to higher

mechanical properties (Song *et al.* 2011; Adzila *et al.* 2013). Hence, higher density and higher hardness are controlled by the bonding amongst the grains in the sintered samples (Adzila *et al.* 2013).The decreasing of hardness could be explained through the existence of closed porosity and/or the increased grain size in the sintered compacts (Thangamani *et al.*2002).



(a) **(b)**

Figure-1. FTIR spectra of synthesized powders of (a) CaP and (b) Mg-CaP at various weight percentages.

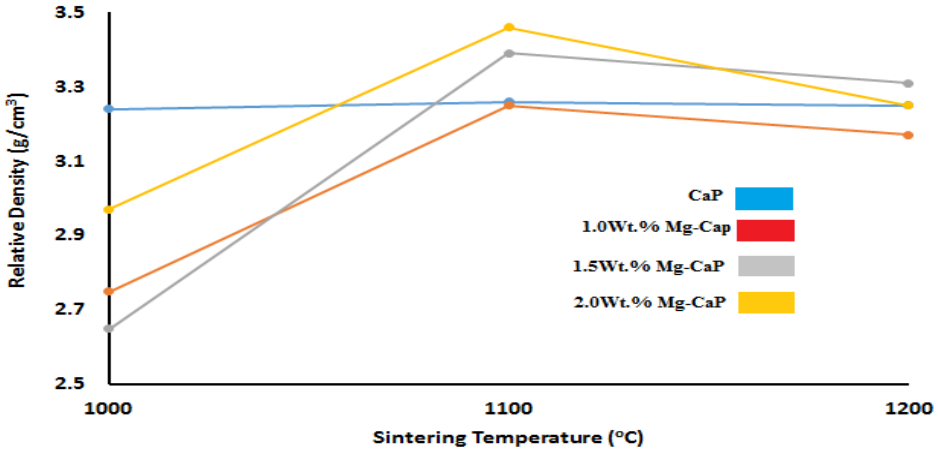


Figure-2. Densities of CaP and Mg-CaP at various weight percentages as a function of sintering temperature.

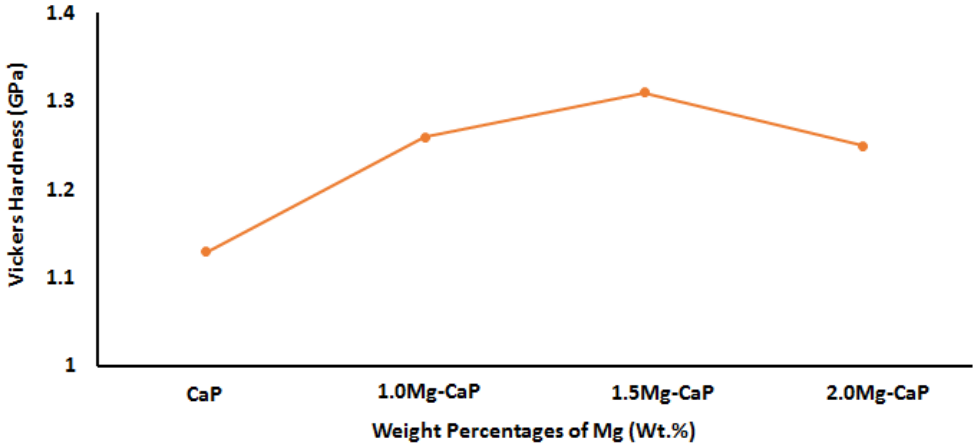


Figure-3. Vickers hardness of CaP and Mg–CaP at 1200 °C as a function of Mg weight percentages.

CONCLUSIONS

From this study, FTIR adsorption band has shown that Mg doped CaP has been successfully synthesized by the simple method through mechanochemical synthesis. Mg doping has improved the densification and the hardness of CaP. The maximum density was achieved at 2.0 wt. % Mg-CaP, 3.46 g/cm^3 when sintered at 1100 ºC and the maximum hardness was achieved by 1.5wt. % Mg-CaP at 1.31 GPa when sintered at 1200 ºC. Further characterization of Mg doped calcium phosphate will be studied in terms of their powder particle size and shape as well as their biocompatibility properties. Doping with Mg ion can be applied in artificial implant in bioactive ceramics of calcium phosphate for future bone implant in load bearing application.

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REFERENCES

[1] Adzila, S., Sopyan, I., Tan, C., Y., Ramesh, S., Wong, Y., H., Purbolaksono, J. and Hamdi, M. (2013). Mechanochemical synthesis of nanohydroxyapatitebioceramics. Indian Journal of Chemistry, 52A, pp. 1570-1575.

[2] Barinov, S., M. (2010). Calcium phosphate-based ceramic and composite materials for medicine. Russian Chemical Reviews, 79, pp. 13-29.

[3] Bigi, A., Falini, G., Foresti, E., Gazzano, M., Ripamonti, A. and Roveri, N. (1993). Magnesium influence on hydroxyapatite crystallization. Journal of Inorganic Biochemistry, 49, pp. 69–78.

[4] Boanini,E., Gazzano, M. and Bigi, A. (2010). Ionic substitutions in calcium phosphates synthesized at low temperature. ActaBiomaterialia, 6, pp. 1882–1894.

[5] Chevalier, J., and Gremillard, L. (2009). Ceramics for medical applications: A picture for the next 20 years. Journal of the European Ceramic Society, 29, pp. 1245–1255.

[6] Detsch, R., Hagmeyer, D., Neumann, M., Schaefer, S., Vortkamp, A., Wuelling, M., Ziegler, G. and Epple, M. (2010). The resorption of nanocrystalline calcium phosphates by osteoclast-like cells. ActaBiomaterialia, 6, pp. 3223–3233.

[7] Franco, J., Hunger,P., Launey,M., E.,Tomsia,A., P., andSaiz, E. (2010). Direct write assembly of calcium phosphate scaffolds using a water-based hydrogel. ActaBiomaterialia, 6, pp. 218–228.

[8] Golden, D., C. and Ming, D., W. (1999). Nutrient-substituted hydroxyapatites:synthesis and characterization. Soil Science Society of American Journal, 63, pp. 657–64.

[9] Hanifi, A., Fathi, M., H.,Mir Mohammad Sadeghi, H. and Varshosaz, J. (2010). Mg^{2+} substituted calcium phosphate nano particles synthesis for non-viral gene delivery application. Journal of Materials Science & Materials Medicine, 21, pp. 2393–2401.

[10] LeGeros, R., Z. (1984). Incorporation of magnesium in synthetic and in biological apatites. In: Fearnhead RW,Suga S, editors. Tooth enamel IV. Amsterdam: Elsevier; pp. 32–36.

[11] LeGeros, R., Z. (2008). Calcium Phosphate-Based Osteoinductive Materials. Chemical Reviews, 108, pp. 4742-4753.

[12] Mayer, I., Schlam, R. and Featherstone, J., D., B. (1997). Magnesium-containing carbonate apatites. Journal of Inorganic Biochemistry, 66, pp. 1–6.

[13] Song, J., Liu, Y., Zhang, Y. and Jiao, L. (2011). Mechanical properties of hydroxyapatite ceramics sintered from powders with different morphologies. Materials Science and Engineering A., 528, pp. 5421–5427.

[14] Suchanek, W., L., Byrappa, K., Shuka, P., Riman, R., E., Janas, V., F. and TenHuisen, K., S. (2004). Mechanochemical-hydrothermal synthesis of calcium phosphate powders with coupled magnesium and carbonate substitution. Journal of Solid State Chemistry, 177, pp. 793–799.

[15] Thangamani, N., Chinnakali, K. and Gnanam, F., D. (2002). The effect of powder processing on densification, microstructure and mechanical properties of hydroxyapatite. Ceramics International, 28, pp. 355-362.