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HYDROTHERMAL TRANSFORMATION OF CALCIUM HYDROGEN PHOSPHATE DIHYDRATE INTO MAGNESIUM WHITLOCKITE

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Abstract: We here report a single-step, rapid synthesis method for magnesium whitlockite (MgWH). The hydrothermal synthesis of MgWH by transformation of calcium hydrogen phosphate dihydrate (DCPD) in formic acid solution was investigated. The fraction of MgWH increased with increasing Mg²⁺ ion concentration. Single-phase MgWH with monodisperse, hexahedral-shaped particles was obtained when the reaction was conducted in the presence of 15 mmol/L Mg²⁺ ions and at 220 °C for more than 3 h. The results also indicated that the hydrothermal transformation into MgWH in the presence of Mg²⁺ ions was not pH-dependent precipitation but thermodynamically stable precipitation. Local structure analysis by ¹H and ³¹P nuclear magnetic resonance confirmed the presence of protonated phosphate (HPO₄²⁻) and showed three distinct phosphate peaks corresponding to the MgWH structure, which were consistent with the crystal structure of conventional MgWH.

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INTRODUCTION

Magnesium whitlockite (MgWH; Ca₁₀Mg₂(HPO₄)₄(PO₄)₂) has been reported to deposit in the human body, for example, dental calculi of human tooth enamel,⁠¹⁻³ human articular cartilage,⁠⁴ and hyper-mineralized osteocyte and lacunae in human alveolar bone.⁠⁵ In a recent study, Hang et al.⁶ demonstrated that MgWH is an osteoconductive material with resorbability intermediate between the resorbabilities of hydroxyapatite and β-tricalcium phosphate (β-TCP).

MgWH can be synthesized directly by precipitation in aqueous solution in the presence of Mg²⁺ ions. However, it only precipitates in a narrow pH range. Thus, extensive studies have been devoted to optimizing the MgWH synthesis conditions.⁷⁻⁹ Jang et al.⁷ showed that single-phase MgWH could be formed at 70 °C; however, aging of the solution by continuous stirring for 24 h was required. Tas⁸ demonstrated the hydrothermal synthesis of MgWH via transformation of calcium hydrogen phosphate dihydrate (DCPD) at 37 °C for 21 days or at 70 or 115 °C for 1 day. As such, to the best of our knowledge, a single-step synthesis with a reaction time shorter than 24 h has not yet been reported.

Therefore, the aim of the present study is to establish a single-step, rapid method for synthesizing MgWH. To this end, MgWH was hydrothermally synthesized by transforming DCPD in formic acid (HCOOH) solution in the presence of Mg²⁺ ions.

MATERIALS AND METHODS

Synthesis method

DCPD (CaHPO₄·2H₂O, Cat. No. C7263), magnesium chloride (MgCl₂, Cat. No. 19-0220-5), and HCOOH (Cat. No. 11-0780-5) were purchased from Sigma-Aldrich, Japan.

HCOOH solution (25 mL, 1 mol/L) was prepared in a polytetrafluoroethylene (PTFE) vessel (50 mL) at a filling ratio of 50 vol.%. and MgCl₂ was dissolved to a concentration of 0, 3, 5, 10, or 15 mmol/L. The pH of each resultant solution was ~1.4 and was not adjusted. After 0.8 g of DCPD powder was added to the solution without stirring, the vessel was transferred to an autoclave (HU-50, SAN-Al Kagaku, Japan). The reaction solution was treated under a pressure of 2.3 MPa at 220 °C for 3, 6, or 12 h in an oven. The resultant precipitate was separated by centrifugation, washed with ultrapure water, and then dried in an oven at 105 °C for 24 h.

Characterization

The crystalline phase was characterized by X-ray diffraction (XRD) using a diffractometer (SmartLab, Rigaku, Japan) equipped with a Cu Ka radiation source (λ = 1.5418 Å, 40 kV, and 50 mA). The crystalline phase was identified by comparison to ICDD PDF reference patterns. The lattice constants and phase composition were calculated using the SmartLab Studio II (Rigaku Corp.) software. The lattice parameters were refined using an external Si reference standard. The phase composition was analyzed by Rietveld refinement using structure templates of MgWH¹⁰ and anhydrous calcium hydrogen phosphate (monetite).¹¹ A scanning electron micro-

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scope (JSM-6610LA, JEOL, Japan) was used at an accelerating voltage of 15 kV to observe the surface morphology of the Au-sputter-coated MgWH particles. The particle size was measured with a laser scattering particle size distribution analyzer (LA-950V2, Horiba, Japan).

$^1$H and $^{31}$P magic angle spinning nuclear magnetic resonance (MAS-NMR) spectra were collected on a 600 MHz (14.1 T) JNM-ECA600 spectrometer (JEOL, Japan) operating at 100.172 and 242.954 MHz for $^1$H and $^{31}$P, respectively. Single-pulse $^1$H and $^{31}$P MAS-NMR experiments were performed at MAS frequencies of 20 kHz with a 3.2 mm-diameter zirconia tube. A 90° pulse width of 2.3 μs and a relaxation delay of 30 s were used in the $^1$H MAS-NMR experiments. The $^{31}$P MAS-NMR experiment was performed with a 90° pulse width of 3.2 μs and a relaxation delay of 100 s. Adamantane ((CH)$_3$CH$_2$) and ammonium dihydrogen phosphate (NH$_4$H$_2$PO$_4$) were used as the secondary external references for $^1$H and $^{31}$P, respectively.

RESULTS AND DISCUSSION

The effect of the Mg$^{2+}$ ion concentration on the formed products was examined. Figure 1 shows XRD patterns for powders synthesized by transformation of DCPD with 0, 3, 5, 10, and 15 mmol/L of Mg$^{2+}$ ions at 220 °C for 12 h. The phase composition of the products is plotted as a function of the Mg$^{2+}$ ion concentration (Fig. 2a). At Mg$^{2+}$ ion concentrations between 0 and 10 mmol/L, a biphase of monetite (CaHPO$_4$, ICDD PDF 01-071-1759) and MgWH (01-070-2064) was formed. The amount of MgWH increased with increasing Mg$^{2+}$ ion concentration: from 2.3 wt.% for 0 mmol/L to 79.2 wt.% for 10 mmol/L. Single-phase MgWH was obtained when the Mg$^{2+}$ ion concentration was 15 mmol/L; the pH after the reaction was 1.7. The lattice constants for the MgWH decreased with increasing Mg$^{2+}$ ion concentration (Fig. 2b) from $a = 10.367 \pm 0.003$ Å and $c = 37.148 \pm 0.017$ Å for 0 mmol/L to $a = 10.354 \pm 0.001$ Å and $c = 37.104 \pm 0.005$ Å for 15 mmol/L. The decreasing lattice constants were agreement with a study by Chickerur et al.$^{12}$ They reported that the lattice constants of MgWH decreased with increase of Mg$^{2+}$ ion concentration in the range of Mg/(Mg+Ca) molar ratio from 0.070 ($a = 10.430$ Å and $c = 37.365$ Å) to 0.190 ($a = 10.129$ Å, $c = 37.100$ Å). The lattice parameters reported by Gopal et al.$^{10}$ for MgWH are $a = 10.350 \pm 0.005$ Å and $c = 37.085 \pm 0.012$ Å, which are similar to those obtained in the present study. However, when those were compared with those by Chickerur et al.$^{12}$ a discrepancy between them was observed. They proposed the MgWH composition of Ca$_{16}$Mg$_{14}$(PO$_4$)$_4$H$_2$ at Mg/(Mg+Ca) = 0.070, while effect of Na$^+$ ions of Na$_2$HPO$_4$, which was used as phosphate source, on the substitution in MgWH was not considered. Although in the synthetic MgWH, Ca(4) site is occupied by H$^+$ ions,$^{10}$ Na$^+$ ions might be also substituted partially in Ca(4) site. As the result, the expansion of unit cell due to the difference of cation radius between H$^+$ and Na$^+$ ions would provoke the longer lattice parameters.

Figure 3 displays XRD patterns showing the effect of the hydrothermal reaction time on the formed products synthesized by transformation of DCPD with 15 mmol/L of Mg$^{2+}$ ions at 220 °C for 3, 6, and 12 h. MgWH was formed at all the reaction time, suggesting that the transformation of DCPD into MgWH completed at more than 3 h of reaction time.

The particle morphologies observed by scanning electron microscopy (SEM) are depicted in Fig. 4a and b. The DCPD particles exhibited a plate-like

FIGURE 1 XRD patterns for the formed products synthesized by transformation of DCPD in the presence of 0 to 15 mmol/L Mg$^{2+}$ ions: 20 = (a) 4 – 60° and (b) 25 – 35°.
MgWH particles synthesized by the transformation of DCPD with 15 mmol/L of Mg\textsuperscript{2+} ions were monodisperse hexahedral-shaped particles (Fig. 4b). The particle size distribution showed single peak with the median particle size of 17.2 μm (Fig. 4c). Hashimoto et al.,\textsuperscript{13} Tas,\textsuperscript{8} and Li et al.\textsuperscript{14} have reported a similar hexahedral morphology for MgWH particles, while the particle size of MgWH differed among them. The particle size of MgWH was 50 μm (reaction temperature: 350 °C) for Hashimoto et al.,\textsuperscript{13} 200 nm (70 °C) for Tas,\textsuperscript{8} 15 μm (180 °C) for Li et al.,\textsuperscript{14} in which the result by Li et al.\textsuperscript{14} was similar to our study. It was considered that increasing reaction temperature resulted in increasing particle size.

The local structure of MgWH synthesized by transformation of DCPD in the presence of 15 mmol/L Mg\textsuperscript{2+} ions was analyzed by \textsuperscript{1}H and \textsuperscript{31}P MAS-NMR. The \textsuperscript{1}H MAS-NMR spectrum shows a peak at 9.8 ppm, which is attributed to protonated phosphate (HPO\textsubscript{4}\textsuperscript{2-}) in the MgWH structure, together with an unidentified peak at 9.5 ppm (Fig. 5a). Figure 5b displays the \textsuperscript{31}P MAS-NMR spectrum, which shows three distinct PO\textsubscript{4}\textsuperscript{3-} peaks centered at 2.2, 1.4, and −0.3 ppm, with integration percentages of 39.9 : 16.8 : 43.4 (= 2.4 : 1.0 : 2.6), respectively. The PO\textsubscript{4}\textsuperscript{3-} sites (P(1), P(2), and P(3)) were assigned on the basis of the \textsuperscript{31}P MAS-NMR peak assignments for Ca\textsubscript{10}Na(PO\textsubscript{4})\textsubscript{7} reported by Grigg et al.\textsuperscript{15} In the \textsuperscript{31}P MAS-NMR spectrum of Ca\textsubscript{10}Na(PO\textsubscript{4})\textsubscript{7}, the main P environments are the P(1) and P(2) sites related to the substitution of Na\textsuperscript{+} ions into the Ca(4) site (i.e., P(1)–Na(4) and P(2)–Na(4)) and the P(3) site related to the Ca(5) site (i.e., P(3)–Ca(5)); the P(3) site was not affected by the Ca(4) site because Na\textsuperscript{+} ions did not substitute into the Ca(5) site. In the MgWH, H\textsuperscript{+} and
Mg$^{2+}$ ions are substituted into Ca(4) and Ca(5) sites, respectively. Thereby, the P(1) and P(2) magnetic environments are related to the H$^+$ ion substitution of the Ca(4) site, i.e., P(1) – H(4) and P(2) – H(4)), whereas the P(3) environment is related to Mg(5) (i.e., P(3) – Mg(5)). As a consequence, the PO$_4^{3-}$ sites in MgWH should be similar to those of Ca$_{10}$Na(P0$_4$)$_4$. The P(3) – Mg(5) site (43% of the observed area) can be assigned to the peak at −0.3 ppm (43.4%) in Fig. 5b. Because the observed areas of P(1) – Na(4) and P(2) – Na(4) were 11.0 : 36.0 (%), the peaks at 2.2 and 1.4 ppm (39.9 : 16.8 (%)) can be attributed to P(2) – H(4) and P(1) – H(4), respectively. McCubbin et al. have demonstrated using $^{31}$P MAS-NMR that the three crystallographically distinct PO$_4^{3-}$ sites in MgWH exist in a 3 : 1 : 3 ratio, which is also consistent with the results of the XRD study by Gopal et al. The P(2) : P(1) : P(3) integration ratio of 2.4 : 1.0 : 2.6 calculated from the $^{31}$P MAS-NMR spectrum in Fig. 5b is consistent with the results of these previous studies.

Chickerur et al. demonstrated that MgWH synthesized with Mg/(Mg+Ca) = 0.070 resulted in Ca$_{10}$Mg$_7$(PO$_4$)$_4$.H$_2$. According to their report, by assuming that all the Ca$^{2+}$ ions of DCPD (4.8 mmol) reacted at Mg/(Mg+Ca) = 0.070, MgWH could be formed as given in Eq. (1), where Mg$^{2+}$ ion concentration was 14.5 mmol/L. The calculated Mg$^{2+}$ ion concentration was good agreement with 15 mmol/L Mg$^{2+}$ ion in the present study. In addition, the yield of MgWH was about 0.5 g, which was similar to the yield (0.55 g) calculated by Eq. (1).

$$18.6\text{CaHPO}_4\cdot2\text{H}_2\text{O} + 1.45\text{MgCl}_2 \rightarrow \text{Ca}_{18.6}\text{Mg}_{1.4}\text{(HPO}_4)_2\text{(PO}_4)_{12} + 0.05\text{Mg}^{2+} + 2\text{H}_2\text{O} + 4.6\text{PO}_4^{2-} + 16.6\text{H}^+ + 2.8\text{Cl}^- \quad \text{Eq. (1)}$$

Meanwhile, in the case of lower Mg$^{2+}$ ion concentration than 15 mmol/L, Mg$^{2+}$ ion concentration was too low to react with all the Ca$^{2+}$ ions of DCPD. Therefore, both MgWH and DCPD were formed. It was also considered that amount of Mg$^{2+}$ ions substituted in MgWH increased with increase of Mg$^{2+}$ ion concentration by 15 mmol/L, as the lattice constants of MgWH decreased with increase of Mg$^{2+}$ ion concentration (Fig. 2b).

The solubility of DCPD and β-TCP decreases with increasing temperature; i.e., the solubility constants (log $K(T)$) of DCPD (0.61) and β-TCP (10.61) at 25 °C decrease to 0.28 and 0.26 at 90 °C, respectively. As such, β-TCP can precipitate together with DCPD at temperatures of 90 °C or greater. Indeed, some fractions of Mg-free whitlockite (2.3%) were formed in the absence of Mg$^{2+}$ ion (0 mmol/L), as shown in Fig. 2a. Upon incorporation of Mg$^{2+}$ ions into the MgWH structure, the solubility of MgWH

FIGURE 4 SEM micrographs showing the particle morphologies of (a) DCPD and (b) MgWH synthesized by transformation of DCPD in the presence of 15 mmol/L Mg$^{2+}$ ions and (c) particle size distribution of MgWH.

FIGURE 5 (a) $^1$H and (b) $^{31}$P MAS-NMR spectra of MgWH synthesized by transformation of DCPD in the presence of 15 mmol/L Mg$^{2+}$ ions. Solid black lines: original spectra; solid red lines: deconvoluted peak models; dashed lines: individual deconvoluted peak models.
would be lower than that of β-TCP, as demonstrated in a previous in vivo study of MgWH. Therefore, MgWH was thermodynamically more stable than DCPD at 220 °C in the presence of Mg ions at a concentration greater than 15 mmol/L, which led to precipitation of single-phase MgWH. Also, Tas has reported that MgWH can precipitate upon transformation of DCPD at 37 °C for 21 days or at 70 or 115 °C for 1 day. Tas used an initial Mg/(Mg+Ca) molar ratio of 0.069, similar to the value of 0.072 used in the present study. Therefore, the rapid precipitation of MgWH for 3 h compared with the precipitation in 1 day reported by Tas is attributable to our higher reaction temperature (220 °C vs 70 or 115 °C by Tas). We also note that, whereas the final pH after transformation was between 4.5 and 5.3 in Tas’s study, the final pH in the present study was 1.7. This result is further evidence that the MgWH transformation at 220 °C was not pH-dependent precipitation but thermodynamically stable precipitation in the presence of Mg ions.

CONCLUSIONS

A single-step, rapid hydrothermal synthesis of MgWH via transformation of DCPD in HCOOH solution was demonstrated. Single-phase MgWH particles with a monodisperse hexahedral shape were obtained when the reaction was conducted in the presence of 15 mmol/L Mg ions and at 220 °C for more than 3 h. The results also indicate that the hydrothermal precipitation of MgWH at 220 °C was not pH-dependent precipitation but thermodynamically stable precipitation. The 1H and 31P MAS-NMR spectra of MgWH showed a peak associated with protonated phosphate (HPO₄²⁻) and three distinct PO₄³⁻ peaks, which are consistent with the crystal structure of conventionally prepared MgWH.

REFERENCES

1. T. Kodaka, K. Debari, M. Abe, Caries Res., 26, 69–76 (1992).
2. T. Kodaka, Y. Ohara, J. Showa Univ. Dent. Soc., 13, 375–379 (1993).
3. T. Kodaka, M. Yamada, Y. Kodaka, O. Anatomy, T. Kodaka, M. Yamada, J. Showa Univ. Dent. Soc., 14, 359–362 (1994).
4. C.A. Scotchford, M. Vickers, S.Y. Ali, Osteoarthr. Cartil., 3, 79–94 (1995).
5. F.A. Shah, B.E.J. Lee, J. Tedesco, C.L. Wexell, C. Persson, P. Thomsen, K. Grandfield, A. Palmquist, Nano Lett., 17, 6210–6216 (2017).
6. H.L. Jang, G.B. Zheng, J. Park, H.D. Kim, H.R. Baek, H.K. Lee, K. Lee, H.N. Han, C.K. Lee, N.S. Hwang, J.H. Lee, K.T. Nam, Adv. Healthc. Mater., 5, 128–136 (2016).
7. H.L. Jang, H.K. Lee, K. Jin, H.Y. Ahn, H.E. Lee, K.T. Nam, J. Mater. Chem. B, 3, 1342–1349 (2015).
8. A.C. Tas, J. Am. Ceram. Soc., 99, 1200–1206 (2016).
9. S. Batool, U. Liaqat, Z. Hussain, M. Sohail, Nanomaterials, 10, 1856 (2020).
10. R. Gopal, C. Calvo, J. Ito, W.K. Sabine, Can. J. Chem., 52, 1155–1164 (1974).
11. M. Catt, G. Ferraris, S.A. Mason, Acta Crystallogr. Sect. B Struct. Crystallogr. Cryst. Chem., 36, 254–259 (1980).
12. N.S. Chickerur, R.C. Lenka, B.B. Sabat, G.H. Nayak, Indian J. Chem., 25A, 181–182 (1986).
13. K. Hashimoto, T. Kobayashi, Y. Toda, T. Kanazawa, S. Udagawa, Inorg. Mater., 6, 110–116 (1999).
14. G.C. Li, P. Wang, C.B. Liu, J. Inorg. Mater., 32, 1128–1132 (2017).
15. A.T. Grigg, M. Mee, P.M. Mallinson, S.K. Fong, Z. Gan, R. Dupree, D. Holland, J. Solid State Chem., 212, 227–236 (2014).
16. F.M. McCubbin, B.L. Phillips, C.T. Adcock, K.T. Tait, A. Steele, J.S. Vaughan, M.D. Fries, V. Atudorei, K.E. Vander Kaaden, E.M. Hausrath, Am. Mineral., 103, 1319–1328 (2018).
17. G. Vereecke, J. Lemaître, J. Cryst. Growth, 104, 820–832 (1990).