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Novel attempts for the synthesis of calcium sulfate hydrates in calcium chloride solutions under atmospheric conditions

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Abstract

The medical grade calcium sulfate is widely used in clinical applications for treating bone defects. A high-purity and predictable calcium sulfate (CS) synthesis process is desirable in the medical industry. The objective of this study was to develop a one-pot method for the direct preparation of calcium sulfate hemihydrates (CSHs; such as the α- and β-forms) in a $CaCl_2$ solution. CS was synthesized by mixing K_2SO_4 and $Ca(NO_3)_2{\cdot}4H_2O$ under various $CaCl_{2(aq)}$ concentrations and reaction temperatures under atmospheric pressure. The calcium sulfate dihydrate (CSD) was found to be an intermediate phase that converts to CSH during the synthesis process, and α-CSH was gradually transformed from β-CSH over time. Moreover, the kinetic of CSD conversion to CSH was strongly accelerated by increasing the $CaCl_2$ concentration. As the reaction temperature was fixed in 90 °C, the form of the CS reactant with an increase in the $CaCl_2$ concentration was in the following sequence: CSD → CSD + β-CSH → CSD + β-CSH + α-CSH → α-CSH. In this study, the synthesis processing window of the CS reactant was established according the test results, and it is worth noting that all phases of CS hydrate could be synthesized with this system and well predicted by the constructed processing window.

Keywords: Calcium sulfate; Calcium chloride; Dehydration; Processing window

1. Introduction

Calcium sulfate (CS) is the subject of much research due to its multifaceted clinical applications for treating bone defects [1,2]. Good control of biodegradation is essential for CS to achieve satisfactory clinical outcomes. It is desirable for CS to have a dissolution rate close to the rate of new bone growth as a bone substitute [3]. The resorption rate of CS can be governed by its particle size and crystalline structure. Medical use CS hydrate can be further classified as dihydrate (CSD, $CaSO_4{\cdot}2H_2O$), β-hemihydrate (β-CSH, β-$CaSO_4{\cdot}0.5H_2O$), and α-hemihydrate (α-CSH, α-$CaSO_4{\cdot}0.5H_2O$) based on the crystal structure and crystalline water content. Unlike β-CSH (microcrystalline crystal), α-CSH is a long and regular needle-like macrocrystalline crystal and requires less hydration water but produces gypsum with greater strength and a longer resorption period [4,5].

According to ASTM F2224-03 standard specifications for high-purity CSH or CSD for surgical implants, the upper limit of heavy metal contents (such as mercury, arsenic, lead, and cadmium) is 10 ppm, and that of iron content is 100 ppm. Generally, CS can be obtained from natural rock mines or industrial by product (e.g., flue gas desulfurization (FGD) gypsum), however, heavy metal elements or impurities are usually present in FGD gypsum and nature gypsum [6], which is not suit for medical application. For this reason, medical industry usually direct synthesis high quality CSD with wet-precipitation method, however the produced CSD still need a process to convert into CSH. Transformation of CS hydrate phases is influenced in a complex manner by temperature, pressure, dissolved electrolytes or organics, and the presence of nuclear seeds [7]. Among them, an autoclaving (high pressure

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steam) method is the typical way to convert CSD to α-CSH [8]. Recently, an alternative approach to transform CSD into α-CSH gypsum with inorganic salts or sulfuric acid under atmospheric pressure without an autoclaving step is possible [9], and the process is relatively milder than the autoclave method [10], moreover the crystal dimensions also can be controlled by electrolyte concentration [11].

To combine the synthesis and conversion process, this paper reports a systematic study that was recently undertaken to seek the one-pot direct synthesis of various CS hydrates by providing Ca^{+} and SO_4^{-} ions in a $CaCl_2$ solution at a suitable temperature, and identified the residue heavy metal content. We also tried to construct a processing window of the design process to provide an alternative for producing medical-grade CSs.

2. Experimental procedures

All reagents used in the study were obtained from Sigma–Aldrich (Seelze, Germany) with no further purification. The synthesis process is summarized in Fig. 1. The CS reactant was prepared by mixing 0.1 mole K_2SO_4 and 0.1 mole $Ca(NO_3)_2{\cdot}4H_2O$ in a beaker containing 100 ml of the designed concentration of a $CaCl_2$ solution (0–5 M) at each preset temperature (25–110 °C) for various reaction times (1–240 min) under atmospheric pressure. The temperature of the system was controlled using an oil bath. All reaction conditions are listed in Table 1. The stoichiometric CS precipitates were harvested by filtration, washed with 95% ethanol, and dried in a freeze-dryer (Christ Co., Osterode am Harz, Germany) overnight to preserve the CS phases without causing undesired rehydration or phase transformation during sample handling.

The crystalline phases of the CS products were investigated by wide-angle X-ray diffraction (WAXD, MaxRC, Rigaku, Japan). The wavelength of the monochromatic X-ray beam was 1.54 Å for CuKα radiation, and the range of the 2θ scan was 5–60° at a scanning rate of 10°/min. The diffraction peaks of various CS phases were analyzed according to the American

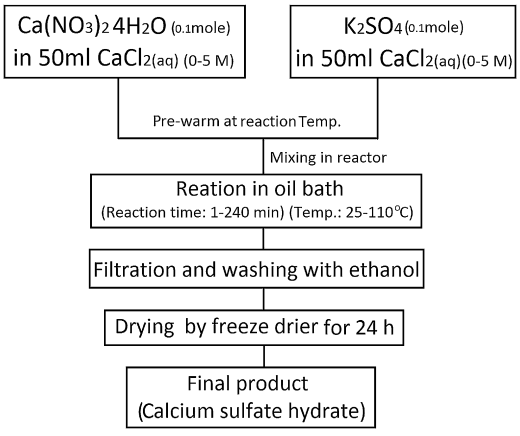

Fig. 1. Schemtic flow chart of the direct synthesis of calcium sulfate (CS) hydrates.

mineralogist crystal structure database. Thermal analysis and SEM observations were conducted to distinguish the crystalline structure between α-CSH and β-CSH. Samples, of 10 mg each, were loaded in onto an aluminum disc and placed in an oven of a differential scanning calorimeter (DSC, TA-Q100, New Castle, DE, USA). The heating rate was 10 °C/min from 20 to 350 °C. CS specimens were sputter-coated using an ion sputter (E-1010, Hitachi, Tokyo, Japan), and the crystal morphology was examined by scanning electron microscope (SEM) (S2400, Hitachi, Tokyo, Japan) at 15 kV with a magnification of 1000×. The content of heave metal was identified by inductively coupled plasma optical emission spectrometer (ICP/OES) (Perkin Elmer Optima 3000 ICP-OES, Waltham, MA, USA)

3. Results and discussion

3.1. Synthesis of CSH in a $CaCl_2$ solution

CSD can be synthesized by a wet precipitation method. The precipitation process involved three stages of supersaturation, nucleation, and crystal growth. We added $CaCl_2$ to this wet precipitation system to regulate the crystalline phases of the CS reactant. In this reaction, 0.1 mole K_2SO_4 and 0.1 mole $Ca(NO_3)_2{\cdot}4H_2O$ were respectively dispersed in the $CaCl_2$ aqueous solution, and the solutions were agitated on a stirring plate to prevent K_2SO_4 aggregation in the $CaCl_2$ solution. When the ratio of K_2SO_4 (mole)/$CaCl_{2(aq)}$ (L) exceeded 3, the reactant slurry was too viscous to react. For operational convenience, the ratio of K_2SO_4 (mole)/$CaCl_{2(aq)}$ (L) of the following experiment was kept constant at 2. According to the solubility of the material and boiling point of the solution, the reaction analysis produced the following conditions: $CaCl_2$ of 0–5 M, a reaction temperature of 25–110 °C, and reaction time of 1–240 min; all conditions are listed in Table 1. As previously reported, CSD could be completely transformed to α-CSH in an over 35% (about 3.15 M) $CaCl_2$ solution at near the boiling point [11,12], thus the reaction temperature and concentration of $CaCl_2$ were controlled to 3.5 M and 90 °C. The effect of the reaction time on the synthesis of CSH was evaluated first. Since the WAXD pattern could only be used to identify the crystalline phases for CSD and CSH, each resulting CS reactant had to be further analyzed by DSC and SEM to distinguish β-CSH and α-CSH.

3.2. Effect of reaction time on the synthesis of CSH

The time effect of CSH synthesis (1, 15, 60, 120, and 240 min) was evaluated by WAXD measurements. The characteristic peaks of CSD located at 11.64°, 20.75°, 23.41°, and 29.14° were correlated with the crystal planes of (0 2 0), (0 2 1), (0 4 0), and (0 4 1), while the characteristic peaks of CSH located at 14.75°, 25.66°, 29.76°, and 31.91° were associated with the crystal planes of (1 1 0), (3 1 0), (2 2 0), and (−1 1 4), respectively. Typical characteristic peaks of AH usually located at 25.47°, 31.37°, 38.66°, and 40.83° were attributed to the crystal planes of (2 0 0), (1 0 2), (0 2 2), and (1 2 2). According to the WAXD results (Fig. 2A), only the

Table 1
Summary of various reaction conditions for calcium sulfates prepared by a wet precipitation method.

Test no.	Reaction condition			Final product
	$CaCl_2$ (M)	Time (min)	Temp. (°C)	
1	3.5	1	90	CSD + β-CSH
2	3.5	15	90	β-CSH
3	3.5	60	90	β-CSH
4	3.5	120	90	α-CSH
5	3.5	240	90	α-CSH
6	3.5	120	25	CSD
7	3.5	120	50	CSD
8	3.5	120	80	CSD
9	3.5	120	90	α-CSH
10	3.5	120	100	α-CSH
11	3.5	120	110	β-CSH
12	0	120	90	CSD
13	0.5	120	90	CSD + β-CSH
14	1	120	90	CSD + β-CSH
15	2	120	90	CSD + β-CSH + α-CSH
16	3	120	90	α-CSH
17	3.5	120	90	α-CSH
18	4	120	90	α-CSH
19	5	120	90	α-CSH
20	0	120	103	CSD + β-CSH
21	0.5	120	100	CSD + β-CSH
22	0.5	120	110	β-CSH
23	1	120	80	CSD
24	1	120	100	CSD + β-CSH
25	2.5	120	100	β-CSH + α-CSH
26	3	120	100	α-CSH
27	3	120	110	β-CSH
28	4	120	80	CSD
29	4	120	110	β-CSH + α-CSH

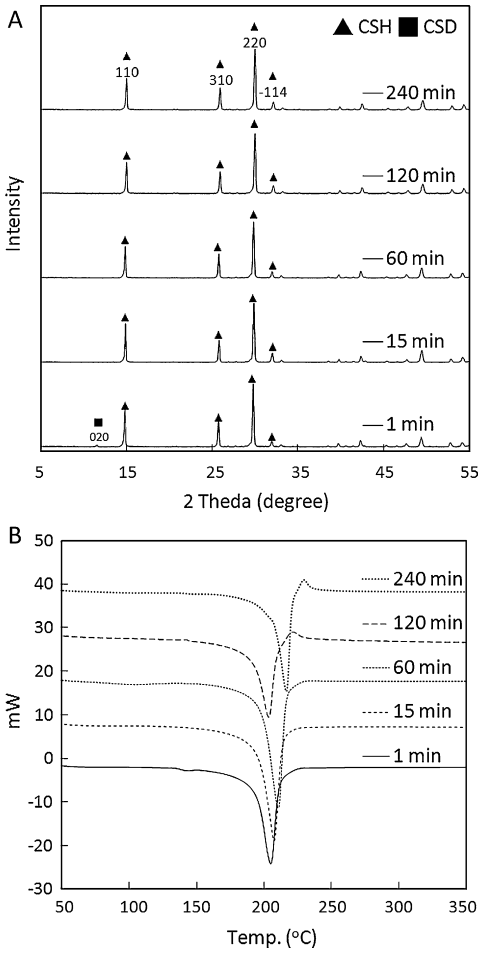

Fig. 2. Reaction time effect on calcium sulfate hydrate synthesis in 3.5 M $CaCl_2$ at 90 °C. (A)Wide-angle X-ray diffraction (WAXD) and (B) differential scanning calorimetry (DSC).

sample with a reaction time of 1 min had a trace of CSD (a weak peak at 11.64° (0 2 0)), and the other samples were mostly CSH. The characteristic peaks of CSH were very sharp and clear, and only small peaks of impurities or un-reacted materials were observed.

Each obtained CS specimen was further investigated by DSC and SEM to distinguish the crystalline phases of β-CSH and α-CSH. The representative DSC thermogram of CSD had two endothermic peaks at ranges of 130–150 °C and 200–210 °C, while the thermogram for CSH mainly had an endothermic peak in a range of 200–210 °C. CSH was classified into α-CSH as evidenced by an exothermic peak at about 210–230 °C (β-CSH had no exothermic peak). Fig. 2B shows the DSC graphs of products synthesized under different reaction times. As the reaction time was 15–60 min, the reactant of microcrystalline β-CSH was obtained (Fig. 3A). With an increase in the reaction time (above 120 min), the exothermic peak of α-CSH following the second endothermic peak occurred on the DSC curve, and the SEM picture (Fig. 3B) confirmed that the reactant was needle-like α-CSH. For this reason, the operating condition of a reaction time of 120 min was chosen for the following experiment.

As can be seen, CSD and β-CSH were intermediate products in the reaction between K_2SO_4 and $Ca(NO_3)_2{\cdot}4H_2O$ at 90 °C in 3.5 M $CaCl_2$. At the reaction conditions of 90 °C with 3.5 M $CaCl_2$, the phase transition route of the reactant was transformed from CSD → β-CSH → α-CSH with an increase in the reaction time. This reveals that the kinetics of phase transformation (CSD–CSH) did not fully coincide with the kinetics of the $K_2SO_4/Ca(NO_3)_2{\cdot}4H_2O$ reaction, which was similar to Ling's report [10]. According to the above results, the microcrystalline β-CSH gradually transformed to macrocrystalline α-CSH with reaction time. Thus, α-CSH formation in this reaction may have been due to crystal growth of β-CSH, which occurred according to the dissolution–crystallization mechanism [13]. However, the effect of reaction time on the α-CSH crystal size and its mechanical properties after hydration still require further study.

3.3. Effect of reaction temperature on the synthesis of CSH

Temperature is the key factor affecting the crystalline phase of CS. To investigate the effect of reaction temperature on the synthesis of CSH and product characteristics, the reaction temperatures were set to 25, 50, 80, 90, 100, and 110 °C respectively. The WAXD and DSC diagrams of the reactants are

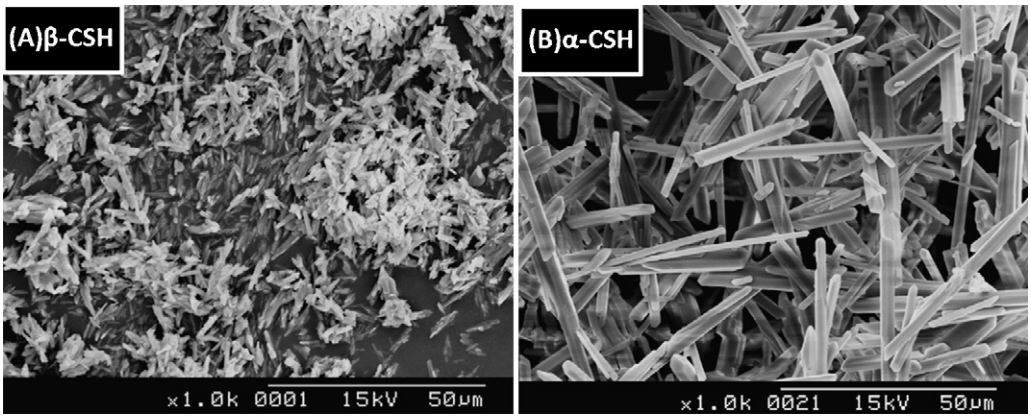

Fig. 3. Representive scanning electron microscope (SEM) pictures of (A) β-calcium sulfate hemihydrate (CSH) and (B) α-CSH.

shown in Fig. 4. At lower temperatures (below 80 °C), CSD was synthesized with 3.5 M $CaCl_2$ for 120 min, while the reaction temperature was 90–100 °C, the reactant was fine α-CSH (SEM data none shown). However, when the temperature exceeded 110 °C, the reactant transformed to β-CSH instead. For this reason, the transition temperature (CSD–CSH) was at 80–90 °C; that is, the production of α-CSH or β-CSH became feasible at lower temperatures when using electrolyte solutions.

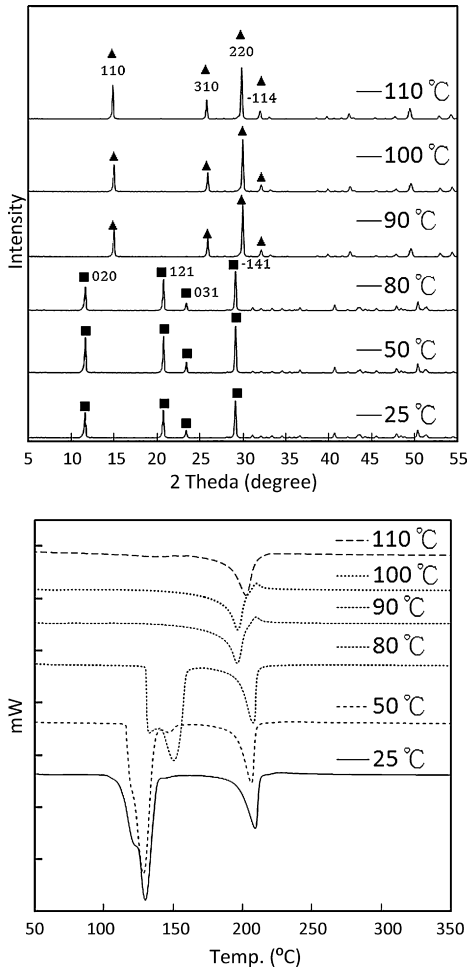

Fig. 4. Temperature effect on calcium sulfate hydrate synthesis in 3.5 M $CaCl_2$ for 2 h. (A) Wide-angle X-ray diffraction (WAXD) and (B) differential scanning calorimetry (DSC).

During the CSH synthesis process, we had to control the synthesis conditions so that they remained above the transition point of CSD–CSH. At the transition point of CSD to CSH, values of $K_{sp,CSD}$ and $K_{sp,CSH}$ are equal [9]. Li et al. mentioned that the intersection of $K_{sp,CSD}$ and $K_{sp,CSH}$ lines corresponding to the transition point of CSD–CSH was about 100 °C [14], which is close to the 98 °C of Partridge et al. but lower then Dahlgren's 104 °C [15,16]. All of them were close to or higher than the boiling temperature, which is not favored for industrial processes. Generally, the added electrolyte can decrease the transition temperature of CSD–CSH [17]. Guan et al. reported a system that was able to transform FGD gypsum to high-value α-CSH in an electrolyte (3 M $CaCl_2$ + 1 M $MgCl_2$) at 95 °C [9], the reaction temperature of which was similar to those of our system. We also found that as the reaction temperature exceeded 110 °C, the precipitated CS was microcrystalline β-CSH. The crystal size of CSH depends on the nucleation and growth rates that are related to variations of supersaturation [18,19], which is the main driving force for crystallization [20]. According to references [19,21], the relative supersaturation of CSH (σ) is defined as follows:

$$\sigma = \left[\frac{\mathrm{IP}}{K_{\mathrm{sp(CSH)}}}\right]^{1/V} - 1 = \left[\frac{c(\mathrm{Ca}^{2+})\gamma\mathrm{Ca}^{2+} + c(\mathrm{SO}_4^{2-})\gamma\mathrm{SO}_4^{2-} - a_w^{0.5}}{K_{\mathrm{sp(CSH)}}}\right]^{1/2} - 1 \quad (1)$$

where IP is the ionic product, K_{sp} is the solubility product of CSH that is only a function of temperature, $c(Ca^{2+})$ and $c(SO_4{}^{2-})$ are the respective concentrations of Ca^{2+} and $SO_4{}^{2-}$, and a_w is the activity of water. The K_{sp} of CSH decreases with temperature [7], which may cause an increase in the relative supersaturation of CSH. When preparing CSH, the higher relative supersaturation condition had a higher nucleation rate that resulted in a smaller crystal size [21]. For this reason, when the system reached the labile region of supersaturation, large numbers of nuclei were formed that may have resulted in formation of microcrystalline β-CSH crystals.

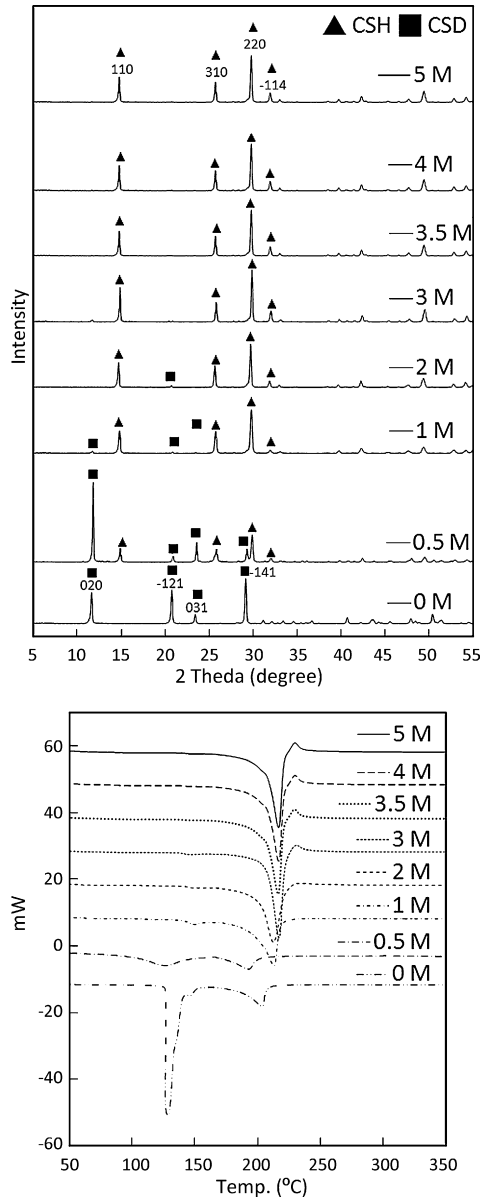

Fig. 5. Effect of the $CaCl_2$ concentration on calcium sulfate hydrate synthesis at 90 °C for 2 h. (A) Wide-angle X-ray diffreaction (WAXD) and (B) differential scanning calorimetry (DSC).

3.4. Effect of $CaCl_2$ concentration on the synthesis of CSH

$CaCl_2$ is also an important factor in controlling the phase of synthesized CS. To investigate the effects of the $CaCl_2$ concentration in the aqueous system on CS synthesis, the $CaCl_2$ concentration of the system was respectively adjusted to 0, 0.5, 1, 2, 3, 3.5, 4, and 5 M, and reaction conditions were fixed at 90 °C for 120 min. From the WAXD analysis (Fig. 5A), the reactant of K_2SO_4 and $Ca(NO_3)_2{\cdot}4H_2O$ was CSD under a condition without $CaCl_2$ at 90 °C. With an increase in the $CaCl_2$ concentration, the characteristic peak of CSD diminished and CSH gradually became evident. When the $CaCl_2$ concentration exceeded 3 M, the reactant was completely CSH. Fig. 5B shows DSC grafts of the reactant with various $CaCl_2$ concentrations. The first endothermic peak (at about 130–150 °C) gradually shrank with an increase in $CaCl_2$. In the DSC curve of 2 M $CaCl_2$, the first endothermic peak (at about 130–150 °C) had almost completely disappeared, and a weak exothermic peak (at about 225 °C) was found; the phase of the reactant was also confirmed by SEM analysis, Fig. 6A shows the reactant composed of irregular CSD, microcrystalline β-CSH, and α-CSH, indicating that the reactants produced in this condition (2 M $CaCl_2$) were combination of the CSD, β-CSH, and α-CSH phases. For synthesis conditions of higher $CaCl_2$ concentrations (>3 M) at 90 °C, the results of DSC and SEM proved the reactants of CS were of the α-form. That is to say, with an increase in the $CaCl_2$ concentration, the form of the CS reactant was in following sequence: CSD → CSD + β-CSH → CSD + β-CSH + α-CSH → α-CSH.

Li et al. reported that the transition temperature of CSD–CSH in 2 M $CaCl_2$ was about 90 °C, and the transition temperature decreased with an increase in $CaCl_2$ [14]. Thus controlled synthesis conditions above the transition temperature (CSD–CSH) should be able to directly synthesize pure CSH. Ling et al. also reported that with an increase in the acidity or electrolyte, the kinetics of CSD conversion to CSH were strongly accelerated [10]. For this reason, the condition with a higher $CaCl_2$ concentration may be able to reduce the reaction time for converting CSD to CSH.

Crystallization was affected by various factors (e.g., impurities, temperature, reaction time, and additives), and supersaturation is the main driving force of nucleation and

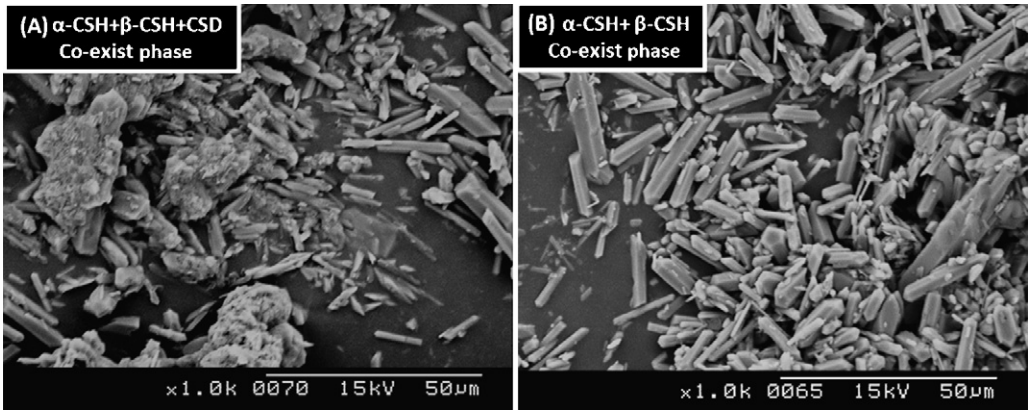

Fig. 6. Representive scanning electron microscope (SEM) pictures of (A) calcium sulfate dihydrate (CSD) + β-calcium sulfate hemihydrate (CSH) + α-CSH, and (B) β-CSH + α-CSH.

growth. Adding $CaCl_2$ reduce the K_{sp} of CSH (common ion effect) which may increase supersaturation [14], and enhance the nucleation and growth rates of the crystallization process [22]. Wang et al. reported that the $CaCl_2$ concentration strong affected the morphology of CSH; as the $CaCl_2$ concentration decreased, the aspect ratio of the powder decreased, which affected the compressive strength of the hydrated CSH. That is to say, $CaCl_2$ not only can reduce the conversion time of CSD to α-CSH but also control the morphology of CSH, which is a very interesting point for future research.

3.5. Processing window of CS synthesis with the $CaCl_2$ solution

Each CS sample synthesized under various conditions was characterized by WAXD, DSC, and SEM, and the conditions and results are summarized in Table 1. Because the crystallization and phase transformation of crystals are very complicated, it is very difficult to effectively optimize and control the process. For this reason, we fixed the reaction time at 120 min to remove the time effect and constructed a precise processing window of CS reactants at various $CaCl_2$ concentrations and reaction temperatures to provide a basis of reaction conditions to forecast the type of reactants. A processing map for CSD, β-CSH, α-CSH, and coexisting phases is graphically presented in Fig. 7. The predicted boiling point line was calculated by followed equation: $\Delta T_b = K_b \cdot m_B$, where the ebullioscopic constant (K_b) is 0.51 °C kg/mol for water and m_B is the molality of the K_2SO_4, $Ca(NO_3)_2{\cdot}4H_2O$, and $CaCl_2$ aqueous solutions. The processing window showed that most reactants were CSD (region I) at lower reaction temperatures (below 80 °C). When the reaction temperature and $CaCl_2$ concentration were 85–103 °C and 0–2 M, respectively, β-CSH began to form, and the reactants in this region were a coexisting phase of CSD + β-CSH (region II). As the $CaCl_2$ concentration exceeded 2 M, α-CSH begun to form. Under conditions with higher $CaCl_2$ concentrations (>2 M) and a suitable reaction temperature (85–103 °C), the reactant was fine α-CSH (region III-α). For this reason, with an increase in the $CaCl_2$ concentration, CSD could transform into β-CSH and then gradually transform into α-CSH. However, we also found that as the reaction temperature was near or over the predicted boiling temperature, the reactant tended to be microcrystalline β-CSH (region III-β).

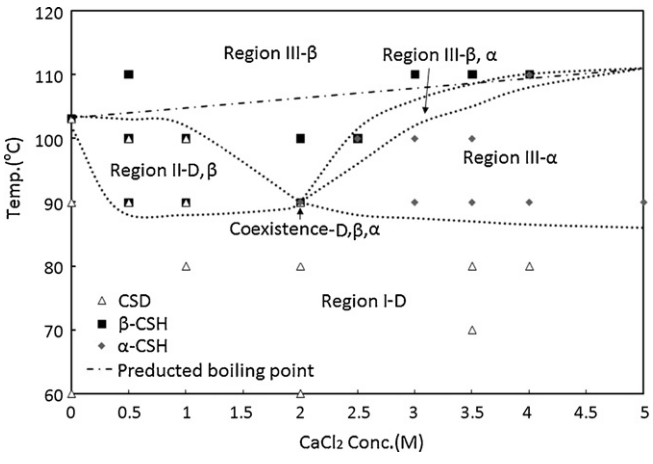

Fig. 7. Processing window of calcium sulfate (CS) synthesis with various $CaCl_2$ concentrations and temperatures (reaction time: 2 h).

From the processing window, the transformation temperature of CSD to α-CSH gradually decreased (103–85 °C) with an increase in the $CaCl_2$ concentration (0–5 M). This behavior can be attributed to the ability of $CaCl_2$ to decrease the water activity which in turn, facilitated the conversion of CSD to CSH; in other words, $CaCl_2$ acts as a dehydrating agent. However, compared to other CS phase-transition diagrams in the $CaCl_2$ system, a discrepancy exists between Li et al.'s report [14] and our experimental observations, the transition temperature of our system (CSD to CSH) was determined to be somewhat higher by 5–10 °C, which may have been because our CSH was synthesized from K_2SO_4 and $Ca(NO_3)_2{\cdot}4H_2O$ in a $CaCl_2$ solution, and the reaction time also differed. In each CS reactant, little un-reacted material and heave metal (data not shown) were found by ICP-MS, which indicated that the quality of the synthesis process was satisfactory. Moreover, no detectable CSA was obtained under synthesis conditions within this processing window. Numerous studies reported that the hydrothermal method was useful to produce α-CSH [9,10,23], however, they also mentioned that CSA usually formed under specific conditions. Li et al. reported that the presence of $CaCl_2$ suppressed the transformation of CSH to CSA, which may explain why little CSA formed in our system [24]. The processing window of direct synthesis the CS hydrant in $CaCl_2$ was first proposed in this study, and it is worth noting that the all phases of CS hydrate could be synthesized using this system, and were well predicted by the constructed processing window.

4. Conclusions

The one-pot method of the direct synthesis CS hydrate in $CaCl_2$ solution at an elevated temperature was developed through multiple analyses. We concluded that all phases of CS hydrate could be synthesized by the designed system, and the quality of reactants was satisfactory. Little CSA and was observed in any of the conditions. A processing window of CS hydrates, namely, CSD, β-CSH, α-CSH, and their coexistence, in the various $CaCl_2$ and reaction temperature systems was successfully established. There were a little heave metal residual in CSs. The phases of CS hydrates could be regulated by adjusting the reaction temperature and $CaCl_2$ concentration. For this reason, this CS hydrate synthesis system may be an alternative for the medical industry.

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