# Intercalation of Natural Cyclodextrins into Layered Double Hydroxide by Calcination–Rehydration Reaction

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Natural α-, β-, and γ-cyclodextrins (CDs) were intercalated in the interlayer of layered double hydroxide (LDH) by calcination–rehydration reaction using the calcined precursor of Mg–Al/$CO_3$/LDH. The intercalated amount was considerably large in spite of nonanionic macrocyclic molecule in the wide CD concentration range. The presence of hydroxyl group on upper and lower rim in CD molecule favors the intercalation driving force by hydrogen bond with the hydroxide basal layer. In addition, CDs in the CD/LDHs were deintercalated by the ion exchange with carbonate ion with regeneration of the pristine Mg–Al/$CO_3$/LDH.

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Layered double hydroxide (LDH) is a layer compound with anion-exchange ability. The chemical composition of LDHs is generally represented as $[M^{2+}{}_{1-x}M^{3+}{}_x(OH)_2]$ $[A^{n-}{}_{x/n}\cdot yH_2O]$. LDHs consist of positively charged octahedral hydroxide layers and an exchangeable interlayer anion with water molecules.[1–4] Recently, anionic drug molecules have been intercalated into LDHs with an aim to determine the feasibility of using these intercalation compounds as materials for the storage, transport and ultimately controlled release of drug molecules.[5–7] Moreover, the intercalation of macrocyclic molecules into LDHs has great attractions to prepare new hybrid materials.[8–12]

Cyclodextrin (CD) is a cyclic oligosaccharide with truncated cylindrical molecular shape that possess a unique nonpolar cylindrical cavity (Figure 1). CDs and derivatives are very useful as microencapsulating agents for stabilizing volatile or toxic organic compounds. CDs are also expected as a new drug to check for adult diseases such as high blood pressure and diabetes. As the earlier studies on the intercalation of CD into inorganic layer materials, cationic modified β-CDs have been incorporated into montmorillonite and α-zirconium phosphates.[13,14] Recently, the intercalation of anionic modified β-CD into LDH by the ion-exchange method has been reported.[9,15–17] However, no information is currently available on the intercalation of natural CDs, nonanionic macrocyclic molecules, into LDH. Concerning the intercalation of nonionized compounds, our group has reported that the nonionized sugar/LDH nanocomposite can be prepared by the calcination–rehydration reaction (reconstruction method) using Mg–Al/$CO_3$/LDH.[18,19] In these studies, the intercalation of sugar for the LDH was found to be greatly influenced by hydrogen bond between hydroxyl group of the intercalated sugar and the LDH hydroxide basal layers. Since CD has many hydroxyl groups on upper and lower rims, we predict that there is a possibility of the intercalation of CDs by hydrogen bond similar to other sugar molecules. As a nonanionic CD has higher structure stability and safety for human body than anionic modified CD, the synthesized materials are expected as high safety medical supplies. In the present study, the intercalation of natural α-, β-, and γ-CDs in the interlayer of LDH has quantitatively been investigated by the reconstruction method using the calcined precursor of Mg–Al/$CO_3$/LDH.

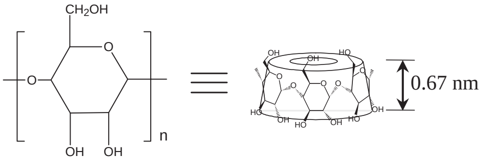

**Figure 1.** Structure of CD; $n = 6$ (α-CD), 7 (β-CD), and 8 (γ-CD).

The Mg–Al/$CO_3$/LDH (Mg/Al molar ratio = 2 and 3) was prepared by the standard aqueous coprecipitation method[3] at pH 10 and 60 °C. The pristine LDH was calcined at 500 °C for 2 h to prepare the Mg–Al oxide precursor. Each CD solution (50 $cm^3$) with various concentrations was placed in a 100 $cm^3$ Erlenmeyer flask together with the oxide precursor (0.2 g) and shaken in a water bath set at 25 °C under $N_2$ atmosphere. The resulting precipitate was washed with distilled water and dried under vacuum at 40 °C for 24 h. All the amount of CDs intercalated was measured for the solid product after dissolved in 0.1 mol/$dm^3$ HCl solution using total organic carbon analyzer (TOC).

The amount of CDs intercalated was found to increase with an increase in the equilibrium concentration of the solution. In all cases, the Freundlich adsorption equation, $\log(X/M) = 1/n(\log C) + \log k$, is applicable. $X$ (mmol) is the amount of CD intercalated, $M$ (g) the amount of the calcined precursor added, $C$ (mmol/$dm^3$) the equilibrium concentration of CD, $k$ (mmol/g-oxide) and $n$ (−) the constants. The Freundlich parameters for the intercalation of CDs (Mg/Al = 2 and 3) are indicated in Table 1. The $k$ value was higher than that expected. Name-

**Table 1.** Chemical composition of CD/LDHs (Mg/Al = 2) and Freundlich's parameters for CD intercalation (Mg/Al = 2 and 3)

| Chemical composition[a)] | CD/Al[a)] | Mg/Al = 2 | | Mg/Al = 3 | |
|---|---|---|---|---|---|
| | | $k$ (mmol/g-oxide) | $n$ (−) | $k$ (mmol/g-oxide) | $n$ (−) |
| $[Mg_{0.66}Al_{0.33}(OH)_{2.33}][(\alpha\text{-CD})_{0.052}\cdot 0.10H_2O]$ | 0.157 | 0.96 | 12.7 | 0.59 | 16.2 |
| $[Mg_{0.66}Al_{0.33}(OH)_{2.33}][(\beta\text{-CD})_{0.035}\cdot 0.09H_2O]$ | 0.106 | 0.53 | 31.5 | 0.42 | 11.4 |
| $[Mg_{0.66}Al_{0.33}(OH)_{2.33}][(\gamma\text{-CD})_{0.036}\cdot 0.13H_2O]$ | 0.109 | 0.71 | 19.6 | 0.41 | 12.5 |

a) Products were obtained in the CD solution of 20 mmol/$dm^3$ initial concentration.

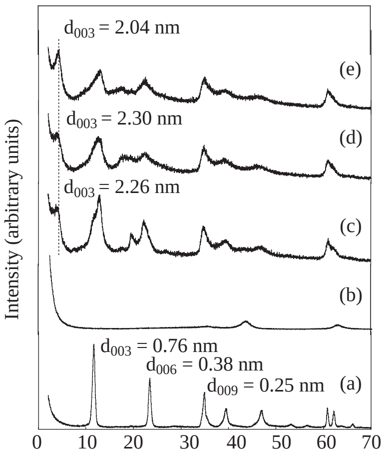

**Figure 2.** XRD patterns of (a) Mg–Al/$CO_3$/LDH, (b) Mg–Al oxide precursor, (c) Mg–Al/$\alpha$-CD/LDH, (d) Mg–Al/$\beta$-CD/LDH, and (e) Mg–Al/$\gamma$-CD/LDH.

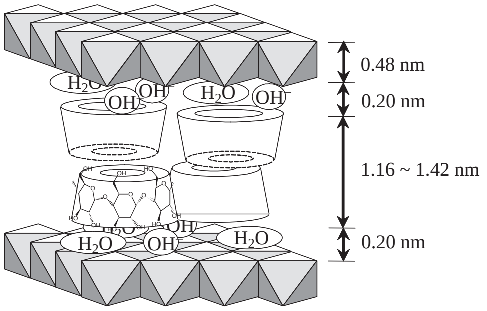

**Figure 3.** Schematic representation of possible CD oriented in interlayer space of Mg–Al LDH.

ly, the intercalated amount was considerably large in spite of nonanionic macrocyclic molecule. The amount of $\alpha$-CD intercalated was almost equal with anionic modified $\beta$-CD, and those of $\beta$- and $\gamma$-CDs were lower than that of anionic modified $\beta$-CD reported by the earlier resarchers.[17] The *n* value was quite high, which suggests that the CD concentration dependence was extremely small.

The oxide precursor (Mg/Al = 2) has slightly higher uptake ability than the oxide precursor (Mg/Al = 3) as indicated in Table 1. Because the former has a higher charge density in the hydroxide basal layer compare to the latter, influencing the cointercalation of hydroxide ion and water molecule. The intercalated amount by the oxide precursor was as follows: $\alpha$-CD > $\gamma$-CD $\geq$ $\beta$-CD. This result indicates that the intercalated amount is influenced by the molecular size and solubility in water. In the case of $\beta$-CD, it is known to have a strongly intermolecular hydrogen bond. Therefore, $\beta$-CD has smaller solubility in water and is comparatively difficult to form a hydrogen bond with the LDH basal layer.

The XRD patterns of the solid products obtained using the oxide precursor (Mg/Al = 2) and the CD solution of 20 mmol/$dm^3$ initial concentration are shown in Figure 2. In these XRD patterns, all the solid products were found to have the expanded LDH structures with a broad basal spacing of 2.0–2.3 nm. The peak intensity of the CD/LDHs was weaker than that of the pristine LDH.

The schematic representation of the CD/LDH is shown in Figure 3. Considering the thickness of the original brucite layer of 0.48 nm and the hydrogen-bonding space of 0.20 nm between the hydroxide basal layers and guest CD,[20,21] the gallery height was calculated as 1.16–1.42 nm. Therefore, CD molecules were speculated to arrange in a bilayer with their cavity axes perpendicular to the hydroxide basal layer by hydrogen bond. Hydroxyl ion was also cointercalated in the interlayer space, causing a broad XRD peak at about 2.0 nm. The FT-IR spectra and $^{13}C$ CP/MAS NMR spectra revealed that there were no changes in the CD structure before and after the intercalation.

The result of the deintercalation experiments confirmed that ca. 100% of CD in the CD/LDH (Mg/Al = 2 and 3) was deintercalated by shaking together with 500 mmol/$dm^3$ $Na_2CO_3$ solution for 24 h. Namely, the CD in the interlayer space of the resulting CD/LDH can be easily deintercalated by the ion exchange with carbonate ions. The XRD pattern of the deintercalated product showed that the pristine Mg–Al/$CO_3$/LDH with $d_{003} = 0.78$ nm was regenerated. According to the FT-IR spectra, the strong peak at 1375 $cm^{-1}$, the stretching mode of carbonate ion, clearly appeared after the deintercalation. This result shows that the cyclic system of intercalation and deintercalation of CD into LDH can be possible.

In summary, natural $\alpha$-, $\beta$-, and $\gamma$-CDs were easily intercalated in spite of nonionic macrocyclic molecules. The presence of hydroxyl group in CD molecule favors the intercalation driving force by the hydrogen bond with the hydroxide basal layer. In addition, CDs in the CD/LDHs were deintercalated by the ion exchange with carbonate ion, resulting the pristine Mg–Al/$CO_3$/LDH. Therefore, the Mg–Al LDH has considerable possibilities as a molecular container or carrier for not only anions, but also nonionic molecules.

### References

1 L. Ingram and H. F. W. Taylor, *Mineral. Mag.*, **36**, 465 (1967).
2 H. F. W. Taylor, *Mineral. Mag.*, **39**, 377 (1973).
3 S. Miyata, *Clays Clay Miner.*, **23**, 369 (1975).
4 S. Miyata and A. Okada, *Clays Clay Miner.*, **25**, 14 (1977).
5 J.-H. Choy, J.-S. Jung, J.-M. Oh, M. Park, J. Jeong, Y.-K. Kang, and O.-J. Han, *Biomaterials*, **25**, 3059 (2004).
6 S.-Y. Kwak, W. M. Kriven, M. A. Wallig, and J.-H. Choy, *Biomaterials*, **25**, 5995 (2004).
7 B. Li, J. He, D. G. Evans, and X. Duan, *Int. J. Pharm.*, **287**, 89 (2004).
8 T. J. Pinnavaia, M. Chibwe, V. R. L. Constantino, and S. K. Yun, *Appl. Clay Sci.*, **10**, 117 (1995).
9 H. Zhao and G. F. Vance, *Clays Clay Miner.*, **46**, 712 (1998).
10 V. Rives and M. A. Uibarri, *Coord. Chem. Rev.*, **181**, 61 (1999).
11 R. Sasai, D. Sugiyama, S. Takahashi, Z. Tong, T. Shichi, H. Itoh, and K. Takagi, *J. Photochem. Photobiol., A*, **155**, 223 (2003).
12 S. Sasaki, S. Aisawa, H. Hirahara, A. Sasaki, and E. Narita, *Chem. Lett.*, **33**, 790 (2004).
13 T. Kijima, J. Tanaka, and M. Goto, *Nature*, **310**, 45 (1984).
14 T. Kijima and Y. Matsui, *Nature*, **322**, 533 (1986).
15 H. Zhao and G. F. Vance, *J. Chem. Soc., Dalton Trans.*, **1997**, 1961.
16 H. Zhao and G. F. Vance, *J. Inclusion Phenom.*, **31**, 305 (1998).
17 J. Wang, M. Wei, G. Rao, D. G. Evans, and X. Duan, *J. Solid State Chem.*, **177**, 366 (2004).
18 S. Aisawa, H. Hirahara, K. Ishiyama, W. Ogasawara, Y. Umetsu, and E. Narita, *J. Solid State Chem.*, **174**, 342 (2003).
19 S. Aisawa, H. Hirahara, S. Takahashi, Y. Umetsu, and E. Narita, *Chem. Lett.*, **33**, 306 (2004).
20 V. Prevot, C. Forano, and J. P. Besse, *J. Mater. Chem.*, **9**, 155 (1999).
21 Q. Yuan, M. Wei, D. G. Evans, and X. Duan, *J. Phys. Chem. B*, **108**, 12381 (2004).

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