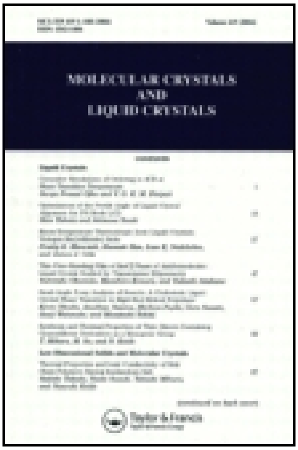

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Layered Double Hydroxide as Gene Reservoir

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Layered Double Hydroxide as Gene Reservoir

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Novel bio-/organic-inorganic hybrid compounds of deoxyribonucleic acid (DNA) and methotrexate (MTX)-layered double hydroxide are prepared by ion-exchange type intercalation reaction. The layered inorganic support, $Mg_2Al(NO_3)$-LDH, is at first obtained by coprecipitation in an aqueous solution, and then the interlayer NO_3^- anions are replaced by guest molecules such as methotrexate (an anticancer drug) and deoxyribonucleic acid (about 500 ~ 1000 base pairs), leading to form new bio-/organic-nanohybrids. Upon intercalating guest molecules into hydroxide layers, the basal spacing of LDH increases from 8.5 Å (NO_3^-) to 20.8 Å (MTX) and 23.9 Å (DNA), respectively. According to the X-ray diffraction and infrared spectroscopic analyses, it is found that the target molecules are safely preserved by hydroxide layers maintaining their chemical and structural properties.

Keywords: bio-/organic-inorganic hybrid; intercalation; gene and drug reservoir; encapsulation; layered double hydroxide

INTRODUCTION

Bio-/organic-inorganic nanohybrids, defined as solid monophasic or polyphasic composite materials between bio-/organic molecules and inorganic matrices on a nanometer scale, are of growing interest from fundamental and practical view-points[1,2]. Artificially organized bio-inorganic nanohybrids may provide a chance to understand biochemical reactions in the living world. In addition, they probably become key materials in developing of reservoirs or delivery carriers for biomolecules including DNA and drugs[3]. For such applications, the inorganic supports should act as not only a protector for the biomolecules against degradation but also a vehicle to transport biological species to target organs or cells. Since the layered double hydroxides (LDHs), so called 'anionic clays', consist of positively charged metal hydroxide layers and exchangeable interlayer anions (usually Cl^-, NO_3^-), various kinds of anionic bio-/organic molecules are expected to intercalate into hydroxide layers by simple anionic exchange route[4]. In the present study, our primary attention was paid to the intercalation of bulky bio-/organic molecules such as DNA and MTX to construct novel nanohybrids.

EXPERIMENTS

A pristine $Mg_2Al(NO_3)$-LDH was prepared by coprecipitation under N_2 atmosphere as follows[5]; the Mg/Al-hydroxide coprecipitate was formed when a mixed aqueous solution containing Mg^{2+} (0.024M, from $Mg(NO_3)_2$) and Al^{3+} (0.012M, from $Al(NO_3)_3$) ions was titrated into NaOH solution with vigorous stirring. And the solution pH and temperature were adjusted to 10 ± 0.2 and 25 ℃, respectively during the titration and aging processes. The resulting white precipitate was collected by centrifugation and washed with deionized water thoroughly. The MTX, a kind of useful drug in the management of acute lymphoblastic leukemia in children[6], and the herring testis DNA were selected as the gallery molecular species. The MTX-LDH was prepared using commercial sterile injectable solution of methotrexate (Yuhan Co., 50mg/2ml) without pre-treatment, but it was necessary to purify and shear the herring testis DNA (Sigma D-6898)[7]. The hybridization between LDH and guest molecule was achieved by simple anion exchange route. The pristine LDH was dispersed in deaerated aqueous solution containing excess of MTX or DNA, and this suspended solution was kept at 50 ℃ for 2 days. The resulting products were then isolated, washed, and used for the further analyses.

RESULTS AND DISCUSSION

The X-ray diffraction patterns for the pristine $Mg_2Al(NO_3)$-LDH and the organic- or bio-LDH hybrids are shown in Figure 1A. A diffraction peak at 8.7 Å for the pristine corresponds to the basal spacing of the NO_3^- interlayered $Mg_2Al(NO_3)$-LDH (Fig. 1A-(a)). Upon replacing the NO_3^- ions by guest molecules, the (00*l*) reflections shift to lower 2θ angle, indicating the further expansion of hydroxide layers due to the intercalation of bulky anionic bio-/organic molecules. Taking into account the thickness of brucite-like hydroxide layers (4.8 Å), the gallery heights for bio-/organic-LDH hybrids are estimated to be 16.0 Å (MTX) and 19.1 Å (DNA), respectively. In the MTX-LDH hybrid, the observed gallery height (16.0 Å) (Fig 1A-(b)) is smaller than the longitudinal molecular length (≈20 Å) of MTX, indicating that the interlayer MTX molecules are arranged in paraffin-like monolayers with the tilting angle of about 53° as illustrated in Fig. 2-(b). From the electrostatic interaction point of view, the attractive electrostatic interaction between the anionic terminal carboxylates and cationic hydroxide layers would be maximized in such a tilted monolayer stacking. Comparing the molecular thickness of DNA (~20.0 Å) with a double helical conformation, the observed interlayer separation (19.1 Å) for the DNA-LDH hybrid allows us to interpret that the DNA molecules are lying parallel to the basal plane of LDH.

According to the infrared spectra for the pristine (a) and bio-/organic molecules intercalated LDHs ((b) and (c)) as shown in Fig. 1B, the characteristic absorption bands of bio-/organic molecules are clearly observed even after immobilizing in LDH layers, suggesting that the guest molecules are stabilized between the layers with preserving their functionalities. The absorption peak at 1360 cm^{-1} (a), due to the stretching vibration of NO_3^- in the pristine LDH, disappears completely after ion-exchange reaction, reflecting the complete replacement of interlayer NO_3^- by biomolecules. On the other hand, the characteristic absorption bands, due to the amide II and aromatic ring stretching vibrations of interlayer MTX molecules[8], are appeared in the range of 1600 ~ 1300 cm^{-1} (Fig. 1B-(b)). The weak absorption bands in the range of 1800~1000 cm^{-1} for the DNA-LDH hybrid (Fig. 1B-(c)), are well assigned to the functional groups in bases of DNA such as aromatic C=C or C=N and conjugates C=O and –N–C=O as denoted in Fig. 1B[9].

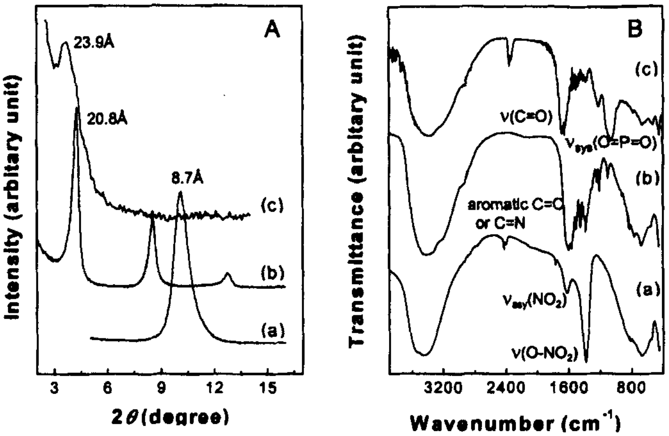

FIGURE 1 Powder X-ray diffraction patterns (A) and the infrared spectra (B) for the (a) pristine $Mg_2Al(NO_3)$-LDH, (b) MTX-LDH, and (c) DNA-LDH, respectively.

Based on these findings, we propose the structure models for the MTX-LDH and DNA-LDH nanohybrids as schematically illustrated in Fig. 2.

In this work, the functional bio-/organic molecules such as MTX and DNA could be intercalated successfully into LDH layers to form bio-/organic-inorganic nanohybrids. According to our very recent experimental results, these hybrids exhibit quite high physicochemical and biological stability, which provide a new way of LDH application as reservoir and delivery carrier of bio-molecules and drugs.

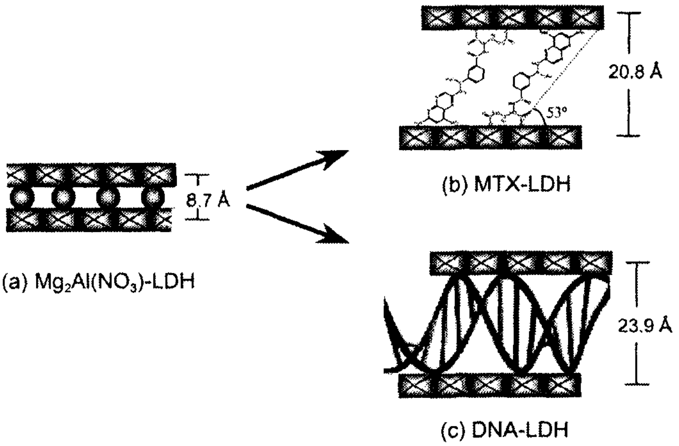

FIGURE 2 Proposed structure models for the bio-/organic molecule-LDH nanohybrids.

Acknowledgements

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References

[1] P. A. Bianconi, *Materials Chemistry – advances in chemistry series* (American Chemical Society, Washington, DC, 1995), p. 510.
[2] J. Portier, G. Campet, N. Treuil, A. Poquet, Y. I. Kim, S. J. Kwon, S. Y. Kwak, and J. H. Choy, *J. Korean Chem. Soc.* **42(4),** 487 (1998).
[3] J. H. Choy, S. Y. Kwak, J. S. Park, Y. J. Jeong, and J. Portier, *J. Am. Chem. Soc.* **121(6),** 1399, (1999).
[4] F. Cavani, F. Trifiro, and A. Vaccari, *Catal. Today,* **11,** 173 (1991).
[5] E. P. Giannelis, D. J. Nocera, and T. J. Pinnavaia, *Inorg. Chem.* **26,** 203 (1987).
[6] A. G. Gilman, L. S. Goodman, and A. Gilman, *The parmacological basis of therapeutics* (Macmilan Publishing Co., Inc., New York, 6th ed. 1980).
[7] J. Sambrook, E. F. Firsch, and T. Maniatis, in *Molecular Cloning. A Laboratory Manual,* (Cold Spring Harbor Lab. Press. 2nd ed. 1989).
[8] C. J. Pouchert, *The Aldrich library of Infrared spectra* (Aldrich Chemical, Milwaukes, 2nd ed.1975).
[9] H. H. Mantsch and D. Chapman, *Infrared spectroscopy of biomolecules* (Wiley-Liss, Inc. 1996).