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Study on Intercalative Nanohybrid of Cordycepin in Layered Double Hydroxide

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Abstract: A novel negatively charged biomolecule-cordycepin has been intercalated within the gallery spaces of [Mg-Al-NO_3]. Results of TEM, PXRD and FT-IR spectroscopy confirmed that cordycepin could be intercalated into [Mg-Al-NO_3] interlayers as the charge-compensating species. Initial studies suggest that the new bioinorganic nanocomposite may be used as a novel inorganic reservoir or carrier of pharmaceutically active compounds.

Keywords: Layered double hydroxide, nanohybrid, cordycepin, intercalate.

Cordycepin, a nucleoside analogue 3'-deoxyadenosine, has been reported to have a broad spectrum of biological activity, such as antibacterial [1] and antifungal activity [2], antiviral activity against HIV-1 *in vitro* [3], and inhibition of RNA [4]. How to protect cordycepin from deamination by the enzyme adenosine deaminase (ADA) and retain its activity is the urgent problem. We hope to find a reservoir or carrier for cordycepin to study its property and may be used in target therapy. Layered double hydroxide (LDH) represented by the general formula $[M^{II}_{1-x}M^{III}_{x}(OH)_2]^{x+}X^{m-}_{x/m} \cdot nH_2O$, abbreviated by: $[M^{II}$-M^{III}-X] [5], where M^{II} is a divalent cation such as Mg, Ni, or Zn, M^{III} is a trivalent metal ion such as Al, Cr, Fe, or Ga, are now well established owing to their intercalation ability of anionic species and other physicochemical properties for application as anion adsorbents, medicine stabilizers, ion-exchangers, ionic conductors, catalysts, catalyst supports and DNA reservoirs [5-8]

[Mg-Al-cordycepin]: [Mg-Al-NO_3] was prepared using a non-steady co-precipitation method [9]. Under N_2 atmosphere, a mixed solution of magnesium and aluminum nitrate was prepared in the molar ratio of 2:1. Then 6% aqueous ammonia was added to the solution. The final pH value was 10.0. The precipitate was aged for 1 h and then washed with deionized water. After that, the filter cake was peptized at 80℃, forming the positive sol. Dense suspensions of [Mg-Al-NO_3] was diluted to 0.5 wt % solid content, and reacted with 0.04 mol/L aqueous solutions of cordycepin at 65℃ for

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4 days, then washed with deionized water, finally dried in air at 60℃.

Transmission electron microscopy (TEM) analysis was performed using a JEM-100CX Ⅱ electron microscope. Powder X-ray diffraction (XRD) patterns were recorded using D/max-YB diffractometer with Cu K α radiation. CZE separations were carried out with a Beckman P/ACE^{TM} system MDQ (Fullerton, CA, USA) utilizing system software version 2.2 for control and data collection. FTIR spectra were recorded in the region 4000-400 cm^{-1} on a Nicole t 50X infrared spectrophotometer.

Figure 1 TEM image of [Mg-Al-Cordycepin]

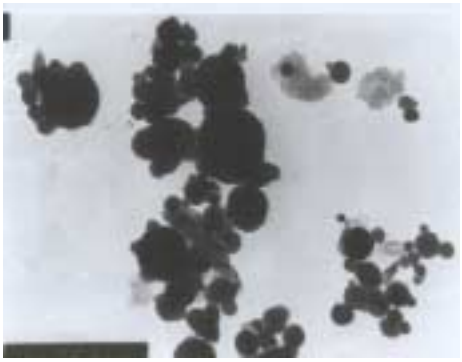
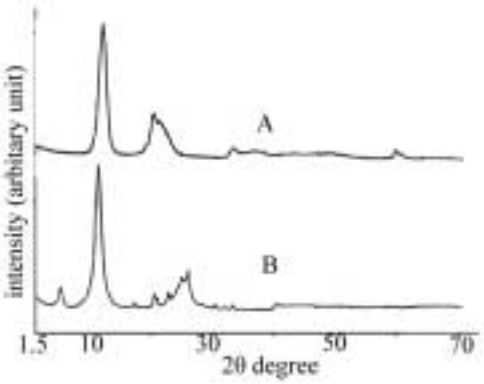


Figure 2 XRD patterns of A) Mg-Al-NO_3], B)[Mg-Al-Cordycepin]



The TEM micrographs for sample [Mg-Al-Cordycepin] are shown in **Figure 1**. [Mg-Al-NO_3] consisted of hexagonal particles approximately 100–120 nm in length [9]. [Mg-Al-Cordycepin] showed some interesting morphological features comparing with [Mg-Al-NO_3]. It was composed of sphere approximately 50-350 nm in diameter.

The XRD data for the LDH samples containing nitrate, cordycepin interlayer species are shown in **Figure 2**. The peak which occurred at approximately 10° (2θ) for [Mg-Al-NO_3] was attributed to the reflections from the (003) family of crystallographic planes (**Figure 2 A**). When cordycepin inserted into the LDH gallery, the d_{003} reflection shifted from 8.4 Å for [Mg-Al-NO_3] to 16.2 Å for [Mg-Al-(Cordycepin)] (**Figure 2 B**).

In the **Figure 3**, the absorption bands at 2800-3000 cm^{-1} and 1200-1400 cm^{-1} suggested the characteristic CH stretching vibration and CH sector mutation vibration of glucoside, respectively. The two absorption bands at 1000-1100 cm^{-1} corresponded to the furan group in cordycepin, and the band at 895 cm^{-1} demonstrated that the glycosidic bond is β type. The characteristic bands of the aromatic C=C and C=N at about 1700-1570 cm^{-1} are also clearly observed as shown in **Figure 3 B**.

The cordycepin-LDH hybrid was dissolved in deionized water and separated by capillary zone electrophoresis. The CZE parameters were set as Ling method [10] except while the voltage was increased to 25 kV. The pristine LDH has no UV absorption, it was baseline separated in 10 min shown as **Figure 4 C**. The intercalated sample exhi-

Figure 3 FTIR spectra of A) [Mg-Al-NO_3], B) [Mg-Al-(Cordycepin)]

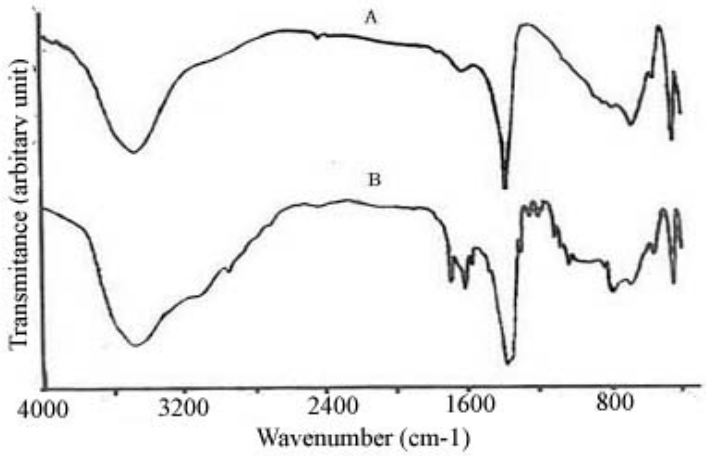
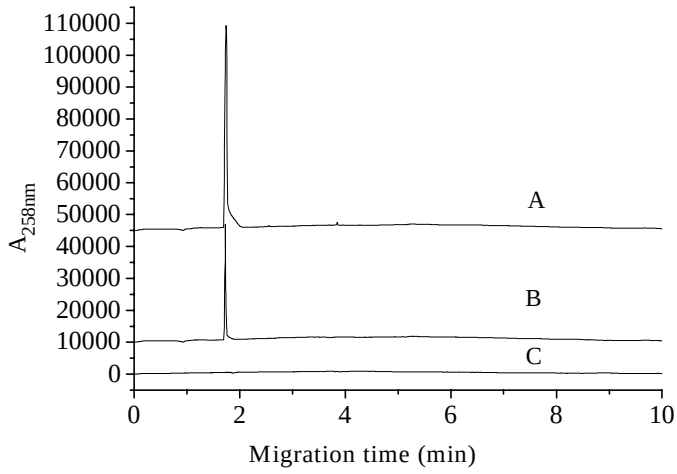


Figure 4 CZE maps of A) [Mg-Al-(Cordycepin)] after adding the standard cordycepin, B) [Mg-Al-(Cordycepin)], C) [Mg-Al-NO_3]



bited characteristic absorption bands in 258 nm which is attributed to $\pi \rightarrow \pi^*$ or $n \rightarrow \pi^*$ transition in the adenine group (**Figure 4 B**). The migration time of cordycepin-LDH was 1.757 min, peak was identified by spiking with the standard of cordycepin (**Figure 4 A**). The results strongly suggested that cordycepin were intercalated in the LDH and preserved its integrity.

This work has clearly demonstrated that cordycepin had been exchanged with the nitrates in the gallery of LDH. The FTIR and XRD results showed that the [Mg-Al-NO_3] could accommodate cordycepin in the interlayer space and got a bigger

basal spacing. Cordycepin also retained its integrity determined by CZE. It is expected that inorganic LDH could be a good host lattice for cordycepin reservoir for using in the target therapy.

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