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# DL-mandelic acid intercalated Zn-Al layered double hydroxide: A novel antimicrobial layered material

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ABSTRACT

DL-mandelic acid (MA) has been intercalated into Zn-Al layered double hydroxide (LDH) by an anion-exchange reaction. After intercalation of MA anions, the basal spacing of the LDH increased from 0.75 to 1.46 nm, suggesting that the MA anions were successfully intercalated into the interlayer galleries of the LDH. The structure and the thermal stability of the samples were characterized by XRD, FT-IR, TG-DTA. Studies of MA release from ZnAl-MA-LDH in hydrochloric solution (pH = 4) imply that ZnAl-MA-LDH is a better controlled release system than pure MA. Meanwhile, the mechanisms of slow release were assessed by using four commonly kinetic models. Finally, the antimicrobial activity of ZnAl-MA-LDH was tested against two kinds of bacteria and a fungus. The study confirms that the mandelic ions intercalated LDHs have the potential application as a slow release preservative in the future.



## 1. Introduction

During the past few decades, the contamination by microorganisms has become an urgent problem to be tackled either by academic or applied. This phenomenon affects many areas, such as food packaging, water purification systems, medical devices, healthcare products and more [1–3]. Researchers are attempting to develop new and effective antibacterial agents. Antimicrobial agents are those materials capable of killing pathogenic microorganisms and they are generally used for the water and soil sterilization, or as antimicrobial drugs or as food preservatives [4].

DL-mandelic acid (MA), an alpha-hydroxy acid derived from the hydrolysis of an extract of bitter almonds, has been studied extensively for its possible uses in healthcare products, such as photoaging, irregular pigmentation, and antimicrobial [5]. The chemical structure of MA is shown in Fig. 2. Unfortunately, MA is very unstable to light, heat and base, resulting in decomposition to biologically inactive compounds [6]. On the other hand, human body requires only a very small amount of MA for physiological functions. High concentration of MA is irritating to the skin and easy to produce allergic reactions [7]. A drug delivery and controlled release system is designed to a more sophisticated drug administration method. Therefore, an effective solution is to choose an appropriate inorganic material as the host matrix to overcome such problems. These systems can not only avoid direct contact with the skin to reduce irritation, but also improve the thermal and optical stability of MA. More importantly, such systems utilize carriers that slowly release their contents in order to maintain antimicrobial concentrations at the desired levels for a longer period of time.

Layered double hydroxides (LDHs), whose structure can be generally expressed as $[M^{2+}_{1-x}M^{3+}_{x}(OH)_2]^{x+}(A^{n-})_{x/n}\cdot mH_2O$ (where $M^{2+}$ are divalent and $M^{3+}$ trivalent metals, respectively, and $A^{n-}$ an anion), are 2D layered materials consisting of positively charged host layers with charge balancing guest anions [8]. One of the most interesting features of these materials is their role as a host matrix for the orientation and dispersion of interlayer anions. Therefore, LDHs show a very broad application in medicine, cosmetics, adsorption, catalysis, photochemistry, filler material and optoelectronic materials [9–13]. A few antibacterial agents have been prepared from LDHs. Supun Samindra et al. have encapsulated curcuminoids into the LDH and studied the release characteristics of curcumin from the nanocomposites [14]. In recently, This research group has also reported the potential of curcuminoids (SEC)-LDH as an antimicrobial nanohybrid [7]. Jayoda Perera et al. have also reported citric acid intercalated layered double hydroxides nanohybrids and have verified its anti-fungal activity [15]. Latip et al. intercalated anionic ciprofloxacin, which is a broad spectrum antibiotic compound in therapeutic, into layered zinc hydroxide nitrate(LZH) and the sustained release and the enhanced toxicity effect were identified [16].

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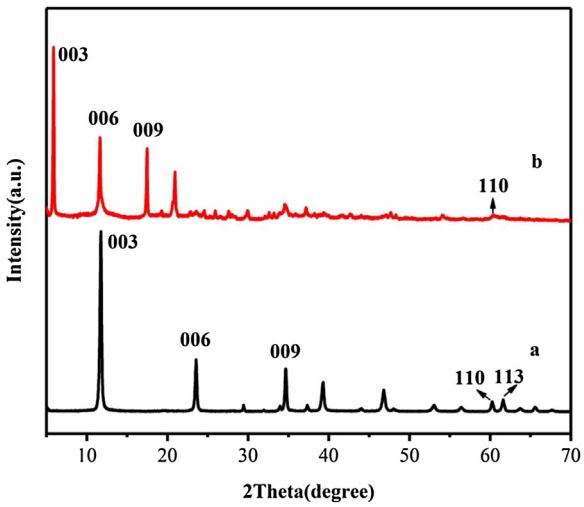


**Fig. 1.** XRD patterns of (a) ZnAl-LDH precursor and (b) ZnAl-MA-LDH.

The aim of this research work was to store the MA anions (MA) in the LDHs interlayer region. For this purpose, ZnAl-LDH was chosen as lamellar host because for its good biocompatibility [17]. Al and Zn are metals largely used both in pharmaceutical and cosmetic formulations, the first as salt for astringent activity, the second as oxide (ZnO) for sun photoprotection and antimicrobial activity [18,19]. In this paper, MA was intercalated into ZnAl-$CO_3$-LDH to improve its thermostability, photostability and release time. Furthermore, the quantity and the kinetics of MA release from the host materials were investigated. Finally, antibacterial activity of ZnAl-MA-LDH and MA have been studied and confirmed. The studies suggest that ZnAl-MA-LDH composites have potential applications as safe and effectively antimicrobial materials.

## 2. Experimental

### 2.1. Synthesis and characterization of ZnAl-MA-LDH

#### 2.1.1. Materials

Analytical grade $Zn(NO_3)_2{\cdot}6H_2O$, $Al(NO_3)_3{\cdot}9H_2O$, NaOH, $NaCO_3$ and MA were purchased from Sinopharm Chemical Reagent Co., Ltd. and used without further purification. The deionized and decarbonated water was used in all the preparation processes.

#### 2.1.2. Preparation of ZnAl-$CO_3$-LDH

The ZnAl-$CO_3$-LDH precursor was prepared by using a method involving separate nucleation and aging steps [20]. 100 mL of an aqueous solution A containing 23.80 g (0.08 mol) $Zn(NO_3)_2{\cdot}6H_2O$ and 15.00g(0.04 mol) $Al(NO_3)_3{\cdot}9H_2O$ and 100 mL aqueous solution B consisting of 7.68 g (0.19 mol) NaOH and 8.48g(0.08 mol) anhydrous $Na_2CO_3$ were added simultaneously under vigorous stirring. The resulting reactant was aged in an autoclave at 100 °C for 6 h. The precipitate was separated

by repeated cycles of centrifugation/washing with deionised water until the pH value of the washings was less than 8. Part of the solid was dried at 60 °C for 18 h for characterization purposes and the remainder was stored (solid content of LDHs in the wet product was ca. 30 wt%) [21].

#### 2.1.3. Preparation of ZnAl-MA-LDH

The MA anion intercalated LDH (ZnAl-MA-LDH) was synthesized by anion-exchange using ZnAl-LDH precursor. 3 g ZnAl-$CO_3$-LDHs (calculated as $Zn_4Al_2(OH)_{12}CO_3{\cdot}4H_2O$, 10 g of the wet precursor obtained above) was decentralized in a 250 mL flask containing 50.0 mL ethylene glycol and the slurry was stirred vigorously. 50.0 mL ethylene glycol of a 2.81 g MA ($MA/CO_3^{2-}$ = 4:1) was added drop-wise into the slurry in air followed by aging at 150 °C for 2 h. The resulting precipitate was centrifuged, thoroughly washed, and dried at 60 °Cfor 18 h.

#### 2.1.4. Characterization

The X-ray diffraction (XRD) patterns of the samples were recorded on an X-ray powder diffractometer (Bruker D2, Karlsruhe, Germany) under the conditions: 30 kV, 10 mA, Cu Ka radiation (λ = 1.5406 A°), with a scanning rate of 5° $min^{-1}$ in the 2$\theta$ range from 5° to 70°. FT-IR spectra were recorded on a Thermo Scientific Nicolet IS 10 instrument in attenuated total reflectance (ATR) mode. CHO analysis was conducted using a vario EL cube. The content of Zn and Al were analyzed by inductively coupled plasma (ICP) emission spectroscopy using solutions prepared by dissolving the samples in 1% $HNO_3$ and 2% HCL. Thermo-gravimetric (TG) analysis was performed on TGA Q5000IR instrument in the temperature range 50–700 °C with a heating rate of 10 °C $min^{-1}$ in air. Scanning electron microscopy (SEM) images were obtained using a Hitachi S-4700 scanning electron microscope operating at 20 kV. Varian CARY-60 single beam scanning spectrophotometer was used for the MA release studies. The color difference (ΔE) of materials aged under UV light was determined in terms of CIE 1976 L*a*b* using a precision colorimeter NR 145 [22].

### 2.2. Release studies of ZnAl-MA-LDH

The release of the MA-LDH (~0.108 g mandelic acid) and pure mandelic acid(0.108 g) were placed in a dialysis membrane bag containing 200 mL hydrochloric solution (pH = 4). The solution was stirred at room temperature and the releasing suspension (4.00 mL) was collected at predetermined time. The concentration of released MA was quantified using the UV–vis spectrophotometer at 257 nm, corresponding to the typical absorption peak of MA.

### 2.3. Determination of antimicrobial activity

The antimicrobial activity of pure MA and ZnAl-MA-LDH were tested against two bacterial species (*Escherichia coli*(ATCC8739),

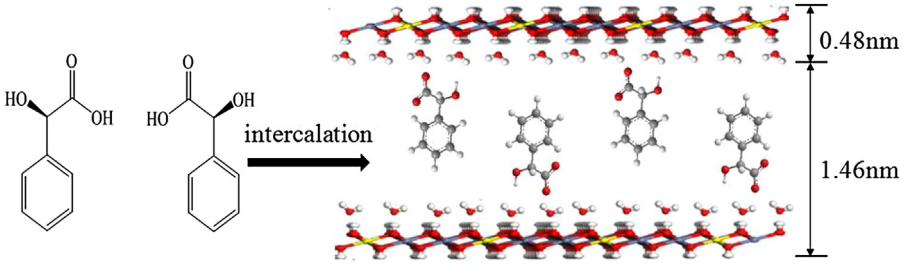


**Fig. 2.** Chemical structural formula of DL-mandelic acid and the structure model of ZnAl-MA-LDH.