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Studies on the intercalation of naproxen into layered double hydroxide and its thermal decomposition by in situ FT-IR and in situ HT-XRD

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Abstract

Layered double hydroxides, novel anionic clay, meet the first requirement as inorganic matrices for encapsulating functional drugs or biomolecules with negative charge in aqueous media. In this study, naproxen has been intercalated into Mg–Al layered double hydroxide by the methods of ion exchange. The structure and composition of the intercalated material have been studied by X-ray diffraction (XRD), UV–vis spectroscopy and inductively coupled plasma emission spectroscopy. A schematic model has been proposed. Furthermore, in situ Fourier transform infrared spectroscopy, in situ high-temperature XRD, and thermogravimetry (TG) have been used to characterize the thermal decomposition of the hybrid material. It has been found that the thermal stability of the intercalated naproxen is significantly enhanced compared with the pure form before intercalation, which suggests that this drug-inorganic layered material may have prospective application as the basis of a novel drug delivery system.

Keywords: Naproxen; Layered double hydroxide; Intercalation; Thermal decomposition; In situ FT-IR; In situ HT-XRD

1. Introduction

Layered double hydroxides, which are widely known as host–guest materials, have received considerable attention due to their special intercalation properties. LDHs can be represented by the general formula $[M^{II}_{1-x}M^{III}_x(OH)_2]^{x+}(A^{n-})_{x/n}\cdot mH_2O$ [1], where M^{II}, M^{III} are di- and tri-valent metal cations, respectively; A^{n-} is an exchangeable inorganic or organic anion, and the x value, i.e., the charge density, is equal to the molar ratio $M^{III}/(M^{II}+M^{III})$. LDHs consist of positively charged metal hydroxide layers, in which the anions (along with water) are stabilized in order to compensate the positive layer charges. Various kinds of inorganic or organic anions have been introduced between the hydroxide layers by simple ion-exchange reaction or coprecipitation. LDHs are now well established as excellent anion-exchange materials and their extensive intercalation chemistry has widespread applications in areas such as heterogeneous catalysis [2,3], optical materials [4,5], biomimetic catalysis [6,7], separation science [8,9], DNA reservoirs [10], and medical science [11,12].

Naproxen, (+)-6-methoxy-α-methyl-2-naphthalene acetic acid (as shown in Fig. 2A), is a non-steroidal anti-inflammatory drug frequently used in the treatment of rheumatic diseases and it is characterized by low water solubility. It is not easily transformable into the amorphous state by freeze drying or spray drying. In order for drug therapy to be most effective, the desired pharmacological response must be obtained at the target without harmful interactions at other sites [13]. This requires the correct amount of drug to be absorbed into the body and transported to the target with control of the drug rate input in order to produce the correct dosage. In previous researches, the binding of naproxen

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to hydrophilic organic molecules such as polyvinylpyrrolidone [14,15] and cyclodextrins [16,17] has been widely studied by different methods. These complexes with drugs are formed in order to improve or enhance their stability, solubility, dissolution rate, bioavailability, etc.

Recently, anionic drug molecules have been intercalated into a variety of LDHs [11,12], with an aim to determine the feasibility of using these intercalation compounds as materials for the storage, transport and ultimately controlled release of the drug. The release properties of the drugs have been investigated by adding their intercalation compounds to samples of simulated gastrointestinal and intestinal fluid. Khan et al. [11] have intercalated a series of pharmaceutically active compounds including diclofenac, gemfibrozil, ibuprofen, and naproxen ect., into LDHs, and studied the release behavior of the drugs. It has been found that release of the drugs in gastrointestinal fluid (pH 4) was instantaneous; however, release in simulated intestinal fluid was much slower (pH 7). So there is a prospective approach of LDHs for the storage than subsequent controlled release of bioactive agents.

However, the thermal stability of the intercalated drugs has not been investigated, and it is a very important aspect which should be considered of using LDHs in drug delivery system.

Ex situ X-ray diffraction (XRD) and thermal analysis have been used to investigate the decomposition process of LDH [18,19]. Ex situ studies have the disadvantage that mixed oxides derived from hydrotalcites may rehydrate and reconstruct to the original structure at ambient temperature in air. In situ infrared spectroscopy has been used to provide structural information about the dehydroxylation and decarbonation process in LDHs [20–22]. Pérez-Ramírez et al. [23] have studied the thermal decomposition of Co–Al and Ni–Al hydrotalcites by in situ Fourier transform infrared (FT-IR) and laser Raman spectroscopies. Furthermore, high-temperature XRD (HT-XRD) has been used as one of the few in situ techniques to investigate the decomposition and reconstruction mechanism over Mg–Al–CO_3 LDHs [24], for the thermally metastable phases which are not recognized by conventional XRD can be determined by in situ HT-XRD technique.

In the present work, the thermal decomposition process of naproxen-intercalated LDH has been investigated by in situ FT-IR, in situ HT-XRD and thermogravimetry (TG). To the best of our knowledge, combined application of in situ techniques to investigate the decomposition of drug molecule intercalated LDH has not been reported elsewhere. Therefore, this work provides an understanding of the thermal stability of drug-LDH hybrid for prospective application as the basis of a novel drug delivery system.

2. Experimental

2.1. Reagents

All chemicals including $Mg(NO_3)_2 \cdot 6H_2O$, $Al(NO_3)_3 \cdot 9H_2O$, NaOH, $NaNO_3$, were analytical grade. Naproxen was purchased from Aldrich, and the others from the Beijing Chemical Plant Limited.

2.2. Synthesis of naproxen/LDH

The precursor $[Mg_4Al_2(OH)_{12}](NO_3)_2 \cdot 4H_2O$, (Mg/Al–$NO_3$LDH) was synthesized by a procedure similar to that described previously [1]. A solution of $Mg(NO_3)_2 \cdot 6H_2O$ (32.0 g, 0.125 mol) and $Al(NO_3)_3 \cdot 9H_2O$ (11.7 g, 0.062 mol) in deionized water (200 cm^3) was added dropwise over 2 h to a solution of NaOH (12.5 g, 0.310 mol) and $NaNO_3$ (18.2 g, 0.210 mol) in water (250 cm^3). The mixture was held at 100°C for 36 h. The precipitate was separated by centrifugation, washed with water and dried at 60°C for 8 h.

The naproxen/LDH was obtained by the method of ion exchange. A solution of naproxen (1.5 g, 6 mmol) in deionized water (50 cm^3) was added to a suspension of Mg/Al–NO_3 LDH (1.0 g, ca. 2 mmol) in water (50 cm^3), and the solution pH was kept 8.0 by adding 0.1 mol/L NaOH solution during reaction. The mixture was heated at 70°C under a nitrogen atmosphere for 39 h (the product remained the same when the time was longer than 39 h, so this reaction time was taken). The product was washed extensively with water, centrifuged and dried at 60°C for 8 h.

2.3. Characterization

In situ HT-XRD measurements were performed on a Rigaku D/max 2500VB2+/PC diffractometer in vacuum, using Cu$K\alpha$ radiation ($\lambda = 0.154$ nm) at 40 kV, 30 mA. The samples as unoriented powders were scanned in steps of 0.02° in the 2θ range 2–70° using a count time of 4 s per step.

In situ FT-IR spectra were recorded using a Nicolet 60sxb spectrometer in the range 4000 between 400 and 2 cm^{-1} resolution. The spectra were obtained every 10° with a heating rate of 5°C/min under the protection of a nitrogen atmosphere. The standard KBr disk method (1 mg of sample in 100 mg of KBr) was used.

TG analysis was measured on a PCT−1A thermal analysis system with a heating rate of 10°C/min under air atmosphere.

Elemental analysis was performed with a Shimadzu ICPS−7500 instrument. C, H, N content was determined using an Elementarvario elemental analysis instrument.

3. Results and discussion

3.1. Structure of naproxen/LDH

The conversion of Mg/Al–NO_3 LDH into the naproxen form has been obtained by an anion-exchange process as described in the experimental part. The XRD patterns of the precursor Mg/Al–NO_3 LDH and the naproxen intercalated LDH are shown in Fig. 1. In each case, the reflections can be indexed to a hexagonal lattice with $R\bar{3}m$ rhombohedral symmetry, commonly used for the description of the LDH structures. Table 1 lists the basal spacing and lattice parameters. The value of the lattice parameter a is a function of the average distance between the metal ions and thus, since Al^{3+} is smaller than Mg^{2+}, gives an indication of the Mg^{2+}/Al^{3+} ratio. The value a of the intercalation product is almost identical to that of the precursor, indicating that there is no significant change in Mg^{2+}/Al^{3+} ratio on intercalation of naproxen. The Mg/Al–NO_3 LDH precursor has an XRD pattern similar to that reported previously [25,26], with an interlayer spacing (d_{003}) of 0.854 nm. After intercalation of naproxen, the interlayer distance increased to 2.347 nm. Since the thickness of the LDH hydroxide basal layer is 0.480 nm [26], the gallery height, i.e., the interlayer distance increased to 1.867 nm.

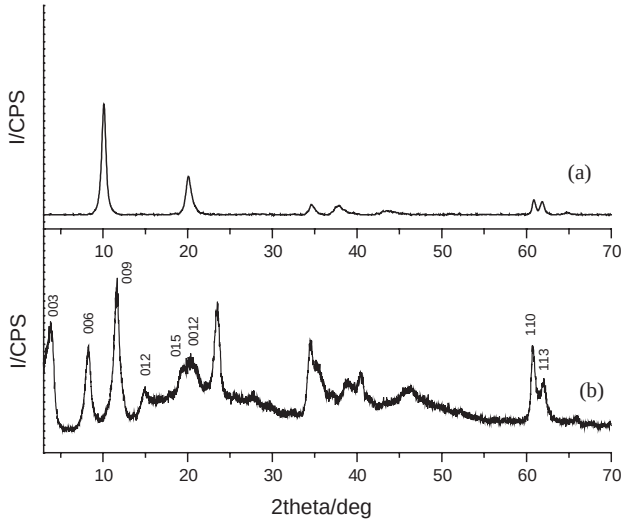

Fig. 1. XRD patterns of: (a) Mg/Al–NO_3 LDH, and (b) naproxen/LDH.

Table 1
Lattice parameters of Mg/Al–NO_3 LDH and naproxen/LDH

Lattice parameter (nm)	Mg/Al–NO_3LDH	Naproxen/LDH
d_{003}	0.854	2.347
d_{006}	0.436	1.072
d_{009}	0.257	0.758
d_{110}	0.152	0.152
Lattice parameter a	0.303	0.304
Lattice parameter c	2.561	7.041

As shown in Fig. 1b, the strongest peak of naproxen/LDH is the (009) reflection, while the (003) reflection has the strongest peak intensity in the diffraction pattern of the LDH precursor. This is possibly related to the presence of a CO_3^{2-} LDH impurity phase which is often observed even when intercalation reactions are carried out under nitrogen. The peak around 11.7° may be a superposition of the (003) reflection of CO_3^{2-} LDH and the (009) reflection of naproxen/LDH, accounting for its enhanced intensity. The peak around 23.5°C can be assigned to the (006) reflection of CO_3^{2-} LDH. This will be discussed further below.

The value of pKa of naproxen is 4.2 [27]. Based on the experimental condition for naproxen/LDH with the ion-exchange solution pH at 8.0, the value of distribution coefficient of monovalent anion (δ) can be calculated as $\delta > 99\%$, thus the naproxen exists mainly as monovalent anion during intercalation. The length of naproxen anion is 1.220 nm, calculated by the method of molecular mechanics. Comparison of the length of naproxen anion with a gallery height of 1.867 nm suggests that the naproxen ions are accommodated in the interlayer region as a monolayer of species partially superimposed with their naphthalene ring perpendicular to the layer plane and with the carboxyl of individual anions attaching alternately to the upper and lower hydroxide layers. The guests strongly interact with each other via $\pi-\pi$ interactions of naphthalene rings, which supply sufficient energy for the observed large interlayer expansion. Besides, hydrogen bonding area (calculated from the result of in situ HT-XRD below) exists between the guest anions and the host layers. A schematic representation of the probable arrangement for naproxen/LDH is shown in Fig. 2B.

3.2. Chemical composition of naproxen/LDH

Elemental analysis data show that the chemical composition of naproxen/LDH is $Mg_{0.73}Al_{0.33}(OH)_2(C_{14}H_{13}O_3)_{0.20}(CO_3)_{0.13}\cdot 0.9H_2O$. It can be seen that all of the NO_3^- anions have been exchanged by naproxen, while some CO_3^{2-} containing LDH coexist with the naproxen/LDH, which is consistent with the XRD results and will be further confirmed by in situ IR and HT-XRD results. The total exclusion of carbonate from the interlayer space of LDHs is known to be difficult in spite of the intercalation reaction under nitrogen atmosphere, which can be readily explained on the basis of the favorable lattice stabilization enthalpy associated with the small and highly charged CO_3^{2-} anions [28]. The Mg/Al molar ratio of the product is a little larger than the theoretical molar ratio (Mg/Al = 2), which may be related to the deviation between experimental and theoretical values, or to the determination stochastic error in elemental analysis.

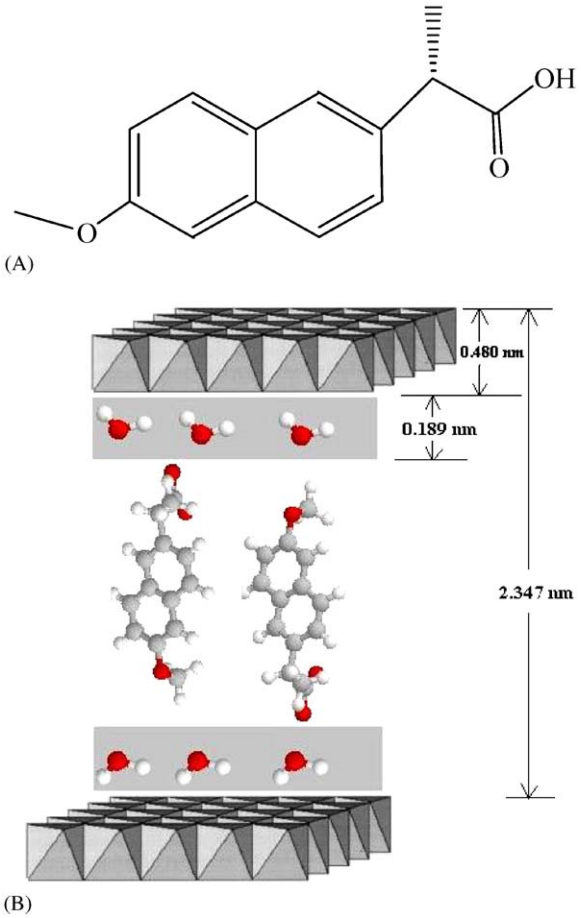

Fig. 2. Structure of naproxen (A), and a schematic representation of the possible arrangement for naproxen/LDH (B).

3.3. Thermal decomposition monitored by in situ FT-IR

Infrared spectra recorded at room temperature, as well as during the decomposition of naproxen, naproxen/LDH in the temperature range 20–300°C and 20–450°C are presented in Figs. 3 and 4, respectively. Naproxen was investigated as a reference sample in this section.

3.3.1. Analysis of as-synthesized samples

As shown in Fig. 3, in the infrared spectrum at room temperature of the as-synthesized naproxen, broad strong adsorption band at 3191 cm^{-1} is observed, which can be attributed to the OH combination stretching vibrations of hydroxyl groups and physically adsorbed water [25]. Adsorption bands at 2964 and 2941 cm^{-1} are due to the asymmetric and symmetric stretching vibrations of $-CH_3$, respectively. Bands at 1687, 1597 and 1506 cm^{-1} are assigned to adsorption of skeletal stretching vibrations of aromatic rings [29]. 1726, 1394 and 1260 cm^{-1} are attributed to $\nu_{C=O}$ stretching vibration, −COOH bend/stretch and stretch/bend vibrations, respectively. Bands at 1026 and 857 cm^{-1} are assigned to absorption of C–O–C in naproxen, while 1173 cm^{-1} is due to the absorption of C–O.

Fig. 4 displays the infrared spectra of naproxen/LDH. The very broad adsorption band centered at 3464 cm^{-1} at room temperature is assigned to the OH stretching vibration of hydroxyl groups, water molecules in the interlayer and physically adsorbed water [25]. The intercalated naproxen and OH groups of the LDH

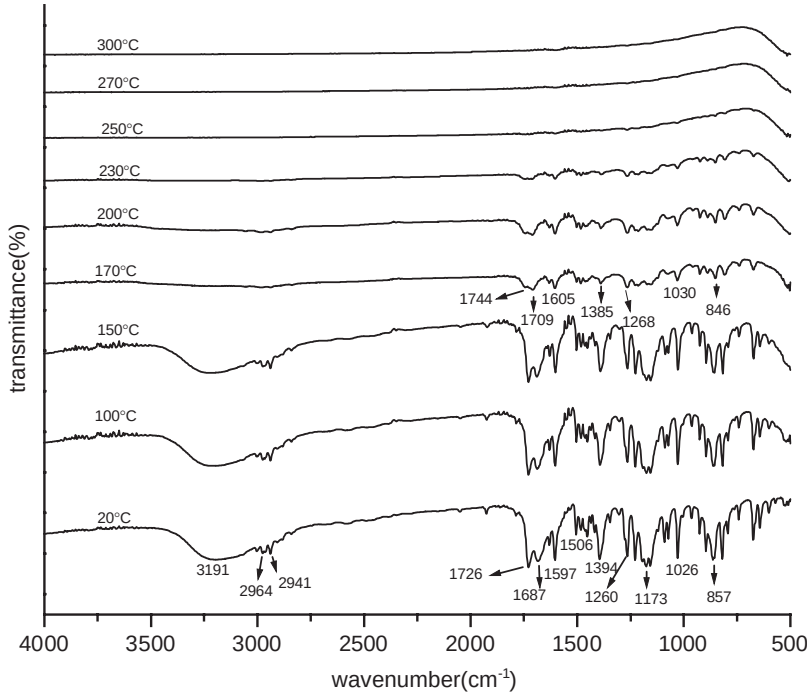

Fig. 3. In situ FT-IR spectra for the thermal decomposition of naproxen.

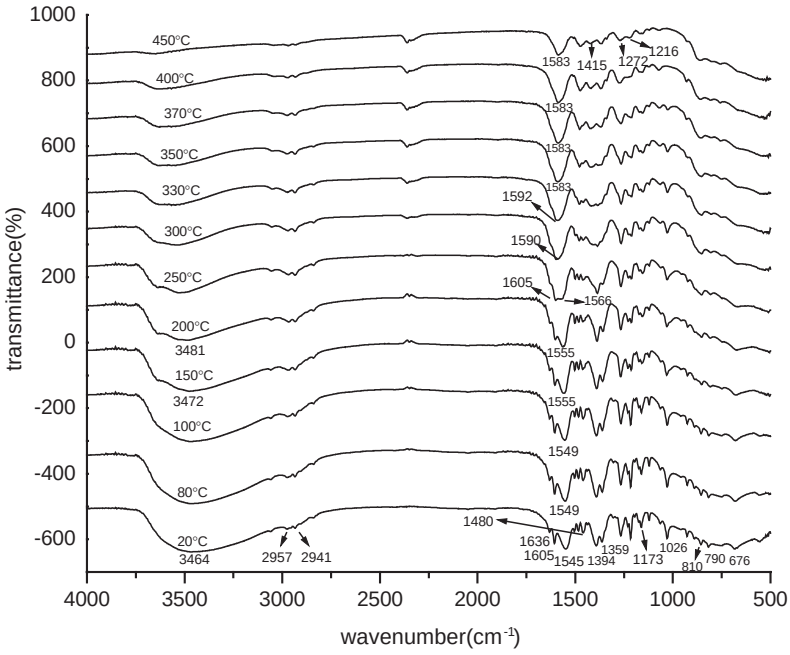

Fig. 4. In situ FT-IR spectra for the thermal decomposition of naproxen/LDH.

layers form a strong hydrogen bonding resulting in a shift of the OH band to higher frequency compared with pristine naproxen (3191 cm^{-1}). The asymmetric and symmetric stretching vibrations of $-CH_3$ are observed at 2957 and 2941 cm^{-1}. Bands at 1545 and 1394 cm^{-1} are attributed to the asymmetric (v_{as}) and symmetric (v_s) stretching vibrations of carboxylate $-COO^-$, respectively. Compared with naproxen, the absorption of $v_{C=O}$ moves to low frequency due to the interaction between guest naproxen and host layers. Prevot et al. [30] have reported that the difference $\Delta v = v_{as} - v_s$ gives information about the symmetry of the interaction between the carboxylated and hydroxylated layers. Since Δv value is similar to that of naproxenum natrium in this study, the naproxen anions are intercalated in the interlayer space and bound by electrostatic interaction as well as hydrogen bonding to the host matrix. Bands at 1636, 1605 and 1480 cm^{-1} are assigned to adsorption of skeletal stretching vibrations of aromatic rings [29]. Bands at 1026 and 810 cm^{-1} are assigned to absorption of C–O–C groups in naproxen, while 1173 cm^{-1} is due to absorption of C–O. The lattice vibrations of metal cations Al^{3+} and Mg^{2+} are observed at 790 and 676 cm^{-1} [31]. It should be noted that the band at 1359 cm^{-1} is due to the stretching vibrations of CO_3^{2-} [32]. This is in agreement with the results of XRD and elemental analysis, and will be further confirmed by in situ HT-XRD in the next section.

3.3.2. *Thermal decomposition monitored by in situ FT-IR*

It can be observed from Fig. 3 that there is not much change of the absorption bands of naproxen upon increasing the temperature from 20°C to 150°C, while the intensity of bands decreases remarkably with somewhat shift at 170°C, indicating the occurrence of the decomposition of naproxen. Moreover, the bands become weaker with the increase of temperature between 170°C and 230°C, and almost disappear at 250°C, corresponding to the complete decomposition of naproxen.

As shown in Fig. 4, infrared spectra of naproxen/LDH recorded at higher temperature are rather different from those of naproxen itself. The absorption band at 3464 cm^{-1} becomes weaker with increasing temperature, and disappears at 450°C, which involves the loss of water molecules as well as hydroxyl of the LDH layers. No remarkable changes of the absorption bands are observed from 20°C to 200°C, indicating that the intercalated product is stable in this temperature range. However, obvious changes at 250°C are observed. Bands at 1636, 1605 and 1480 cm^{-1} attributed to the stretching vibrations of aromatic rings as well as the one at 1359 cm^{-1} corresponding to interlayer CO_3^{2-} decrease considerably, and all of them disappear at 300°C. This implies two processes as follows: (1) The decomposition of intercalated naproxen occurs at 250°C, and there is a remarkable structure change at 300°C. It can be concluded that the thermal stability of intercalated naproxen enhances remarkably compared with the pristine naproxen whose decomposition occurs at 170°C. (2) The destruction of MgAl–CO_3 LDH starts at 250°C and ends at about 300°C. This would be further discussed in the section of in situ HT-XRD. The change of band centered at 1545 cm^{-1} which is

attributed to asymmetric stretching vibration of C=O is very interesting. When the temperature increases to 330°C, the band of $\nu_{C=O}$ increases from 1545 to 1592 cm^{-1} gradually, while it shifts in the reverse direction to 1583 cm^{-1} at 350°C and maintains the same position in the temperature range 350–450°C. This process is possibly related to the destruction of hydrogen bonding between naproxen and interlayer water molecules. Prevot [30] reported that there are hydrogen bonding distances between guest and host (0.27 ± 0.01 nm), i.e., guest interacts with host by the formation of hydrogen bonding through water molecules. In this study, physically adsorbed and interlayer water loss with the increase of temperature from 20°C to 330°C, leading to the gradual disappearance of hydrogen bonding distances as well as the decrease of d_{003} (which will be discussed in HT-XRD). As a result, the band of $\nu_{C=O}$ moves to high frequency. The deintercalation of gallery water almost completes when the temperature is above 330°C [33], so $\nu_{C=O}$ keeps invariable at 1583 cm^{-1}. It can be observed that only absorption bands corresponding to carboxylate remain at 450°C, indicating the interaction between carboxylate and host is rather stable.

3.4. Thermal decomposition monitored by in situ HT-XRD

The in situ HT-XRD patterns of the intercalation product naproxen/LDH in the temperature range 20–700°C are shown in Fig. 5. The relationships between the d_{003} basal spacing of naproxen/LDH and CO_3^{2-} LDH and the temperature are shown in Figs. 6a and b, respectively.

It can be observed in Fig. 5 that the (003), (006) and (009) diffraction peaks of naproxen/LDH clearly move to higher-angle 2θ with the increase of temperature. There are two sharp decreases of d_{003} value in Fig. 6a. The first is from 20°C to 150°C with the d_{003} basal spacing decreasing from 2.347 to 1.971 nm. Since there is no decomposition of naproxen in this temperature range, which has been confirmed by in situ FT-IR (Fig. 4), this decrease of d_{003} is related to the destruction of hydrogen bonding area as a result of deintercalation of interlayer water molecules. Therefore, the height of interlayer hydrogen bonding area is calculated to be

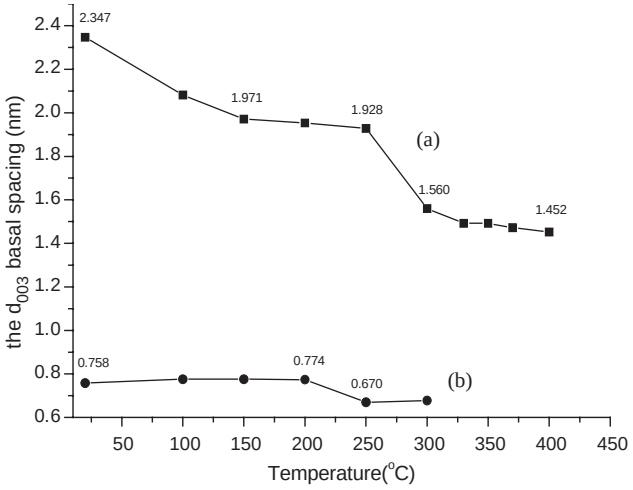

Fig. 6. The relationship between the d_{003} basal spacing and temperature: (a) naproxen/LDH, and (b) CO_3^{2-} LDH.

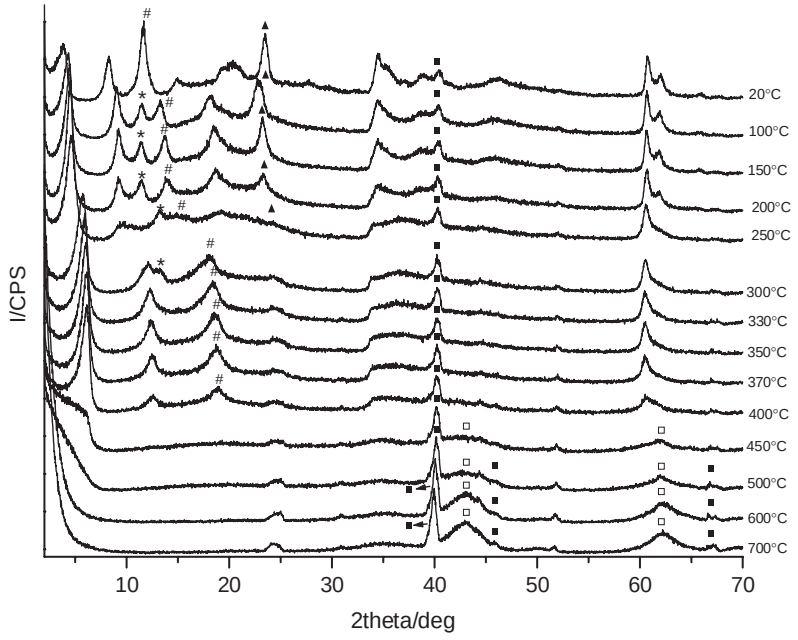

Fig. 5. In situ HT-XRD patterns of naproxen/LDH in the temperature range 20–700°C.

0.376 nm, and the unilateral distance is 0.189 nm (as illustrated in Fig. 2B). The distance of hydrogen bonding area of this study is larger than that of the previous report [30], which might be due to the different interlayer guests (tartrate anion in their study) and different study technologies (non in situ technologies in their study). The second fall is from 250°C (1.928 nm) to 300°C (1.560 nm), which is attributed to the decomposition of naproxen. In situ FT-IR (Fig. 4) has approved that the decomposition of intercalated naproxen occurs at 250°C, and there is a remarkable structure change at 300°C. So the results are in accordance with each other. The (009) peak of naproxen/LDH (marked with # in Fig. 5) and (003) peak of CO_3^{2-} LDH (marked with * in Fig. 5), which overlap at room temperature, are separated at 100°C. This change probably results from the destruction of the interlayer hydrogen bonding area [30] in naproxen/LDH associated with the loss of gallery water. When the temperature is above 400°C, reflections of MgO phase appear at about 43° and 62° (marked with □ in Fig. 5), which has been confirmed by Kanezaki et al. [24].

For the impurity phase CO_3^{2-} LDH, its (006) peak is observed at room temperature (marked with ▲ in Fig. 5); while its (003) diffraction peak (marked with * in Fig. 5) is observed at 100°C due to the shift in position of the (009) peak of the naproxen/LDH phase, which was previously coincident with it. It can be seen from Fig. 6b that the change in d_{003} basal spacing of CO_3^{2-} LDH is negligible in the range between 20°C and 200°C, in contrast to that of the naproxen/LDH phase. However, there is a decrease of d_{003} value at 250°C and both reflections of the CO_3^{2-} LDH phase disappear at 330°C, indicating complete decarbonation which is consistent with the results from in situ FT-IR spectroscopy at 300°C.

It should be noted that the peaks at about 40°, 46° and 67° which become stronger with the increase of temperature are attributed to the characteristic reflections of platinum substrate used in the in situ HT-XRD experiment (marked with ■ in Fig. 5).

3.5. Thermal decomposition studied by TG

The TG curves for the pure naproxen, the Mg/Al–NO_3 LDH precursor and the resulting naproxen/LDH complex are shown in Fig. 7. The naproxen used as reference sample (Fig. 7c) exhibits three weight loss events. The first slow event in the temperature range 20–170°C is attributed to the loss of adsorbed water; the second sharp event (170–310°C) is due to the decomposition of naproxen, which corresponds to the disappearance of absorption peaks of naproxen at around 250°C by the analysis of in situ FT-IR (Fig. 3); the third weight loss between 310°C and 470°C is the result of combustion of naproxen. The Mg/Al–NO_3 LDH precursor also exhibits three weight loss stages (Fig. 7a). The first (20–120°C) and second (120–300°C) correspond to the removal of surface water (from both the external surfaces and the internal gallery surface); the third (300–540°C) is due to dehydroxylation of the brucite-like layers as well as decomposition of the NO_3^- anions.

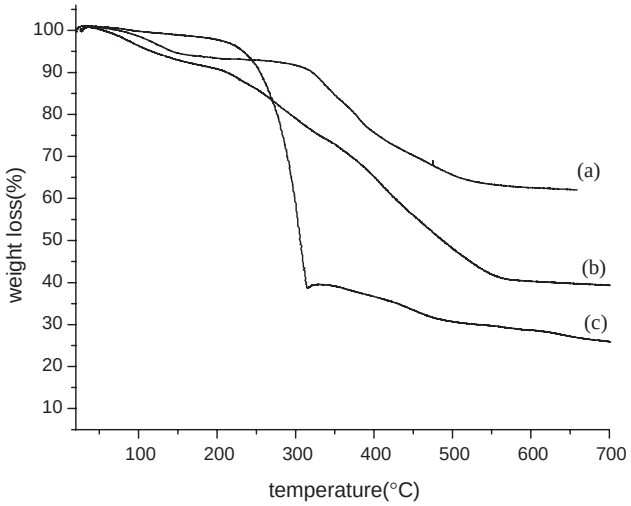

Fig. 7. TG curves of: (a) Mg/Al–NO_3 LDH, (b) naproxen/LDH, and (c) naproxen.

The thermal decomposition of naproxen/LDH complex is characterized by three steps (Fig. 7b): the first (20–200°C) is due to loss of both adsorbed and interlayer water molecules which has been confirmed by the shift of (003) reflection to higher-angle 2θ by in situ HT-XRD (Fig. 5); the second (200–300°C) is a consequence of the naproxen decomposition. This has been approved by in situ FT-IR of the decrease of vibration absorption of aromatic rings from 200°C to 250°C and the disappearance at 300°C (Fig. 4) as well as by in situ HT-XRD of the sharp decrease of d_{003} of the naproxen/LDH between 200°C and 300°C (Fig. 6a). The third loss event (300–570°C) can be attributed to the further decomposition and deintercalation of naproxen as well as dehydroxylation of the host layers. It can be observed from in situ FT-IR that the absorption bands corresponding to naproxen and its decomposition products decrease gradually above 300°C (Fig. 4) and from in situ HT-XRD that the LDH phase disappears little by little and MgO phase appears gradually above 400°C (Fig. 5).

4. Conclusion

Naproxen/LDH was obtained by the intercalation of naproxen anions into magnesium–aluminum layered double hydroxide by the method of ion exchange. XRD was used to confirm the intercalation structure, with

$d_{003} = 2.347$ nm. Taking into account the dimension of the naproxen anion and the rule of charge balance, the guest can only adopt a monolayered arrangement with the naphthalene ring perpendicular to the layer plane and with the carboxyl of individual anions attaching alternately to the upper and lower hydroxide layers. The guests interact with each other via $\pi-\pi$ interactions of naphthalene rings, and hydrogen bonding area exists between the guest anions and the host layers. A schematic model of the intercalation structure has been proposed.

In situ FT-IR spectroscopy and in situ HT-XRD were used to study physicochemical changes during the thermal decomposition of naproxen/LDH. The spectroscopic changes observed during the decomposition process correlate well with TG analysis.

As shown by infrared spectroscopy, the decomposition of intercalated naproxen occurs at 250°C, and there is a great structure change at 300°C. Only absorption bands corresponding to carboxylate remain at 450°C, indicating the interaction between carboxylate and host is rather stable. The band of $\nu_{C=O}$ increases first from 24°C to 330°C, then decreases at 350°C and remains invariable between 350°C and 450°C. This process is possibly related to the destruction of the hydrogen bonding between naproxen and interlayer water molecules. It can be concluded that the thermal stability of intercalated naproxen enhances remarkably compared with the pristine naproxen whose decomposition occurs at 170°C.

In situ HT-XRD shows that there are two sharp decreases of d_{003} value of naproxen/LDH with the increase of temperature. The first decrease from 20°C to 150°C is related to the destruction of the hydrogen bonding area as a result of deintercalation of interlayer water molecules; the second one between 250°C and 300°C is attributed to the decomposition of intercalated naproxen. MgO phase appears when the temperature is above 400°C. For the impurity phase CO_3^{2-} LDH, its (006) diffraction peak is observed at room temperature while its (003) peak is observed at 100°C due to the shift of (009) peak of naproxen/LDH phase to higher-angle 2θ, and both reflections of CO_3^{2-} LDH disappear at 330°C.

Acknowledgments

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