JOURNAL OF OPTOELECTRONICS AND ADVANCED MATERIALS Vol. 9, No. 11, November 2007, p. 3376 - 3378

Controlled release of salycilate from the lamella ZnAl layered double hydroxide nanocomposite

M. FRUNZA*, M. I. POPA, V. HULEA[a]
Department of Chemical Engineering, Faculty of Chemical Engineering, Technical University Iasi, Bd. D. Mangeron 71A, 700050, Iasi, Romania
[a] *Ecole Nationale Superieure de Chimie de Montpellier, 8 rue de l'Ecole Normale 34296 Montpellier Cedex, France*

This paper reports the kinetic study of the release of salycilate (SAL) in layered double hydroxides. SAL was intercalated into ZnAl-layered double hydroxides lamella as an inorganic host by ion exchange technique. Powder X-ray diffractogram shows that the basal spacing of the ZnAl layered double hydroxide with salicylate as the intergallery anion expanded from 8.7 Á to 15.4 Á. The release of SAL anion from the lamella of an organic-inorganic nanohybrid material, ZnAlLDH_SAL nanocomposite, was found to be floe-rates and pH dependent. The release of SAL from the lamella of hydrotalcites at pH 2.0, 5.5, 8.0 was controlled by first-order kinetics.

(Received March 23, 2007; accepted November 1, 2007)

Keywords: Layered double hydroxide, Ion exchange, Intercalation, Salicylate, Controlled release

1. Introduction

Nanohybrid systems drug-inorganic supports have attracted considerable interest due to their synergistic effects and potential applications. For example, various drugs were inserted within interlayer or interleaved with the layers of inorganic matrix of layered double hydroxides (LDH) [1-4] resulting in the formation of the so-called layered nanocomposite materials. LDH have many applications as catalysts, optical and electrical functional materials. LDHs- based controlled release systems have also been studied [5-9].

Salicylate (SAL) is used in rheumatism treatment, but its adverse secondary effects, such a gastric and duodenal ulcer formation are quite common. The effect of LDHs in preventing taurcholate induced gastric injury in rat was demonstrated in the literature [10].

In this work we have investigated the intercalation behavior of SAL into ZnAlLDHs by ion-exchange reaction and the kinetic study of release of SAL intercaled in the layered double hydroxides (LDH).

2. Experimental

2.1. Materials

All chemicals including $Zn(NO_3)_2 \cdot 6H_2O$, $Al(NO_3)_3 \cdot 9H_2O$, NaOH were analytical grade. Salicylate was purchased from Aldrich.

2.2. Preparation ZnAlLDH

100 ml of an aqueous solution of $Zn(NO_3)_2 \cdot 6H_2O$ (0.2mol)/$Al(NO_3)_3 \cdot 9H_2O$ (0.1mol) and an aqueous solution of NaOH 1M, were mixed together by drop wise addition. During the whole process the flow was controlled in such a way that the pH was kept at a constant value of 8.5. The resulting white precipitate was aged at 338 K for 24 h under stirring. After the ageing step, the precipitate was separated by centrifugation, washed extensively with warm deionized water until sodium free and dried under vacuum at 40 °C.

2.3. Preparation of ZnAlLDH_SAL nanocomposites

ZnAlLDH_SAL nanocomposite samples were prepared by anion exchange reaction. 150 ml of 0,1M Sal aqueous solution were added into 250 ml aqueous dispersion containing 1g ZnAl-LDH under nitrogen atmosphere and vigorous magnetic stirring. The pH of the mixture was held constant at 8 by simultaneous addition of 1M NaOH solution. The exchange reaction was allowed to proceed at room temperature for 24 h.

The obtained precipitates were filtered, washed with deionized water and dried at 37°C.

2.4. Characterization

Powder X-ray diffraction (XRD) was performed on a Brunker AXS D8 diffractometer using CuK α radiation (λ = 0.154 nm) at 40 KV and 35 mA between 4^o and 70^o (2θ) with a graphite secondary monochromator.

The intercalation of SAL in LDH was effectuated by ion-exchange method. The profile of release from LDH was determined with a BOECO S-22 UV-visible spectrophotometer at λ = 280 nm. A series of aqueous solutions with various pH values and various flow rates were used to observe the effect on the release rate of SAL from the organic-inorganic nanohybrid.

2.5. Salicylate release measurements

The study of SAL release from the LDH was carried out by an elution technique in aqueous medium of different pH and flow-rates values using the apparatus described in diffusional system based on tolazoline hydrochloride included in a reticulated carboxymethylcellulose hydrogel [13]

3. Results and discussion

3.1. Powder X-ray diffraction (XRD)

The powder XRD patterns of the precursor NO_3^- ZnAlLDH and the sample produced by reaction of SAL with LDH are shown in Fig. 1. The ZnAlLDH precursor has an XRD pattern similar to those reported previously [11], with a basal spacing (d_{003}) of 8.7 Å (Fig. la). After reaction with SAL, the powder XRD pattern of the product maintains the characteristic features of ZnAlLDH (Fig. 1b). The main diffraction peaks of ZnAILDH structure appear at 5.07°, 11.7° and 17.5°, with an expanded basal spacing (d_{003}) of 15.4 Å. The diffraction peak at 15.4 Å is assigned the d_{003}, proving that the guest molecules are lying horizontally to the hydroxide region in a monolayer [12].

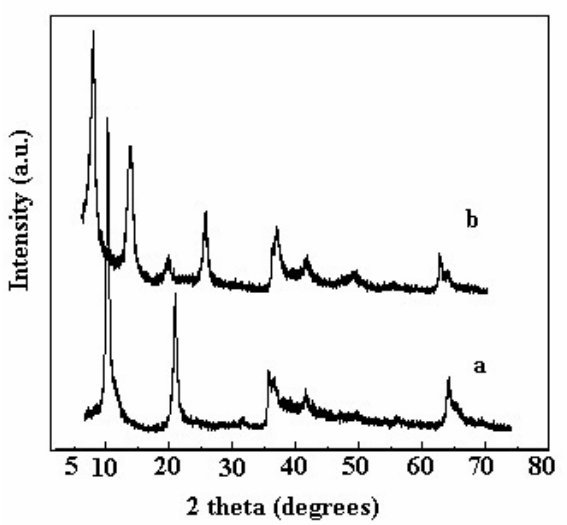

Fig. 1. The XRD spectra (a) ZnAlLDH, (b) *ZnAILDH_SAL*

The peak at 17.5° 2θ might be the reflection of the unchanged LDH-NO_3^- precursor.

This indicates that there is very little of the unexchanged LDH-nitrate phase remaining in the product. The peak at 11.7° 2θ is the superposition of (003) reflection of the precursor and (006) reflection of the intercalation product, accounting for its enhanced intensity. The peak at around 23.55° 2θ observed in Fig. 1b is possibly related to the presence of an LDH-CO_3^{2-} impurity phase that is often observed even when intercalation reactions are carried out under nitrogen.

3.2. Kinetics study

The amount of SAL released from ZnAlLDH_SAL was evaluated using a spectrophotometric method. A calibration curve was first obtained from the study of six aqueous solutions of SAL, with concentrations in the range 0 - 700 μg/mL. All solutions were prepared by diluting a standard solution with the concentration of 0.1 g/dL. The absorbance was measured at 280 nm using a spectrophotometer with a 1 cm or 0.5 cm thick quartz cell, depending on the sample concentration.

The calibration curves are plotted in figure 1 and 2. In all cases the experimental points were found on the same straight line, with an error of less than 1%. The equations of these curves were obtained by the least - square method and are shown below:

A = 0.002 x C (μg/mL) in the range 0-700 μg/mL, (C - concentration of the SAL solution, A - absorbance). They can be used for direct determination of SAL concentration.

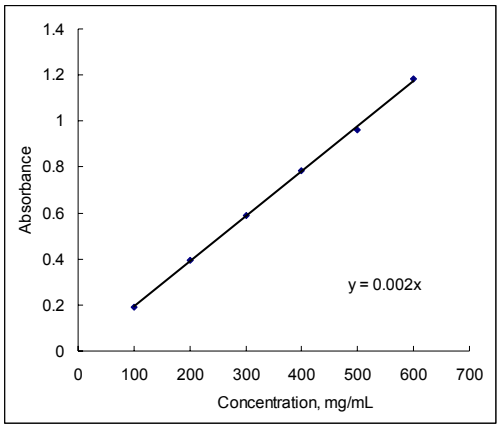

Fig. 2. Calibration curve for SAL in the range 0-700 mg/mL

The release kinetics of SAL has been followed for 12 hours. The release curves obtained are plotted in Fig. 3, 4, and 5.

The amount of SAL released from the samples was calculated as:

$$m_{SAL} = c_n \cdot V_e + \sum_{i=0}^{n-1} c_i \cdot V_i \qquad (1)$$

where: m_{SAL} is the amount of SAL released from the sample at a certain time (μg); c_d is the concentration of drug in the extracted sample (μg/mL); V_e is the volume of eluent from the system (50 mL); V_i is the volume of extracted sample, *i*, (2 mL); and c_i is the concentration of SAL in the extracted sample, *i*, (μg/mL) determined spectophotometrically.

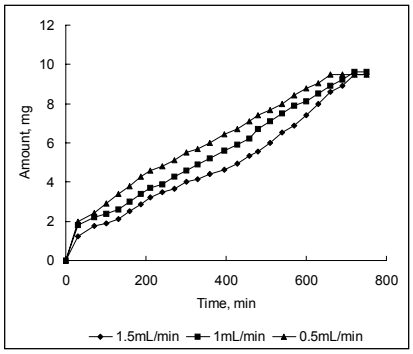

Fig. 3. Release profile of SAL from ZnAlLDH into aqueous solution at various flow rates. Conditions: 0.200 g sample in 50 mL aqueous solution at room temperature, pH=2.0.

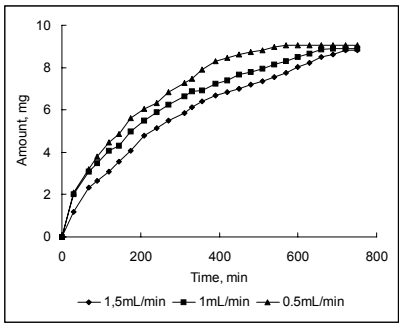

Fig. 4. Release profile of SAL from ZnAlLDH into aqueous solution at various flow rates. Conditions: 0.200 g sample in 50 mL aqueous solution at room temperature, pH=5.5.

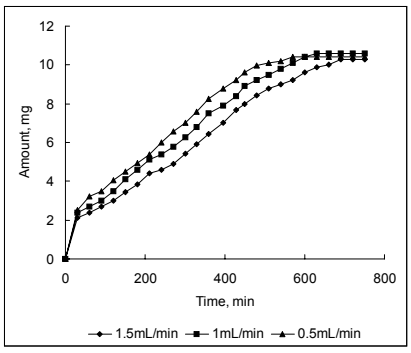

Fig. 5. Release profile of SAL from ZnAlLDH into aqueous solution at various flow rates. Conditions: 0.200 g sample in 50 mL aqueous solution at room temperature, pH=8.0.

A series of aqueous solutions with various pH values were used to observe the pH effect on the release rate of SAL from the organic-inorganic nanohybrid. Figs. 3, 4 and 5 show the release profile of SAL from the lamellae of ZnAlLDH into the aqueous solution at various initial pH values and different flow-rates.

The accumulated SAL released into the aqueous solution increased with contact time and flow-rate when SAL-LDHs were put in contact with aqueous solution. The release rate was found to be faster in the first 20 mint from the initial time of the experiment, thereafter a slower release was observed. The stationary state of SAL release from nanohybrid is obtained in the all cases after 800 mints when the release proceeds according to a zero order kinetics. To explain this gradual decrease of the dissolution rate, some considerations may be draw. The rate of drug diffusing out of the matrix is controlled by the rigidity of the layers and the diffusion path length.

4. Conclusions

SAL-LDH was obtained by the intercalation of salicylate anions into Zn-Al layered double hydroxide by the method of ion exchange. XRD was used to confirm the intercalation structure. According to XRD, the basal spacing of Sal-LDH was expanded to 15.4 Å

The SAL releases from the SalZnAlLDH demonstrate that the LDHs intercalated with SAL, may be a promising system for drug delivery, which also provides a sustained release pattern.

Acknowledgements

This work has been supported by Ministry of Education and Research Romania, by CEEX 108/ 2006.

References

[1] V. Ambrogi, G. Fardella, G. Grandolini, L. Perioli, Int. J. Phar. **220**, 23-32 (2001).
[2] M. Wei, S. Shi, J. Wang, X. Duan, J. Solid State Chem, **177**, 2534-2541 (2004).
[3] Z. Wang, E. Wang, L. Gao, L. Xu, J. Solid State Chem. **178**, 736-741 (2005).
[4] B. Li, D. Evans, X. Duan, Appl. Clay Sci. **27**, 199-207 (2005).
[5] A. I. Khan, L. Lei, A. J. Norquist, D. O'Hare, Chem. Commun. 2342-2343 (2001).
[6] M. Frunza, G. Carja, M. I. Popa, Scientific Study & Research, **VI** (2), 173-180 (2005).
[7] Z. Wang, E. Wang, L. Gao, L. Xu, J. Solid State Chem. **178**, 736-741(2005).
[8] B. Li, J. He, D. G. Evans, X. Duan, Appl. Clay Sci. **27**(3-4), 199-207 (2004).
[9] M. Del Arco, E. Cebadera, S. Gutirrez, C. Martin, M. J. Montero, V. Rives, J. Rocha, M. A. Sevilla, J. Pharm. Sci. **93** (6), 1649-1658 (2004).
[10] B. P. Yu, J. Sun, M. Q Li, H. S. Luo, J. P. Yu, World J. Gastroenterol. **9**, 1427-1430 (2003).
[11] Z. P. Xu, H. C. Zeng, J. Phys. Chem. B, **105**, 1743-1749 (2001).
[12] S. H. Hwang, Y. S. Han, J. H. Choy, Bull. Korean. Chem. Soc. **22**(9) 1019-1022 (2001).
[13] M. Popa, N. Bajan, A. A. Popa, Polymer-Plastics Technology and Engineering, **45**(1), 9-21 (2006).

*Corresponding author: mfrunza@ch.tuiasi.ro