Electronic Supplementary Information

New Insights on two Intercalated Ciprofloxacin Arrangements into Layered Double Hydroxide Carrier Material

Nawal Fodil Cherif,[†,§,⊀] Vera Regina Leopoldo Constantino,[‡] Oualid Hamdaoui,[¥] Fabrice Leroux[†] and Christine Taviot-Guého[*†]

†Institut de Chimie de Clermont-Ferrand, UMR-CNRS 6296. Université Clermont Auvergne. Campus des Cézeaux, 24 avenue des Landais. B.P. 800 26. 63171 Aubière, France.
§Laboratory of Environmental Engineering. Badji Mokhtar-Annaba University. P.O. Box 12, 23000 Annaba. Algeria.
⊀Centre de Recherche Scientifique et Technique en Analyses Physico-Chimiques. B.P. 384, Zone Industrielle Bou-Ismail. Tipaza. Algérie.
¥ Chemical Engineering Department, College of Engineering, King Saud University, P.O. Box 800, Riyadh 11421, Saudi Arabia.
‡ Instituo de Quimica, Universidade de Sao Paulo. Av. Prof. Lineu Prestes 748, 05508-000 Sao Paulo, Brazil.

Table of Contents

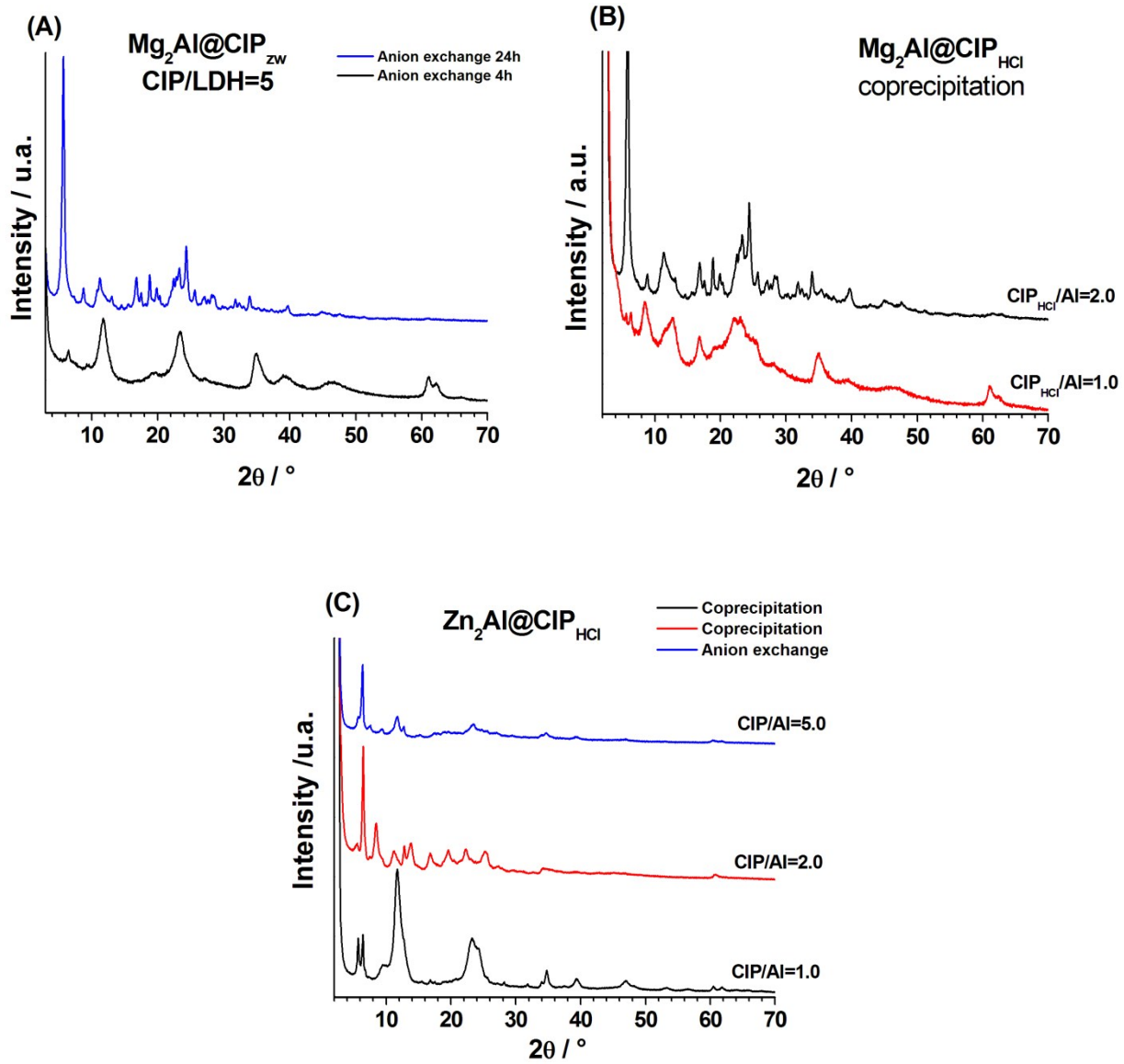


Figure ESI1. PXRD patterns of LDH samples prepared by anion exchange or by coprecipitation with different excesses of CIP_{HCl}.

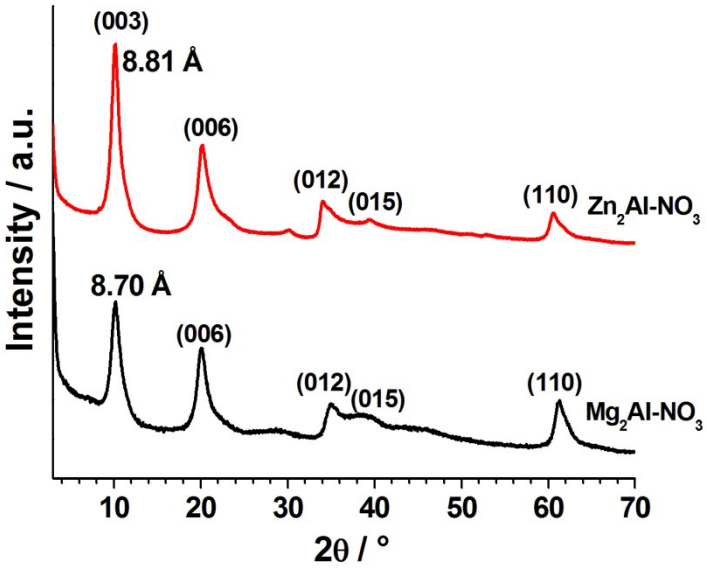


Figure ESI2. PXRD patterns of $Mg_2Al\text{-}NO_3$ and $Zn_2Al\text{-}NO_3$ LDH precursors.

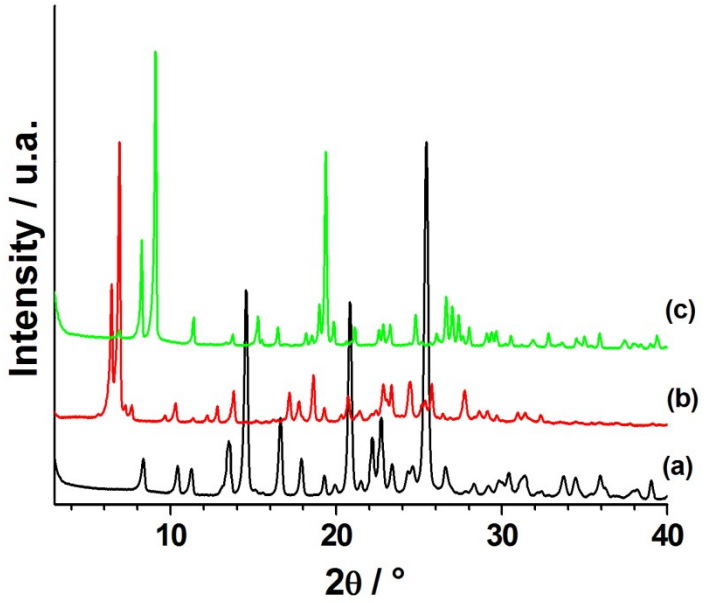


Figure ESI3. PXRD patterns of (a) CIP_{zw} zwitterion salt, (b) CIP_{zw} after dissolution in water and recrystallization upon drying, (c) CIP_{HCl} hydrochloride salt.

As shown in Figure ESI3, the XRD pattern of re-precipitated CIP_{zw} (after dissolution in water and recrystallization through evaporation at 50°C) is modified and probably corresponds to a different polymorph of CIP.[1]

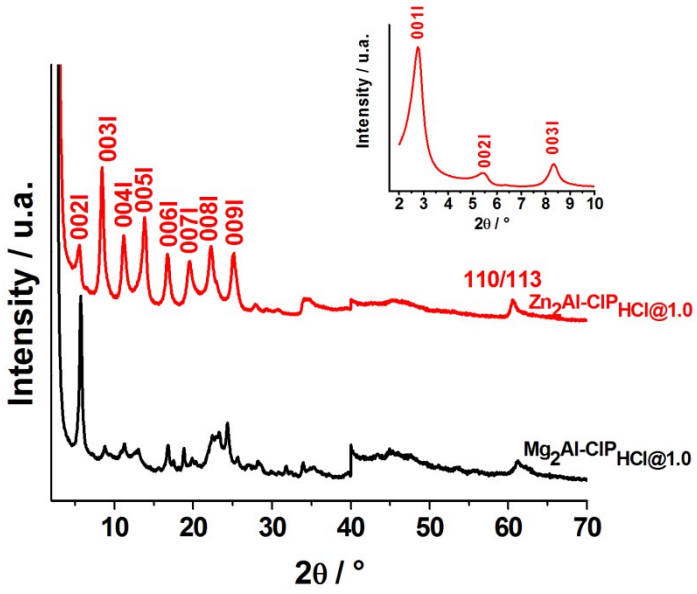


Figure ESI4. PXRD patterns of Zn_2Al-CIP and Mg_2Al-CIP samples obtained by coprecipitation using CIP_{HCl}/Al = 1.0.

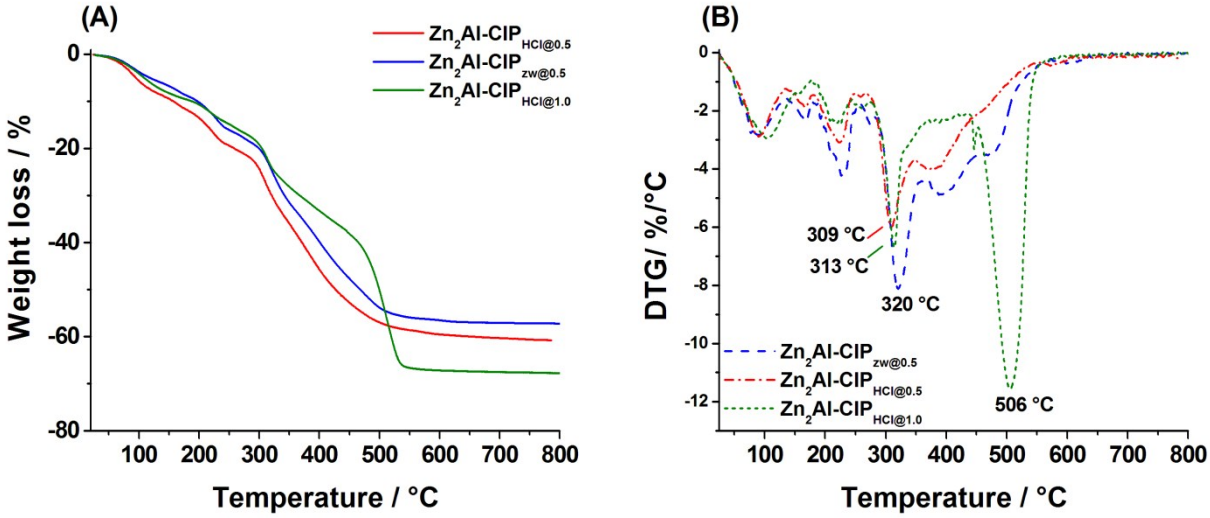


Figure ESI5. (A) TGA and (B) DTG curves for Zn_2Al-CIP samples.

For all samples, a continuous weight loss is observed up to 550°C (Figure ESI5 A) with five inflection points identified by DTG curves (Figure ESI5 B) in the temperature ranges 80-110°C, 150-180°C, 210-240°C, 280-350°C and 350-580°C. The first and second weight loss events are attributed to the removal of interlayer water molecules while the third one is assigned to the dehydroxylation of LDH layers.[2]The next events are associated to the decomposition of CIP species as evidenced by TG-MS analysis performed in air atmosphere (Figure ESI6). TG-MS analysis of CIP_{HCl} and CIP_{zw}

(data not shown) indicate a similar thermal decomposition process for both CIP salts with first the release of water molecules (m/z mass-to-charge ratio = 18) around 150°C and 300°C. For CIP_{HCl} a departure of HCl (m/z = 36) is also observed around 300°C. Finally, a release of CO2 (m/z = 44) is obtained between 300-600°C for CIP_{HCl} and 300-700°C CIP_{zw}.

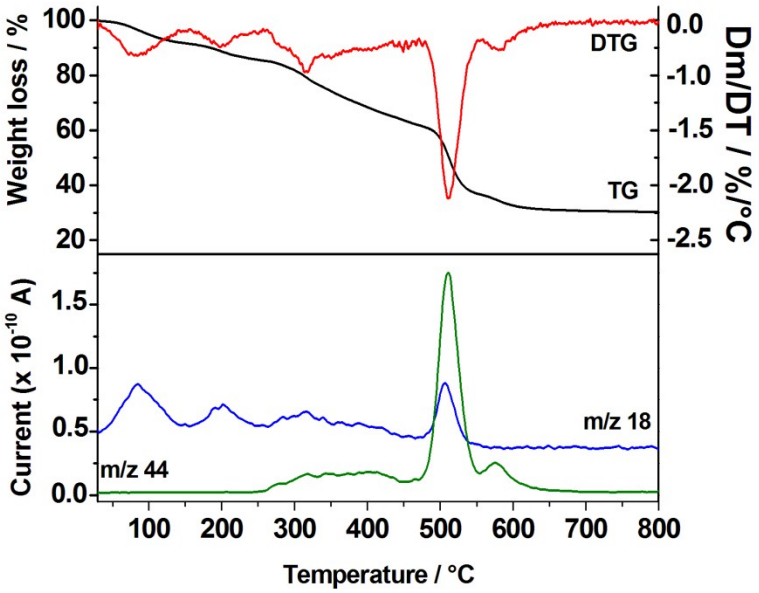


Figure ESI6. TGA-DTG-MS curves for Zn_2Al-$CIP_{HCl@1.0}$.

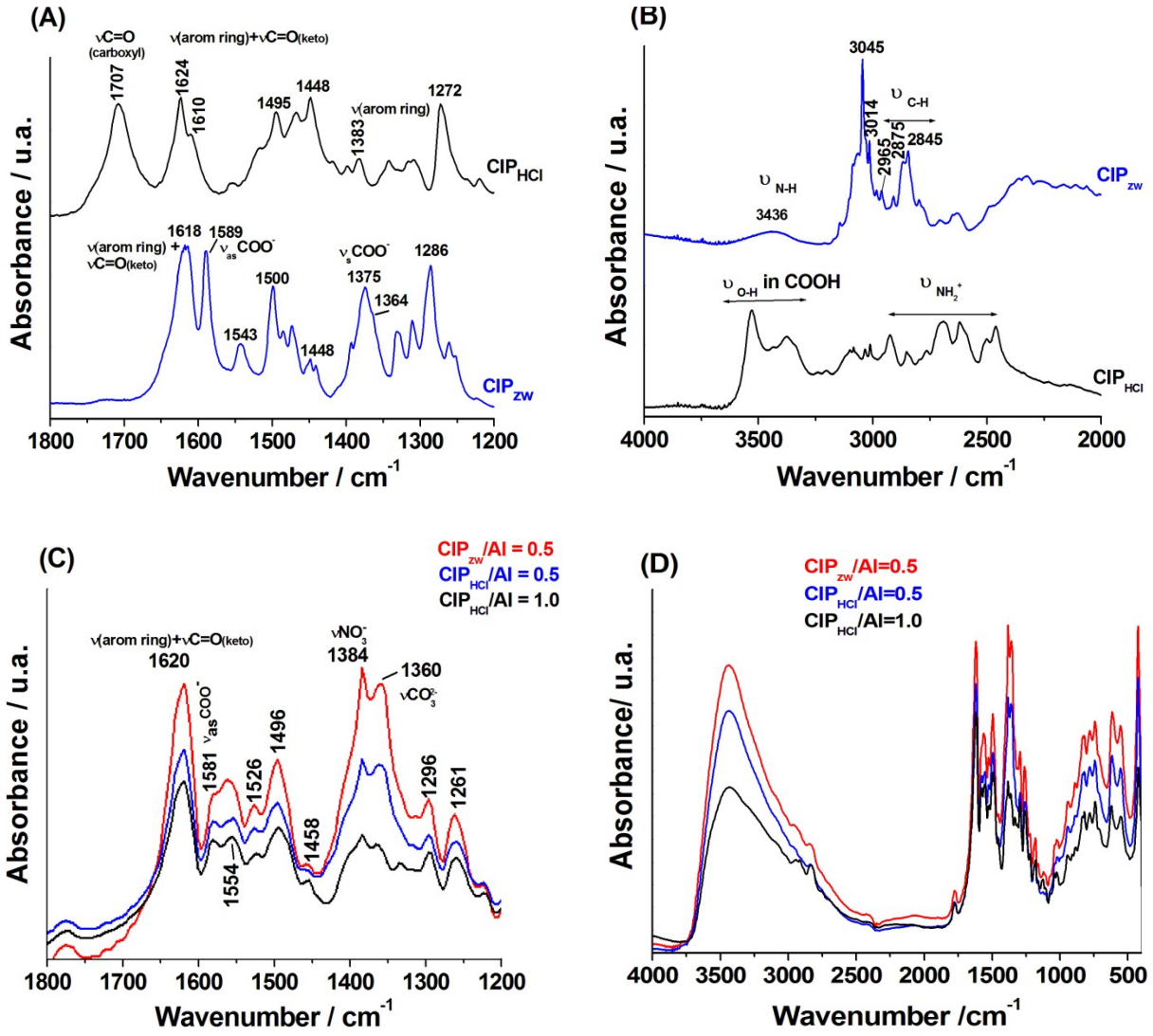


Figure ESI7. FTIR spectra CIP salts in the range (A) 1800-1200 cm^{-1}, (B) 4000-2000 cm^{-1} and Zn_2Al-CIP samples in the range (C) 1800-1200 cm^{-1} and (D) 4000-400 cm^{-1}.

Figure ESI7A shown the most characteristic vibrational bands of CIP in the 1800-1200 cm^{-1} spectral range. The band observed at 1707 cm^{-1} in CIP_{HCl} spectrum can be ascribed to the C=O stretching mode of the carboxylic group (νCOOH). This band is not present in the IR spectrum of CIP_{zw} in accordance with the zwitterion form i.e. carboxyl group is deprotonated. Instead, it is observed a band at about 1590 cm^{-1} corresponding to the combination of ketone group stretching (νC=O) and the antisymmetric stretching of carboxylate group ($\nu_{as}COO^-$), and also a band at 1375 cm^{-1} attributed to a combination of aromatic ring stretching and symmetric stretching of carboxylate group (ν_sCOO^-).[3]The bands at 1624 and 1610 cm^{-1} for CIP_{HCl} (Figure ESI7 A), as well as the band at about 1618 cm^{-1} in for CIP_{zw}, correspond to the stretching mode of aromatic quinolone ring (νC=C and νC=N) combined to the ketone group stretching.[3]For CIP_{HCl}, the several bands located between 2800-2300 cm^{-1} (Figure ESI7 B) are attributed to stretching

vibrations of piperazinium group (νNH_2^+) and those ones located between 3500 to 3200 cm^{-1} are assigned the νO-H stretching of the carboxylic group.[4] CIP_{zw} exhibited broad band with small intensity around 3500-3400 cm^{-1} assigned to NH stretching vibration (Figure ESI7 B).

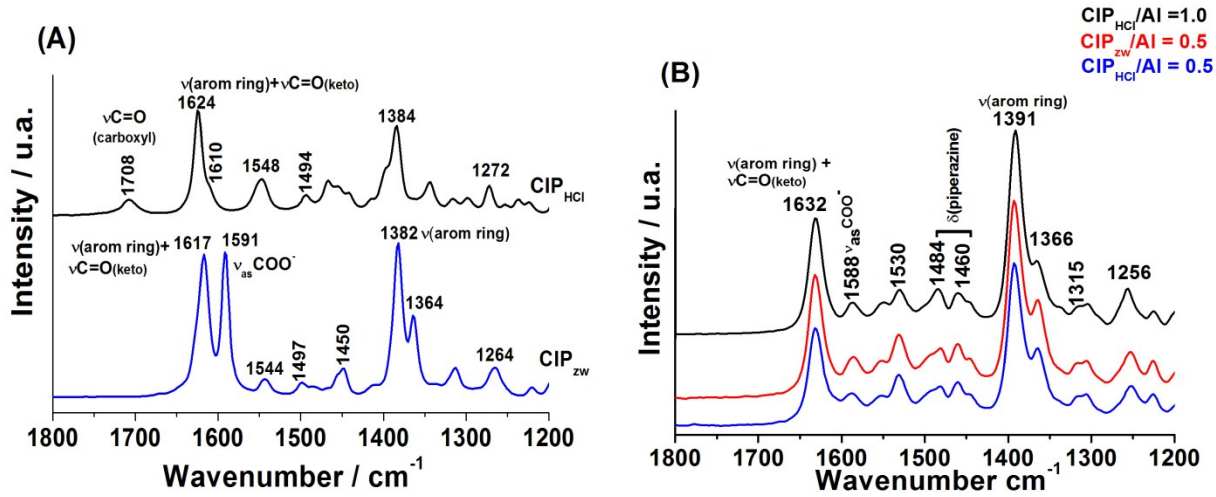
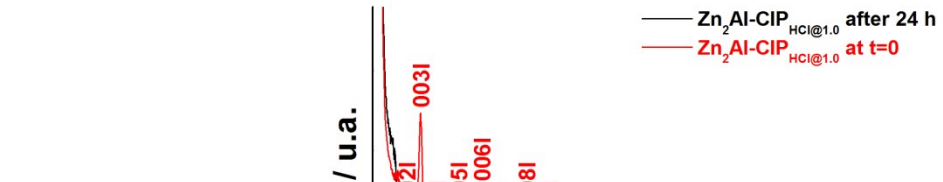


Figure ESI8. FT-Raman spectra of: (A) CIP salts, (B) Zn_2Al-CIP intercalated samples.

(A)



(B)

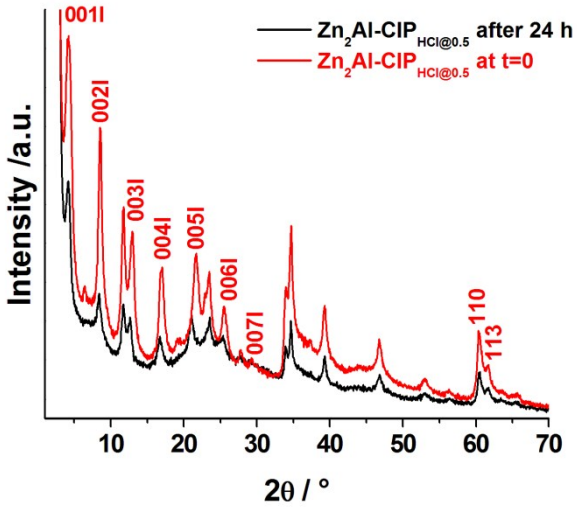
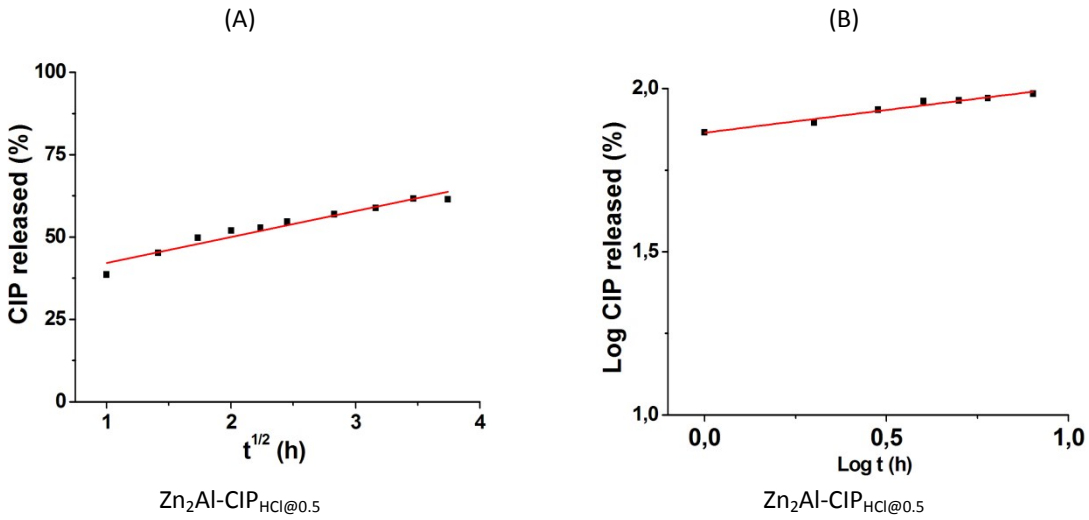
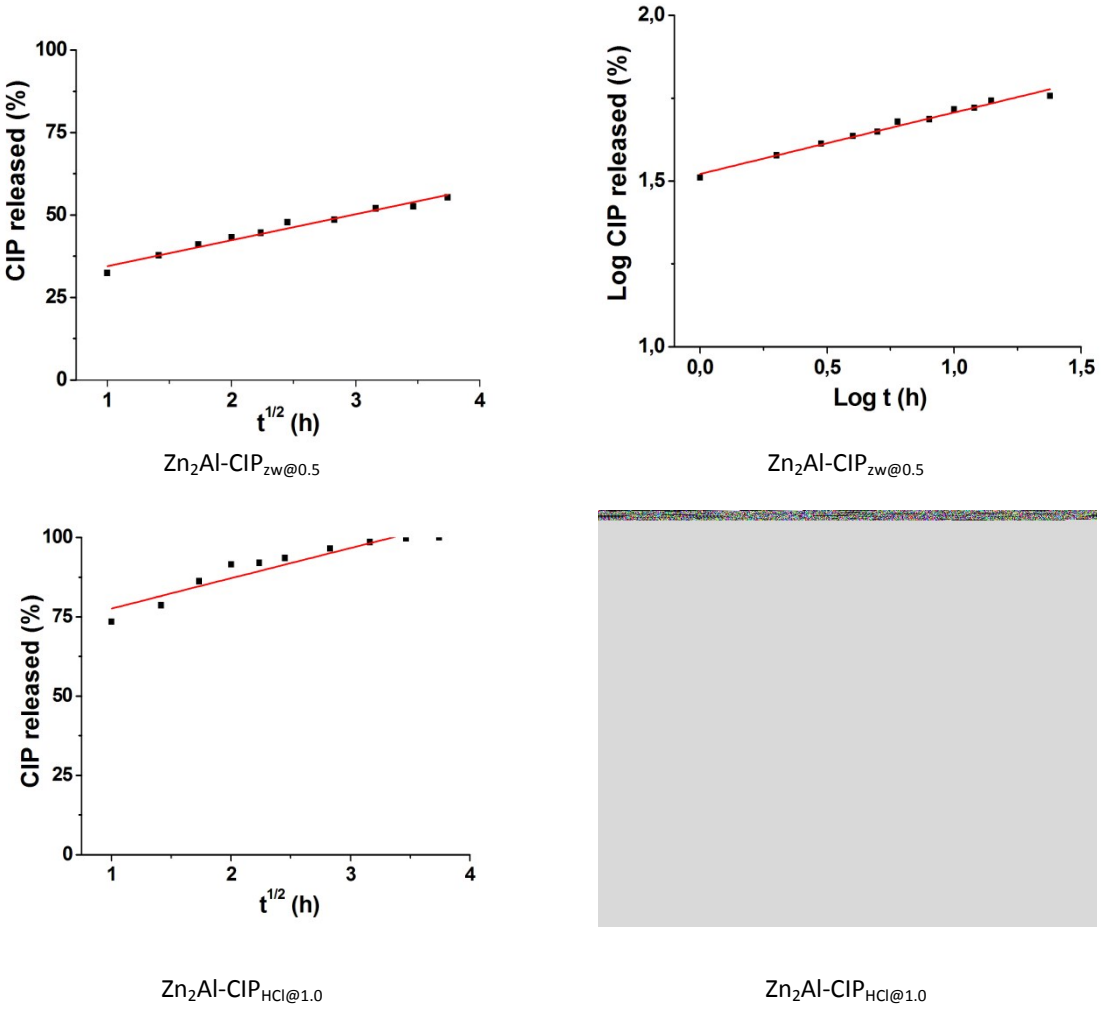


Figure ESI9. PXRD patterns of (A) $Zn_2Al\text{-}CIP_{HCl@1.0}$ and (B) $Zn_2Al\text{-}CIP_{HCl@0.5}$ samples recovered after a contact time of 24 h in PBS solution. The symbol * denote the diffraction peaks due to phosphate species.





Figures ESI10. Adjustment of the CIP release data from Zn_2Al-CIP in PBS medium to (A) Higuchi and (B) Korsmeyer-Peppas kinetic equations.[5]

TableESI1. ^{13}C CPMAS chemical shifts of CIP salts and intercalated Zn_2Al-LDH.[6]

Sample / Assignement	CIP_{HCl} (ppm)	$Zn_2Al\text{-}CIP_{HCl@0.5}$ (ppm)	$Zn_2Al\text{-}CIP_{HCl@1.0}$ (ppm)	CIP_{zw} (ppm)	$Zn_2Al\text{-}CIP_{zw@0.5}$ (ppm)
C4	175.5	177 ; 175.5	177 ; 175.5	178	177 ; 175
C3a	168.0	172	172.4	178	172
C6	151.2	164	153	158 ; 154	164
C2	148.2	148.1	148.2	148	148

C7	145	144	148.2	148	148
C10	138.4	138.1	138.8	143	138.5
C9	1180	127.6	127.7	128	127.3
C3	110.0	119.9	119.4	125	120.2
C5	108.5	111.5 ; 114.6	111.3 ; 114	120	111.4 ; 114
C8	104.0	105.9	106	115	105.7 ; 104
C2'6'	49.0	45.47	45.57	51.26	50.9
C3'5'	45.5			47.80	45.4
C1a	37.1	36.19 ; 34.50	36.04; 34.31	40.77	35.9 ; 34.5
C1b	9.2	8.12 ; 5.72	8.31 ; 6.26	13	8.02

REFERENCES

1 F.P.A. Fabbiani, B. Dittrich, A.J. Florence, T. Gelbrich, M.B. Hursthouse, W.F. Kuhs, N. Shankland and H. Sowa, *Cryst. Eng. Comm.,* 2009, **11**, 1396.

2 C. Forano, U. Costantino, V. Prévot and C. Taviot-Gueho in *Handbook of Clay Science*, ed. F. Bergaya, G. Lagaly, Elsevier, Amsterdam, 2013, 745-782.

3 U. Neugebauer, A. Szeghalmi, M. Schmitt, W. Kiefer, J. Poppa and U. Holzgrabe. *Spectroc. Acta A* 2005, **61**, 1505.

4 V.L. Dorofeev, *Pharm. Chem. J.* 2004, **38**, 693 ; V.L. Dorofeev, *Pharm. Chem. J.* 2004, **38**, 698.

5 M.L. Bruschi in *Mathematical Models of Drug Release* in *Strategies to Modify the Drug Release From Pharmaceutical Systems*, ed. M.L. Bruschi, Woodhead Publishing, Elsevier,.2015, 63-86.

6 L. Mafra, S.M. Santos, R. Siegel, I. Alves, F.A. Almeida Paz, D. Dudenko and H. W. Spiess, *J. Am. Chem. Soc.* 2012, **134**, 71; A.K. Chattah, Y.G. Linck, G.A. Monti, P.R. Levstein, S.A. Breda, R.H. Manzo and M.E. Olivera, *Magn. Reson. Chem.* 2007, **45**, 850.