Supporting Information

Conventional or mechanochemically-aided intercalation of diclofenac and naproxen anions into the interlamellar space of CaFe-layered double hydroxides and their application as dermal drug delivery systems †

Márton Szabados,[a,b] Attila Gácsi,[b,c] Yvette Gulyás,[b] Zoltán Kónya,[d,e] Ákos Kukovecz,[d] Erzsébet Csányi,[c] István Pálinkó[a,b] and Pál Sipos[b,f*]

[a]*Department of Organic Chemistry, University of Szeged, Dóm tér 8, Szeged, H-6720 Hungary*

[b]*Material and Solution Structure Research Group, Institute of Chemistry, University of Szeged, Aradi vértanúk tere 1, Szeged, H-6720 Hungary*

[c]*Institute of Pharmaceutical Technology and Regulatory Affairs, University of Szeged, Eötvös utca 6, Szeged, H-6720 Hungary*

[d]*Department of Applied and Environmental Chemistry, University of Szeged, Rerrich B. tér 1, Szeged, H-6720 Hungary*

[e]*MTA-SZTE Reaction Kinetics and Surface Chemistry Research Group, Rerrich B. tér 1, Szeged, H-6720 Hungary*

[f]*Department of Inorganic and Analytical Chemistry, University of Szeged, Dóm tér 7, Szeged, H-6720 Hungary*

Table S1
Comparative literature for drug release of Mg- and Zn-based LDH solids summarizing the applied kinetic models, *n* release exponents, and R^2 linear correlation coefficients.

Investigated nanocomposites	Intercalation method	Kinetic models	*n*	R^2	References
MgAl-LDH−naproxen	Co-precipitation	Korsmeyer–Peppas	0.9	0.997	Rojas et al., 2014
MgAl-LDH−naproxen	Co-precipitation	Korsmeyer–Peppas	0.89	0.996	Carriazo et al., 2010
MgAl-LDH−diclofenac / Eudragit	Direct anion exchange	Higuchi	0.5	0.995	Ambrogi et al., 2008
MgAl-LDH−diclofenac	Direct anion exchange	Higuchi	0.5	0.989	Ambrogi et al., 2002
ZnAl-LDH/diclofenac / Polycaprolactone	Direct anion exchange	Ritger-Peppas	0.37	0.933	Wang et al., 2019
ZnAl-LDH−diclofenac	Direct anion exchange	Ritger-Peppas	0.21	0.991	Joy et al., 2017
ZnAl-LDH−diclofenac	Direct anion exchange	Higuchi	0.5	0.986	Perioli et al., 2011

† This publication is dedicated to the memory of our mentor, friend and colleague, Prof. István Pálinkó, who passed away shortly after the submission of the current manuscript

*corresponding author
sipos@chem.u-szeged.hu (Pál Sipos)

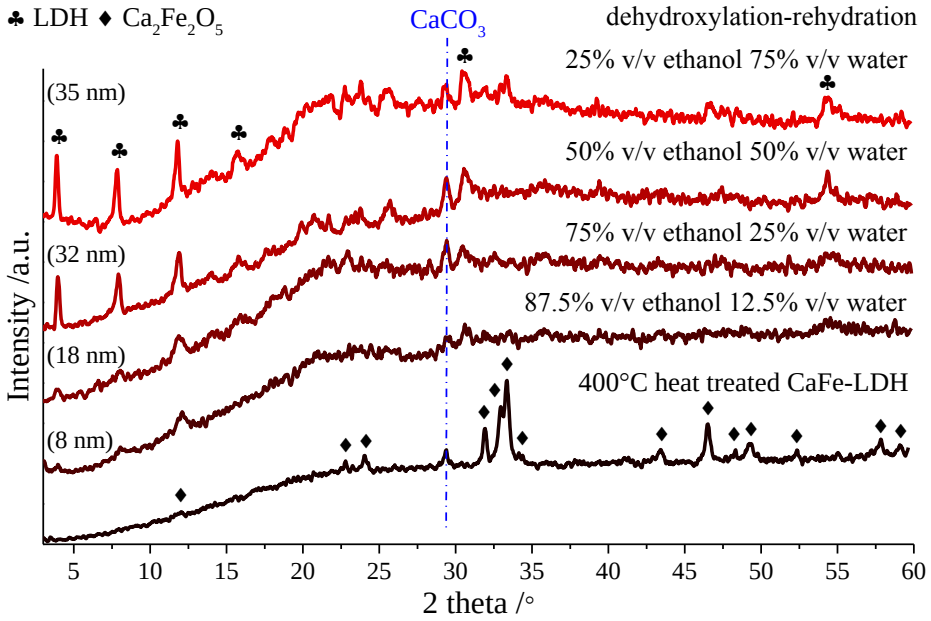

Fig. S1 X-ray diffractometry patterns of diclofenac anion-intercalated LDH samples intercalated in ethanol-water mixtures of varying compositions (1:1 Fe(III):diclofenac anion molar ratio, 25°C) and the as-prepared LDH after calcination at 400°C.

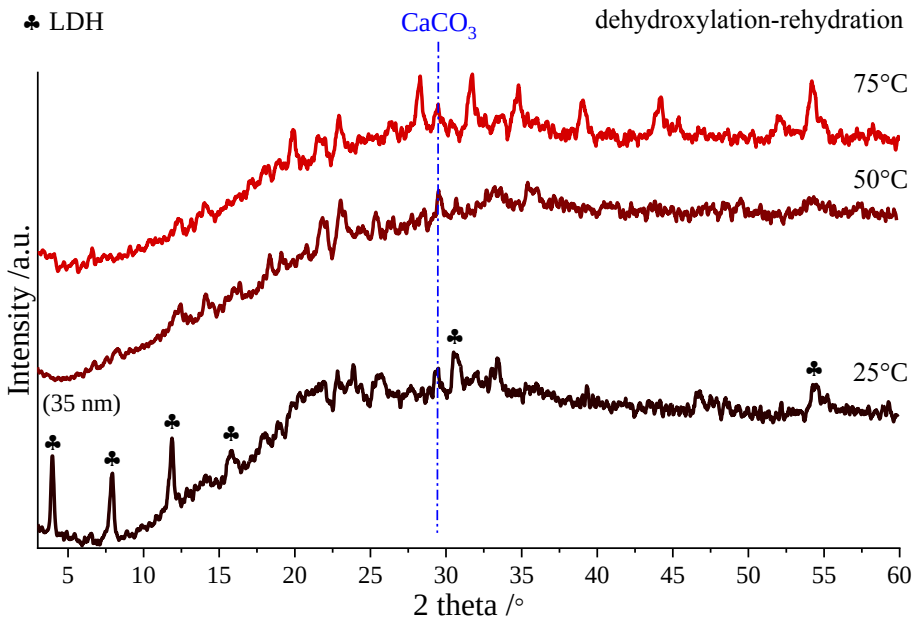

Fig. S2 X-ray diffraction patterns of solids obtained at varying stirring temperature (1:1 Fe(III):diclofenac anion molar ratio, 25% v/v ethanol-water mixture).

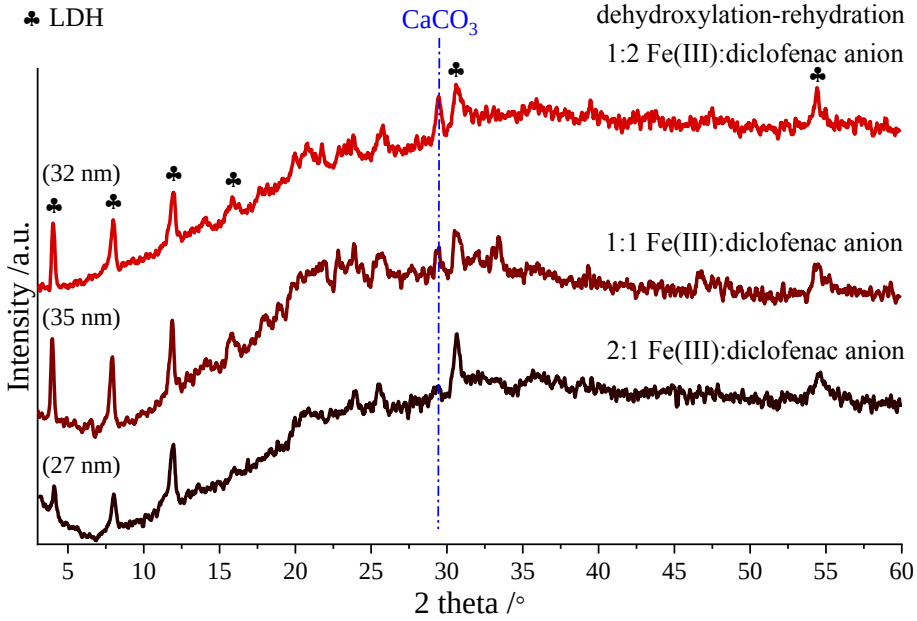

Fig. S3 X-ray diffraction patterns of the LDH composites at different Fe(III):diclofenac anion molar ratios (25% v/v ethanol-water mixture, 25°C).

Table S2

Crystal, size, heterogeneity parameters and zeta potential of pristine and organic CaFe-LDH solids (average predominant solvodynamic diameter – $Z_{avg.}$, polydispersity index – PDI, average zeta potential – $\zeta_{avg.}$).

Samples	*d*-value (nm)[x]	*a* (nm)[y]	$Z_{avg.}$ (nm)	PDI	$\zeta_{avg.}$ (mV)
CaFe−NO_3-LDH	0.854	0.586	255 ± 60	0.42	−12.9 ± 1.6
co-precipitation LDH−diclofenac	2.291	0.586	1220 ± 330	0.13	−9.5 ± 1.1
direct anion exchange LDH−diclofenac	2.304	0.582	1140 ± 330	0.17	−9.3 ± 2.7
dehydroxylation-rehydration LDH−diclofenac	2.271	0.586	675 ± 185	0.35	−11.5 ± 3.4
mechanochemically-aided intercalation LDH−diclofenac	2.276	0.584	540 ± 170	0.21	−12.4 ± 1.8
co-precipitation LDH−naproxen	1.943	0.586	760 ± 180	0.46	−4.7 ± 1.5
direct anion exchange LDH−naproxen	1.935	0.586	2280 ± 605	0.22	−5.4 ± 3.4
dehydroxylation-rehydration LDH−naproxen	1.926	0.584	2770 ± 760	0.22	−2.5 ± 1.3
mechanochemically-aided intercalation LDH−naproxen	1.902	0.584	3125 ± 585	0.45	−3.9 ± 1.4

[x] *d*-value = d_{001} or the first reflections

[y] Lattice parameter *a* is calculated by estimation: $a = 2d_{110}$

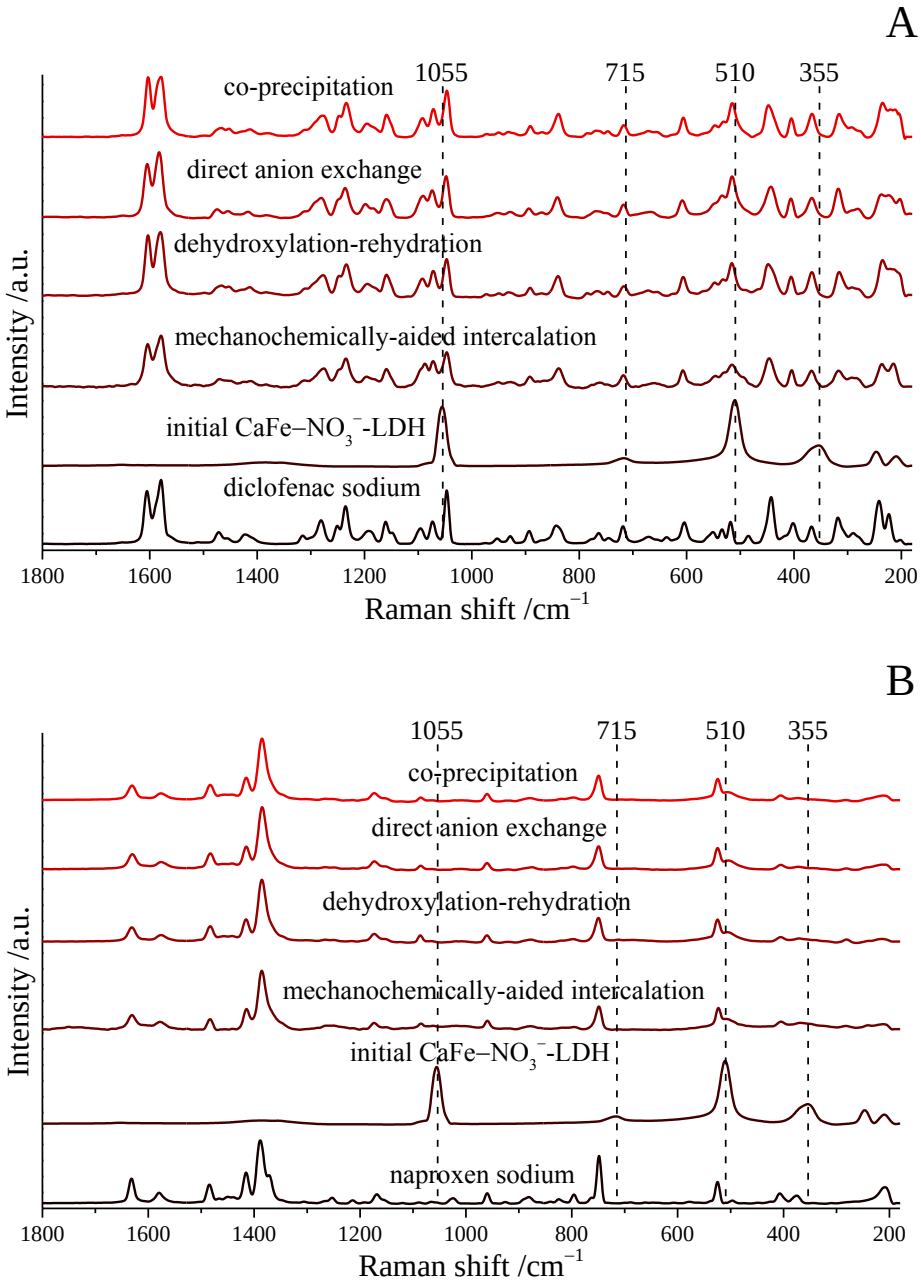

Fig. S4 Raman spectra of the diclofenac (A) and naproxen (B) anion-intercalated LDH samples and those of the as-prepared CaFe-LDH and starting drugs.

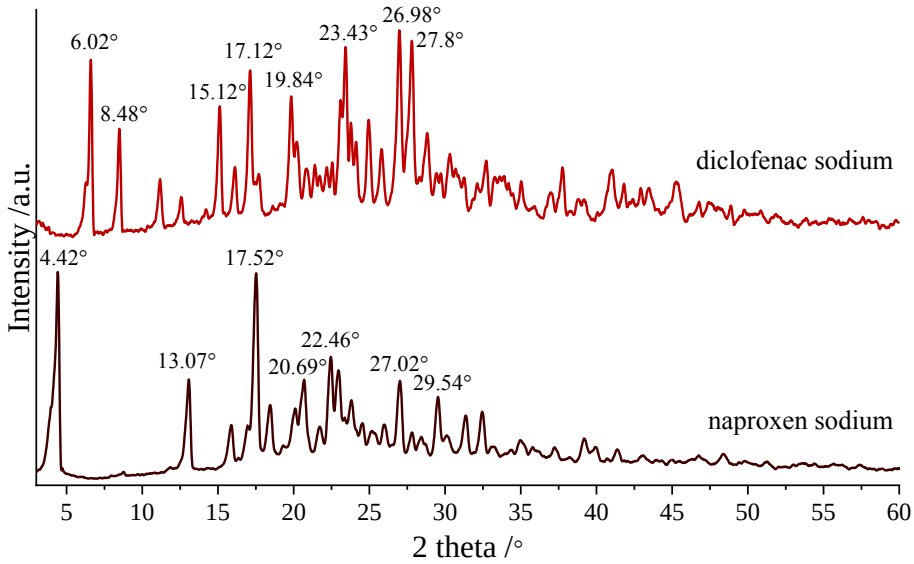

Fig. S5 X-ray diffractograms of the naproxen and diclofenac sodium salts.

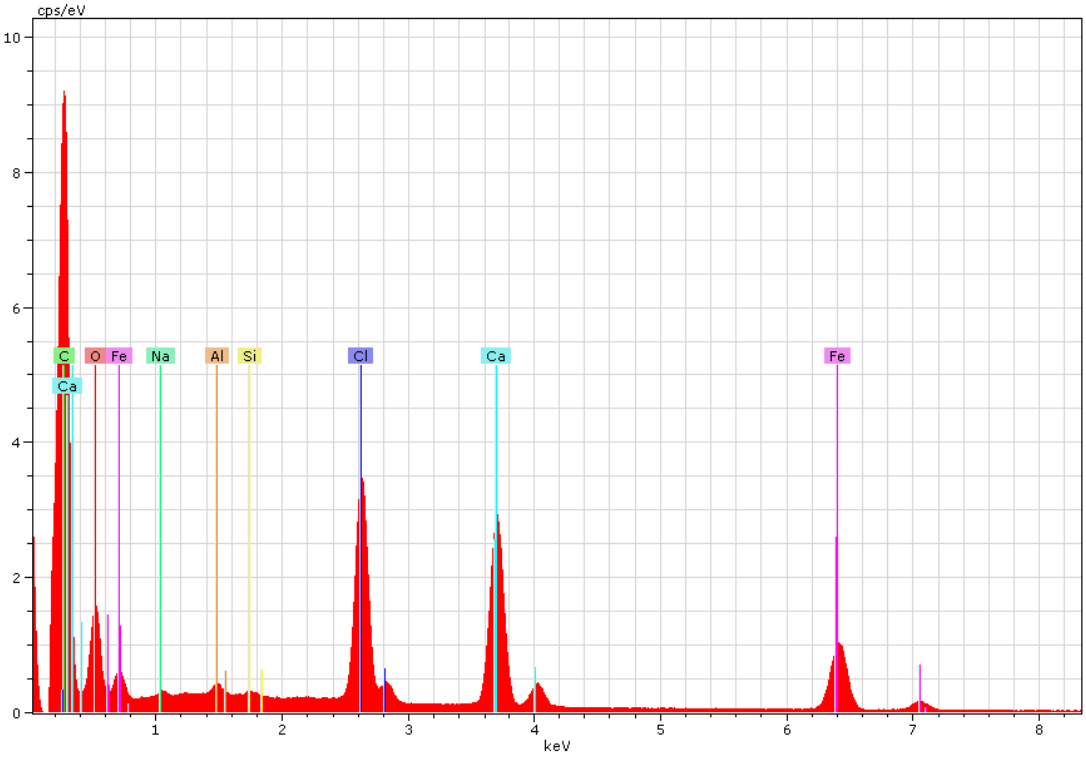

Fig. S6 Energy dispersive X-ray analysis spectrum of diclofenac anion−CaFe-LDH composite (signals of silicon and aluminium are originated from the adhesive tape/sample holder).

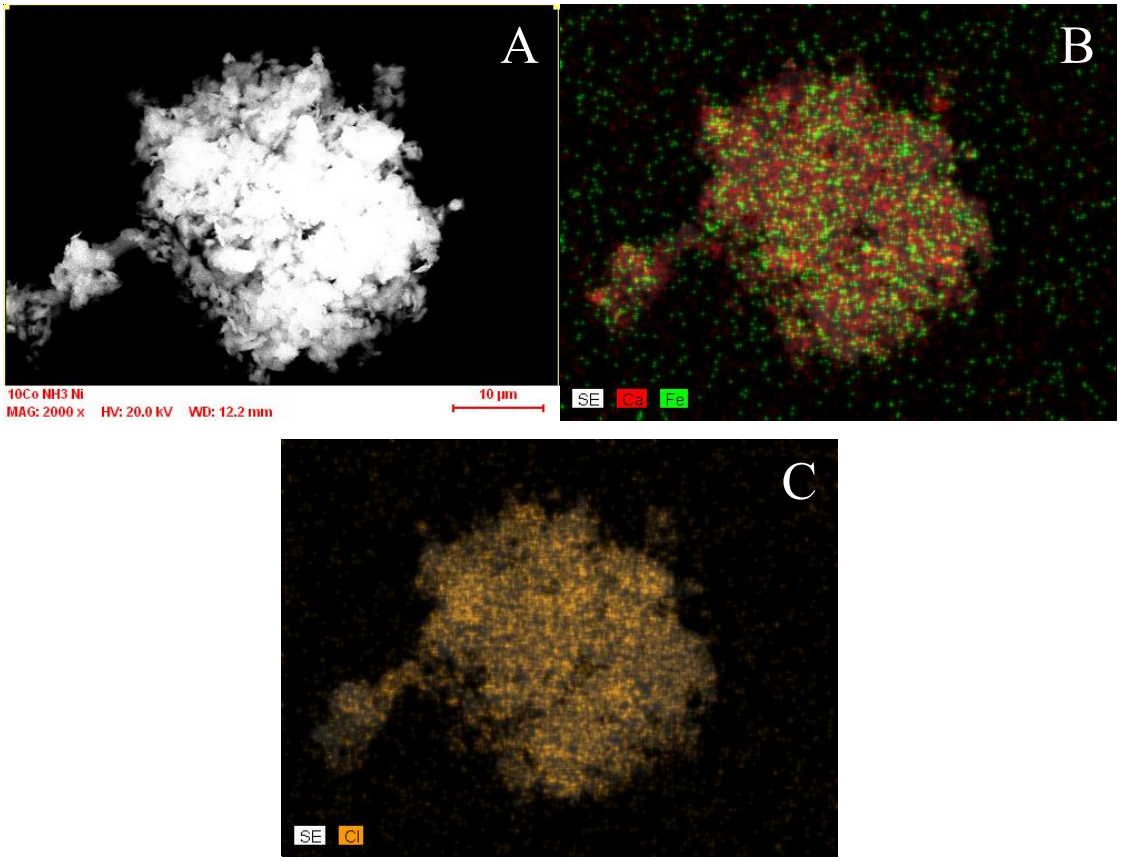

Fig. S7 SEM (A) and elemental map (B and C) images from the diclofenac anion−CaFe-LDH.

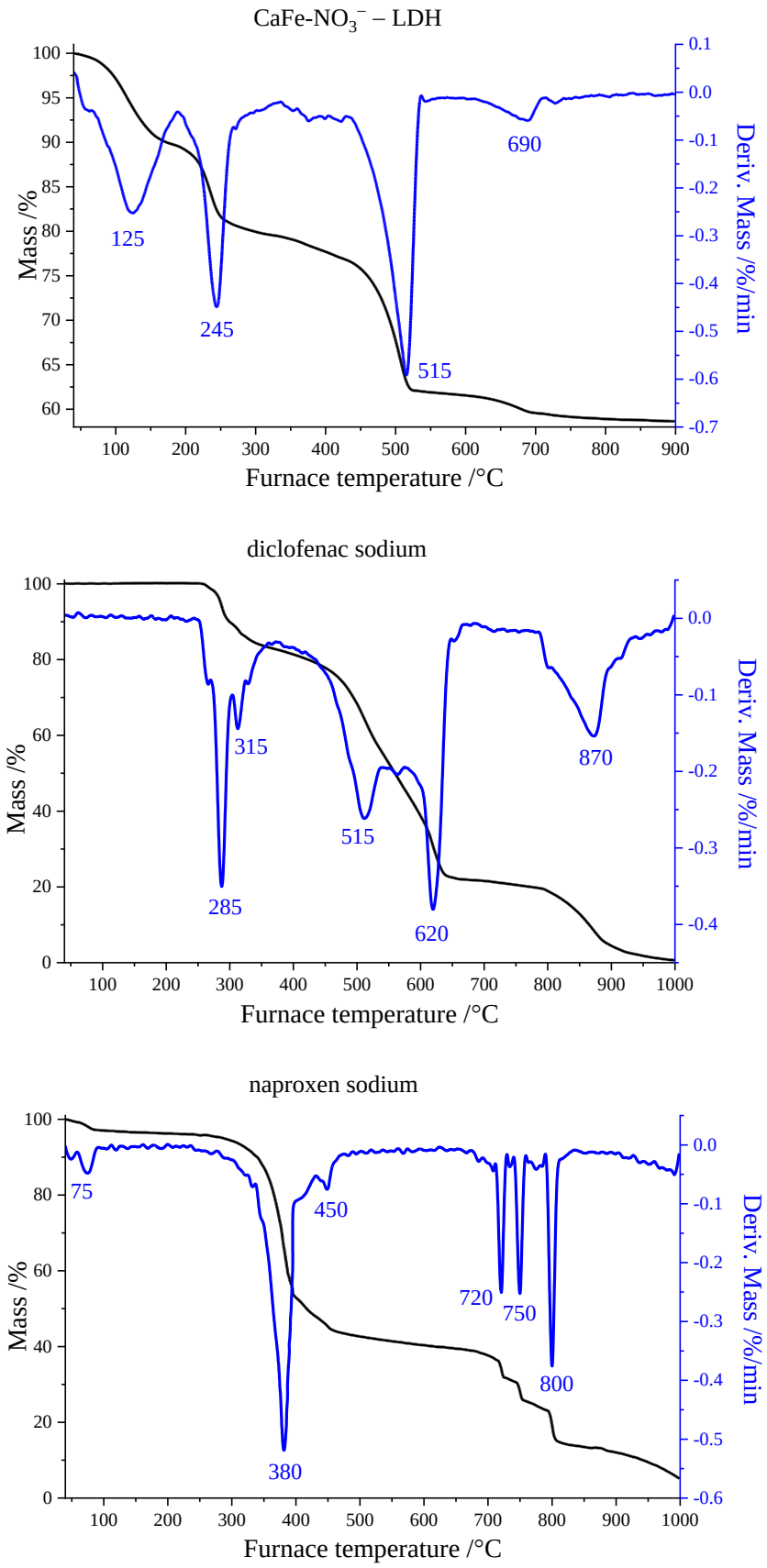

Fig. S8 Thermal behaviour of the pristine CaFe-LDH and sodium salts of diclofenac and naproxen.

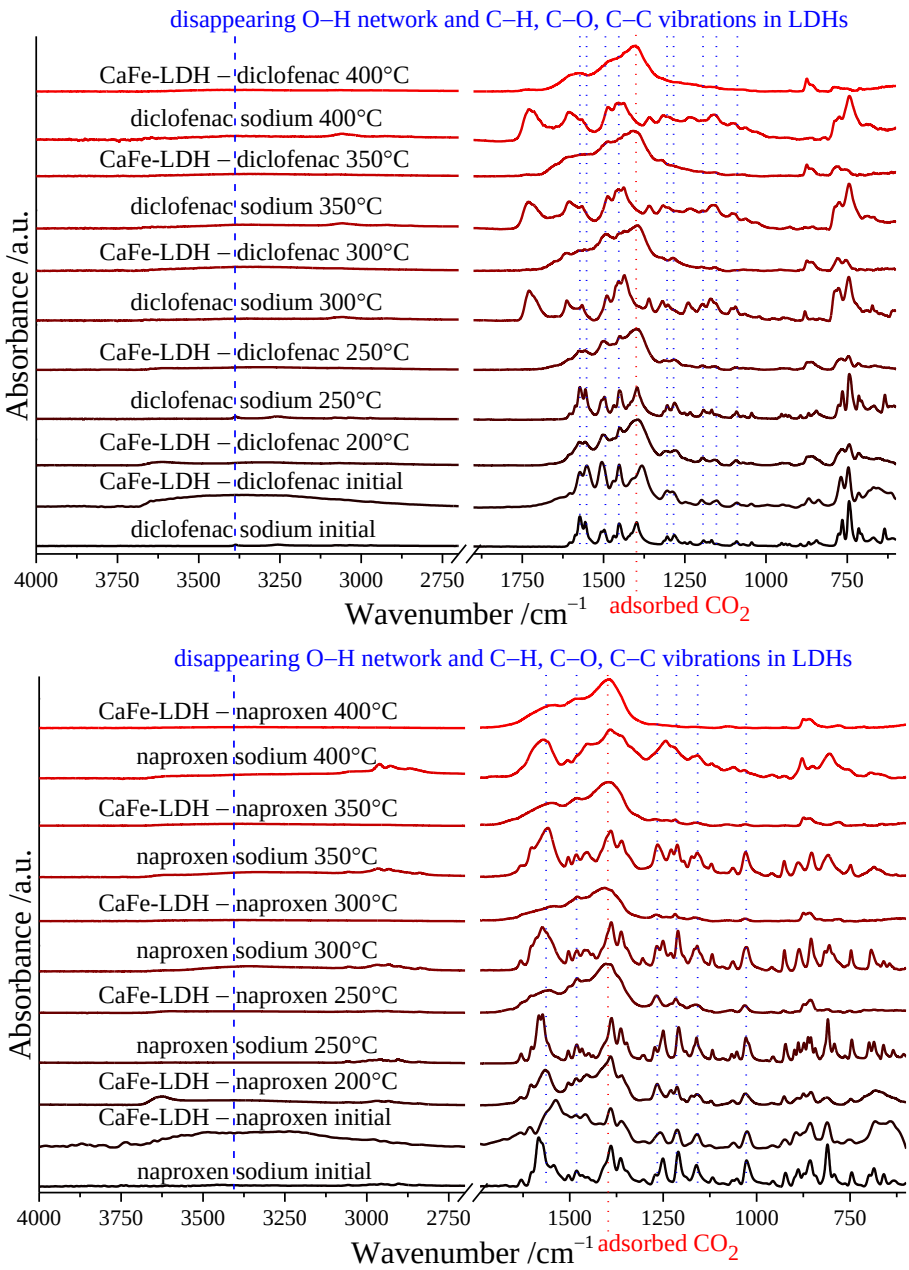

Fig. S9 Infrared spectra of diclofenac, naproxen sodium salts and drug-intercalated (by the dehydroxylation-rehydration technique) LDH solids after heat treatments at various temperatures.

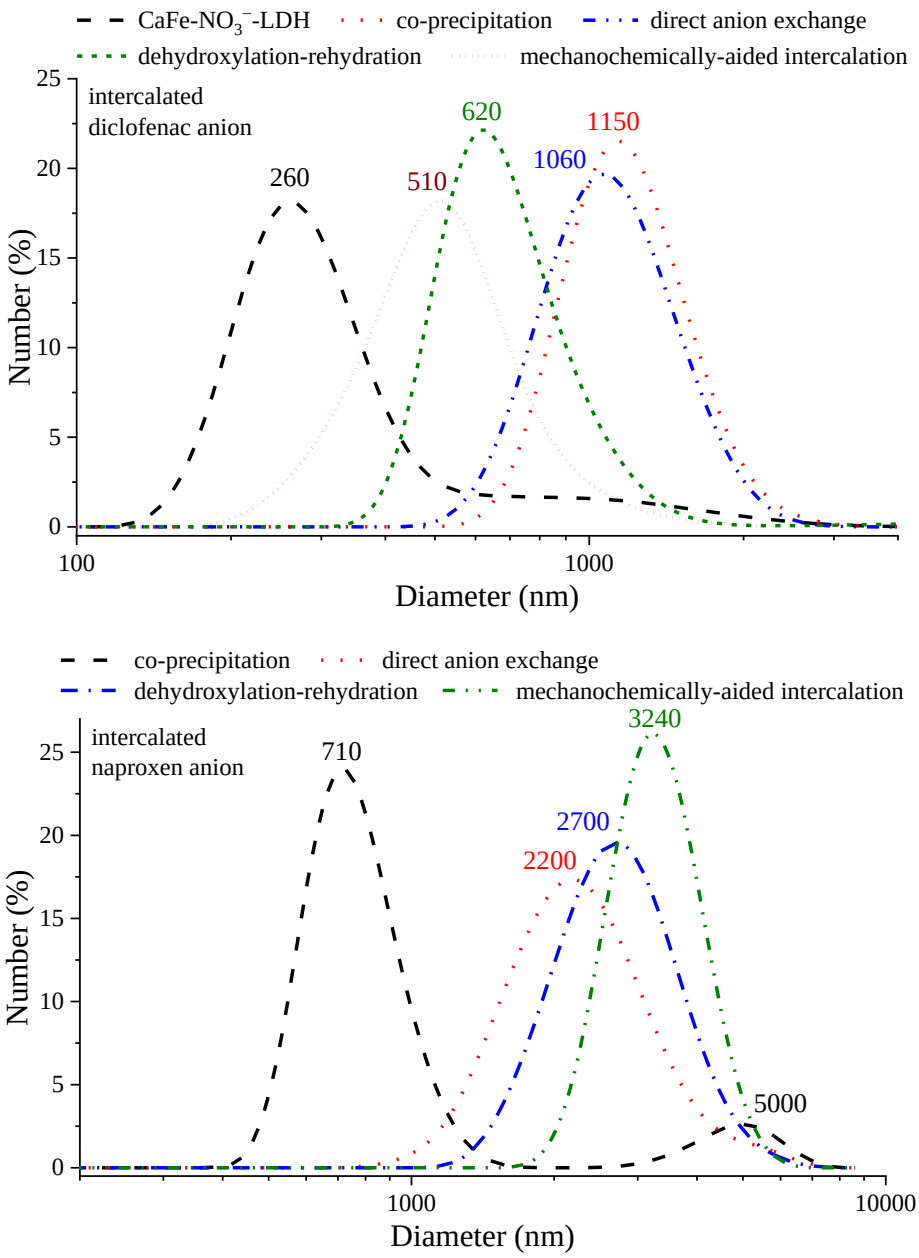

Fig. S10 The number-weighed size distribution patterns of the as-prepared (nitrate-containing), the diclofenac and the naproxen anion-intercalated CaFe-LDH particles (the numbers show the predominant solvodynamic diameters).

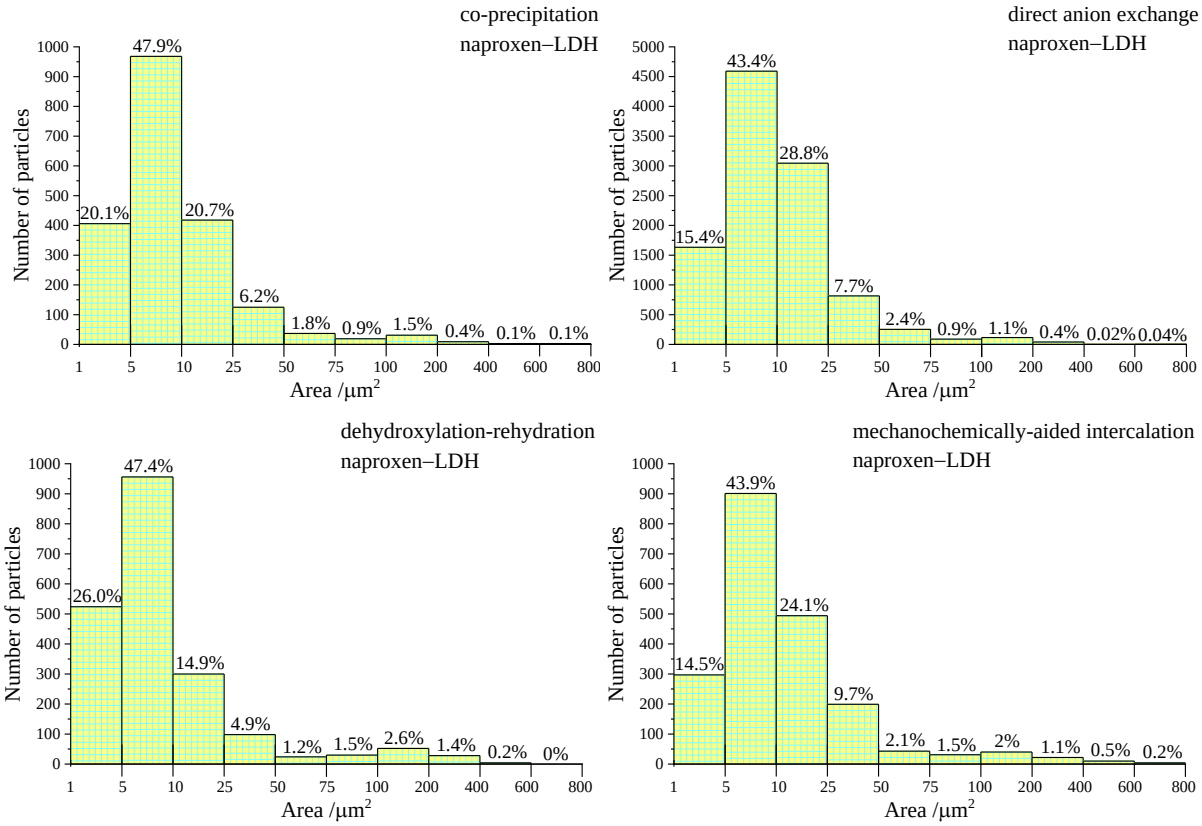

Fig. S11 Particle size distribution histograms of the naproxen anion-intercalated CaFe-LDH solids dispersed in hydrogels.

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