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Supplementary Information

Structural and morphological aspects of (fluor)quinolones delivery by layered double hydroxide nanoparticles.

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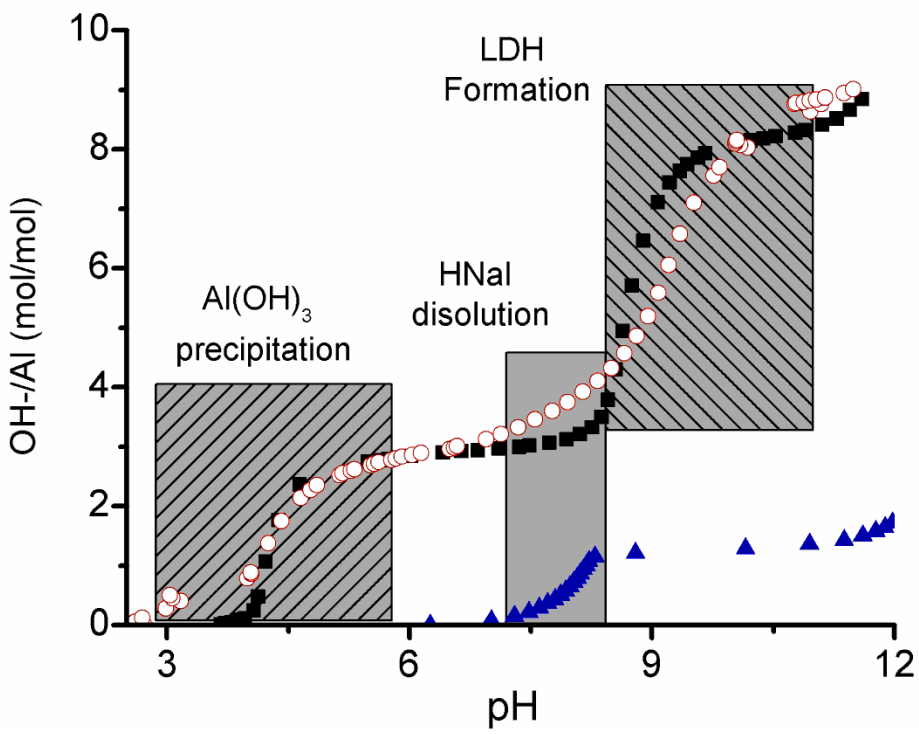

Figure S1. Titration curves of $MgCl_2$+$AlCl_3$ (3:1molar ratio) (filled squares)$MgCl_2$+$AlCl_3$+HNal (3:1:1) and pure HNal as a reference. The marked zones indicate the reactions produced in each pH range.

SI.1. Reactions involved in the synthesis of LDH-Nal-DSs.

In order to study the reactions involved in the synthesis of the LDH-Nal-DSs and the dependence of their composition with the synthesis conditions, $MgCl_2$ 0.3 mol $L^{-1}$and $AlCl_3$ 0.1 mol L^{-1} solutions (100 mL) with and without the presence of HNal (0.01 mol) were titrated with a 1 mol L^{-1}NaOH solution (Figure S1). A HNal dispersion was also titrated as a reference. A Titrando 905 automatic titrator (Metrohm) controlled by Tiamo software and coupled to a Metrohm 9.0262.100 combined pH electrode and a Dosino 800 dosing unit was used in these experiments. The titrant volumes were adjusted to achieve regular pH gaps, while equilibrium was considered reached at a 2 mV/min electrode drift.

The titration curve of the metal salts without HNal showed two OH^- consumption steps. The first one, placed between pH 3.5 and 5, corresponded to the formation of $Al(OH)_3$, which present a lower solubility than $Mg(OH)_2$[1]:

$$Al^{3+}_{(aq)} + 3\ OH^-_{(aq)} \rightarrow Al(OH)_{3(s)} \quad [1]$$

Accordingly, the plateau was obtained for a OH/Al ratio of 3 approximately. The second step, produced at pH=8-9.5, was assigned to the formation of the chloride intercalated 3:1 Mg-Al-LDH:

$$Al(OH)_{3(s)} + 3Mg^{2+}_{(aq)} + 5OH^-_{(aq)} + Cl^-_{(aq)} \rightarrow Mg_3Al(OH)_8Cl\cdot nH_2O_{(s)} \quad [2].$$

Then, the overall reaction was:

$$3Mg^{2+}_{(aq)} + Al^{3+}_{(aq)} + 8OH^-_{(aq)} + Cl^-_{(aq)} \rightarrow Mg_3Al(OH)_8Cl\cdot nH_2O_{(s)} \quad [3]$$

The titration curve in the presence of HNal exhibited these two steps but also a step assigned to the deprotonation of nalidixic acid. Nevertheless, an important aspect of the formation of the LDH-Nal conjugates was related to the interactions of Nal^- with Mg^{2+} and Al^{3+} ions [2,3]. First, the titration curves begin at a lower pH, which indicated that a portion of Nal^- ions deprotonated to interact with the metal ions concurrent in the media. Also, once the $Al(OH)_3$(s) formation and HNal dissolution begins, the generated Nal^- anions were expected to interact with Mg^{2+} ions to precipitate $Mg(Nal)_2\cdot 4H_2O$ complex:

$$Mg^{2+}_{(aq)} + 2HNal + 2OH^-_{(aq)} + 2H_2O_{(l)} \rightarrow Mg(Nal)_2\cdot 4H_2O_{(s)}. \quad [4]$$

This is the reaction competing with Nal-intercalated LDH formation in the synthesis of LDH-Nal-DSs. In the case of the titration experiment the LDH layers are formed as pH increases, according to the reaction

$$Al(OH)_{3(s)} + 2.5\ Mg^{2+}_{(aq)} + 5OH^-_{(aq)} + 0.5\ Mg(Nal)_2\cdot 4H_2O_{(s)}. \rightarrow Mg_3Al(OH)_8Nal\cdot nH_2O_{(s)} \quad [5]$$

The overall reaction for this titration can then be written as

$3Mg^{2+}_{(aq)} + Al^{3+}_{(aq)} + HNal_{(aq)} + 9OH^{-}_{(aq)} \rightarrow Mg_3Al(OH)_8Nal \cdot nH_2O_{(s)}$ [6]

This reaction was consistent with the plateau reached at a OH/Al ratio around 8.8. Note that, if $Mg(Nal)_2 \cdot 4H_2O_{(s)}$ had not dissolved, the theoretical OH/Al value would be lower, according to the following reaction.

$3Mg^{2+}_{(aq)} + Al^{3+}_{(aq)} + HNal_{(aq)} + 8OH^{-}_{(aq)} \rightarrow 0.5\ MgNal_{2(s)} + Mg_{2.5}Al(OH)_7Cl \cdot nH_2O_{(s)}$ [7]

Then, the reactions involved in the synthesis of LDH by coprecipitation at constant or variable pH would be those represented in eq. [4] and [6]. The preference for one or another and, consequently, the phases obtained would be determined by the synthesis conditions, specially $[OH]^-$ during the synthesis. Conditions were a large excess of OH^- anions were maintained (low supersaturation, variable pH→LDH-Nal-pHvar) favored reaction [6], while those where OH^- is just enough to produce LDH precipitation (low supersaturation, constant pH, LDH-Nal-pHcte) produced competition between reactions [4] and [6].

SI.2. NaI affinity for LDH layers and effect of $Mg(NaI)_2$ on LDH-NaI-DSs.

To complete the study of the interaction of NaI anions with the LDH layers and its effect on the properties of the obtained LDH-NaI conjugates, 1.00 g L^{-1} LDH-Cl dispersions with increasing NaI concentration ([NaI] ranging from 0.07 to 5.9 mmol L^{-1}) were equilibrated overnight. [NaI] in the supernatants was measured by UV-Vis spectrophotometry at λ=330 nm to determine NaI uptake (Γ) by LDH-Cl. Also, the hydrodinammic diameter (d) and zeta potential (ζ) of the particles was determined and portion of the solids obtained were dried to obtain their PXRD patterns.

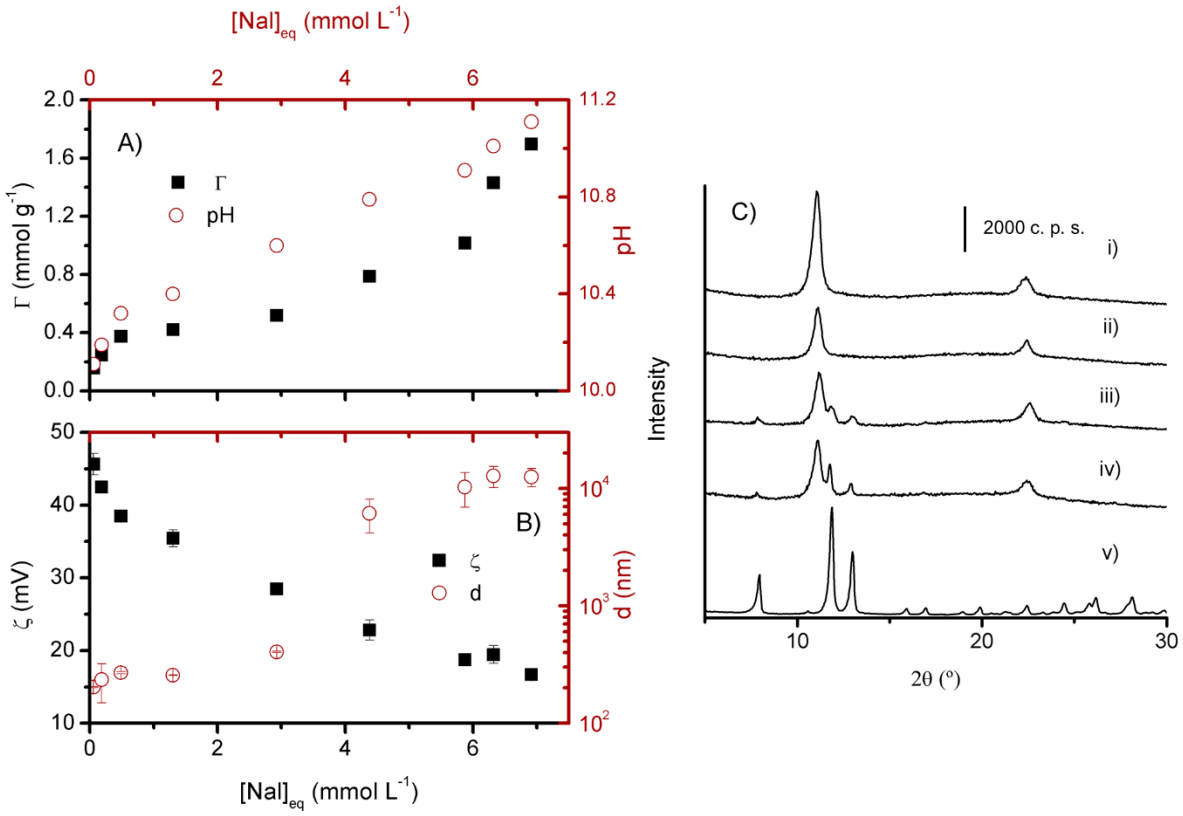

Figure S2. NaI uptake (Γ), pH, ζ and d vs. [NaI] curves (A and B) in 1 g L^{-1} LDH-Cl dispersions with increasing initial [NaI]. C) PXRD patterns of the solids obtained at 0.1 g L^{-1} (i), 0.4 g L^{-1} (ii), 1.2 g L^{-1} (iii), 1.8 g L^{-1} (iv); as well as a that of $Mg(NaI)_2$ (v).

The sorption isotherm showed two stages:at low [NaI], there is a first uptake that reached a plateau at around Γ=0.4 mmol g^{-1}, corresponding to 15 % of the anion exchange capacity (AEC) of LDH-Cl. This stage was associated with adsorption of NaI anions. In this stage, a ζ decrease was produced, which indicated that NaI anions possessed higher affinity fpr LDH surface than chloride anions. Nevertheless, the ζ diminution did not produced a charge reversal, which indicated that nalidixate only held electrostatic interactions with the LDH surface [4]. As a consequence of the small ζ diminution, the LDH-Cl particles did not aggregate and, consequently, maintained their small particle size. A second stage that did not reach a plateau value in the [NaI] range of the experiments was developed at $[NaI]_{eq}$>2.5 mmol L^{-1}. This stage was associated with the partial dissolution of the Mg^{2+} ions from LDH layers and the formation of a salt with NaI^- ions:

$$Mg_3Al(OH)_8Cl\cdot nH_2O_{(s)} + 2xNaI^-_{(aq)} \rightarrow xMg(NaI)_2 + Mg_{3-x}Al(OH)_{(8-2x)}NaI\cdot nH_2O_{(s)} + 2OH^-_{(aq)} \quad [5]$$

Quite accordingly, the PXRD patterns of the solids obtained in this stage showed peaks of $Mg(NaI)_2$ reference sample. Also, the pH increase in this stage was concordant with the reaction proposed in Eq. [5]. This process led to a ζ decrease and a d increase, which was consistent with the larger size and negative zeta potential of $Mg(NaI)_2$ (see main text). These results underline the equilibrium existing between the LDH phases and $Mg(NaI)_2$ complex, which can be displaced by changes in [NaI].

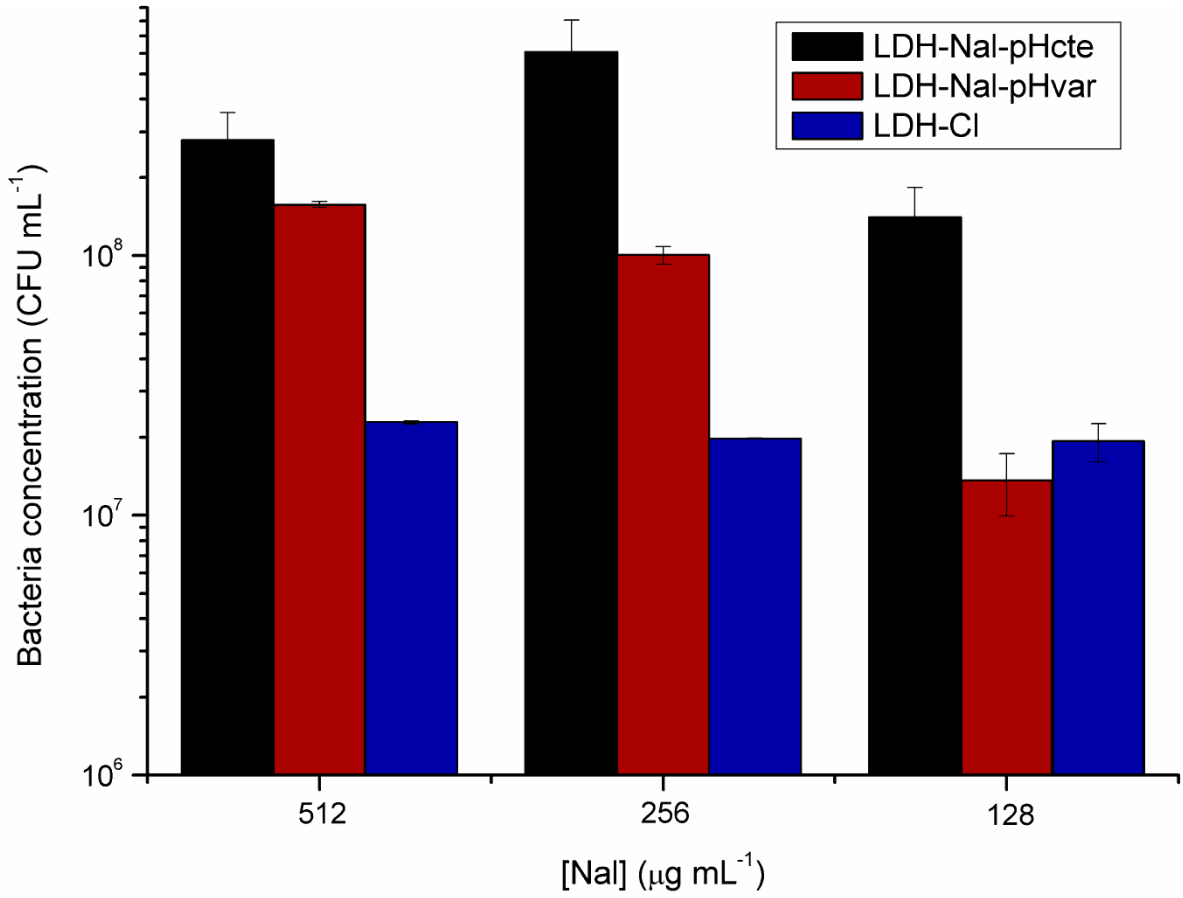

Figure S3. Bacteria count of lawn cultures on Mueller Hinton agar seeded with Mueller-Hinton broth (10^5CFU mL^{-1}) that contained [Nal] above the MIC of the samples.

References

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