

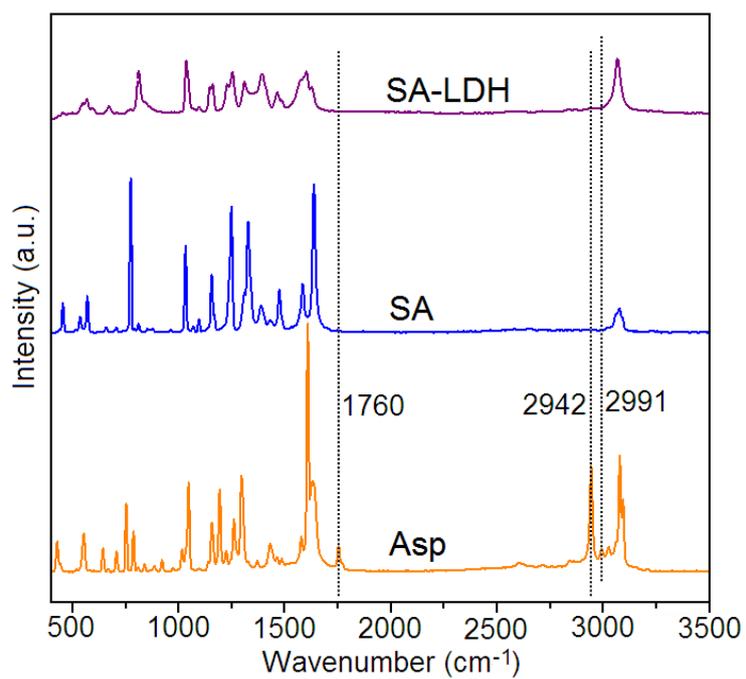
## **Supporting Information**

### **Novel Morphology-Controlled Hierarchical Core@Shell Structural Organo-Layered Double Hydroxides Magnetic Nanovehicles for Drug Release**

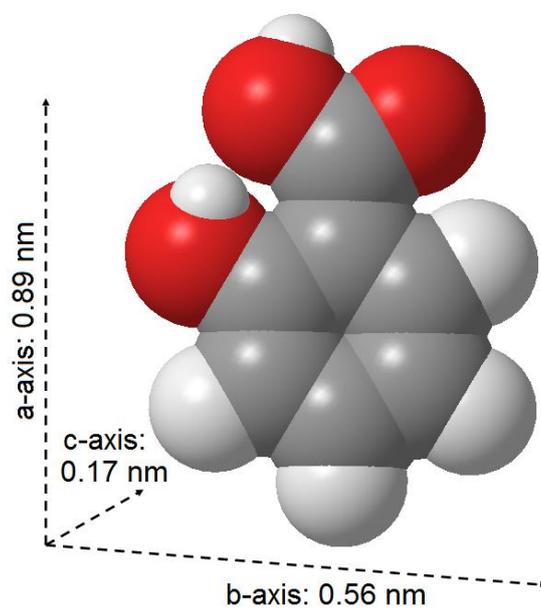
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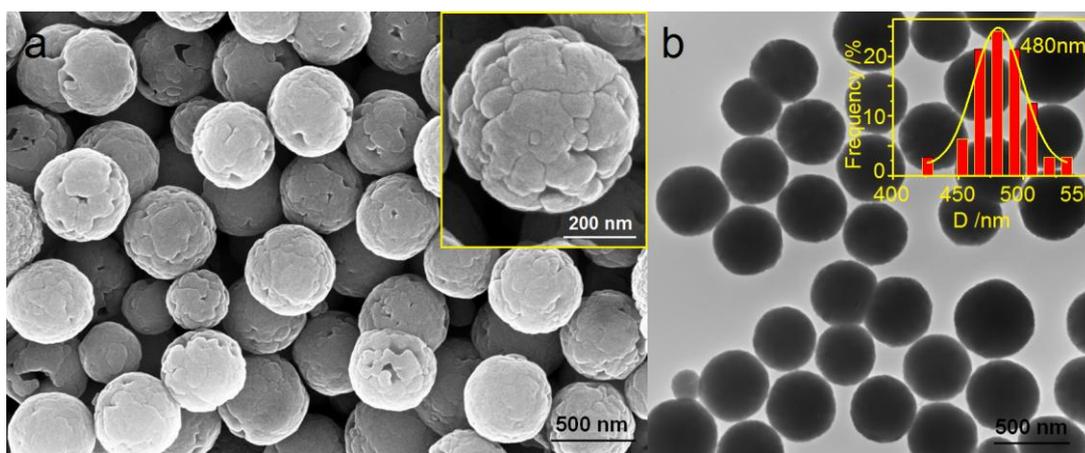
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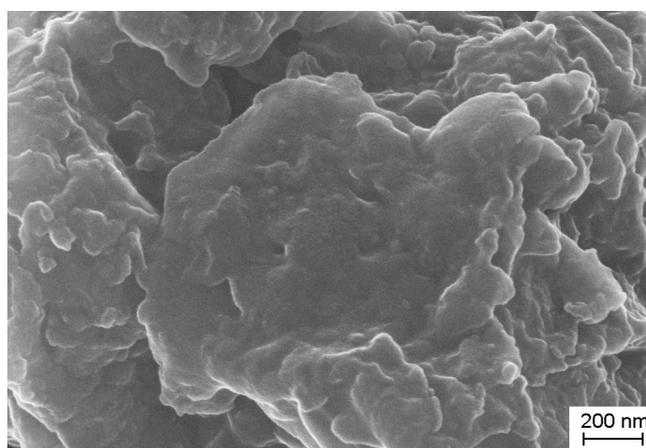
**Figure S1.** FT-Raman spectra of SA-LDH, salicylic acid (SA), and aspirin (Asp).



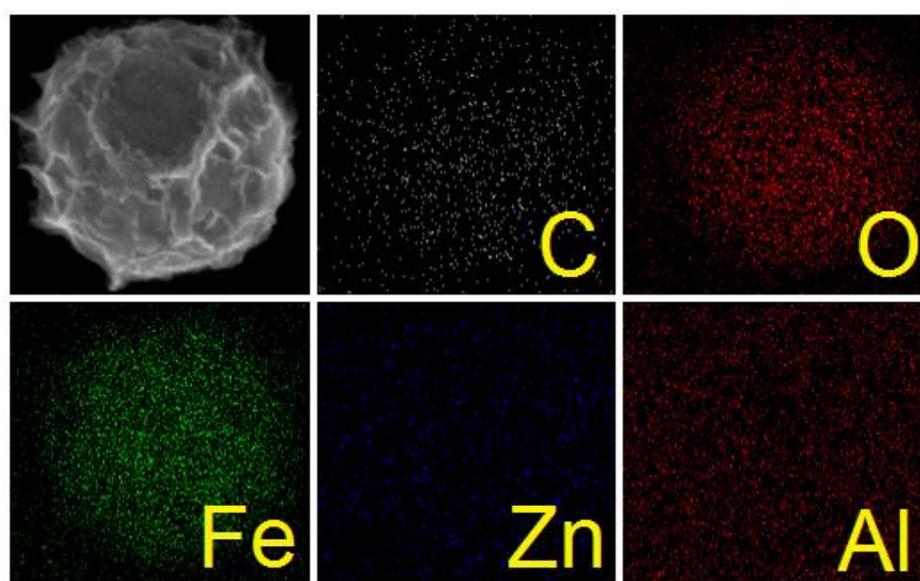
**Figure S2.** Three-dimension model of SA obtained by Chemdraw Ultra 8.0.



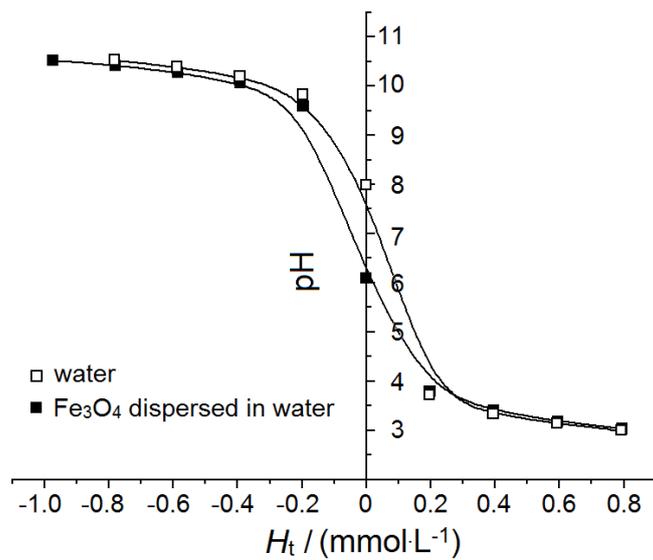
**Figure S3.** SEM (a) and TEM (b) images of  $\text{Fe}_3\text{O}_4$  nanoparticles.



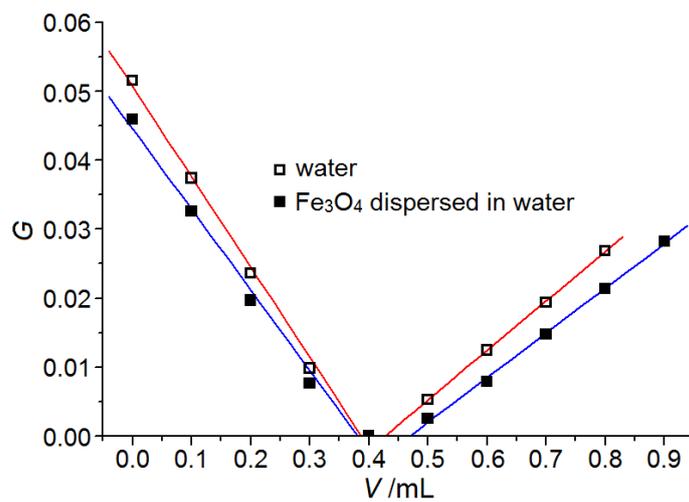
**Figure S4.** SEM image of pure SA-LDH.



**Figure S5.** EDX mapping analysis of  $\text{Fe}_3\text{O}_4@$ SA-LDH-3.85.



**Figure S6.** pH of  $\text{Fe}_3\text{O}_4$  aqueous suspension as a function concentration of the total  $\text{H}^+$  ions added to the system ( $H_t$ ).



**Figure S7.** Gran functions ( $G$ ) for the  $\text{Fe}_3\text{O}_4$  sample.

### Determination of surface OH site density ( $D_s$ ) of $Fe_3O_4$ sample.

0.08 g  $Fe_3O_4$  sample is dispersed in 50 mL of  $NaNO_3$  aqueous solution (0.1 M) under vigorous stirring in  $N_2$  flow for 2 h. 0.1 mL of HCl aqueous solution (0.1 M) is added into above  $Fe_3O_4$  suspension at set intervals (5 min) until the pH value reaches 3.0. Then, the obtained acidic  $Fe_3O_4$  suspension is inversely titrated using 0.1 mL of NaOH aqueous solution (0.1 M) at set intervals (5 min) until the pH value reaches 10.5. The pH values and the volumes of HCl and NaOH aqueous solutions are recorded.

The total acid concentrations ( $H_t$ ) and Gran ( $G$ ) function are calculated as following equations:<sup>1,2</sup>

$$H_t = (V_{at} \times C_a - V_b \times C_b) / (V_0 + V_{at} + V_b)$$

$$G \text{ (acidic side)} = (V_0 + V_{at} + V_b) \times 10^{-pH}$$

$$G \text{ (alkaline side)} = ((V_0 + V_{at} + V_b) \times 10^{-(13.8-pH)})$$

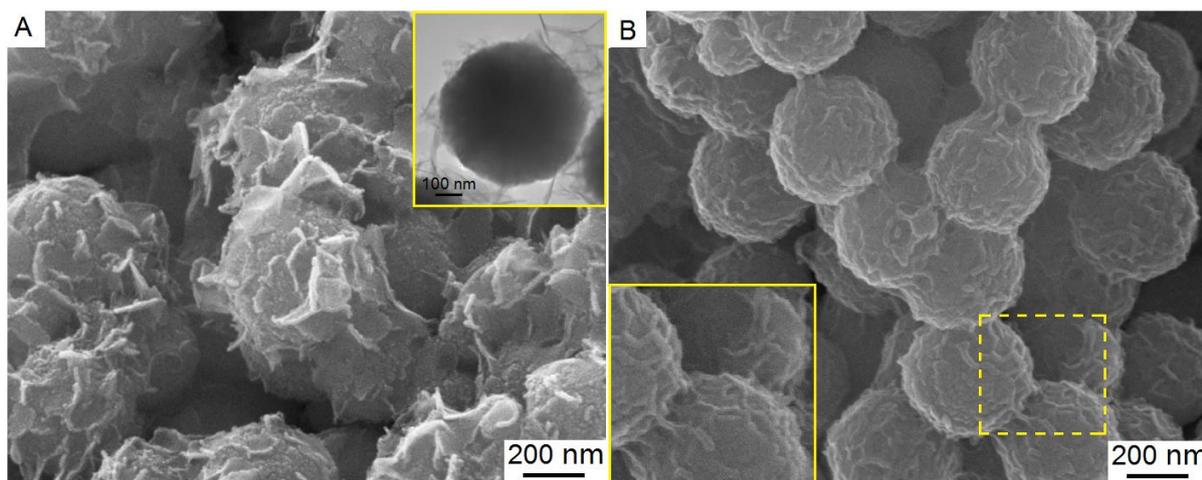
Upon the  $G$  functions, the total surface site concentration ( $H_s$ ) is calculated as following equation:

$$H_s = [(V_{e2} Fe_3O_4 - V_{e1} Fe_3O_4) \times C_b - (V_{e2} \text{ blank} - V_{e1} \text{ blank}) \times C_b] / V_0$$

The  $D_s$  is calculated as following equation:

$$D_s = (H_s \times N_A) / (S \times C_s \times 10^{18})$$

In above equations,  $V_0$ ,  $V_{at}$ ,  $V_b$  are the initial volume (50 mL) of  $Fe_3O_4$  aqueous suspension, the volume of HCl and NaOH aqueous solutions added to the suspension, respectively.  $C_a$  and  $C_b$  are the concentrations of HCl and NaOH added to the suspension, respectively.  $V_{e1}$  and  $V_{e2}$  are the volume of NaOH solution at equivalent point 1 and 2.  $N_A$  is the Avogadro constant ( $6.02 \times 10^{23}$ ).  $S$  is the specific surface area of  $Fe_3O_4$  sample ( $2.2 \text{ m}^2 \cdot \text{g}^{-1}$ ).  $C_s$  is the concentration of  $Fe_3O_4$  suspension ( $1.6 \text{ g} \cdot \text{L}^{-1}$ ).

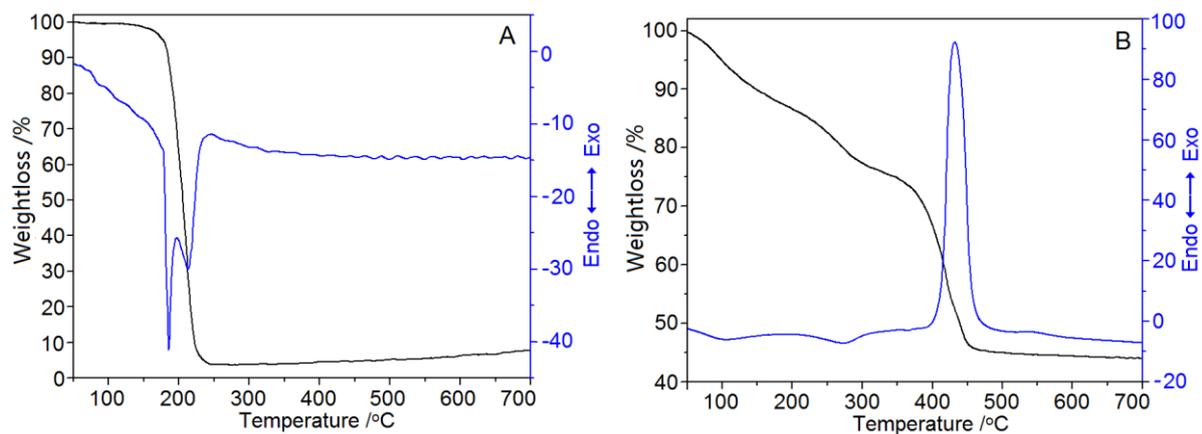


**Figure S8.** SEM images of Fe<sub>3</sub>O<sub>4</sub>@LA-ZnAl-LDH (A, inset refers to TEM image) and Fe<sub>3</sub>O<sub>4</sub>@SA-MgAl-LDH (B, inset refers to a topical magnification) nanovehicles.

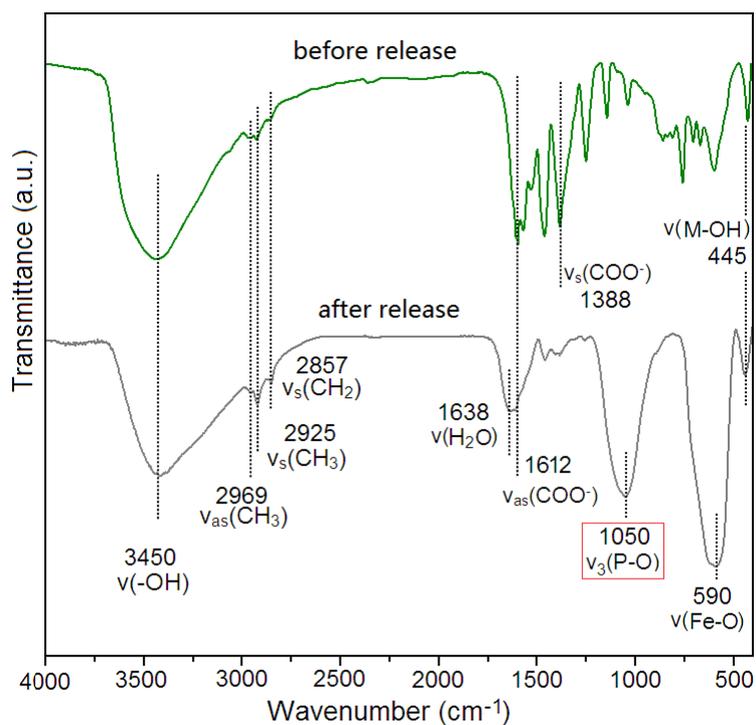
### **Synthesis experiment of L-lactic acid (LA) intercalated ZnAl-LDH and SA intercalated MgAl-LDH on the surface of Fe<sub>3</sub>O<sub>4</sub> cores.**

A uniform suspension were obtained by ultrasonically dispersing Fe<sub>3</sub>O<sub>4</sub> (0.348 g) nanoparticles in 100 mL of methanol for 15 min, and then transferred into a 500 mL four-necked flask keeping vigorous stirring at room temperature. An alkaline solution containing NaOH (2.4 g) in 80 mL of methanol as was added dropwise into above Fe<sub>3</sub>O<sub>4</sub> suspension under vigorous stirring in N<sub>2</sub> atmosphere to modulate the pH to ~8.5 and kept for 5 min for stabilization. Then, a mixed salts solution with Zn(NO<sub>3</sub>)<sub>2</sub>·6H<sub>2</sub>O (1.34 g), Al(NO<sub>3</sub>)<sub>3</sub>·9H<sub>2</sub>O (0.56 g) and LA (0.34 g) in 60 mL of methanol ([Zn<sup>2+</sup>]/[Al<sup>3+</sup>]=3, [LA]/[Al<sup>3+</sup>]=2.5) and the alkaline solution were simultaneously added dropwise into above Fe<sub>3</sub>O<sub>4</sub> suspension under vigorous stirring in N<sub>2</sub> flow with constant pH ~8.5 for 1.5 h. The resultant was aged at 60 °C for 24 h, separated by a magnet of 0.15 T, washed with deionized water until pH 7.0 and dried in vacuum at 60 °C for 24 h giving the product Fe<sub>3</sub>O<sub>4</sub>@LA-ZnAl-LDH.

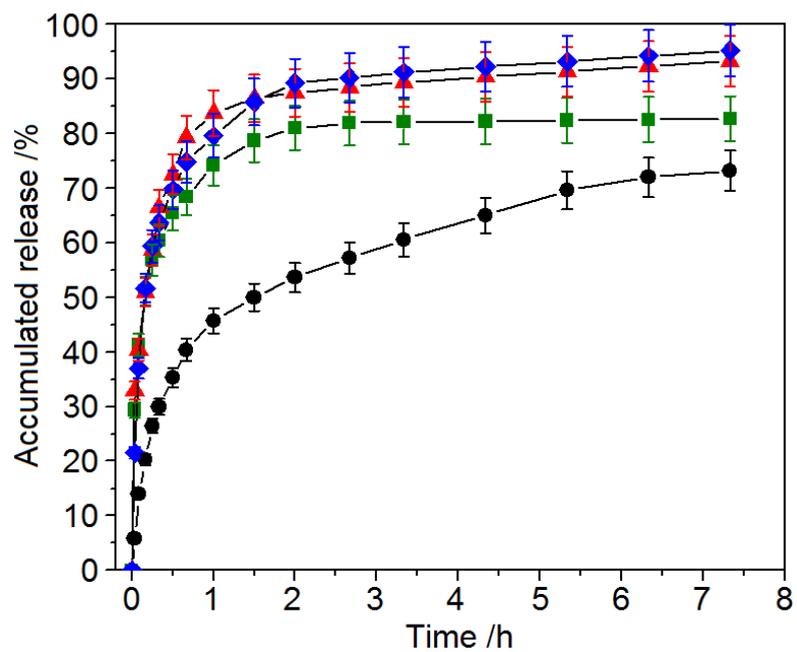
The synthesis procedure of SA intercalated MgAl-LDH on Fe<sub>3</sub>O<sub>4</sub> surface (denoted as Fe<sub>3</sub>O<sub>4</sub>@SA-MgAl-LDH) is similar to that of Fe<sub>3</sub>O<sub>4</sub>@SA-LDH-3.85 except the mixed salts solution containing Mg(NO<sub>3</sub>)<sub>2</sub>·6H<sub>2</sub>O (11.534 g), Al(NO<sub>3</sub>)<sub>3</sub>·9H<sub>2</sub>O (5.6 g) and Asp (6.8 g) with molar ratio of [Asp]/[Mg<sup>2+</sup>]/[Al<sup>3+</sup>]=2.5/3/1) and the coprecipitation pH kept at 10.0.



**Figure S9.** TG-DTA curves of pure SA (A) and SA-LDH (B).



**Figure S10.** FT-IR spectra of Fe<sub>3</sub>O<sub>4</sub>@SA-LDH-3.85 before and after *in vitro* drug release test.



**Figure S11.** *In vitro* release profiles of SA-LDH (black dot) and Fe<sub>3</sub>O<sub>4</sub>@SA-LDH-r (1.93: green square; 3.85: red triangle; 7.71: blue diamond) in pH 4.60 PBS.

**Table S1.** XRD structural parameters and chemical compositions of the Fe<sub>3</sub>O<sub>4</sub>@SA-LDH-r magnetic nanovehicles and related samples.

Samples	$d_{003}/\text{nm}$	$d_{110}/\text{nm}$	$a/\text{nm}^a$	GH /nm <sup>b</sup>	Zn/Al ratio		Zn/Fe ratio		$x^e$	$S$ /nm <sup>2</sup> /e <sup>f</sup>	SA loading /wt% <sup>g</sup>
					bulk <sup>c</sup>	Surf. <sup>d</sup>	bulk <sup>c</sup>	Surf. <sup>d</sup>			
SA-LDH	1.47	0.1521	0.3042	0.988	3.24	2.89	—	—	0.24	0.340	19.2 (19.3)
Fe <sub>3</sub> O <sub>4</sub> @SA-LDH-1.93	1.36	0.1540	0.3080	0.885	3.07	3.14	0.25	9.72	0.25	0.334	2.7 (2.5)
Fe <sub>3</sub> O <sub>4</sub> @SA-LDH-3.85	1.38	0.1536	0.3072	0.899	3.10	2.58	0.43	23.9	0.24	0.335	3.3 (3.1)
Fe <sub>3</sub> O <sub>4</sub> @SA-LDH-7.71	1.40	0.1534	0.3068	0.918	3.38	2.51	0.85	27.5	0.23	0.357	5.5 (5.2)
Sal-Mg <sub>2</sub> Al-LDH <sup>h</sup>	1.63	0.1515	0.303	1.150	1.97(Mg/Al)	—	—	—	0.37	0.236	29.8

<sup>a</sup> Based on hexagonal crystal system,  $a = 2d_{110}$ .

<sup>b</sup> Gallery height (GH) =  $d_{003} - 0.48$  nm (the thickness of LDH layer is 0.48 nm).

<sup>c</sup> The Zn/Al and Zn/Fe molar ratios in bulk phase are obtained from ICP analysis.

<sup>d</sup> The Zn/Al and Zn/Fe molar ratios in surface are obtained from XPS analysis.

<sup>e</sup>  $x = \text{Al}/(\text{Zn}+\text{Al})$ , refers to the LDH layer charge density.

<sup>f</sup>  $S$ : available surface area per unit charge of the LDH layer,  $S_{\text{unit-charge}} = (a^2 \cdot \sin 60^\circ)/x$ .<sup>3</sup>

<sup>g</sup> Drug loadings are based on CHN data while those in blanket upon the UV measurement of the dissolved samples.

<sup>h</sup> Data taken from the reference 36 in the manuscript.

**Table S2.** XPS results of the Fe<sub>3</sub>O<sub>4</sub>@SA-LDH-r magnetic nanovehicles and related samples.

Samples	Zn 2p <sub>3</sub> /eV	Al 2p <sub>3</sub> /eV	Fe 2p <sub>3</sub> /eV	C 1s/eV			O 1s/eV		
				O=C=O	C-OH	C-C/C-H	H <sub>2</sub> O/-OH	Zn-O-Al	O <sup>2-</sup>
Fe <sub>3</sub> O <sub>4</sub> @SA-LDH-1.93	1022.2	74.7	709.9	288.5	285.6	284.7	533.3	532.2	531.4
Fe <sub>3</sub> O <sub>4</sub> @SA-LDH-3.85	1022.0	74.2	710.3	289.0	285.5	284.6	532.9	532.0	530.9
Fe <sub>3</sub> O <sub>4</sub> @SA-LDH-7.71	1022.8	74.1	708.9	287.3	286.5	284.1	533.4	—	531.6
SA-LDH	1021.9	74.4	—	289.0	285.5	284.6	532.8	531.9	531.0
Fe <sub>3</sub> O <sub>4</sub>	—	—	710.4	—	—	—	532.1	—	529.7

**Table S3.** The ion products and coprecipitation pH values in the synthesis process of varied LDH systems. <sup>a</sup>

Samples	$[M^{2+}][OH^-]^2$ (M= Zn, Mg, or Ni) <sup>b</sup>	$[Al^{3+}][OH^-]^3$ <sup>b</sup>	pH	Refs <sup>c</sup>
Fe <sub>3</sub> O <sub>4</sub> @SA-LDH-1.93	$3.75 \times 10^{-16}$	$3.95 \times 10^{-23}$	constant at 8.5	This work
Fe <sub>3</sub> O <sub>4</sub> @SA-LDH-3.85	$7.50 \times 10^{-16}$	$7.91 \times 10^{-23}$	constant at 8.5	This work
Fe <sub>3</sub> O <sub>4</sub> @SA-LDH-7.71	$1.50 \times 10^{-15}$	$1.19 \times 10^{-22}$	constant at 8.5	This work
SA-LDH	$2.50 \times 10^{-15}$	$2.75 \times 10^{-22}$	constant at 8.5	This work
5-ASA-LDH/MgFe <sub>2</sub> O <sub>4</sub>	$5.70 \times 10^{-11}$	$1.29 \times 10^{-14}$	adjusted to 8.4	[20]
IBU-Zn <sub>2</sub> Al-LDH	$2.76 \times 10^{-7}$	$1.31 \times 10^{-10}$	adjusted to 10.0	[9]
5-ASA-LDHcp2	$9.38 \times 10^{-12}$	$5.86 \times 10^{-16}$	adjusted to 8.4	[38]
Lactate-ZnAl-LDH(ZAL313)	$1.87 \times 10^{-12}$	$5.40 \times 10^{-17}$	constant at 10	[48]
Zn <sub>3</sub> AlCO <sub>3</sub>	$2.50 \times 10^{-14}$	$8.33 \times 10^{-20}$	constant at 9.0	[49]
IBU-MgAl-LDH/MgFe <sub>2</sub> O <sub>4</sub>	$5.00 \times 10^{-8}$	$1.25 \times 10^{-11}$	adjusted to 10.0	[22]
DIC-MgAl-LDH/MgFe <sub>2</sub> O <sub>4</sub>	$5.00 \times 10^{-8}$	$1.25 \times 10^{-11}$	adjusted to 12.8	[23]
Fe <sub>3</sub> O <sub>4</sub> @MgAl-LDH	$4.50 \times 10^{-13}$	$1.50 \times 10^{-17}$	constant at 10	[26]
Fe <sub>3</sub> O <sub>4</sub> @CuMgAl-1	$5.86 \times 10^{-13}$	$2.34 \times 10^{-17}$	constant at 10	[28]
Fe <sub>3</sub> O <sub>4</sub> @CuMgAl-2	$3.75 \times 10^{-13}$	$1.50 \times 10^{-17}$	constant at 10	[28]
Fe <sub>3</sub> O <sub>4</sub> @CuNiAl-LDH	$1.70 \times 10^{-14}$ – $1.70 \times 10^{-13}$	$2.37 \times 10^{-19}$ – $2.37 \times 10^{-18}$	constant at 9.5–10.0	[27]

<sup>a</sup> The  $K_{sp}$  of Zn(OH)<sub>2</sub>, Mg(OH)<sub>2</sub>, Ni(OH)<sub>2</sub>, and Al(OH)<sub>3</sub> are  $3.0 \times 10^{-17}$ ,  $5.6 \times 10^{-12}$ ,  $2 \times 10^{-15}$ , and  $1.33 \times 10^{-33}$ , respectively.

<sup>b</sup> The constant [OH<sup>-</sup>] values in the double-drop coprecipitation method are obtained upon the pH value, while the initial [OH<sup>-</sup>] values in the single-drop coprecipitation method are obtained upon the concentration of alkali.

<sup>c</sup> The sequence number of the references is same as those in the manuscript.

**Table S4.** Kinetic parameters about the homogeneous nucleation process of Zn(OH)<sub>2</sub> and Mg(OH)<sub>2</sub>.<sup>a</sup>

Hydroxides	[Zn <sup>2+</sup> ][OH <sup>-</sup> ] <sup>2</sup> or [Mg <sup>2+</sup> ][OH <sup>-</sup> ] <sup>2</sup>	K <sub>sp</sub>	S	v <sub>0</sub> /m <sup>3</sup> mol <sup>-1</sup>	C* /mol m <sup>-3</sup>	D /m <sup>2</sup> s <sup>-1</sup>	σ /J m <sup>-2</sup>	A /m <sup>3</sup> s <sup>-1</sup>	J /m <sup>3</sup> s <sup>-1</sup>	J' <sup>b</sup> /m <sup>3</sup> s <sup>-1</sup>
Zn(OH) <sub>2</sub>	7.50×10 <sup>-16</sup>	3×10 <sup>-17</sup>	24	5.41×10 <sup>-29</sup>	2.021×10 <sup>-3</sup>	8.8×10 <sup>-10</sup>	1.054	1.217×10 <sup>8</sup>	2.914×10 <sup>9</sup>	4.056×10 <sup>14</sup>
Mg(OH) <sub>2</sub>	7.50×10 <sup>-16</sup>	5.6×10 <sup>-12</sup>	—	4.11×10 <sup>-29</sup>	0.1651	2×10 <sup>-9</sup>	1.193	2.627×10 <sup>10</sup>	—	4.683×10 <sup>11</sup>

<sup>a</sup> Concentration of Zn<sup>2+</sup> or Mg<sup>2+</sup> ions is same as the [Zn<sup>2+</sup>] in the synthesis process of Fe<sub>3</sub>O<sub>4</sub>@SA-LDH-3.85.

<sup>b</sup> The [Mg<sup>2+</sup>][OH<sup>-</sup>]<sup>2</sup> or [Zn<sup>2+</sup>][OH<sup>-</sup>]<sup>2</sup> values are designed as 10<sup>-10</sup> to make sure that the Mg<sup>2+</sup> ions can be precipitated into Mg(OH)<sub>2</sub>.

## REFERENCES AND NOTES

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- (2) Zhang, W. M.; Yang, Z. D.; Liu, J.; Sun, Z. X. Determination of Acid-Base Equilibrium Constants on Aqueous Mesoporous Silica Surfaces. *Acta Phys. -Chim. Sin.* **2010**, *26*, 2109–2114.
- (3) Xu, Z. P.; Zeng, H. C. Abrupt Structural Transformation in Hydrotalcite-Like Compounds Mg<sub>1-x</sub>Al<sub>x</sub>(OH)<sub>2</sub>(NO<sub>3</sub>)<sub>x</sub>·nH<sub>2</sub>O as a Continuous Function of Nitrate Anions. *J. Phys. Chem. B* **2001**, *105*, 1743–1749.