Table S1. Supporting data summary for reviewers

LDH	(XRD, FTIR, SEM/TEM, PSD) Availability	Z-Average size (nm)	PDI	ζ-potential (mV)	Note
1. LDH	(XRD, FTIR, TEM, PSD)	110	0.14	43	
2. sLDH	(XRD, FTIR, TEM, PSD)	50	0.17	39	
3. lLDH	(TEM, PSD)	210	0.18	43	
4. LDH-BSA in H2O	(FTIR, TEM, PSD)	150	0.22	-20	
5. LDH-BSA in PBS		180	0.20	-15	LDH:BSA = 2:25
6. LDH-FITC	(XRD, FTIR, TEM, PSD)	100	0.20	41	10% FITC in total anions exchanged
7. LDH-FITC-BSA in H2O		180	0.29	-23	As above
8. LDH-FITC-BSA in PBS		167	0.24	-13	As above
9. LDH-LMWH	(XRD, FTIR, SEM, PSD)	123	0.23	35	10% LMWH in total anions exchanged
10. LDH-LMWH-BSA in H2O		198	0.26	-19	As above. LDH:BSA = 2:12.5
11. LDH-LMWH-BSA in culture medium		165	0.24	-17	As above. LDH:BSA = 2:12.5
12. LDH-MTX	(XRD, FTIR, SEM, PSD)	103	0.16	40	10% MTX in total anions exchanged
13. LDH-MTX-BSA in H2O		173	0.25	-17	As above.
14. LDH-MTX-BSA in culture medium		179	0.25	-15	As above
15. LDH-BSA-ODN in H2O	(PSD)	170	0.15	-24	LDH:ODN = 40:1
16. LDH-BSA-ODN in PBS	(PSD)	173	0.19	-16	LDH:ODN = 40:1
17. LDH-ODN (10:1)	(XRD, TEM)	200-700	--	-26 to 40	Different ODNs

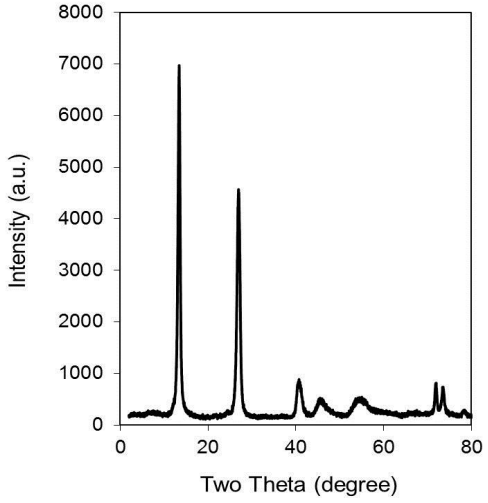
a) Following supplementary figures were displayed sequentially;

b) LDH:BSA mass ratio was 2:5, and otherwise indicated.

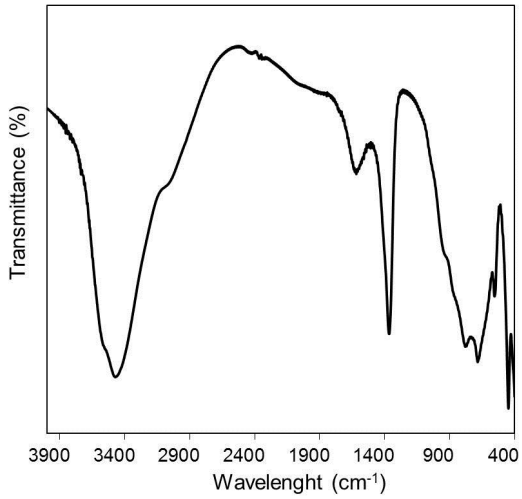
Supplementary Figures

1. LDH

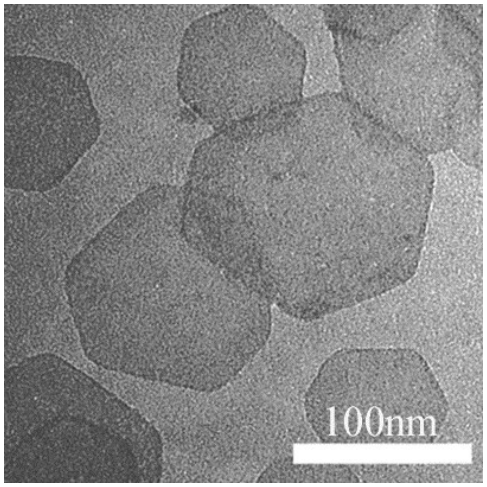
XRD



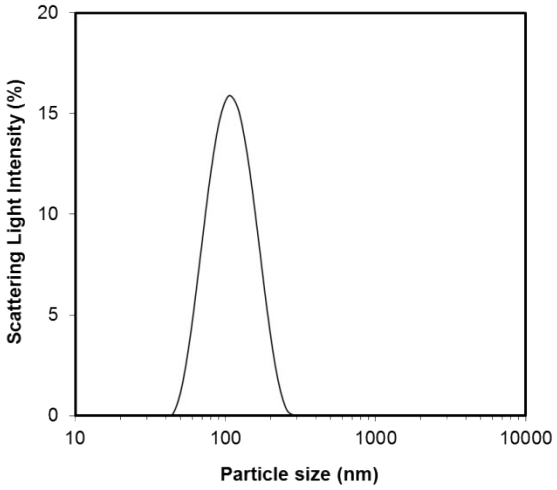
FTIR



TEM



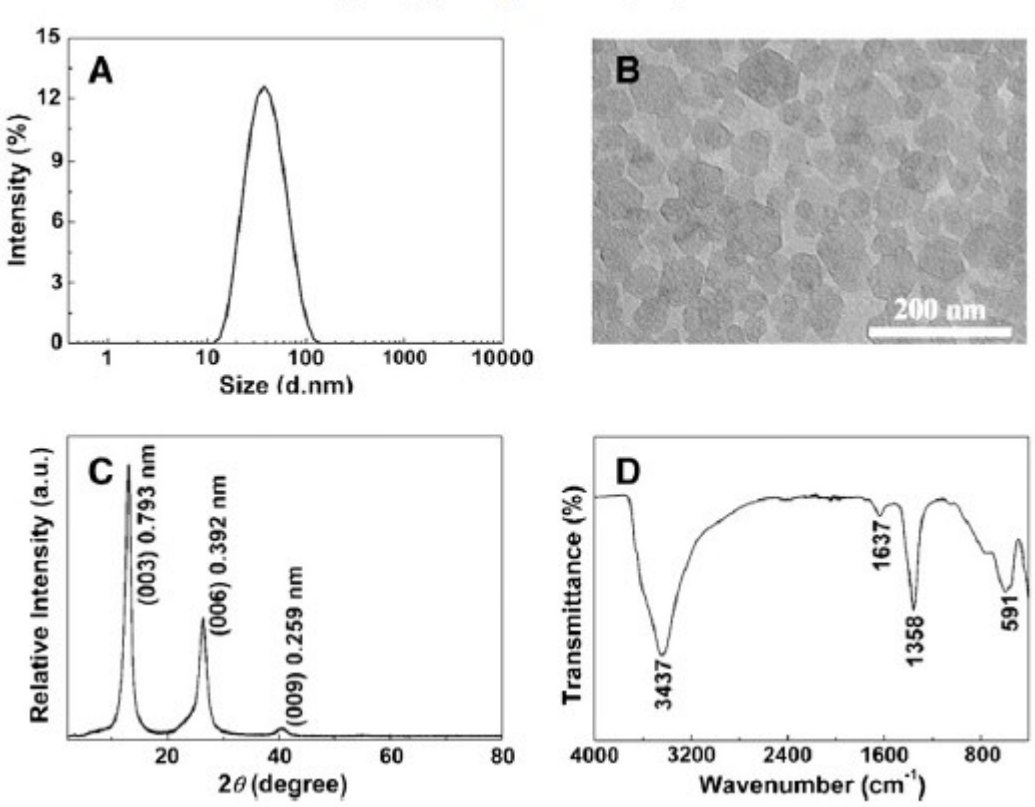
PSD



Refs:

Xu, ZP; Stevenson, G; Lu, CQ; Lu, GQ Max; Bartlett, PF; Gray, PP: *J. Am. Chem. Soc.* **128**, 36-37, 2006; **Xu, ZP**; Stevenson, G; Lu, CQ; Lu, GQ: *J. Phys. Chem. B* **110**, 16923-16929, 2006; **Xu, ZP**; Kurniawan, ND; Bartlett, PF; Lu, GQ Max: *Chem. Eur. J.* **13,** 2824-2830, 2007; **Xu, ZP**; Walker, TL; Liu, K-L; Cooper, HM; Lu, G.Q. Max; Bartlett, PF: *Inter. J. Nanomed.* **2**, 163-174, 2007; **Xu, ZP**; Jin, YG; Liu, SM; Hao, ZP; Lu, GQM: *J. Colloid Interface Sci.* **326**, 522-529, 2008

2. sLDH



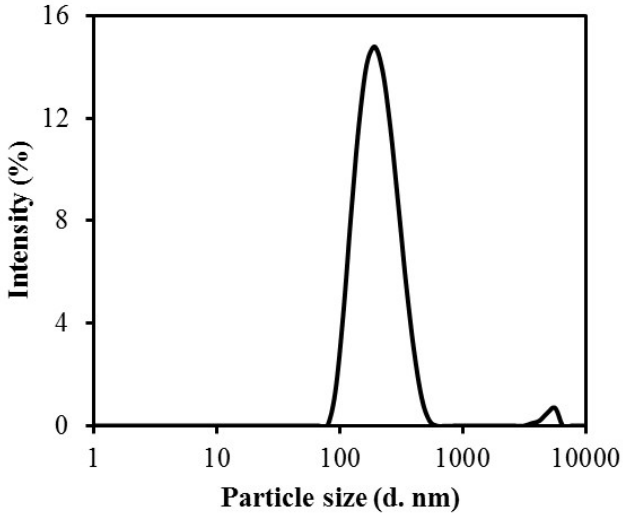
A. PSD; B. TEM; C. XRD; D. FTIR

Refs:

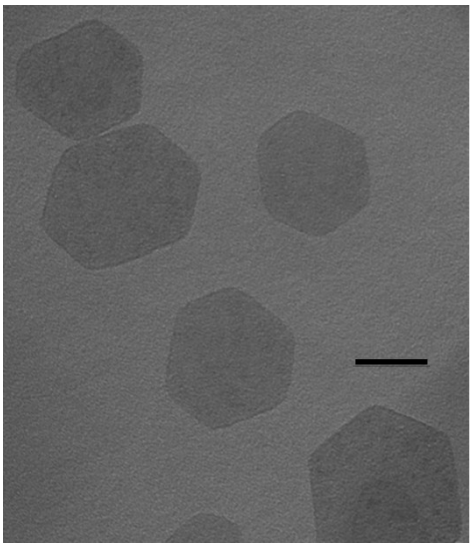
Dong HY; Parekh HS; **Xu ZP**: *Journal of Colloid and Interface Science,* **437**, 10-16, 2014; Dong HY; Chen M; Rahman S; Parekh HS; Cooper HM; **Xu ZP**: *Applied Clay Science*, **100**, 66-75, 2014; Chen, M; Cooper, HM; Zhou, JZ; Bartlett, PF; Lu, G.Q. (Max); **Xu, ZP**: *Journal of Colloid and Interface Science* **390**, 275-281, 2013.

3. lLDH

PSD



TEM

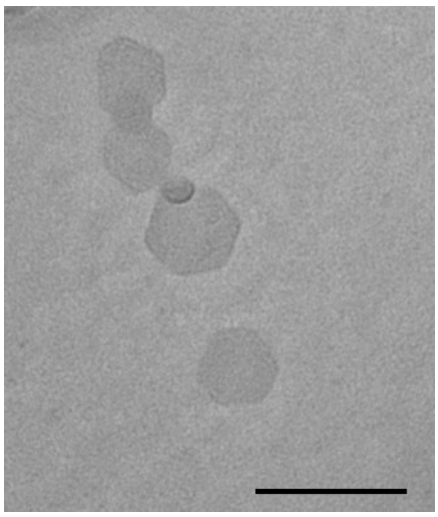


Ref:

Xu, ZP; Stevenson, G; Lu, CQ; Lu, GQ: *J. Phys. Chem. B* **110**, 16923-16929, 2006; TEM not published.

4. LDH-BSA in H2O

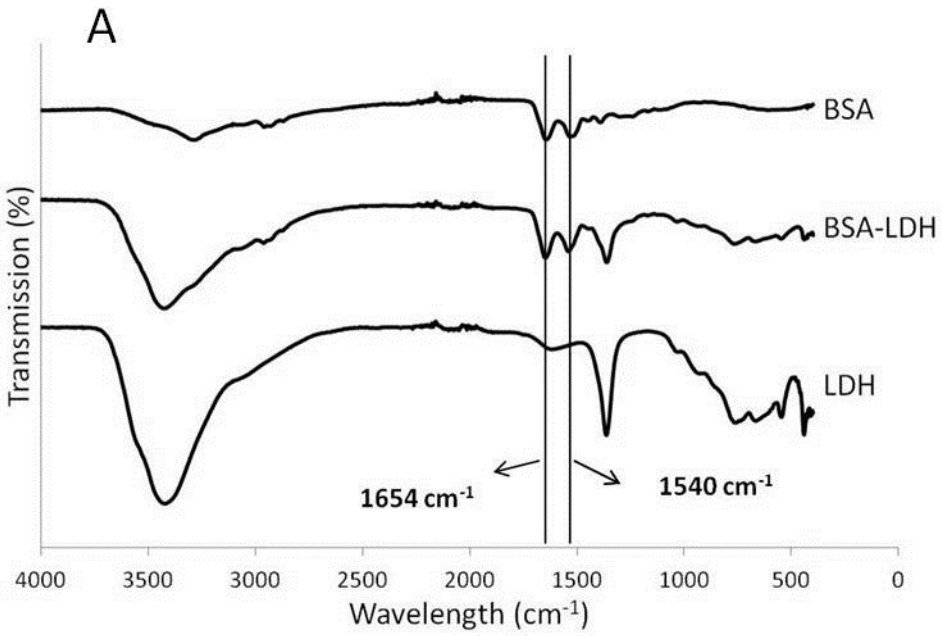
TEM (LDH-BSA 5:2 in water)



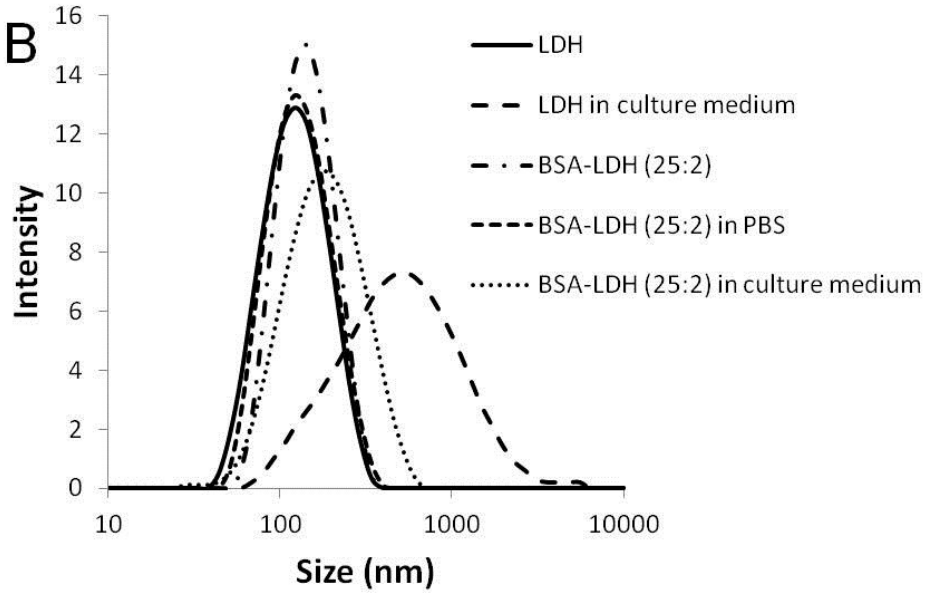
(Bar length = 200 nm)

(Figure 1E)

FTIR: **Refer to Fig 5A in the manuscript**

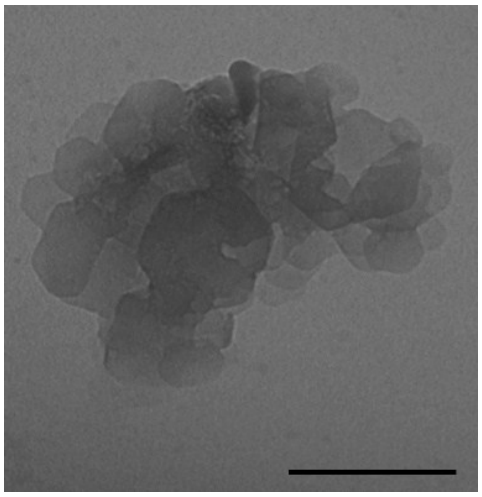


PSD: **Refer to Fig 1B in the manuscript**

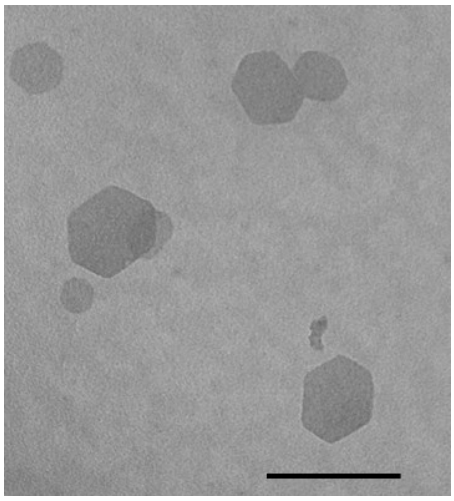


5. LDH-BSA in PBS

LDH in PBS (Figure 1D)

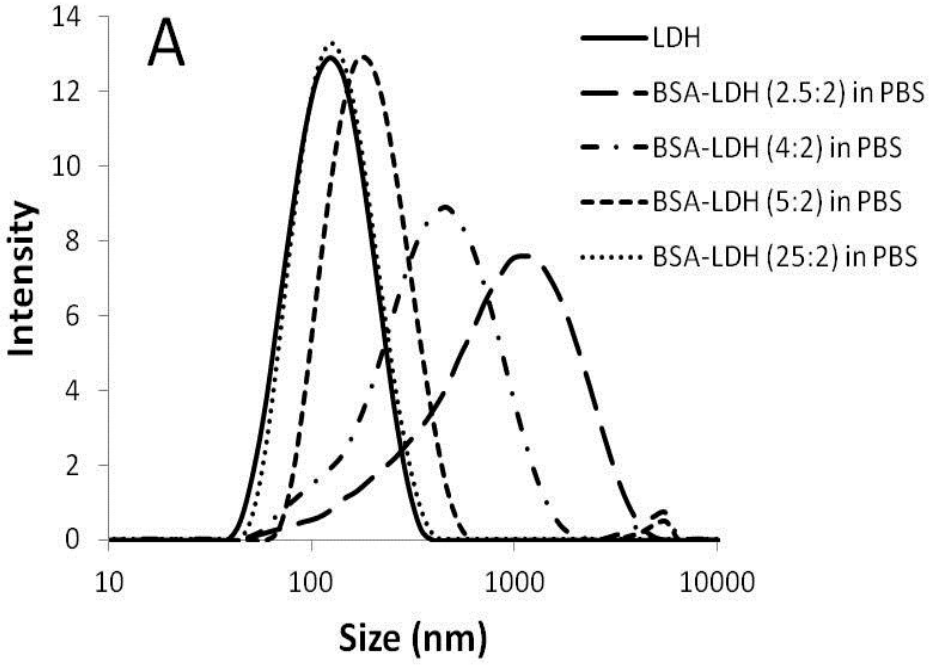


LDH-BSA in PBS (Figure 1F)



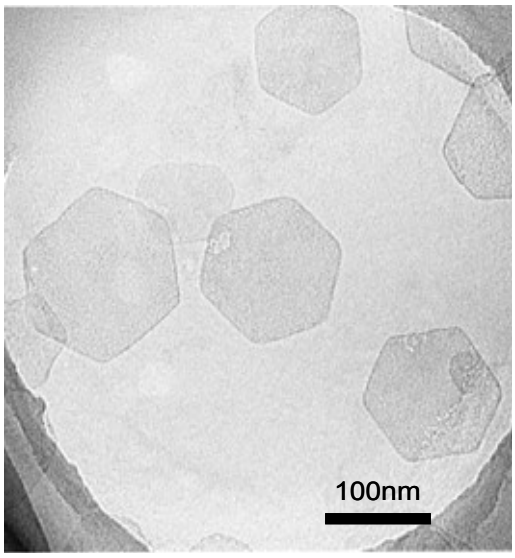
(Scale bar = 200 nm, not published yet)

PSD: refer to Fig 2A in the manuscript



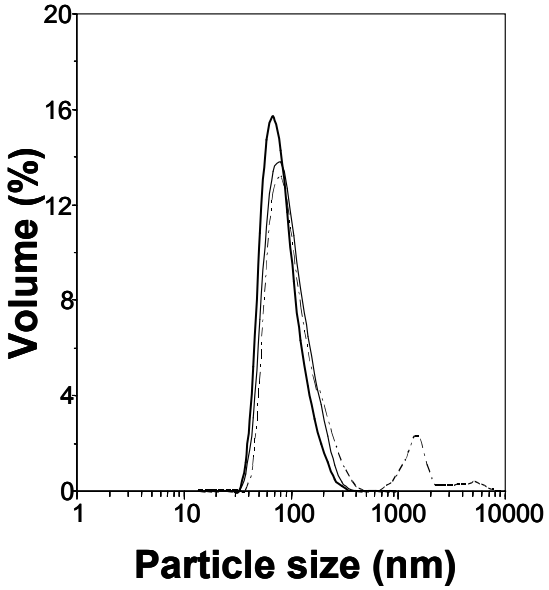
6. LDH-FITC

TEM



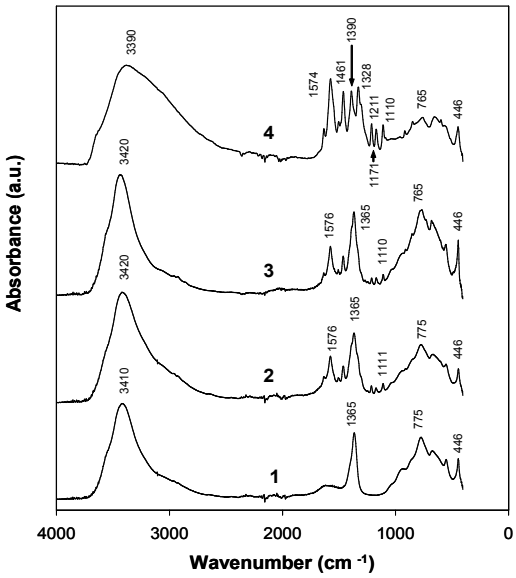
PSD (thin line)

B



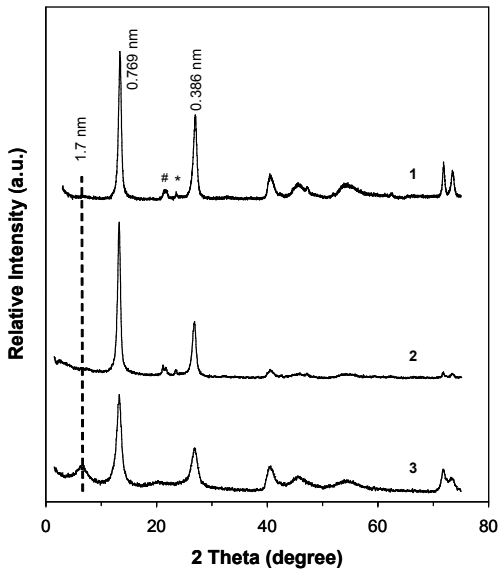
FTIR

A



XRD

B



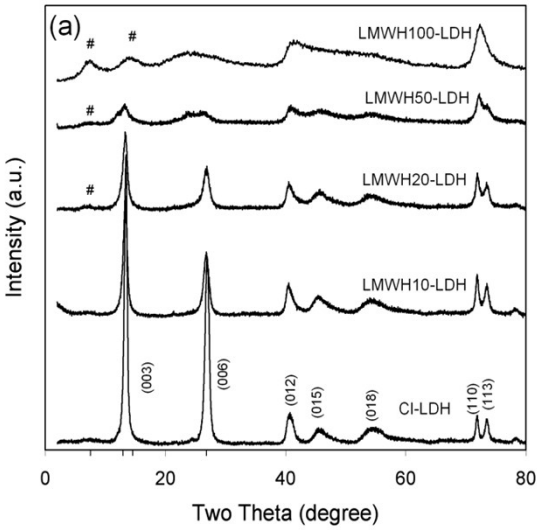
(**A**) Infrared spectra of (1) hexagonal LDH-Cl; (2) rod-like $LDH_{FITC\text{-}ROD}$ (10% Cl^- equivalent FITC); (3) hexagonal $LDH_{FITC\text{-}HEX}$ (10% Cl- equivalent FITC); and (4) LDH_{FITC} with 50% of Cl^- ions exchanged by FITC; (**B**) XRD patterns of LDH-Cl/FITC samples. (1): hexagonal $LDH_{FITC\text{-}HEX}$ (10% Cl^- equivalent FITC); (2) rod-like $LDH_{FITC\text{-}ROD}$ (10% Cl-equivalent FITC); and (3) LDH_{FITC} (50% Cl^- equivalent FITC). #: brucite-like phase; *: gibbsite phase.

Ref:

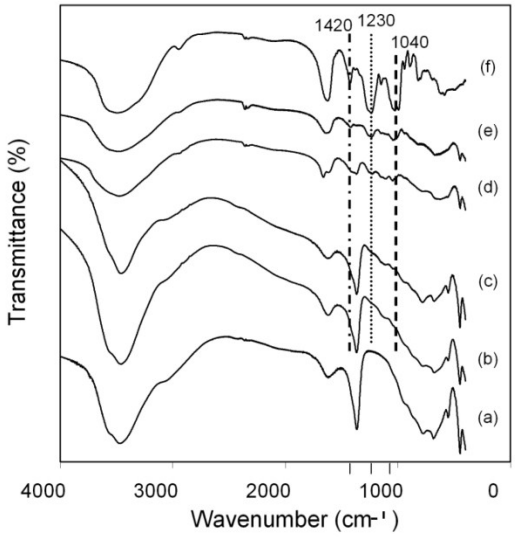
Xu, ZP; Niebert, M; Porazik, K; Walker, TL; Cooper, HM; Middelberg, APJ; Gray, PP; Bartlett, PF; Lu, GQM: *J Control Release.* **130**, 86-94, 2008.

9. LDH-LMWH

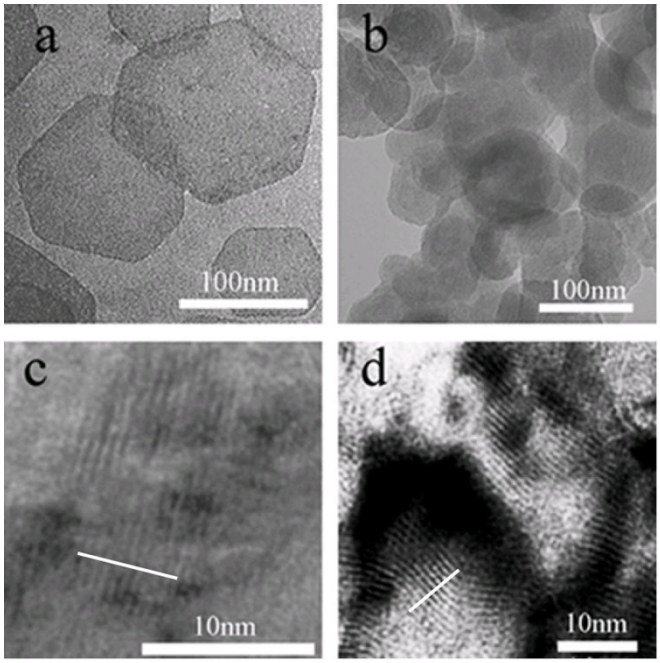
XRD



FTIR



TEM



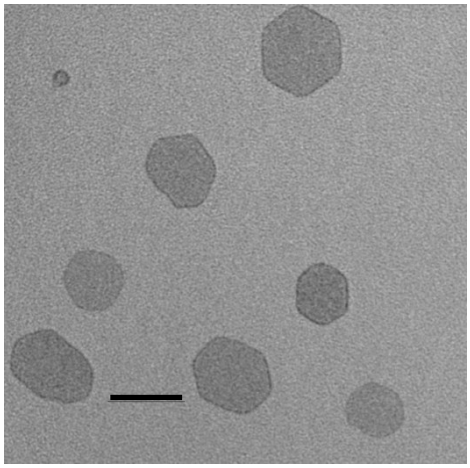
XRD, FTIR spectra and TEM of (a) Cl-LDH, (b) LMWH10-LDH, (c) LMWH20-LDH, (d) LMWH50-LDH, (e) LMWH100-LDH, (f) heparin sodium salt (MW = 4~6 kD).

Ref:

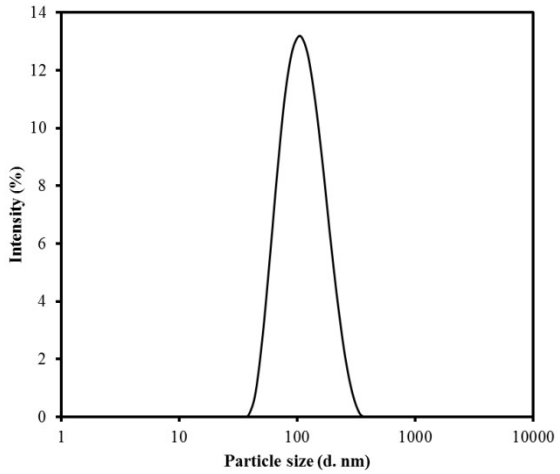
Gu, Z; Thomas, A; **Xu, ZP**; Campbell, J; Lu, GQ Max: *Chem. Mater.* **20**, 3715-3722, 2008.

12. LDH-MTX

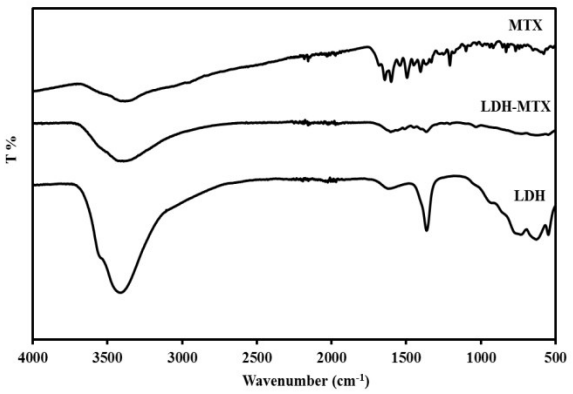
TEM (bar =100 nm)



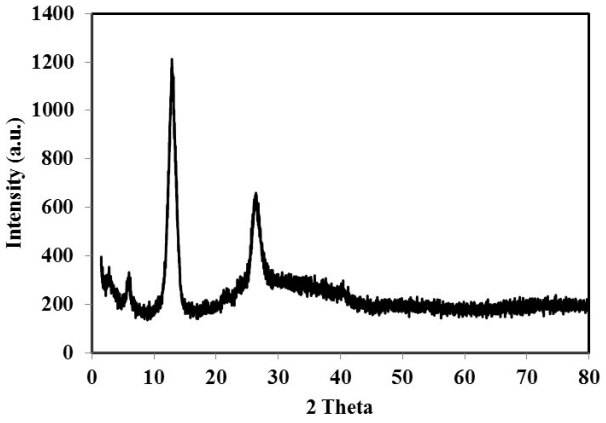
PSD



FTIR



XRD

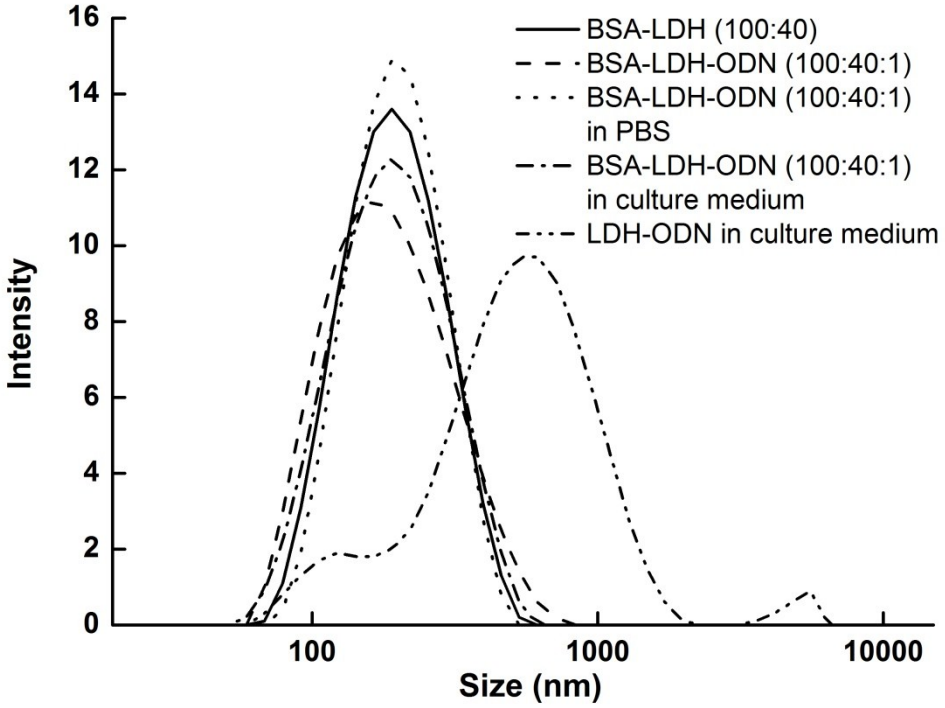


Data were not published yet.

Note that in this LDH, there were 90% Cl^- and 10% MTX^- in the interlayer to balance the positive charges in the hydroxide layers. In XRD pattern, the major phase was attributed to LDH-Cl (peaks at 14 and 28^o) with a small portion of minor phase LDH-MTX (peak at 6^o).

As also shown in the XRD patterns for Data 6 and 9, when there was more LMWH/FITC, the XRD peak belonging to LDH-LMWH/FITC became more obvious. However, the aggregation of LDH-LMWH/FITC nanoparticles became severe, increasing the particle size and losing the monodispersivity (PCS data not shown). Therefore, for a particular drug, LDH-drug nanoparticles are normally dispersed well in aqueous suspension when the drug loading in LDH is equivalent to replacing 10-20% of total Cl^- in precursor LDH-Cl, which avoids any aggregation while the drug loading is high enough for subsequent biological tests. So in this research, we chose this loading range (Refer to Section 2.2.2 in the main text) in order to obtain well dispersed LDH suspensions.

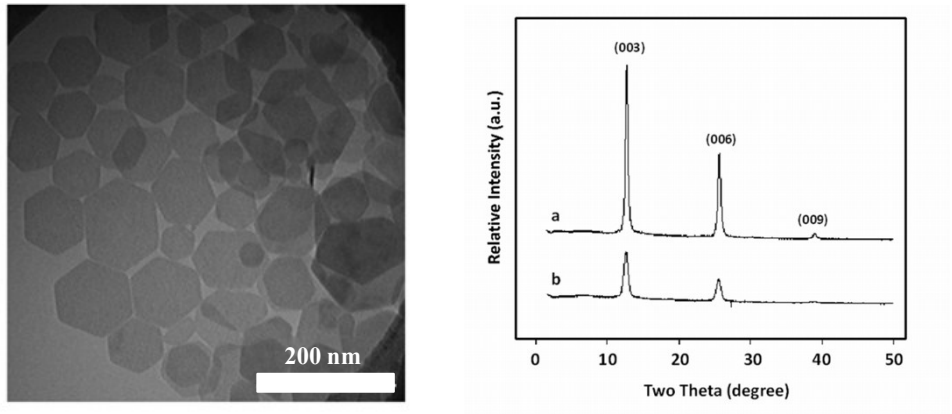
15,16. BSA-LDH-ODN (100:40:1) in water, PBS and culture medium



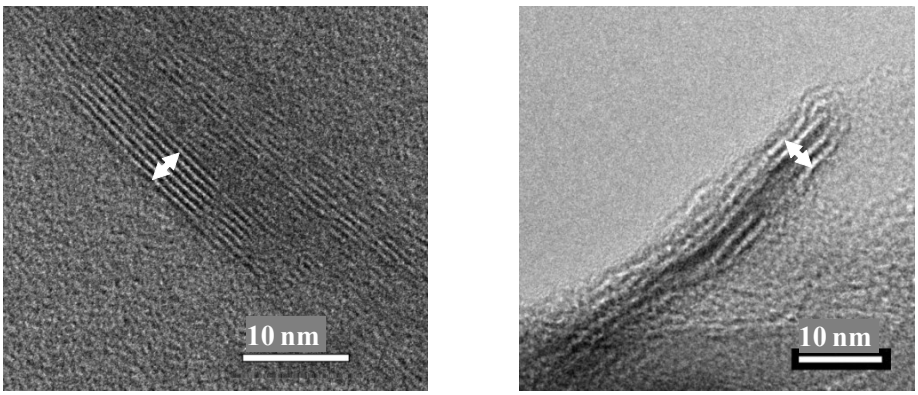
In the manuscript, Fig.3 was changed to the graph above (BSA-LDH-ODN in PBS was added):

17. LDH-ODN

(A) (B)



(C) (D)



(A) TEM image of LDHs; (B) XRD patterns of LDH (a) and dsDNA-Htt#1-LDH (b); High resolution TEM images of LDH (C) and dsDNA-Htt#1-LDH (D), Bars; interlayer width without dsDNA intercalation, arrow; expansion due to dsDNA intercalation.

Ref:

Wong, YY; Cooper, HM; Zhang, K; Chen, M; Bartlett; PF; **Xu, ZP**: *J Colloid Interface Sci.* **369**, 453-459, 2012.