Electronic Supplementary Information

Experimental and theoretical evaluation of nanodiamonds as pH triggered drug carriers

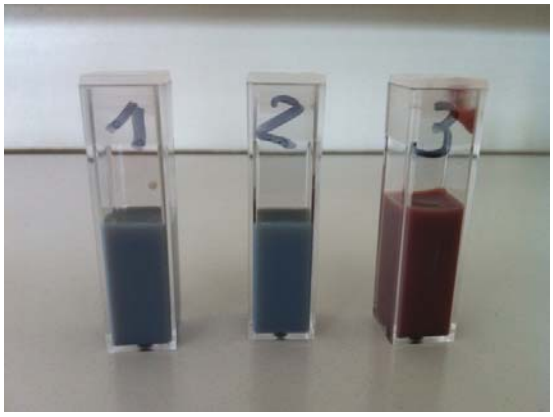
Jingjing Yan,[a] Yong Guo,[a] Azza Altawashi,[b] Basem Moosa,[a] Sébastien Lecommandoux,[c] and Niveen M. Khashab*[a]

[a] Advanced Membranes and Porous Materials Center, Chemical and Life Sciences and Engineering Division, King Abdullah University of Science and Technology (KAUST), Thuwal 23955-6900, Kingdom of Saudi Arabia.

[b] Chemical and Life Sciences and Engineering Division, King Abdullah University of Science and Technology (KAUST), Thuwal 23955-6900, Kingdom of Saudi Arabia.

[c] Université de Bordeaux, IPB-ENSCBP, F-33600 Pessac, France. CNRS, LCPO, UMR 5629 F- 33600 Pessac, France

**Address correspondence to Niveen Khashab, niveen.khashab@kaust.edu.sa*



5.00 mg/ml in DI water **0.100 mg/ml in DI water**

1. NDs after calcination 2. Fc-NDs 3. Fc-NDs-DOX

Table S1

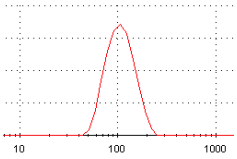
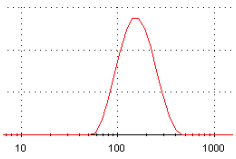
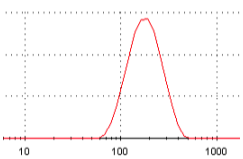
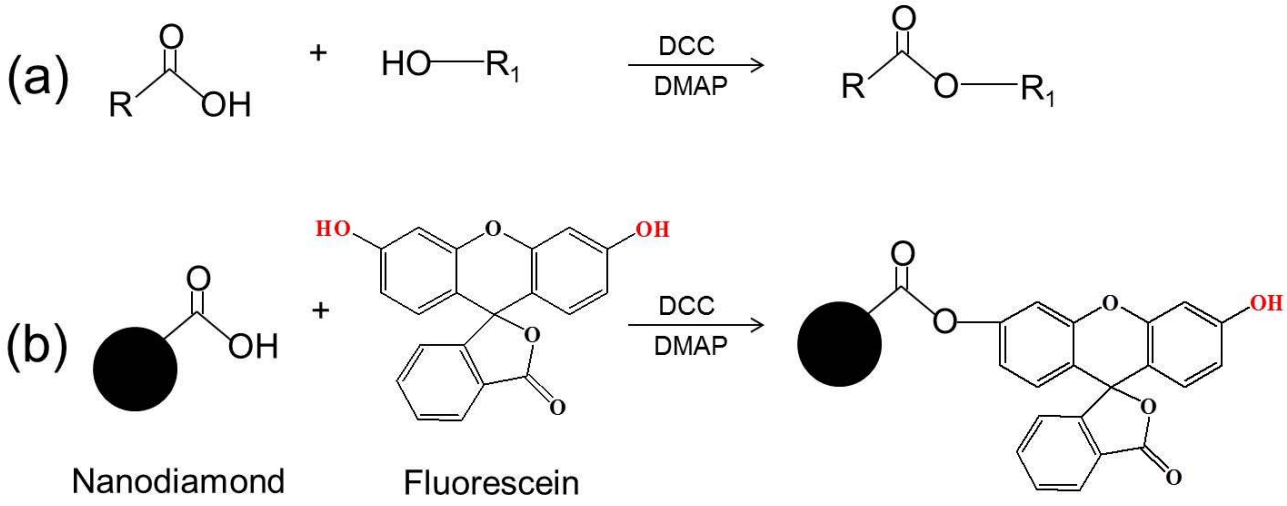
	NDs after calcined	Fc-NDs	Fc-NDs-DOX
ζ potential (mV)	**-57.8 ± 9.69**	**-49.8 ± 5.75**	**-45.0 ± 7.74**
Hydrodynamic diameter (nm)	 **D_H = 120 nm Polydispersity PDI = 0.120**	 **D_H = 143 nm Polydispersity PDI = 0.140**	 **D_H = 165 nm Polydispersity PDI = 0.130**

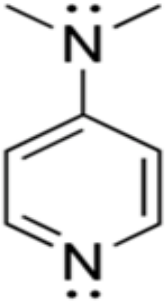
Table S1. ζ Potential and hydrodynamic sizes of the different native and functionalized nanodiamonds.

Figure S1



(c)

N,N'-Dicyclohexylcarbodiimide
(DCC)



4-Dimethylaminopyridine
(DMAP)

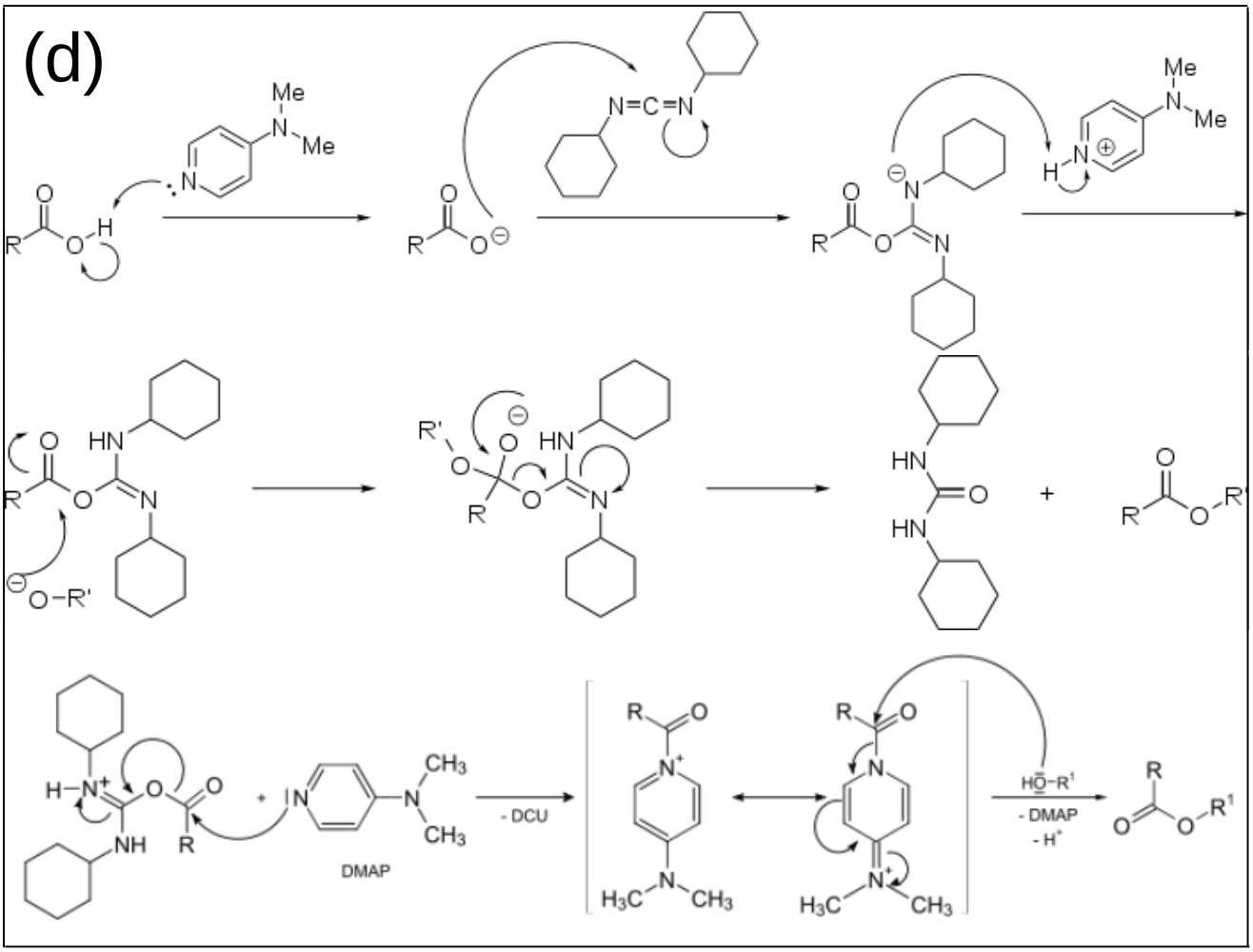


Figure S1. Schemes of (a) Steglich esterification[1] and (b) reaction of NDs carboxyl group and fluorescein hydroxyl group (there are two hydroxyl groups on each fluorescein molecule, and for better understanding ,we only drew the reaction for one hydroxyl group, while, the other hydroxyl group of fluorescein may also react with NDs carboxyl groups). (c) the structures of N,N' Dicyclohexylcarbodiimide (DCC) and 4-Dimethylaminopyridine (DMAP), (d) the mechanism of Steglich esterification.[1]

Figure S2

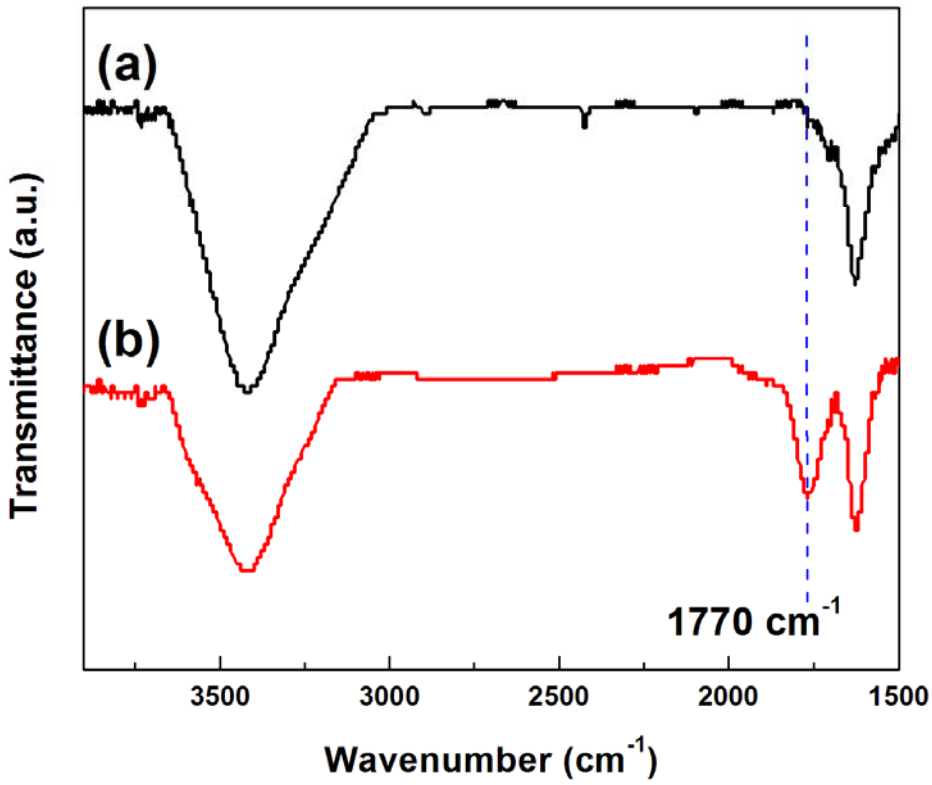


Figure S2. FTIR spectra of (a) pristine NDs and (b) NDs after calcination at 425 ^{o}C for 4 hours. In Figure S1b, there is a new peak that appears at 1770 cm^{-1}, which belongs to the carboxyl group formed by oxidation.

Figure S3

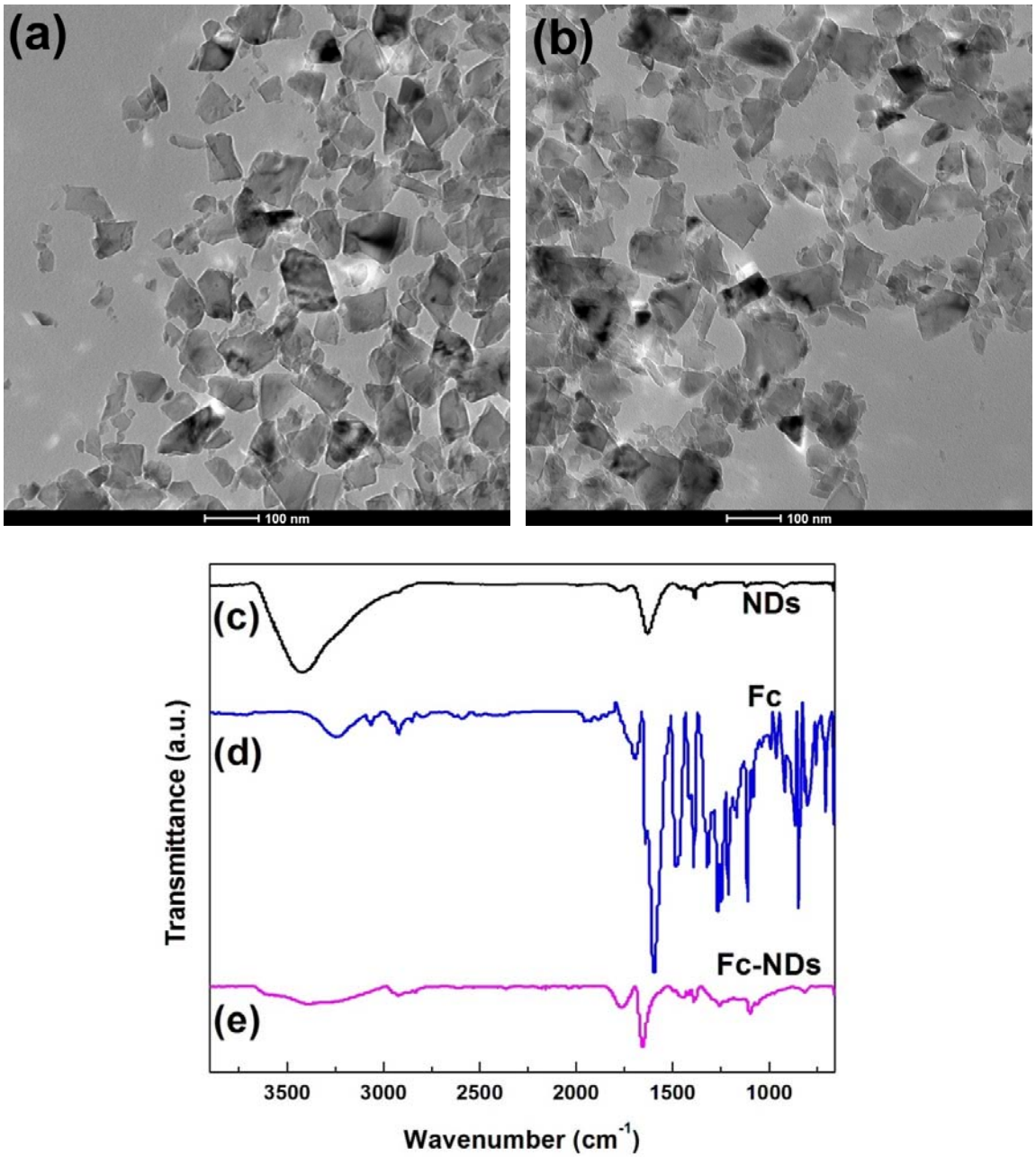


Figure S3. TEM images of (a) NDs and (b) Fc-NDs (scale bar is 100 nm). From the two images, we can see there is no obvious difference of morphology between NDs and Fc-NDs; (c), (d) and (e) are the FTIR spectra of NDs, fluorescein and Fc-NDs. The characteristic peaks of fluorescein range from 1000 cm^{-1} to1500 cm^{-1}. By comparing these spectra, we can conclude that fluorescein has been successfully coupled onto NDs.

Figure S4

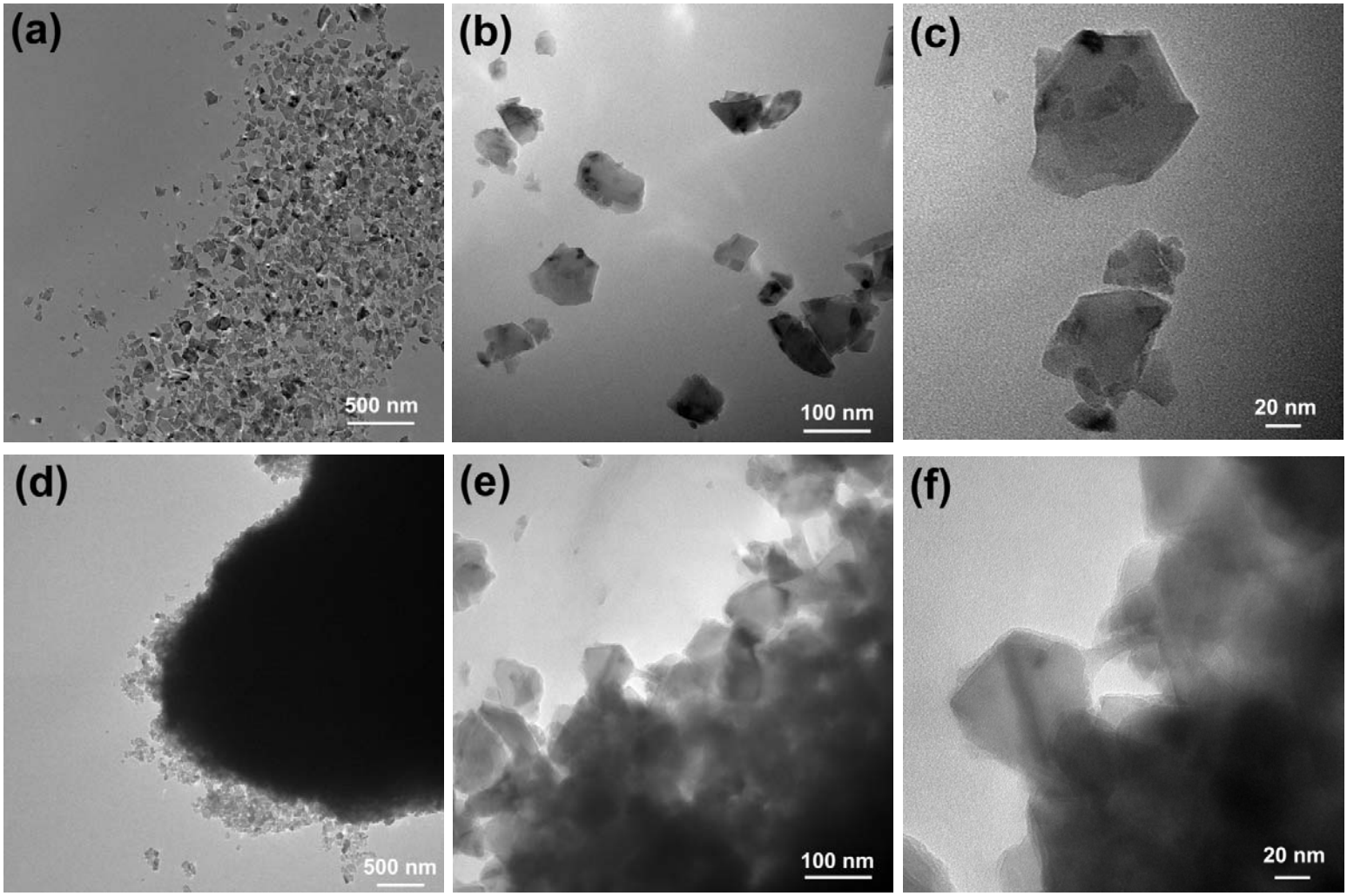


Figure S4. TEM images of Fc-NDs (a, b, c) and Fc-NDs-DOX (d, e, f).

Figure S5

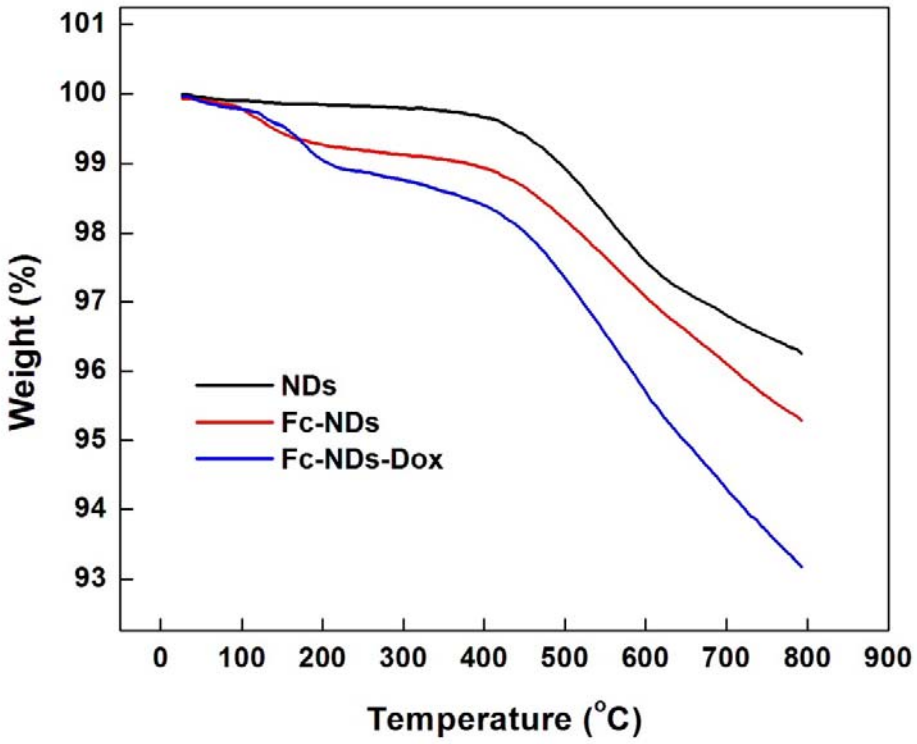


Figure S5. The TG curves of NDs, Fc-NDs and Fc-NDs-DOX, confirming that Fluorescein and DOX have been successfully attached onto NDs.

Figure S6

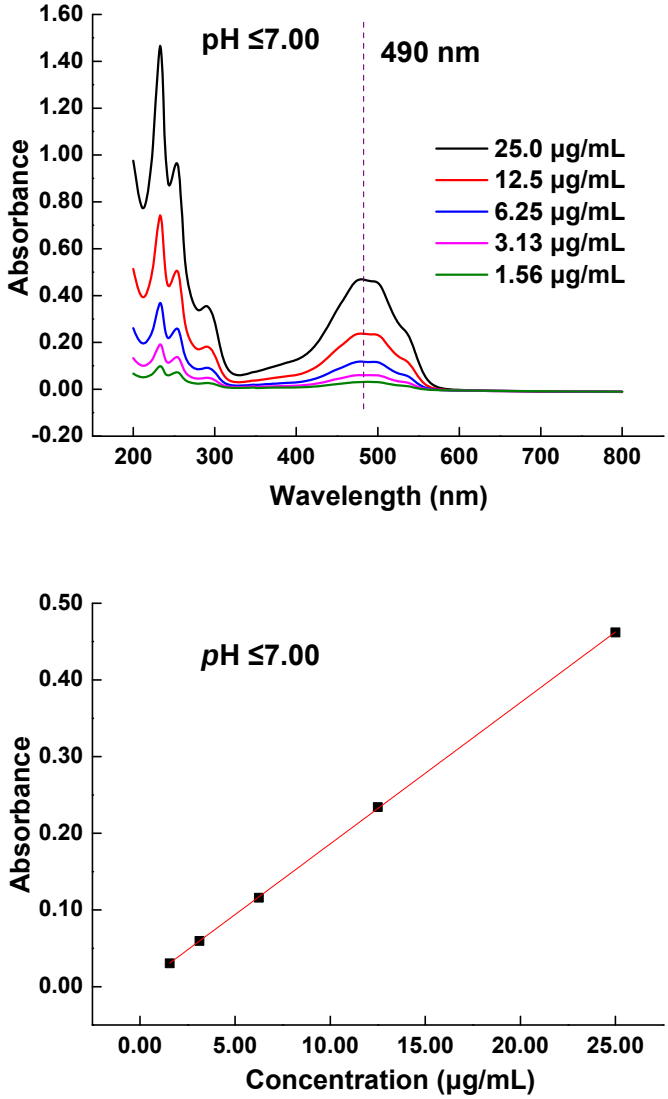


Figure S6. The UV-Vis spectra of Doxorubicin (pH ≤ 7) at different concentrations and the liner equation of the concentration of and its absorbance at 490 nm. Absorbance = A + B * Concentration

Parameter	**Value**	**Error**
A	0.0467	0.0274
B	0.0154	$2.38E^{-4}$

R	**SD**	**N**	**P**
0.99993	0.06725	10	<0.0001

Figure S7

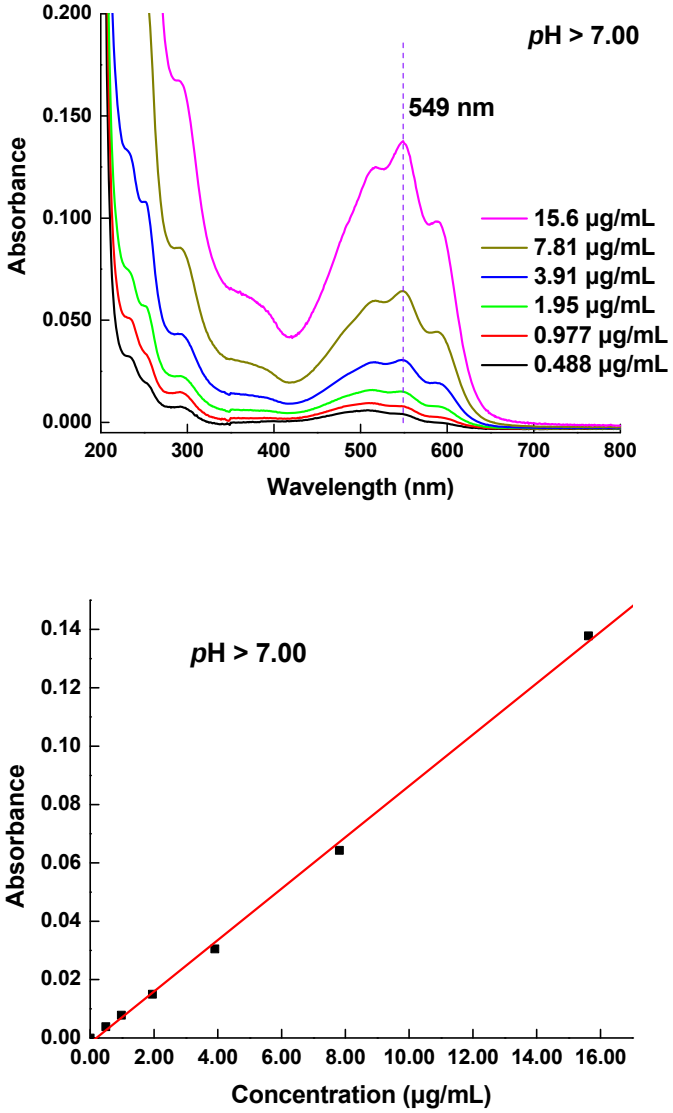


Figure S7. The UV-Vis spectra of Doxorubicin (pH > 7) at different concentrations and the liner equation of the concentration of and its absorbance at 549 nm. Absorbance = A + B * Concentration

Parameter	**Value**	**Error**
A	-0.00162	0.00103
B	0.0088	$1.51757E^{-4}$

R	**SD**	**N**	**P**
0.99926	0.00209	7	<0.0001

Figure S8

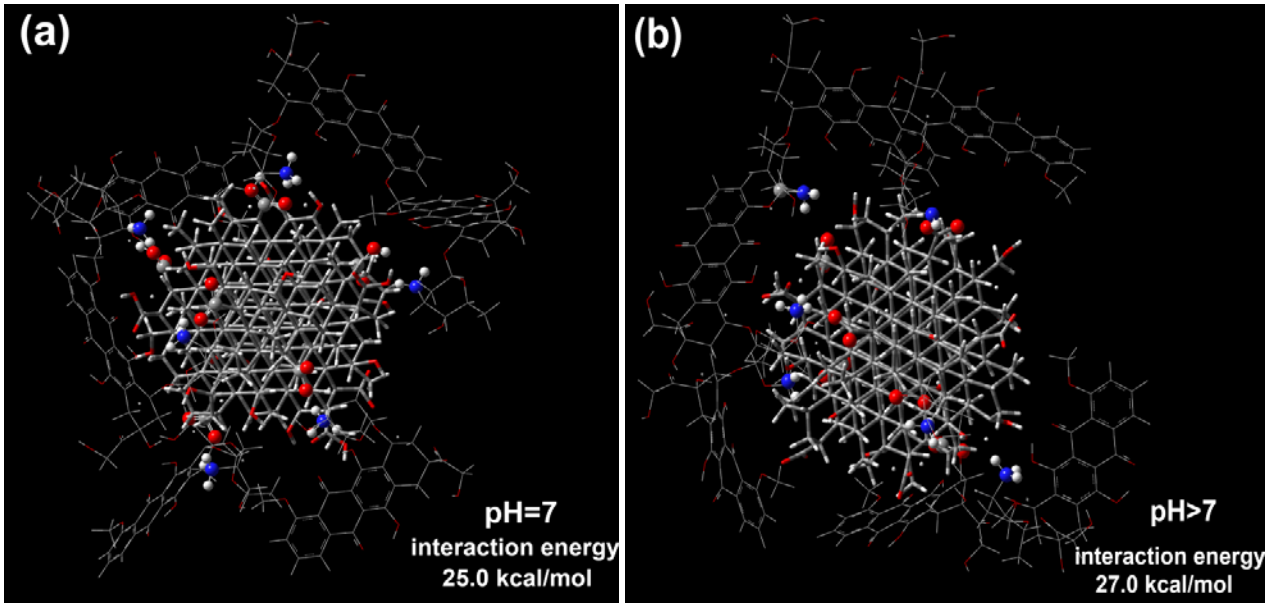


Figure S8. Optimized structure models of the interaction between ND surface groups and DOX in (a) pH=7 and (b) pH>7. The interaction energies are 25.0 kcal/mol and 27.0 kcal/mol respectively.

References

(1) B. Neises and W. Steglich, *Angewandte Chemie-International Edition in English*, 1978, **17**, 522-524.