Electronic Supplementary Material (ESI) for RSC Advances.

Supporting Information

Self-assembly of multifunctional integrated nanoparticles loaded with methotrexate-phospholipid complex: combining simplicity and efficacy in both targeting and anticancer effect

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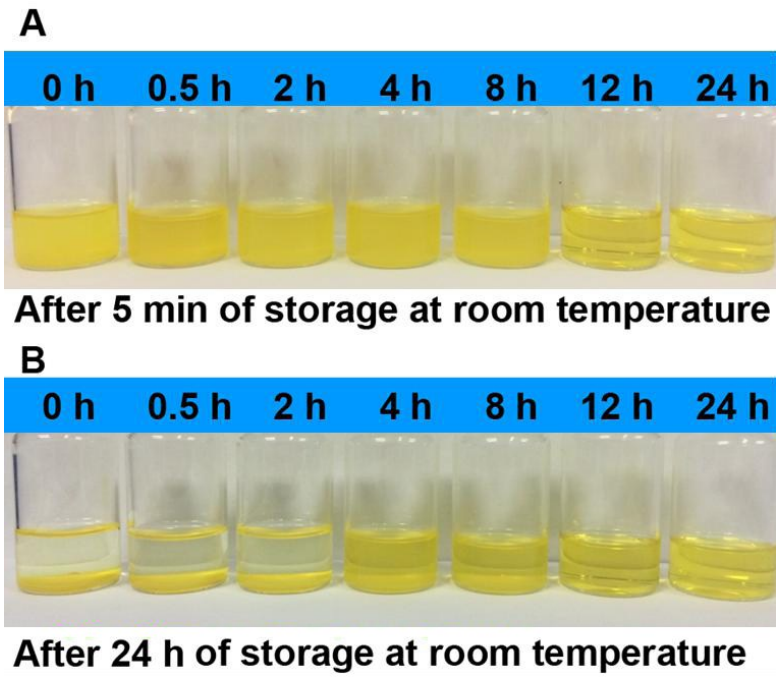

Figure S1. (A, B) Optical images of the MTX-PC complex dispersed in THF after (A) 5 min and (B) 24 h of storage at room temperature. The MTX-PC complex was prepared by a co-solvent method between MTX and PC in reaction solvent (THF) for

different reaction times (0, 0.5, 2, 4, 8, 12, and 24 h). Subsequently, the reaction solvent was removed by evaporation under reduced pressure. THF was added into the film followed by vigorous vortexing and the obtained dispersion was photographed.

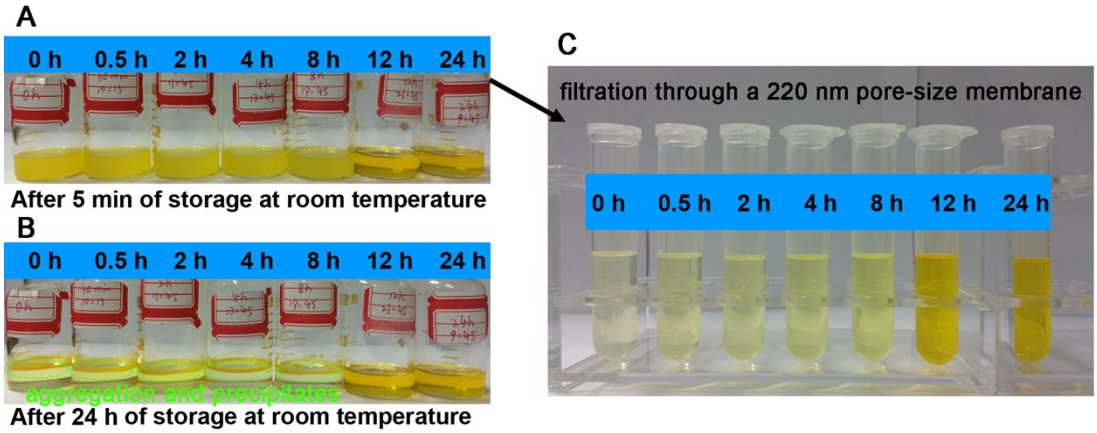

Figure S2. (A, B) Optical images of the MTX-PC complex dispersed in DCM after (A) 5 min and (B) 24 h of storage at room temperature. (C) Optical images of the MTX-PC complex dispersed in DCM after filteration through a 220 nm pore-size membrane filter. The MTX-PC complex was prepared by a co-solvent method between MTX and PC in reaction solvent (THF) for different reaction times (0, 0.5, 2, 4, 8, 12, and 24 h). Subsequently, the reaction solvent was removed by evaporation under reduced pressure. DCM was added into the film followed by vigorous vortexing and the obtained dispersion was photographed.

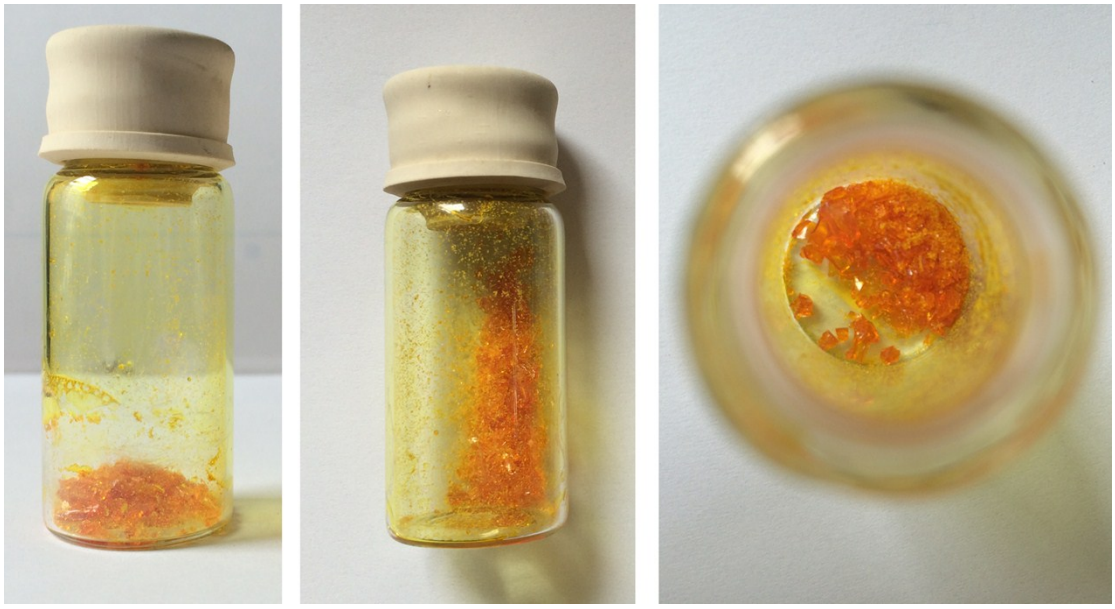

Figure S3. Optical images of the dried MTX-PC complex. The MTX-PC complex was prepared by a co-solvent method between MTX and PC in reaction solvent (THF). Subsequently, the reaction solvent was removed by evaporation under reduced pressure. The film was added into DCM followed by vigorous vortexing. The purified MTX-PC complex was obtained by filteration through a 220 nm pore-size membrane

filter to remove the uncomplexed MTX precipitates followed by rotary evaporation and vacuum drying.

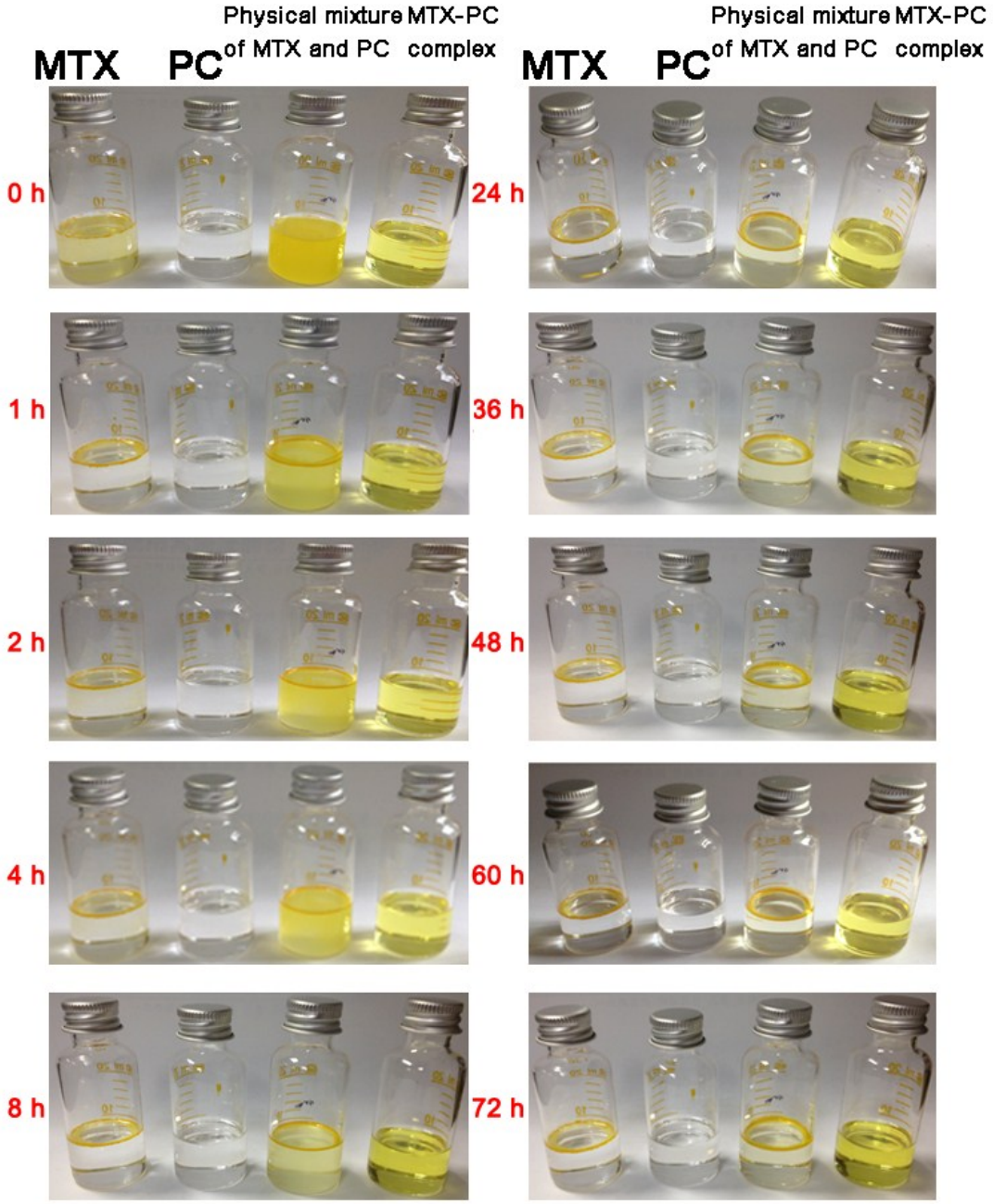

Figure S4. Optical image of MTX, PC, physical mixture of MTX and PC, and MTX-PC complex dispersed in DCM for 72 h of storage.

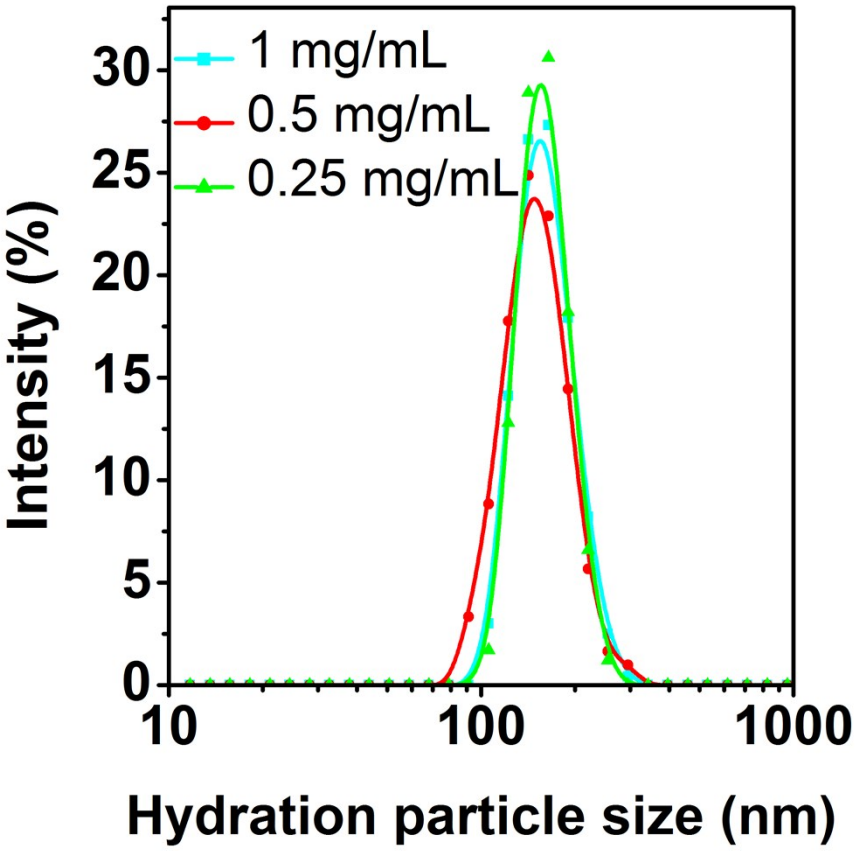

Figure S5. Hydrodynamic particle size and hydrodynamic particle size distribution of the MTX-PC NPs in water.

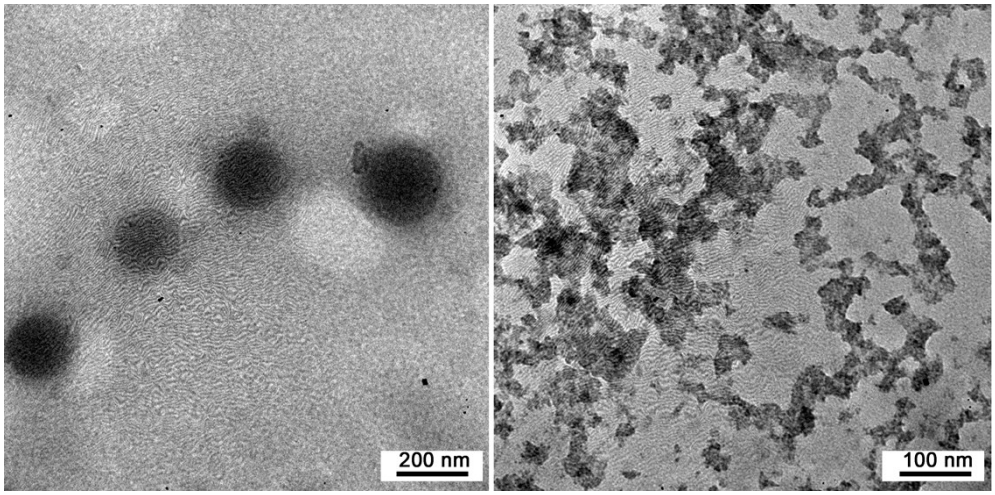

Figure S6. TEM images of the MTX-PC NPs in PBS incubated at (A) pH 7.4 and (B) pH 5.0 for 4 h.

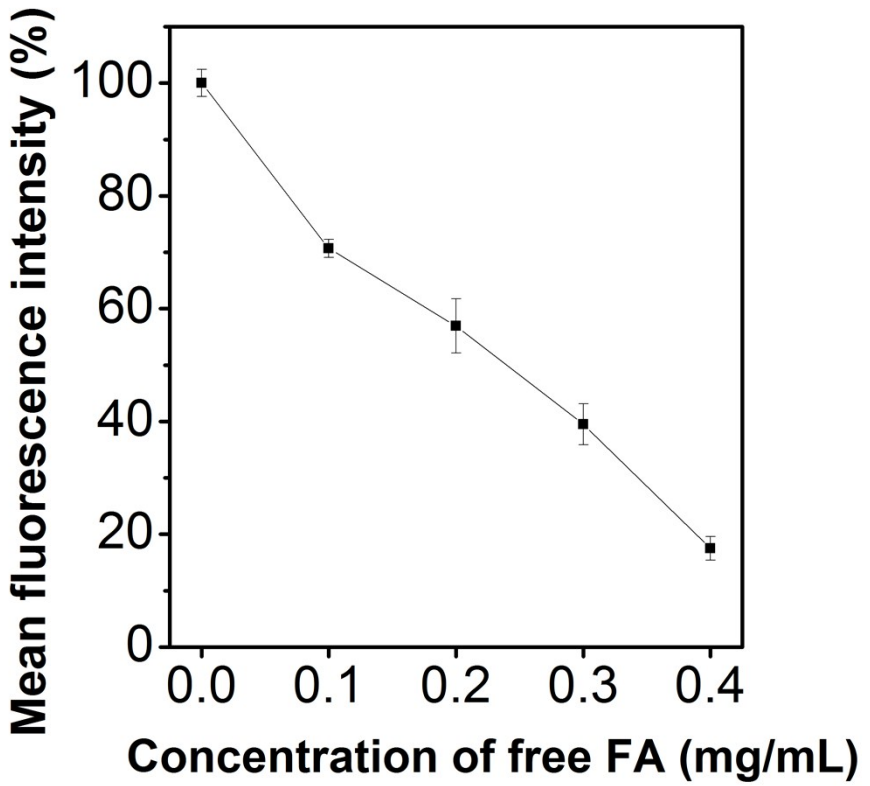

Figure S7. Fluorescence measurements of HeLa cells incubated with the MTX-PC NPs@DiD in the presence of the free FA at different concentration after 4 h of incubation. Data are presented as mean ± s.d. (n = 4)