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## **Supporting Information**

## Delivery of system $x_c$ inhibitor by a redox-responsive levodopa prodrug nanoassembly for combination ferrotherapy

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**Scheme S1.** The synthesis route of **DSSD**.

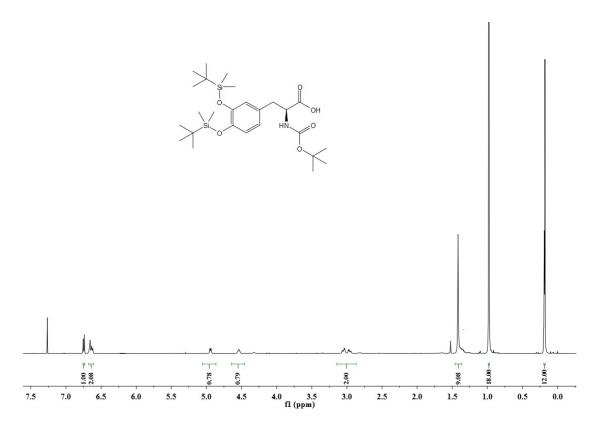


Fig. S1  $^1\text{H-NMR}$  spectrum of compound DOPA-TB (in CDCl $_3$ ).

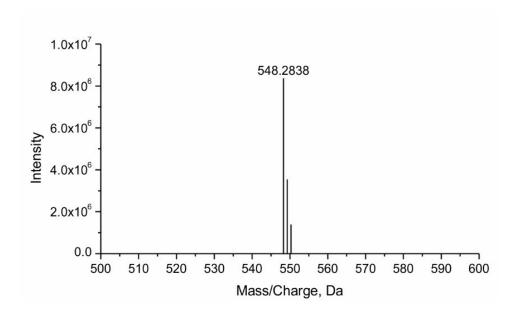


Fig. S2 HR-MS of compound DOPA-TB.

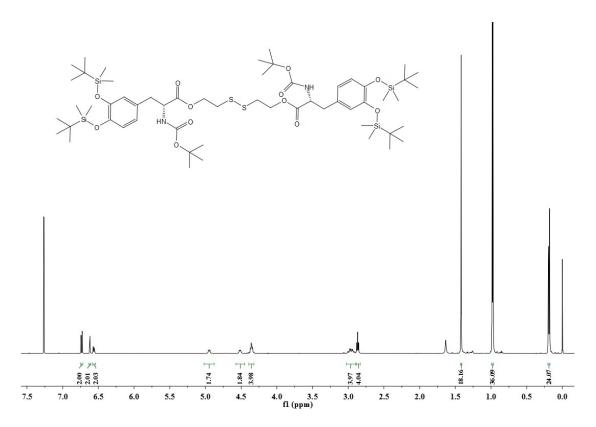


Fig. S3 <sup>1</sup>H-NMR spectrum of compound DSSD-TB (in CDCl<sub>3</sub>).

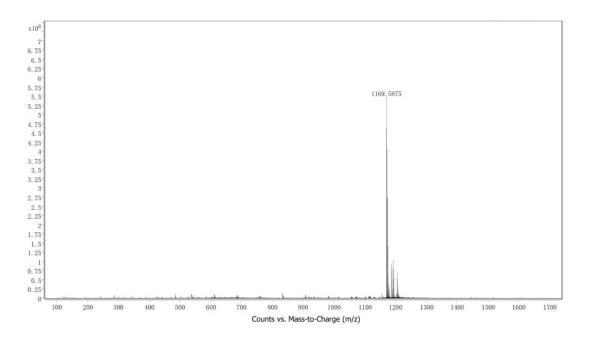


Fig. S4 HR-MS of compound DSSD-TB.

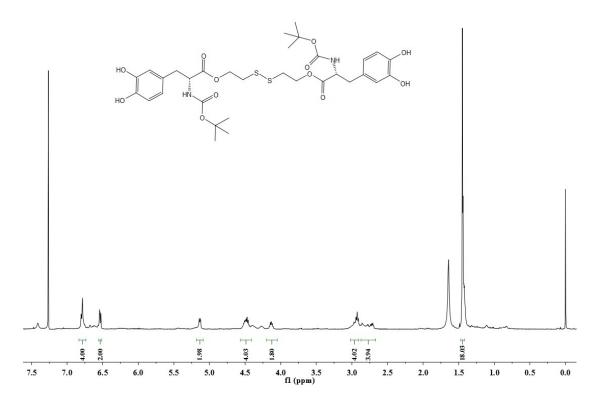


Fig. S5 <sup>1</sup>H-NMR spectrum of compound DSSD-B (in CDCl<sub>3</sub>).

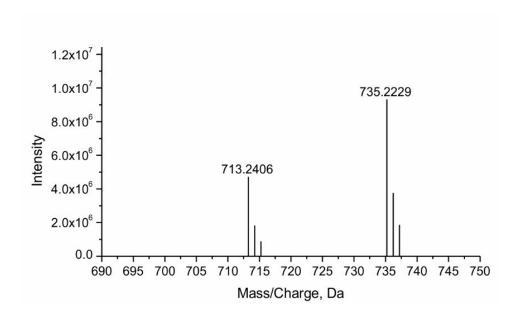


Fig. S6 HR-MS of compound DSSD-B.

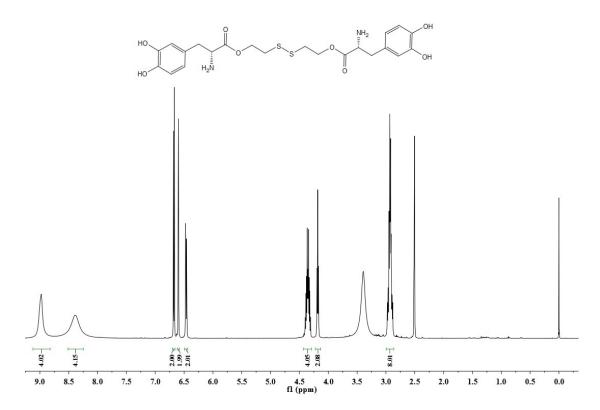


Fig. S7  $^1$ H-NMR spectrum of compound **DSSD** (in DMSO-d<sub>6</sub>).

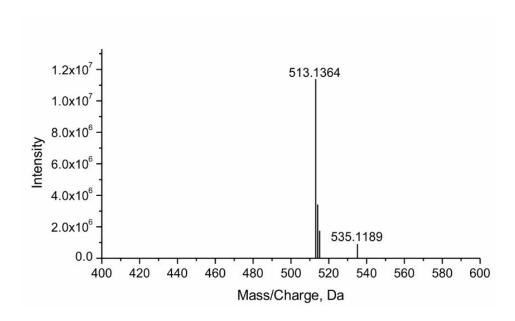


Fig. S8 HR-MS of compound DSSD.

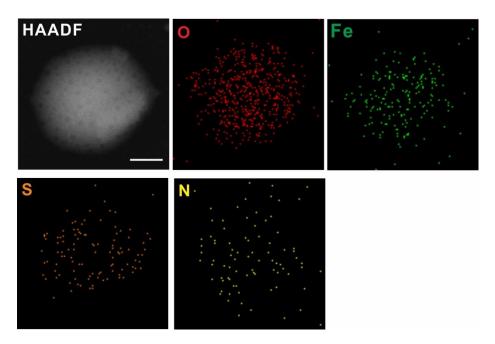
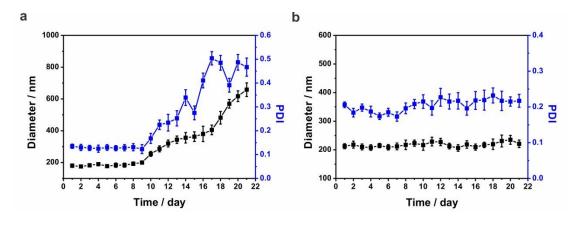
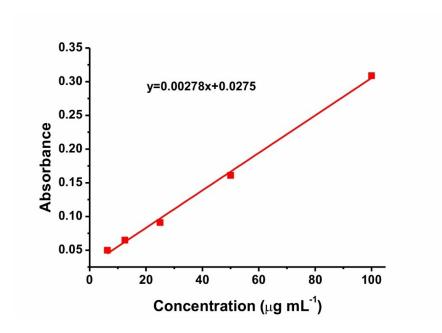


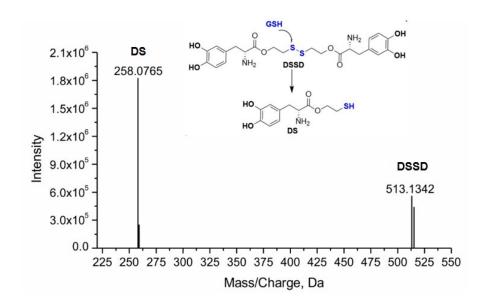
Fig. S9 HAADF-STEM and EDS mapping of SSZ-Fe<sup>2+</sup>@DSS (Scale bar: 50 nm).



**Fig. S10** Diameters for (a)SSZ@DSSD and (b)SSZ-Fe<sup>2+</sup>@DSSD (0.5 mg mL<sup>-1</sup>) in pH 7.4 PBS buffer at 37 °C as determined by DLS for 21 days.



**Fig. S11** Calibration curves for DSSD measured by absorption spectrometry.  $\lambda abs = 361 \text{ nm}$ .



**Fig. S12** High-resolution mass spectrum of the DSSD (50  $\mu$ g mL<sup>-1</sup>) treated with GSH (10 mM) for 20 min. The signals at m/z 258.0765 and 513.1342 represent DS and DSSD, respectively.

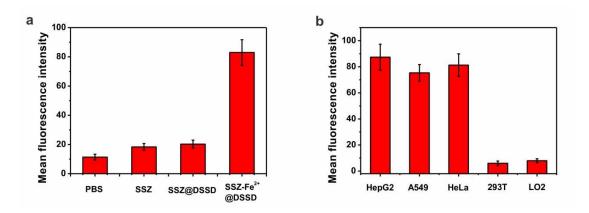


Fig. S13 Quantitative analysis of the fluorescence intensity of (a)Fig. 2d and (b)2e.

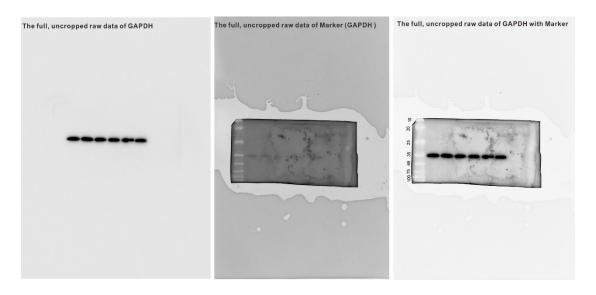


Fig. S14 The full, uncropped raw data of GAPDH with markers.

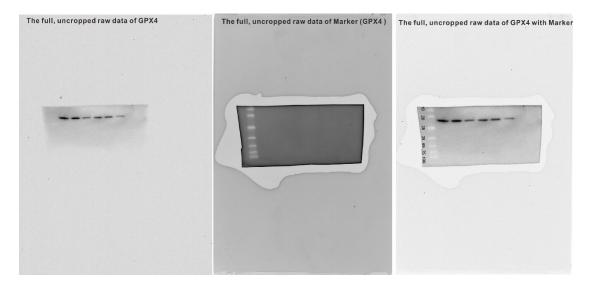
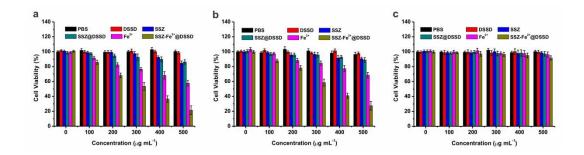
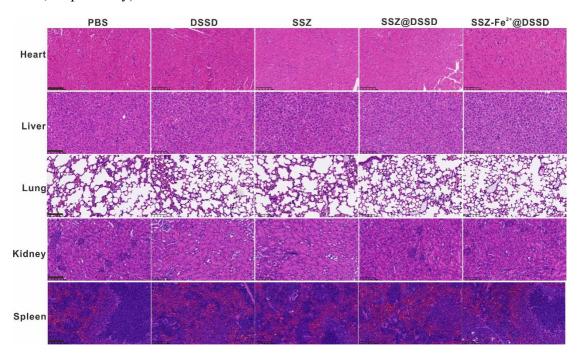


Fig. S15 The full, uncropped raw data of GPX4 with markers.



**Fig. S16** The viability of (a)HepG2, (b)A549 and (c)LO2 cells after incubation with different formulations at various concentrations (0, 100, 200, 300, 400 and 500  $\mu$ g mL<sup>-1</sup>, respectively).



**Fig. S17** H&E staining results of the major organs (heart, liver, spleen, lung and kidney) with different formulations. The scar bar:  $100 \, \mu m$ .