Supplementary Information

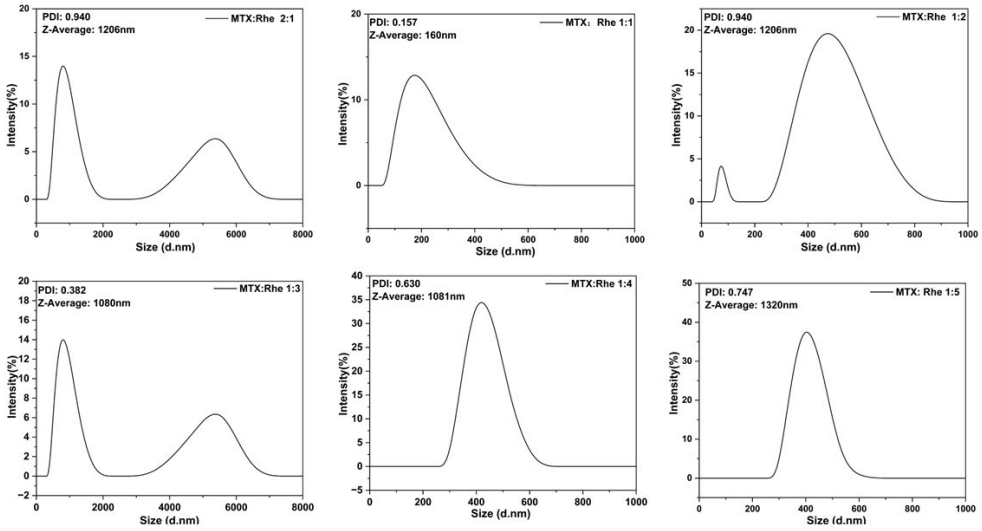

Figure S1. Effect of different molar ratios on MR particle size and distribution.

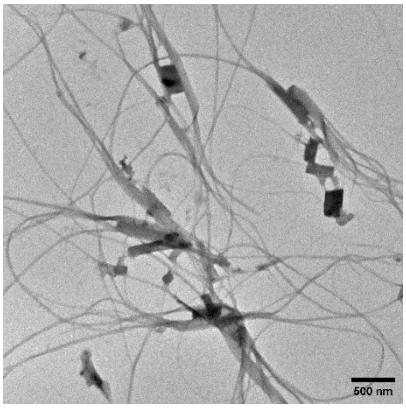

Figure S2. TEM image of Rhe. Scale bar: 500 nm.

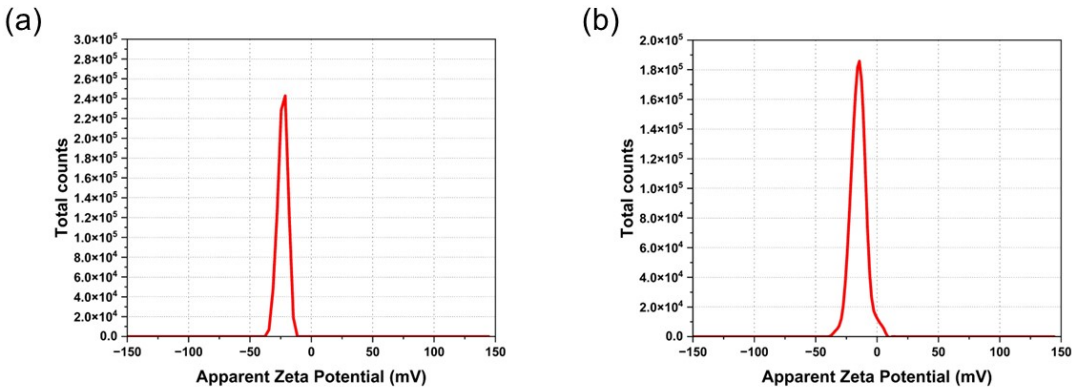

Figure S3. Zeta potential of MTX (a) and Rhe (b).

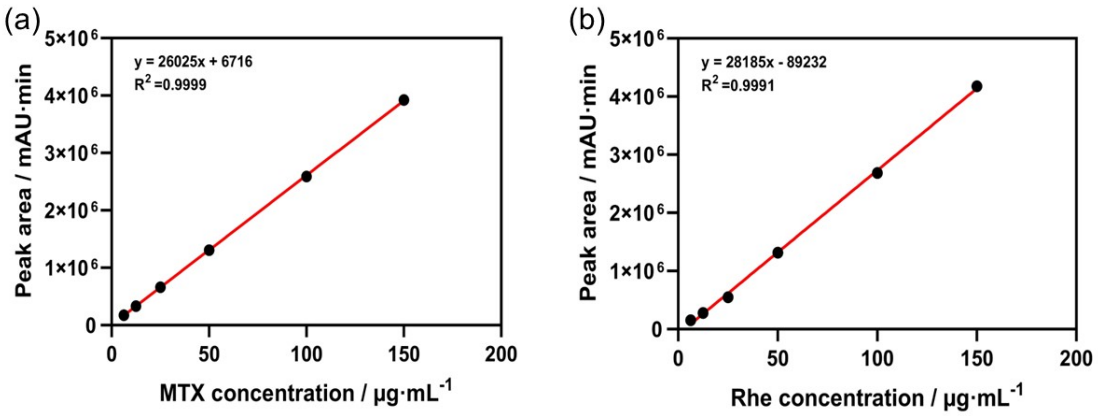

Figure S4. Standard curves of MTX (a) and Rhe (b).

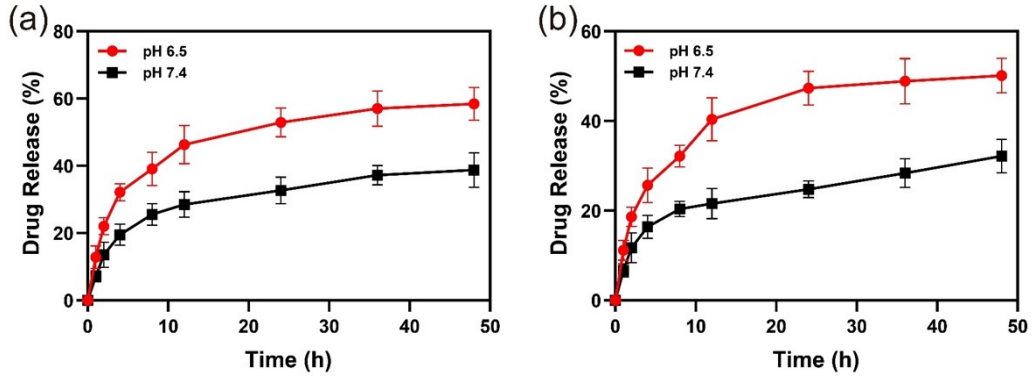

Figure S5. Release of MTX (a) and Rhe (b) from MR at pH 6.5 and 7.4.

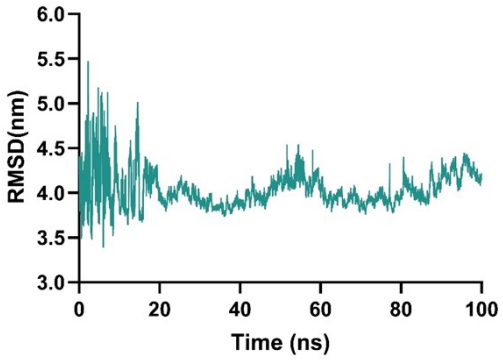

Figure S6. RMSD of MR system during the simulation time.

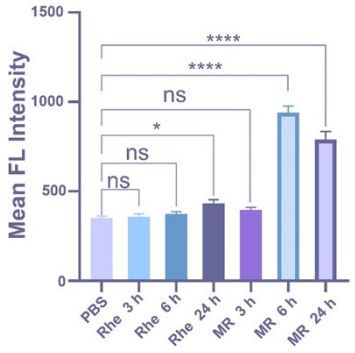

Figure S7. Quantitative analysis results of cellular uptake by flow cytometry. Data are mean ± SEM (n = 3).

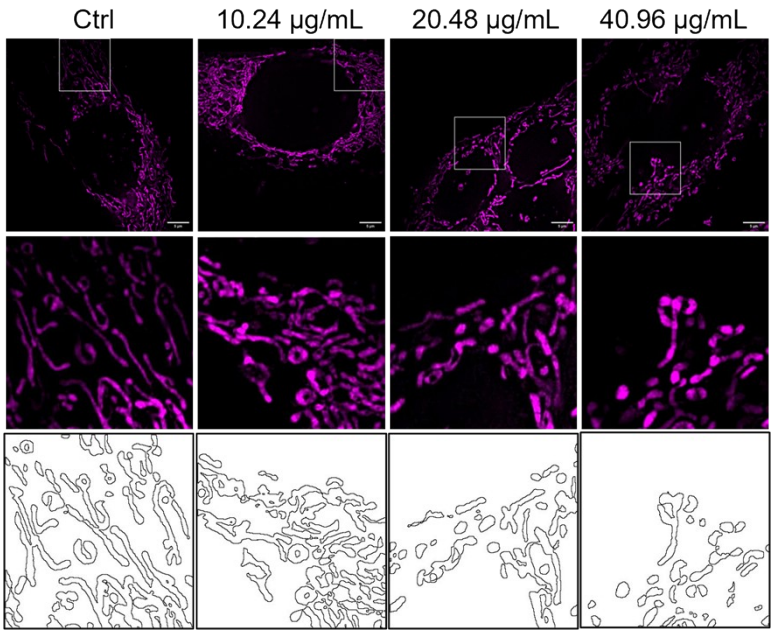

Figure S8. SIM images of MCF-7 cells subjected to various concentrations of Rhe, with mitochondria stained using Mito-Tracker deep red (λ_{ex} = 640 nm). Scale bar: 5 μm.

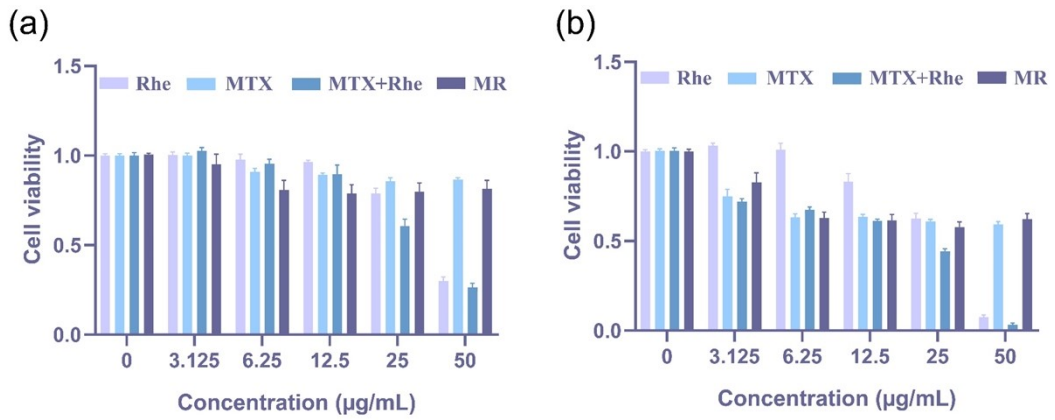

Figure S9. (A) Cell viability of MCF-10A cells cultured with MTX, Rhe, MTX + Rhe, and MR for 24 hours was

detected by CCK-8 assay. Data are mean ± SEM (n = 3). (B) Cell viability of MCF-10A cells cultured with MTX, Rhe, MTX + Rhe, and MR for 48 hours was detected by CCK-8 assay. Data are mean ± SEM (n = 3).

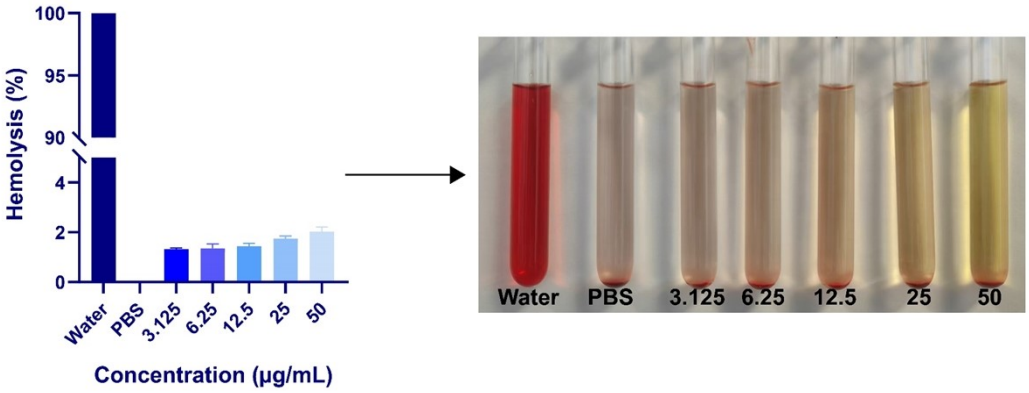

Figure S10. Hemolysis assessment and hemolysis rate of MR. Data are mean ± SEM (n = 5).