Figure S1. Photomicrographs of CEP- or TET-treated 2D MCF-7 and MDA-MB-231 monolayer cells stained with calcein, Hoechst or PI. MCF-7 and MDA-MB-231 cells were treated with 0.3, 1, 30 or 100 μg/ml CEP or TET and stained with calcein (green), Hoechst (blue) or PI (red), which represent the cytoplasm, chromatin (nuclei) or dead cells, respectively. CEP induced chromatin aggregation and cell death. Scale bar, 200 μm. CEP, cepharanthine; TET, tetrandrine; PI, propidium iodide.

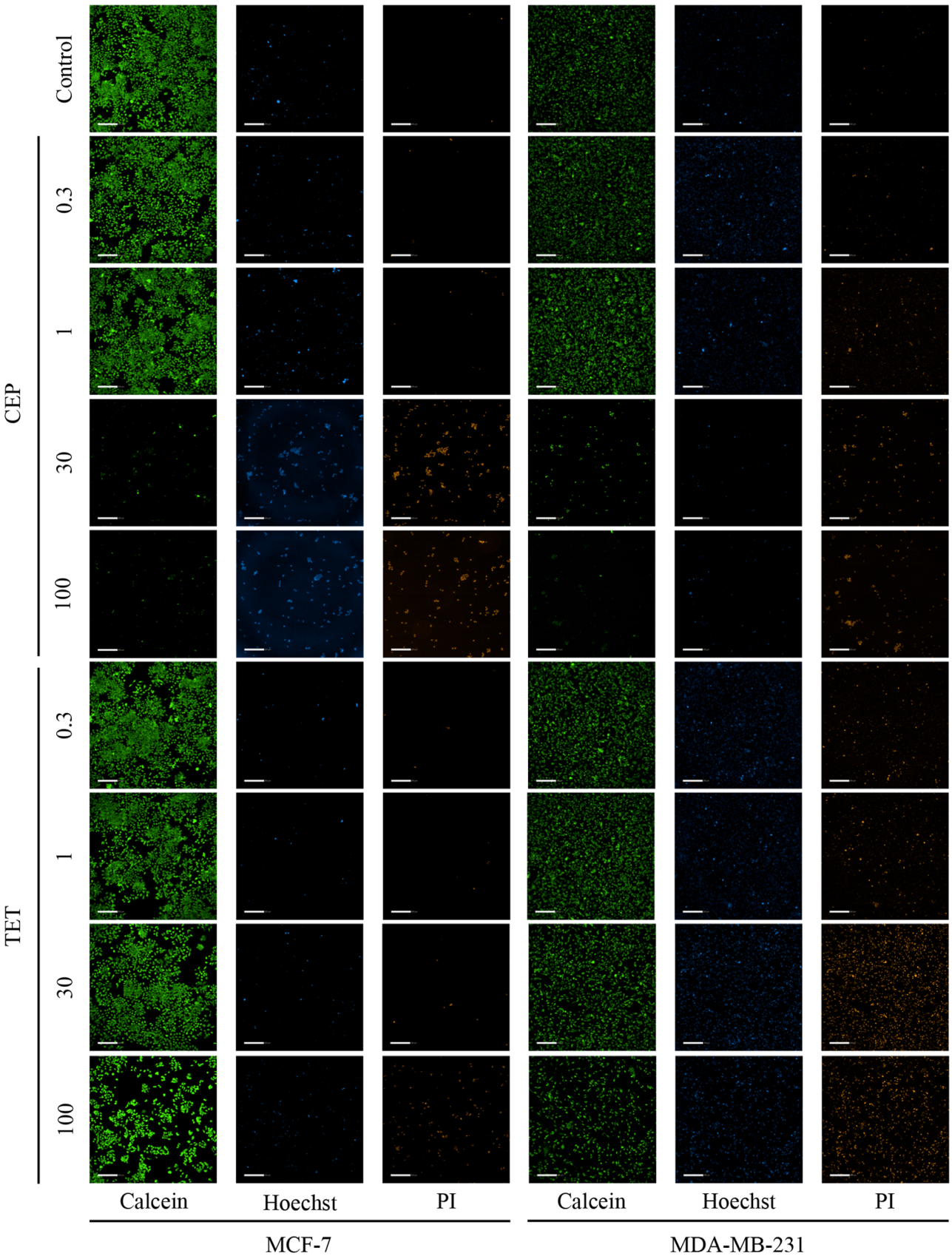

Figure S2. Photomicrographs of CEP- or TET-treated 3D MCF-7 and MDA-MB-231 spheroids stained with calcein or PI. MCF-7 and MDA-MB-231 spheroids were treated with 1, 3, 30 or 100 μg/ml CEP or TET and stained with calcein (green) or PI (red), representing the cytoplasm or dead cells, respectively. Scale bar, 500 μm. CEP, cepharanthine; TET, tetrandrine; PI, propidium iodide.

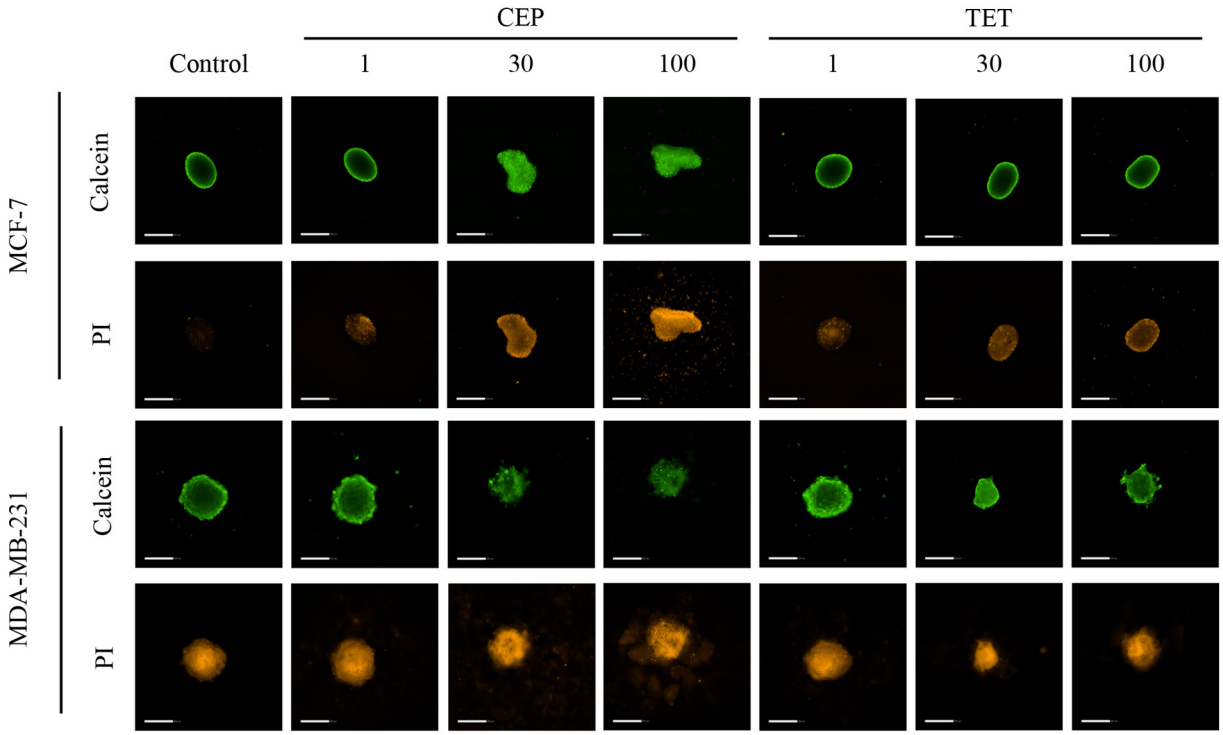

Figure S3. Flow cytometry plots of CEP- or TET-treated 2D MDA-MB-231 and MCF-7 cells. MDA-MB-231 and MCF-7 monolayer cells were treated with 1, 3, 10 or 30 μg/ml CEP or TET and stained with Annexin V-FITC and PI, and classified into four groups based on different quadrants: Viable cells (bottom left), early apoptotic cells (bottom right), late apoptotic cells (upper right) and necrotic cells (upper left). C/CEP, cepharanthine; T/TET, tetrandrine; PI, propidium iodide.

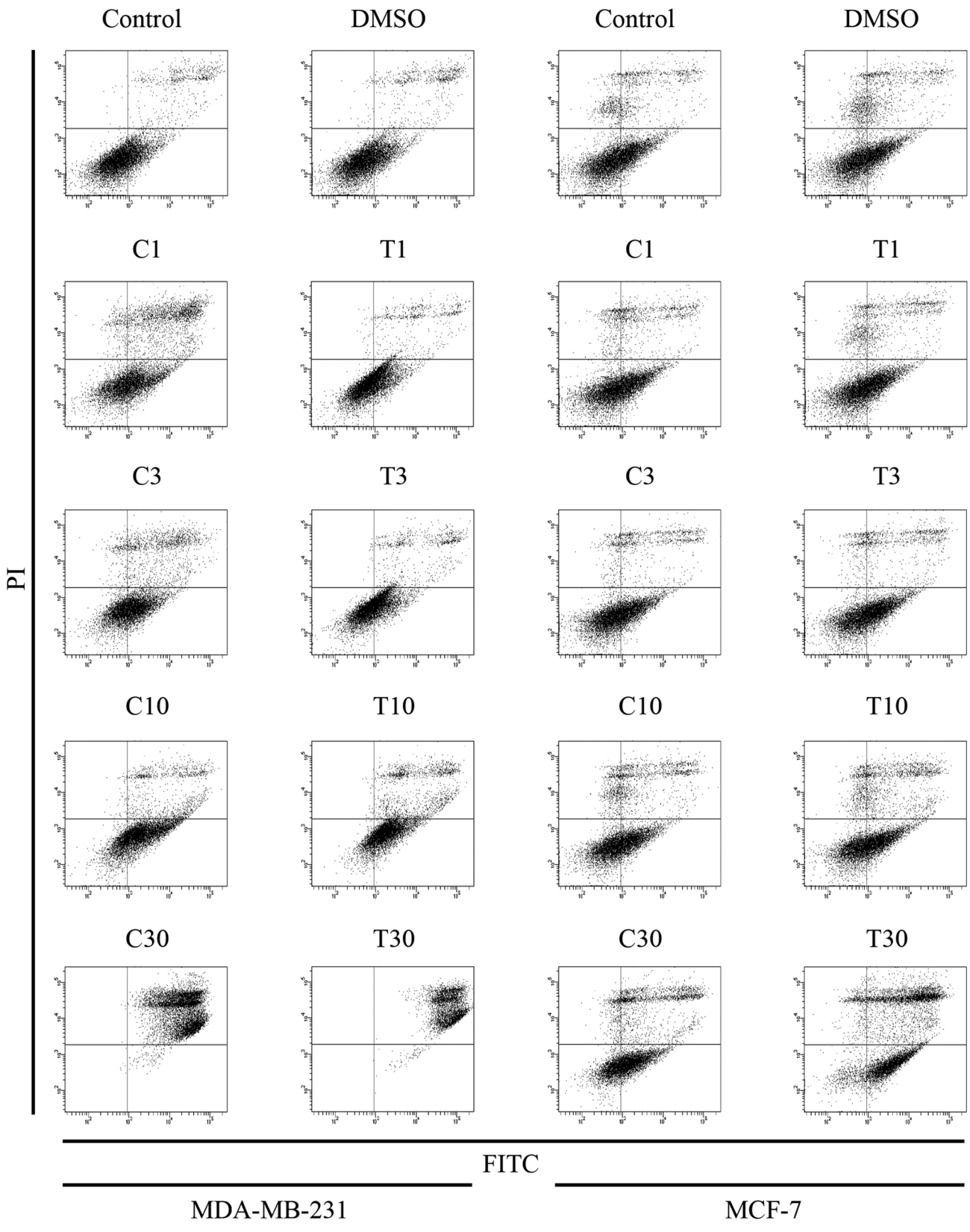

Figure S4. Flow cytometry plots of CEP- or TET-treated 3D MDA-MB-231 and MCF-7 spheroids. MDA-MB-231 and MCF-7 spheroid were treated with 1, 3, 10 or 30 μg/ml CEP or TET and stained with Annexin V-FITC and PI, and classified into four groups based on different quadrants: Viable cells (bottom left), early apoptotic cells (bottom right), late apoptotic cells (upper right) and necrotic cells (upper left). C/CEP, cepharanthine; T/TET, tetrandrine; PI, propidium iodide.