Electronic Supplementary Information

Inherently targeted estradiol-derived carbon dots for selective killing of ER (+) breast cancer cells via oridonin-triggered p53 pathway activation

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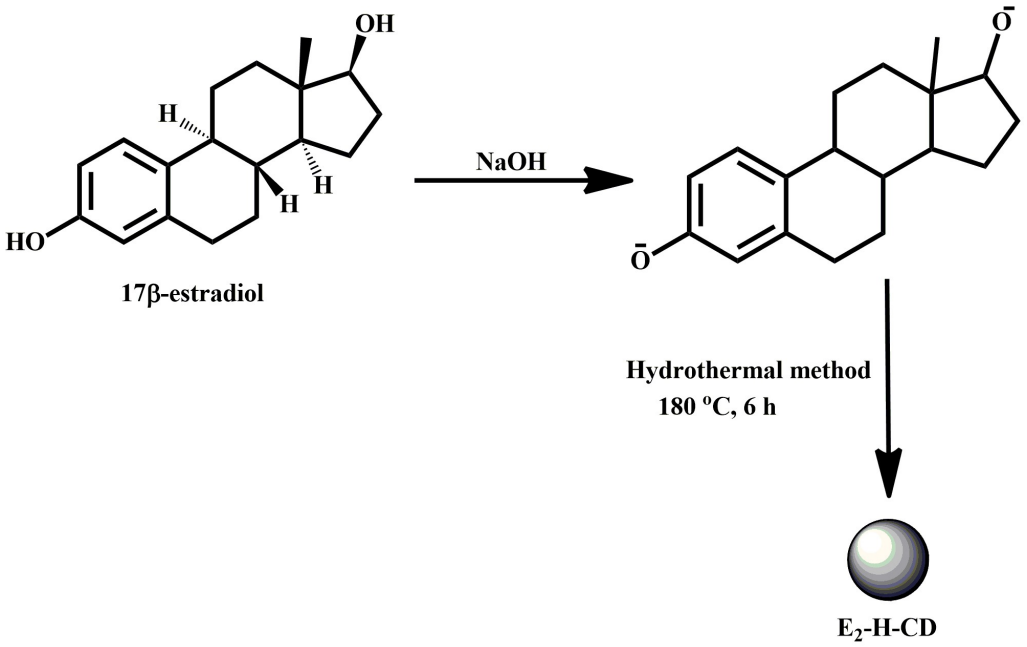
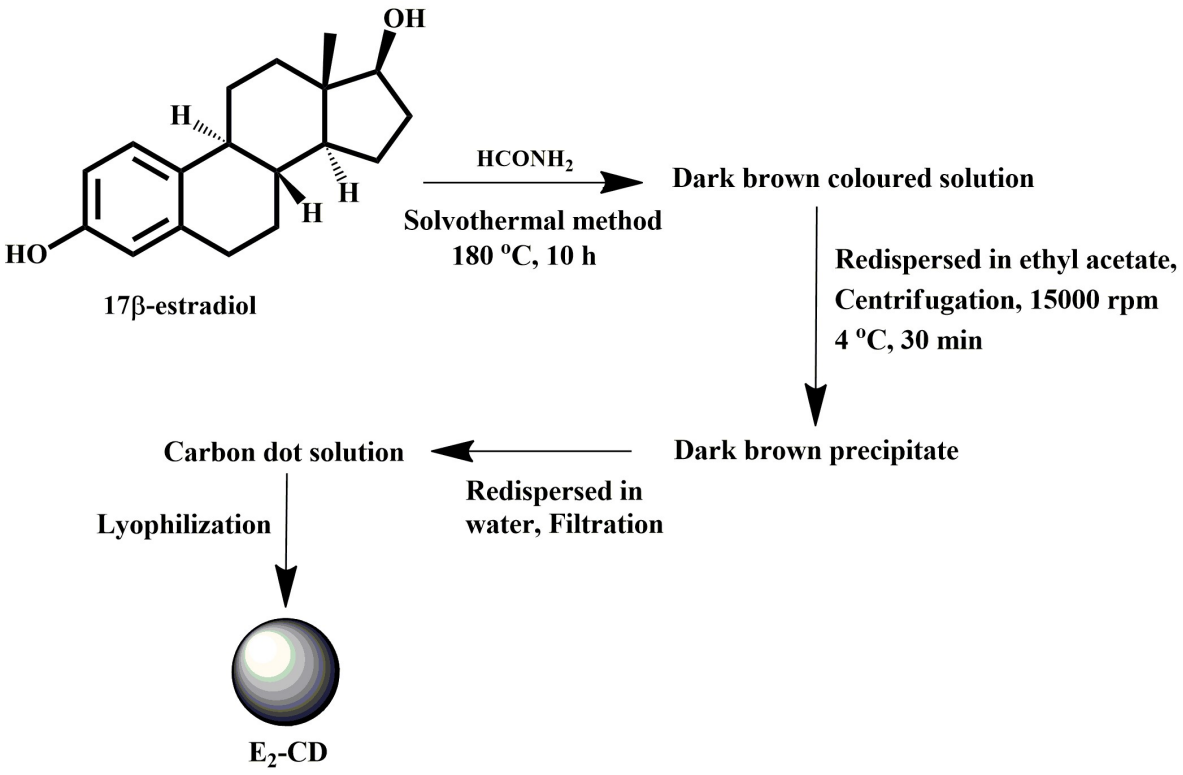
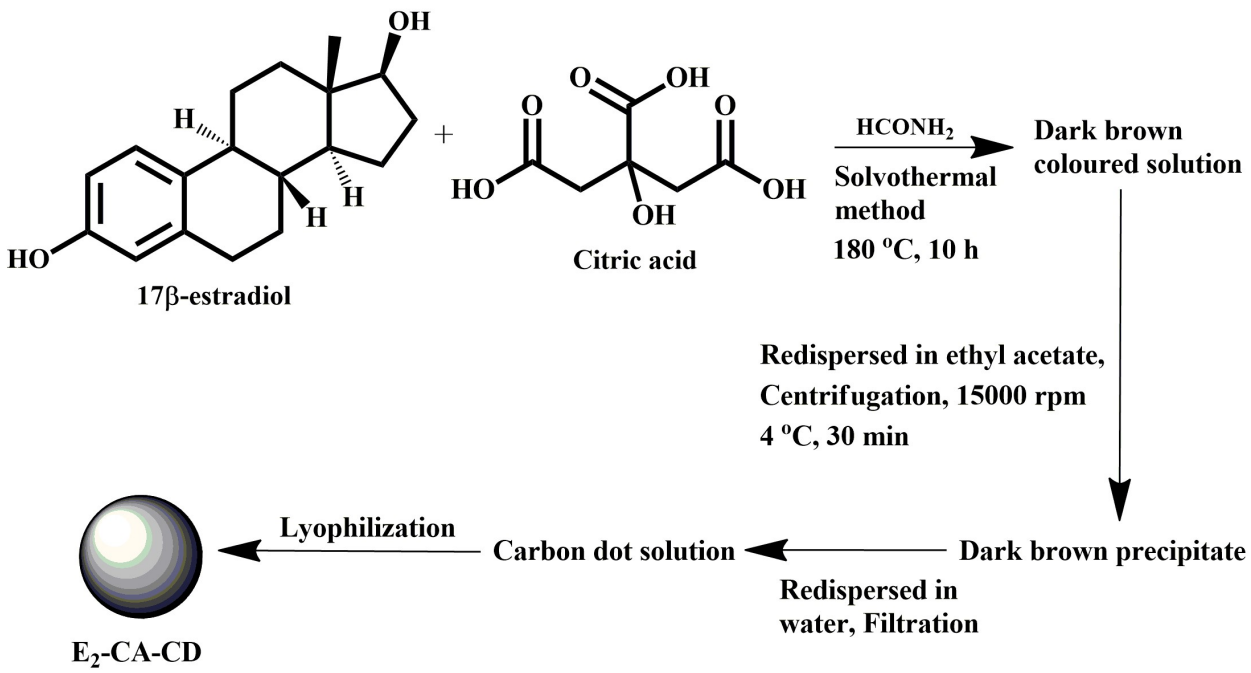


Scheme S1. Synthetic scheme of **E_2-H-CD** by hydrothermal method.



Scheme S2. Synthetic scheme of **E_2-CD** by solvothermal method.



Scheme S3. Synthetic scheme of **E_2-CA-CD** by solvothermal method.

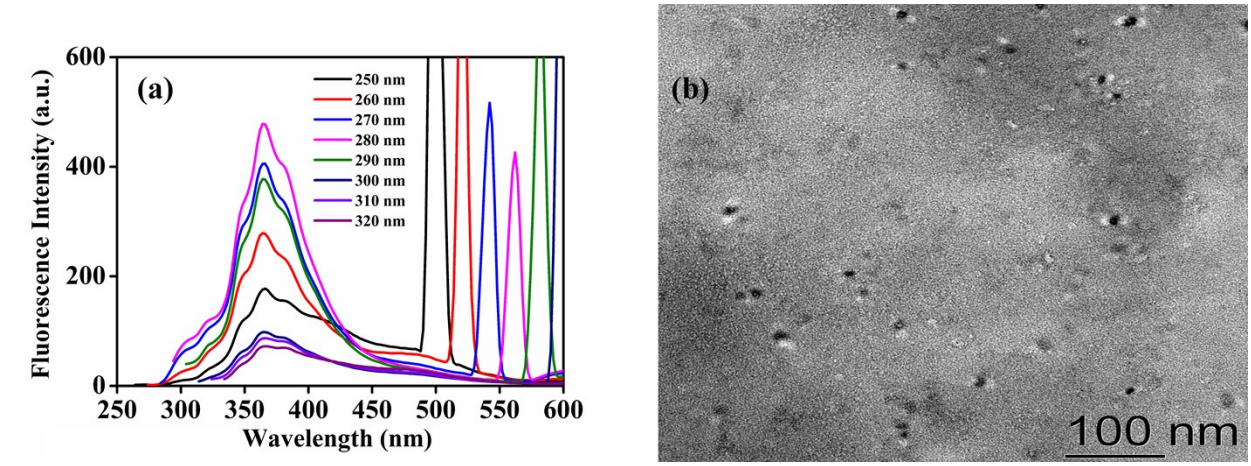


Fig. S1. (a) Fluorescence spectra and (b) FEG-TEM image of **E_2-H-CD**.

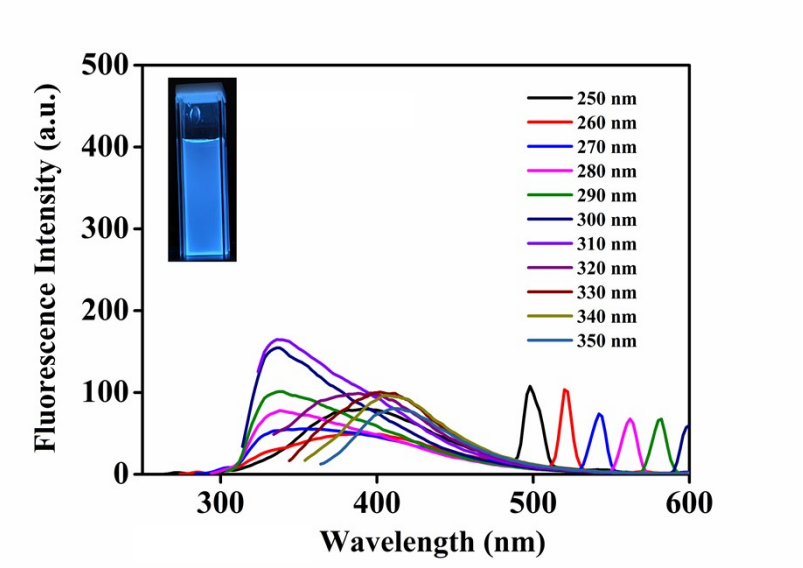


Fig. S2. Fluorescence spectra of **E_2-CD**.

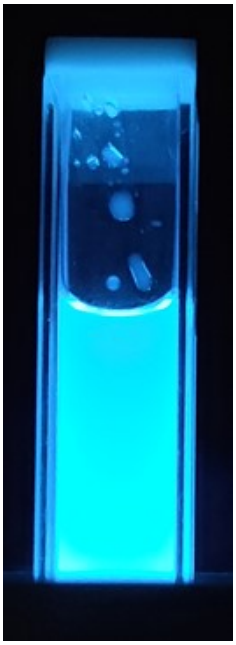


Fig. S3. Blue fluorescence of **E_2-CA-CD** observed under UV torch irradiation (excitation 365 nm)

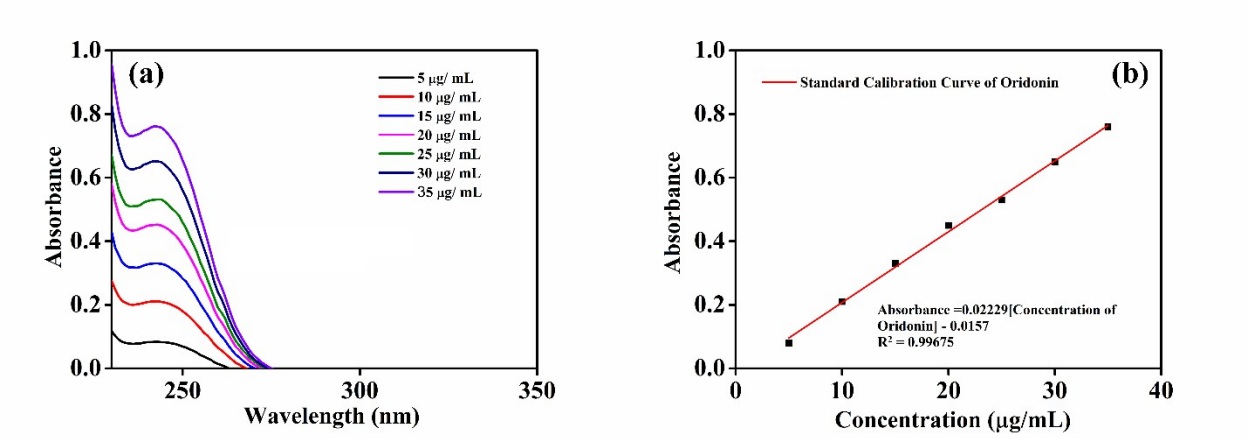


Fig. S4. (a) UV-vis spectra and (b) standard calibration curve of oridonin.

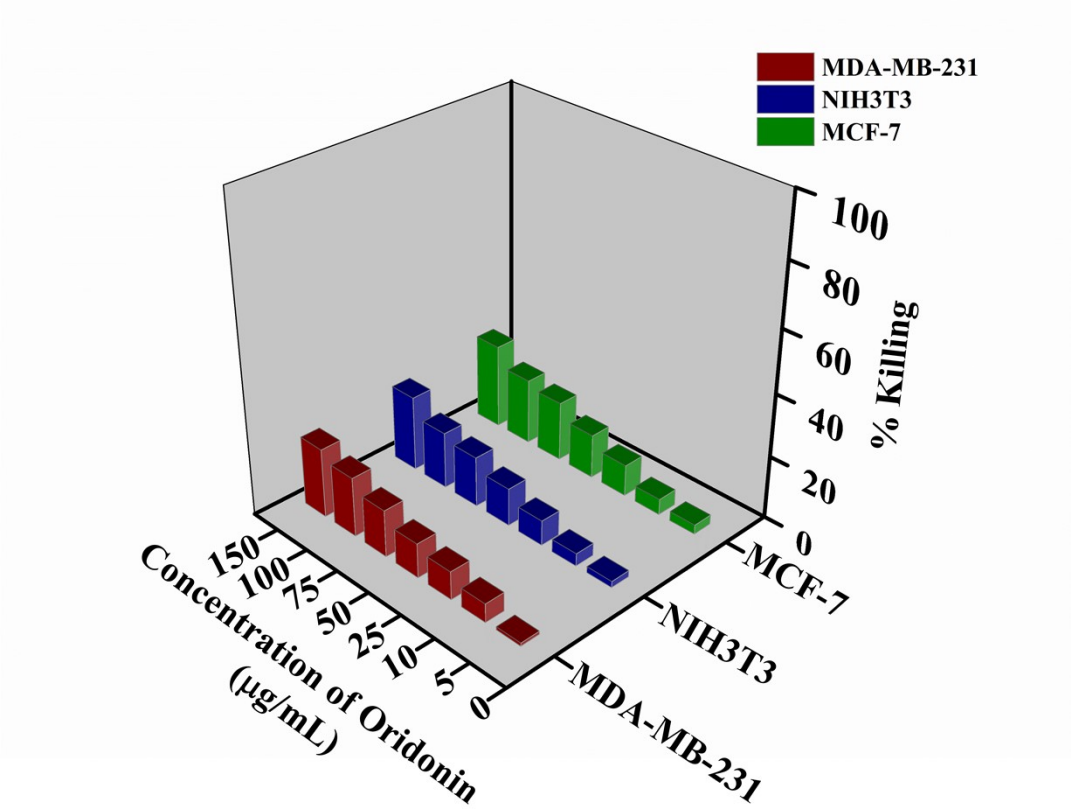


Fig. S5. % killing of MDA-MB-231, NIH3T3 and MCF-7 cells determined by MTT assay incubated with varying concentrations of oridonin (5-150 μg/mL) for 24 h. The experimental errors were in the range of 1-3% in triplicate experiments.

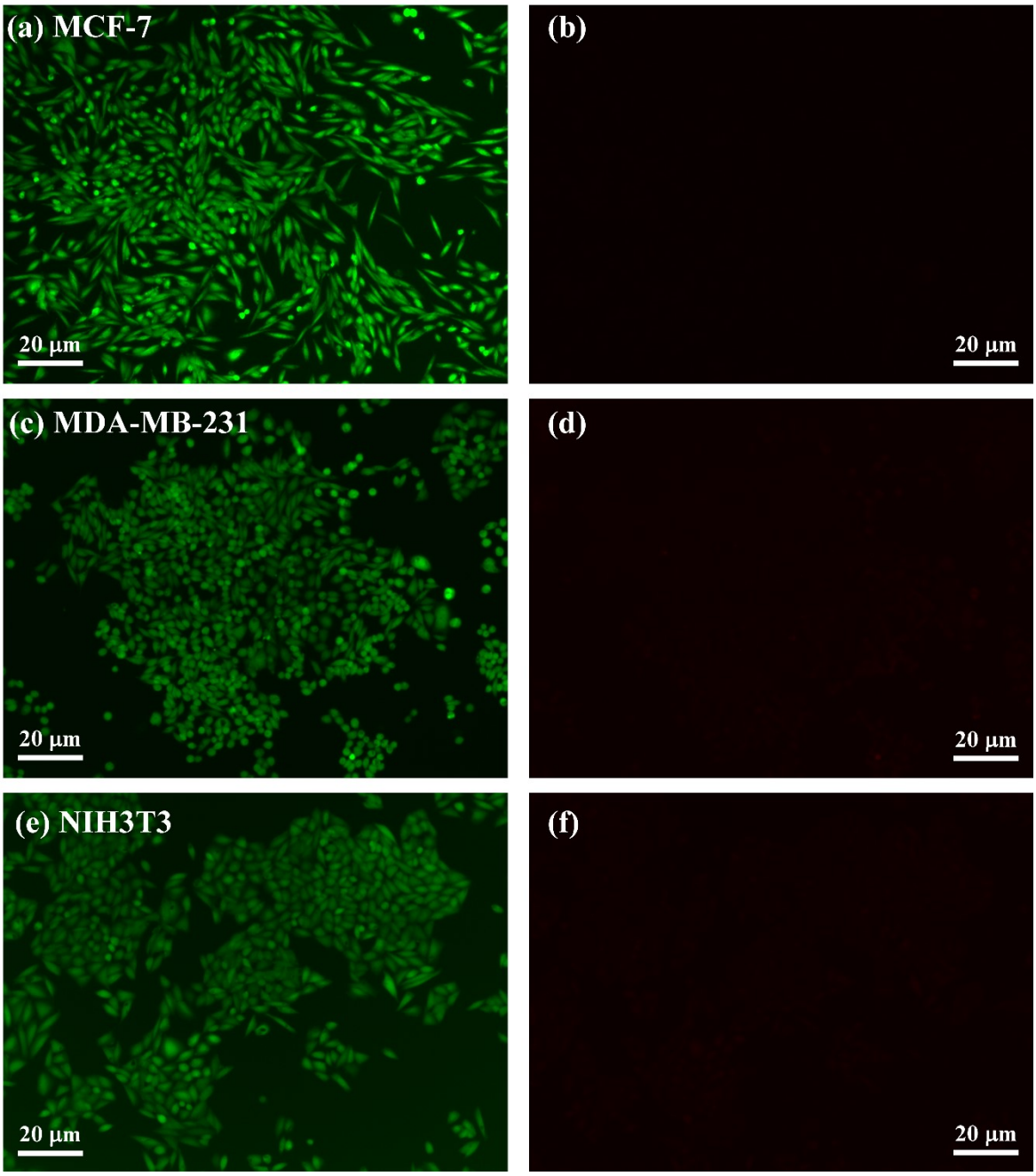


Fig. S6. LIVE/DEAD fluorescence microscopic images of (a and b) MCF-7, (c and d) MDA-MB-231, (e and f) NIH3T3 cells incubated for 12 h with **E_2-CA-CD** ([**E_2-CA-CD**] = 250 µg/mL). Scale bars correspond to 20 µm.

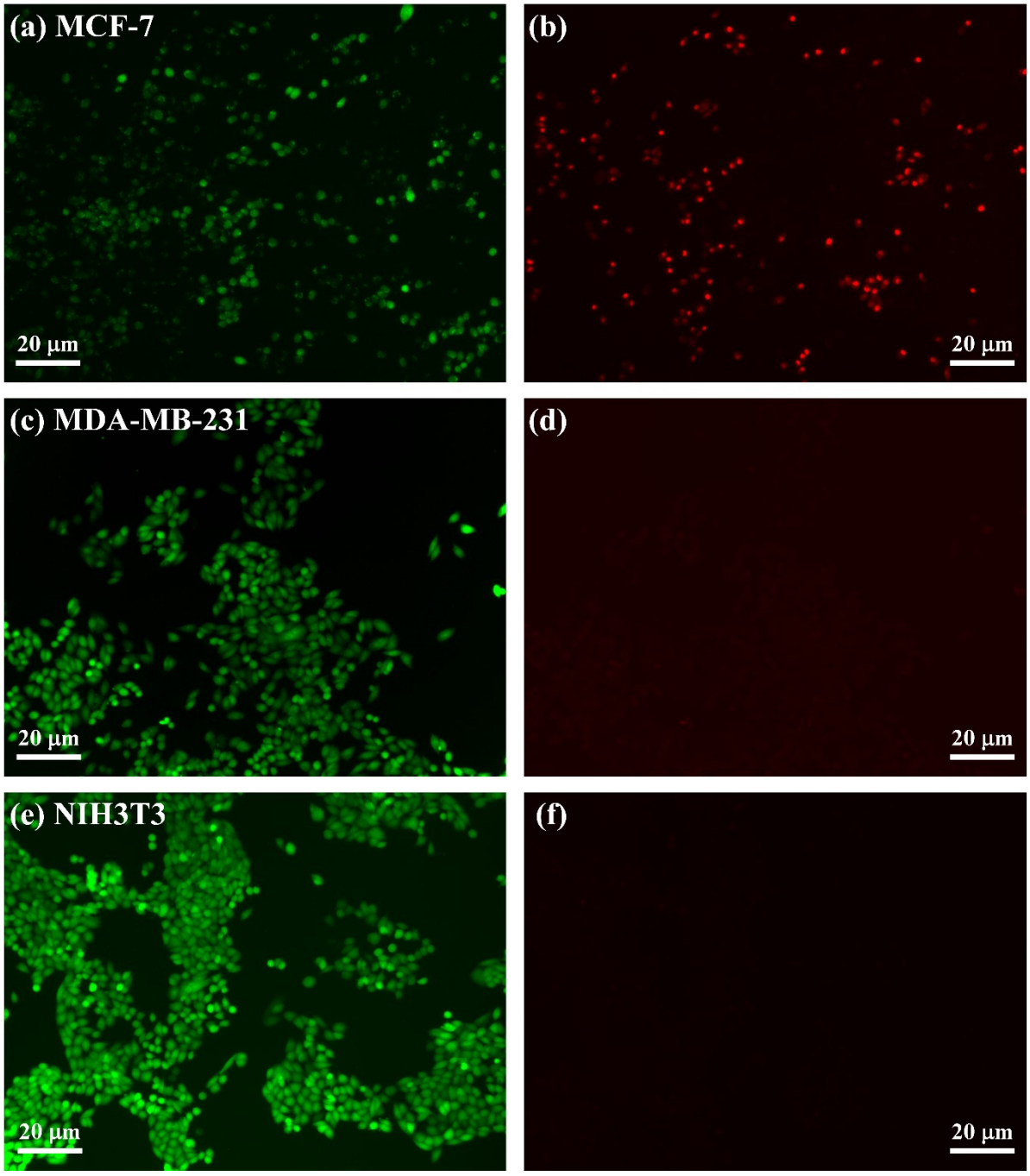


Fig. S7. LIVE/DEAD fluorescence microscopic images of (a and b) MCF-7, (c and d) MDA-MB-231, (e and f) NIH3T3 cells incubated for 12 h with **E_2-CA-CD**-Ori ([**E_2-CA-CD-**Ori] = 250 μg/mL, [Oridonin]=75 μg/mL). Scale bars correspond to 20 μm.

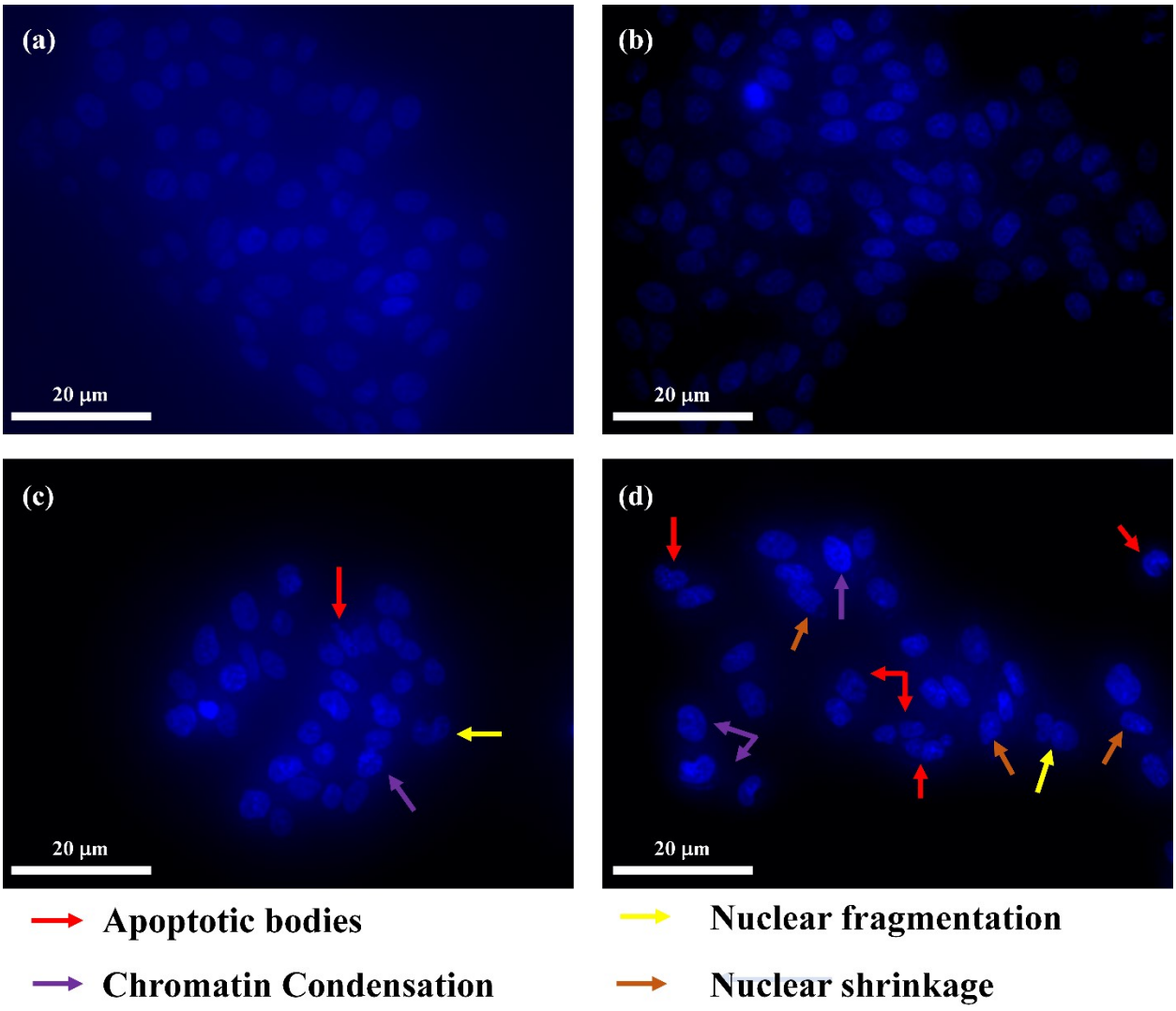


Fig. S8. Nucleus Staining with Hoechst 33342 dye of (a) MCF-7 cells; following incubation with (b) **E_2-CA-CD**, (c) native oridonin and (d) **E_2-CA-CD**-Ori for 12 h.

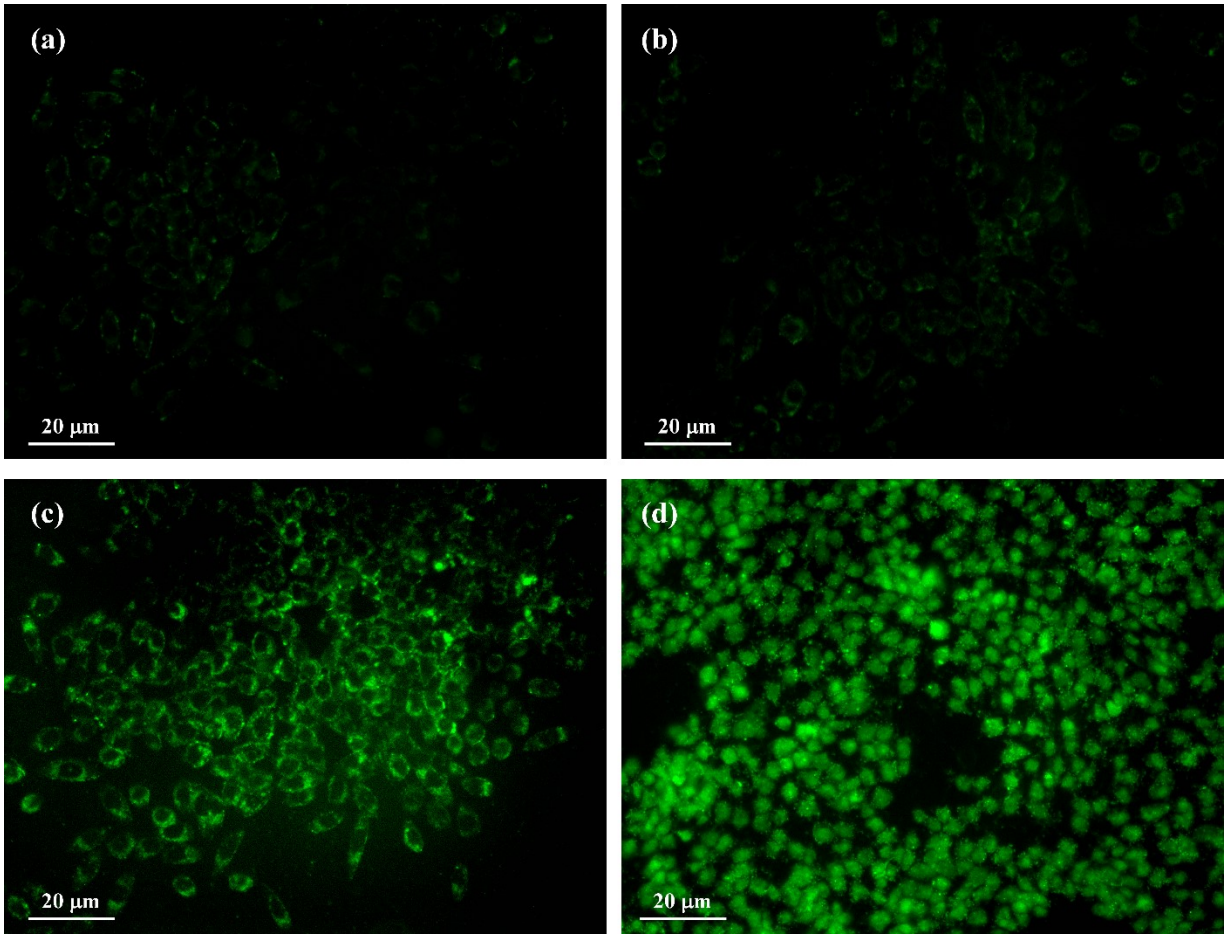


Fig. S9. Fluorescence microscopic images depicting intracellular ROS generation as indicated by green fluorescence of DCF in (a) MCF-7 cells, following incubation with (b) **E_2-CA-CD** (250 μg/mL), (c) native oridonin (75 μg/mL), and (d) **E_2-CA-CD**-Ori (250 μg/mL) for 12 h.

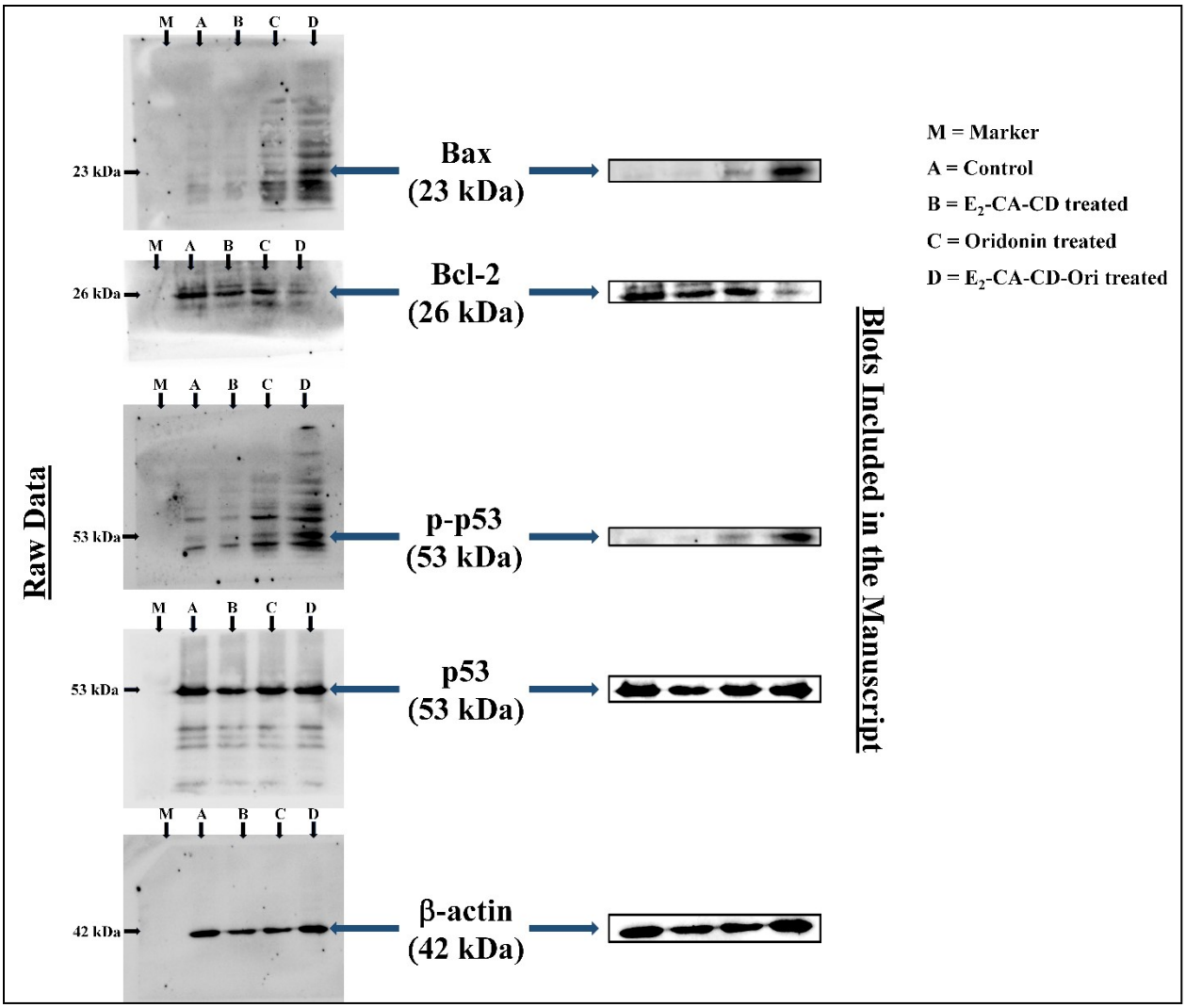


Fig. S10. Raw data along with submitted data of immunoblots corresponding to Fig. 9.

Herein, we have used PageRular Plus Prestained Protein Ladder, 10-250 kDa (Thermo Scientific) for determining the molecular weight of the desired proteins. The advantages of using pre-stained protein ladders are from the color of the markers, monitoring of protein migration during SDS-polyacrylamide gel electrophoresis and monitoring of protein transfer onto membranes after western blotting can be followed easily which is not possible in case of unstained markers. Therefore, we have chosen this type of pre-stained protein ladders which is also widely used. The blots were developed using Clarity Western ECL Substrate (Bio-rad) kit and imaging was done using ChemiDoc Gel Imaging system (Bio-rad). As we have used pre-stained protein markers which do not get stained in presence of ECL substrate, therefore splitting of bands of the marker depending on the molecular weight cannot be observed in ChemiDoc

imaging and the marker lane of the membrane appeared to be blank under chemiluminescence. However, the marker lane's different colors were clearly visible to the naked eye. On the basis of the colors of protein markers depending on their molecular weight, we have labelled the respective protein in our Western blot as given above in the original raw data blot.