SUPPLEMENTARY MATERIAL

A. Stability of liposomes formulation on time and in the presence of Fetal Bovine Serum (FBS)

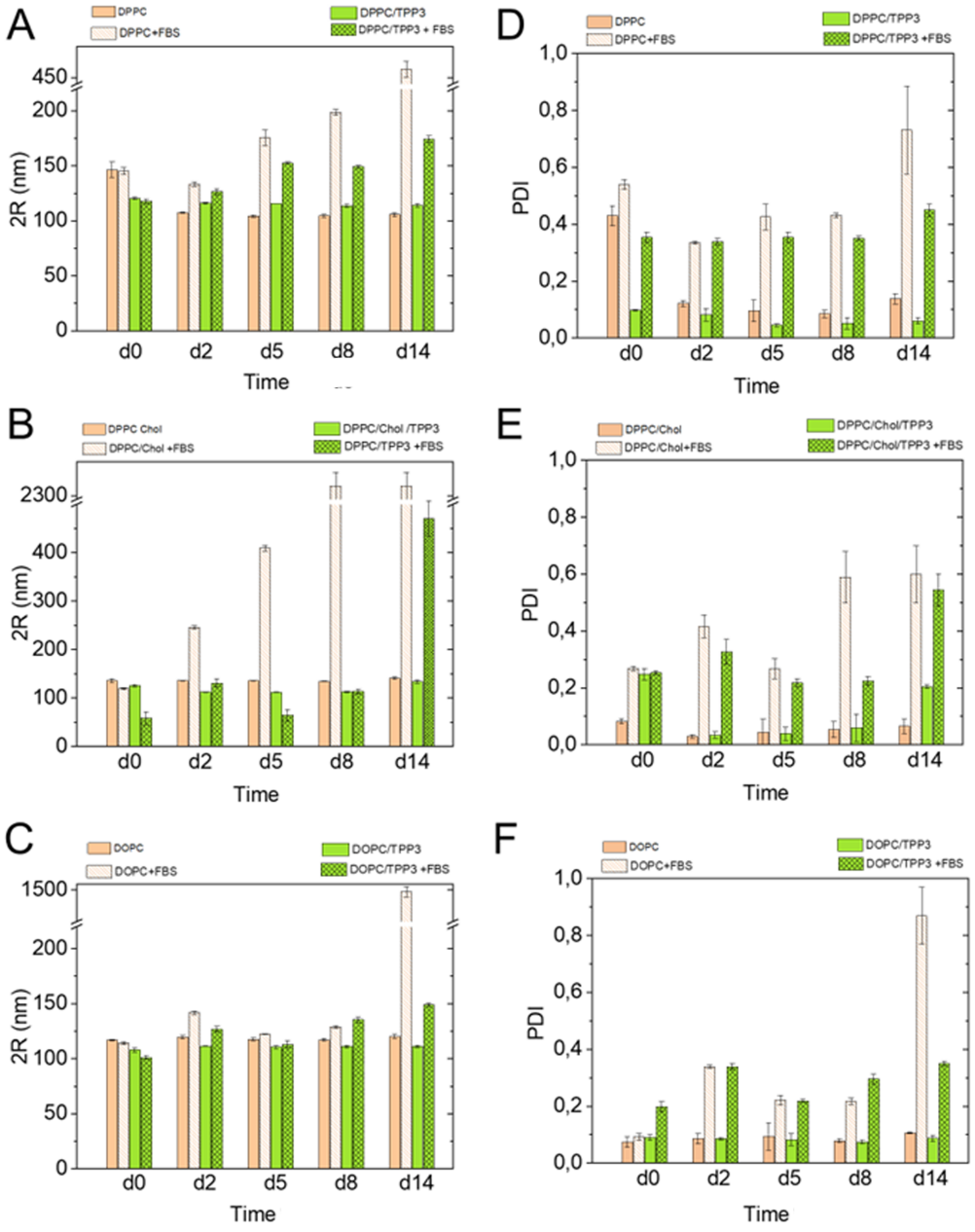

FIG. S1. Values of hydrodynamic diameter (2R, panels A-B-C) and polidispersity (PDI, panels D,E,F) of liposomal formulation measured soon after the preparation (d0) and after 2,5,8, 14 days. Measurements have been performed at 25 °C.

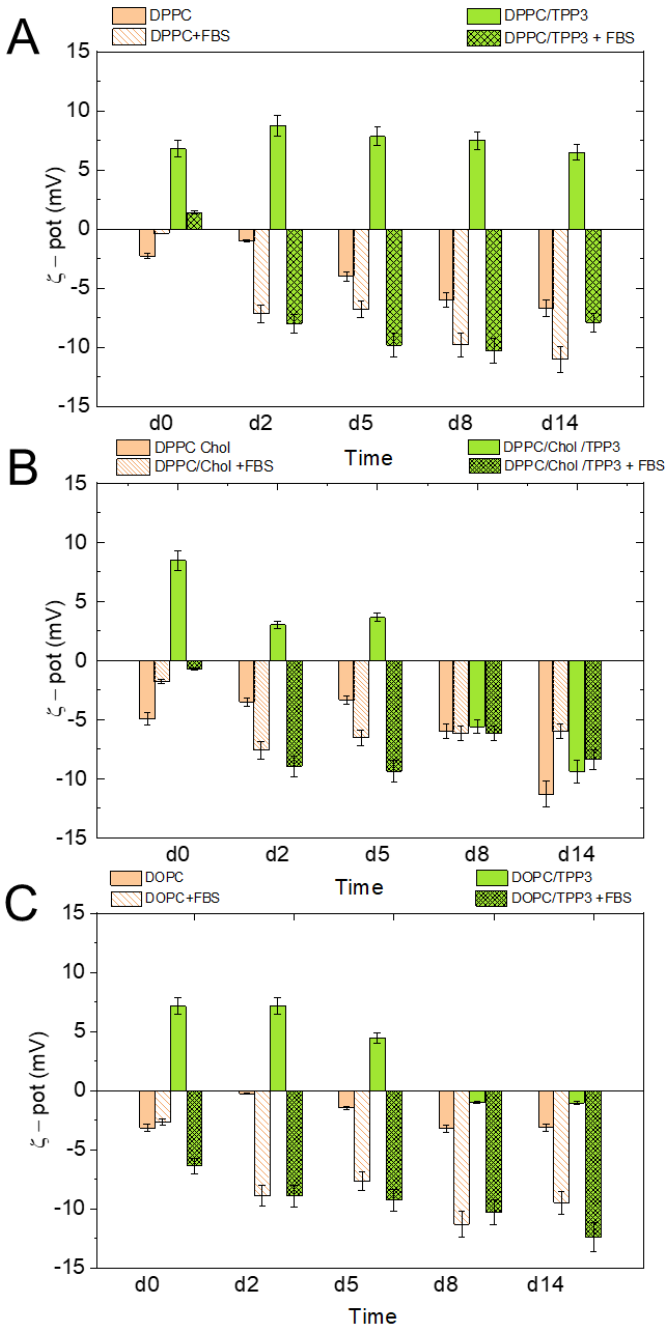

FIG. S2. Values of $\zeta-$potential of liposomal formulation measured soon after the preparation (d0) and after 2,5,8, 14 days. Measurements have been performed at 25 °C.

B. Flow cytometry analysis of mitochondrial membrane potential

Mitochondrial membrane potential was evaluated by flow cytometry in MDA-MB-231 cells labelled with the cationic fluorescent probe TMRM (tetramethylrhodamine methyl ester). TMRM, after crossing the plasma membrane, is readily incorporated in active mito-

chondria in a voltage-dependent manner. In this context, it diffuses across the mitochondrial membrane and accumulates in the organelle matrix which is negatively charged. Fluorescence intensity derived from TMRM directly correlates with the mitochondrial membrane potential.

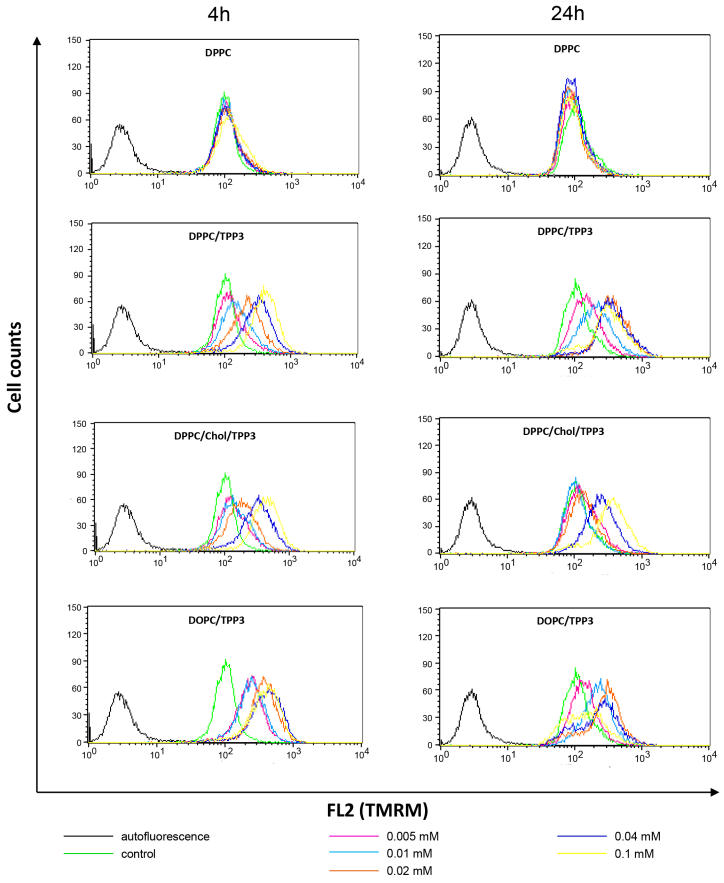

FIG. S3. Cells were treated for 4 (left panels) and 24 hours (right panels) with increasing concentration of DPPC, DPPC/TPP3, DPPC/Chol/TPP3 and DOPC/TPP3 liposomes. Histogram profiles from one representative experiment are shown; the profile obtained from unlabeled sample (to set autofluorescence signal) is also reported. x-axis refers to FL2 signal deriving from TMRM probe; y-axis refers to cell counts. Treatment of MDA-MB231 cells with liposomal formulations, in particular those containing TPP3, induces a mitochondrial membrane hyperpolarization. The consequent increase of TMRM fluorescent signal is reflected in the right shift of the flow cytometric profiles.

C. Determination of the first dissociation constant K_{a1} of *trans* resveratrol

The calibration plot of calculated $logC_H$ + values *vs* experimental pH readings is linear in the range 2–17; the relation between the pH values read on the instrument and the proton concentration is the following: $log[H_+] = a + bpH_{read}$. The extrapolation gives the value of the pK_{a_1} relative to the first dissociation constant of *trans* resveratrol.

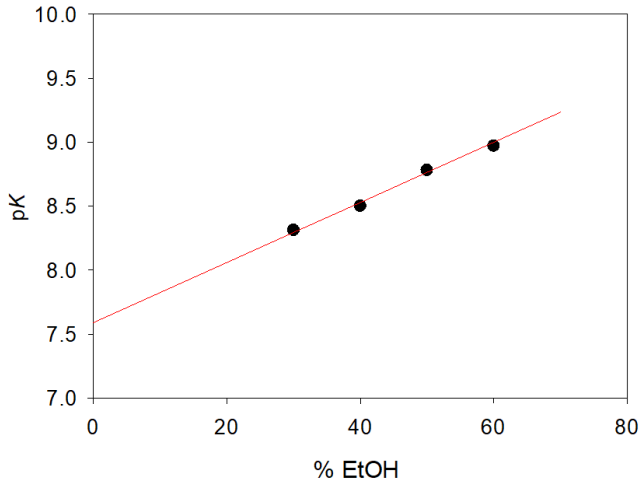

FIG. S4. Determination of the first dissociation constant K_{a1} of *trans* resveratrol. The straight line provides the extrapolated value in absolute H_2O.

D. Trolox stability as a function of pH.

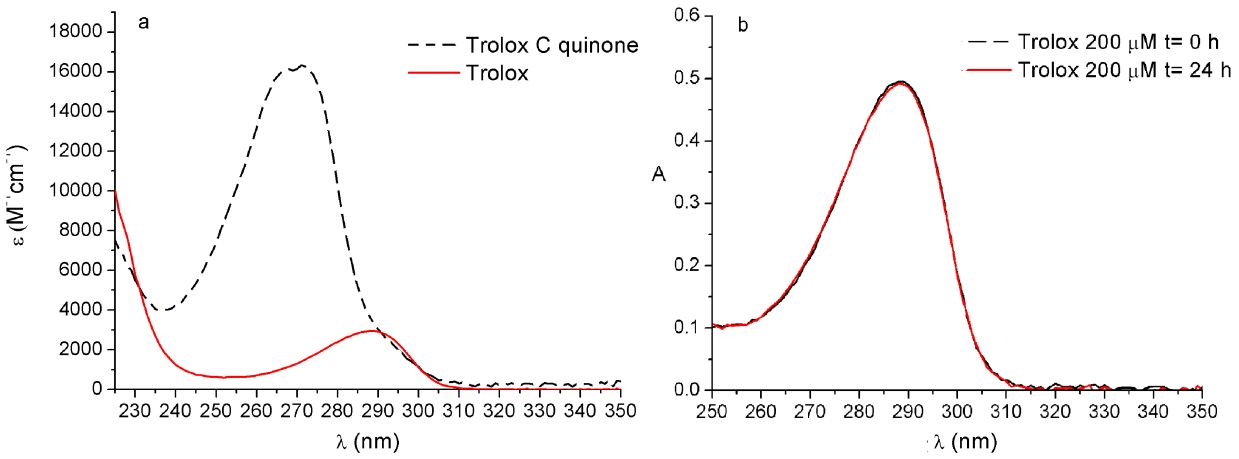

FIG. S5. a) Normalized UV spectrum of Trolox and Trolox C in PBS: Isopropanol 1:1. b) UV absorbance spectra of Trolox (200 μM) in calcium acetate 150 mM registered within 24h.