**Supporting Information for**

Enhanced Apoptosis and Mitochondrial Cell Death by Paclitaxel loaded TPP-TPGS1000 Functionalized Nanoemulsion

**Table S1**

**Synthesis and characterization of cationic TPP-TPGS1000**

TPP-TPGS1000was synthesized by using DCC/DMAP chemical reaction. Lyophilized product was characterized and confirmed by different spectroscopies such as proton nuclear magnetic resonance spectroscopy (1H NMR 400 MHz, Bruker AVANCE III 400), FTIR spectroscopy (Perkin Elmer spectrum version 10.03.06), and matrix-assisted laser desorption ionization time-of-flight mass spectrometry (MALDI-TOF-MS)[1,2].

**Figure S1**

**Determination of critical micellar concentration using UV hydrophobic probes**

The I2-UV-spectroscopy method was used to analyze the critical micellar concentration of TPGS and TPP-TPGS1000. The absorption intensity was plotted against the logarithm of the polymer mass concentration, and the cross-point of these two lines can be calculated to know the CMC value of synthesized TPP-TPGS1000. [3–5]

**Figure S2**

**Determination of rheological property of nanoemulsion**

The rheological properties of developed nanoformulation at different temperatures [6,7].

**Figure S3**

***In vitro* physicochemical characterization and hemolysis study**

Particle size, PDI and zeta potential of the developed TPP-TPGS1000-PTX-NE were analyzed using zetasizer (Nano-ZS, Malvern instrument, UK). In order to confirm the *in vitro* toxicity as well as *ex-vivo* hemolysis, TPP-TPGS1000-NE, and TPP-TPGS1000-PTX-NE were screened out for their hemolytic profile [8].

**Figure S4**

**Determination of drug loading and encapsulation efficiency of TPP-TPGS1000-PTX-NE**

A Shimadzu HPLC system integrated with binary modular, SIL-20AC HT, binary pump LC20DA, column oven CT0-10AS VP and a rheodyne® injector (model 7125, 20 µL loop) was used for chromatographic method development and validation. The chromatographic resolution was accomplished on a C18 Phenomenex Luna column (150 x 4.6 mm, 5μ) at 20 °C of column temperature. PTX was eluted using a mobile phase consisting 60: 40 (% v/v) ratio of acetonitrile and water. The flow rate was 1 ml/min and run time for each injection was 9 min. All the solvents were filtered and sonicated by utilizing a bath sonicator at room temperature for 9 min before the experiment. The eluent was monitored for PTX at λ = 227 using Shimadzu SPD-M20A UV-PDA detector [8,9].

**Chromatographic conditions for LC-MS/MS and pharmacokinetic drug profile of Taxol vs TPP-TPGS1000-PTX-NE in tissue samples**

**Source Parameters:** Sheath gas= 50, Auxiliary gas = 10, sweep gas = 0, Spray voltage (V) = 4000, Vaporizer temp (°C) = 325.

**Compound Parameters:** Precursor ion = 876.338 (M+Na), Product ion = 308.071, Collision energy (V) = 28.01, CID gas (mTor) = 1.5, RF (V) = 206, Q1 resolution = 0.7, Q3 resolution = 0.7, Dwell time (ms) = 100. For internal standard (Phenacetin), Precursor ion = 179.9, Product ion = 109.9, Collision energy (V) = 20, RF (V) = 30, CID gas (mTor) = 1.5, RF (V) = 206, Q1 resolution = 0.7, Q3 resolution = 0.7, Dwell time (ms) =100

**Chromatographic separation:** Phenomenex Luna (C18), 150 × 4.6 mm, 5μ) column was used for chromatographic separation of PTX. Formic acid (0.1 % v/v) in methanol (MeOH):10 milli molar ammonium acetate, 75:25 (v/v) used as mobile phase, with 0.6 ml/min flow rate.

Tissue drug concentration data (ng/g) vs. time data were plotted for pharmacokinetic and statistical analysis. Blood volume correction factors (Tumor-0.03, Kidney-0.24, and Liver-0.31) were applied to collected relevant tissue concentration data in the computation of final tissue concentration. Further, concentration was then evaluated using WinNonlin (Pharsight, Mountain View, CA) software utilizing a non-compartmental analytical approach [10–13].

**Table S2**

**Table S3**

**References**

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