Polymeric Micellar Co-delivery of Resveratrol and Curcumin to Mitigate In Vitro Doxorubicin Induced Cytotoxicity

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**Purpose**
To investigate micellar delivery of curcumin (CUR) and resveratrol (RES) in combination with doxorubicin (DH) on cancer cells in vitro. CUR has chemotherapy enhancing properties which may enhance cytotoxicity in SKOV-3 (human ovarian adenocarcinoma cells). CUR and RES have strong antioxidant properties which provide protective effects on H9C2 (rat embryonic derived myocytes).

**Methods**
Pluronic® F127 with RES:CUR 5:1 micelles were prepared by solvent casting method. Micelle size was characterized by Dynamic Light Scattering. Micelle loading was assessed by HPLC on a C18 column. Cytotoxicity of RES, CUR, DH in DMSO and RES:CUR 5:1 micelles with DH for a final ratio of all drugs at 10:2:1 was assessed in SKOV-3 and H9C2 cells using Cell Titer Blue Cell Viability Assay by fluorescence (EX/EM 560/590 nm).

**Results**
Micelle sizes were ~30 nm and RES and CUR loading in micelles was 13.14 mM and 2.63 mM respectively. The IC50 values for each treatment group were as follows: RES 53.9 µM, CUR 5.6 µM, DH 0.1 µM, micelles RES:CUR:DH 0.1 µM in SKOV-3 cells and RES 153.3 µM, CUR 10.7 µM, DH 0.01 µM, and micelles RES:CUR:DH 0.04 µM in H9C2 cells. The combination index (CI) for micelles RES:CUR:DH 10:2:1 is 0.58 in SKOV-3 indicating synergy and 3.43 in H9C2 indicating antagonism.

**Conclusion**
The micellar formulation of RES and CUR upon co-administered with DH at therapeutically relevant concentrations can exhibit synergy in vitro in cancer cells while being cardioprotective. This system provides potential for further development as a therapeutic option for patients using doxorubicin for chemotherapy.