suitable nanoemulsion region for preparing the SNEDDS formulation. RESULTS: The prepared formulations were characterized through in vitro, in situ, and in vivo studies to evaluate the biopharmaceutical performance. In vitro drug release studies showed 2.8- to 3.4-fold enhancement in the dissolution rate of both drugs from SNEDDS as compared with the pure drug suspension. Cell line studies revealed 1.5- to 2.7-fold reduction in the cytotoxicity on MCF-7 cells by plain PTX-SNEDDS and PTX-Cu-SNEDDS vis-à-vis the PTX-suspension. In situ intestinal perfusion studies revealed significant augmentation in permeability and absorption parameters of drug from PTX-Cu-SNEDDS over the plain PTX-SNEDDS and PTX-suspension ($p < 0.001$). In vivo pharmacokinetic studies also showed a remarkable improvement (i.e., 5.8- to 6.3-fold) in the oral bioavailability (Cmax and AUC) of the drug from PTX-SNEDDS and PTX-Cu-SNEDDS vis-à-vis the PTX-suspension. CONCLUSIONS: Overall, the studies corroborated superior biopharmaceutical performance of PTX-Cu-SNEDDS.

Singh, B. et al. (2014). "Synthesis and anti-proliferative activities of new derivatives of embelin." *Bioorg Med Chem Lett* 24(20):4865–4870.

Embelin (1), a benzoquinone isolated from *Embelia ribes*, is known to possess variety of biological activities. Despite of several promising biological activities, preclinical efforts on embelin were hampered because of its poor aqueous solubility. In order to address the solubility issue, herein, we have synthesized a series of Mannich products of embelin by treating it with various secondary amines. The synthesized compounds were screened for antiproliferative and antimicrobial activities. In cytotoxicity screening, the benzyl-piperidine linked derivative 8m was found to possess better antiproliferative activity compared to parent natural product embelin against a panel of cell lines including HCT-116, MCF-7, MIAPaCa-2 and PC-3 with IC50 values of 30, 41, 34 and 36 μM, respectively. The mechanistic study of compound 8m revealed that it exhibits cytotoxicity via induction of apoptosis and mitochondrial membrane potential loss. Further, the compounds were tested for antimicrobial activity where dimethylamino-8a and piperidine linked derivative 8b displayed antibacterial activity against *Staphylococcus* aureus with MIC values of 8 and 16 μg/mL, respectively. Mannich derivatives did now show improved aqueous solubility, however their hydrochloride salts 8a. HCl, 8b. HCl and 8m. HCl showed significantly improved aqueous solubility without affecting biological activities of parent Mannich derivatives.

White, J. A. et al. (2017). "Preformulation studies with the Escherichia coli double mutant heat-labile toxin adjuvant for use in an oral vaccine." *J Immunol Methods* 451:83–89.

Double mutant heat-labile toxin (dmLT) is a promising adjuvant for oral vaccine administration. The aims of our study were to develop sensitive methods to detect low concentrations of dmLT and to use the assays in preformulation studies to determine whether dmLT remains stable under conditions encountered by an oral vaccine. We developed a sandwich ELISA specific for intact dmLT and a sensitive SDS-PAGE densitometry method, and tested stability of dmLT in glass and plastic containers, in saliva, at the pH of stomach fluid, and in high-osmolarity buffers. The developed ELISA has a quantification range of 62.5 to 0.9 ng/mL and lower limit of detection of 0.3 ng/mL; the limit of quantification of the SDS-PAGE is 10 μg/mL. This work demonstrates the application of dmLT assays in preformulation studies to development of an oral vaccine containing dmLT. Assays reported here will facilitate the understanding and use of dmLT as an adjuvant.