Pre-formulation Studies of Trans-Resveratrol
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Purpose
trans-Resveratrol, a natural compound found in grapes have potential chemopreventive effects. This compound has very low oral bioavailability in humans. Therefore, the purpose of this study is to evaluate the solubility, pH stability profile, plasma protein binding, and stability in plasma for trans-resveratrol.

Methods
Solubility of trans-resveratrol was measured in 10 common solvents at 25°C. Sufficient amounts of trans-resveratrol were added to scintillation vials in triplicate while protected from light. Vials were shaken vigorously to reach drug saturation and analyzed by an established HPLC method. The solution state pH stability of trans-resveratrol was assessed in various USP buffers ranging from pH 2-10 for 24 hours at 37°C. Standard solution of 1mg/mL trans-resveratrol in acetonitrile was added to each buffer in 1:10 ratio (n=3). Samples were analyzed up to 24 hours. Human plasma protein binding was determined using ultracentrifugation technique. Standard solutions of drug were spiked to blank human plasma to yield final concentrations of 5, 12.5, or 25 µg/mL (n=3) for determination. Finally, stability of trans-resveratrol in human and rat plasma was also assessed at 37°C. Aliquots of blank plasma was spiked with a standard drug concentration to yield final plasma concentration of 50 µg/mL (n=6). Samples were analyzed for trans-resveratrol concentration up to 96 hours.

Results
trans-Resveratrol has wide solubility ranging from 0.05 mg/mL in water, 0.14 mg/mL in soybean oil, 7.46 mg/mL in tween-80, and 374 mg/mL in PEG-400. trans-Resveratrol is not stable in basic conditions with a mean apparent degradation half life of 40 hours. The mean plasma protein binding of trans-resveratrol is 98.3%. trans-Resveratrol degrades in human and rat plasma in a first order process with mean half lives of 54 and 25 hours, respectively.

Conclusion
trans-resveratrol is soluble in alcohol and PEG-400. It binds highly to plasma proteins, and degrades slower in human then rat plasma.