**SN-38-Cyclodextrin Complexation: Influence on Solubility, Stability and In Vitro Anticancer Activity against Ovarian Cancer**

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**Purpose**
SN38, an active metabolite of irinotecan, is about 100-1000 times more potent than irinotecan. But the clinical use of SN38 is limited by its extreme hydrophobicity and instability at physiological pH. In an effort to enhance solubility and stability, SN-38 was complexed with cyclodextrins and their influence on SN-38 solubility, stability and *in-vitro* cytotoxicity was studied on ovarian cancer cell lines.

**Methods**
SN-38 was complexed with four different types of β-cyclodextrins, namely, sodium sulfobutyl ether β-cyclodextrin (SBEβCD), hydroxyl propyl β-cyclodextrin (HPβCD), randomly methylated β-cyclodextrin (RMβCD), methyl β-cyclodextrin (MβCD). Phase solubility studies were conducted to understand the pattern of SN-38 solubilization. SN-38-cyclodextrin complexes were characterized by DSC, FTIR and XRPD. Stability of SN-38-SBEβCD complex in pH 7.4 PBS was evaluated and compared against free SN-38. Cytotoxicity of SN-38-SBEβCD complex was studied in two ovarian cancer cell lines, A2780 and 2008.

**Results**
Phase solubility studies revealed that SN-38 solubility increased linearly as a function of β-cyclodextrin concentration and the linearity was characteristic of an *A*_<sub>p</sub>-type system and suggested formation of complexes in 1:2 SN-38/CD molar ratio. The aqueous solubility of SN-38 was enhanced by 10-16 times by cyclodextrin complexation. DSC, FTIR, XRPD studies confirmed the formation of inclusion complexes. Stability studies in PBS revealed that cyclodextrin complexation significantly increased the hydrolytic stability of SN-38 at physiological pH 7.4. 1% SBEβCD improved the stability of SN-38 by >3 fold, after 5 h of incubation at pH 7.4. Cytotoxicity of SBEβCD-SN-38 complex was significantly high in A2780 and 2008 cells in comparison to SN-38 and its parent drug molecule irinotecan (*p* < 0.01, student’s t-test). IC<sub>50</sub> values of irinotecan, SN-38, and SBEβCD-SN-38 complex for A2780 cells were 4.15±0.109 µM, 76.07±0.50 nM, and 21.42±1.09 nM, respectively. Whereas IC<sub>50</sub> values for 2008 cells were 26.38±0.844 µM, 140.27±3.06 nM, and 133.30±2.82 nM, respectively.

**Conclusion**
Based on the results from this study it was concluded that SBEβCD could be a better complexing agent for enhancing the solubility, stability and thereby cytotoxicity of SN-38.