Effect of Surfactant, Gastric Emptying and Dosage Form on Supersaturation of Dipyridamole in an In Vitro Model Simulating the Stomach and Duodenum

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**Purpose**
To investigate the impact of surfactant, gastric emptying and dosage form on supersaturation of dipyridamole.

**Methods**
A Simulated Stomach and Duodenum in-vitro dissolution model was developed using two compartments representing the stomach and duodenum. The two compartments are connected using a pump capable of achieving first order emptying rate. Simulated gastric and intestinal fluids were simultaneously pumped into their respective compartments. Sodium dichromate solution was first used to validate the dissolution model. The impact of surfactant on dipyridamole supersaturation was then studied using tween 80, sodium lauryl sulphate (SLS) and lutrol F68. For each surfactant, concentration was chosen such that surface tension is similar to in-vivo (~40 mN/m). In all cases, concentrations were less than critical micelle concentrations (CMC). Samples were taken from the stomach and duodenum compartments over three hours and analyzed (HPLC). At each time point, pH was also recorded. The effect of gastric emptying rate and dosage form (solution vs powder) were also studied.

**Results**
The concentration of dipyridamole in the duodenum compartment was significantly higher than would be predicted from the pH solubility profile (e.g. concentration at pH 5.8 in the simulated duodenal compartment at 20 min was found to be 90 µg/mL, which is much higher than the 12 µg/mL predicted from the pH solubility profile). This supports supersaturation of dipyridamole upon passage from the stomach (pH~2) to the duodenum (pH~5.5). The extent of supersaturation was significantly higher with SLS compared to tween 80 and lutrol F68, whereby the supersaturation ratios were 3-fold and 3.8-fold respectively at 20 min. Since surface tension was similar for all surfactant solutions, surfactant concentrations <CMC and pH was accounted for, the difference in supersaturation is likely due to specific interactions between surfactant and dipyridamole. Dipyridamole dosage form (solution vs powder) was not found to have a significant impact on supersaturation (α>0.05). Drug supersaturation in the duodenal compartment was maintained for longer periods when slower gastric emptying rates were utilized.

**Conclusion**
A Simulated Stomach and Duodenum dissolution model was developed and utilized to assess supersaturation of a model compound dipyridamole.