



## Pharmaceutical Sciences Seminar Series

Wednesday, September 6, 2023

4:00pm

2548 North University Building

[Zoom](#)

### “CO<sub>2</sub>-H<sub>2</sub>O Reaction: Implications for Intestinal Drug Dissolution and Solubility”

Presented by:



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**Abstract:** Drug (and sometimes excipient) dissolution *in vivo* is very often governed by its acid-base interaction with the hydrochloric acid in the stomach and the bicarbonate buffer in the intestine. When it comes to intestinal dissolution, bicarbonate buffer shows a peculiar behavior both at interfaces and in the bulk. This is related to the reversible hydration of CO<sub>2</sub> into H<sub>2</sub>CO<sub>3</sub>. In bulk, the volatility of CO<sub>2</sub> often limits the accumulation of the conjugate acid in case of acid dissolution (or its net decline in case of base dissolution). This strengthens the buffer capacity over a wide pH range thus enabling the intestine to be effectively buffered over a broad range of pH values between 5.5 and 7.5. It also increases the saturation solubilities of ionizable compounds. However, at interfaces, the relatively slow kinetics of this reaction (comparable to diffusional kinetics) results in a non-equilibrium situation at the dissolving surface. This weakens the ability of the intestinal fluid to buffer the interface resulting in a lower extent of ionization. Accordingly, dissolution in intestinal bicarbonate tends to be slower (sometimes far slower) than in “ordinary” buffers typically used in pharmaceutical dissolution testing. This discrepancy between enhanced bulk saturation solubility and lowered interfacial “solubility” also results in saturation solubility being a poor indicator of the dissolution rate in intestinal fluids. Those unique physico-chemical properties are not present in the typical pharmaceutical buffers which results in the performed dissolutions tests tending to overestimate drug product dissolution (sometimes quite strongly). The implications of this range from failed bioequivalence tests to the clinical failure of some drug products like the case of enteric-coated aspirin.

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