Modeling Dissolution in GastroPlus

PSCI-518, Spring 2024

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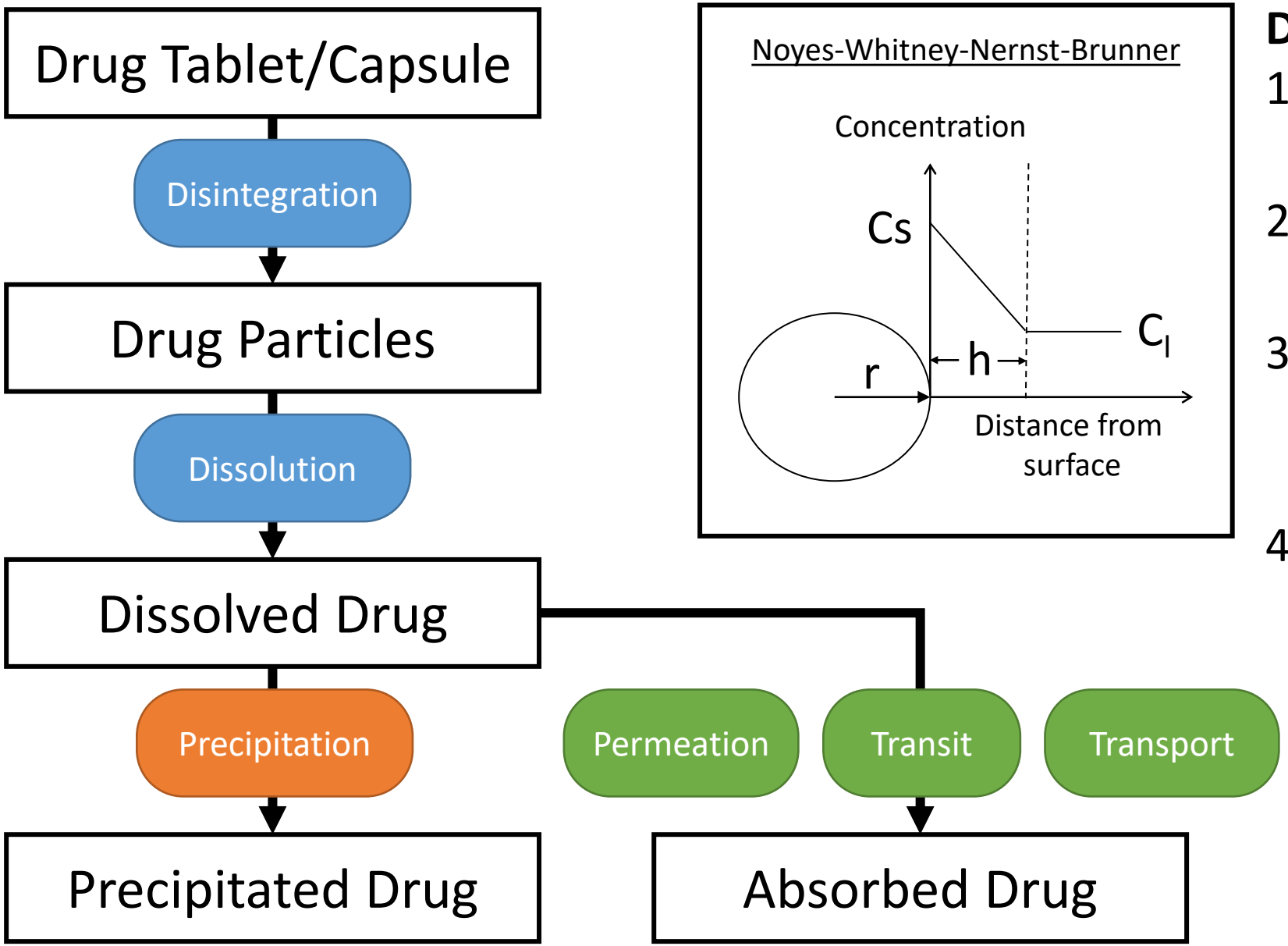
Dissolution Processes



Dissolution Models in GP:

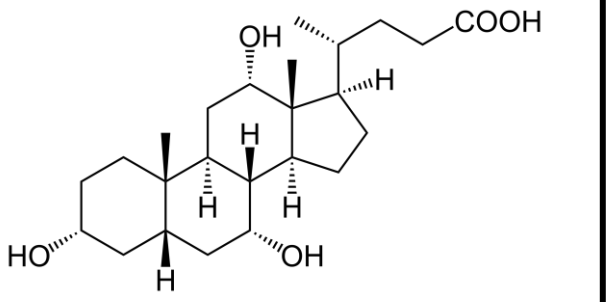
1. Johnson
   - Shaped Particles
2. Wang-Flanagan
   - Spherical Particles
3. Instant
   - Instant, up to solubility
4. Z-Factor
   - Rate constant

Nomenclature

- Intrinsic Solubility – solubility of the neutral form of a compound
- Reference Solubility – solubility of a compound at a given pH (ideally mostly unionized)
- Ionic Solubility – solubility of the ionized form of a compound
- Solubility Factor (SF) – ratio of ionic/intrinsic solubility (extent that solubility increases as a function of ionization)
- Biorelevant Solubilities/Media – SGF, FeSSIF, FaSSIF, etc.
- Solubilization Ratio (SR) – effect of solubilizing agents (bile salts) on solubility *in situ*

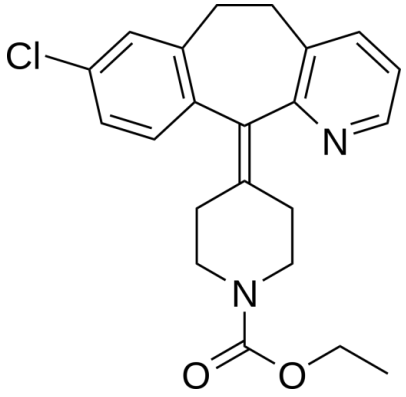
Physiologic Processes Affecting Dissolution

- pH Dependence – Solubility Factor (SF)
- Bile Salts – Solubilization Ratio (SR)
- GI Motility – Mixing
- Sink Effect – Absorption



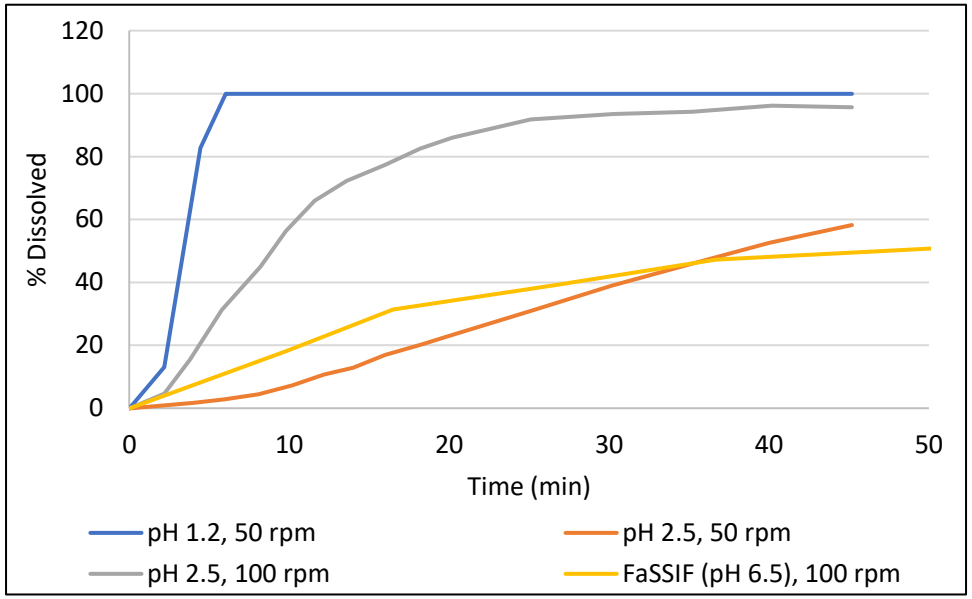
Cholic Acid

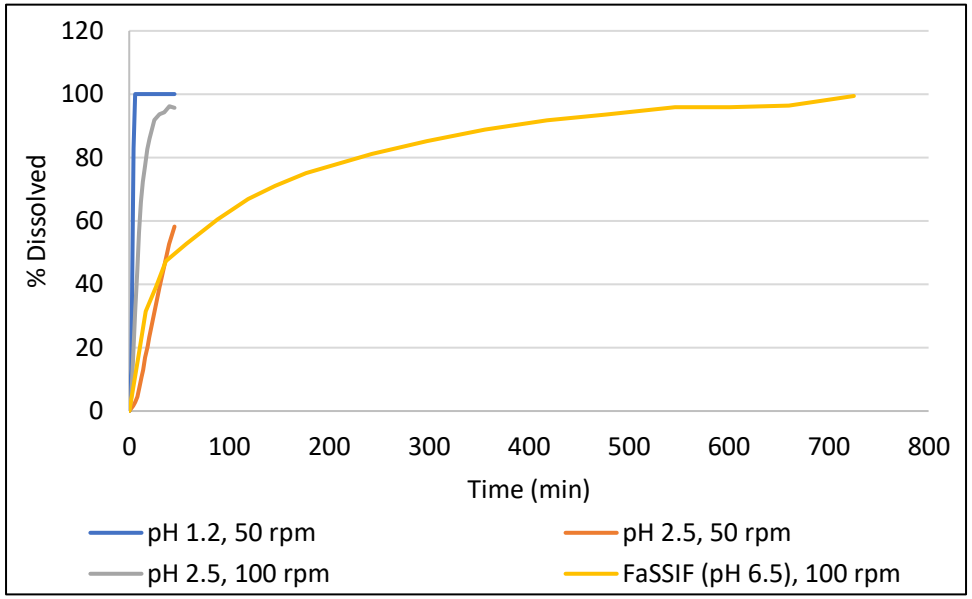
Duodenal Concentrations
Fasted: 2.8 mM
Fed: 14.4 mM



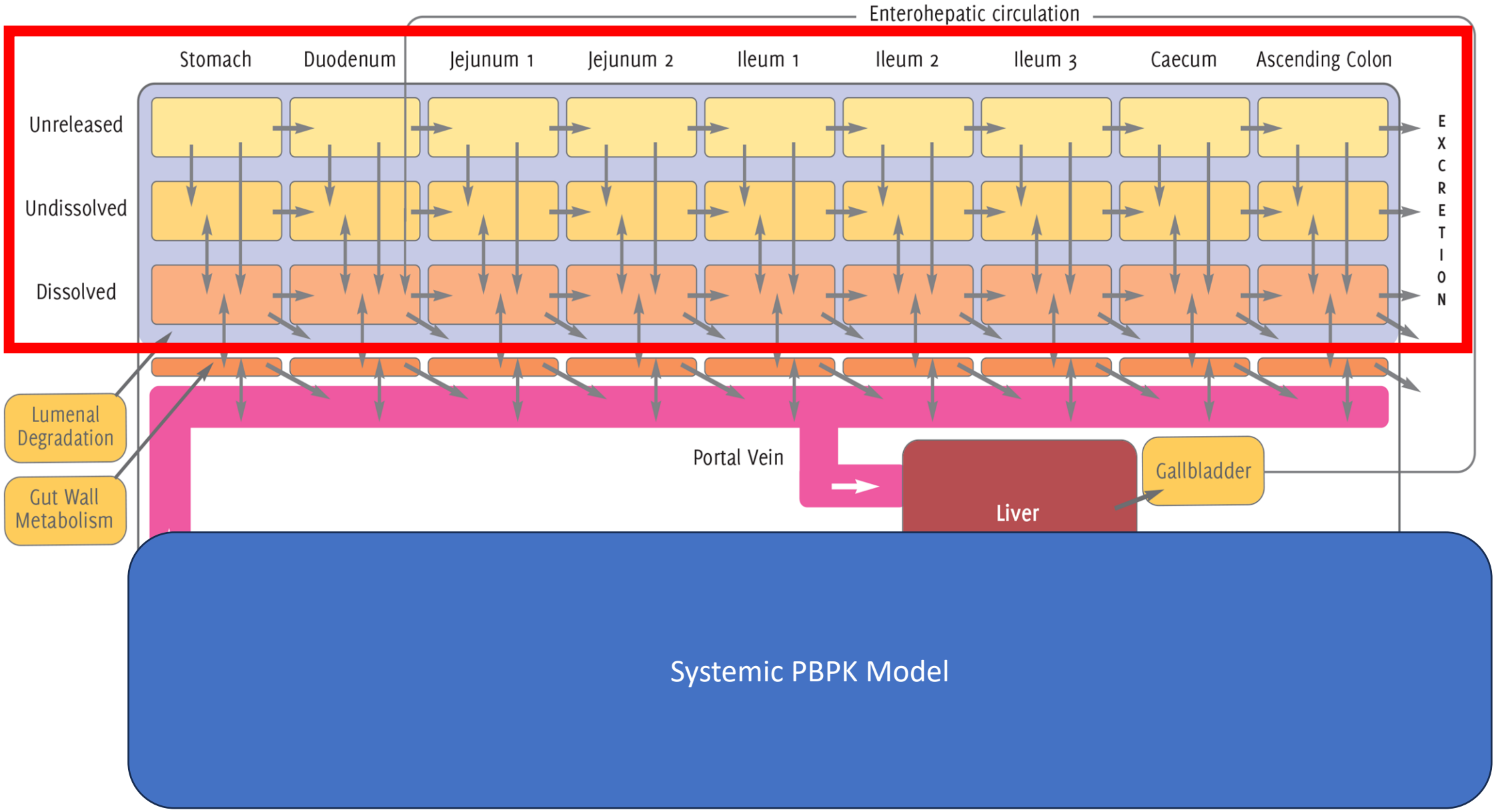
Loratadine

Fig. 1. Solubility Profile of Loratadine Tested in Physiologically Relevant pH Media of the Gastrointestinal Tract





Advanced Compartmental Absorption and Transit Model (ACAT™)



GastroPlus Activities

- Copy IV record to make PO record(s), set dosage form/route/amount
- Enter reference solubility, solubility factor
- Add/examine biorelevant solubilities
- Run simulation and examine Dissolution-Absorption-Time and Cp-time plots