

Osmotic Capsules for Preclinical Assessment of Extended Release Drug Delivery Feasibility

March 31, 2023

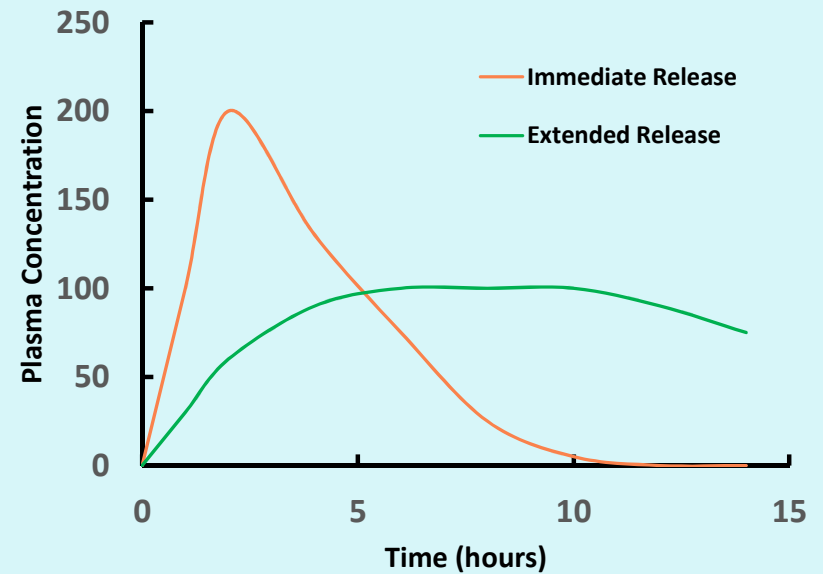
Jessica Kelly



Why Extended Release

Extended release delivery of drugs provides advantages over immediate release

- Reduced dosing frequency
 - May enable qd (once-daily) or bid (twice-daily) dosing over tid (three times daily) or qid (four times daily)
 - Can significantly improve patient compliance
- Decreased peak blood levels of drug
 - Reducing high peak blood levels (C_{max}) can decrease side effects and safety issues



Challenges with Extended Release

- GI regional absorption
 - Absorption can be limited past the duodenum (first part of small intestine)
- First-pass metabolism
 - Extending the drug release may lead to greater first-pass metabolism
- Efflux
 - Drug can be pumped back into the gastro-intestinal (GI) tract after absorption: greater tendency in lower GI tract
- Dosage form performance *in vivo*
 - pH varies
 - Water content varies
 - Shear forces change

Benefits of Osmotic Oral Extended Release

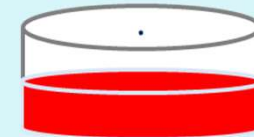
Common oral extended release technologies



matrix tablets



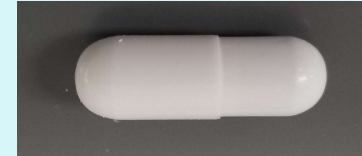
coated beads



osmotic tablets

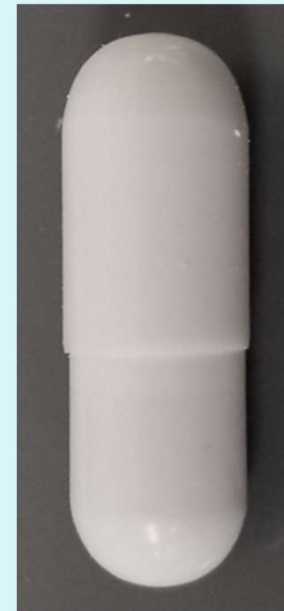
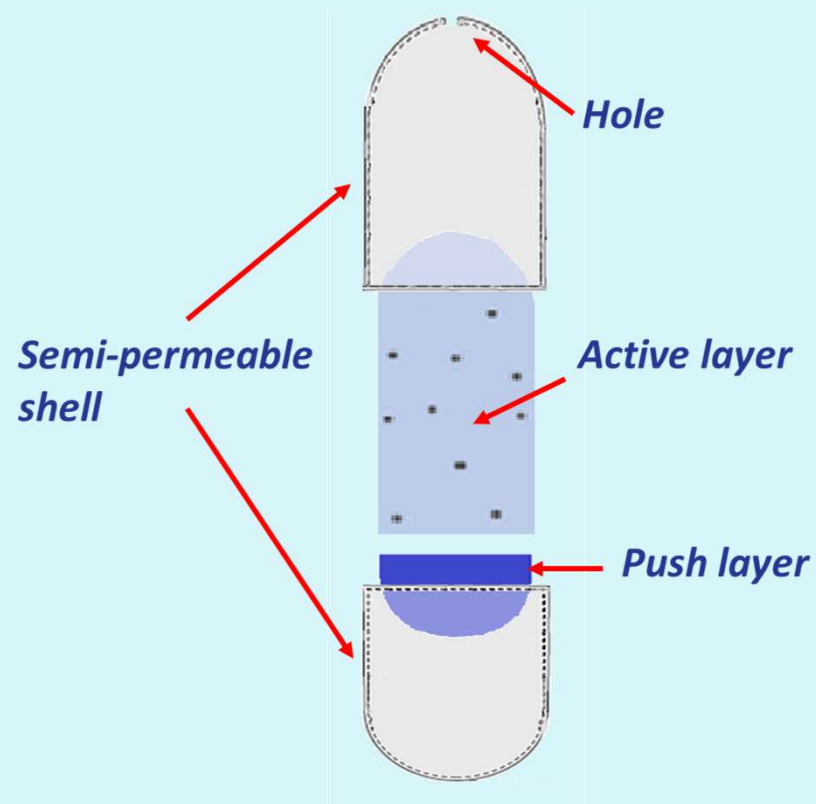
- Osmotic tablets
 - Advantages
 - Robust drug delivery independent of drug solubility/pH sensitivity
 - Best *in vitro*–*in vivo* correlation
 - Less affected by fed state
 - Disadvantages
 - Require specialized/expensive equipment (e.g., bilayer tablet press, solvent coater, laser drill, side recognition)
 - Longer development time due to complex manufacturing

What is OzmoCAP®



- Oral extended release (ER) osmotic capsule
 - A mechanism similar to osmotic tablets
 - Provides benefits of osmotic controlled release tablets without manufacturing/timeline disadvantages
 - Releases drug over an extended duration — not enteric (delayed) release
 - Offers range of drug release durations controlled by capsule
 - Release is independent of drug properties
 - Release is independent of pH
 - Release is independent of capsule position in GI tract
 - Supplies can be rapidly produced for feasibility/proof of concept studies in animals
 - Results from animal studies can be used to assess viability of extended release dosage forms

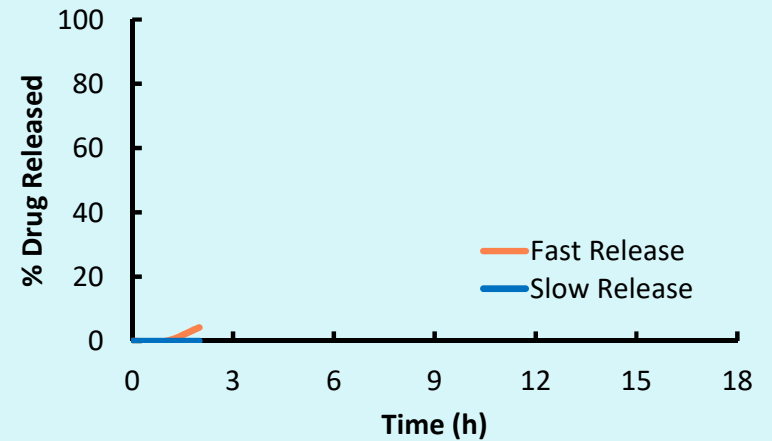
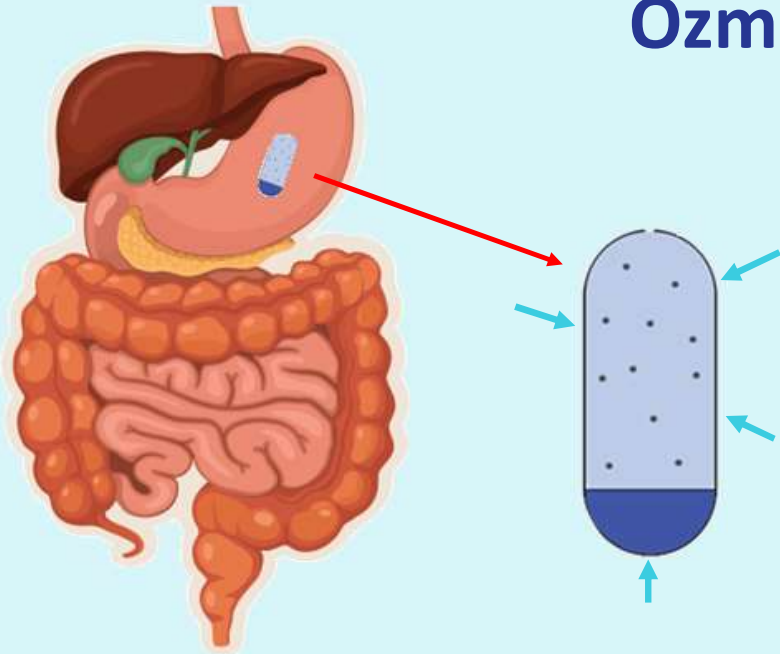
OzmoCAP[®] Assembly



OzmoCAP®: Formulating for Extended Release

- Solid API is processed with excipients by the OzmoCAP® team and compressed into an active layer
 - Dose range is 1–150 mg API
- Active and push layers are filled into capsule shells
- Capsule shell is sealed and ready to dose
- Capsule shells are prepared using a proprietary process
 - Size 00
 - Three different release profile options:
 - Fast: 80% API released in 6 hours
 - Medium: 80% API released in 10 hours
 - Slow: 80% API released in 14 hours

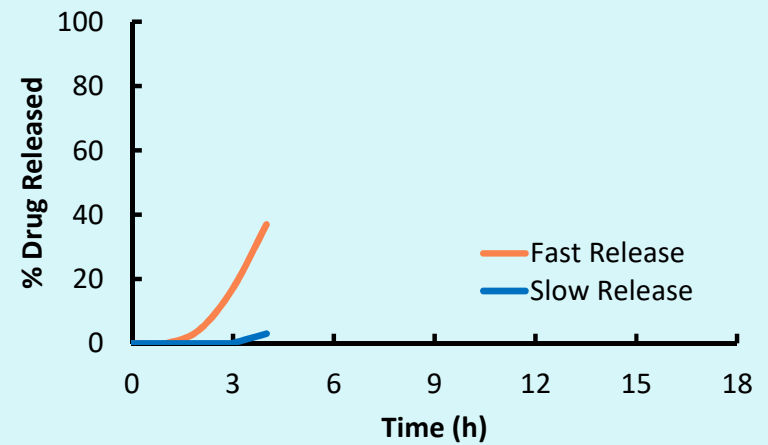
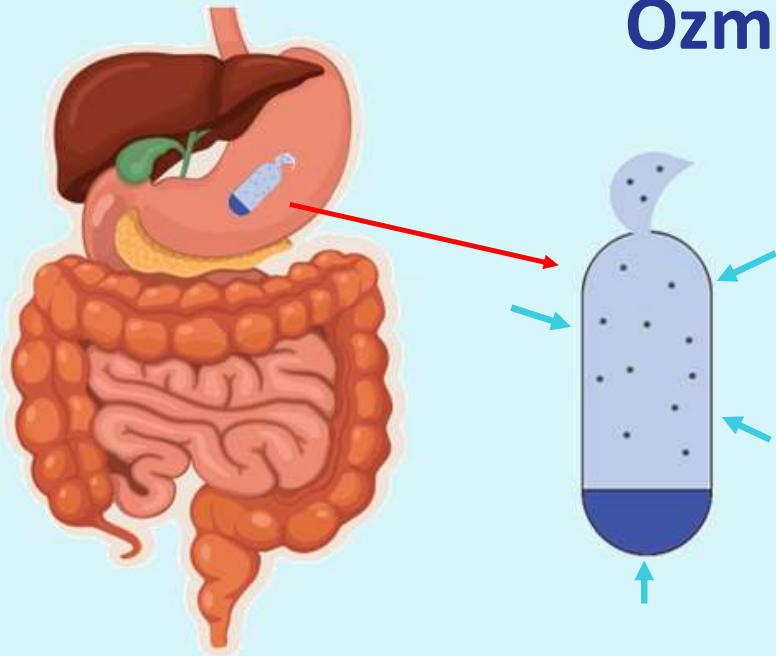
OzmoCAP[®] in Action



- Swallowed capsule enters stomach and water is osmotically drawn through semipermeable capsule shell

- Both fast and slow release OzmoCAP[®] capsules show lag before releasing drug

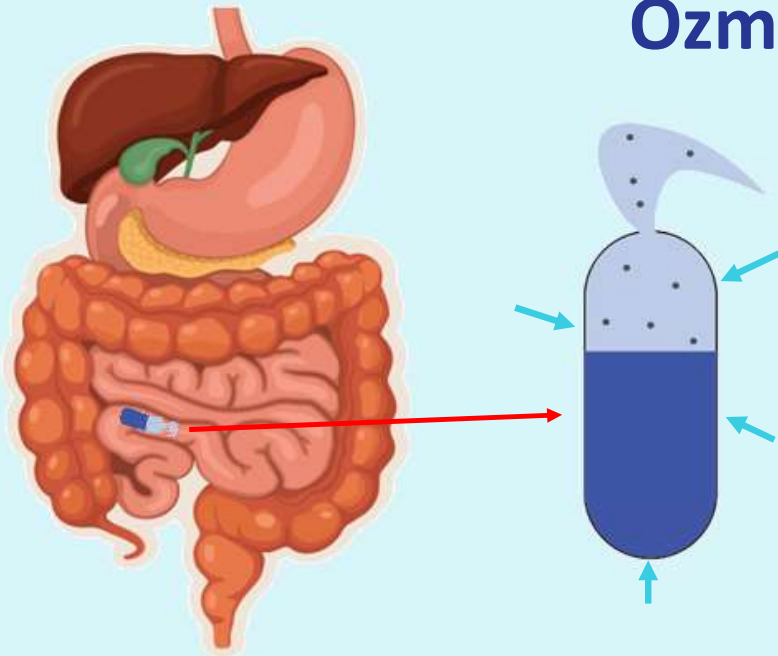
OzmoCAP® in Action



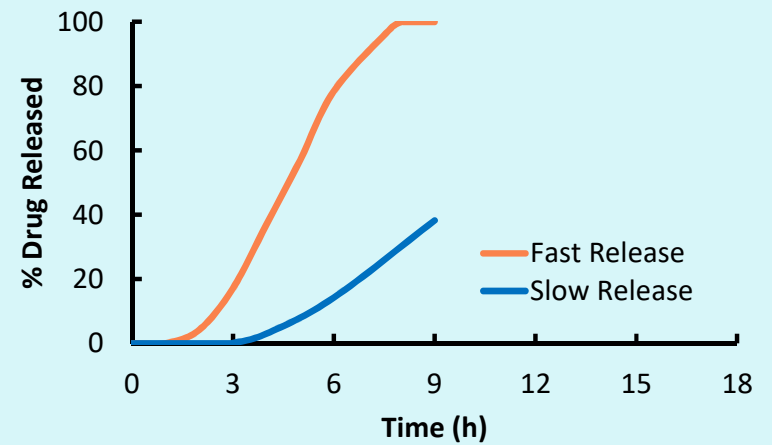
- Water ingress converts active layer into suspension
- Osmotic pressure pushes drug out capsule hole
- Duration in stomach:
 - 0–2 hours fasted
 - 1–12 hours fed

- Fast release OzmoCAP® capsules have a shorter lag than the slow release OzmoCAP® capsules

OzmoCAP[®] in Action

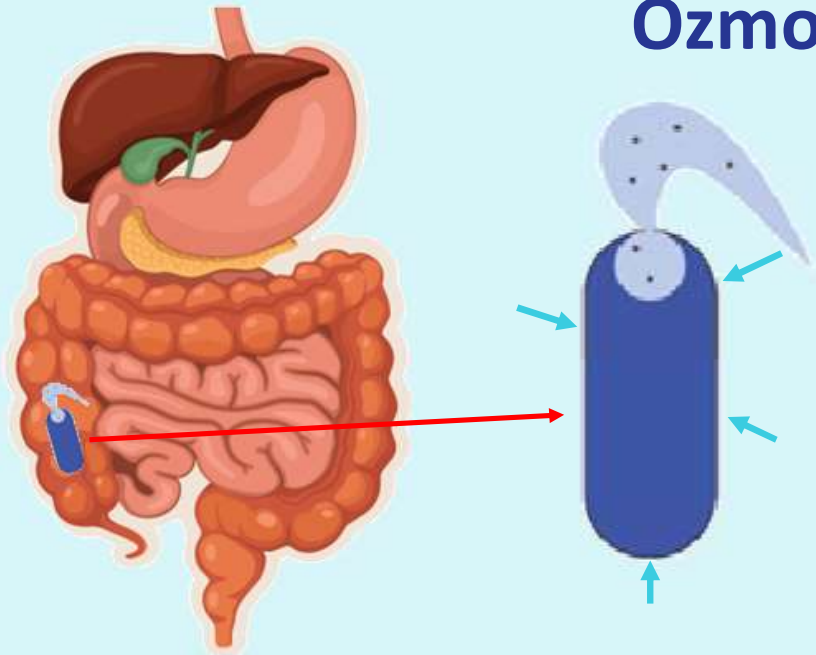


- In small intestine, drug continues to release in suspension form with assistance from push layer expansion
- Duration in small intestine:
 - ~4 hours

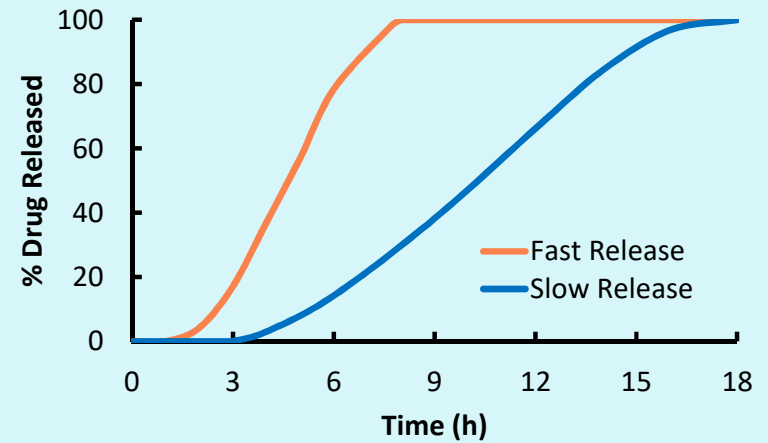


- After lag, drug release from capsule is linear and independent of drug properties

OzmoCAP® in Action



- In colon, drug continues to release in suspension form with assistance from push layer expansion
- Duration in ascending colon:
 - 1–20 hours



- Drug release from capsule continues even with little water present, but drug dissolution/absorption may be limited
- Useful data to determine viability of extended release dosage forms

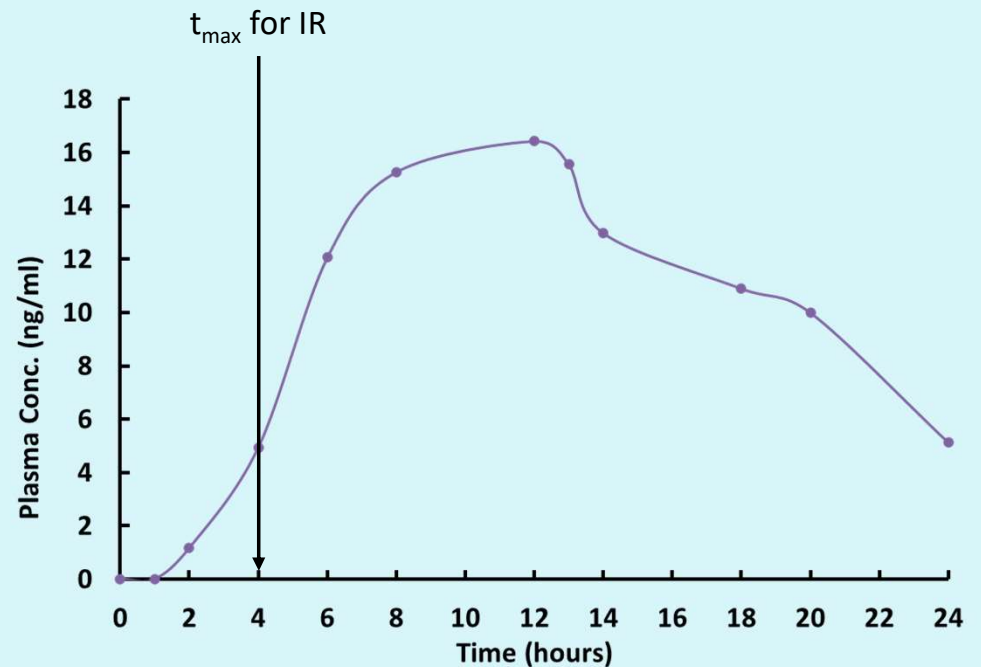
OzmoCAP® Case Study: Compound X*

- Compound X already an immediate release (IR) oral dosage form for twice-daily (bid) dosing
- Once-daily (qd) oral product desired
 - Reduced dosing frequency for patient compliance
 - Blunting C_{\max} to decrease side effects
- Important to understand drug absorption throughout the GI tract
- OzmoCAP® dosage form was developed and dosed into dogs to evaluate ER drug absorption *in vivo*

**Study in conjunction with Boehringer Ingelheim*

Compound X OzmoCAP[®] Dog Data

- Study conducted in fed dogs
- IR dosage form has 4-hour t_{\max}
- Fast release OzmoCAP[®] extended absorption and shifted t_{\max} to 10–12 hours
- Development of ER dosage form progressed with release durations based on upper GI absorption



Summary

- Extended release dosage forms can be beneficial for improving patient compliance
- Osmotic tablets provide reliable extended release drug delivery but can be time consuming and expensive to develop
- OzmoCAP® enables rapid development and dosing into animals for rapid assessment of extended release drug delivery viability
- Animal data can facilitate an extended release drug development strategy

Acknowledgements

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