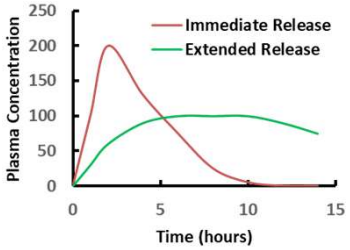
# Osmotic Capsules for Preclinical Assessment of Extended Release Drug Delivery Feasibility

Jennifer Chu, Sammy Bell & Kenneth C. Waterman

OzmoCAP®, a division of FreeThink Technologies, Inc.

## Introduction

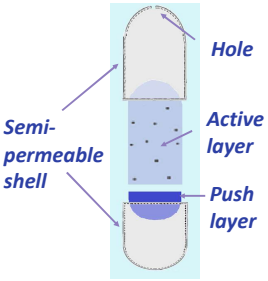
- Oral extended release (ER) delivery of drugs can provide multiple advantages over oral immediate release delivery.
  - Patient compliance: An effective ER dosage form can improve patient compliance by reducing how frequently patients are dosed
  - Safety: An effective ER dosage form can decrease peak blood levels ($C_{max}$) of drug, reducing the potential for adverse events
  - Drug efficacy: An effective ER dosage form can increase minimum blood levels ($C_{min}$), which may provide greater efficacy




- A drug's suitability and optimal ER profile depend on many factors.
  - Gastrointestinal (GI) regional absorption is affected by:
    - pH (ranges from <2 to >7.5 through the GI tract)
    - Water content (lowest in the large intestine)
    - Intestinal permeability (highest in the upper small intestine)
    - Shear forces (greatest in stomach)
    - First pass metabolism (can impact bioavailability when ER slows drug absorption)
    - Efflux (absorbed drug is pumped back into GI tract and excreted, which depends on interactions between drug and efflux transporter)
- Optimizing ER oral drug delivery rates *in vivo* is valuable

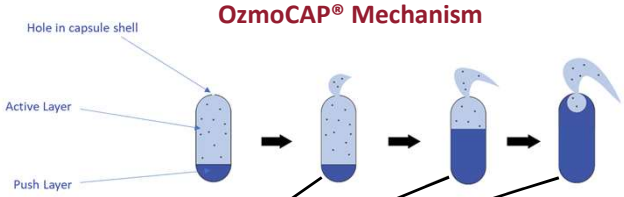
## Osmotic Drug Delivery

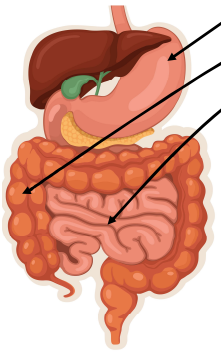
- Osmotic ER delivery is not enteric—release rate and release duration are independent of:
  - drug properties
  - environmental pH
  - dosage form position in GI tract
- Osmotic delivery has better *in vitro-in vivo* correlation (IVIVC) than other oral ER dosage forms such as matrix tablets and coated beads.
- While osmotic tablet preparation requires a complex manufacturing processes and long development timelines, OzmoCAP® can be developed and manufactured rapidly.




OzmoCAP® internal view

## OzmoCAP® Mechanism

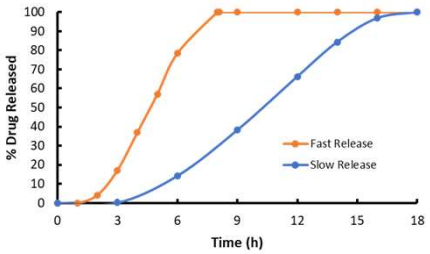


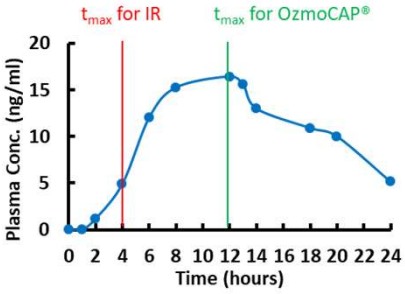
- When OzmoCAP® enters the GI tract, water is osmotically drawn in at a rate determined by the capsule shell permeability (the shell never dissolves).
- A combination of pressure buildup inside the capsule + expansion of the push layer delivers the drug as a viscous solution/suspension out of the hole in the capsule shell.

## OzmoCAP® Dissolution Profiles

- Various release durations possible:
  - **Fast**: 80% drug released ~6 h
  - **Medium**: 80% drug released ~10 h
  - **Slow**: 80% drug released ~14 h
- Drug release is independent of:
  - media pH
  - stir rate




## Case Study




- Compound X is already an oral immediate release tablet for twice-daily dosing.
- Once-daily product is desired to reduce dosing frequency and decrease $C_{max}$-related side effects.
- It is important to understand Compound X absorption throughout the GI tract to determine the feasibility of developing an oral ER dosage form.

- Fast + slow release OzmoCAP® developed and dosed into fed dogs
  - Immediate release dosage form has 4 h $t_{max}$
  - Fast release OzmoCAP® extended absorption + shifted $t_{max}$ to 10–12 h
  - Slow release OzmoCAP® shows very low blood levels (data not shown)
- Absorption in small but not large intestine led to progressing an ER dosage form with release duration corresponding to upper GI absorption.

## Conclusion

- Oral ER dosage forms can be beneficial drug product enhancements.
- Determining an optimum release profile is often a critical step in ER dosage form development yet can be convoluted by dosage form performance.
- OzmoCAP® enables rapid development and *in vivo* dosing for quick assessment of an optimal ER drug delivery profile.

## Acknowledgments

- The authors would like to acknowledge Boehringer Ingelheim for its support of this project.
- The authors would also like to acknowledge the following for their assistance with the development efforts:
  - Jessica Kelly
  - Lili Chen
  - Edward Harrington
  - Michael McDermott
  - Zachary Soffer

## Contact

jennifer.chu@freethinktech.com | david.lucey@freethinktech.com

OzmoCAP® 2023