Welcome

Oral Drug Delivery Workshop
Technology of Today and Tomorrow

Ali Rajabi-Siahboomi, Sandip Tiwari and Daniel Treffer

Monday, July 14, 2025

CRS 2025 ANNUAL MEETING & EXPOSITION
PHILADELPHIA, PA
JULY 13-18, 2025

NEXT-GENERATION DELIVERY INNOVATIONS

Many Thanks to Sponsors

Agenda (Morning Session)

Session 1: The basics of oral drug delivery – level setting

09:10 – 09:45	Andre Hermans, Merck	Understanding oral route for drug delivery
09:45 – 10:20	Ali Rajabi-Siahboomi, Colorcon	Designing oral drug delivery formulation

10:20 – 10:40 Networking Coffee Break

Session 2: Role of Excipients in Oral Drug Delivery

10:40 – 11:00	Rainer Dobrawa, BASF	Current trends in complex oral formulations & digital developments
11:00 – 11:20	Xiaoling Li, UP & Triastek	Excipients for MED 3D Printing: A Systemic Approach for Materials Selection
11:20 – 11:40	Vasu Sethuraman, Syntis	Using an in-situ synthetic polymer lining, to unlock the full therapeutic potential of the small intestine
11:40 – 12:00	Ahmed Elkhabaz, Merck	Implications of solution-phase phenomena and nanodroplet formation upon dissolution of amorphous dispersions

12:00 – 13:00 Lunch Break

Agenda (Afternoon Session)

Session 3: Latest Innovation for bench research

13:00 – 13:20	Christine Allen, Intrepid	Driving efficiency in oral dosage form development using AI and robotics
13:20 – 13:40	Anil Kane, ThermoFisher	Understanding commercial CMC in complex formulations
13:40 – 14:00	Vincent Jannin, Lonza	Peptides (Exenatide) in Lipid-Based Formulations for the gut
14:00 – 14:20	Randy Mrsny, Agor Therapeutics	Biological strategies to improve the oral absorption of protein and peptide
14:20 – 14:40	Arvind Bansal, NIPER	Effect of polymer type and drug loading on the mechanism of nano-species generation during dissolution of amorphous solid dispersions of aprepitant
14:40 – 15:00	Jim Mullin, Simulation Plus	When Mechanistic IVIVC Falls Short: The Case for IVIVR in Oral Drug Delivery

15:00 – 15:20 Afternoon break

Session 4: Novel Methods Empowering Oral Drug Delivery

15:20 – 15:40	Daniel Treffer, MeltPrep	Formulations developed with milligrams
15:40 – 16:00	Anette Mullertz, Bioneer	Using the Dynamic Gastrointestinal Model for predicting oral drug pharmaco kinetics
16:00 – 16:20	Grzegorz Garbacz, Physiolution	Predict the unpredictable - physiology driven testing of oral dosages
16:20 – 16:40	Vivik Gera, Lucine	AI / ML potentials in oral drug design and development
16:40 – 17:00	General Q&A and closing remarks	

Designing Oral Drug Delivery Formulations

Ali Rajabi-Siahboomi, Ph.D.

Chief Innovation Officer, Colorcon

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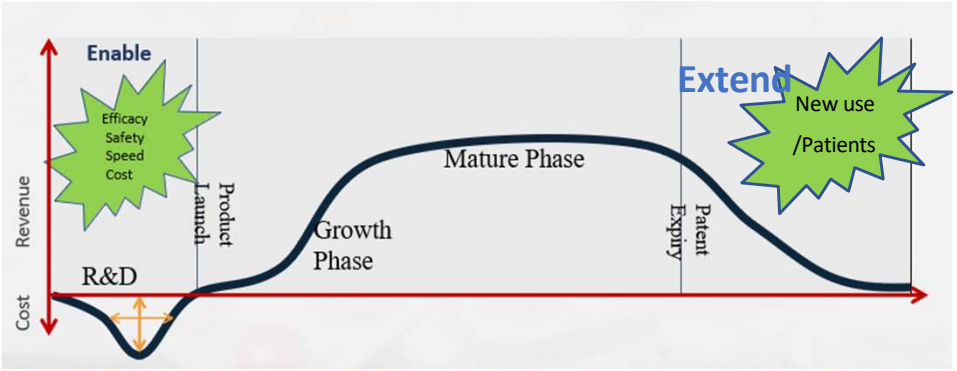
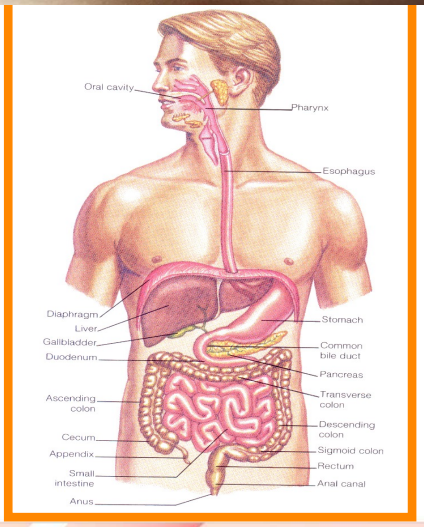
NEXT-GENERATION DELIVERY INNOVATIONS

General Considerations

- Get to know the oral route for drug delivery
- Accurate dosing, patient convenience
- Deal with API challenges and sensitivities (Solubility, compatibility, nitrosamine, sensitivity to light, moisture, heat, oxygen, …)
- Manufacturability – predictability at scale, productivity (cost), consistency (trouble free)
- Patient / consumer acceptability and trust - taste / odor, easy swallow, recognition (Age-appropriate dosages)





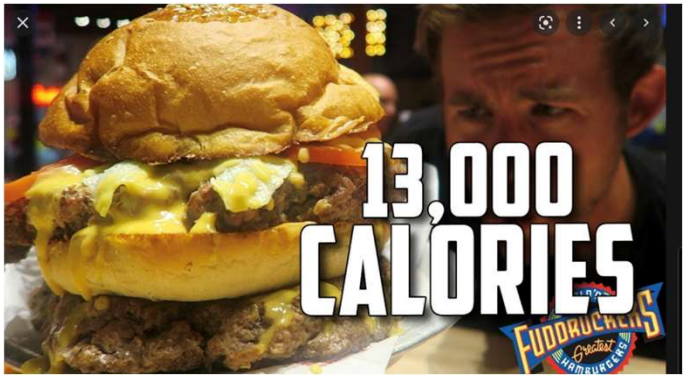
From Food to Poison to Medicine

Acknowledging - Prof Clive Wilson

- Foraging diet (cereals, nuts, berries and meat)
- Glycosides accidentally ingested

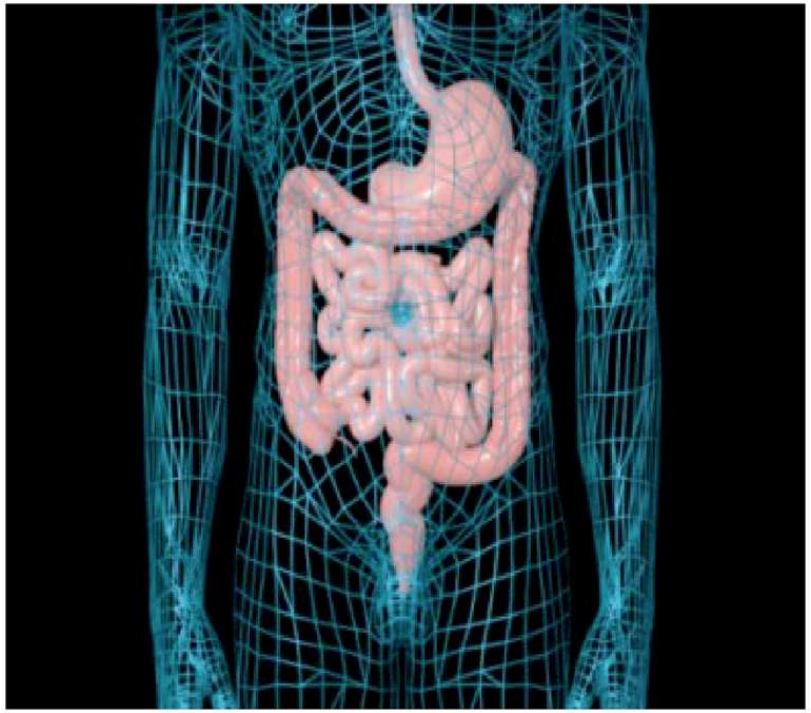
Our body recognizes poisons as a bad thing…
bitter taste, gut wall barrier, metabolism…

We have to make rational decisions to make & take medicines



For food – different game!

The Gastrointestinal Tract – Quick Reminders



A long muscular tube with epithelium lining and two reservoir areas

Preparation

⇩

Regulation, supply & process to slurry

⇩

Continue process to small molecules and absorb

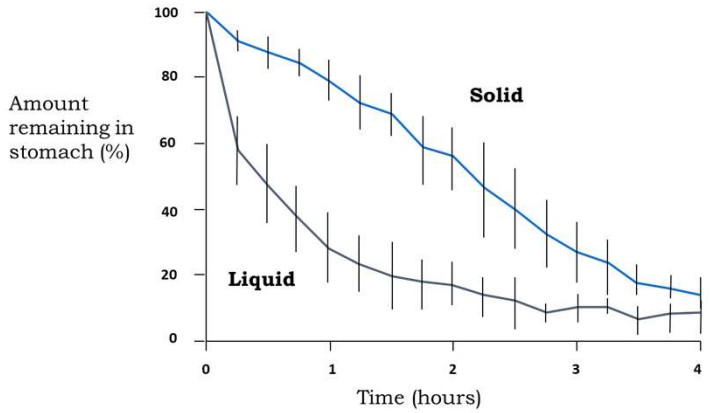
⇩

Reclaim water and store to be excreted

The Gastrointestinal Tract – Quick Reminders

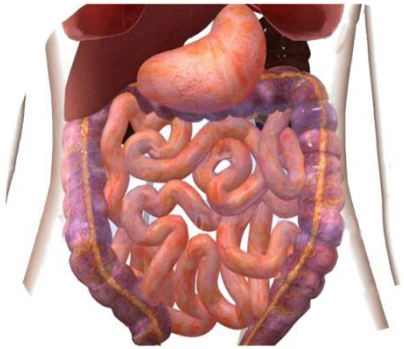
Gastric Emptying

- Phased process – restarting every time we eat
- Preparation, mixing through contractions
- House keeping waves for complete emptying
- Different meal components empty at different rates
- More food = longer fed phase
- Nutrition density (calories) controls / slows gastric emptying



Small Intestine

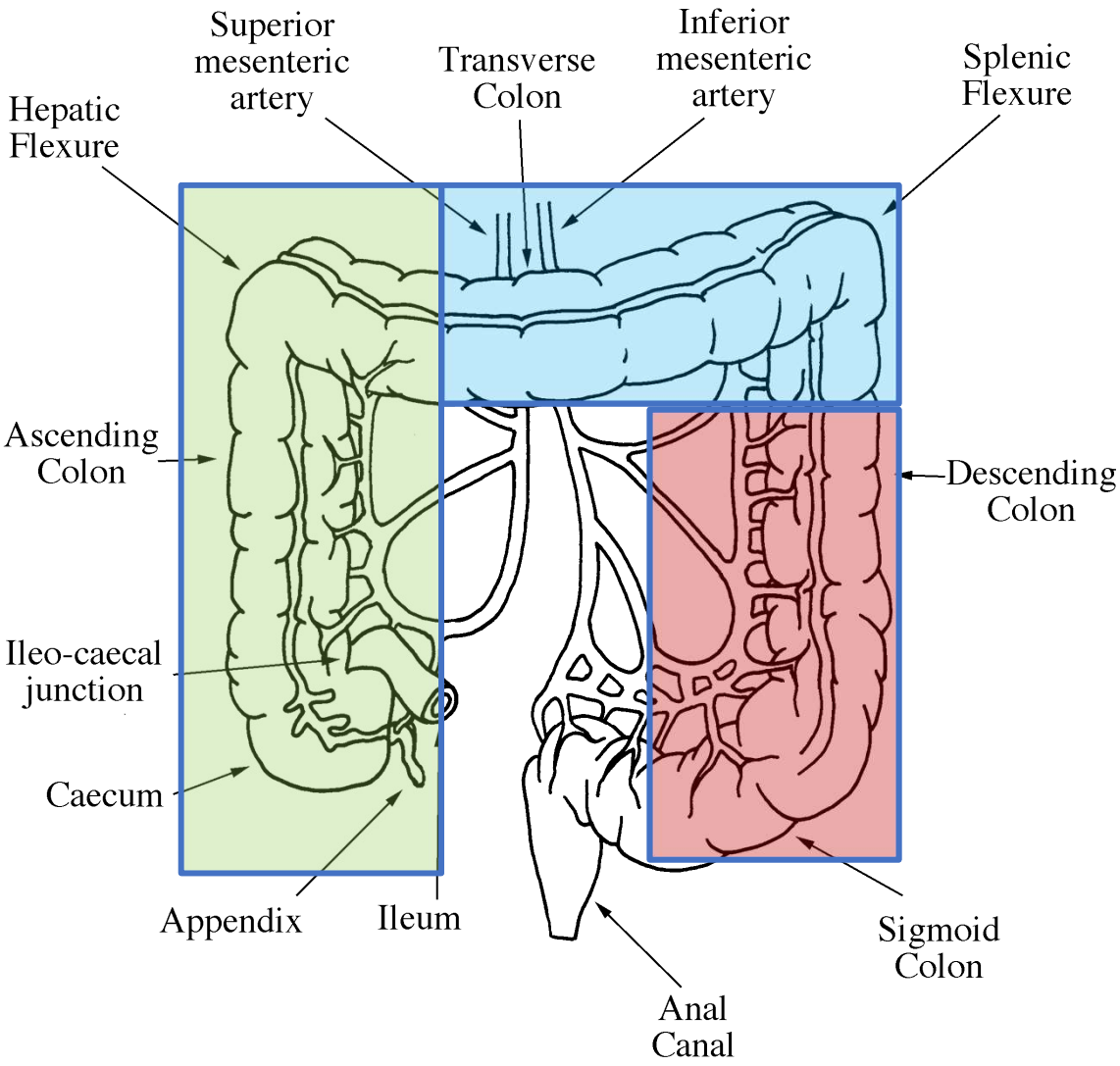
- Longest section of digestive tract, with highest absorption capacity
- Duodenum 20-30cm
- Jejunum 2.5m
- Ileum 3.5m
- No anatomical distinction, but differences in secretion and absorptive capacity



Colon

- 3 Distinct regions
- Long transit time
- Limited availability of water

  (only in ascending colon)
- Fermentation and gas in transverse colon
- Microbiome



Designing Oral Delivery: Release Profiles

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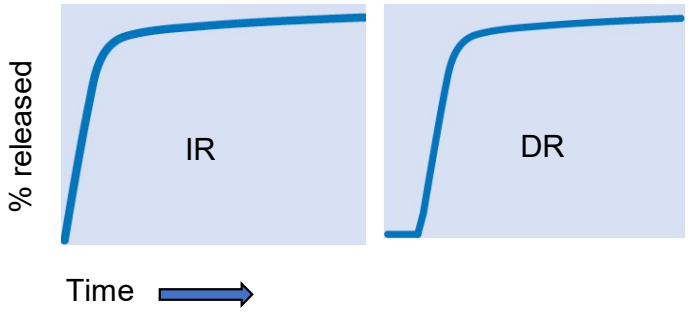
NEXT-GENERATION DELIVERY INNOVATIONS

Release Profile Terminologies

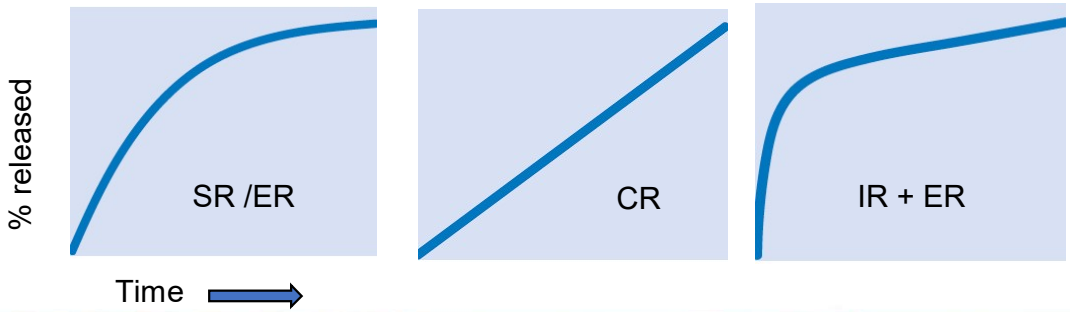
Immediate release
Swallow whole – drug release in the stomach
Fast release – drug release in oral cavity (mouth - taste masking)



Modified release

Delayed release
Taste masking – don't release the drug in the mouth (one approach)
Enteric coated – don't release the drug in the stomach
Colonic release - release drug in the colon (for local or systemic delivery)

Extended release
Slow / sustained release
Controlled release
Complex release, chrono-, pulsatile …



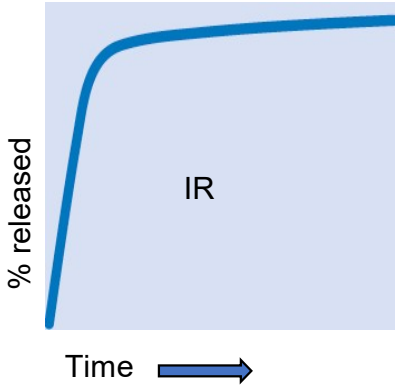
Immediate Release Oral Dosage Forms

Typical formulation considerations:

- API
  Solubility enhancement - solubility / wetting agents / stabilizers

- Excipients: bulk, functionality & or process improvers (filler, binder, glidant, disintegrant …)
  Although physiologically inert, have significant effect on drug product

- Other considerations
  Patient centricity – trade dress & functionality (color / coatings)
  Early capsules to tablets for commercial



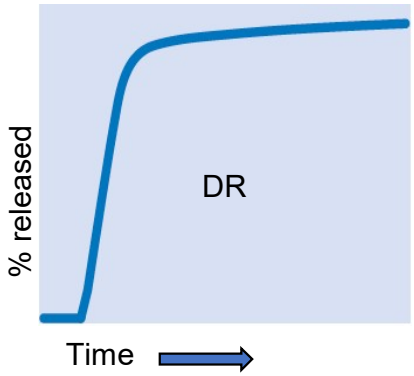
- ➢ Ideal for acute treatment (pain, nausea, antibiotics …), may require multiple doses daily
- ➢ All the dose is delivered in oral cavity or stomach (quick onset, high Cmax: side effects)
- ➢ Typical fillers: microcrystalline cellulose, lactose, starches, mannitol, dicalcium phosphate

Profile modulation & performance: filler type, binder type & level, disintegrant & coating

Delayed Release Oral Dosage Forms

Typical formulation considerations:

- Delay the release of drug (compared to immediate release) to:
- Avoid release in the mouth (taste masking)
- Avoid release in stomach – protect drug (PPIs) or stomach (NSAIDS) / or taste / smell (fish oil)
- Delay till arrival in the colon – mainly for local treatment



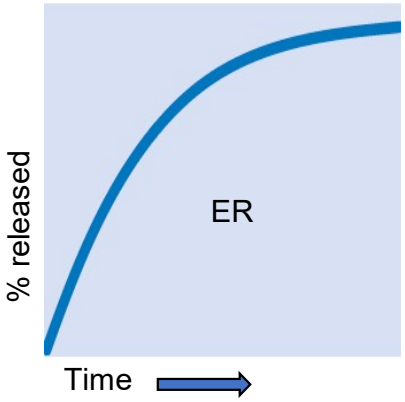
- ➢ Majority of technologies rely on coating of dosage form
- ➢ Biopharmaceutics consideration – release reliably at intended place or time
- ➢ Typical polymers: Methacrylates, Phthalates (PVAP, HPMCP, CAP), Acetyl-succinate (HPMCAS)

Release profile modulation & performance: core properties & enteric coating; polymer type & level (mg/cm^2), seal-coat, process conditions -- BE very challenging

Extended-Release Oral Dosage Forms

Typical formulation considerations:

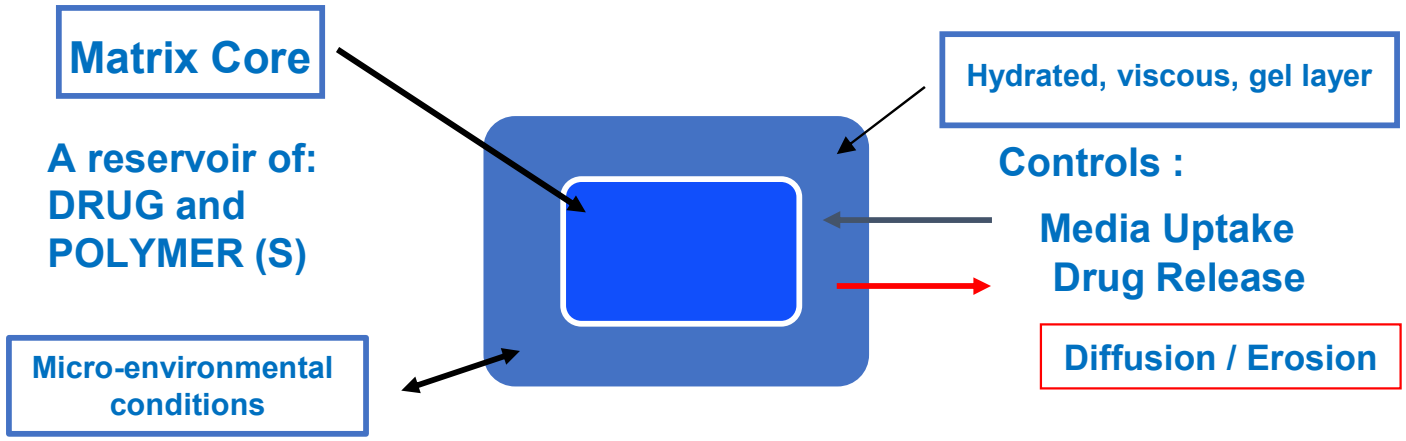
- Slow drug release over a period of time (for once or twice daily dosing)
- Most common technologies:
  - Matrices - hydrophilic polymers (cellulose ethers), lipids and insoluble polymers
  - Barrier membrane coating – ethylcellulose, methacrylates, cellulose & vinyl acetates
  - Push-pull osmotic pumps – polyethylene oxide, cellulose acetate



- ➢ Define target time for release – consider GI transit, absorption, first pass metabolism & elimination half-life
- ➢ Critical to ensure robustness of release – reduce / avoid dose dumping
- ➢ Formulation, process, physiology factors & food effect

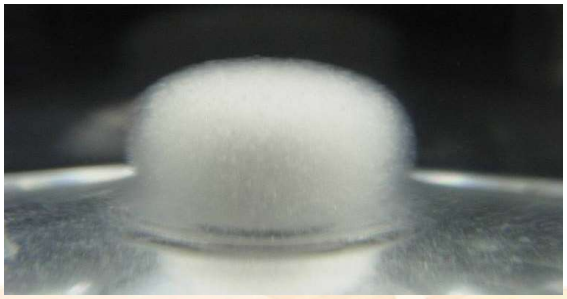
Release profile modulation & performance: Choice of technology, polymer (type & level), other ingredients, process conditions, appropriate specification setting

Hydrophilic Matrix ER



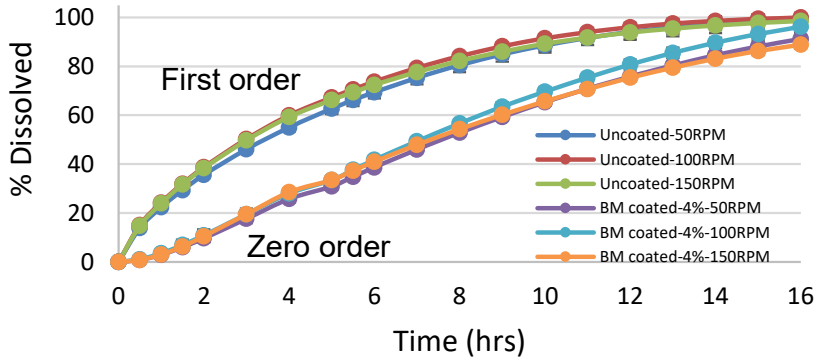
FDC
Biphasic Release

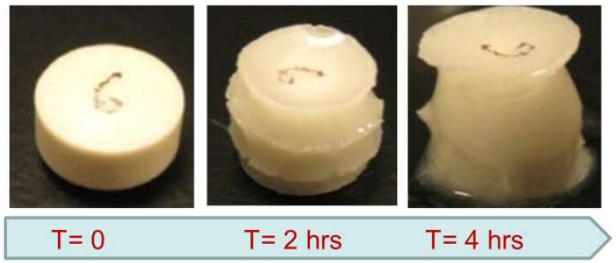
Metformin + …



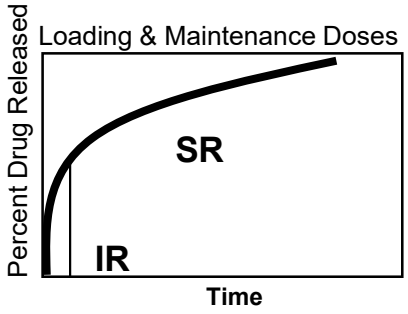
High viscosity Hydrophilic polymers

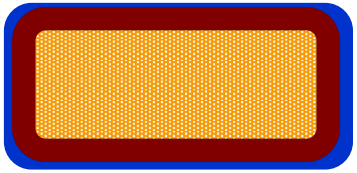
Example of ER Matrix System

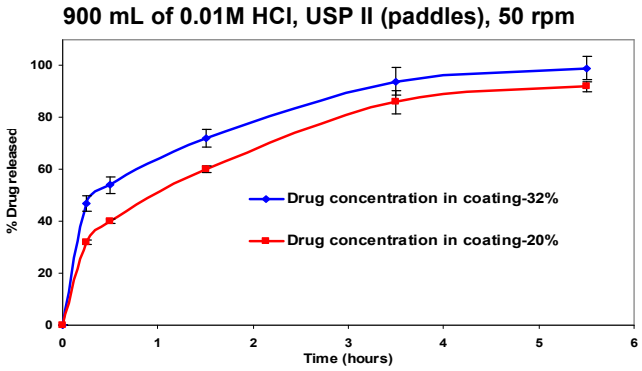




First order kinetics: for long plasma half-life, wide therapeutic index, and many indications
Zero order kinetics: Short plasma half-life, narrow therapeutic index or managing side effects

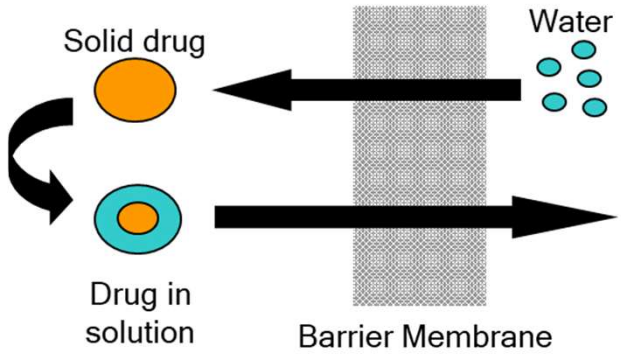






Multiparticulate Dosage Forms

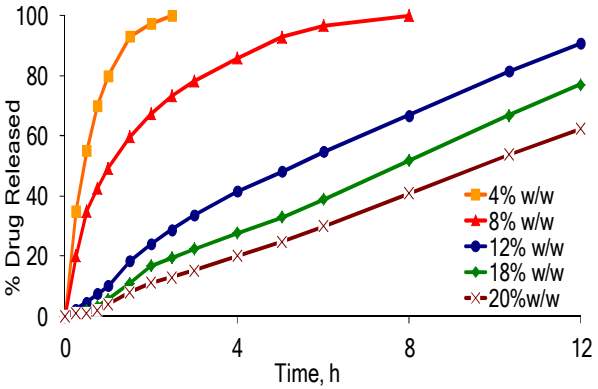
MP & Microencapsulation –
For taste masking & release modulation: DR, ER, Complex

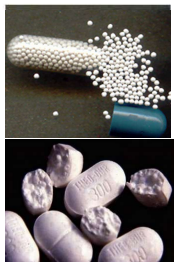


Fick's 1st law of diffusion:

$$J = \frac{dM}{dt} = \frac{DSK(C_d - C_r)}{h}$$

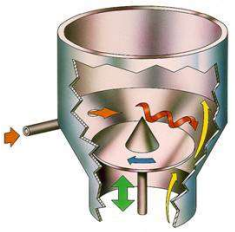
S = surface area (cm^2) C = concentration
D = diffusion coefficient K = partition coefficient
h = thickness of barrier J = Flux



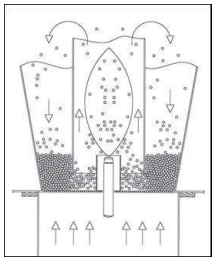


Processing:

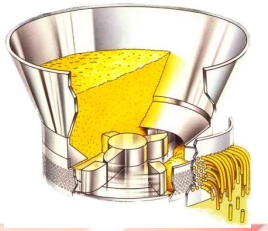
- **Powder layering**



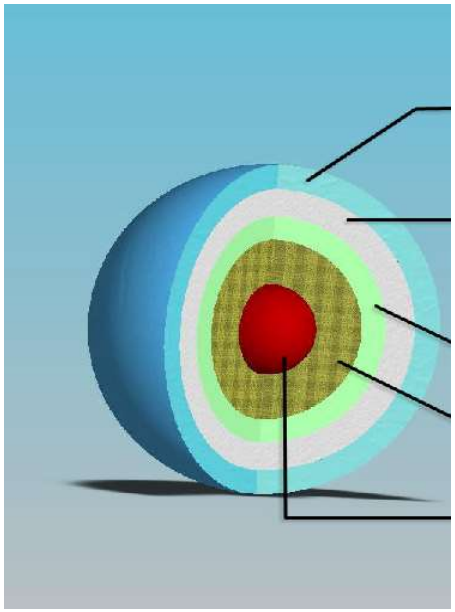
- **Solution/suspension layering**



- **Extrusion-spheronization**



A typical MP formulation may consist of multiple layers



Type – Inert core
Particle size
Size distribution
Sphericity
Friability
Roughness

Drug separation
Surface smoothness
Drug migration
Strength of drug layer

Process Parameters:
Spray rate,
Air flow,
Atomization,
Product temperature

Static charge
Wetting agent
Curing conditions

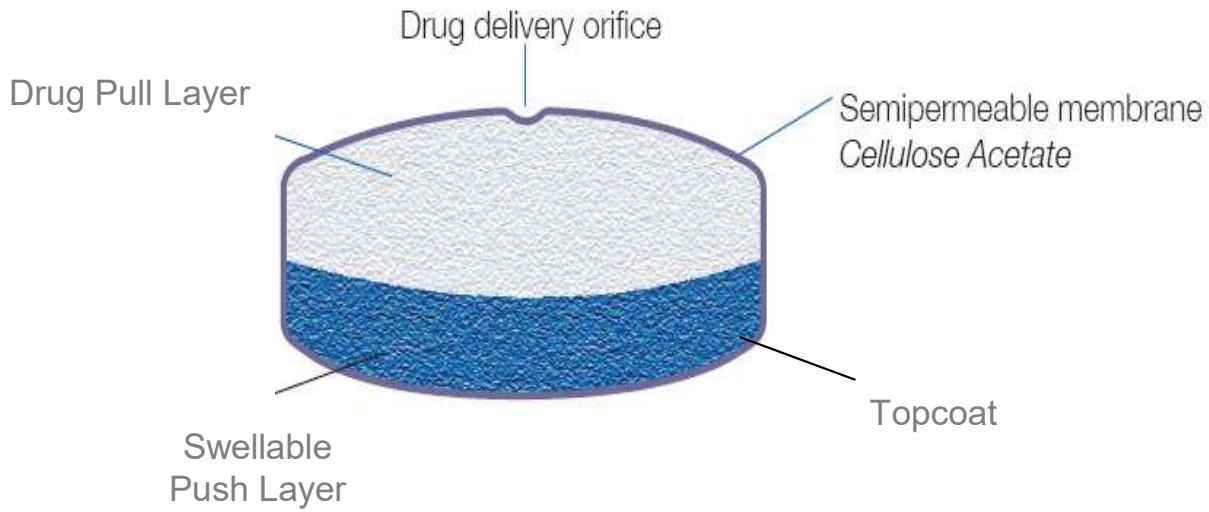
Beads - starter seeds → Drug layer → Seal-coat → Functional Coatings → Top-coat

Drug solubility
Binder selection
API form
API particle size

Polymer, DR or ER
Weight gain,
Permeability,
Aqueous vs organic
Batch to batch variability

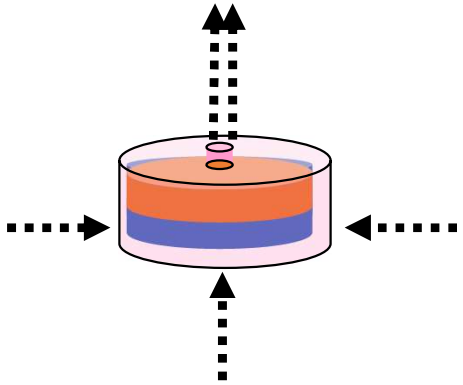
Osmotic Technology

for Zero-Order Release



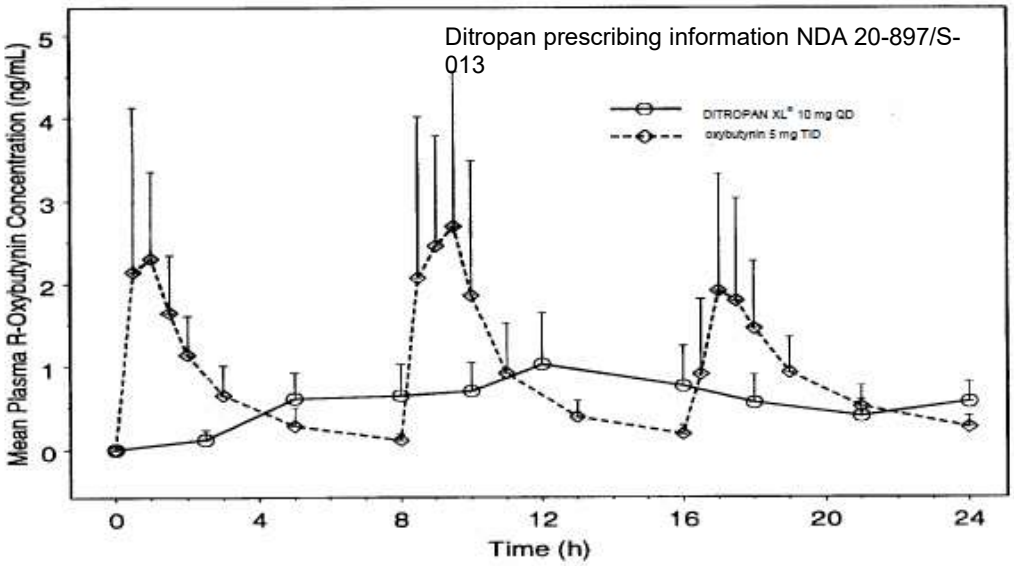
Release rate = (Water flux)(Mass fraction of drug)

$$\frac{dM}{dt} = \frac{dV}{dt} x_d$$

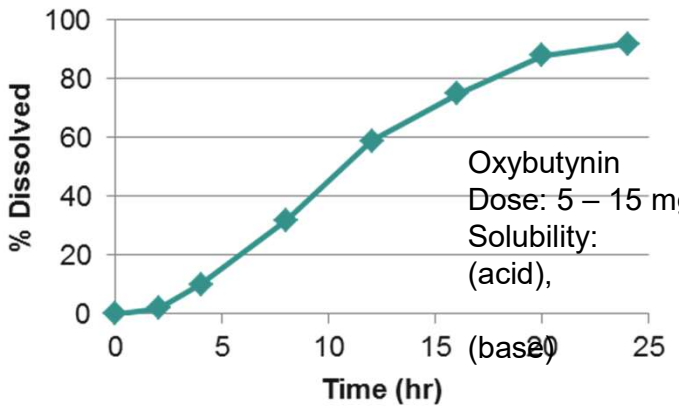


Ditropan XL Pharmacokinetic Profile

Pharmacokinetic Profiles



***In-Vitro* Release Profiles**

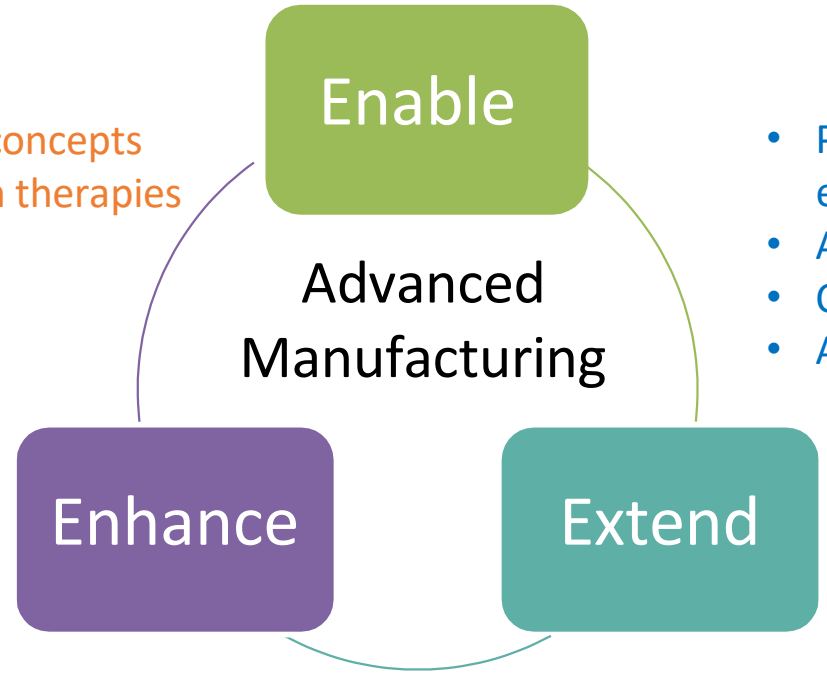


Oxybutynin
Dose: 5 – 15 mg
Solubility: 70 mg/ml (acid),
1 mg/ml (base)

- Two to three times daily dosing to once daily dosing
- 3-fold reduction in peak to through ratio
- Low variation in pharmacokinetic performance

Value of Excipients in Oral Drug Delivery

- Improve API developability
- Reduce Med Chem “Redos”
- Faster PoC for new therapeutic concepts
- Advancement of next generation therapies

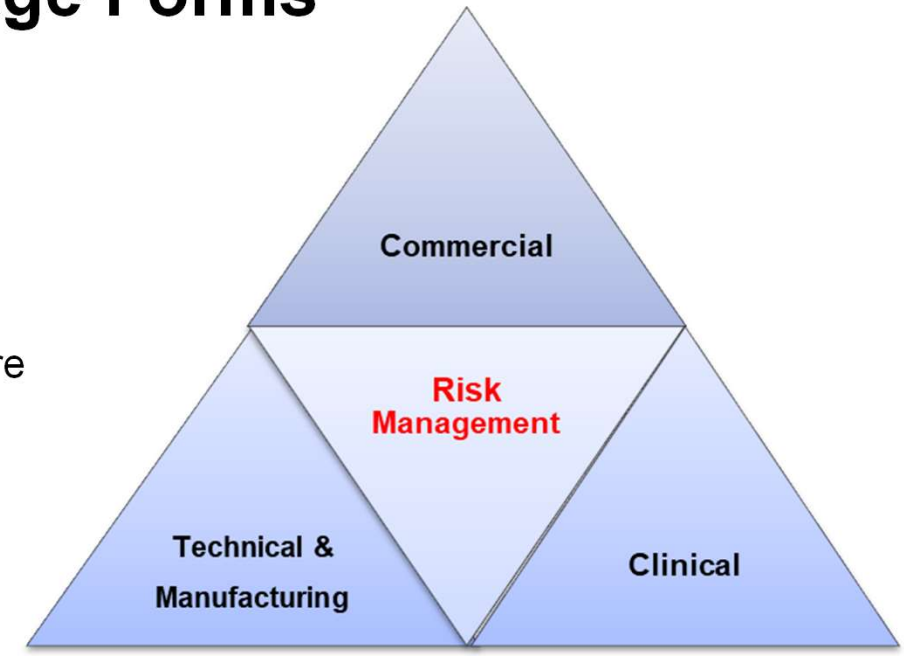


- Patient-centric formulations e.g. pediatrics
- Alternate ways of delivery
- Combination therapies
- Anti-abuse formulations

- Eliminate/reduce food effect
- Reduce dosing frequency
- Improved shelf/use life
- Better tolerability

Designing Oral Solid Dosage Forms

- Keep patients in mind - Safety by Design
- Apply ‘KISS’ - Keep it stupid simple
- Most marketed products used technologies described here
- Having experience (or access to experience) accelerates development and avoids potential future challenges during manufacturing or when in market



QbD: CQAs = f (CPP_1, CPP_2, CPP_3...CMA_1, CMA_2, CMA_3)

Balance between development, manufacture, profitability & patient safety