

Sugar Spheres: “Improving clinical effectiveness with multiparticulate drug delivery systems”

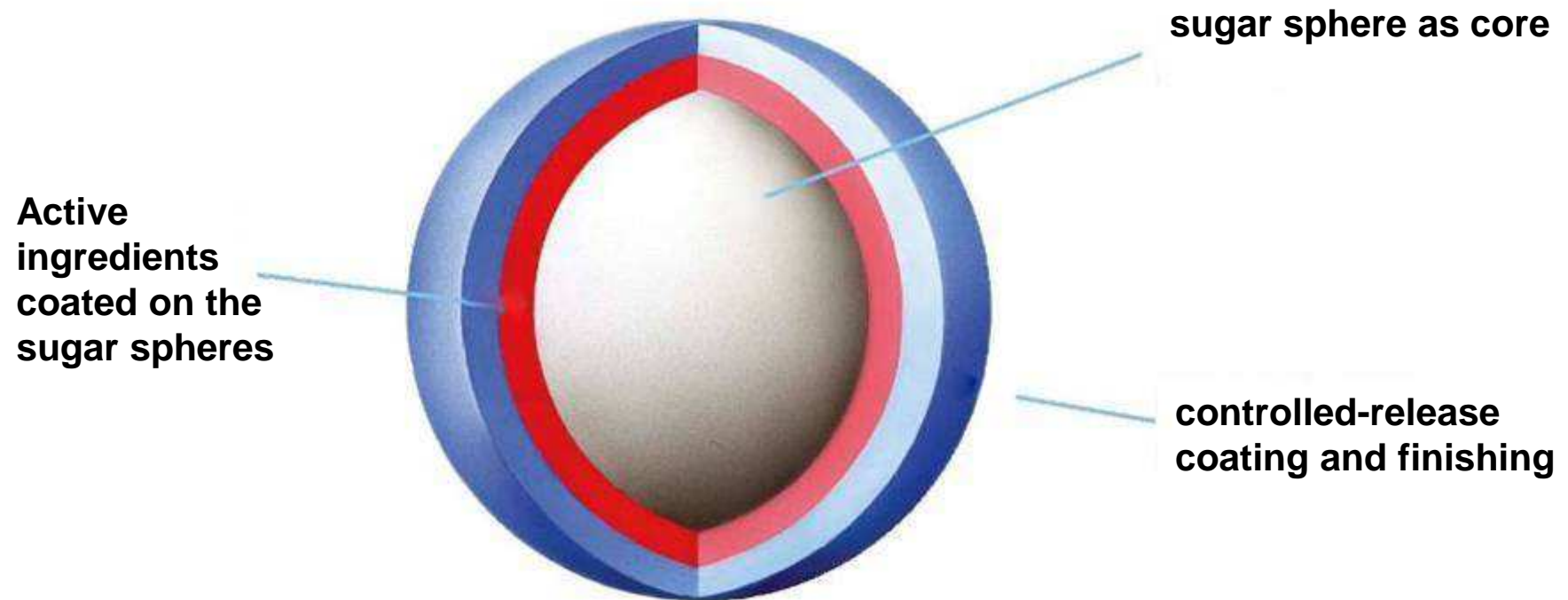
Philipp Werner

A thick, grey, wavy line arches across the bottom of the slide, mirroring the one at the top.



pharm-a-spheres[®]

Introduction



Pharmaceutical product portfolio

Standard and
custom sized
sugar spheres
(EP and USP/ NF)

Micropellets

Globuli sacchari

xylitol and
lactose globuli

nutritional
supplements

Introduction

What are **multiparticulate** oral dosage forms?

Types of **pellets**

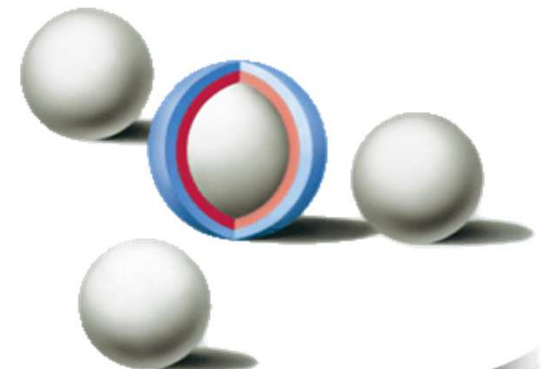
Sugar spheres and their benefits

Multiparticulates improve **clinical effectiveness**?

Technological benefits of multiparticulates

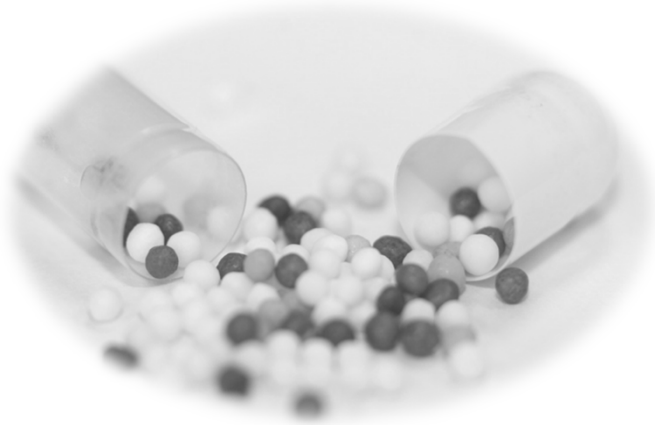
Focus: **Modified release** formulations

Mechanisms of **coating**



Multiparticulate drug delivery systems

*Multiparticulate drug delivery systems are mainly **oral dosage forms** consisting of a **multiplicity** of small **discrete** units, each exhibiting some desired **characteristics**.*



Pellets



Microtablets

Which types of pellets are there?

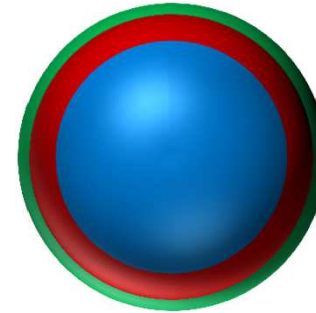
Matrix Pellets

- By extrusion, granulation or spheronisation.



Coated starter core

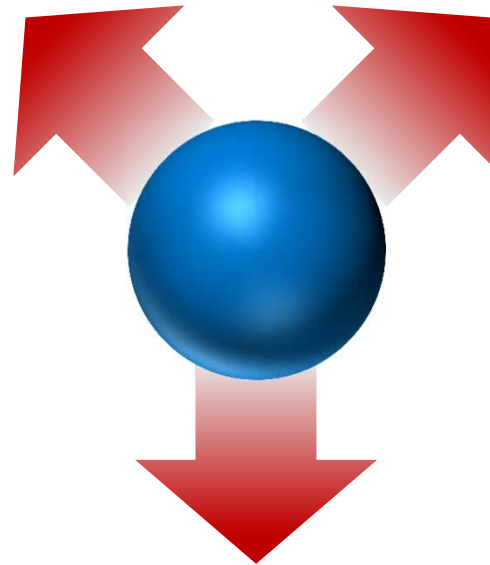
- By coating of an already existing starter core



*Both kind of pellets will normally be **finished** by at least one coating*

High patient compatibility

- *Easy digestible*
- *No side effects*
- *No Microbial contamination*



Technologically suitable

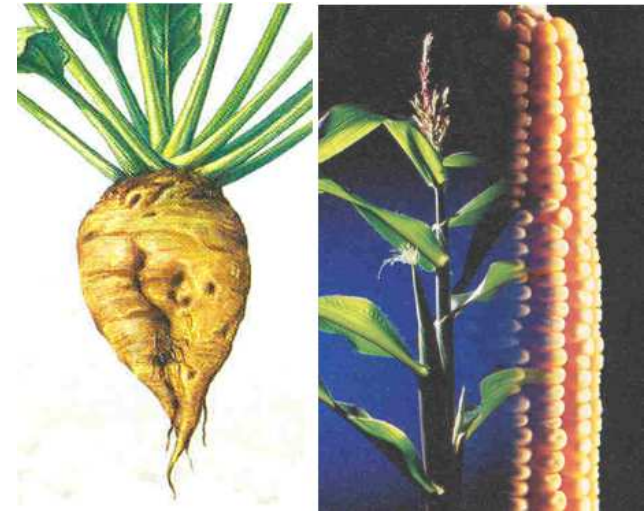
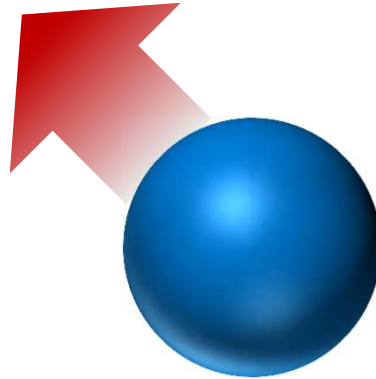
- *Good coating properties*
- *High yield (low friability)*
- *Uniformity of particle size*
- *Easy to use*

In compliance!

- *In respect to EP & USP*

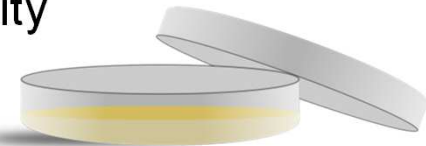
High patient compatibility

- *Easy digestible*
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- *No Microbial contamination*



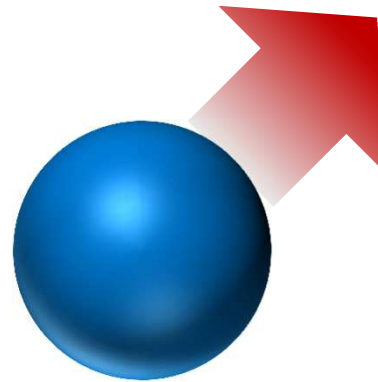
- Only sugar & corn starch
- All natural
- Digestible
- Biodegradable

- Outstanding microbial Quality



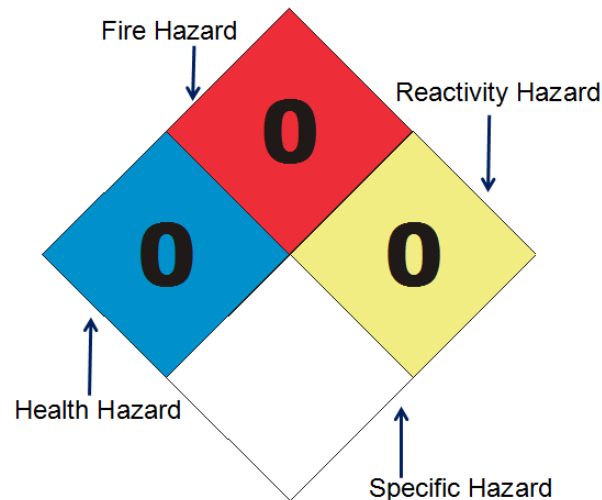
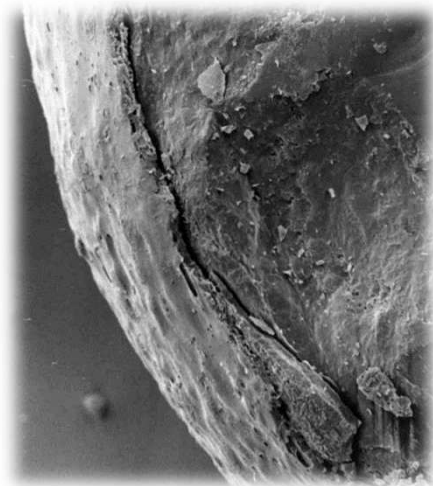
Starter cores - sugar spheres

- High degree of sphericity
- Smooth surface
- Chemically indifferent excipients
- No incompatibilites
- High mechanical stability
- No attrition
- Low friability



Technologically suitable

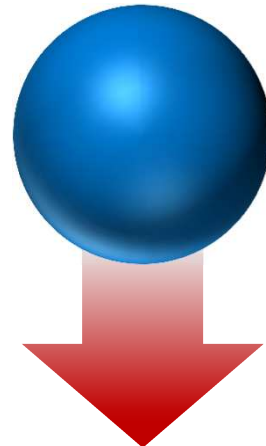
- Good coating properties
- High yield (low friability)
- Uniformity of particle size
- Easy to use



Starter cores - sugar spheres



➤ USP/NF: „sugar spheres“



➤ EP: 1570 „sugar spheres“

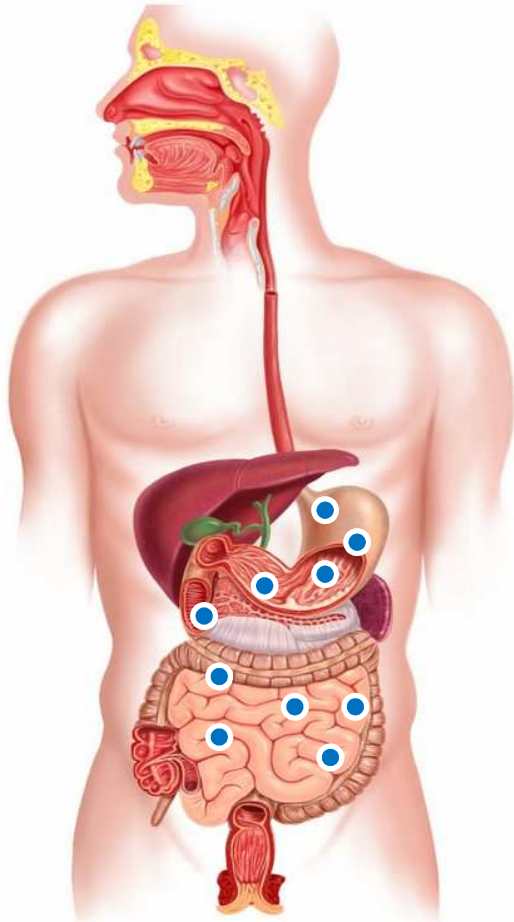
Worldwide acceptance!

In compliance!

➤ *In respect to EP & USP*

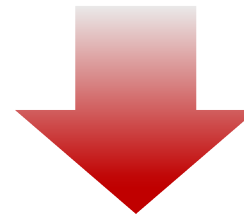
Easy application registration!

Improving clinical effectiveness

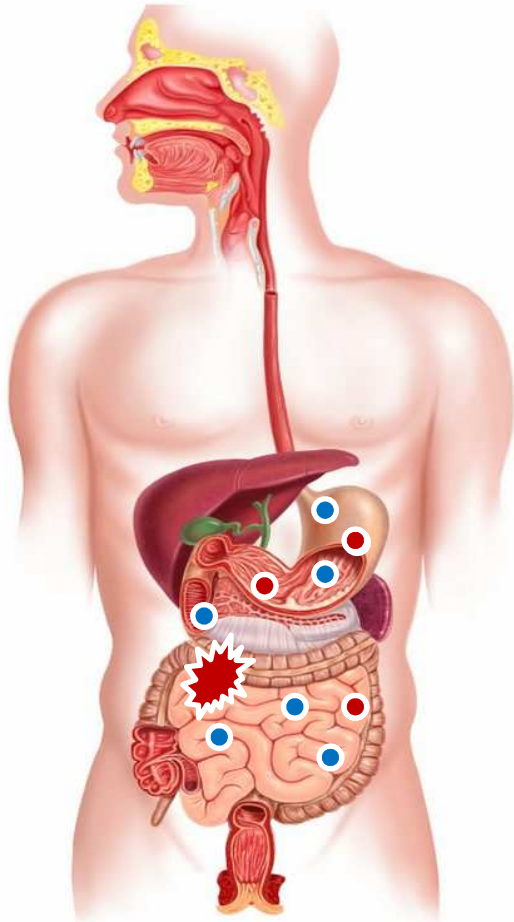


Why use multiparticulate drug delivery systems?

- **Subsequently** drawn from the stomach
- The **effect of food** on gastrointestinal tract is minimized

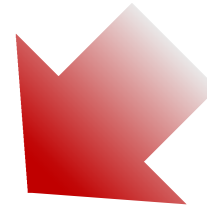


Greater and more **reproducible** dispersion throughout the gastrointestinal tract can be achieved.



Why use multiparticulate drug delivery systems?

Greater and more reproducible dispersion throughout the gastrointestinal tract can be achieved.

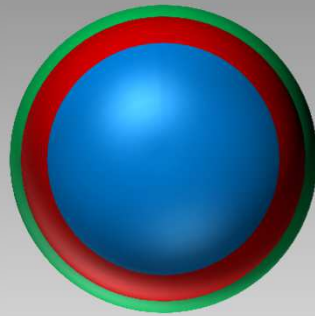


The risk of local toxicity decreases



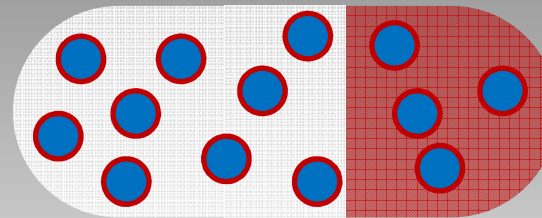
The risk of dose dumping is strongly decreased due to mutual redundancy of a single unit

Easy coating at a constant thickness



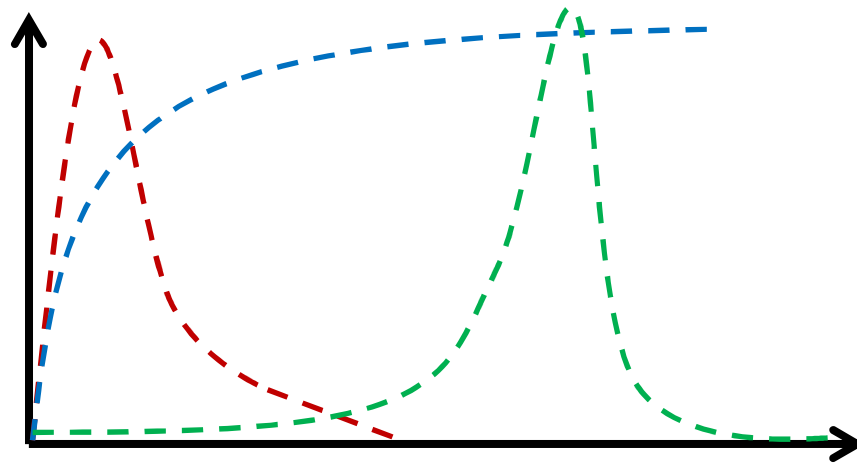
- Highly controllable
- Low stress on API (coating)

Stable mixtures - Easy assembly



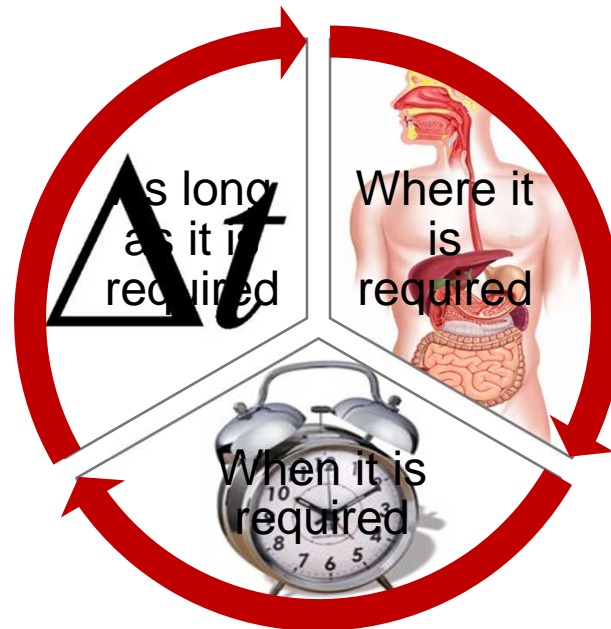
- Easy dose adjusting
- Simultaneous release of incompatible APIs

„The single most important factor responsible for the proliferation of pelletized products is the popularity of controlled release technology in the delivery of drugs“

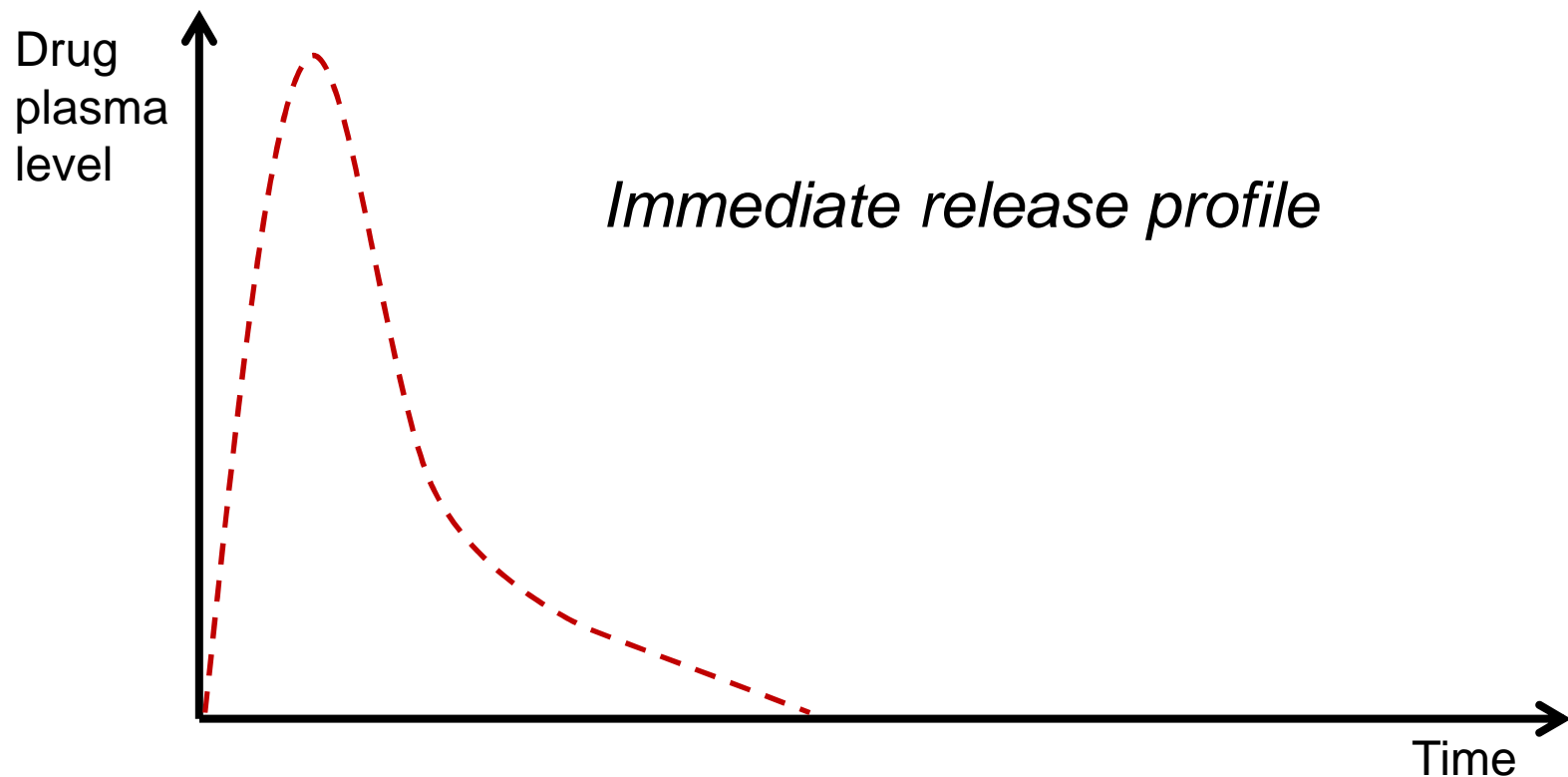


- Potentially any release profile
- Potentially several APIs
- Several ways of achieving modified release

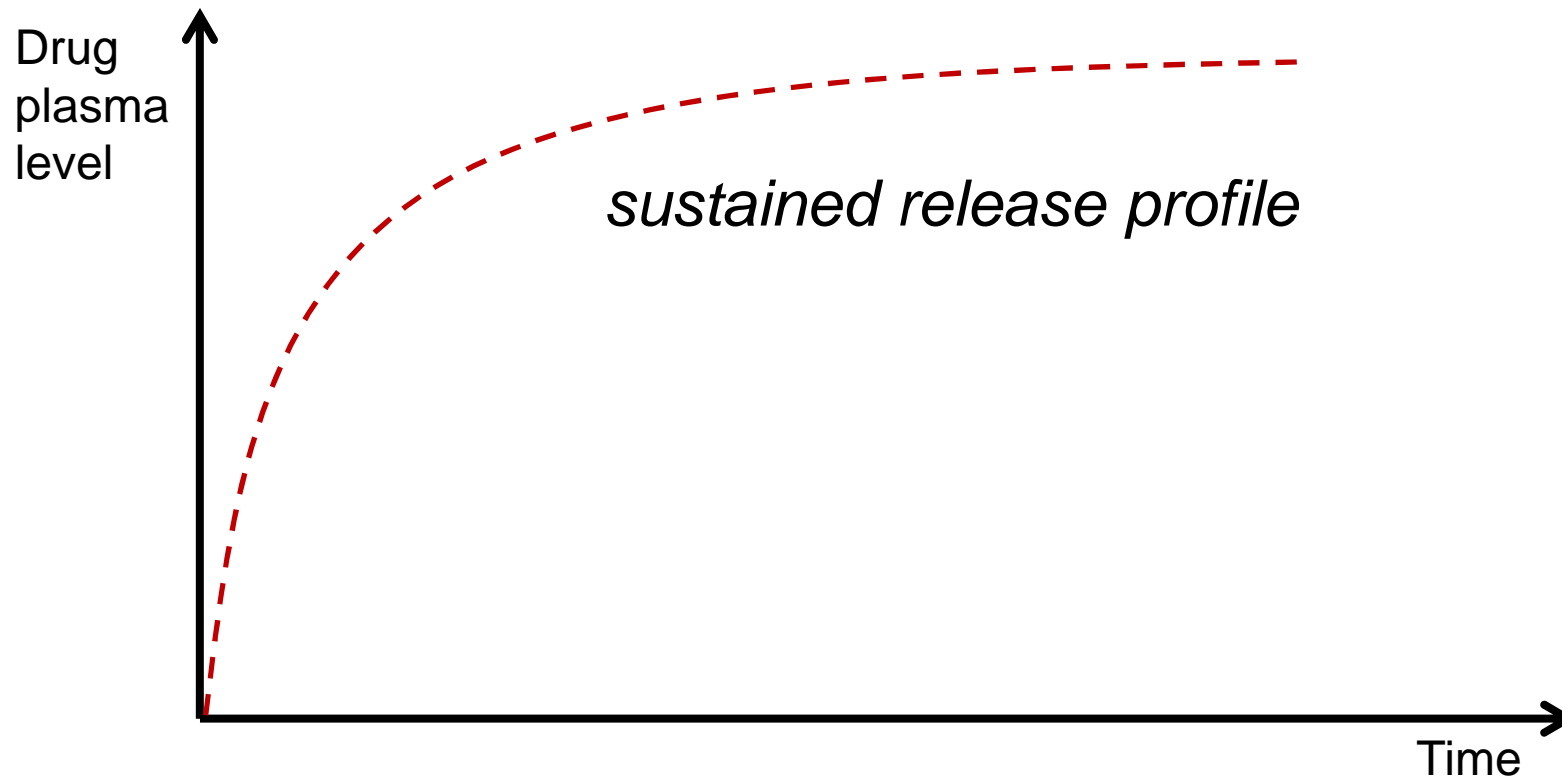
“The term modified release is used to identify drug delivery systems that are designed to achieve or extend therapeutic effect by continuously releasing medication over an extended period of time after administration of a single dose.”



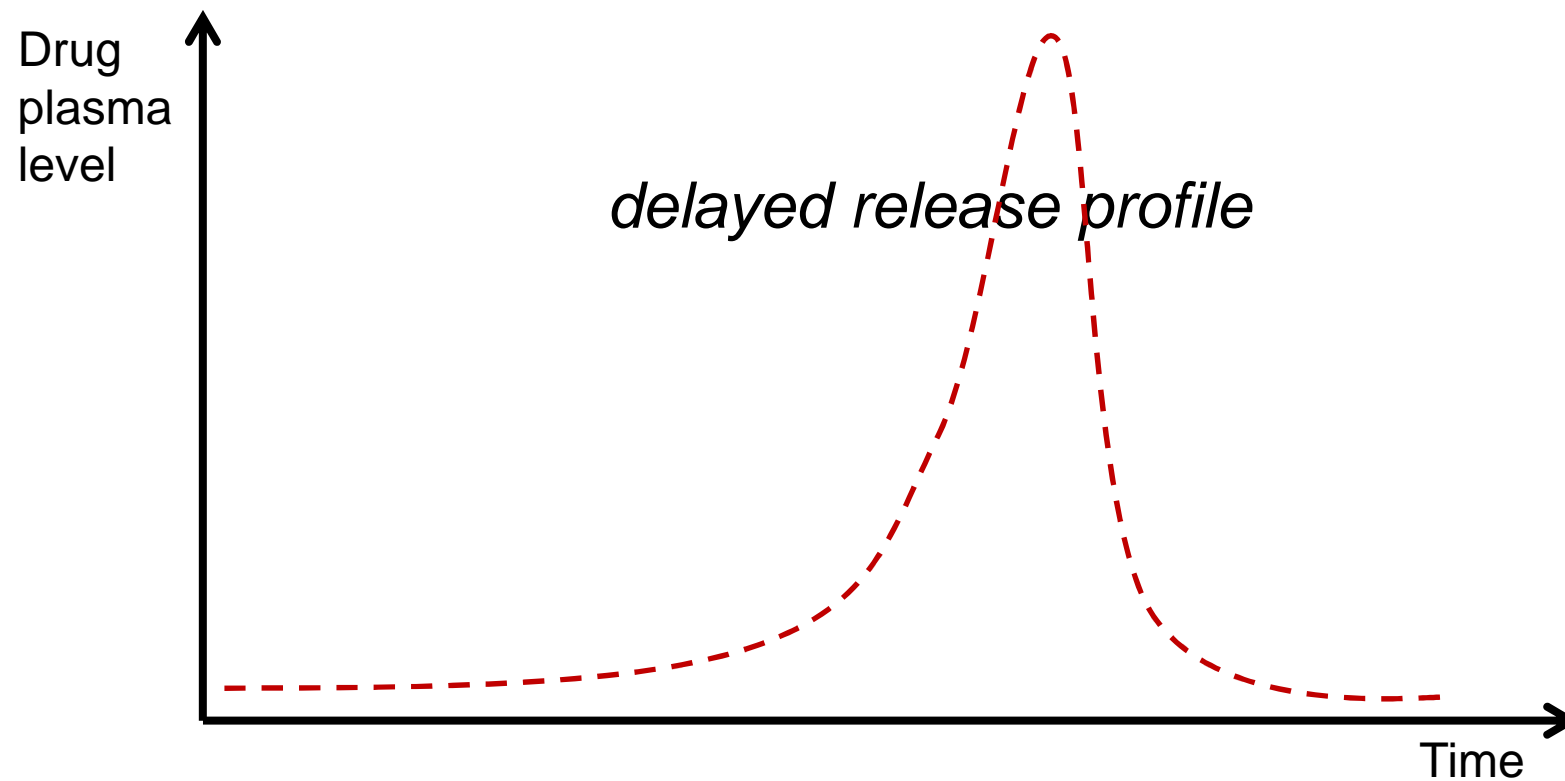
Focus: Modified release formulations



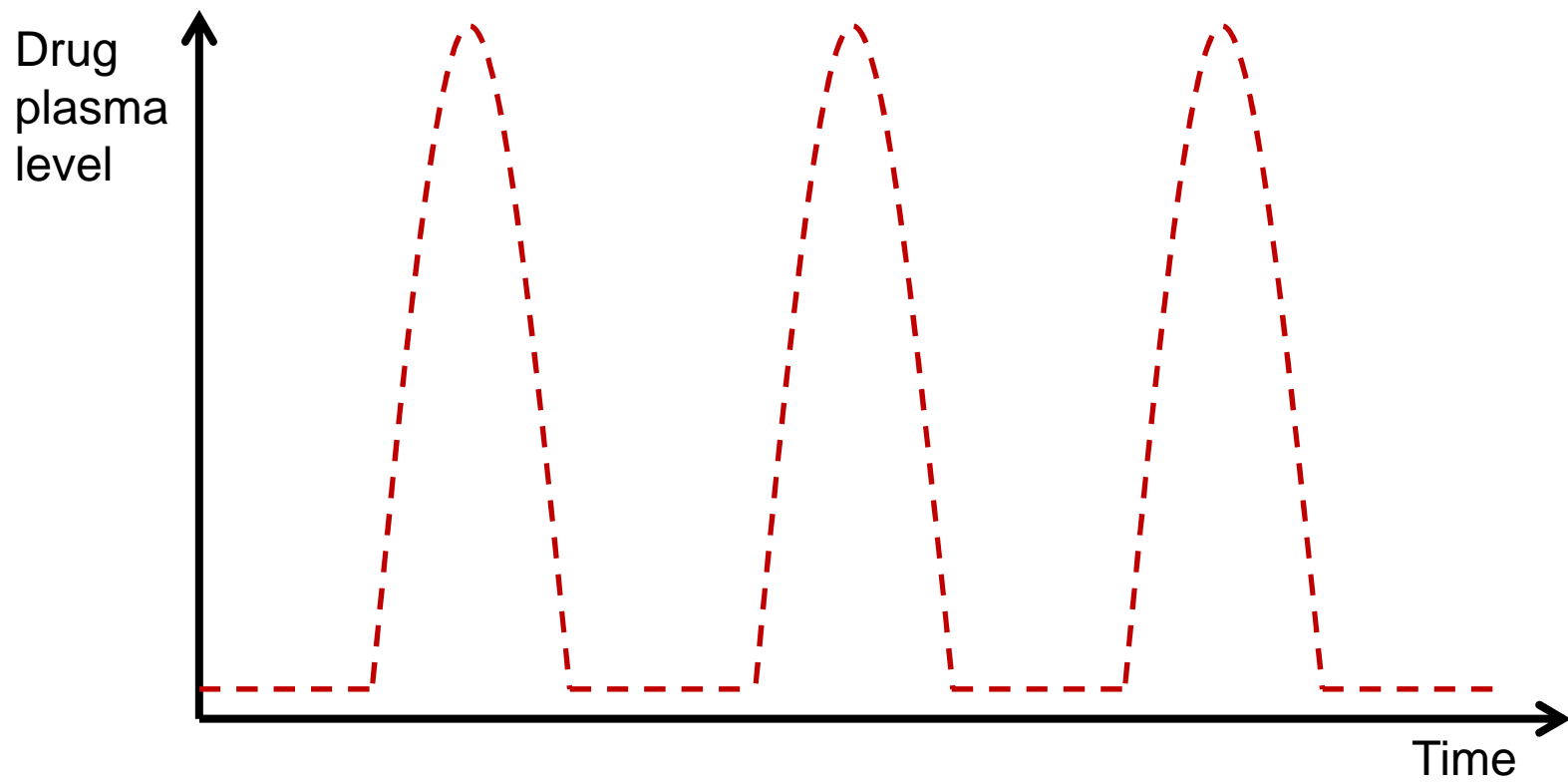
Focus: Modified release formulations

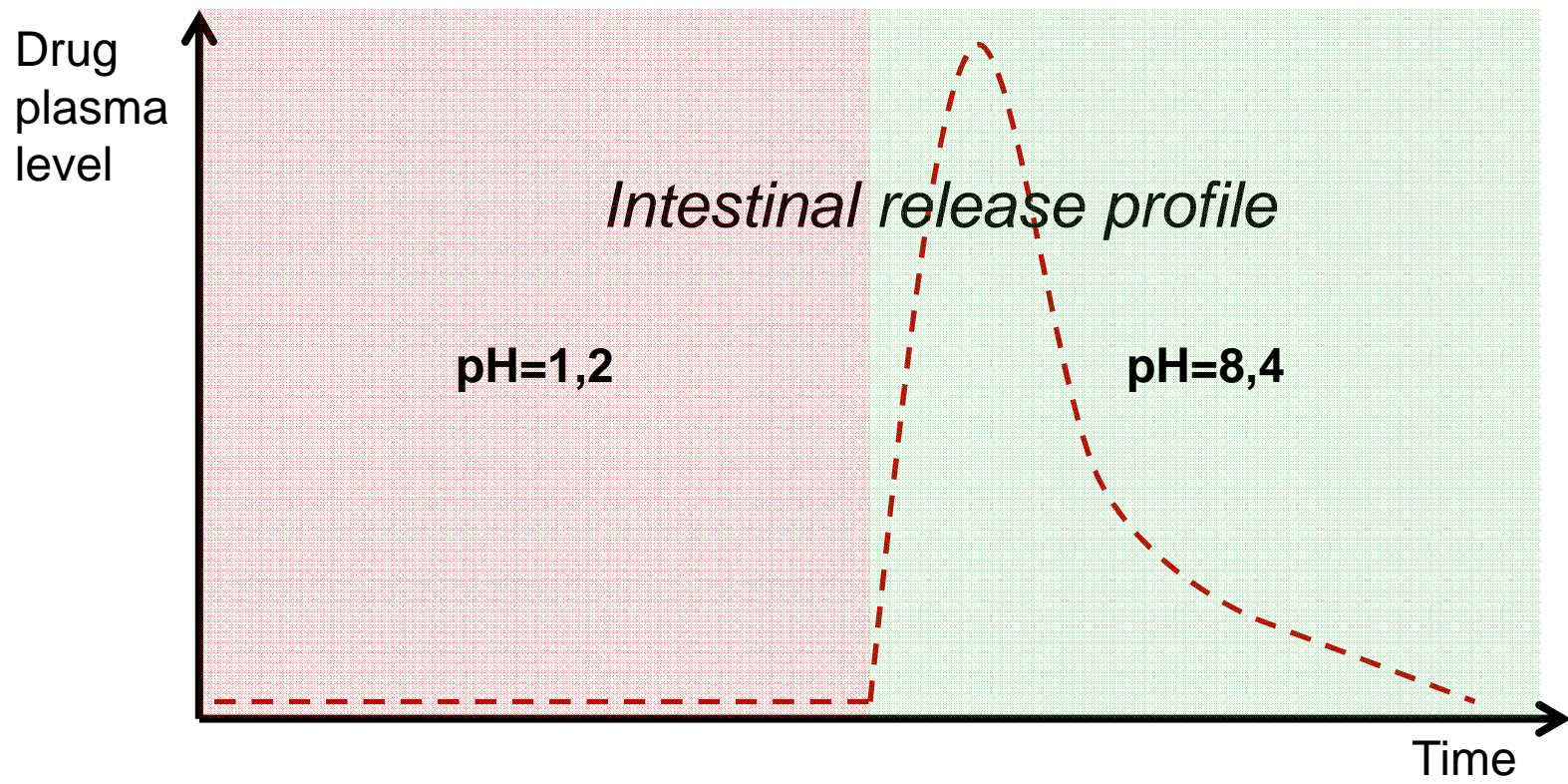


Focus: Modified release formulations



pulsed release profile



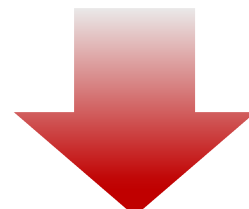
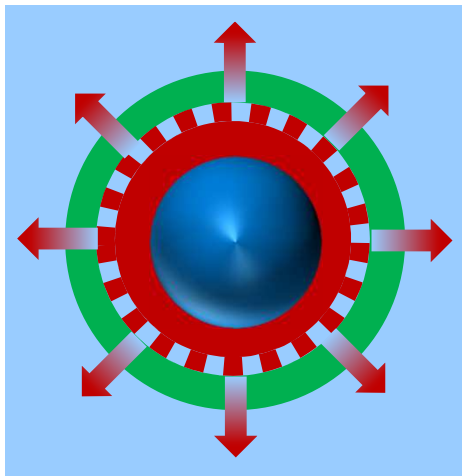


How to control the release?

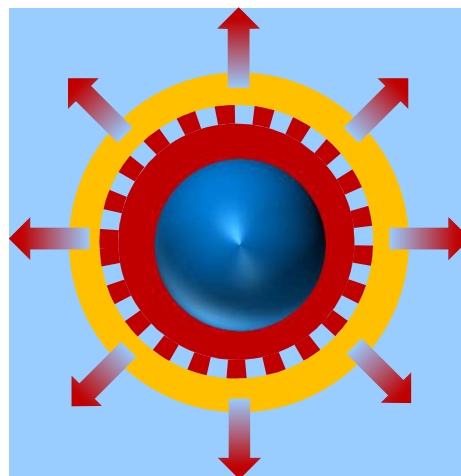
Mechanisms of membrane controlled drug release



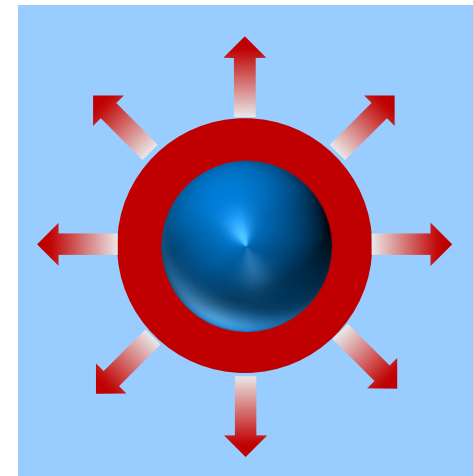
Diffusion



Osmosis

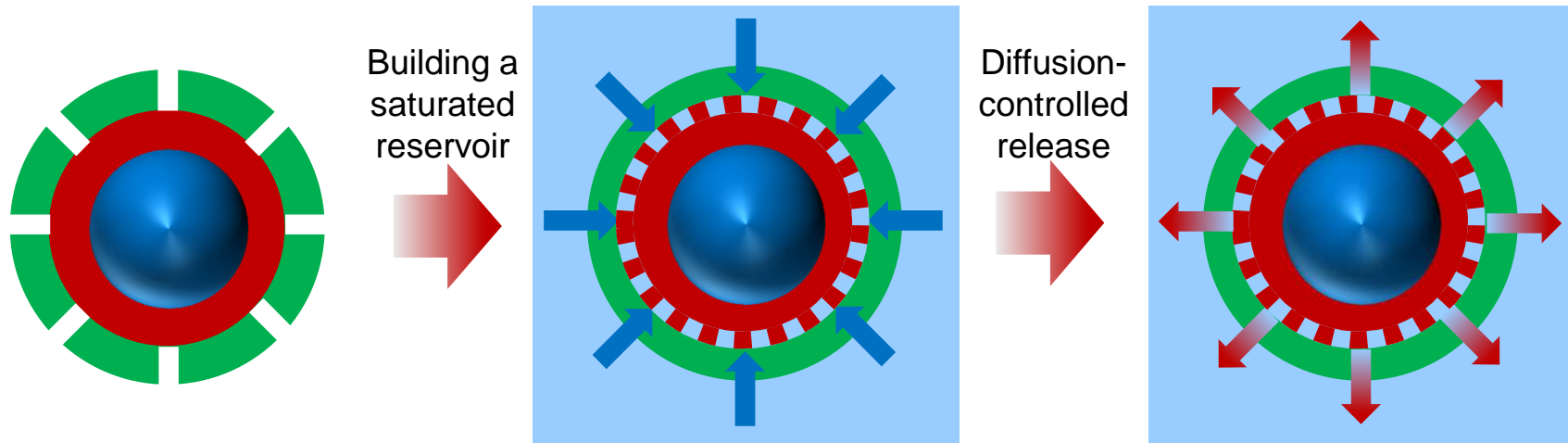


Erosion



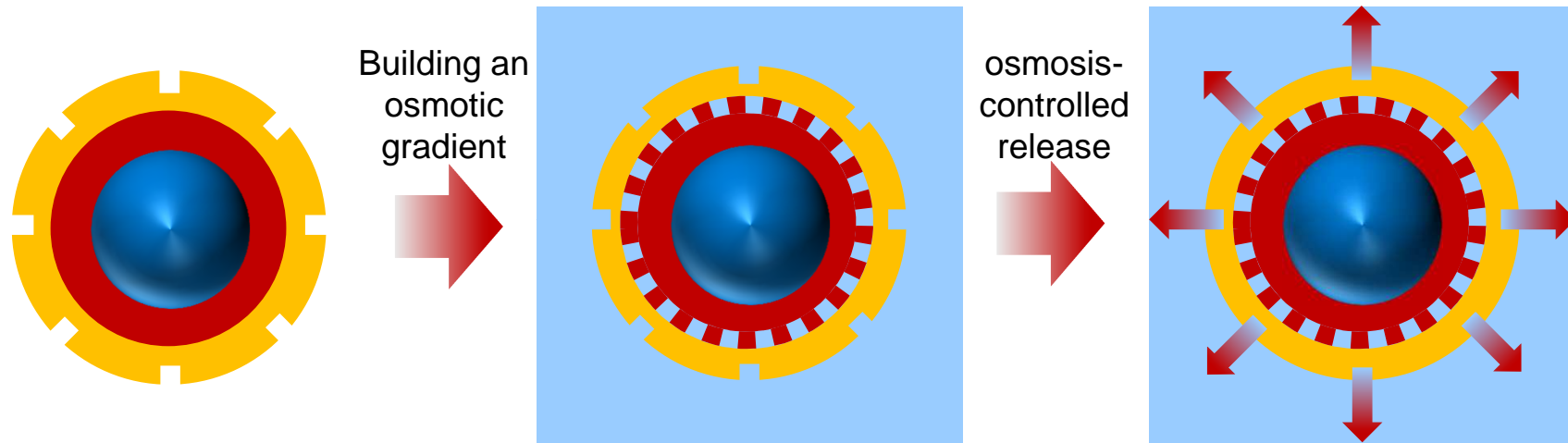
How to control the release?

Control drug release by: Diffusion



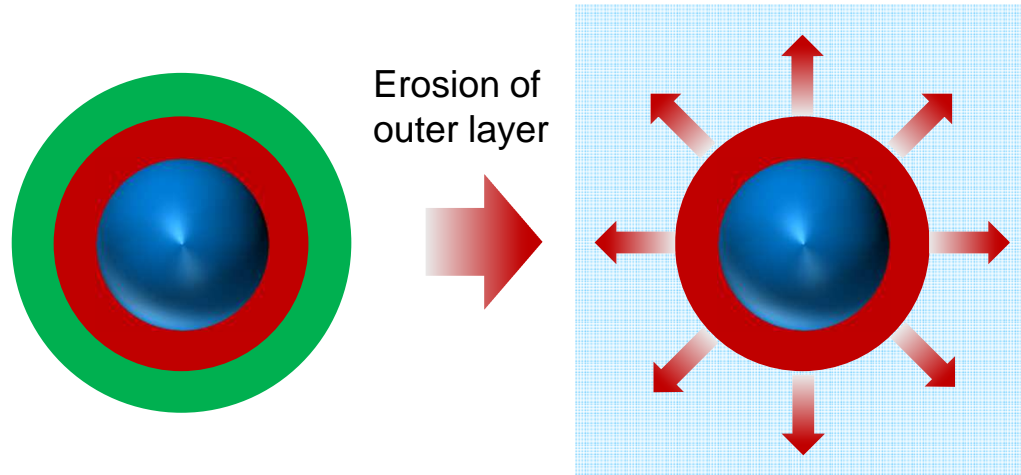
- Membrane permeable for surrounding medium and API
- API decreases if concentration is lower than saturation

Control drug release by: Osmosis



- Membrane permeable for surrounding medium, NOT for API
- API decreases if osmotic pressure decreases with API concentration

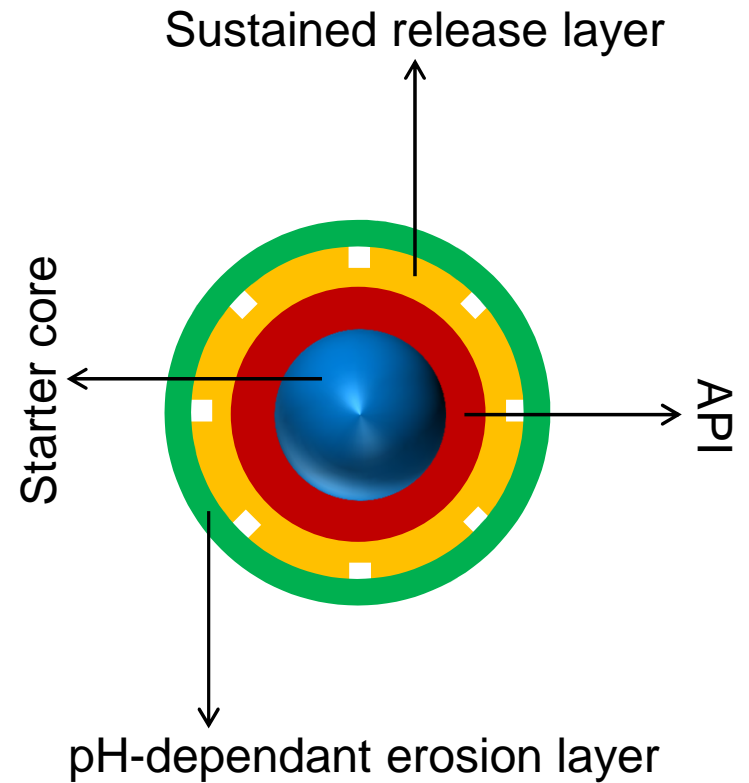
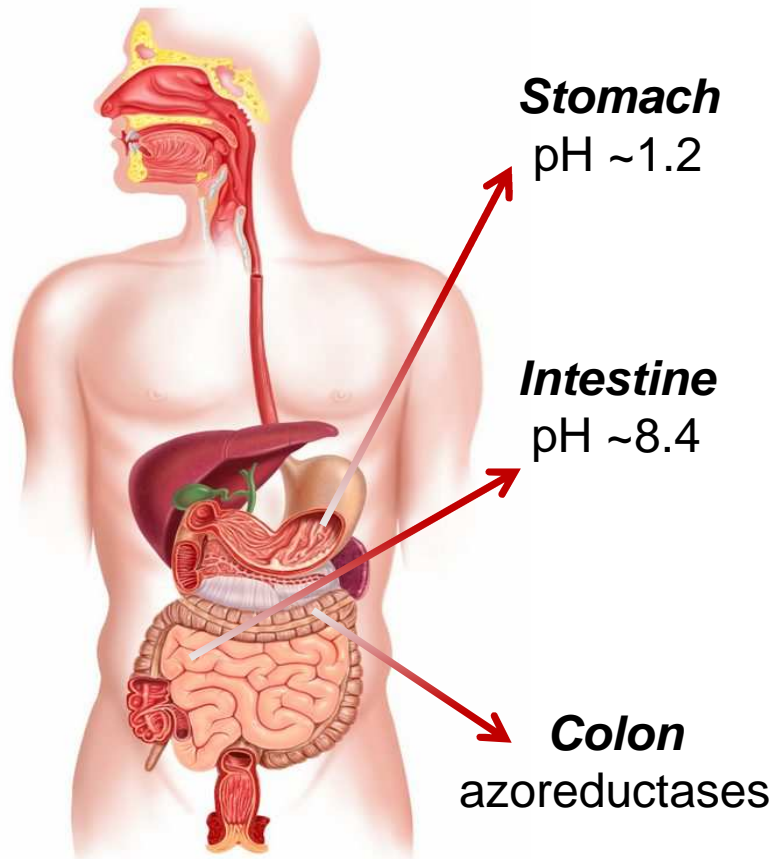
Control drug release by: Erosion



- Outer layer is soluble in the surrounding medium
- API is released after erosion of the outer layer

How to control the release?

Controlling point of release by Erosion



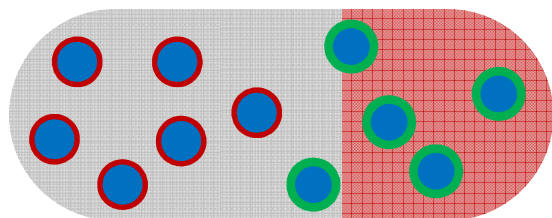
How to control the release?



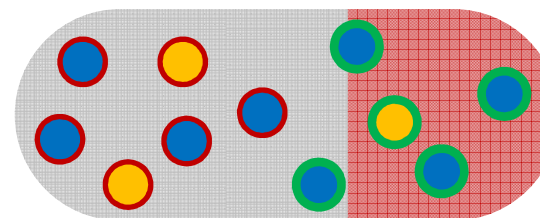
Controlling release profiles by heterogeneous mixtures of multiparticulates

Heterogeneous Multiparticulates

Same API - Different release profiles

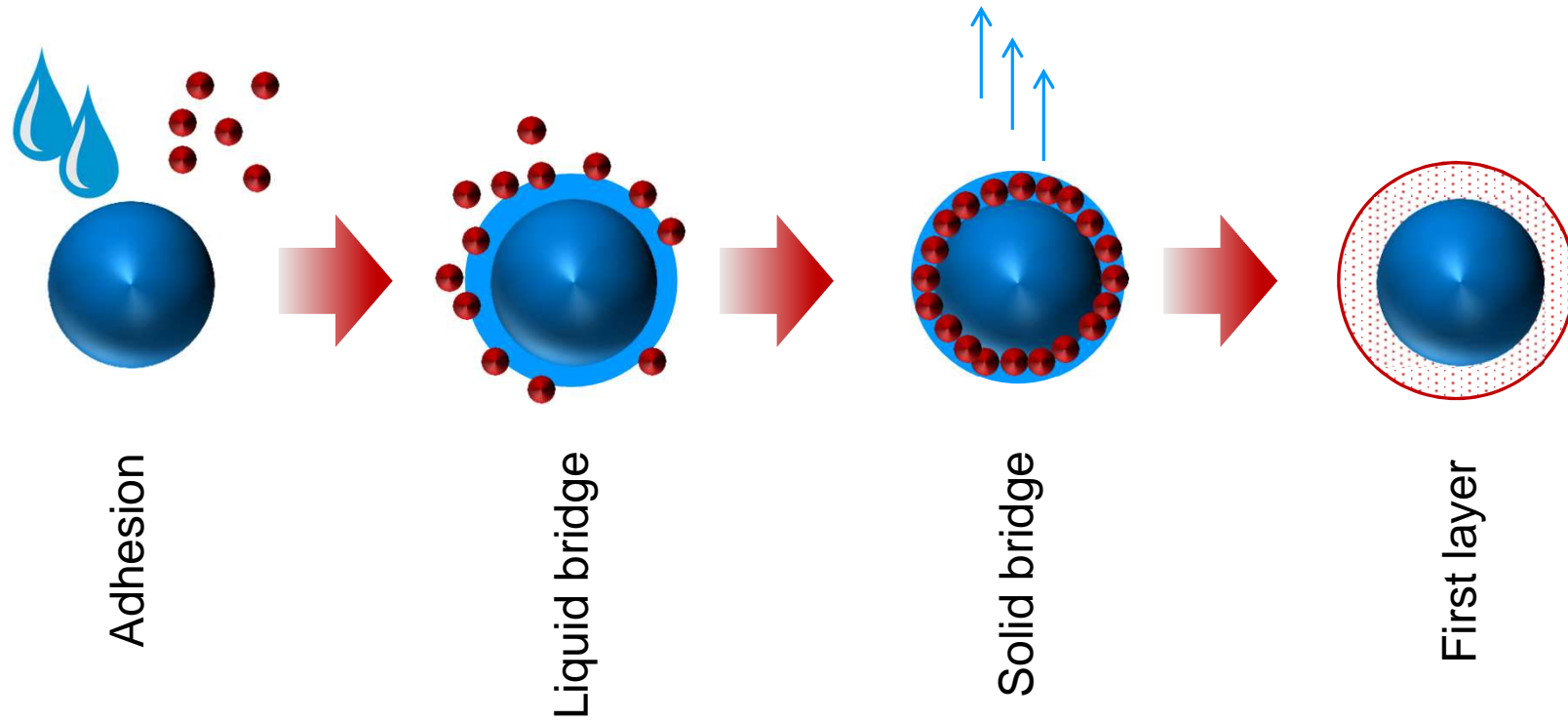


Different API - several release profiles

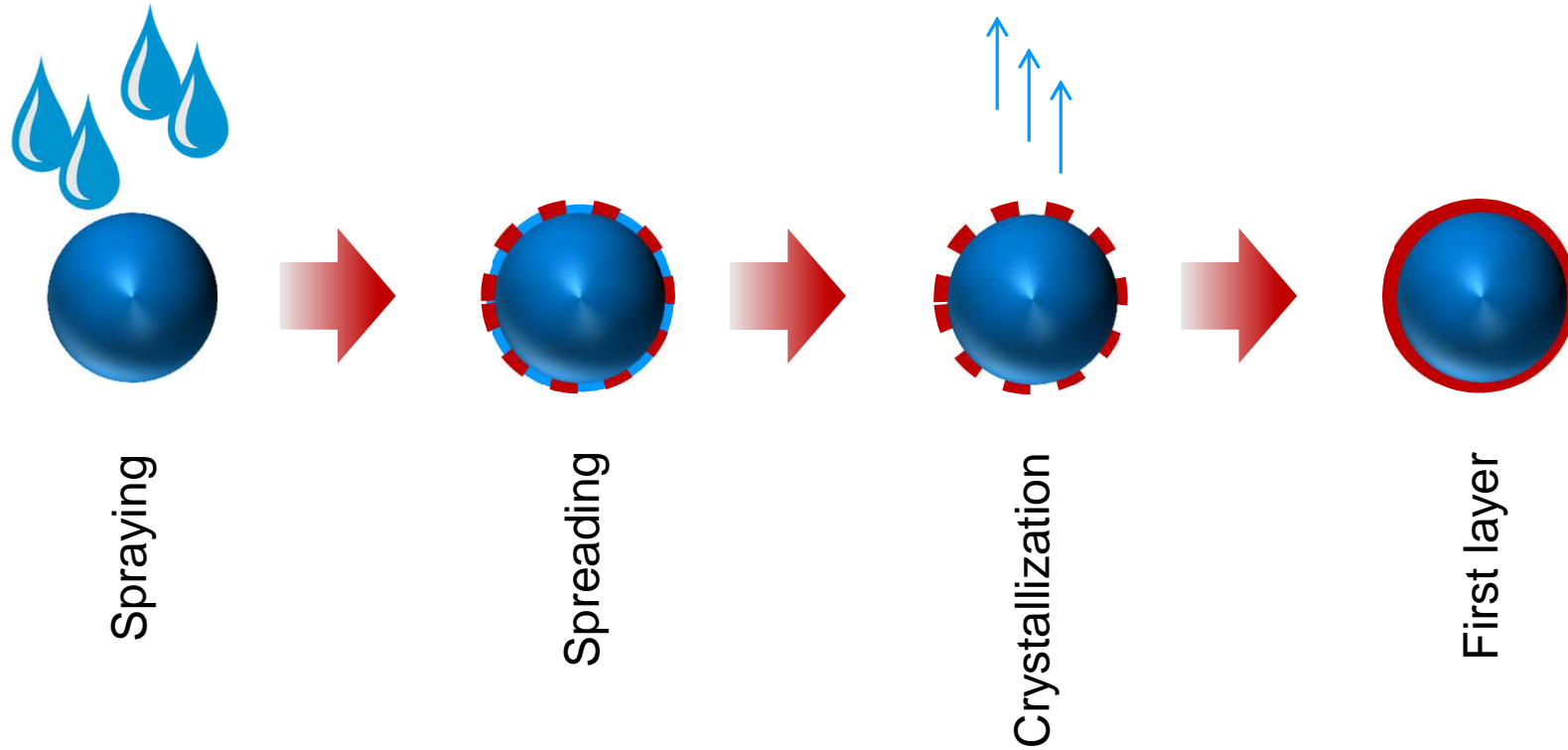


- Multiparticulates with different release profiles can easily be assembled in one capsule
- Even different APIs with different release profiles can be combined this way

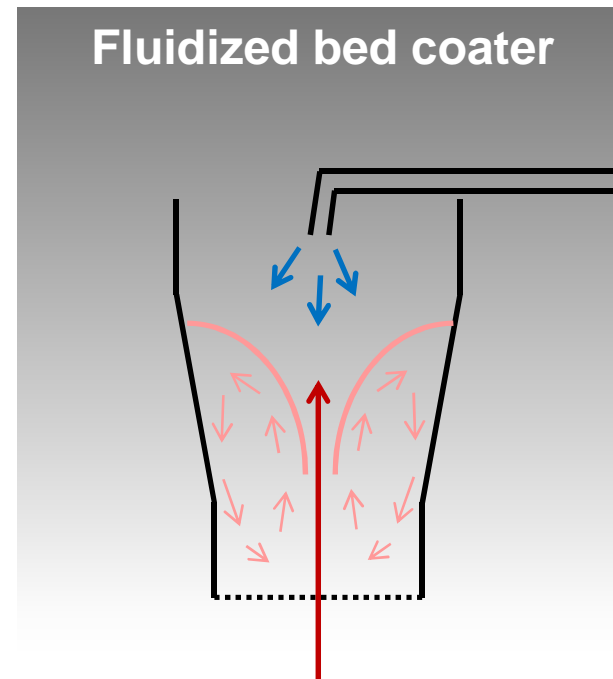
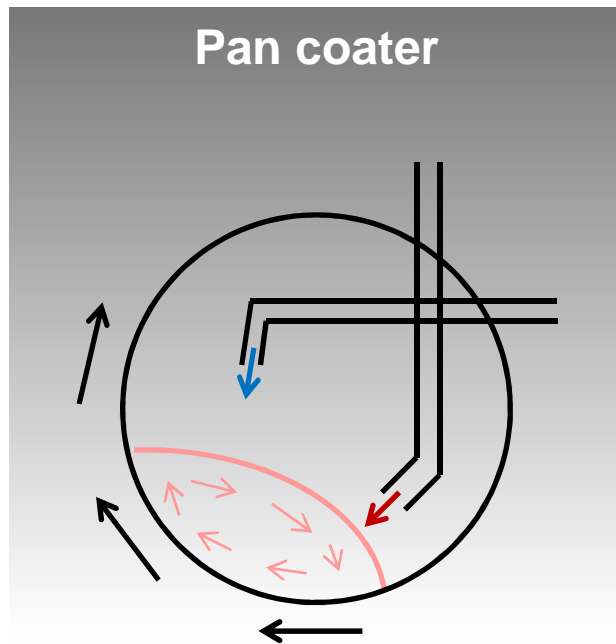
Powder layering

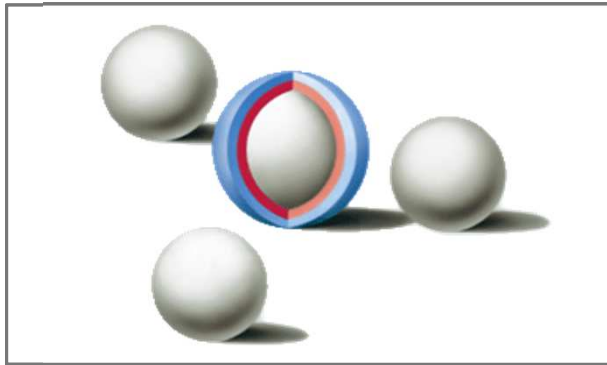


Suspension layering

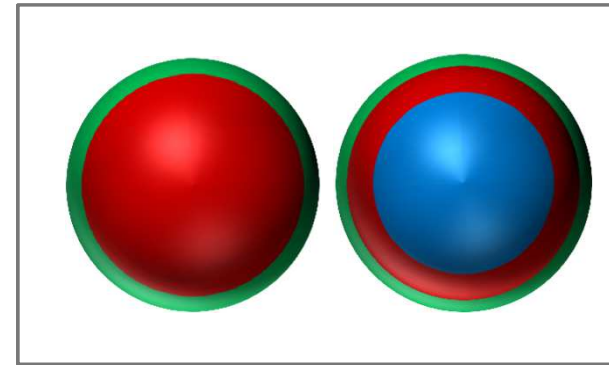


Depending on the **required properties** of the pellet several coating processes are possible. The most popular are **pan coating** and **fluid bed coating**.



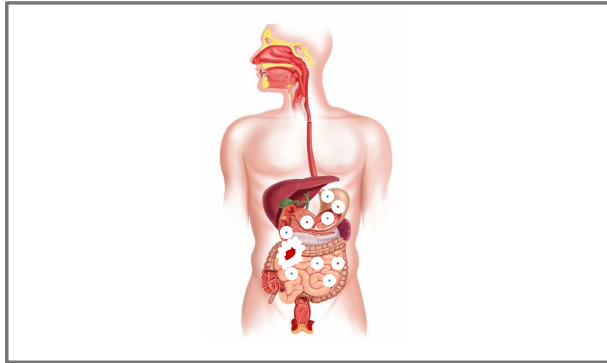


Multiparticulate drug delivery systems are mainly *oral dosage forms* consisting of a *multiplicity* of small *discrete* units, each exhibiting some desired *characteristics*.

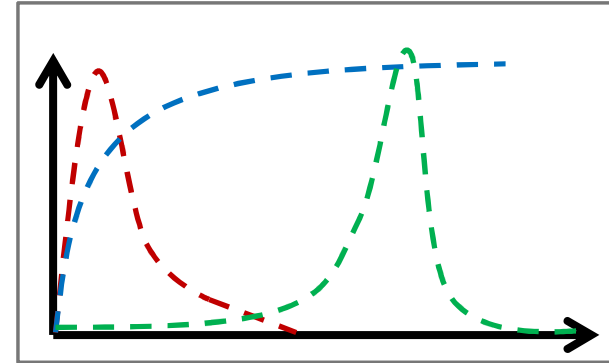


Pellet based systems either consist of *matrix pellets* or *coated starter cores*. For several reasons „*sugar spheres*“ spheres are widely used as starter cores.

Summary

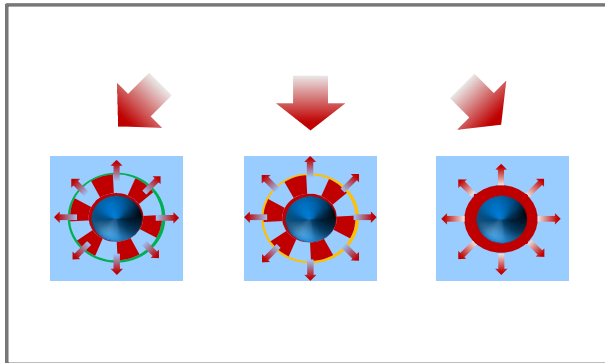


Due to **their small size** and **multiple redundance** multiparticulates can greatly **improve clinical effectiveness** and **safety** of pharmaceutical formulations

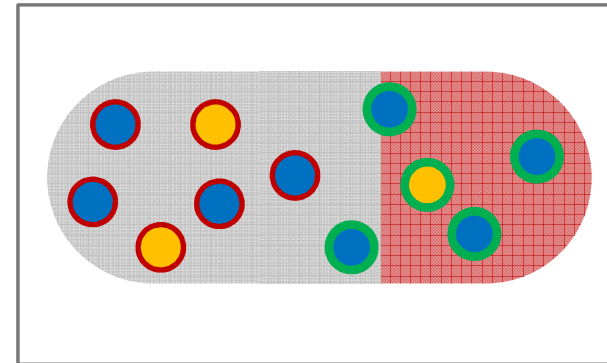


The single most important factor responsible for the proliferation of **pelletized products** is the popularity of **controlled release technology** in the delivery of drugs

Summary

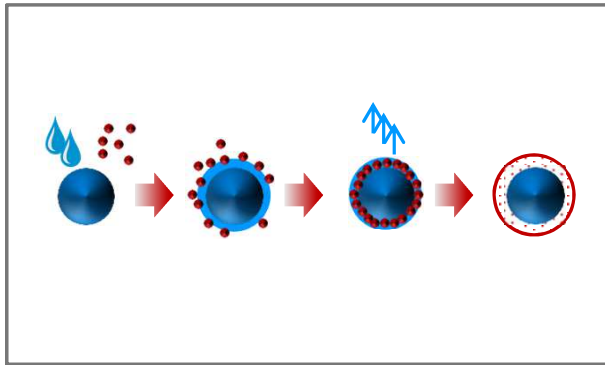


There are different ways to achieve **membrane controlled** drug release. Most important mechanisms are: **Diffusion**, **osmosis** and **erosion**

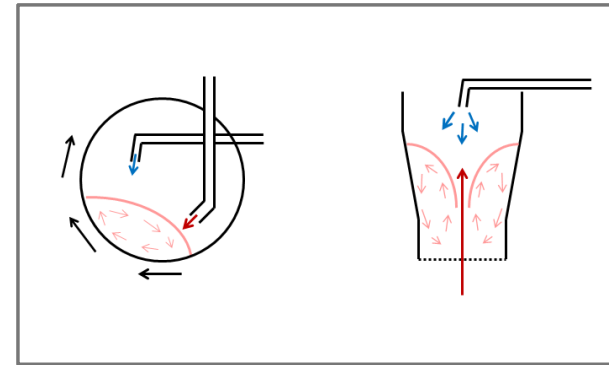


Heterogeneous multiparticulate dosage forms can be utilized to easily achieve **complex** release profiles of **one or several APIs**

Summary



Basic mechanisms of coating are **powder coating** and **suspension layering**. Which one to use depends on the required properties and especially the anticipated **API-load**



Widely used processes in manufacturing coated multiparticulate oral dosage forms are **pan coating** or **fluidized bed technology**

תודה
Dankie Gracias
Спасибо شکرًا
Köszönjük Merci Takk
Grazie Dziękujemy Terima kasih
Děkujeme Vielen Dank Děkojame
Kiitos Täname teid 谢谢
Thank You Tak
感謝您 Obrigado Teşekkür Ederiz
Σας ευχαριστούμε 감사합니다
Bedankt Děkujeme vám
ありがとうございます
Tack