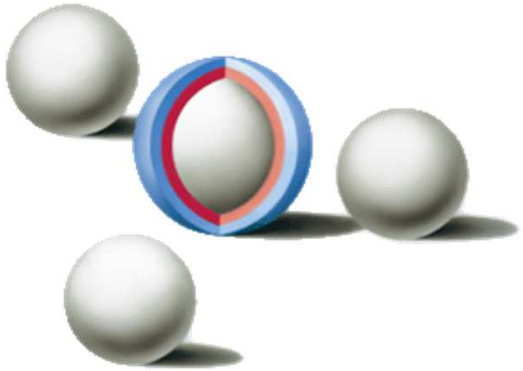
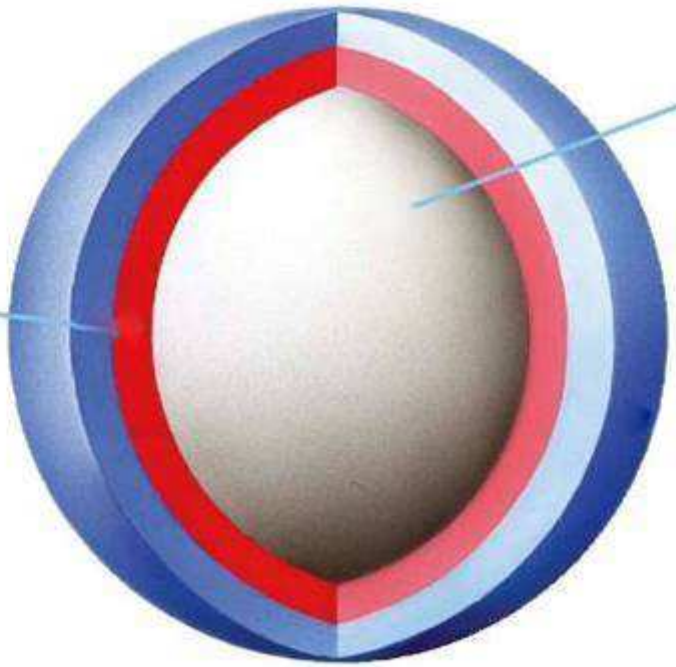


Sugar Spheres: “Improving clinical effectiveness with multiparticulate drug delivery systems”

Philipp Werner

pharm-a-spheres®



sugar sphere as core

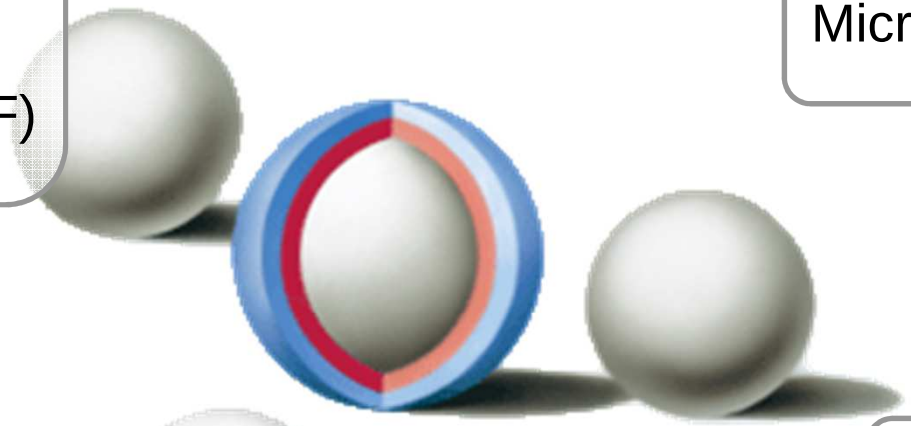
Active ingredients coated on the sugar spheres

controlled-release coating and finishing

Pharmaceutical product portfolio

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

Micropellets



Globuli sacchari

xylitol and lactose globuli

nutritional supplements

What are multiparticulate oral dosage forms?

Types of pellets

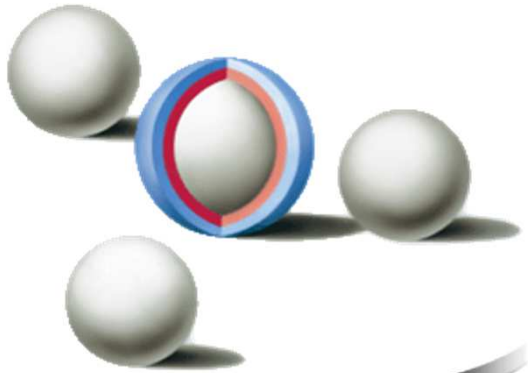
Sugar spheres and their benefits

Multiparticulates improve clinical effectiveness?

Technological benefits of multiparticulates

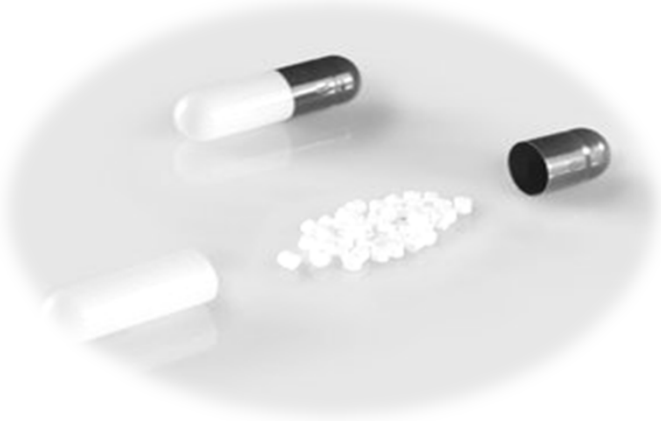
Focus: Modified release formulations

Mechanisms of coating



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

Pellets



Microtablets

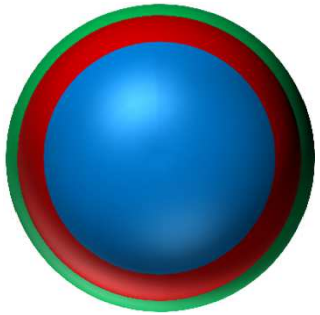
pharm-a-spheres®

Matrix Pellets

➢ By extrusion, granulation or spheronisation.

Coated starter core

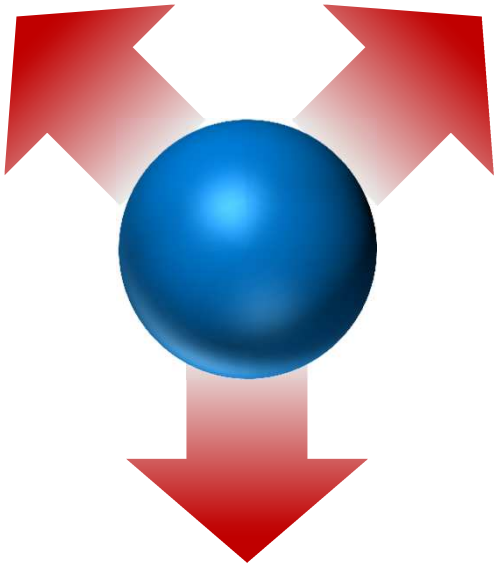
➢ By coating of an already existing starter core



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*

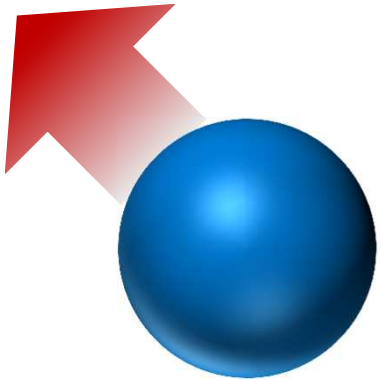
In compliance!

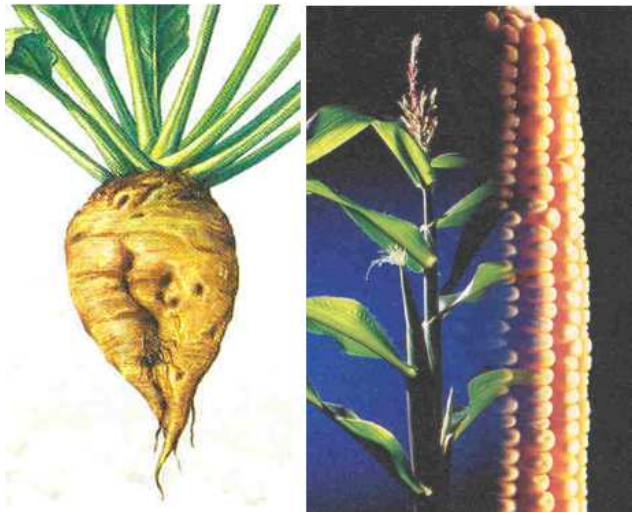
- *In respect to EP & USP*

pharm-a-spheres®

High patient compatibility

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





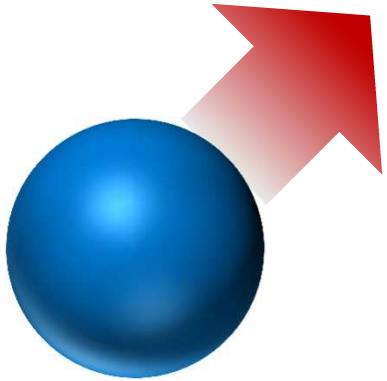
- Only sugar & corn starch
- All natural
- Digestible
- Biodegradable

- Outstanding microbial Quality

- High degree of sphericity
- Smooth surface

- Chemically indifferent excipients
- No incompatibilites

- High mechanical stability
- No attrition
- Low friability



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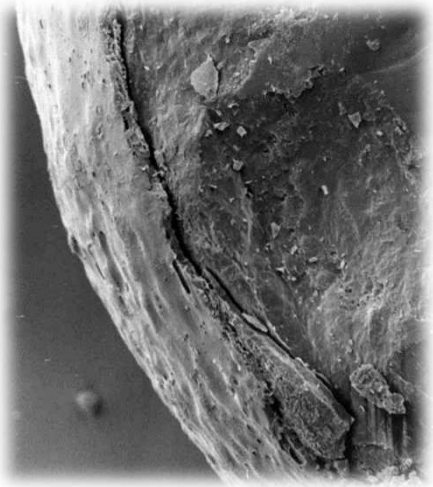
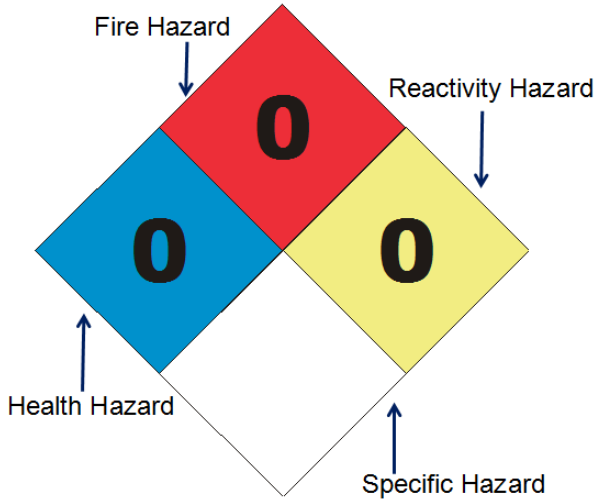
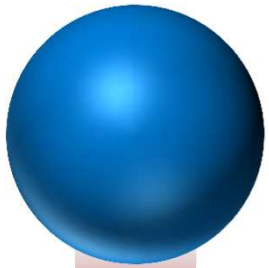




pharm-a-spheres®



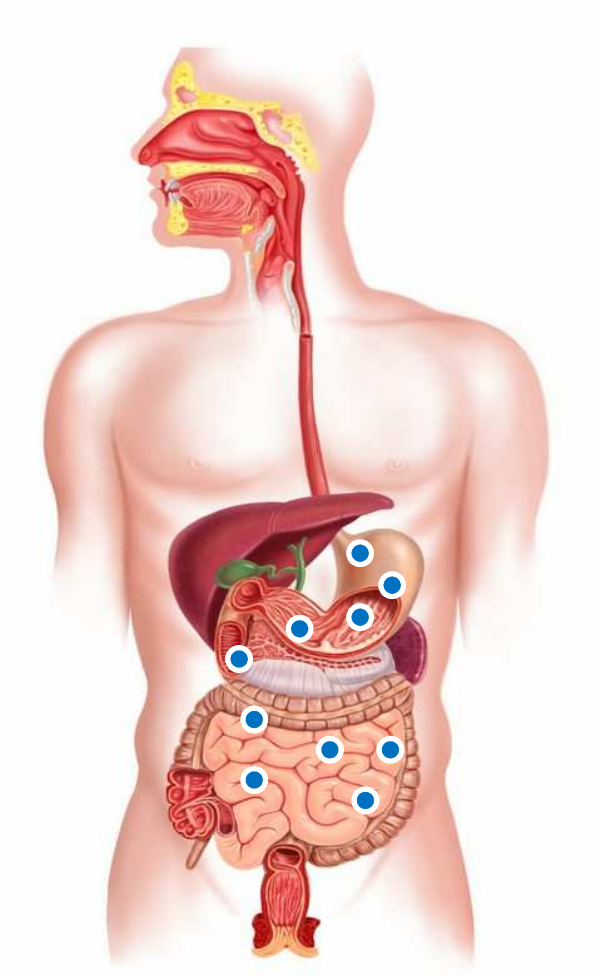
- USP/NF: „sugar spheres“
- EP: 1570 „sugar spheres“

Worldwide acceptance!

In compliance!

- *In respect to EP & USP*

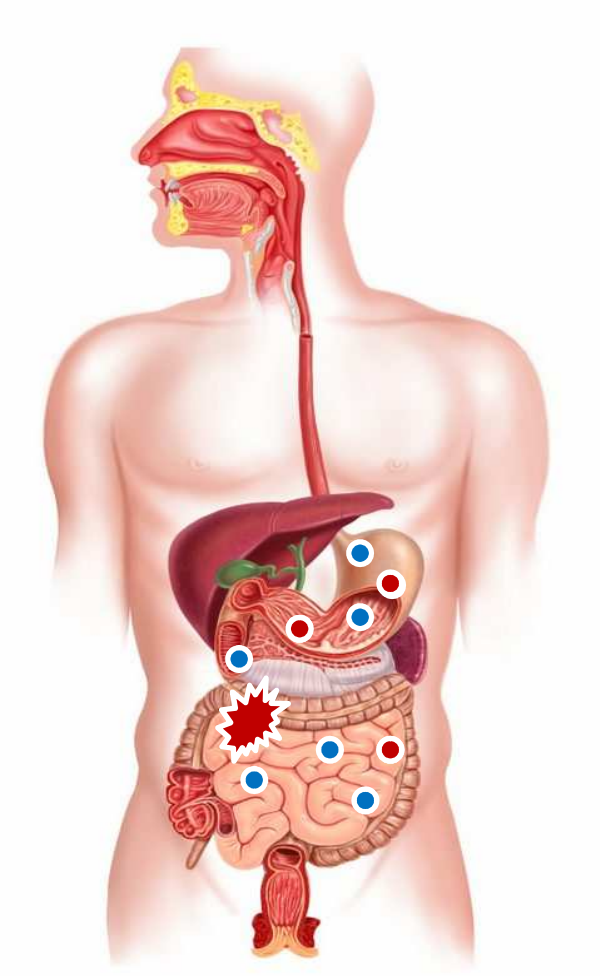
Easy application registration!



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?

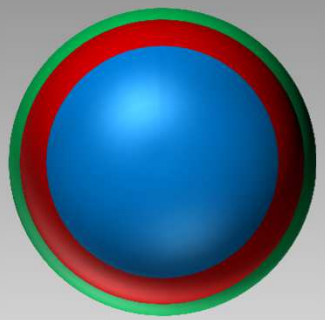
Greater and more reproducible dispersion throughout the gastrointestinal tract can be achieved.

The risk of local toxicity decreases

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

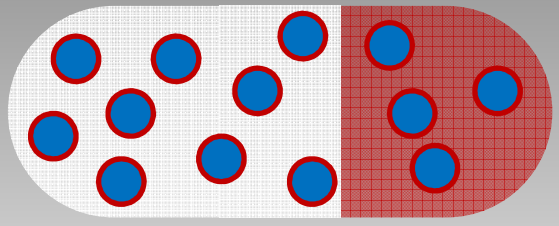
pharm-a-spheres®

Easy coating at a constant thickness



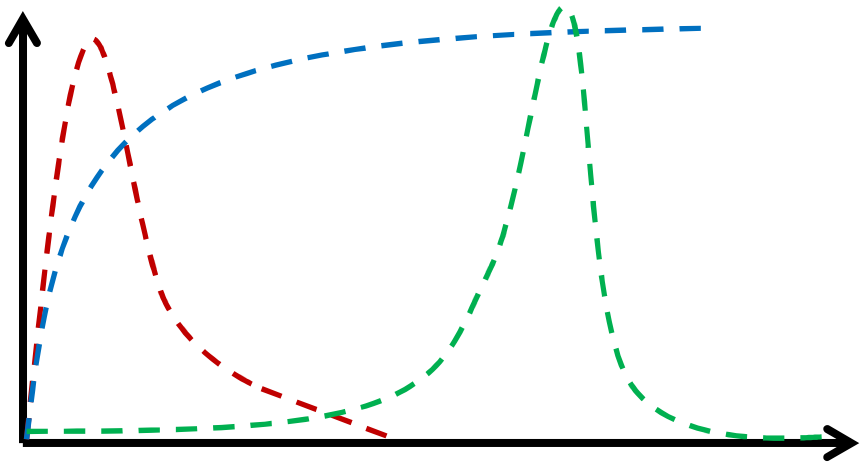
- Highly controllable
- Low stress on API (coating)

Stable mixtures - Easy assembly



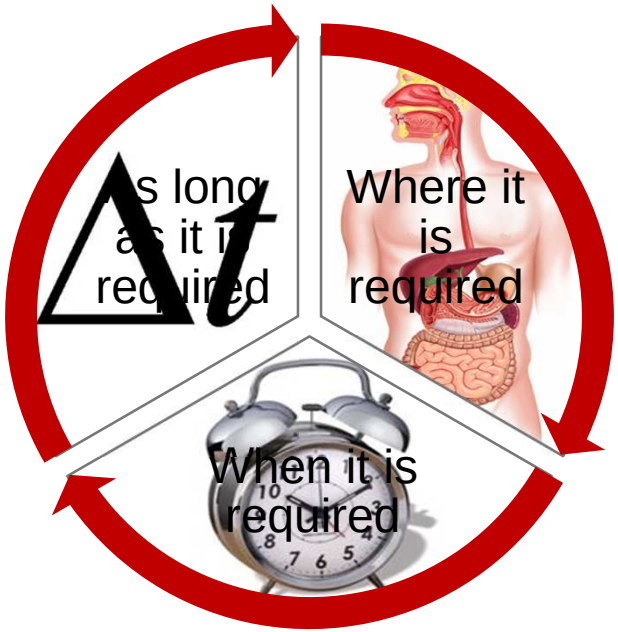
- Easy dose adjusting
- Simultaneous release of incompatible APIs

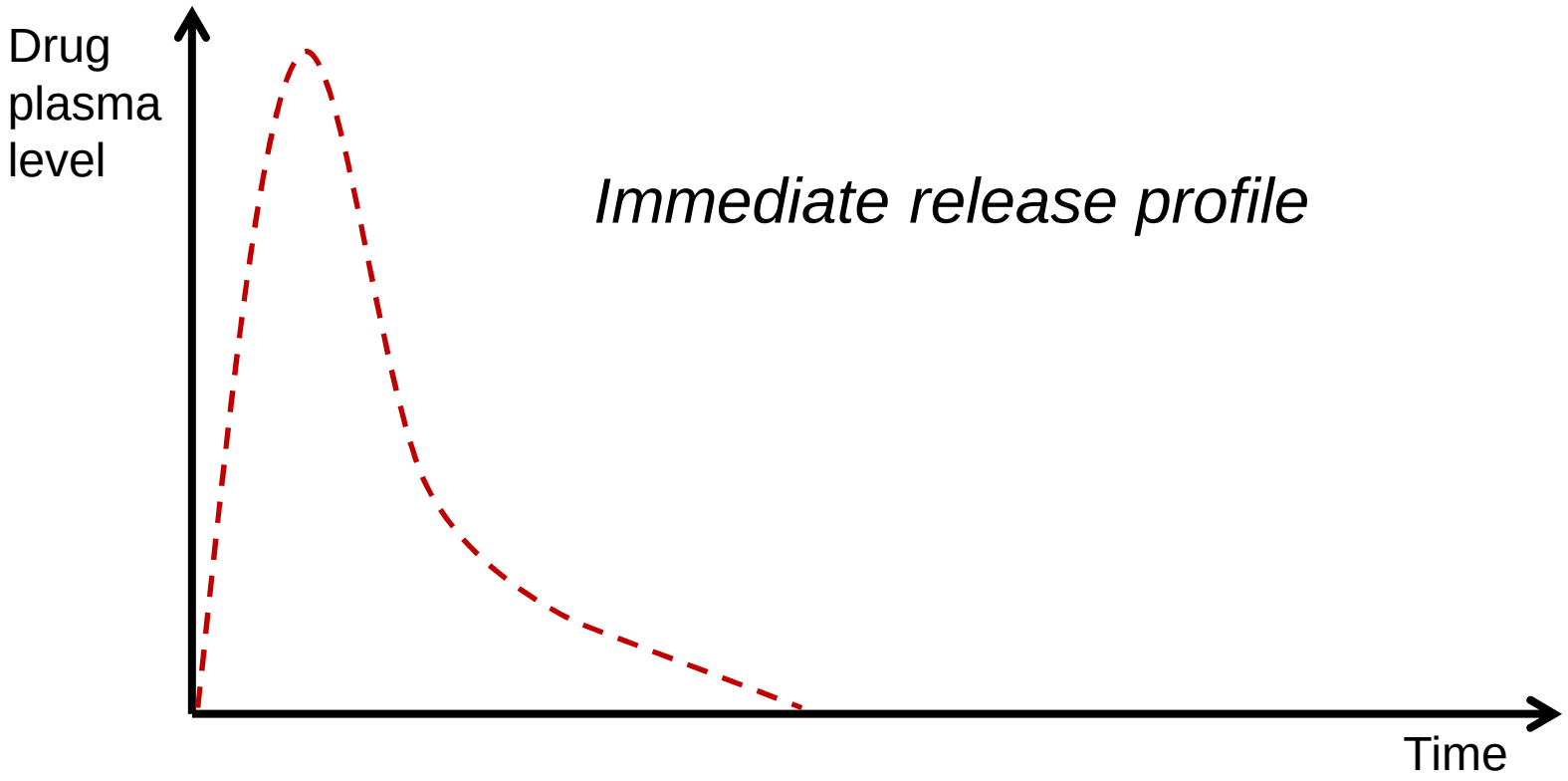
„The single most important factor responsible for the proliferation of pelletized products is the popularity of controlled release technology in the delivery of drugs“

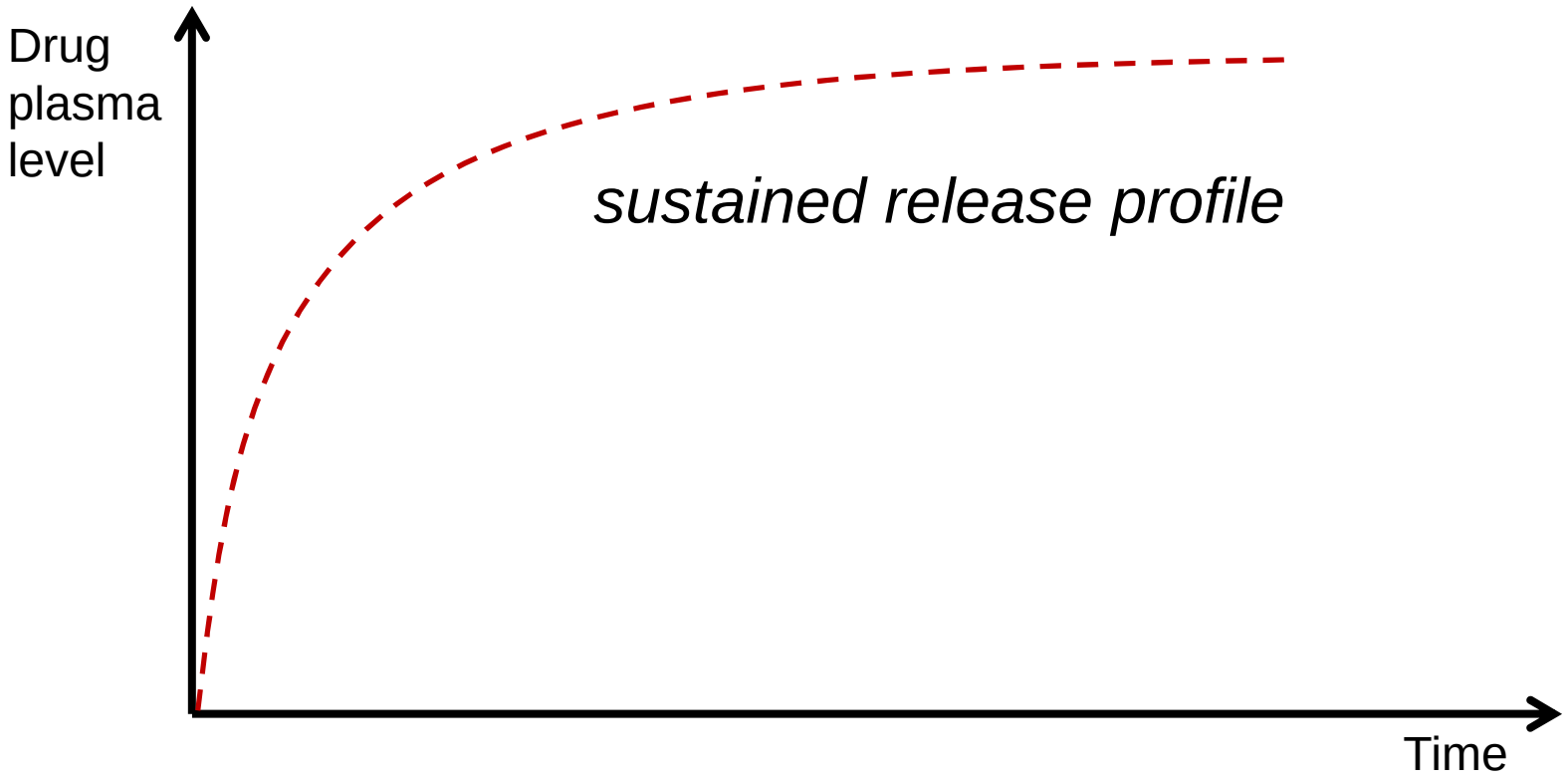


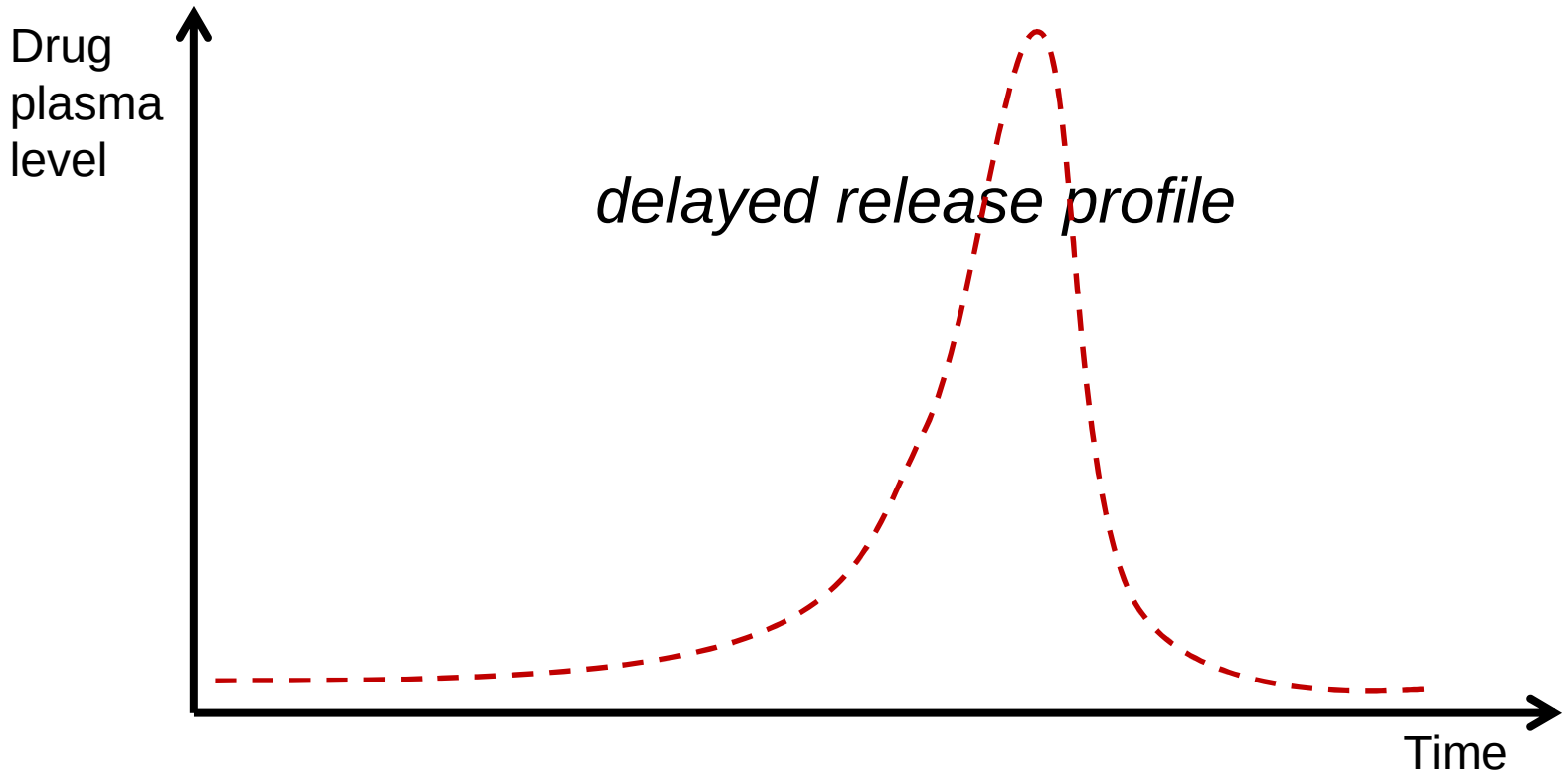
- Potentially any release profile
- Potentially several APIs
- Several ways of achieving modified release

"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."



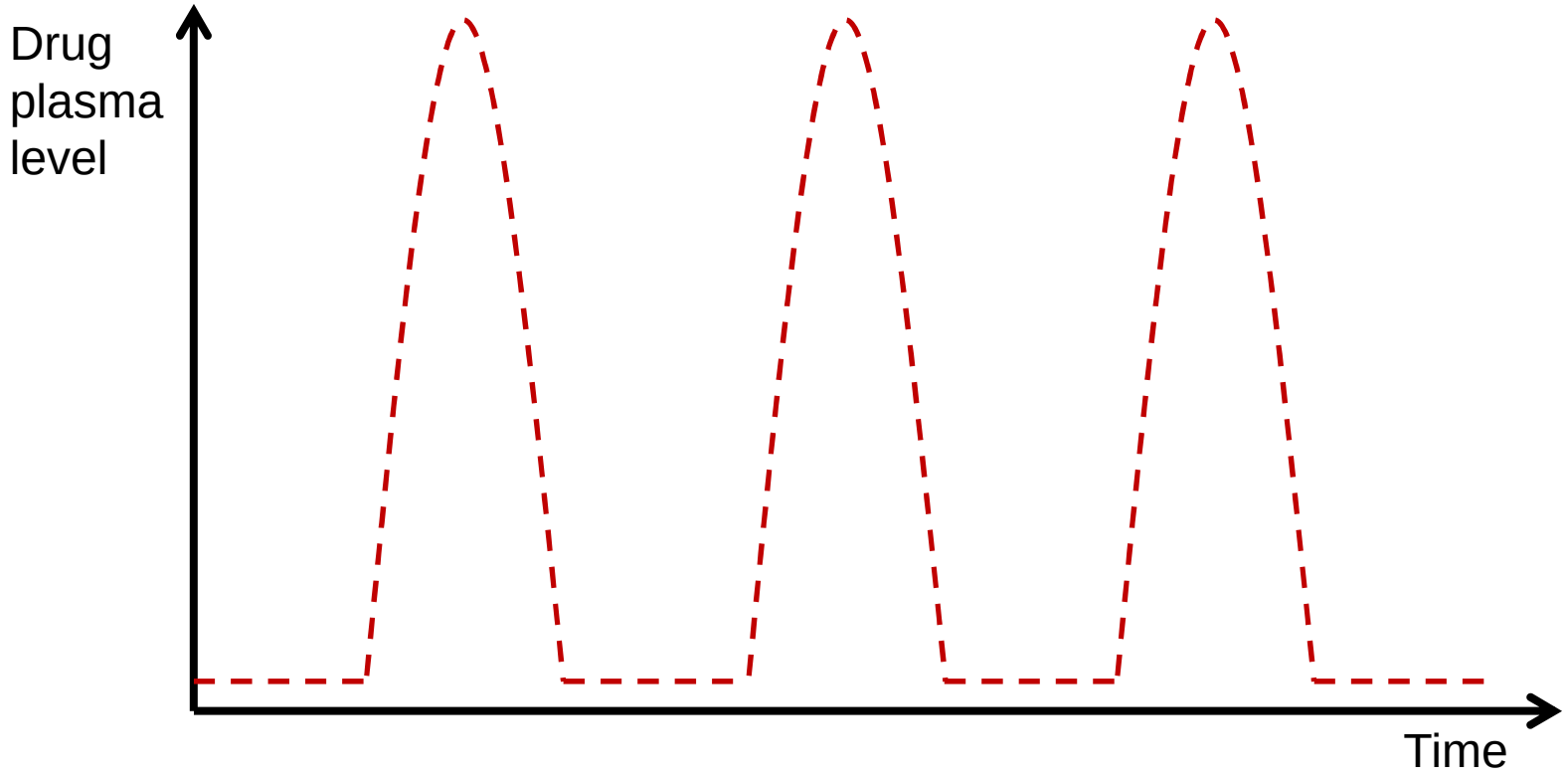

Drug plasma level
Immediate release profile
Time

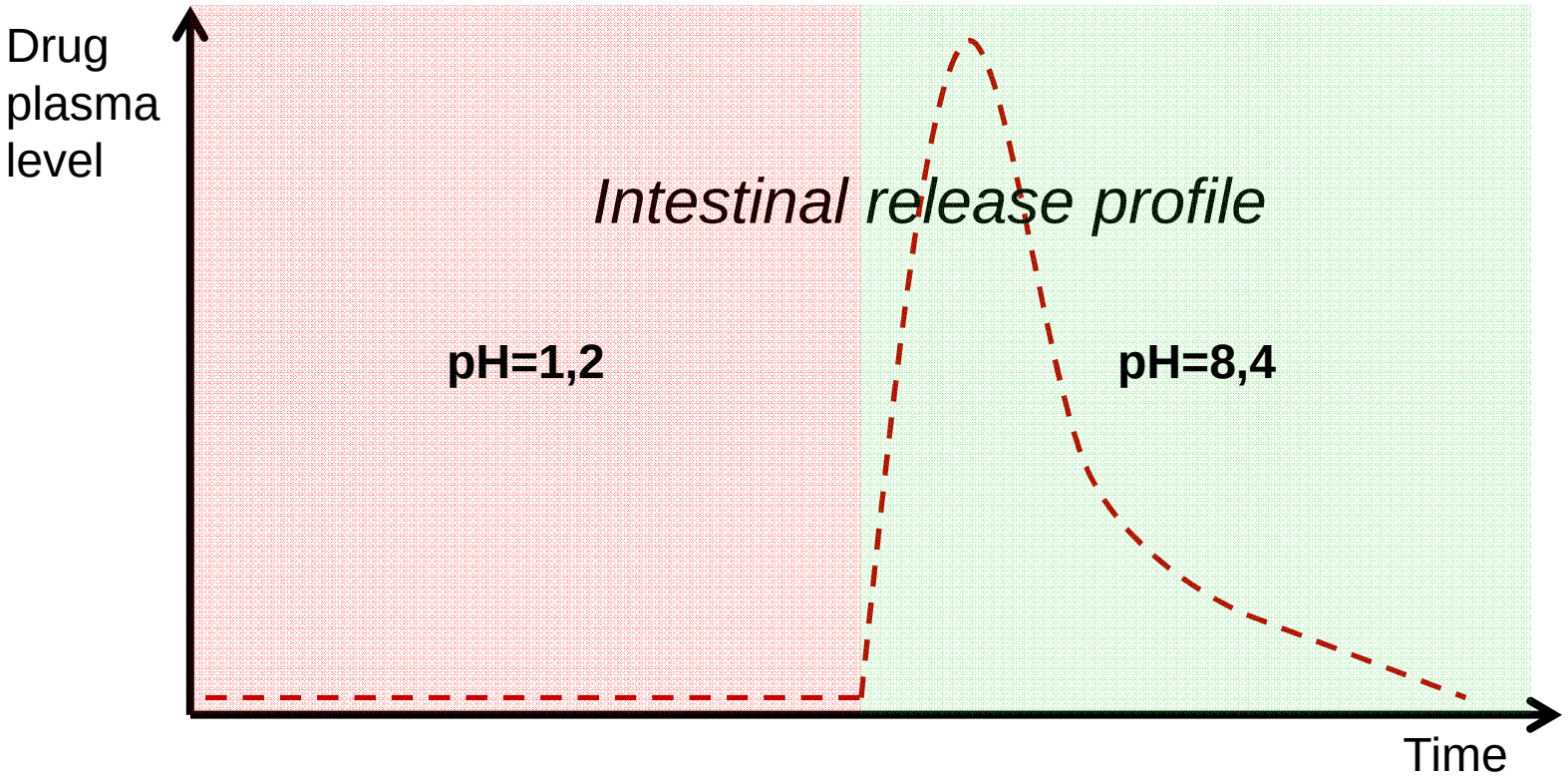

Drug
plasma
level
sustained release profile
Time


Drug
plasma
level
delayed release profile
Time

pharm-a-spheres®

pulsed release profile

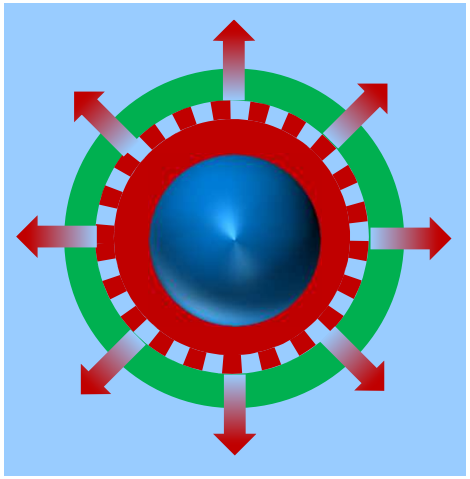



Drug plasma level
Intestinal release profile
pH=1,2
pH=8,4
Time

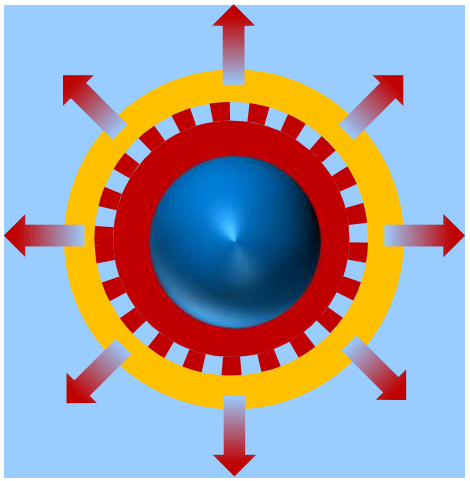
pharm-a-spheres®

Mechanisms of membrane controled drug release

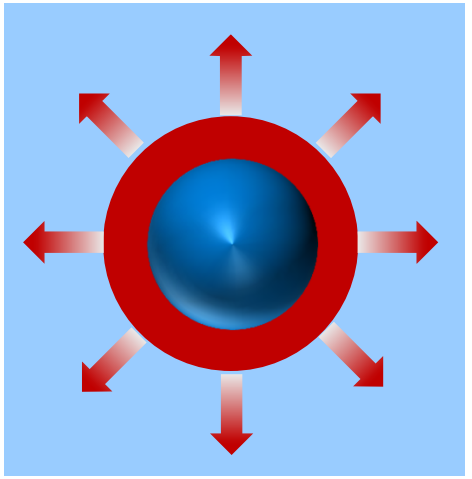
Diffusion



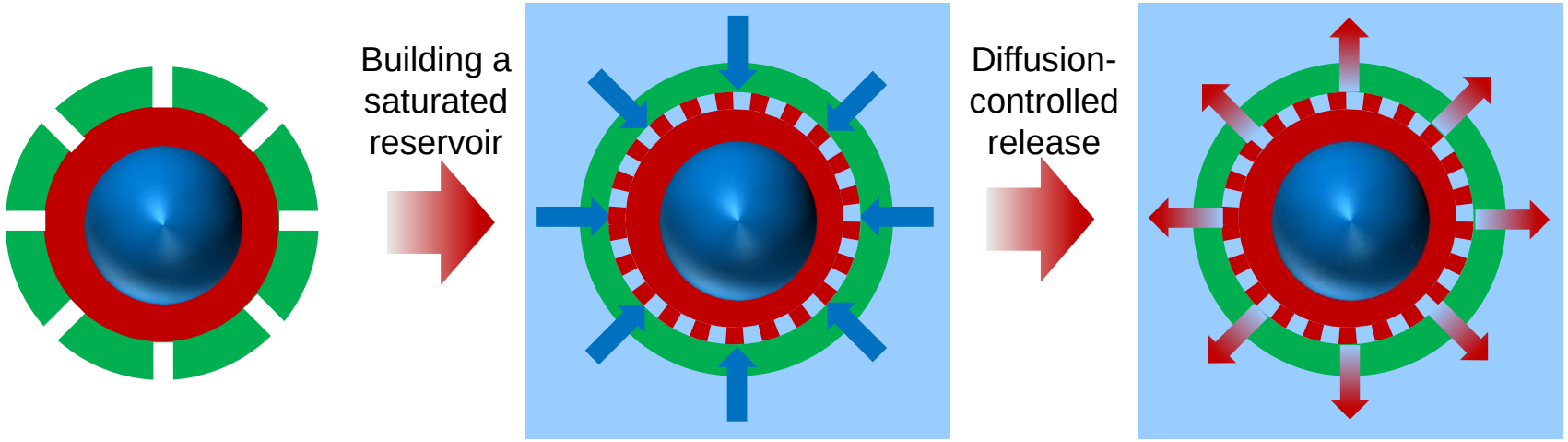
Osmosis



Erosion

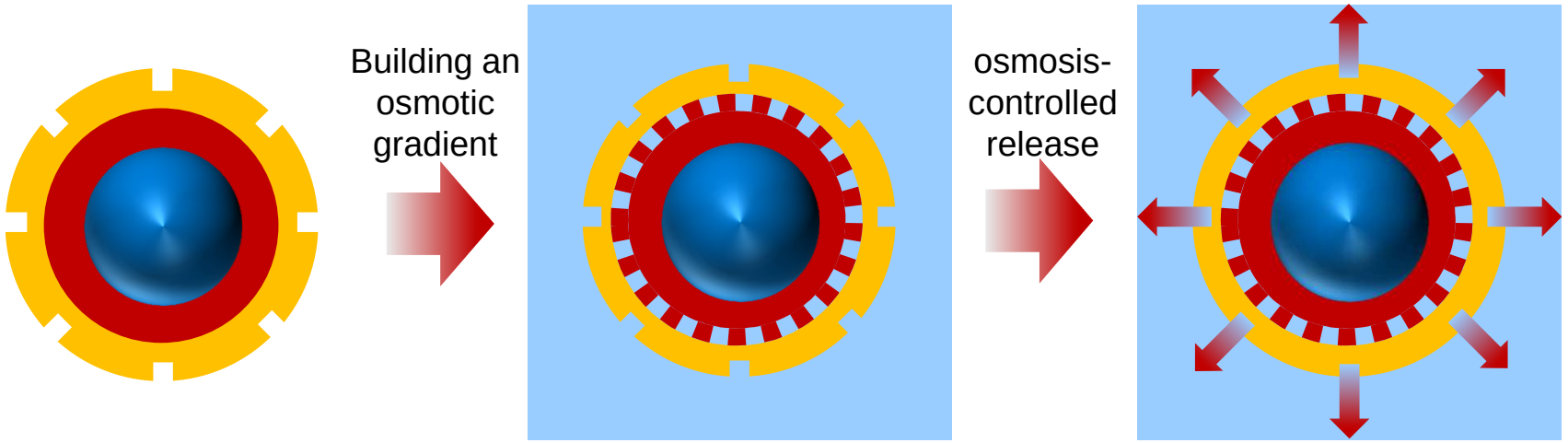


Control drug release by: Diffusion



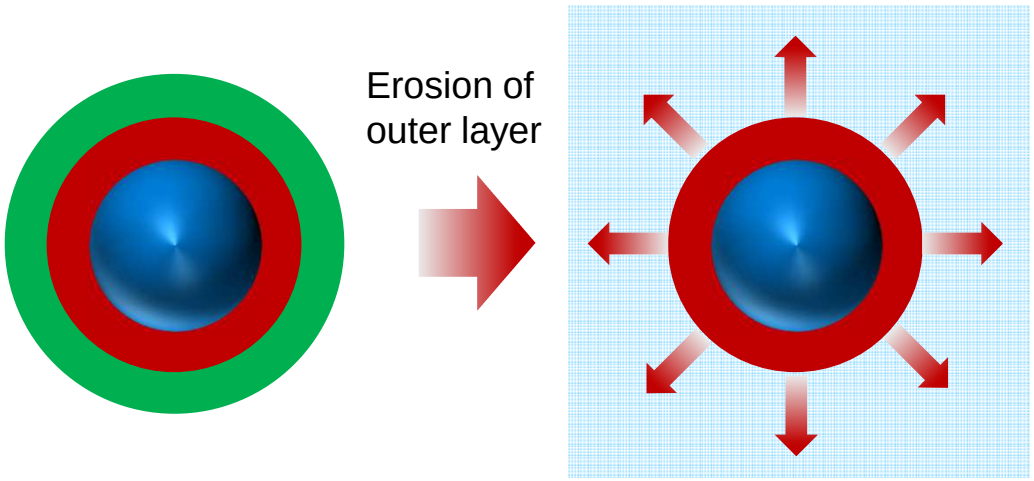
- Membrane permeable for surrounding medium and API
- API decreases if concentration is lower than saturation

Control drug release by: Osmosis



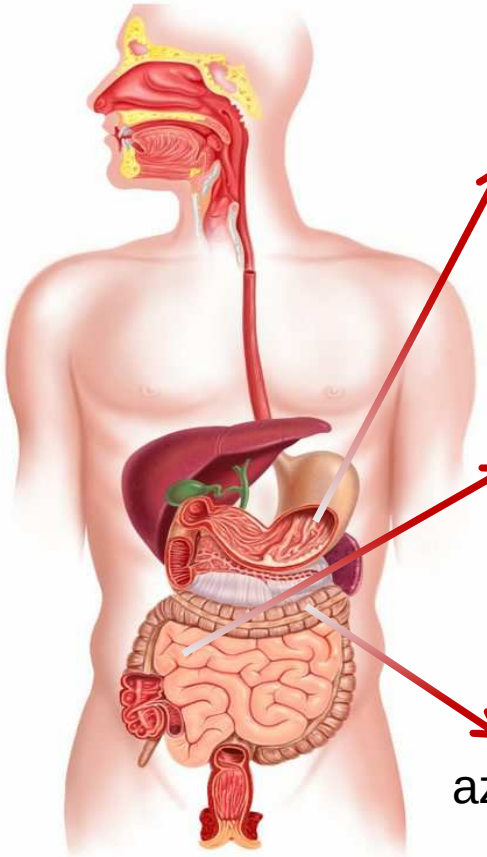
- Membrane permeable for surrounding medium, NOT for API
- API decreases if osmotic pressure decreases with API concentration

Control drug release by: Erosion



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

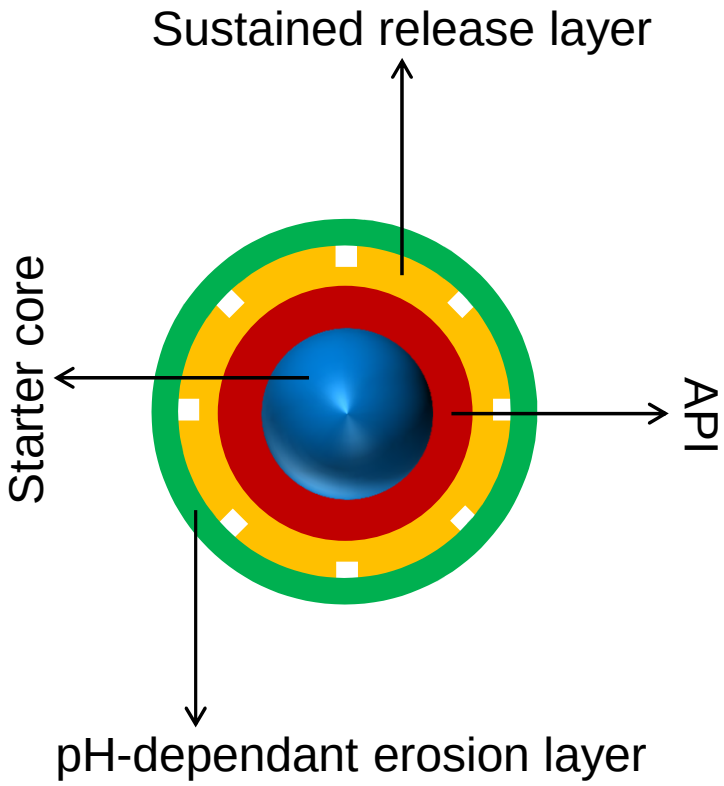
Controlling point of release by Erosion



Stomach
pH ~1.2

Intestine
pH ~8.4

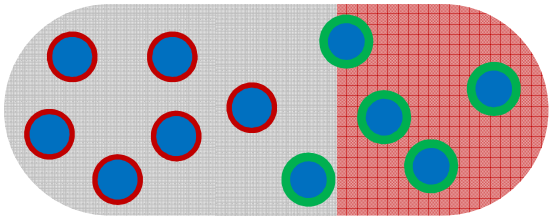
Colon
azoreductases



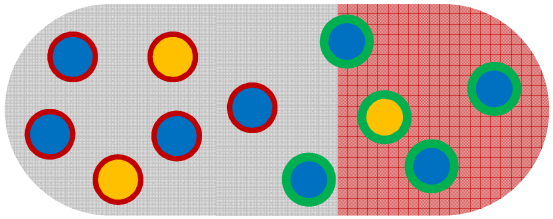
Controlling release profiles by heterogeneous mixtures of multiparticulates

Heterogeneous Multiparticulates

Same API - Different release profiles



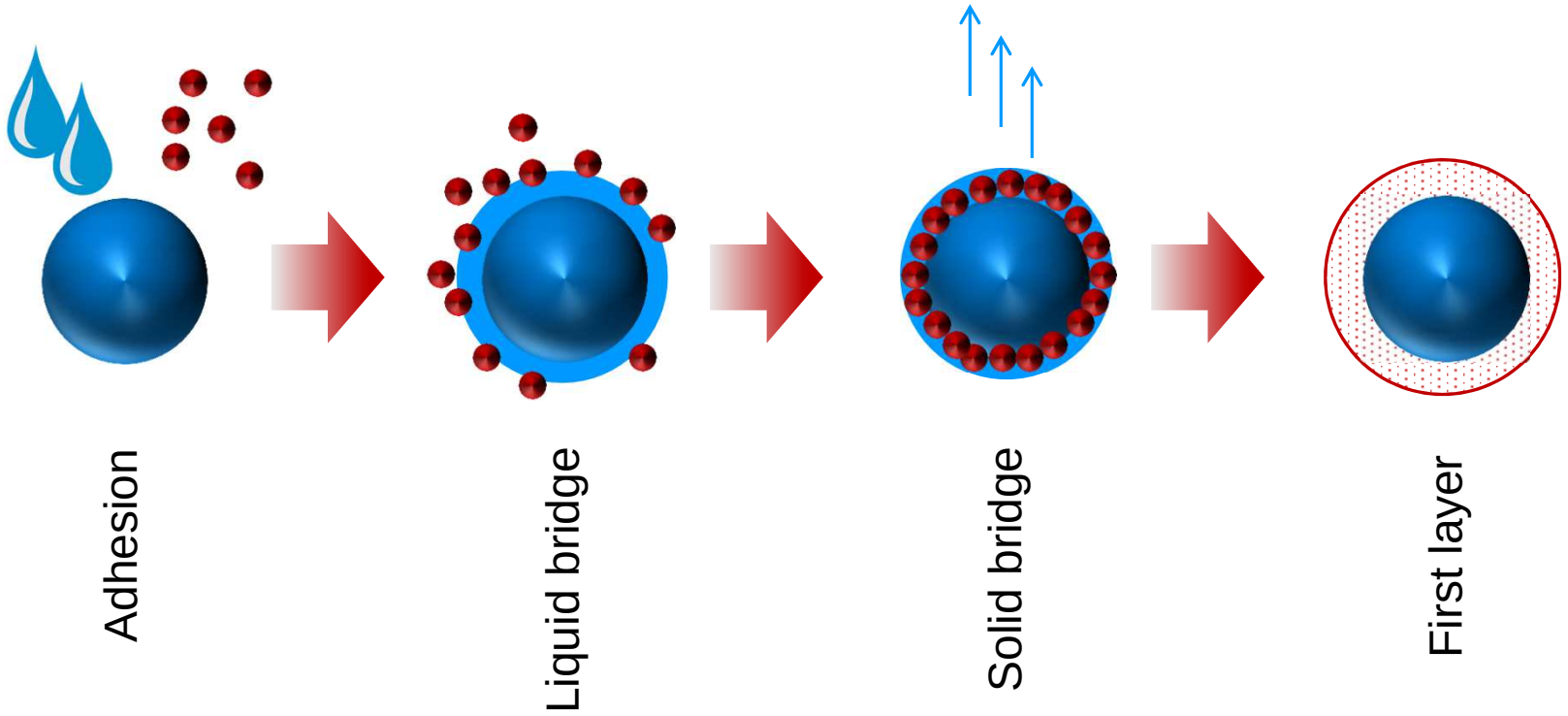
Different API - several release profiles



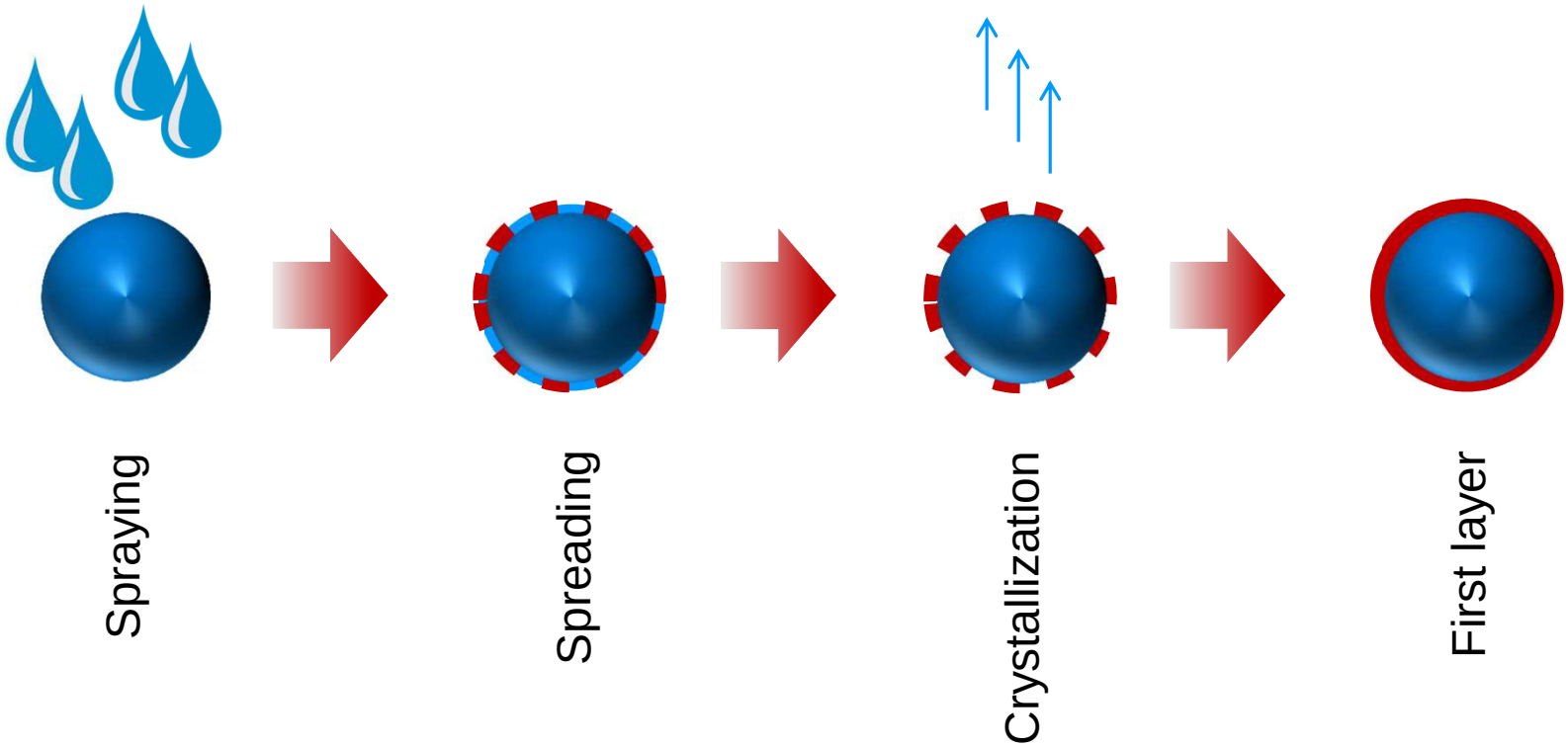
- Multiparticulates with different release profiles can easily be assembled in one capsule

- Even different APIs with different release profiles can be combined this way

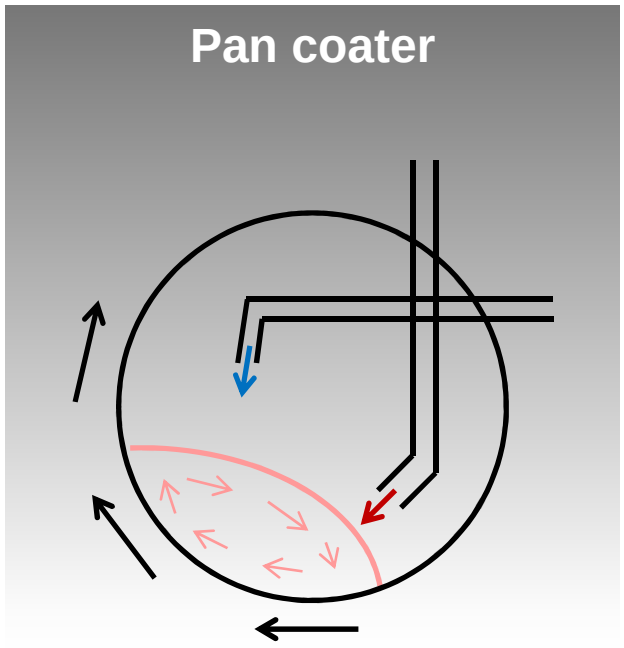
Powder layering

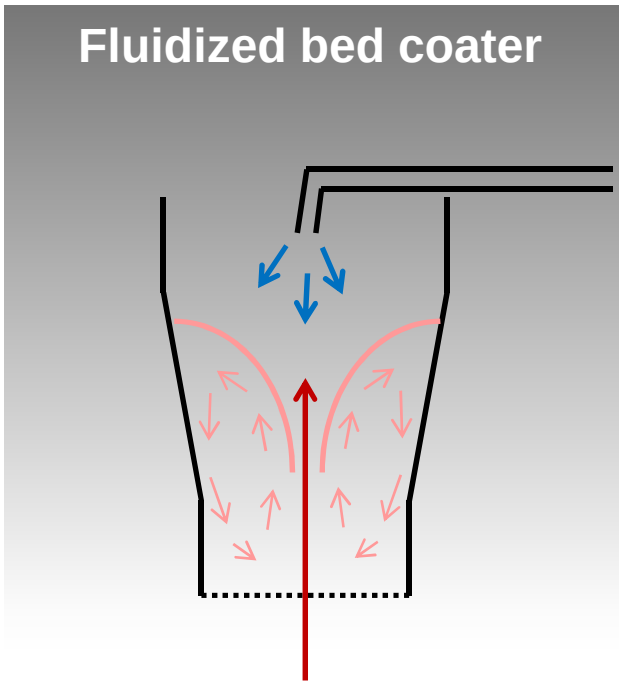


Suspension layering

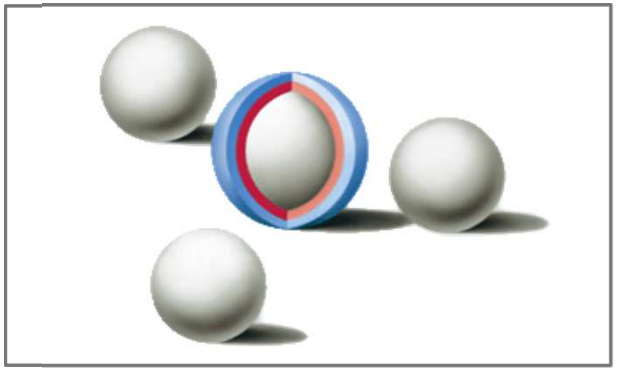


Depending on the required properties of the pellet several coating processes are possible. The most popular are pan coating and fluid bed coating.

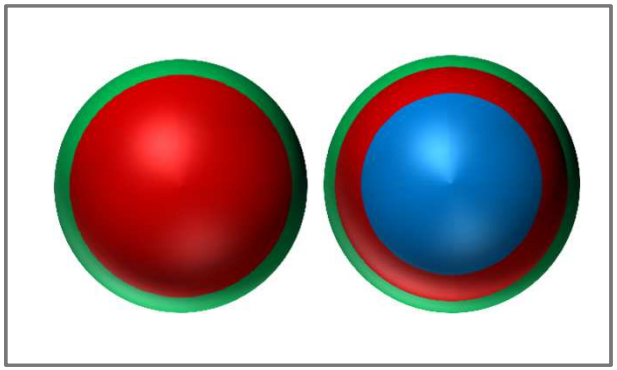




Summary

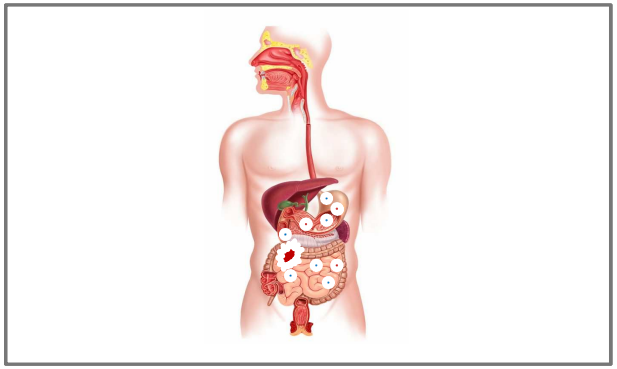


Multiparticulate drug delivery systems are mainly oral dosage forms consisting of a multiplicity of small discrete units, each exhibiting some desired characteristics.

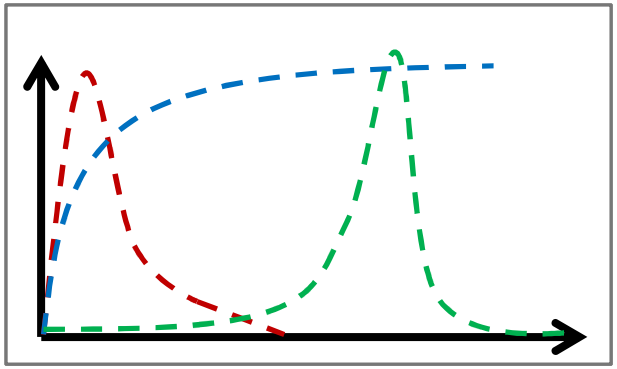


Pellet based systems either consist of matrix pellets or coated starter cores. For several reasons „sugar spheres“ spheres are widely used as starter cores.

Summary

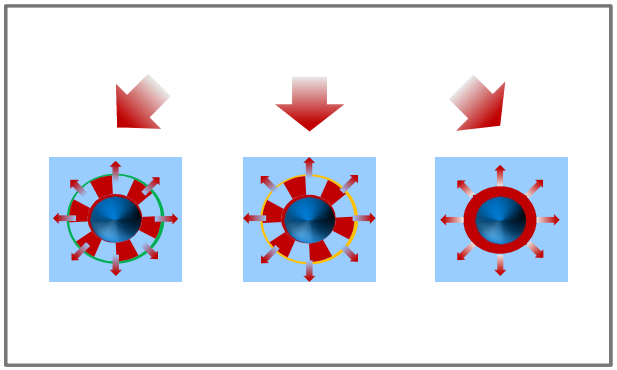


Due to their small size and multiple redundance multiparticulates can greatly improve clinical effectiveness and safety of pharmaceutical formulations

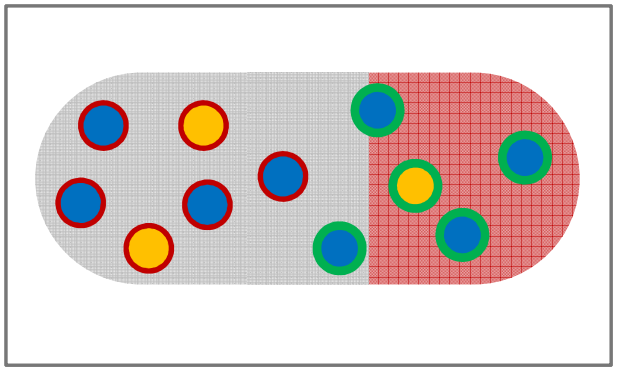


The single most important factor responsible for the proliferation of pelletized products is the popularity of controlled release technology in the delivery of drugs

Summary

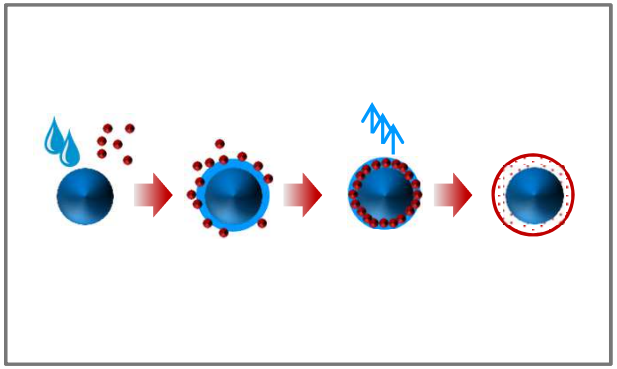


There are different ways to achieve membrane controlled drug release. Most important mechanisms are: Diffusion, osmosis and erosion

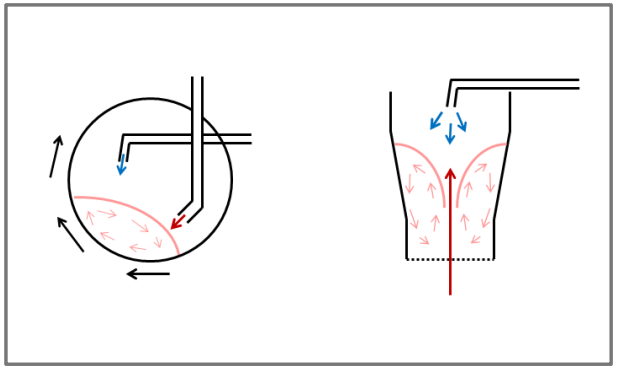


Heterogeneous multiparticulate dosage forms can be utilized to easily achieve complex release profiles of one or several APIs

Summary



Basic mechanisms of coating are powder coating and suspension layering. Whicht o 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

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