PRINCIPLES AND SYSTEMS OF DRUG DELIVERY · SEMINARS 1–2

Drug delivery systems: aims, evolution and classification

Educational program “Pharmacy” · 4th year · Al-Farabi Kazakh National University

After these seminars you will be able to

- Define a dosage form, a drug delivery system (DDS) and a therapeutic system
- Explain the clinical reasons for controlled delivery using a plasma-level curve
- Describe three generations of DDS with marketed examples
- Classify a product by route, release mechanism and release rate
- Use Ph. Eur. terms: prolonged, delayed, pulsatile and modified release
- Name the drug properties that decide whether a DDS is worth making

From dosage form to delivery system

Dosage form

The physical form in which a drug is given: tablet, capsule, ointment, injection.

Goal: correct dose, stability, convenience.

Drug delivery system

A formulation or device that controls the **rate**, **time** or **place** of drug release in the body.

Goal: right amount, right place, right time.

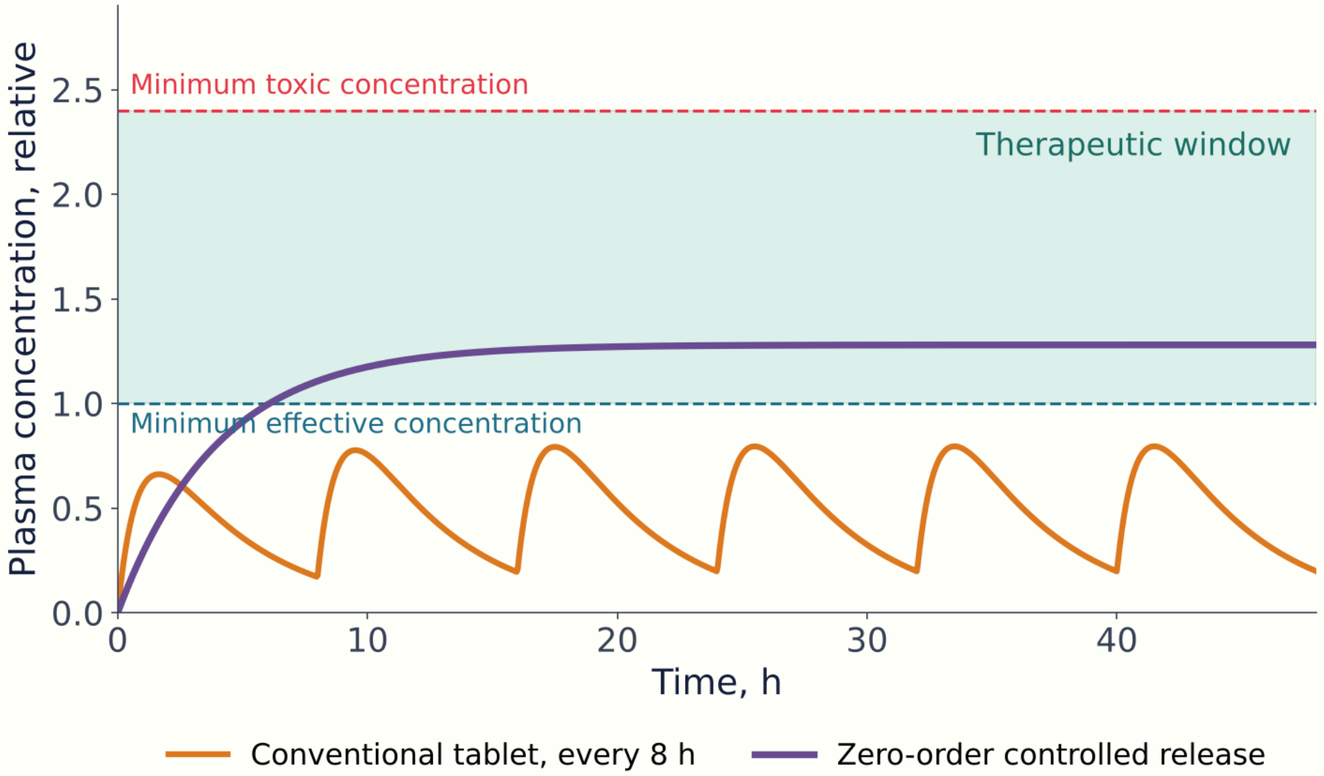
Therapeutic system

A DDS with a defined, pre-programmed release rate over a set period (term introduced by Alza, 1970s).

Example: 7-day estradiol patch.

A DDS has three parts: the **drug**, a **carrier** (polymer, lipid, device) and a **control element** (membrane, matrix, osmotic pump, ligand).

Why control drug release?



Peaks → side effects

Troughs → loss of effect

Flat level → steady effect, fewer doses, better adherence

Most useful when the therapeutic window is narrow and half-life is short.

Seminars 1–2 · Simulated one-compartment model (ka 1.2 h^{-1}, ke 0.25 h^{-1})

Aims of a drug delivery system

Temporal control

Constant or programmed release over hours to years

Spatial control

Drug reaches the target organ, cell or tissue

Protection

Shields peptides, proteins and nucleic acids from enzymes and pH

Adherence

Once daily, weekly or less often; fewer injections

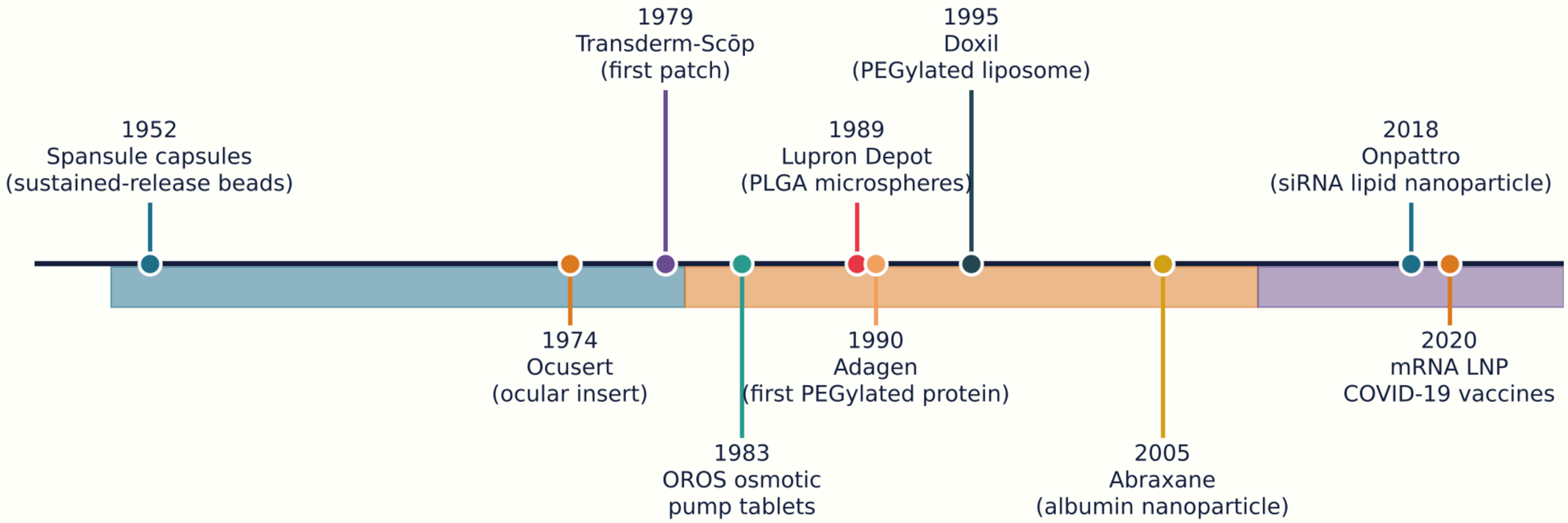
Safety

Lower peaks, less local irritation, lower total dose

Life-cycle value

New product from a known molecule (e.g. once-daily version)

Seventy years of drug delivery



Is a drug a good candidate for a DDS?

Property	Favourable for extended release	Unfavourable
Half-life	2–8 h	< 1 h (huge dose) or > 12 h (no need)
Dose	Small (mg range)	> 0.5–1 g: tablet too large
Solubility	Moderate in GI fluids	Very low (< 0.01 mg/mL) or pH-dependent
Absorption window	Whole GI tract	Upper small intestine only
Therapeutic index	Narrow: benefit from flat levels	—
First-pass effect	Low, or avoided by route	Saturable, dose-dependent

Classification by route of administration

Oral
Matrix, reservoir, osmotic, gastro-retentive, colon-targeted

Parenteral
Microspheres, in situ implants, oily depots, liposomes, nanoparticles

Transdermal
Patches, microneedles, iontophoresis

Pulmonary
pMDI, DPI, nebulizers, soft mist inhalers

Nasal, buccal
Mucoadhesive sprays, films, sublingual tablets

Ocular, otic
In situ gels, inserts, intravitreal implants

Vaginal, uterine
Rings, intrauterine systems

Implants
Subcutaneous rods, pumps, drug-eluting stents

Each route has its own barrier, residence time and maximum dose; these decide which systems are possible.

Classification by release mechanism

Mechanism	How release is controlled	Example
Diffusion: reservoir	Membrane around a drug core	Nicotine patch, Ocusert
Diffusion: matrix	Drug dispersed in polymer; path grows with time	Nexplanon implant
Swelling, erosion	Hydrophilic gel layer or polymer degradation	HPMC tablets, PLGA microspheres
Osmotic	Water influx pushes drug through an orifice	OROS nifedipine (GITS)
Ion exchange	Drug bound to resin, exchanged by ions in GI fluid	Dextromethorphan polistirex
Stimulus-responsive	pH, temperature, enzymes, glucose, light	Enteric coatings, in situ gels

Classification by rate and timing of release

Immediate

Conventional release; usually ≥ 85% dissolved in 30 min

Prolonged

Slower release over a long time; “extended”, “sustained”

Delayed

Release starts later, e.g. enteric-coated tablets

Pulsatile

Sequential pulses after a lag; chronotherapy

The European Pharmacopoeia groups prolonged, delayed and pulsatile release as **modified-release** dosage forms; targeted delivery adds control of **where** the drug goes.

CLASSIFY ONE PRODUCT THREE WAYS

Nifedipine GITS 30 mg: oral · osmotic · prolonged release, zero order for about 24 hours

Now do the same for: an estradiol patch, Lupron Depot, an enteric-coated aspirin tablet.

Questions for discussion

1. What is the difference between a dosage form and a DDS?
2. Why is a drug with a 24-hour half-life a poor candidate for extended release?
3. Name one product from each generation of DDS.
4. What is dose dumping and which systems are at risk?
5. Is an enteric-coated tablet a controlled-release system? Explain.
6. Which route avoids first-pass metabolism and allows release for years?

References

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