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Recently published articles

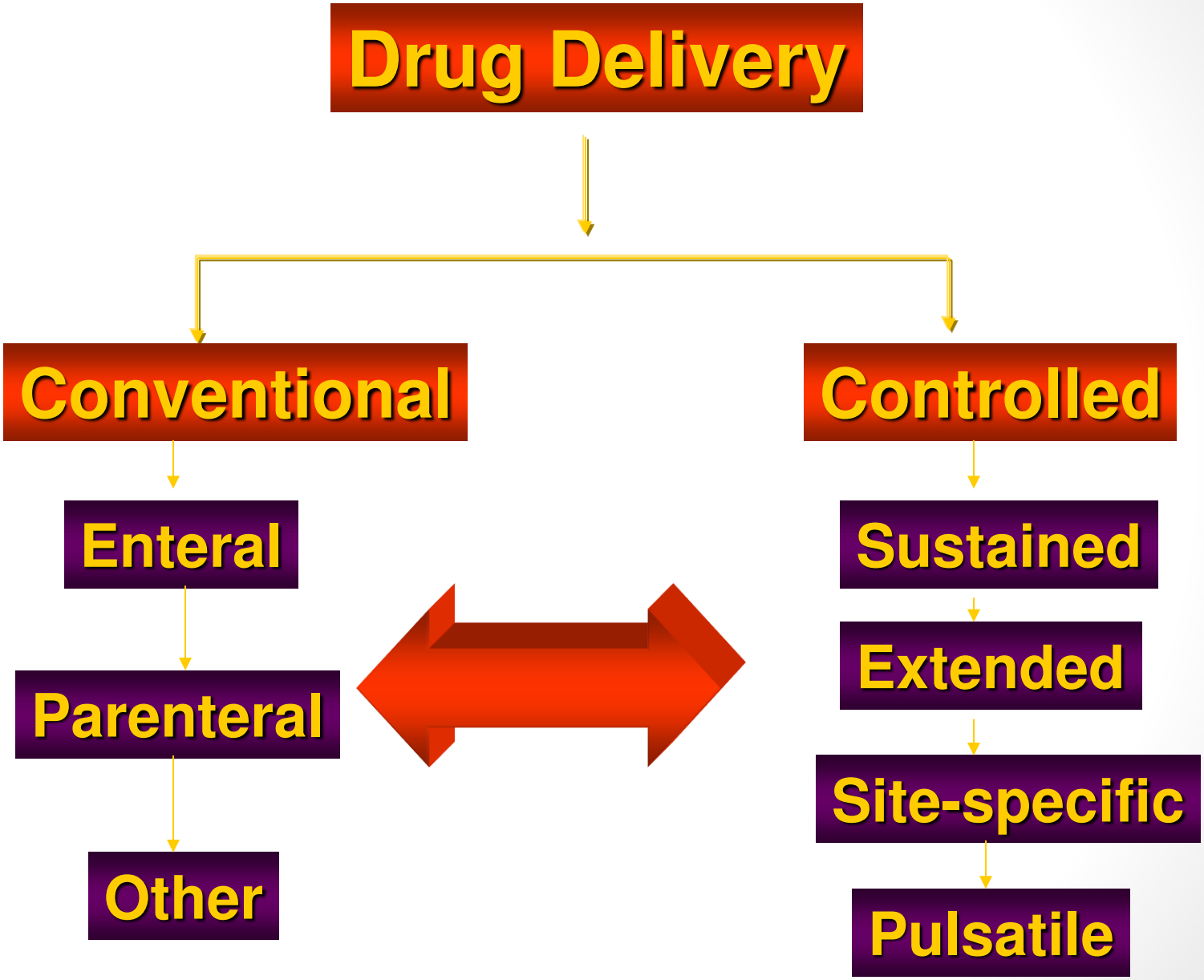
1. Factors Involved in the biochemical etiology of human seminal plasma hyperviscosity
2. Percutaneous drug delivery systems for improving antifungal therapy effectiveness.
3. Pharmaceutical optimization of lipid-based dosage forms for the improvement of taste-masking, chemical stability and solubilizing capacity of phenobarbital.
4. Development, characterization and in vitro evaluation of tamoxifen microemulsions
5. Solubility of amphotericin B in water-lecithin-dispersions and lecithin-based submicron emulsions.
6. Formulation strategies, characterization and *in vitro* evaluation of lecithin-based nanoparticles for siRNA delivery.
7. Polyphenols and antimicrobial activity in extracts of *Lippia alba* (Mill.).
8. An antibody recognizing the apical domain of human transferrin receptor 1 efficiently neutralizes all New World hemorrhagic fever arenaviruses.

Principles of Drug Delivery

Drug Delivery

- **Definition**
  - **The appropriate administration of drugs through various routes in the body for the purpose of improving health**
  - **It is highly interdisciplinary**
  - **It is not a young field**
  - **It has recently evolved to take into consideration**
    - **Drug physico-chemical properties**
    - **Body effects and interactions**
    - **Improvement of drug effect**
    - **Patient comfort and well being**

Controlled Drug Delivery


Drug Delivery
Conventional
Controlled
Enteral
Parenteral
Other
Sustained
Extended
Site-specific
Pulsatile

Oral Administration

- Advantages
  - Patient: Convenience, not invasive, higher compliance
  - Manufacture: well established processes, available infrastructure
- Disadvantages
  - Unconscious patients cannot take dose
  - Low solubility
  - Low permeability
  - Degradation by GI enzymes or flora
  - First pass metabolism
  - Food interactions
  - Irregular absorption

Oral Administration

- Traditional oral delivery systems
  - Tablets
  - Capsules
  - Soft gelatin capsules
  - Suspensions
  - Elixirs

Buccal/Sublingual

- Advantages
  - By-pass First pass metabolism
  - Rapid absorption
  - Low enzymatic activity
- Disadvantages
  - Discomfort during dissolution
  - Probability of swallowing- lost of effect
  - Small doses

- Traditional delivery system/devices
  - Tablets
  - Chewing gum

Rectal

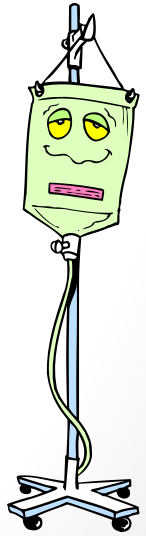
- Advantages
  - By-pass first pass metabolism
  - Useful for children
- Disadvantages
  - Absorption depends on disease state
  - Degradation by bacterial flora
  - Uncomfortable

- Traditional delivery system/devices
  - Suppository
  - Enema

Intravenous (IV)

- **Advantages**
  - **Drug 100% bioavailable**
  - **Rapid response**
  - **Total control of blood concentration**
  - **Maximize incorporation of degradable drugs**
  - **By-pass FPM**
- **Disadvantages**
  - **Invasive**
  - **Trained personnel**
  - **Possible toxicity due to incorrect dosing**
  - **sterility**

- Traditional delivery system/devices
  - Injection-bolus
  - IV bag - infusion



Subcutaneous

- Advantages
  - Patient self-administration
  - Slow, complete absorption
  - By-pass FPM
- Disadvantages
  - Invasive
  - Irritation, inflammation
  - Maximum dose volume - 2mL

Intramuscular

- Advantages
  - Patient can administer the drug himself
  - Larger volume than subcutaneous
  - By-pass first pass metabolism
- Disadvantages
  - Invasive – patient disconfort
  - Irritation, inflamation
  - May require some training

Inhalers

- Advantages
  - By-pass FPM
  - Gases are rapidly absorbed
- Disadvantages
  - Solids and liquids can be absorbed if size is below 0.5um

Transdermal

- Advantages
  - Local effect
  - Ease of administration
- Disadvantages
  - Low absorption for some drugs
  - May cause allergic reactions

- Requirements
  - Low dosage <10 mg/mL
  - MW< 1,000

Factors Influencing the Selection of the Delivery Route

- Drug physico-chemical properties
  - **Drug molecular size (molecular weight)**
  - **Half-life**
  - **Chemical stability**
  - **Loss of biological activity in aqueous solution**
    - **Proteins**
      - **Denaturation, degradation**

Factors Influencing the Selection of the Delivery Route

- **Solubility in aqueous solution (hydrophobicity/hydrophilicity)**
  - **pH**
  - **pKa - ionization**
  - **Temperature**
  - **Concentration**
  - **Crystalinity**
  - **Particle size**
  - **State of hydration**

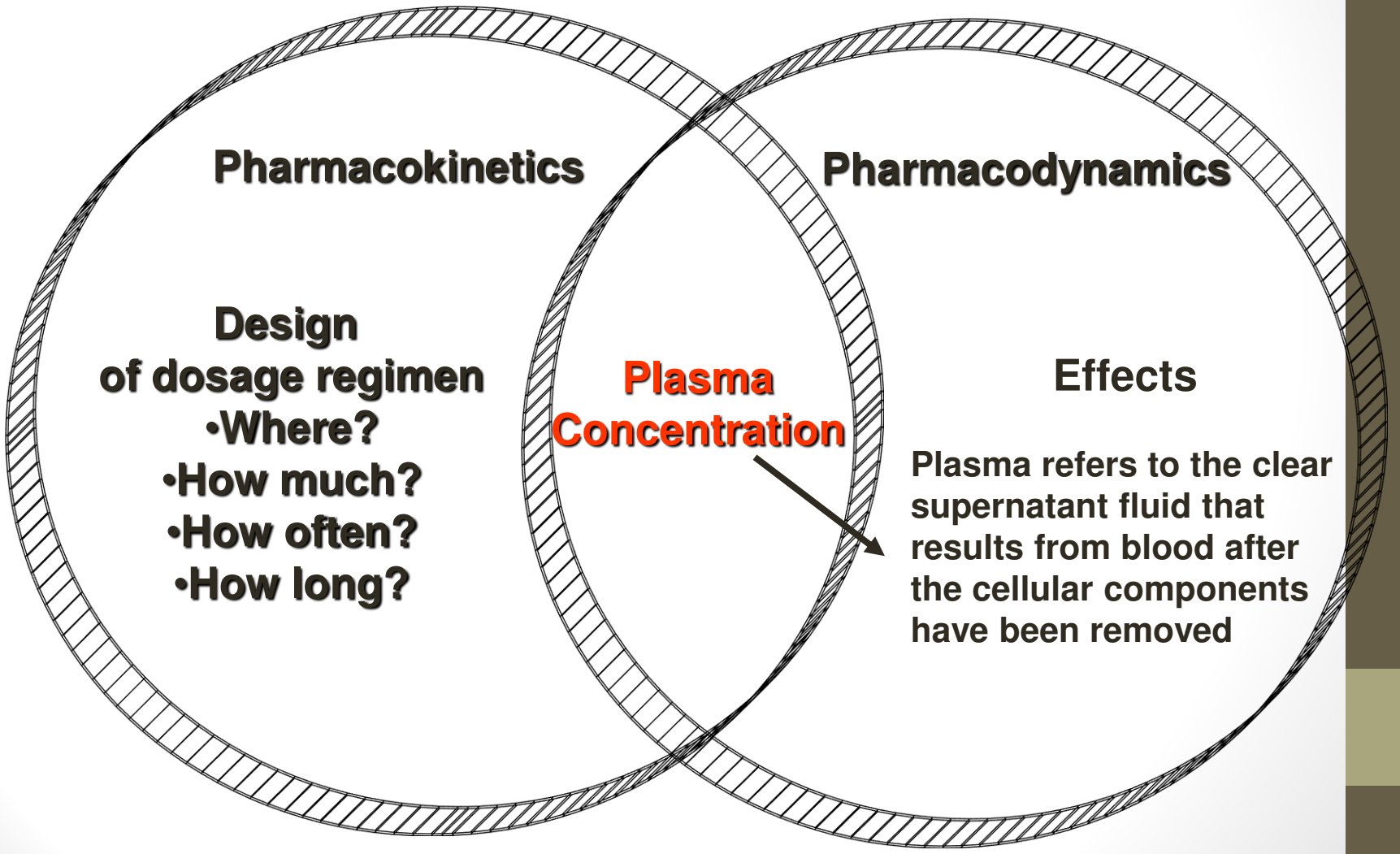
Factors Influencing the Selection of the Delivery Route

- Drug biological interactions
  - **Sensitive to FPM**
  - **Low membrane permeabiltiy**
    - **Efflux pumps (MRP, MDR) – cancer drugs**
    - **Hydrophilicity**
    - **High-density charge**
  - **Enzymatic degradation**
  - **Bacterial degradation**
  - **Half-life**
  - **Side effects**
    - **Irritation**

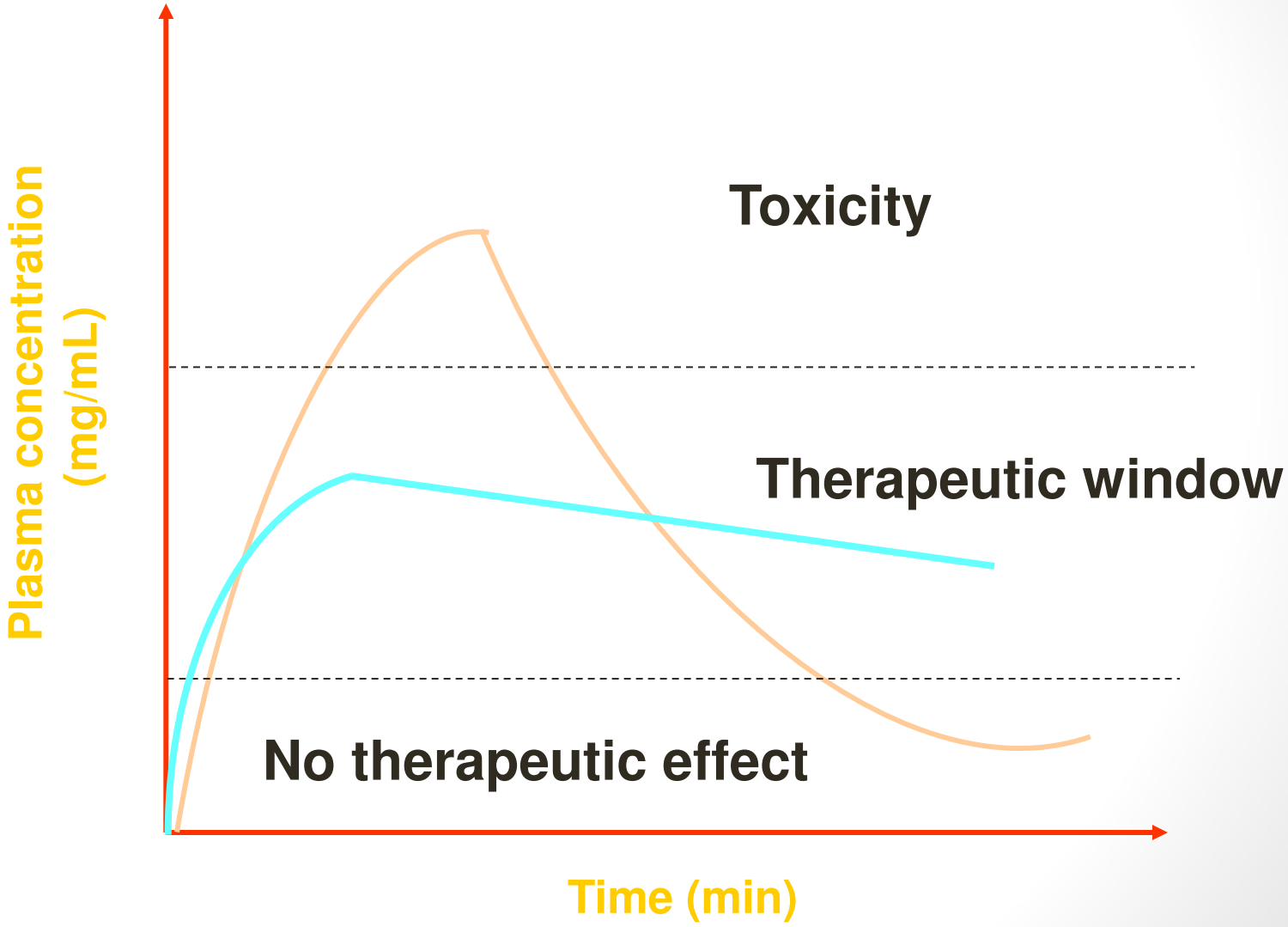
Factors Influencing the Selection of the Delivery Route

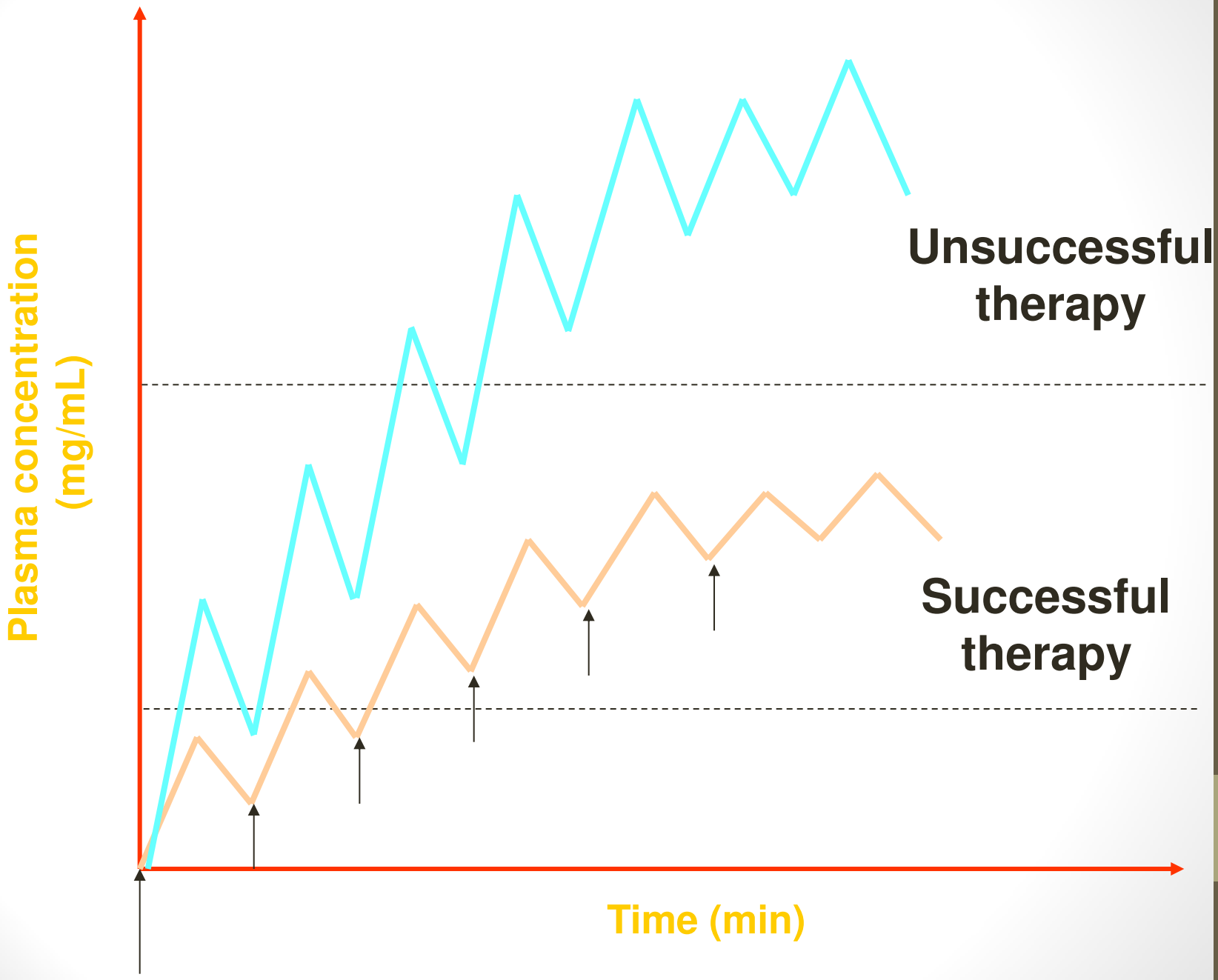
- Desired pharmacological effect
  - **Local**
    - **topical, vaginal**
  - **Systemic**
    - **oral, buccal, IV, SC, IM, rectal, nasal**
  - **Immediate response**
    - **IV, SC, IM, nasal**
  - **Dose size**
  - **Drug molecular size**

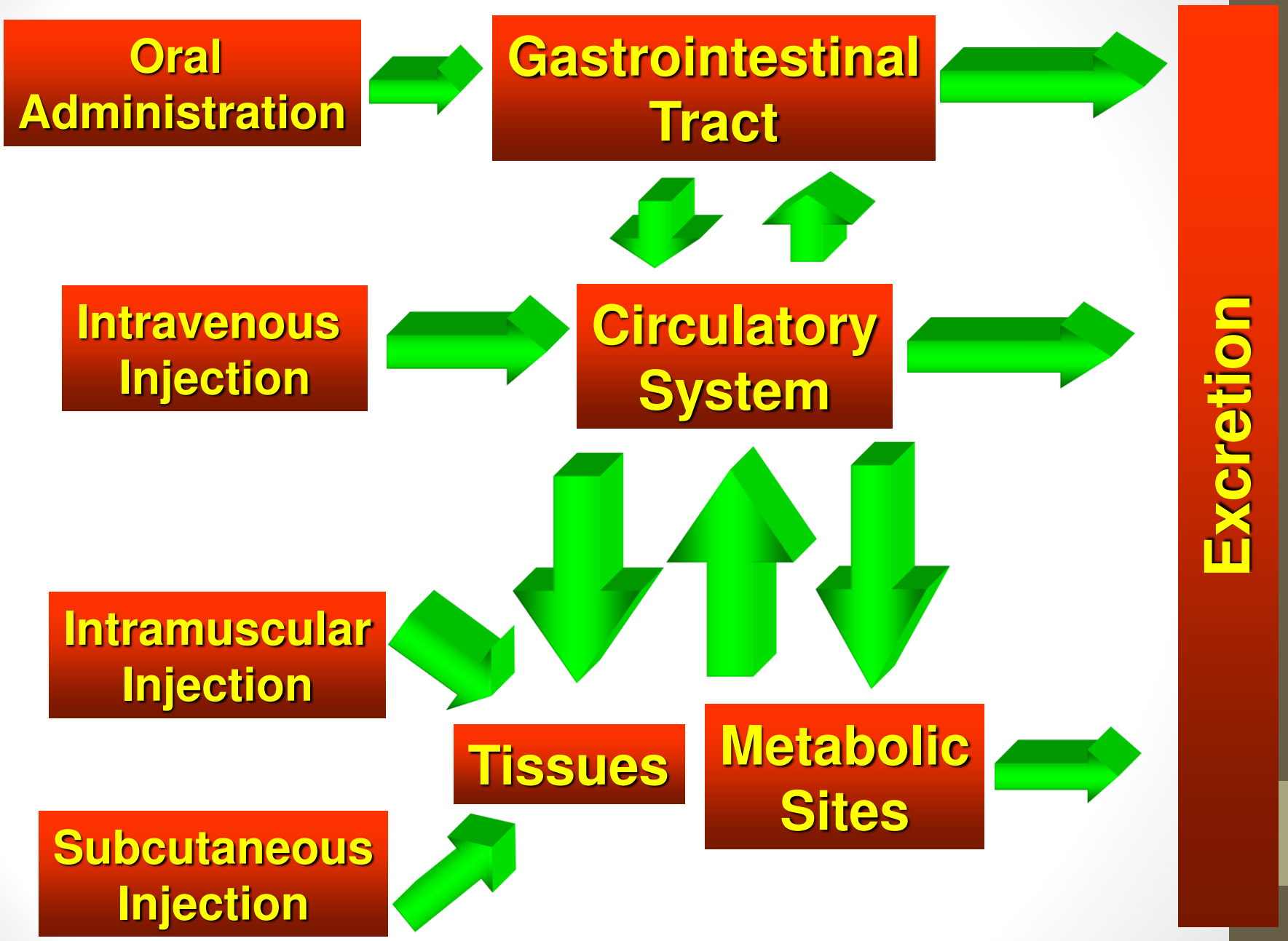
Pharmacokinetics and Pharmacodynamics



Plasma Concentration



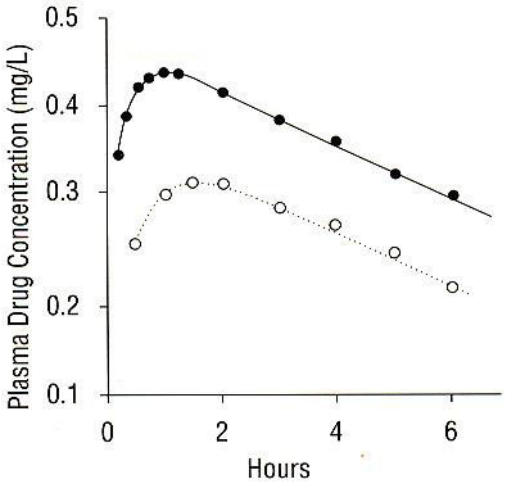

Plasma concentration (mg/mL)
Unsuccessful therapy
Successful therapy
Time (min)


Oral Administration
Gastrointestinal Tract
Excretion
Intravenous Injection
Circulatory System
Intramuscular Injection
Tissues
Metabolic Sites
Subcutaneous Injection

Absorption of drugs could vary within different administration routes

- 500 mg dose given
  - intramuscularly
  - orally

**to the same subject on separate occasions



- Biological barriers greatly affect the extent of drug absorption

Journal of Nanomedicine & Biotherapeutic Discovery

- Journal of Nanomedicine & Biotherapeutic Discovery
- Journal of Nanomedicine & Nanotechnology

Journal of Nanomedicine & Biotherapeutic Discovery

- International Conference on Nanotek & Expo
- International Conference on Signal Processing

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