Dosage Form Design: Biopharmaceutical and Pharmacokinetic Considerations

Summarized by Dr. Mazen Rajab

Ref. Pharmaceutical dosage forms and drug delivery systems, Ansel's 9th ed 2011 pp 143-183

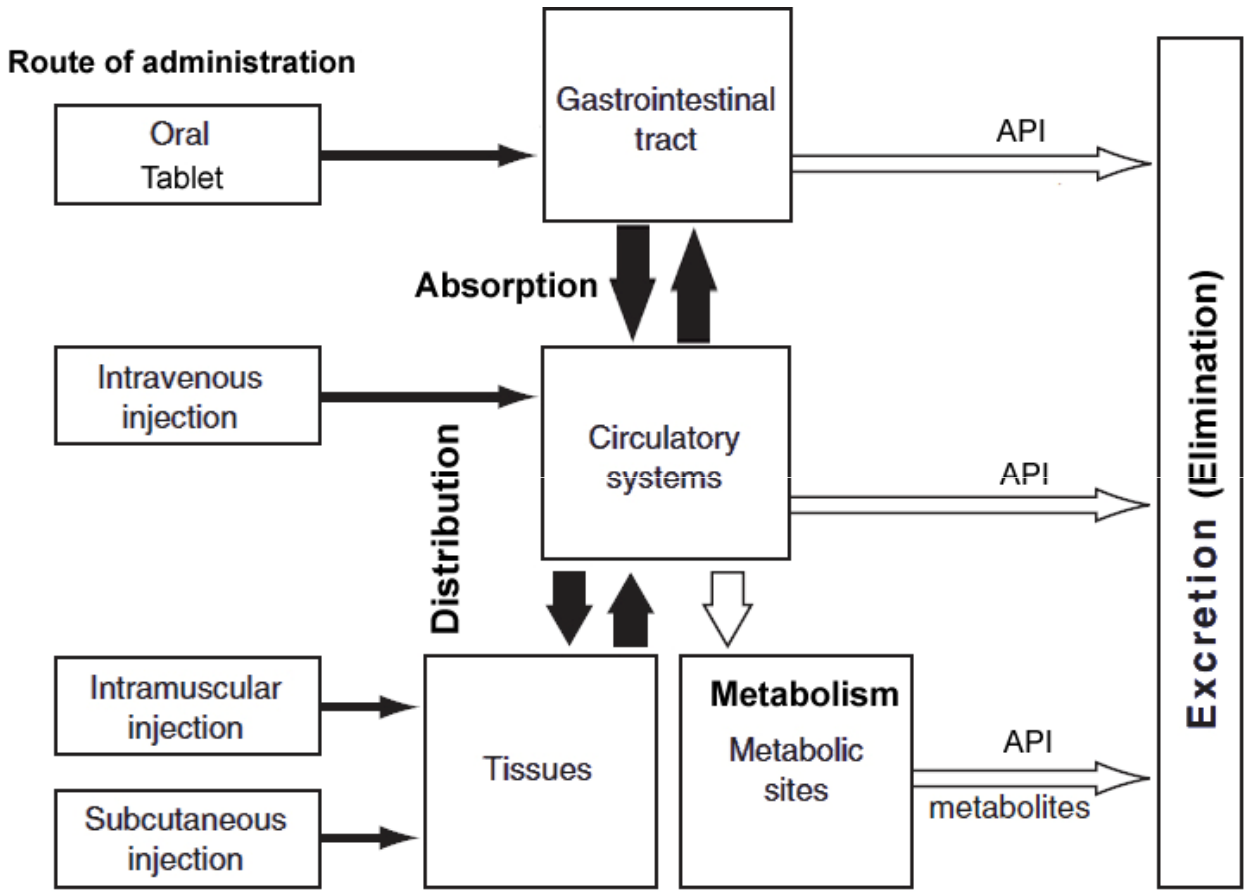
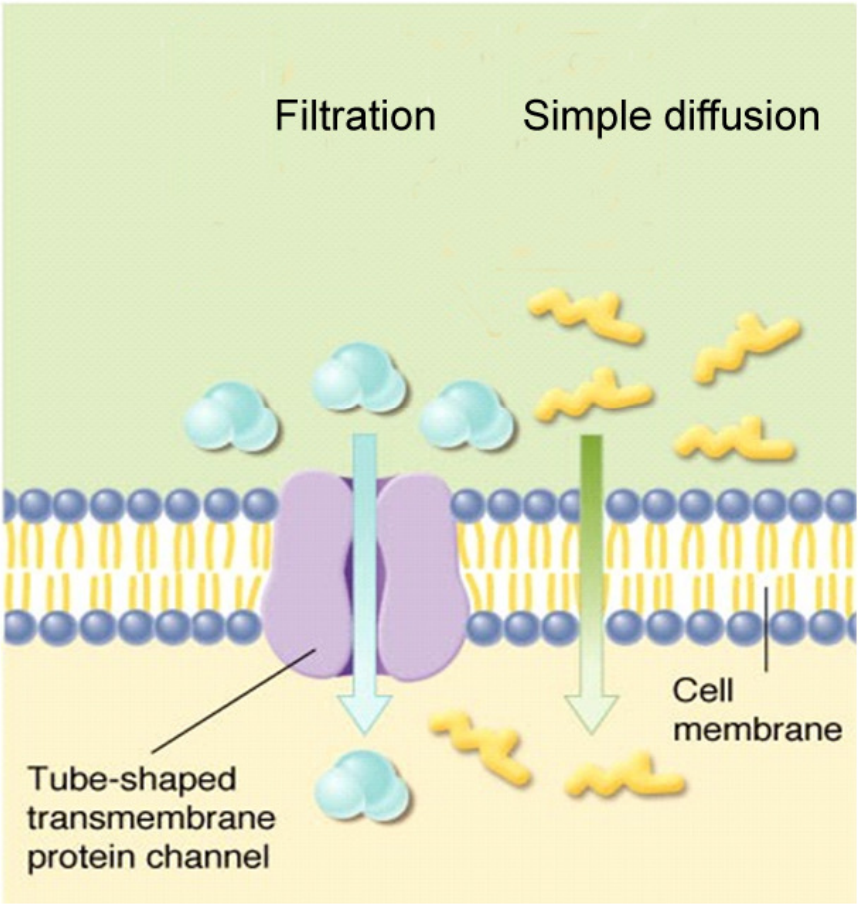
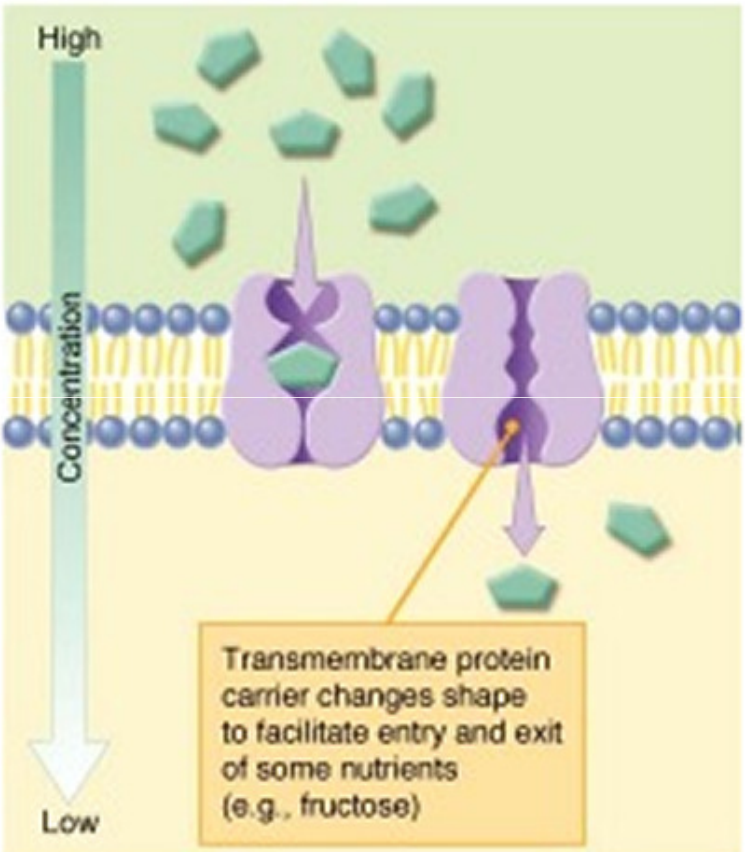


FIGURE 5.1 Events of absorption, metabolism, and excretion of drugs after their administration

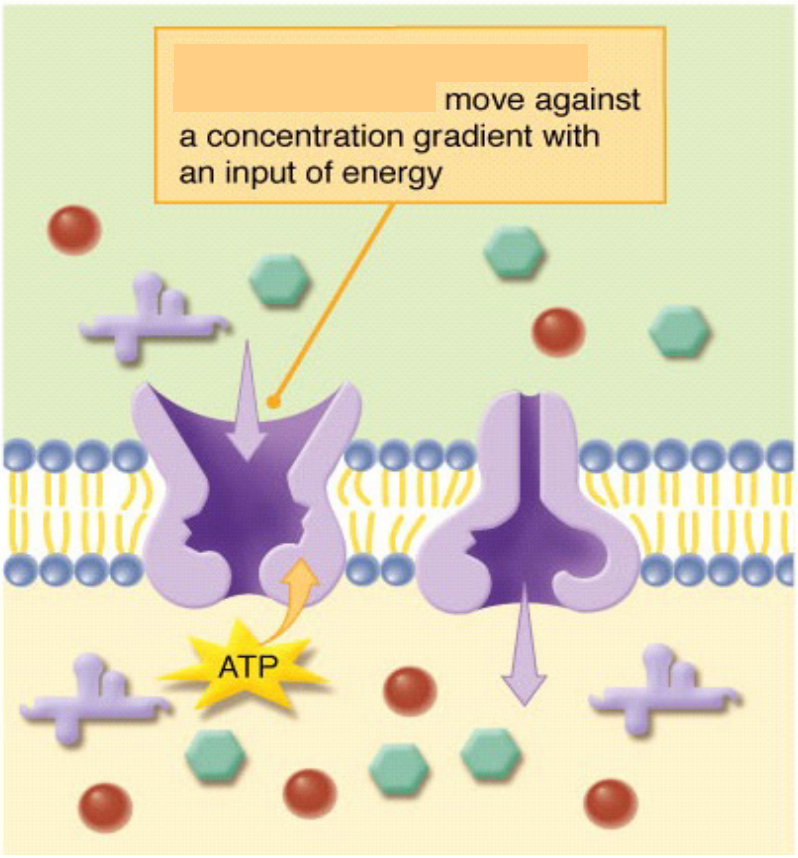
PASSIVE DIFFUSION



FACILITATED DIFFUSION



ACTIVE TRANSPORT



API absorption mechanisms

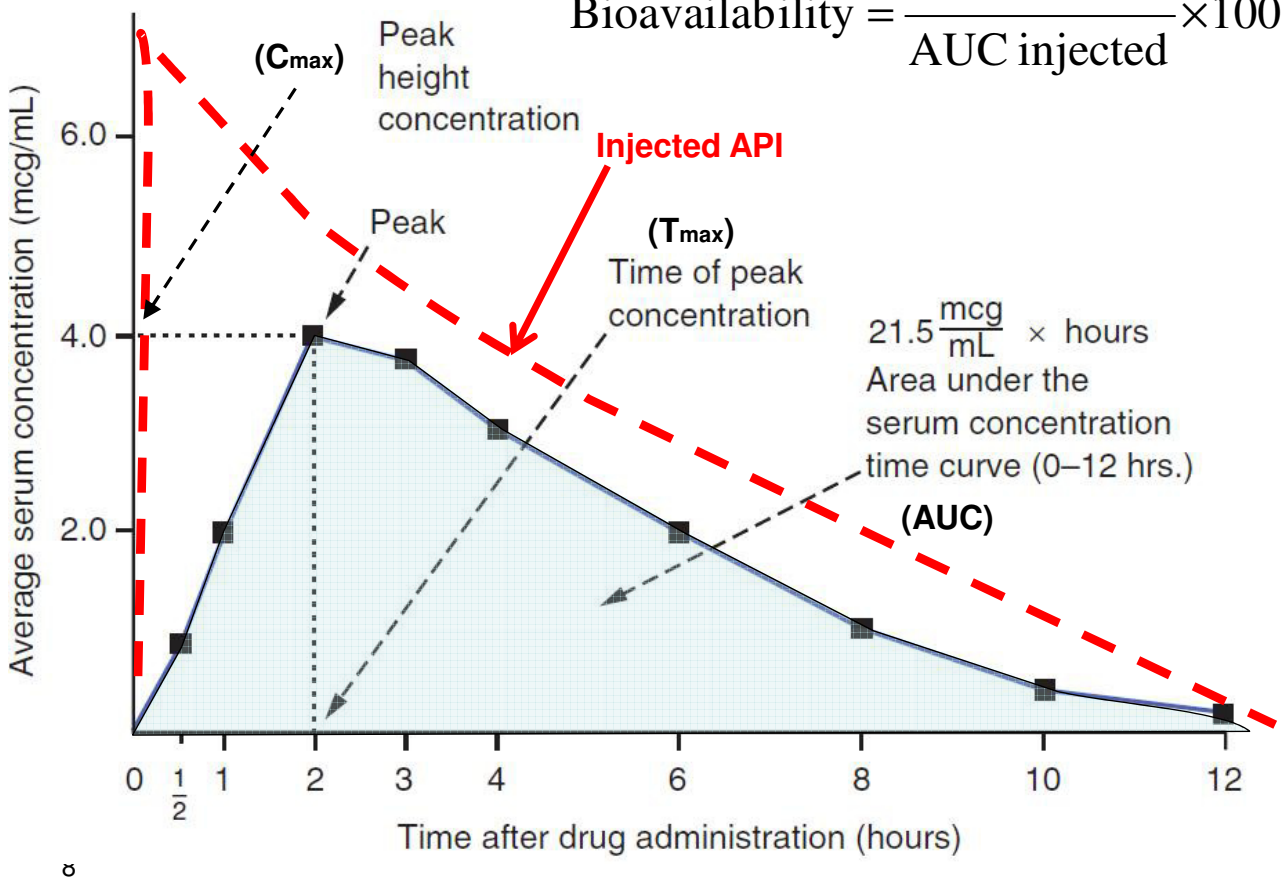
- Passive transfer **(without carriers)**
  - Simple diffusion: 90% of API, Fick's first law, Membrane permeability, hydrophobic molecules, Concentration gradient, **(Erythromycin base)**
  - Filtration: Hydrostatic or the osmotic pressure, Aqueous pores (4-40 A°), molecules sizes, Concentration gradient, **(Water, ethanol)**
- Specialized transport **(with carriers)**

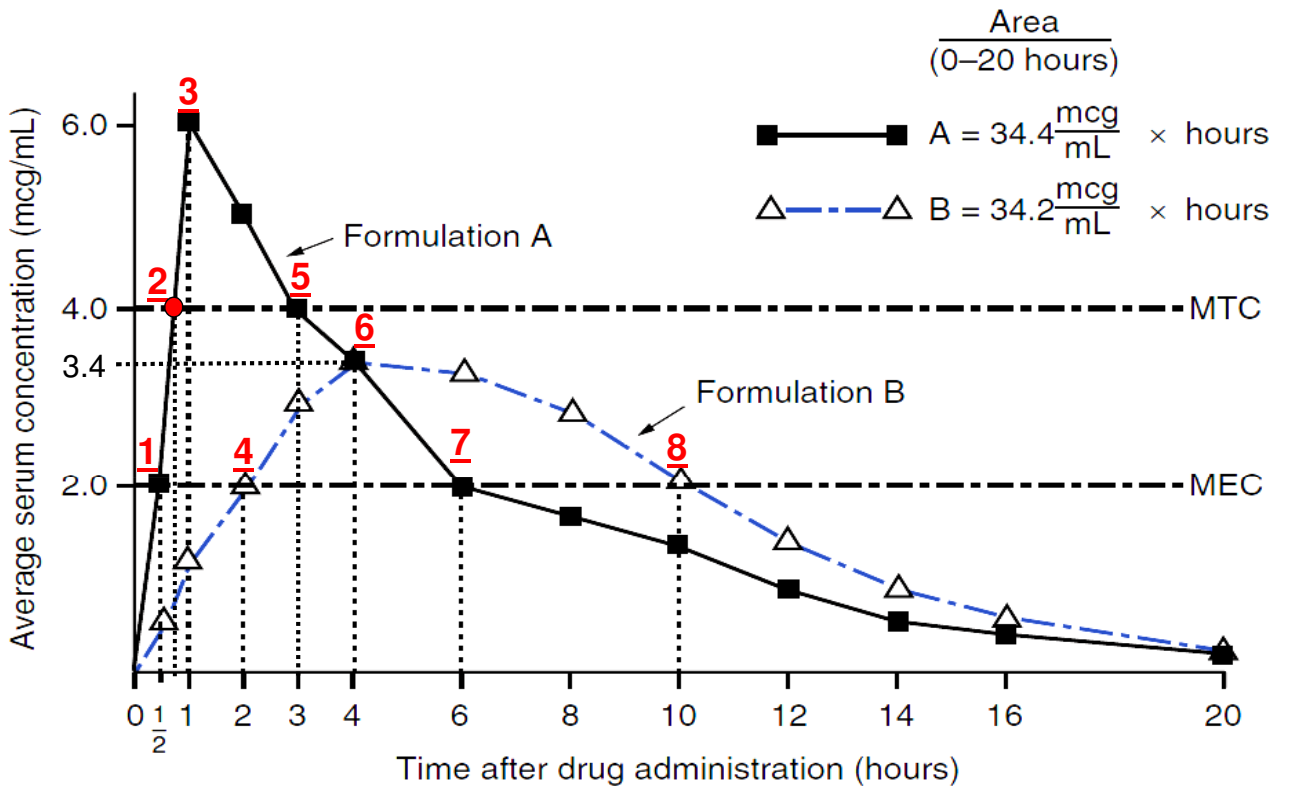
  Influenced by carrier (protein) specificity and amount
  - Facilitated diffusion: Concentration gradient **(sugars, amino acids)**
  - Active transport: **No Concentration gradient, energy is required**, **(thiamine, methyldopa, K^+, Ca^{++}, Na^+)**

Bioavailability and bioequivalence

- **Bioavailability:** is the rate and extent to which an API is absorbed from a drug product and becomes available at the site of action.
- **Bioequivalence:** is the comparison of bioavailabilities of different formulations, drug products or batches of the same drug product.

$$\text{Bioavailability} = \frac{\text{AUC oral}}{\text{AUC injected}} \times 100$$

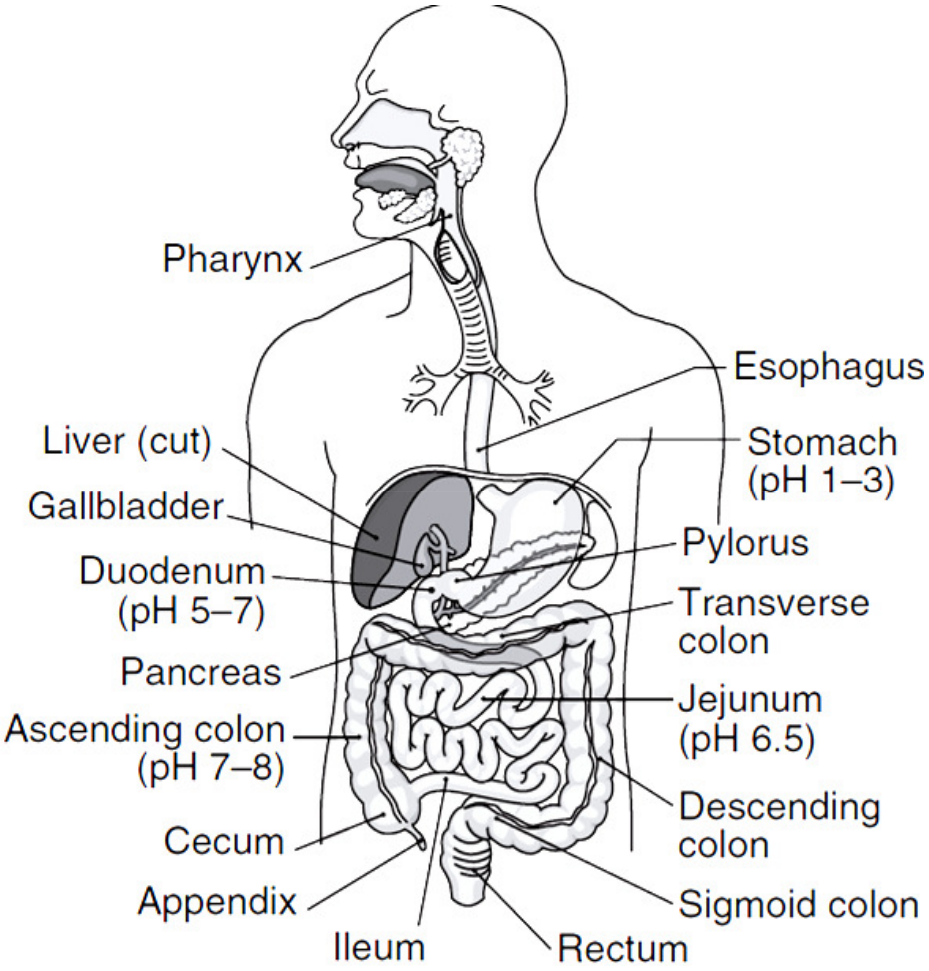




(1) For (A), time to reach MEC is ½ h.
(2) For (A), time to reach MTC is near ¾ h.
(3) For (A), peak T_{max}=1 h, C_{max}=6 mcg/mL
(4) For (B), time to reach MEC is 2 h
(5) For (A), time to go under MTC is 3 h
(6) For (B), peak T_{max}=4 h,C_{max}=3.4 mcg/mL
(7) For (A), time to go under MEC is 6 h
(8) For (B), time to go under MEC is 10 h

Factors that influence bioavailability of oral drugs

- **API physiochemical properties**
  - Particle size
  - Crystalline or amorphous form
  - Salt form
  - Hydration
  - Lipid or water solubility
  - pH and pKa
- **Excipients**
  - Fillers
  - Binders
  - Coatings
  - Disintegrating agents
  - Suspending agents
  - Surface active agents
  - Flavoring, Coloring agents
  - Preservative agents
  - Stabilizing agents
- **Dosage form characteristics**
  - Disintegration rate (tablets)
  - Dissolution time of dosage form
  - Product age and storage conditions
- **Physiologic factors and patient characteristics**
  - Gastric emptying time
  - Intestinal Transit Time
  - Gastrointestinal abnormality or pathologic condition
  - Gastric contents
  - Other drugs
  - Food
  - Fluids
  - Gastrointestinal pH
  - Drug metabolism (gut and during first passage through liver).



Route of administration and delivery system of primary dosage forms (Part 1/4)

Oral	Tablets
	Capsules
	Solutions
	Syrups
	Elixirs
	Suspensions
	Magmas
	Gels
	Powders
Sublingual	Tablets
	Troches, lozenges
	Drops (solutions)

Route of administration and delivery system of primary dosage forms (Part 2/4)

Conjunctival	Contact lens inserts
	Ointments
Intraocular, intra-aural	Solutions
	Suspensions
Intranasal	Solutions
	Sprays
	Inhalants
	Ointments
Intrarespiratory	Aerosols

Route of administration and delivery system of primary dosage forms (Part3/4)

Epicutaneous, transdermal	Ointments
	Gels
	Creams
	Infusion pumps
	Pastes
	Plasters
	Powders
	Aerosols
	Lotions
	Transdermal patches, discs.
	Solutions
Parenteral	Solutions
	Suspensions

Route of administration and delivery system of primary dosage forms (Part4/4)

Rectal	Solutions
	Ointments
	Suppositories
	Gels
Vaginal	Solutions
	Ointments
	Emulsion foams
	Gels
	Tablets
	Inserts, suppositories, sponge
Urethral	Solutions
	Suppositories