# Transportation Across Biological Membrane (Drug Absorption)

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## Contents of the Lecture:

- Cell Membrane
- Drug Absorption
- Transportation Mechanism

# Biological Membrane

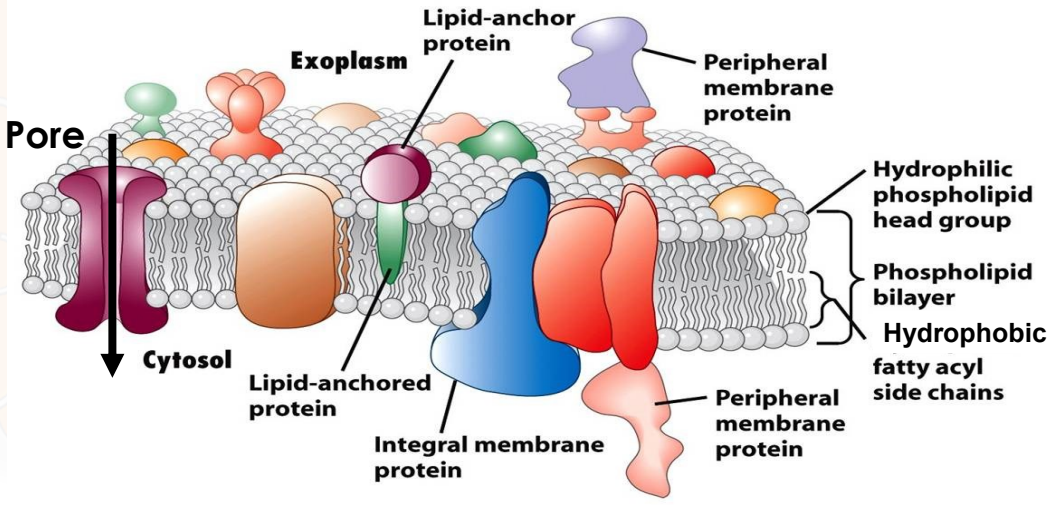


Figure 10-1
*Molecular Cell Biology, Sixth Edition*


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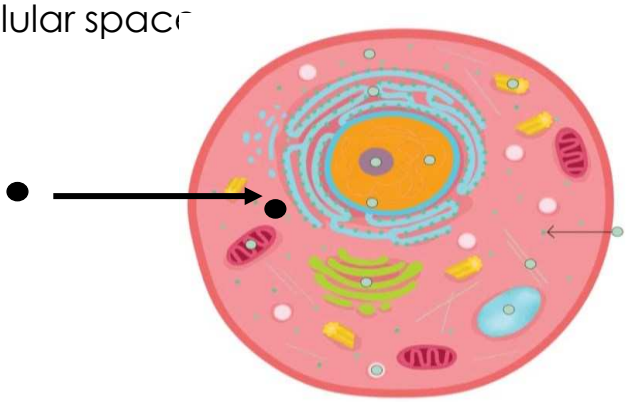
# Trasportation

- **Transportation:** movement of substances from Extracellular space to Intracellular space



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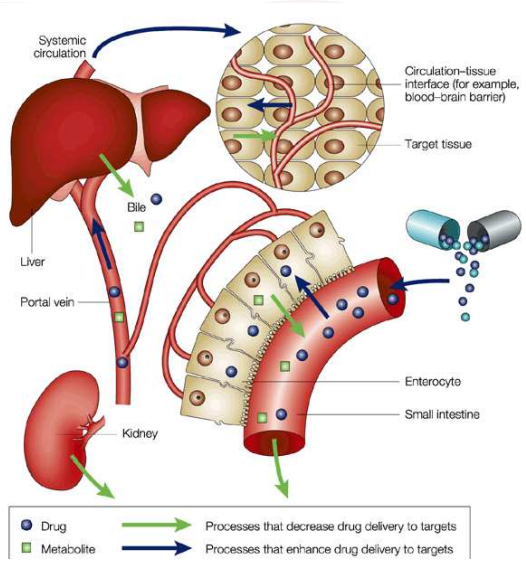
# Drug Absorption

- **Drug Absorption**: The absorption is the **transportation** of the drug across the biological membranes into systemic circulation via portal vein.

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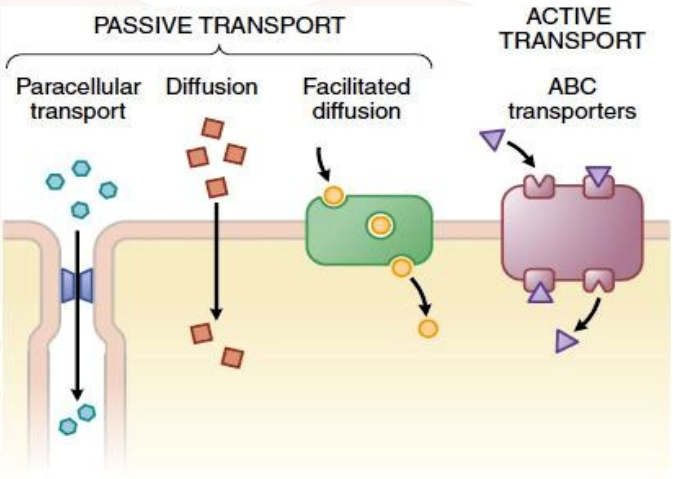
# Transport Mechanism

**Transportation Mechanism**

- Passive (simple) diffusion
- Filteration/pore/paracellular
- Carrier Mediated Transport System
  - Facilitated diffusion
  - Active transport
- Electrochemical/ionic diffusion
- Ion pair transport.
- Endocytosis: Phagocytosis & Pinocytosis

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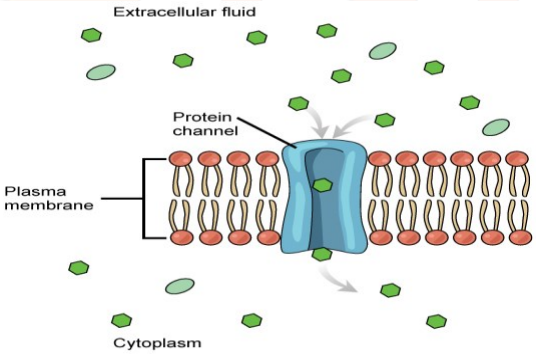
# Transport Mechanism

## 1. Filtration/pore/paracellular

- **highly water-soluble drugs** across via the **aqueous pores (4 A°)** found on the cell membrane (i.e. caffeine, ascorbic acid, acetylsalicylic acid, nicotinamide, urea, glucose).

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# Transport Mechanism

## 1. Filtration/pore/paracellular

- Aqueous pores **do not** play a major role in the transportation of the drugs across the cell membrane.
- Mol. Wt should less then 100 Dalton.
- In case of capillaries (like kidney, Liver), pore size is extent to 40 A° to filter large molecules.
- Capillary absorption/filteration is important on Renal excretion, removal of drug from CSF, and entry of drug into lever.

**Rate of Filtration = N $R^2$ A (dC)/η h**

N = no. of pores; R = radius; A = area; dC = conc. Gradient; η = viscosity; h = thicknes

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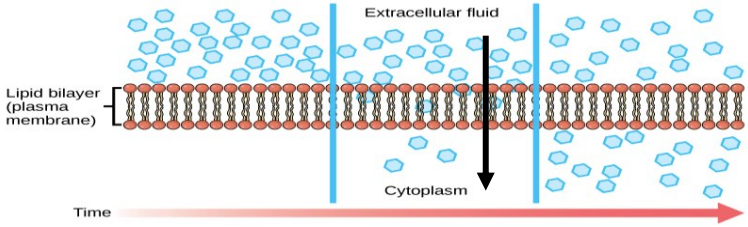
# Transport Mechanism

## 2. Passive (simple) diffusion

- The major role for the transportation of the **lipid soluble drugs** across the cell membrane is simple (passive) diffusion.
- The substances move across a membrane according to a concentration gradient (High to Lower; Downhill direction).
- **The concentration gradient** and the **lipid solubility** of the drug are the two main factors that determine the diffusion rate (speed) of the drug.
- **Energy Independent**.
- **There is no special transport (carrier) protein**.
- **No saturation**

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# Transport Mechanism

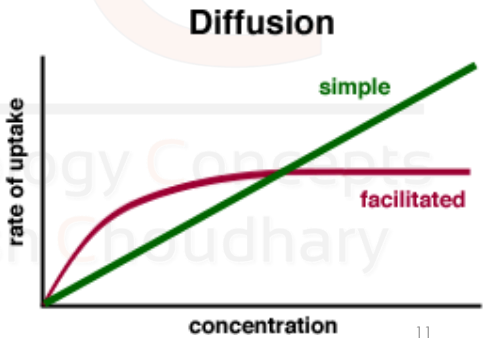
## 2. Passive (simple) diffusion

- Molecular weight of the high lipophilic drugs is not important as much as in the drugs that are soluble in water, BUT MW OVER 1000 is generally restrictive!!!
- **Fick's first law of diffusion (Rate a Conc. Gradients)**
- The rate of diffusion (**dn/dt**) is the change in the number of diffusing molecules inside the cell over time.

$$Dn/dt = DA(C_{out} - C_{in})/dx$$

- **D= Diffusion Cofficient**
- **A= Cross sectional Area**
- **C= Concentration**
- **dx= membrane thickness**

- **First Order Kinetic**

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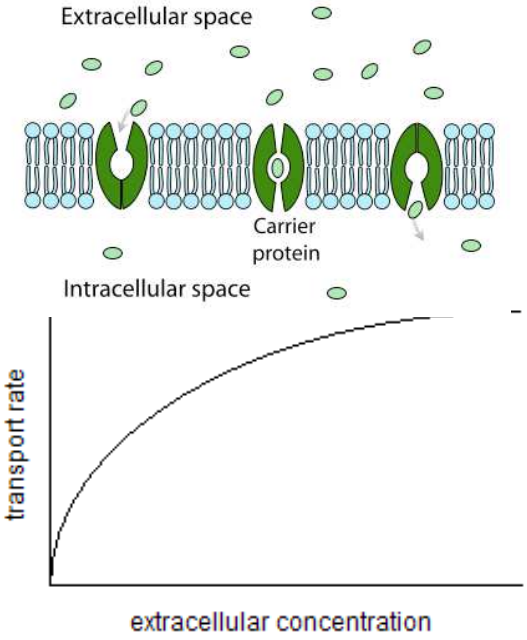
# Transport Mechanism

**3. Carrier Mediated Transport system**

- Require a **carrier protein/system** (PERMIASE) to transport the drug across the membrane.
- It is a **saturable** Process
- **Mixed Order kinetics**



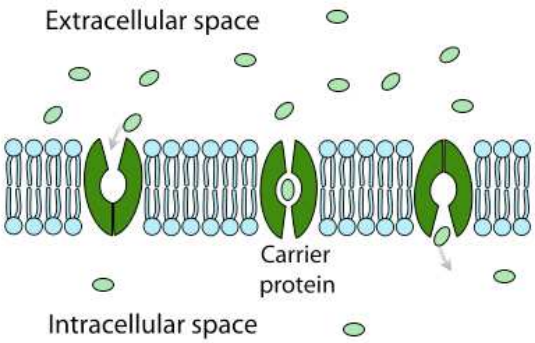



# Transport Mechanism

**3. Carrier Mediated Transport system**

**A. Facilitate Diffusion**

- Require a **carrier protein/system** and It is a **saturable** Process
- Net flux of drug molecules is **from the high concentration to low concentration (Downhill process).**
- **No energy is required.**
- **Polar drugs. E.g., trasport of glucose (GLUTs), Trasport of Vit B 12 [intrinsic factor-1 (IF-1)-glycoprotein]**



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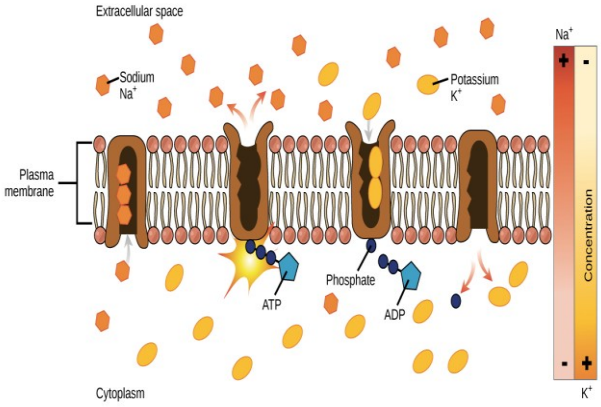
# Transport Mechanism

### 3. Carrier Mediated Transport system

### B. Active Transport System

- Require a carrier protein/system and It is a saturable Process
- The transportation of the drug molecules across the cell membrane against a concentration or an electrochemical gradient.
- Net flux of drug molecules is from the low concentration to high concentration (uphill process).
- It requires energy (ATP) and a special transporter (carrier) protein.

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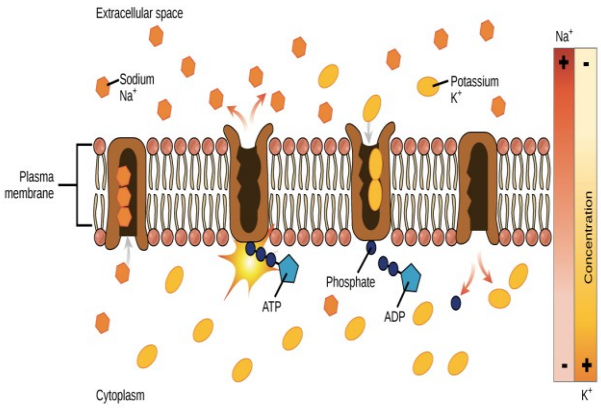
# Transport Mechanism

### 3. Carrier Mediated Transport system

### B. Active Transport System

- Due to energy dependent process, it is inihibited by metabolic poisons like cyanide, fluoride.
- E.g., L-dopa (alfa-amino acid transport), 5FU (pyrimidine trnasport), ACEIs (peptide transport).

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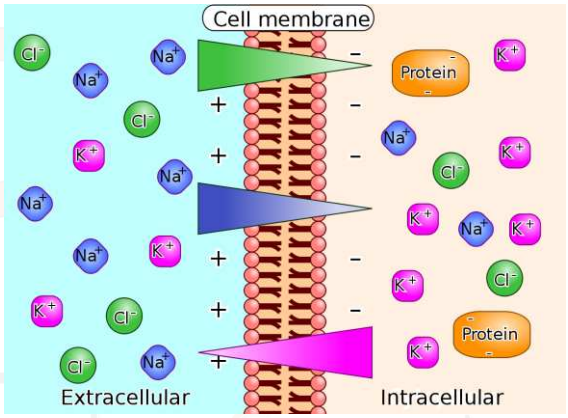
# Transport Mechanism

## 4. Electrochemical Diffusion

- Downhill process, depends upon conc. Gradients.
- Union>Anion>Cation




## 5. Ion Pair Transport

- Quaternary ammonium compounds and Sulfonic acids drugs are ionized at all pH media. Therefore, they transport via ion-pair system.
- Endogeneous mucin (anionic) neutralized the cations and transport across to the membrane.



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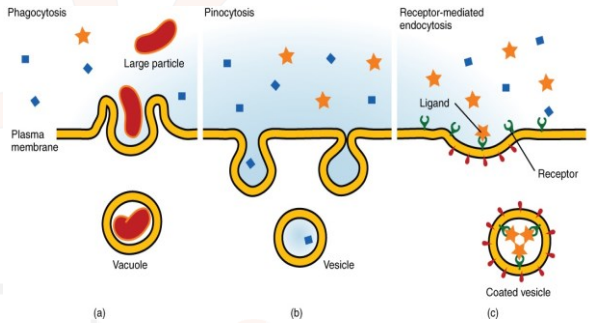
# Transport Mechanism

## 4. Endocytosis

- **Phagocytosis: cell eating**
- **Pinocytosis: Cell Drinking**
- The drugs which have MW over 900 can be transported by pinocytosis.
- It requires **energy**.
- The drug molecule holds on the cell membrane and then surrounded with plasma membrane and inserted into the cell within small vesicles.
- E.g., Sabin polio vaccin, Fat soluble Vit. (A,D,E,K) and Neurotransmitter uptake.

****Neurotransmitter release/secretion is a exocytosis process**



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