Unit - I

Solubility of drugs

Diffusion:

"Mass transfer of individual molecules of a substance caused by random molecular motion, associated with the driving force such as the concentration gradient".

(Or)

"A physical process that refers to the net movement of molecules from a region of high concentration to lower concentration under the influence of concentration gradient".

Diffusion phenomena applied in pharmaceutical sciences include:

- ✓ Release of drug from dosage form
- ✓ Ultrafiltration, microfiltration, dialysis, hemodialysis.
- ✓ Permeation & distribution of drug in living tissues
- ✓ Estimation of molecular weight of polymers
- ✓ Prediction of absorption & elimination of drug.

Types of diffusion

Passive diffusion:

- ✓ Net moment of material from an area of high concentration to an area of low concentration.
- ✓ The difference between high and low concentration is termed as concentration gradient.

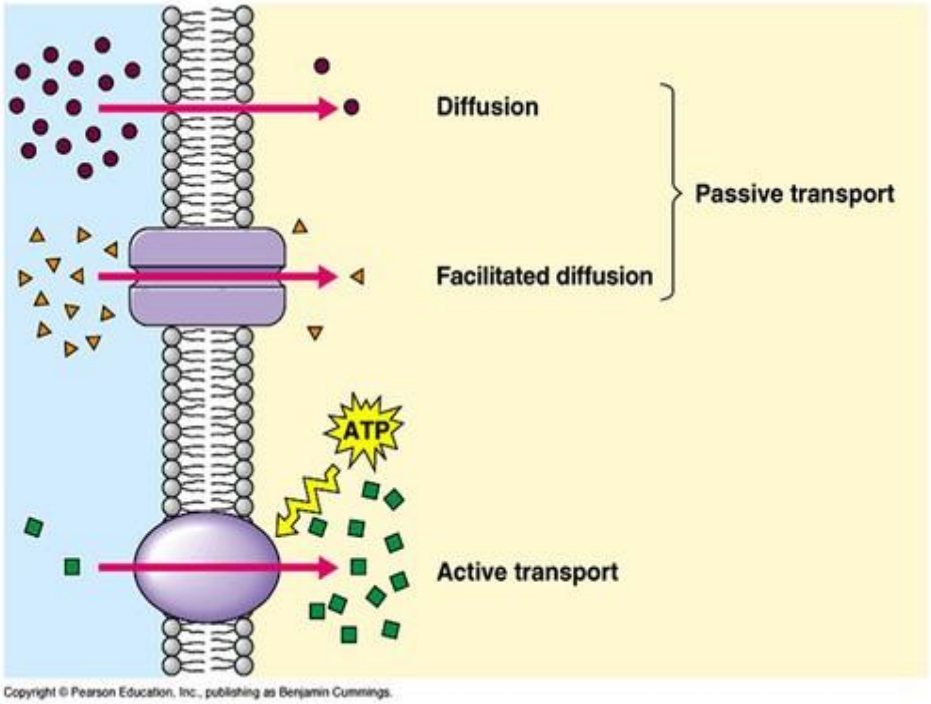
- ✓ Diffusion will continue until the gradient has been eliminated.

Facilitated (carrier mediated) diffusion:

- ✓ Facilitated diffusion also called carrier- mediated diffusion.
- ✓ It is moment of molecules across the cell membrane via special transport proteins that are embedded within the cellular membrane.
- ✓ Not energy-dependent.

Active transport:

- ✓ Movement of molecules across a membrane from a region of lower concentration to higher concentration, against the concentration gradient.



Filtration:

- ✓ Movement of solvent or solute molecules, influenced by hydraulic pressure.

- ✓ Depending on the size of the membrane pores, only solutes of a certain size may pass through it.

Laws of diffusion:

Fick's first law of diffusion: "Diffusion flux is directly proportional to concentration gradient under the assumption of steady state diffusion"

$$J = -D \frac{dc}{dx}$$

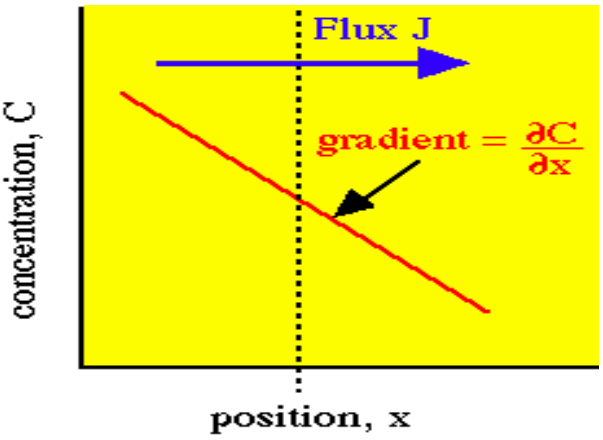
Where,

J= diffusion flux (g/ sq. cm/s)

D= Diffusion coefficient or diffusivity (cm sq/sec)

dc= change in concentration of material (g/cubic cm)

dx= change in distance (cm)

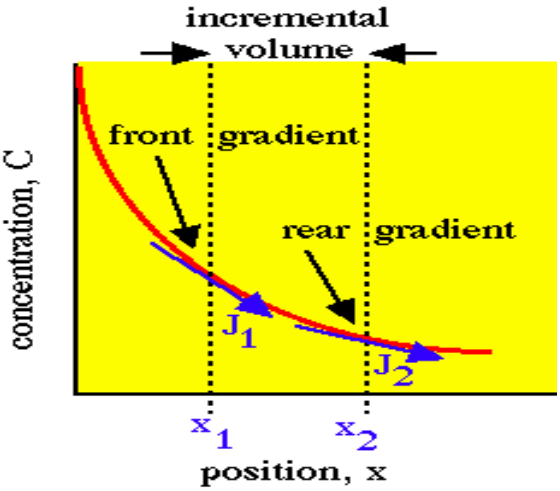


Diffusion flux (J) is mass transfer through a unit Cross section area in unit time.

$$J = dM/S\,dt$$

Fick's second law of diffusion: "Change in concentration with time in a particular region is proportional to the change in concentration gradient at that point in the system".

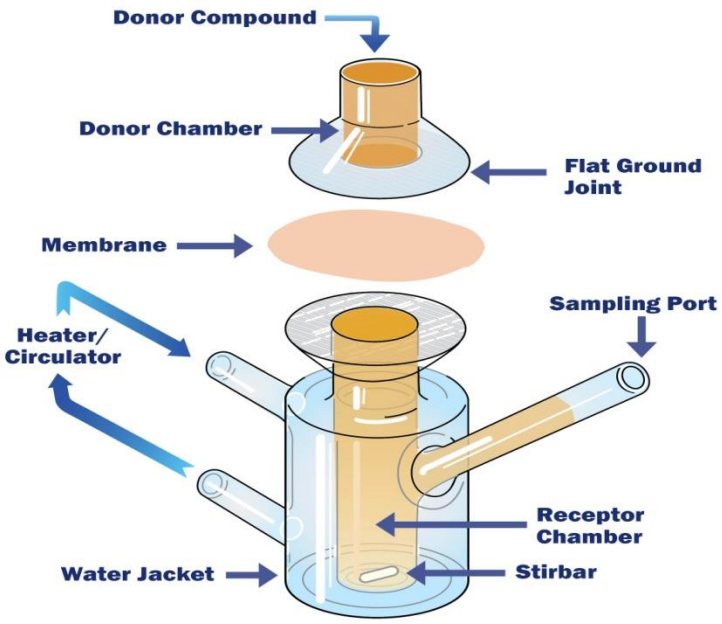
$$dc/dt = -dJ/dx$$



Measurement of diffusion:

Franz diffusion cell

- ✓ Franz cell apparatus contain two chambers separated by a membrane.
- ✓ Donor chamber consist of known concentration of solute.
- ✓ Receptor chamber contain fluid from which samples are taken at a regular interval for analysis.
- ✓ Temperature is maintained at 37˚C.
- ✓ Membrane may be of excised tissue, tissue constructs & cadaver tissue to synthetic membranes.
- ✓ When experiment starts, solute from donor chamber diffuses through membrane into receptor chamber.
- ✓ From receptor chamber, solution is periodically removed for analysis.
- ✓ The test determine amount of diffusant that has permeated the membrane.
- ✓ The solution of receptor chamber is replaced with new solution after each sampling.



Diffusion controlled release system:

Reservoir (laminated matrix) device:

- ✓ A hollow system containing an inner core surrounded in water insoluble membrane.
- ✓ Polymer can be applied by coating or encapsulation.
- ✓ Drug partitions into membranes and exchange with surrounding fluid by diffusion.
- ✓ Drug will enter membrane, diffuse to periphery & exchange with surrounding fluid.
- ✓ Polymer content in coating, thickness of coating & hardness of microcapsules are rate controlling parameters.
- ✓ Release follow fick's first law of diffusion.

Matrix (Monolithic) devices:

- ✓ Solid drug is dispersed or distributed in an insoluble matrix.
- ✓ Outer layer of drug is exposed to bathing solution in which it is first dissolved. Then drug diffuses out of matrix.
- ✓ Matrix diffusion system are of two types:
  - ❖ Rigid matrix
  - ❖ Swellable matrix.