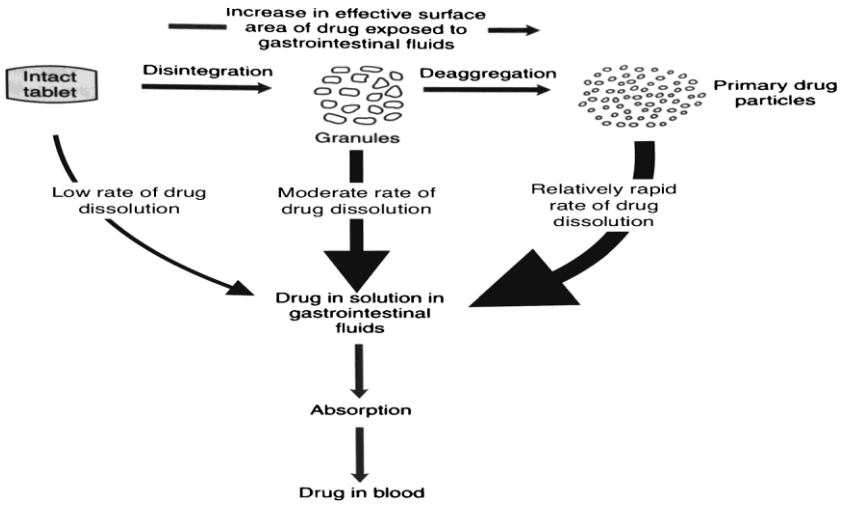
Dissolution refers to the process by which a solid phase (e.g., a tablet or powder) goes into a solution phase

Therefore, drug dissolution (drug release) is the process by which drug molecules are liberated from a solid phase and enter into a solution phase



The dissolution process is of special important in drug development process since ……

Dissolution and Solubility

Dissolution is the process by which a solid drug substance becomes dissolved in a solvent over time.

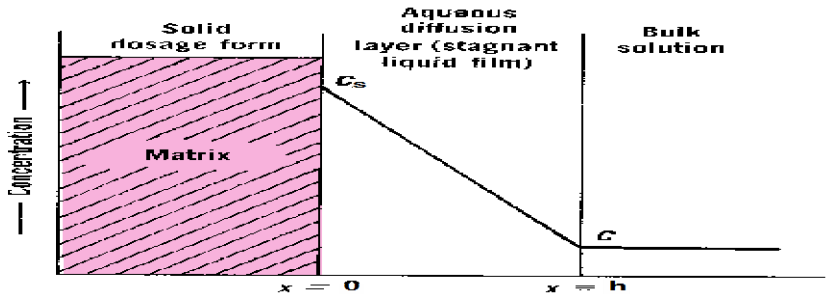
Solubility is the mass of solute that dissolves in a specific mass or volume of solvent at a given temperature (eg, 1 g of NaCl dissolves in 2.786 mL of water at 25□C).

Factors Affecting on the dissolution process

The overall rate of drug dissolution may be described by the *Noyes–Whitney equation*

$$\frac{dC}{dt} = \frac{DA}{h}(C_s - C)$$

where dC/dt = rate of drug dissolution at time t, D = diffusion rate constant, A = surface area of the particle, C_s = concentration of drug (equal to solubility of drug) in the stagnant layer, C = concentration of drug in the bulk solvent, and h = thickness of the stagnant layer .

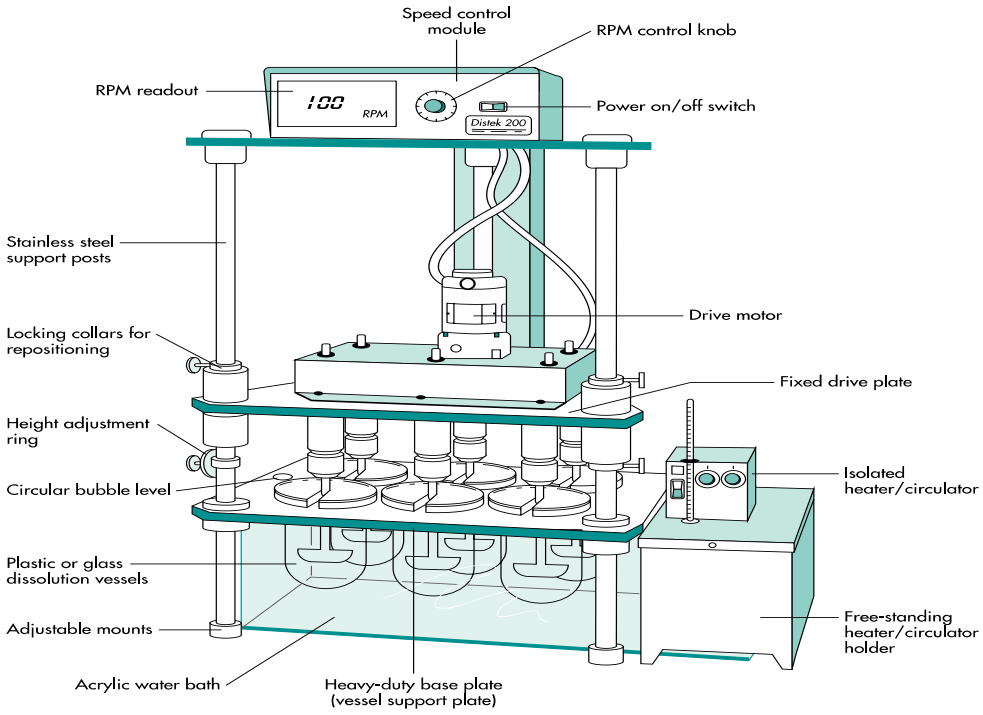


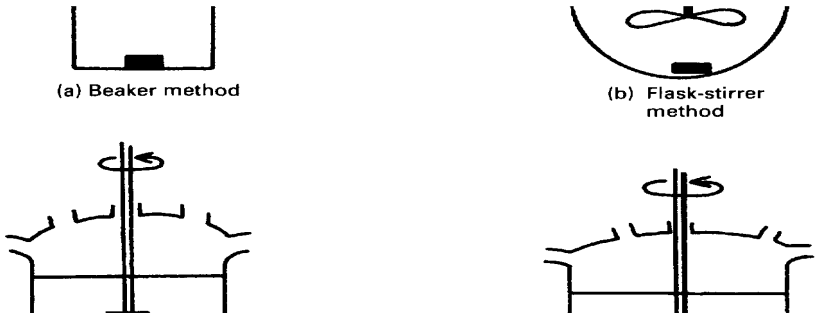
In vitro variables

Chemical stability in dissolution media ، Medium Volume pH Molarity Co-solvents, added enzymes/surfactants ،Temperature of medium Apparatus ، Agitation rate .

In vivo variables

…… (H.W.)





Basket type

Rate-Limiting step for drug occurnce in systemic circulation

For solid oral, immediate-release drug products (eg, tablets, capsules), the rate processes include

1. Dissolution of the drug in an aqueous environment.
2. Absorption across cell membranes into the systemic circulation.

Note1:

The slowest step in a series of kinetic processes is called the *rate-limiting step* .

Note 2 :

- When the rate of absorption (ka) >>> rate of dissolution (Kd) so the rate limiting step is the dissolution process.
- When the rate of absorption (ka)<<< rate of dissolution (Kd) so the rate limiting step is the absorption process.

Name of the experiment:

Dissolution testing of ACV tablet in 0.1 N HCL

Aim of the experiment:

Determination of the dissolution rate constant for ACV in 0.1 N HCL

Procedure:

1- Fill the Jar with 900 ml of Artificial gastric fluid
2- Switch on the heater contected to the water bath until the temperature of the dissolution fluid reaches to 37^0 C .
3- Put on tablet into the Jar and start the instrument immediately at a speed of 50 r.p. m.
4- Draw 5 ml after 5 ,10 ,15, 20 ,30, 40 , 50 min. from the surface of the dissolution media. Stop the apparatus while withdrawing samples. Substitute the volume each interval with 5ml fresh gastric fluid.

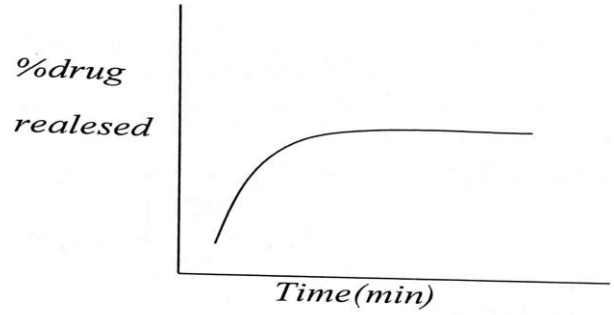
   Note: In vivo, After dissolution, absorption will occur . In vitro dissolution testing, there is no absorption and drug will start to accumulate when saturation solubility is exceeded , therefore replacement with fresh media is required to maintain sink condition.

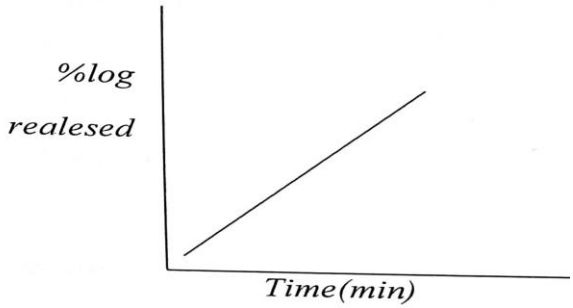
   sink condition: drug concentration in the dissolution media should not exceeds 20% of the saturation solubility of the drug

5- Start the instrument again.
6- Analyte the withdraw samples of ACV by measuring the absorbance at 252 by using the spectrophotometer.
7- Calculate the concentration of the drug from the absorbance by using the calibration curve equation Y=a + b X
8- List the result in the following table

Collection time	Abs. (Y)	Conc. (X) in mg / ml	Amount released (mg)	% Amount released

9- Draw the following curve to calculate the dissolution rate constant





Note: According to first order reaction :

$$\text{Log } C_t = \text{Log } C_0 + \frac{k}{2.303} t$$

x- axis (t), y-axis (Log $C_{t\,\%}$)

Slope = $\frac{k}{2.303}$

K (min^{-1} or hr^{-1}) = Slope X 2.303

Practical issue 1 :

In vitro dissolution can give idea about the in vivo dissolution and drug bioavailability, How? are their any challenges for establishing such correlation?

Practical issue 2 :

Tablet A and Tablet B both contain the same drug and in the same potency , will the provide similar dissolution profile or behavior upon performing in vitro dissolution testing ? Explain …

Practical issue 3 :

Rate limiting step for drug in BSC I is…….. because …… , While BSC II is…….. because ……