UNIT

III

DRUG DISSOLUTION

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INTRODUCTION

Dissolution is the process of mass transfer from the solid surface to the liquid phase of a solid substance in a particular solvent.

Dissolution Rate: The amount of solid substance that dissolves per unit time under standard conditions of temperature, pH, solvent composition, and constant solid surface area is referred to as **dissolution rate**.

Theories of Drug Dissolution:

Important theories to explain dissolution are as follows:

1. Diffusion layer model/Film theory,
2. Danckwert's model/Penetration or Surface renewal theory, and
3. Interfacial barrier model/Double-barrier or Limited solvation theory

DIFFUSION LAYER MODEL/FILM THEORY

The most prevalent theory for dissolution that occurs in two stages:

1. At the solid/liquid contact, a stationary film or diffusion layer forms quickly.
2. Diffusion of the soluble solute from the stationary layer to the bulk of the solution; this is the rate-determining stage in drug dissolution because it is slower.

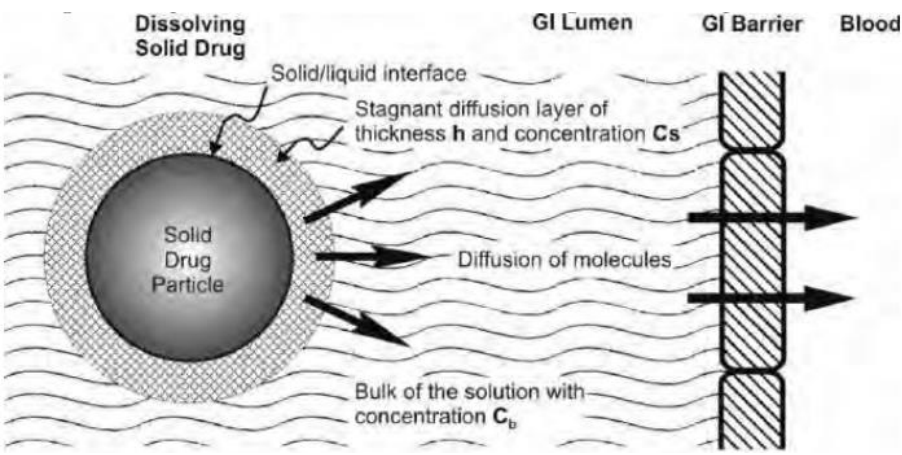

Figure 3.1: Diffusion layer model for drug dissolution

Noyes and Whitney give the following diffusion controlled dissolution rate:

$$\frac{dC}{dt} = k(C_s - C_b)$$

Where, $\frac{dC}{dt}$ = dissolution rate of the drug,

k = dissolution rate constant,

C_s = concentration of drug in the stagnant layer (= saturation or maximum drug solubility),

C_b = concentration of drug in the bulk of the solution at time t.

This equation was further adjusted by Nernst and Brunner by incorporating Fick's first law of diffusion as follows-

$$\frac{dC}{dt} = \frac{DAK_{w/o}(C_s - C_b)}{Vh}$$

where, D = diffusion coefficient of the drug,

A = surface area of the dissolving solid,

$K_{w/o}$ = water/oil partition coefficient of the drug or intrinsic dissolution rate constant,

V = volume of dissolution medium,

h = thickness of the stagnant layer,

(C_s – C_b) = concentration gradient for diffusion of drug.

Danckwert's Model (Penetration or Surface Renewal Theory)

Given the concept of macroscopic mass of eddies or packets, Danckwert ruled out the existence of a stationary layer. Due to eddy currents, these pockets of solute reach the solid/liquid contact at random, absorb the solute through diffusion, and transport it to the bulk of the solution. The hypothesis is called surface renewal theory because it occurs every time a new surface is exposed to solvent pockets. The equation that expresses Danckwert's model is:

$$V\frac{dC}{dt} = \frac{dm}{dt} = A(C_s - C_b)\sqrt{\gamma D}$$

Where, γ = rate of surface renewal

A = surface area

m = mass of solid dissolve

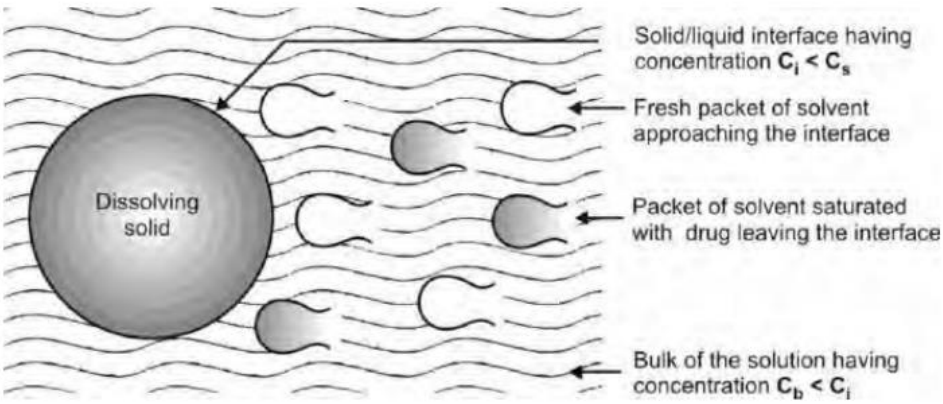

Figure 3.2: Penetration or surface renewal model for drug dissolution

Interfacial Barrier Model (Double Barrier or Limited Solvation Theory)

According to this concept, as a result of the solvation mechanism, an intermediate concentration can exist at the interface, and each face of the crystal will have a different interfacial barrier. The following equation expresses such a concept:

$$G = K_i(C_s - C_b)$$

where, G = dissolution rate per unit area, and

K_i = effective interfacial transport constant