"बेटी बचाओ, बेटी पढ़ाओ"

JAYOTI VIDYAPEETH WOMEN'S UNIVERSITY, JAIPUR

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Course - B.Pharm (3rd sem)

Session - Physical Pharmaceutics – (Diffusion Principle in biological system – Part I)

AcademicDaystartswith–

- Greeting with saying **'Namaste'** by joining Hands together following by 2-3 MinutesHappy session, Celebrating birthday of any student of respective class and **National Anthem**

DIFFUSION PRINCIPLES IN BIOLOGICAL SYSTEMS

From places of high concentration to areas of lower concentration, matter diffuses along energy gradients. The size of the concentration gradient, particle size, and temperature all affect the rate of diffusion. The selectively permeable cell in biology two unique forms of diffusion are produced by membranes: osmosis for the diffusion of water, and dialysis for the solute diffusion

Diffusion is one principle method of movement of substances within cells, as well as for essential small molecules to cross the cell membrane. Cell membranes act as barriers to most, but not all, molecules. A cell membrane that could allow some materials to pass while prevent the movement of other molecules is a major step in the development of the cell.

The cell membrane functions as a semi-permeable barrier, allowing a very few molecules across it while holding majority of chemicals inside the cell. Cell membranes separate the inner cellular environment from the outer cellular (or external) environment.

Most of the molecules move from higher to lower concentration, although there will be some molecules that move from low to high. The overall movement is thus from high to low concentration. If there is no energy input into the system, the molecules reaches a state of equilibrium and gets uniformly distributed throughout the system. A cell membrane is composed of phospholipids and proteins.

Absorption of drugs across the stomach lining/mucosa and the blood/brain barrier are two representative examples of transport phenomenon. Skin is another great example of a membrane for the entry of drugs. The transport of drug molecules through a non-porous membrane occurs by diffusion. Transport through porous cell membranes occurs by diffusion and convection. The rate of diffusion is expressed by equation.

$dM/dt = DSK (C1 - C2) h$ …

Where,

M is amount of drug dissolved,

t is time,

D is diffusion coefficient of the drug,

S is surface area of membrane,

K is oil/water partition coefficient,

h is thickness of the liquid film,

C1 is the concentration of drug at donor side of membrane and

C2 is the concentration of drug at receptor side and

C1 – C2 is concentration gradient.

C_1 and C_2 are not measured since these are values varies within the membrane. Typically, the gradient is measured as $C_d - C_r$, representing the partition at each phase, namely $K_{o/w} = C_1/C_d$ and $K_{o/w} = C_2/C_r$. The rate of drug transport into diffusional system is predominantly dependent upon the magnitude of the concentration gradient considering the other parameters constant.

Water, carbon dioxide, and oxygen are among the few simple molecules that can cross the cell membrane by diffusion (or a type of diffusion known as osmosis).

Gas exchange in lungs operates by diffusion process. All cells because of cellular metabolic processes produce carbon dioxide. Since the source is inside the cell, the concentration gradient is constantly being replenished/re-elevated; leading to net flow of CO_2 out of the cell.

Metabolic processes in animals and plants usually require oxygen, which is in lower concentration inside the cell, have the net flow of oxygen into the cell through diffusion.

SOLUBILITY OF GAS IN LIQUIDS

Solubility of gas in liquids is the concentration of dissolved gas in the liquid when it is in equilibrium with the pure gas above the solution. The example of gas in liquid includes effervescent preparations containing dissolved carbon dioxide, ammonia water and hydrochloride gas. Aerosol products containing nitrogen or carbon dioxide as propellant are also considered to be solution of gases in liquids

Factors Affecting Solubility of Gas in Liquids:

The solubility of gas in liquids depends on pressure, temperature, salt present, chemical reaction and micellar solubilization.

Pressure: Liquids and solids exhibit practically no change of solubility with changes in pressure. When considering solubility of gases in liquids, the pressure of the gas in contact with the liquid is important. At higher gas pressure, more gas is dissolved in liquids. For example, the soda bottle is packed at high pressure of carbon dioxide before sealing. When the cap of bottle is opened, the pressure above the liquid is reduced to 1 atm and the soda fizzes. This fizzing is just carbon dioxide that was dissolved in soda, is getting released. Therefore, if lower is the pressure less carbon dioxide is soluble.

The effect of pressure on the solubility of gas is given Henry's law which states that in dilute solution the mass of gas which dissolves in each volume of liquid solvent at constant temperature is directly proportional to partial pressure of gas. Mathematically it is expressed as

$$Sg = KHPg \ldots$$

Where, Sg is solubility of gas, expressed as mol/L;

KH is Henry law constant which is different for each solute-solvent system and Pg is partial pressure of the gas in mmHg.

The amount of undissolved gas above the solution is obtained by subtracting the vapor pressure of the pure liquid from the total pressure of the solution.

SOLUBILITY OF LIQUIDS IN LIQUIDS

Binary Solutions

It is very common for two or more liquids to be mixed together to make a solution. Therefore, we need to know what liquids can be mixed together without precipitation. Examples of pharmaceutical solutions of liquid dissolved in liquids are hydro alcoholic solutions, aromatic waters, spirits, elixirs, lotions, sprays and some medicated oils that contain mixture of two or more miscible oils.

When two or more liquids mixed together they can be completely miscible, partially miscible or practically immiscible. Completely miscible liquids mix uniformly in all proportions and hence do not get separated. Partially miscible liquids form two immiscible liquid layers, each of which is saturated solution of one liquid in the other. Such liquid pairs are called as conjugated liquid pairs.

The mutual solubility of partially miscible liquids, being temperature specific, is affected by changes in temperature. For binary phase systems, such as phenol-water system, the mutual solubility of two conjugate liquid phase increases with increase in temperature called as conjugate temperature, whereas above this temperature they are soluble in any proportions.

Other examples of partial miscibility include conjugate liquid pair of nicotine and water, ether and water, and triethnolamine and water. Immiscibility refers to those systems which do not mix with each other at all such as water and liquid paraffin or water and oil.

The dielectric constant of a substance also affects the solubility of substance. It is known fact that the polarity of solvent is dependent on the dielectric constant. Also, remember that LIKE DISSOLVES LIKE.

The influence of a foreign substance on a liquid-liquid system is like the idea of three component system in the phase rule. Ternary systems are produced by addition of third component to a pair of partially miscible liquids to produce a solution. If added component is soluble in only one of the two components or if its solubility in the two liquids is markedly different, the mutual solubility of the liquid pair is decreased.

If added solute is roughly soluble in both the liquids approximately to the same extent, then the mutual solubility of the liquid pair is increased. This is called blending.

An example of this is when succinic acid is added to the phenol-water mixture.

The succinic acid is soluble or completely miscible in each phenol and water therefore it causes a blending of the liquids making the mixture one phase.

Ideal Solutions

Dilute solutions consists of negligible amount of solute compared to pure solvents. These solutions are referred as ideal solutions. An ideal solution is one in which there is no change in the properties of the components other than dilution when they are mixed to form the solution.

No heat is evolved or absorbed during the solution formation. The final volume of real solution is an additive property of the individual component. In another way it can be stated as a solution which shows no shrinkage or expansion when components are mixed to form solution.

Ideal solutions are formed by mixing different substances having similar properties and therefore there is complete uniformity of attractive intermolecular forces. For example, when equal amounts of methanol and ethanol are mixed together, the final volume of the solution is the sum of the volumes of the methanol and ethanol.

Solutions used in pharmacy consist of wide variety of solutes and solution. The basis of solubility and solution theory is based on ideal solution. In ideal solution there is a complete absence of attractive or repulsive forces and therefore the solvent does not affect solubility.

The solubility in this case depends on temperature, the melting point of solute and the molar heat of fusion (ΔHf). In ideal solution heat of solution is equal to ΔHf . Therefore solubility in an ideal solution can be expressed by,

$$-\log Xi2 = \Delta Hf\ 2.303R\ (To - T)/\ ToT$$

Where,

Xi2 is the ideal solubility in terms of mole fraction, R is gas constant;

T is the temperature of solution and

To is the temperature (Kelvin) of solute.

The equation. Can be used to calculate molar heat of fusion by plotting the log solubility versus reciprocal of absolute temperature which results in a slope of $-\Delta Hf/2.303R$. Unfortunately most of the solutions are non-ideal (real) because there may be interaction between solute and solvent. In these solutions mixing of solute and solvent can release or absorb heat into or from surroundings, respectively. While describing non-ideal solution, activity of solute must be considered. Activity of solute is defined as concentration of solute multiplied by the activity coefficient (X2).

- **Next Topic-**

➢ Physical Pharmaceutics-I (Raoult's law – Part I)

- **Academic Day ends with-**

National song' Vande Mataram'

Reference

1. Dr. Hajare A. Ashok A text book of physical pharmaceutics nirali prakashan first edition, july 2018