**INTRODUCTION TO BIOPHARMACEUTICS AND PHARMACOKINETICS**

Biopharmaceutics is the study which shows how the drug absorption rate is affected by various factors like physical and chemical properties of the drug, the dose form of the drug and the route through which the drug is administered.

It includes the study of the following:   
1. The stability of the drug  
2. The liberation of the API from the dosage form  
3. The rate at which the drug is getting converted into solution  
4. And finally the absorption of the drug into the systemic circulation

It includes the study of various tests that have took place in the laboratory and in the animals.

**Pharmacokinetics:**  
"Pharmacokinetics is defined as the study of rate processes involved in absorption, distribution, metabolism and excretion"It will decide the how much drug should to be given to the patient, and the route through which the drug must be administered, the time taken by the drug to start its action, and how long the drug ction will remain.

Absorption is the movement of the drug into the systemic circulation from where the drug has been delivered. Once its absorbed it will move to the other parts of the body which is called distribution. Metabolism is the phenomenon of the chemical changes that drug undergo within the body. Excretion is the moving out of the drug from the body.

**APPLICATIONS**

**Biopharmaceutics**  
1. If a company is trying to develop the new dosage form and when it is given to the human beings, in some cases the drug may release very slowly. Or else the entire drug may be released one at a time. Both the conditions are not required. To obtain the required action, the exact formulation can be obtained by using the principles of biopharmaceutics.  
2. If a company tries to change the ingredients of the tablet dosage forms. FDA will approve the change only if the bioavailability is equal to the initial formulation and the bioavailability can be studied by the principles of biopharmaceutics.  
3. Similarly if there is tablet dosage form of the drug and if the company tries to release the drug in the form of transdermal route, the bioavailability is compared and will be only released if the bioavailability is similar.

**Pharmacokinetics**  
1. The pharmacokinetics equations are very much useful in the determination of bioavailability.  
2. How many times the drugs should be given to the patient can be determined by pharmacokinetics principles.  
3. In case of controlled release dosage forms, how much drug should be given can be determined by pharmacokinetics principles.  
4. In the patients whose kidney got failed, the amount of the drug that should be administered can be calculated by using pharmacokinetics. Here the drug elimination will be less.

## ****Mechanism of Absorption of DRUG****

By four ways the drug can be migrated:

* Simple diffusion (Diffusion directly through lipid)
* Facilitated diffusion (Carrier mediated)
* Active transport (Carrier mediated)
* Pinocytosis (Drinking of cell)

**Simple diffusion:**  
Polar substances dissolve freely in polar solvents and vice versa (like dissolves like). It means non polar substances dissolves freely in lipids( non polar substance), therefore, penetrates cell membrane very freely. It occurs due to conc. gradient, it is moving from high to low conc. no need of energy supply for simple diffusion.  
Example: Water- it is moved through the GIT due to gaps between endothelial and along with it .

smaller water soluble substances can be passed such as urea and alcohol etc.  
Gases: the gases can be diffused in the lungs by simple diffusion, not due to conc. gradient but due to partial pressure differences of gases i.e., oxygen.

**Active diffusion:**

 Carrier proteins, ion channels are required for this type of diffusion. Here, a carrier protein moves molecules against the conc. gradient.  
The drug molecule combine with carrier protein and then it transferred drug to the other side of membrane, there it leaves the molecule and come back to normal situation or form. It is energy mediated. Drugs like L-dopa moves by this way  
Through ionized channel, the ions like k+, Ca++, Na+ are transferred.  
In simple diffusion, the rate of transport is directly proportional to conc. gradient. Whereas, in carrier mediated transport, the rate of transport is not related with conc. of drug. But it depends on the amount of carriers by which the drug molecules can be bound.

**Facilitated diffusion:**

 In this case also the carrier proteins are required, but transfer is occurred due to absorption of other molecule, which facilitate movement of drug molecule.  
The glucose is transported along with sodium from the GIT membrane.  
Example: fluorouracil

 **Pinocytosis:**  
It is also called as drinking of cell. The drug molecule, when comes in contact with membranes the invagination occurs (pseudopods). They trap the drug molecule and forms vesicles in which the drug molecule is present and taken into the cell. In the cell, some lysozymes are present which acts on the drug molecule and forms active form.  
This process occurs rarely.  
Example: Barium sulfate. Some molecules like insulin can enter to BBB (blood brain barrier) by this process.  
In follicular cells of the thyroid, the colloids are taken by same process and releases T3 and T4 which are useful residues.

**DISTRIBUTION**

**Distribution** in [pharmacology](https://en.wikipedia.org/wiki/Pharmacology) is a branch of [pharmacokinetics](https://en.wikipedia.org/wiki/Pharmacokinetics) which describes the reversible transfer of drug from one location to another within the body.

* Once a drug enters into systemic circulation by absorption or direct administration, it must be distributed into interstitial and intracellular fluids.
* Each organ or tissue can receive different doses of the drug and the drug can remain in the different organs or tissues for a varying amount of time.
* The distribution of a drug between tissues is dependent on[vascular permeability](https://en.wikipedia.org/wiki/Vascular_permeability), regional blood flow, cardiac output and [perfusion](https://en.wikipedia.org/wiki/Perfusion) rate of the tissue and the ability of the drug to bind tissue and [plasma proteins](https://en.wikipedia.org/wiki/Plasma_protein) and its lipid solubility.
* [pH partition](https://en.wikipedia.org/wiki/PH_partition)  plays a major role as well. The drug is easily distributed in highly perfused organs such as the liver, heart and kidney.
* It is distributed in small quantities through less perfused tissues like muscle, fat and peripheral organs.
* The drug can be moved from the plasma to the tissue until the equilibrium is established (for unbound drug present in plasma).

There are many factors that affect a drug’s distribution throughout an organism-.

### Physical volume of an organism

This concept is related to multi-compartmentalization. Any drugs within an organism will act as a [solute](https://en.wikipedia.org/wiki/Solution) and the organism’s tissues will act as [solvents](https://en.wikipedia.org/wiki/Solvents).

The differing specificities of different tissues will give rise to different concentrations of the drug within each group.

Therefore, the chemical characteristics of a drug will determine its distribution within an organism. For example, a liposoluble drug will tend to accumulate in body fat and water-soluble drugs will tend to accumulate in extracellular fluids.

The [volume of distribution](https://en.wikipedia.org/wiki/Volume_of_distribution)(VD) of a drug is a property that quantifies the extent of its distribution. It can be defined as the theoretical volume that a drug would have to occupy (if it were uniformly distributed), to provide the same concentration as it currently is in blood plasma. It can be determined from the following formula

{\displaystyle Dc={\frac {Vd.Cp}{Da.B}}}

### Removal rate

A drug's removal rate will be determined by the proportion of the drug that is removed from circulation by each organ once the drug has been delivered to the organ by the circulating blood supply.[[1]](https://en.wikipedia.org/wiki/Distribution_(pharmacology)#cite_note-Carmine-1) This new concept builds on earlier ideas and it depends on a number of distinct factors:

* The drugs characteristics, including its pKa.
* Concentration differential between tissues.
* Exchange surface.
* Presence of natural barriers. These are obstacles to a drug's diffusion similar to those encountered during its absorption. The most interesting are:
  + Capillary bed permeability, which varies between tissues.
  + Blood-brain barrier: this is located between the blood plasma in the cerebral blood vessels and the brain’s extracellular space. The presence of this barrier makes it hard for a drug to reach the brain.
  + Placental barrier: this prevents high concentrations of a potentially toxic drug from reaching the foetus.

### Plasma protein binding

* Some drugs have the capacity to bind with certain types of proteins that are carried in blood plasma. This is important as only drugs that are present in the plasma in their free form can be transported to the tissues.
* Drugs that are bound to plasma proteins therefore act as a reservoir of the drug within the organism and this binding reduces the drug’s final concentration in the tissues.
* The binding between a drug and plasma protein is rarely specific and is usually [labile](https://en.wikipedia.org/wiki/Labile) and reversible.
* The binding generally involves [ionic bonds](https://en.wikipedia.org/wiki/Ionic_bond), [hydrogen bonds](https://en.wikipedia.org/wiki/Hydrogen_bond), [Van der Waals forces](https://en.wikipedia.org/wiki/Van_der_Waals_force) and, less often, [covalent bonds](https://en.wikipedia.org/wiki/Covalent_bond).
* This means that the bond between a drug and a protein can be broken and the drug can be replaced by another substance (or another drug) and that, regardless of this, the protein binding is subject to [saturation](https://en.wikipedia.org/wiki/Saturation_(chemistry)).
* An equilibrium also exists between the free drug in the blood plasma and that bound to proteins, meaning that the proportion of the drug bound to plasma proteins will be stable, independent of its total concentration in the plasma.
* the most important plasma proteins are the [albumins](https://en.wikipedia.org/wiki/Albumin) as they are present in relatively high concentrations and they readily bind to other substances.
* Other important proteins include the [glycoproteins](https://en.wikipedia.org/wiki/Glycoprotein" \o "Glycoprotein), the [lipoproteins](https://en.wikipedia.org/wiki/Lipoprotein) and to a lesser degree the [globulins](https://en.wikipedia.org/wiki/Globulin).
* It is therefore easy to see that clinical conditions that modify the levels of plasma proteins (for example, [hypoalbuminemias](https://en.wikipedia.org/wiki/Hypoalbuminemia" \o "Hypoalbuminemia) brought on by renal dysfunction) may affect the effect and toxicity of a drug that has a binding rate with plasma proteins of above 90%.