**INTRODUCTION TO BIOPHARMACEUTICS**

**ABSTRACT**Biopharmaceutics examines the interrelationship of the physical/chemical properties of the drug, the dosage form (drug product) in which the drug is given, and the route of administration on the rate and extent of systemic drug absorption. The importance of the drug substance and the drug formulation on absorption, and in vivo distribution of the drug to the site of action, is described as a sequence of events that precede elicitation of a drug's therapeutic effect. First, the drug in its dosage form is taken by the patient either by an oral, intravenous, subcutaneous, transdermal, etc, route of administration. Next, the drug is released from the dosage form in a predictable and characterizable manner. Then, some fraction of the drug is absorbed from the site of administration into either the surrounding tissue, into the body (as with oral dosage forms), or both. Finally, the drug reaches the site of action. A pharmacologic response results when the drug concentration at the site of action reaches or exceeds the minimum effective concentration (MEC). Biopharmaceutics consideration often determine the ultimate dose of a drug in a dosage form. For example, the quantity of a locally acting drug in a topical dosage form such as an ointment is often expressed in concentration or as a percentage of the active drug in the formulation (e.g., 0.5% w/w hydrocortisone ointment). The amount of drug applied is not specified because the concentration of the drug at the active site relates to the pharmacodynamic action. In contrast, the quantity of a systemically active drug in a dosage form such as a tablet is expressed as milligrams. In this case, the dose is based on the amount of drug that is absorbed systemically and dissolved in an apparent volume of distribution to produce a desired drug concentration at the target site.

**KEYPOINTS**

**BIOPHARMACEUTICS: -**The study of the relationships between the physical and chemical properties, dosage, and form of the administration of drug and its activity in the living body.**PHARMACOKINETICS: -**The kinetics of drug absorption, distribution, metabolism, and excretion (ADME) and their relationship with the pharmacological, therapeutics or toxicological response in man and animals.**PHARMACODYNAMICS: -**The relationship between drug concentration at the site of action and the resulting effect, including the time course and intensity of therapeutic and adverse effects.

**ABSORPTION: -**The process of movement of unchanged drug from the site of administration to the systemic circulation.

**DISTRUBUTION**: - The reversible movement of the drug to and from the blood and various tissue of the body.

**BIOTRANSFFORMATION:-** It is an irreversible conversion of drugs from one chemical form to another, by the enzymes present in the body.**ELIMANATION:** - The process of removal of medication from the body.**PROTEIN DRUG BINDING**: - The phenomenon of complex formation of drugs with proteins. **BIOAVILABILITY: -** The rate and extent (amount) of absorption of unchanged drugs from its dosage form.**BIOEQUIVALENCE:** - It is a relative term which denotes that the drug substance in two or more identical dosage forms, reaches the systemic circulation at the same relative rate and to the same relative extent.

**MINIMUM EFFECTIVE CONCENTRATION (MEC) :** The minimum dose of drug required at the receptor site for action by producing desired pharmacological effect.

**MINIMUM TOXIC CONCENTRATION (MTC):** The minimum dose of drug which starts producing toxic effect.

**ON SET OF TIME:** The time taken by a drug to reach MEC.

**AREA UNDER CURVE (AUC) :** It is the sum total area between two given limits calculated by integration.

**DURATION OF ACTION :** Difference occur between onset time and time taken for drug to reach back its MEC.

**Cmax (MAXIMUM CONCENTRATION) :** After administration of drug , the maximum concentration of that drug in blood, cerebrospinal fluid, or target organ.

**Tmax (MAXIMUM TIME) :** The time taken by a drug to attain its maximum concentration (Cmax).

**HALF LIFE (t 1/2) :** It is a time taken by amount of drug’s active substance to reduced by half in the body.

**VOLUME OF DISTRUBUTION (Vd) :** It is that apparent volume into which the drug is distributed to provide the concentration which is in the blood plasma.

**INTRODUCTION**

BIOPHARMACEUTICS involves the study of the interrelationship of the physiochemical properties of the drug, the dosage form in which the drug is given and the route of administration on the rate of extent of systemic drug absorption. It is also the study of factors influencing the rate and amount of drug that reaches the systemic circulation and the use of these information to optimize the therapeutic efficacy of drug products. It helps to obtain the drug concentration time profiles but it does not explain the desirable, pharmacological, toxicological or clinical response. Biopharmaceutics also consider the impact of the various manufacturing methods and technologies on the intended performance of the drug product. It uses quantitative methods and theoretical models to evaluate the effect of the drug substance, dosage form and the routes of drug administration on the therapeutic requirements of the drug and drug product in a physiological environment. It also allows for rational design of drug products to deliver the drug at specific rate to the body in order to optimize the therapeutic effect and minimize any adverse effects. The concept of biopharmaceutics and pharmacokinetics in pharmaceutical sciences was first induced in 1960s by DR. G. LEVY.It observed therapeutics response after its administration. Studies of biopharmaceutics involves both in-vivo and in-vitro methods. In-vivo methods involves the measurements of systemic drug availability after administering adrug product to an animal or human.In-vitro methods involve test apparatus without involving laboratory animals or humans.

E.g., disintegration tests, dissolution tests etc.

Thus, biopharmaceutics deals with the factors that influence the:

* Protection and stability of the drug within the product.
* The rate of drug release from the product.
* The rate of dissolution of the drugs at the absorption site.
* The availability of the drug at its site of action.

Biopharmaceutics involves pharmacokinetics and pharmacodynamics. Pharmacokinetics is the kinetics of drug absorption, distribution, metabolism, and excretion (ADME) and their relationship with the pharmacological, therapeutics or toxicological response in man and animals. Pharmacodynamics is defined as the body’s biological response to drugs.

Pharmacokinetics description; -

* Absorption
* Distribution
* Metabolism
* Excretion

Drug in dosage

Drug release

**PHARMACOKINETICS** Drug at absorption site **BIOPHARMACEUTICS**

Drug absorption

Drug in systemic circulation

Elimination metabolism **DISPOSITION**

excretion

Drug in extravascular tissues

Drug at site of action

**Pharmacodynamics**

In normal body

Pharmacology response

**Therapeutics**

In diseased body

Therapeutic effect at therapeutic dose

Toxic effect at toxic dose

**Fig.1 Schematic representation of the process involved in drug therapeutics**

**Absorption** is the process of movement of unchanged drug from the site of administration to the systemic circulation.

Mechanism of drug absorptionThe main mechanisms by which absorption occurs include:(a) Transcellular or intracellular transport(b) Paracellular or intercellular transport(c)Vesicular transport or endocytosis

1.Transcellular/Intracellular Transport is defined as the passage of drugs across the GI epithelium. It is the most common pathway for drug transport.2. Paracellular/Intercellular Transport is defined as the transport of drugs through the junctions between the GI epithelial cells. This pathway is of minor importance in drug absorption.3. Vesicular or Corpuscular Transport (Endocytosis) – Like active transport, these are also energy dependent processes but involve transport of substances within vesicles into a cell. Since the mechanism involves transport across the cell membrane, the process can also be classified as transcellular.

**A. PHARMACEUTICAL FACTORS:** include factors relating to the physicochemical properties of the drug, and dosage form characteristics and pharmaceutical ingredients.

**I. Physicochemical Properties of Drug Substances**

1. Drug solubility and dissolution rate.

2. Particle size and effective surface area

3. Polymorphism and amorphism

4. Pseudopolymorphism (hydrates/solvates)

5. Salt form of the drug

6. Lipophilicity of the drug

7. PK of the drug and gastrointestinal pH }pH-partition hypothesis

8. Drug stability

9. Stereochemical nature of the drug

**II. Dosage Form Characteristics and Pharmaceutical Ingredients**

(Pharmaco-technical Factors)

1. Disintegration time (tablets/capsules)

2. Dissolution time

3. Manufacturing variables

4. Pharmaceutical ingredients (excipients/adjuvants)

5. Nature and type of dosage form

6. Product age and storage conditions

**(B) PATIENT-RELATED FACTORS**: include factors relating to the anatomical, physiological and pathological characteristics of the patient

1. Age

2. Gastric emptying time

3. Intestinal transit time

4. Gastrointestinal pH

5. Disease states

6. Blood flow through the GIT

7. Gastrointestinal contents:

(a) Other drugs

(b) Food

(c) Fluids

(d) Other normal GI contents

8. Contact time with gastrointestinal mucosa

9. Presystemic metabolism by:

(a) Luminal enzymes (b) Gut wall enzymes

(c) Bacterial enzymes (d) Hepatic enzyme

Hydrophobic Small uncharged Large uncharged Ions

Molecules polar molecules polar molecules

Lipoidal Membrane

Outside

Inside

**Fig.2 Schematic representation of Absorption.**

**ROUTE OF DRUG ADMINISTRATION**

It is the path by which a drug/ medicine or any other substance is taken into the body.

**Routes of administration can broadly be divided into:**

**1. Topical:** Drugs are applied topically to the skin or mucous membranes, primarily for containing local action.

2. **Oral :** Drugs are introduced by buccal cavity or sublingual. Primarily for systemic action (non local action).

**3. Parenteral:** A drug administered parenterally i.e other than oral route, is one injected via a hollow needle into the body at various sites and to varying depth.

**4. Rectal:** Drugs are introduced by rectum .

**5. Inhalation:** For absorption of drug the lungs provide an excellent surface, Drugs are delivered in gaseous form ,aerosol or ultrafine solid particle form.

**A. Topical Route:-**

When drugs are applied externally to the surface for attaining localized action. Drugs can be efficiently delivered to the localized lesions on skin, oro pharyngeal /nasal mucosa, eyes, ear canal, anal canal or vagina. The dosage forms are lotion, ointment, cream, powder, paints, drops, spray, lozenges, suppositories or pessaries. Non absorbable drugs given orally (sucralfate, vancomycin), inhalation of drugs for action on bronchi (salbutamol, cromolyn sodium) and irrigating solutions/jellys (povidone iodine,lidocaine) applied to urethra.

**Advantage:**

1. Convenient for use.
2. Encouraging for patient.

**B. Oral Route:-**

It is use by swallowing. It is intended for systemic effects resulting from drug absorption through the various epithelia and mucosa of the gastrointestinal tract.

**Advantages:**

1- Convenient - portable, no pain, easy to take.

2- Cheap no need to sterilize, compact, multi-dose automated machines produce tablets in large quantities.

3- Variety tablets, capsules, suspensions, mixtures.

**Disadvantages:**

1- Sometimes inefficient low solubility drugs may suffer poor availability e.g. Griseofulvin

2- First-pass mechanism- drugs absorbed orally are transported to the general circulation via the liver. Thus drugs which are extensively metabolized will be metabolized in the liver during absorption. e.g. propranolol.

**C. Buccal/Sublingual route:-**

Some drugs are taken as smaller tablets which are held in the mouth (buccal tablet) or under the tongue (sublingual tablet). Buccal tablets are often harder tablets [4 hour disintegration time], designed to dissolve slowly. E.g, Nitroglycerin, as a softer sublingual tablet .

**D. Parenteral Route:-**

**A- Intravascular (IV, IA):** placing a drug directly into blood stream. –Might be - Intravenous (into a vein) or intraarterial (into an artery).

**Advantages**

Precise, accurate and immediate onset of action, 100% bioavailability.

**Disadvantages**

1. Sometime swelling at site of injection if admistered wrongly.
2. High concentrations attained rapidly leading to greater risk of adverse effects.
3. Pain at site of injection.

**B-Intramuscular :**(into the skeletal muscle).

**Advantages**

Suitable for injection of drug in aqueous solution (rapid action) and drug in suspension or emulsion (sustained release).

**Disadvantages**

Pain at injection site for certain drugs.

**C-Subcutaneous** (under the skin), e.g. insulin.

**D- Intradermal**, (into the skin itself) is used for skin testing some allergens.

**E- Intrathecal** (into the spinal canal) is most commonly used for spinal anesthesia.

**Drug distribution** refers to the reversible transfer of a drug between the blood and the extra vascular fluids and tissues of the body. Drugs come into the circulation after absorption. From plasma, drugs have to cross the capillary membrane to come to interstitial space. And then need cross the cell-membrane to enter into the intracellular fluid.

**FACTORS AFFECTING DISTRIBUTION OF DRUGS:**

**Tissue Permeability of the Drugs.** a**.** Physiochemical Properties of the drug like Molecular size, pKa and o/w Partition coefficient.b. Physiological Barriers to Diffusion of Drugs.c. Organ / Tissue Size and Perfusion Rate.d. Binding of Drugs to Tissue Components binding of drug to blood components binding of drug to extra cellular components. Miscellaneous Factors Age, Pregnancy, Obesity, Diet, Disease states, and Drug Interactions.

A drug in the body can interact with several tissue components of which the two major categories are blood and extravascular tissues. The interacting molecules are generally the macromolecules such as proteins, DNS and adipose tissue. The phenomenon of complex formation of drug with protein is called as protein binding of drugs. As a protein bound drug is neither metabolized nor excreted hence it is pharmacologically inactive due to its pharmacokinetic and Pharmacodynamic inertness.

**Protein + drug ⇌ Protein-drug complexProtein binding may be divided into: –**1. Intracellular binding–2. Extracellular binding **MECHANISMS OF PROTEIN DRUG BINDING:**  Binding of drugs to proteins is generally of reversible & irreversible.Reversible generally involves weak chemical bond such as: a. Hydrogen bondsb. Hydrophobic bondsc. Ionic bondsd. Van der Waal’s forces. Irreversible drug binding, though rare, arises as a result of covalent binding and is often a reason for the carcinogenicity or tissue toxicity of the drug.**FACTORS AFFECTING PROTEIN DRUG BINDING**1. Drug-related factorsa) Physicochemical characteristics of the drugsb) Concentration of drugs in the bodyc) Affinity of drug for particular binding components2. Protein / Tissue related factorsd) Physicochemical characteristics of the protein or binding agentse) Concentration of protein or binding componentsf) Number of binding sites on the binding agents 3. Drug interactionsg) Competition between drugs for the binding site b) Competition between the drug and normal body constituentsi) Allosteric changes in protein molecule4. Patient-related factorsj) Agek) Intersubjective variationsl) Disease states

**Biotransformation,** is also called metabolism, is defined as the biochemical conversion of drug into another chemical form. Biotransformation includes enzymatically driven chemical conversion, but some of the drugs may be chemically changed by a non-enzymatic process. Xenobiotics, which are substances foreign to the body, are, metabolized or biotransformed to more water-soluble compounds, because water soluble compounds are more readily excreted. It is one of the most important mechanisms that the body has for detoxifying and eliminating drugs and other foreign substances. Drugs delivered by the oral route must pass through the liver before reaching the general circulation. Biotransformation at this point is called “firstpass metabolism,” which can limit systemic exposure for drugs despite good absorption. Oxidation, reduction, hydrolysis, and conjugation are the most common metabolic pathways, generally leading to more hydrophilic compounds that can be readily excreted. Cytochrome P450 (CYP-450) enzymes are a family of drug metabolizing enzymes that are responsible for the majority of drugs’ metabolism as well as many drug–drug interactions. Although the primary role of metabolism is to facilitate elimination of drugs from the body, secondary effects include transformation of drugs into other active or toxic species, which could be desirable in the case of prodrugs or undesirable with respect to toxic metabolites.

**PHASES OF DRUGS METABOLISM**

**The biotransformation of drugs generally occurs in two phases. Phase- I reaction and Phase-II reactions.**

**Phase-I reaction and Phase-II reactions**

**Phase-I** **Phase-II**

**Expose or add functional group.**

**XENOBIOTIC PRIMARY PRODUCT SECONDARY PRODUCT**

**Conjugation**

**Oxidation, Reduction**

**hydrolysis**

**EXCREATION**

**HYDROPHILIC**

**LIPOPHILIC**

**Fig.3 Schematic representation phases of drug metabolism**

**Excretion** is defined as the process whereby drugs and/or their metabolites are irreversibly transferred from internal to external environment. Kidney is the most important organ involved in excretion of most drugs especially which are water soluble or having low molecular weight. Nephron is the functional unit of kidney consisting of various parts viz glomerulus, proximal tubule, loop of Henle, distal tubule and the collecting tubule.

**FACTORS AFFECTING RENAL EXCRETION OF DRUGS**a. Different factors that affect renal excretion of drugs are b. Physicochemical properties of the drugc. Plasma concentration of the drugd. Distribution and binding characteristics of the druge. Urine pHf. Blood flow to the kidneysg. Biological factorsh. Drug interactionsi. Disease states

Urinary Excretion

Oral Administration BILE DISTRUBUTION TO TISSUE

**ENTEROHEPATIC CIRCULATION OF DRUGS**

SMALL INTESTINE LIVER

FAECAL EXCRETION BLOOD

**Fig 2**. **Schematic representation of the process involved in Excretion.**

**Plasma concentration curve:-**

It is the curve which shows the concentration or amount of drug that effectively reaches into the systemic circulation in specific time that is influenced by the degree of bioavailability and by the rate at which elimination occurred.

Peak plasma concentration

**Cmax (** absorption rate =elimination rate **)**

Plasma drug concentration

Toxic level

Intensity of action

Absorption phase Post absorption phase

**Therapeutic range**

Termination of action

Onset of action

Duration of action Minimum effective concentration (MEC)

**Area under the curve (AUC)**

On set time Time for peak concentration (tmax)

Time

**Fig.4 Schematic representation of plasma concentration curve.**

**COMPARTMENT MODELLING**

The time course of drug concentration determined after its administration can be satisfactorily explained by assuming the body as a single well-mixed compartment with first-order disposition processes.

**ONE-COMPARTMENT OPEN MODEL** (Instantaneous Distribution Model)

The one-compartment open model is the simplest model. Owing to its simplicity, it is based on following assumptions 1. The body is considered as a single, kinetically homogeneous unit that has no barriers to the movement of drug.

2. Final distribution equilibrium between the drug in plasma and other body fluids (i.e., mixing) is attained instantaneously and maintained at all times. This model thus applies only to those drugs that distribute rapidly throughout the body.

3. Drugs move dynamically, in (absorption) and out (elimination)of this compartment.

4. Elimination is a first order (monoexponential) process with first order rate constant.

5. Rate of input (absorption) > rate of output (elimination). 6. The anatomical reference compartment is plasma and concentration of drug in plasma is representative of drug concentration in all body tissues i.e., any change in plasma drug concentration reflects a proportional change in drug concentration throughout the body.

However, the model does not assume that the drug concentration in plasma is equal to that in other body tissues. The term open indicates that the input (availability) and output (elimination) are unidirectional and that the drug can be eliminated from the body. Fig. 9.1 shows such a one-compartment model. One-compartment open model is generally used to describe plasma levels following administration of a single dose of a drug.

Metabolism

**KE**

**Ka**

Blood and other body tissues

Drug

Output (Elimination)

Input (Absorption)

Excretion

Depending upon the rate of input, several one-compartment models can be defined:

One-compartment open model, i.v. bolus administration.

One-compartment open model, continuous i.v. infusion.

One-compartment open model, e.v. administration, zero-order absorption.

One-compartment open model, e.v. administration, first-order absorption.

**MULTICOMPARTMENT MODELS:**

One-compartment model adequately describes pharmacokinetics of many drugs. Instantaneous distribution equilibrium is assumed in such cases and decline in the amount of drug in the body with time is expressed by an equation with a monoexponential term (i.e., elimination). However, instantaneous distribution is not truly possible for an even larger number of drugs and drug disposition is not monoexponential but bi- or multi-exponential. This is because the body is composed of a heterogeneous group of tissues each with different degree of blood flow and affinity for drug and therefore different rates of equilibration. Ide ally, a true pharmacokinetic model should be the one with a rate constant for each tissue undergoing equilibrium, which is difficult mathematically. Multicompartment models are thus based on following.

1. Blood/plasma and the highly perfused tissues such as brain, heart, lung, liver and kidneys constitute the central compartment.

2. Other tissues with similar distribution characteristics are pooled together to constitute peripheral compartment tissues on the basis of similarity in their distribution characteristics.

3. Intravenously administered medications are introduced directly into the central compartment.

4.Irreversible drug elimination, either by hepatic biotransformation or renal excretion, takes place only from the central compartment.

5.Reversible distribution occurs between central and peripheral compartments, with a finite time required for distribution equilibrium to be attained.

6.After drug equilibration between central and the peripheral compartments, elimination of drug follows first-order kinetics.

7. All rate processes involving passage of drug in and out of individual compartment are first-order processes and plasma level-time curve is best described by sum of series of exponential terms each corresponding to first-order rate processes associated with a given compartment.

8. The peripheral compartment is usually inaccessible to direct measurement and is not a site of drug elimination or clearance.

Multicompartment characteristics of a drug are best understood by giving it as i.v. bolus and observing the manner in which the plasma concentration declines with time. The number of exponentials required to describe such a plasma level-time profile determines the number of kinetically homogeneous compartments into which a drug will distribute.

**TWO-COMPARTMENT OPEN MODEL**

The commonest of all multicompartment models is a two-compartment model. In such a model, the body tissues are broadly classifiedinto 2 categories--

1. **Central Compartment** or **Compartment 1** comprising of bloodand highly perfused tissues like liver, lungs, kidneys, etc. thatequilibrate with the drug rapidly.Elimination usually occurs from this compartment.

2.**Peripheral** or **Tissue Compartment** or **Compartment 2**comprising of poorly perfused and slow equilibrating tissues such as muscles, skin, adipose, etc. and considered as a hybrid of several functional physiological units.

**Two-Compartment Open Model**

**Intravenous Bolus Administration**

The model can be depicted as shown below with elimination from the central compartment.

**K12**

1.Central compartment

2.Peripheral compartment

**K21**

**KE**

**Bioavailability** refers to the extent and speed with which the active part (drug or metabolite) enters the systemic circulation, accessing the site of action.**OBJECTIVES OF BIOAVAILABILITY STUDIES**1. Bioavailability studies are one of the factors that link in-vivo performance of the drug product used in clinical studies (for determination of evidence of safety and efficacy). 2. Bioavailability studies provide useful information important to establish dosage regimen and to support drug labeling. 3. These studies help in determining the influence of excipient, patient related factors and possible interaction with other drugs on the efficiency of absorption. 4. Bioavailability studies estimates the quality control of a drug product during the early stages of marketing so that the influence of processing factors, storage and stability on drug absorption can be determined.**Bioequivalence Studies**  It is a relative term which denotes that the drug substance in two or more identical dosage forms, reaches the circulation at the same relative rate &to same relative extent i.e., their plasma concentration-time profiles will be identical without significant statistical differences.”**Applications of bioequivalence studiesa.** Bioequivalence studies allow substitution of one product by another product which is equally effective.b. Efficiency and safety of product from batch to batch produced by same company are reduced.c. Bioequivalence studies also reduce the formulation variables.d. Limitations of bioequivalence studies e. It is very difficult, time consuming and expensive process.f. Therapeutically equivalent drug products may not be equally suitable for a particular patient.

**BIOPHARMACEUTICAL CLASSIFICATION SYSTEM:**

Biopharmaceutical classification system was first developed in the year 1995 by a group of scientists (Amidon and his team). It is a scientific frame work for classifying substances based on their aqueous solubility and intestinal permeability. It acts as predicting tool for bio equivalence study design through accurate invivo study.

High solubility and High permeability. E.g Metoprolol, Propranolol

CLASS- I

Low solubility and High permeability. E.g Naproxen, Nifedipine

CLASS-II

High solubility and Low permeability. E.g Cemitidine, Metformin

CLASS-III

Low solubility and Low permeability. E.g Taxol, Chlorthiazole

CLASS-IV

**Fig 3**. **Schematic representation of BCS Classification of drugs.**

**BIOPHARMACEUTICS CONSIDERATION IN DRUG PRODUCT DESIGN :**

1. **Pharmacodynamics consideration**

* Therapeutic objective
* Toxic effects
* Adverse effect

**2. Drug considerations**

* Particle size
* pka & pH profile
* Polymorphism
* Hygroscopicity
* Partition coefficient
* Excipient interaction
* pH stability profile
* Solubility

1. **Drug product considerations**

* Pharmacokinetics of drug
* Bioavailability consideration
* Route of administration
* Desired dose of drug
* Dosing frequency

1. **Patient considerations**

* Acceptability & Compliance of drug product
* Cost

1. **Manufacturing considerations**

* Cost
* Availability of raw materials
* Stability

**SIGNIFICANCE AND APPLICATIONS OF BIOPHARMACEUTICAL STUDIES**

1. The aim of biopharmaceutics is to adjust the delivery of a drug to the site of action to provide optimal therapeutic activity for the patient.2. Biopharmaceutical considerations in the design of a dosage form to deliver the active drug with the desired bioavailability characteristics and therapeutic objectives include (1) the physicochemical properties of the drug molecule, (2) the finished dosage form (e.g., tablet, capsule, etc.), (3) the nature of excipients in the drug product, (4) the manufacturing method, and (5) the route of drug administration. 3. Biopharmaceutical studies must be performed to ensure that the dosage form does not irritate, cause an allergic response, or allow systemic drug absorption from a topical dosage form. 4. Biopharmaceutics has an important role in establishing a link between the in vivo dosage form performance (such as bioavailability, onset of action, safety, and efficacy of the drug to be released from the dosage form) to the dosage form manufacturing process parameters and drug- excipients properties (such as tablet hardness, disintegrants, etc.). Both in vitro (e.g., dissolution) and in vivo methods (bioavailability) are used to evaluate a dosage forms quality and its performance.

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