INTRODUCTION TO BIOPHARMACEUTICS & PHARMACOKINETICS

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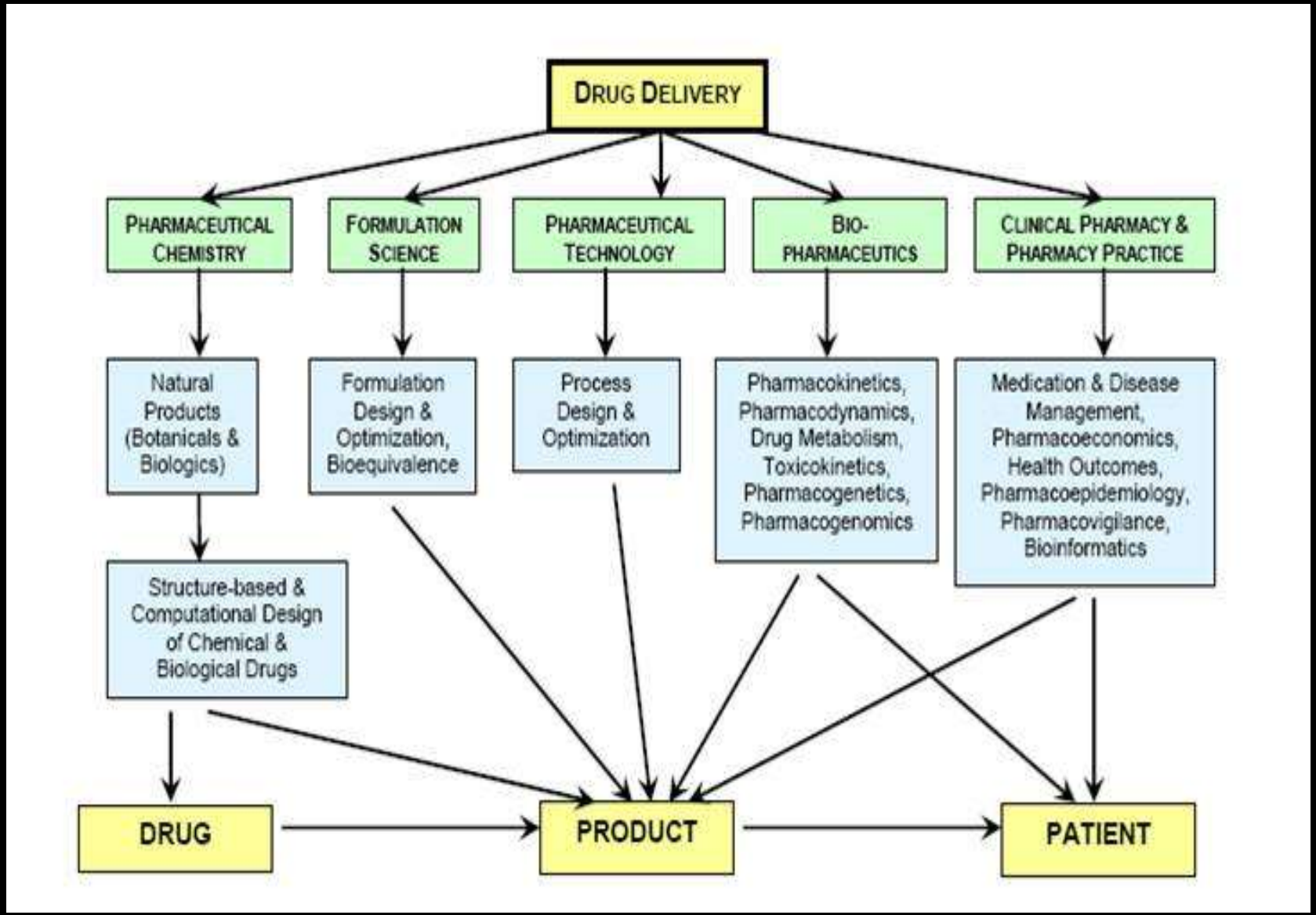
DRUG DELIVERY
PHARMACEUTICAL CHEMISTRY
FORMULATION SCIENCE
PHARMACEUTICAL TECHNOLOGY
BIO-PHARMACEUTICS
CLINICAL PHARMACY & PHARMACY PRACTICE
Natural Products (Botanicals & Biologics)
Formulation Design & Optimization, Bioequivalence
Process Design & Optimization
Pharmacokinetics, Pharmacodynamics, Drug Metabolism, Toxicokinetics, Pharmacogenetics, Pharmacogenomics
Medication & Disease Management, Pharmacoeconomics, Health Outcomes, Pharmacoepidemiology, Pharmacovigilance, Bioinformatics
Structure-based & Computational Design of Chemical & Biological Drugs
DRUG
PRODUCT
PATIENT

- Drugs, whether obtained from plant, animal or mineral sources or synthesized chemically, are rarely administered in their pure chemical form.
- Often, they are combined with a number of inert substances (excipients/adjuvants) and transformed into a convenient dosage form that can be administered by a suitable route.
- Earlier, it was believed that the therapeutic response to a drug is an attribute of its intrinsic pharmacological activity. But today, it is very much understood that the dose-response relationship obtained after drug administration by different routes—for example, oral and parenteral, are not the same.
- The physicochemical characteristics of the active pharmaceutical ingredient (API, or drug substance), the dosage form or the drug, and the route of administration are critical determinants of the *in-vivo* performance, safety and efficacy of the drug product.

- The properties of the drug and its dosage form are carefully engineered and tested to produce a stable drug product that upon administration provides the desired therapeutic response in the patient.

- Both the pharmacist and the pharmaceutical scientist must understand these complex relationships to comprehend the proper use and development of pharmaceuticals.

- To illustrate the importance of the drug substance and the drug formulation on absorption, and distribution of the drug to the site of action, one must first consider the 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.
- The actual dosing regimen (dose, dosage form, dosing interval) was carefully determined in clinical trials to provide the correct drug concentrations at the site of action.
- This sequence of events is profoundly affected—in fact, sometimes orchestrated—by the design of the dosage form, the drug itself, or both.

- Historically, pharmaceutical scientists have evaluated the relative drug availability to the body *in vivo* after giving a drug product to an animal or human, and then comparing specific pharmacologic, clinical, or possible toxic responses.
  - For example, a drug such as isoproterenol causes an increase in heart rate when given intravenously but has no observable effect on the heart when given orally at the same dose level.

- In addition, the *Bioavailability* (a measure of systemic availability of a drug) may differ from one drug product to another containing the same drug, even for the same route of administration.

- This difference in drug bioavailability may be manifested by observing the difference in the therapeutic effectiveness of the drug products.
  - In other words, the nature of the drug molecule, the route of delivery, and the formulation of the dosage form can determine whether an administered drug is therapeutically effective, toxic, or has no apparent effect at all.
- Variations are also observed when the same drug is administered as different dosage forms or similar dosage forms produced by different manufacturers, which in turn depend upon the physicochemical properties of the drug, the excipients present in the dosage form, the method of formulation and the manner of administration.
- A new and separate discipline called *Biopharmaceutics* has therefore been developed to account for all such factors that influence the therapeutic effectiveness of a drug.

- BIOPHARMACEUTICS is defined as the study of factors influencing the rate and amount of drug that reaches the systemic circulation and the use of this information to optimise the therapeutic efficacy of the drug products.

- The process of movement of drug from its site of administration to the systemic circulation is called as ABSORPTION.

- The concentration of drug in plasma and hence the onset of action, and the intensity and duration of response depend upon the bioavailability of drug from its dosage form.

- BIOAVAILABILITY is defined as the rate and extent (amount) of drug absorption. Any alteration in the drug's bioavailability is reflected in its pharmacological effects.

- *Biopharmaceutics* is the science that examines this interrelationship of the physicochemical properties of the drug, the dosage form in which the drug is given, and the route of administration on the rate and extent of systemic drug absorption.

- Thus, biopharmaceutics involves factors that influence

  - the stability of the drug within the drug product,
  - the release of the drug from the drug product,
  - the rate of dissolution/release of the drug at the absorption site, and
  - the systemic absorption of the drug.

- The study of biopharmaceutics is based on fundamental scientific principles and experimental methodology.
- Studies in biopharmaceutics use both *in-vitro* and *in-vivo* methods.
- *In-vitro* methods are procedures employing test apparatus and equipment without involving laboratory animals or humans.
- *In-vivo* methods are more complex studies involving human subjects or laboratory animals.
- These methods must be able to assess the impact of the physical and chemical properties of the drug, drug stability, and large-scale production of the drug and drug product on the biologic performance of the drug.

- Other processes that play a role in the therapeutic activity of a drug are distribution and elimination. Together, they are known as DRUG DISPOSITION.

- The movement of drug between one compartment and the other (generally blood and the extravascular tissues) is referred to as DRUG DISTRIBUTION.

- Since the site of action is usually located in the extravascular tissues, the onset, intensity and sometimes duration of action depend upon the distribution behaviour of the drug.

- The magnitude (intensity) and the duration of action depend largely upon the effective concentration and the time period for which this concentration is maintained at the site of action which in turn depend upon the elimination processes.

- Moreover, biopharmaceutics considers the properties of the drug and dosage form in a physiologic environment, the drug's intended therapeutic use, and the route of administration.

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- ELIMINATION *is defined as the process that tends to remove the drug from the body and terminate its action.*

- Elimination occurs by two processes— BIOTRANSFORMATION (*metabolism*), which usually inactivates the drug, and EXCRETION which is responsible for the exit of drug/metabolites from the body.

- In order to administer drugs optimally, knowledge is needed not only of the mechanisms of drug absorption, distribution, metabolism and excretion (*ADME*) but also of the rate (kinetics) at which they occur i.e. PHARMACOKINETICS.

Elimination of drugs from the body

MAJOR

KIDNEY
filtration
secretion
(reabsorption)

LIVER
metabolism
secretion

MINOR

LUNGS
exhalation

OTHERS
mother's milk
sweat, saliva etc.

PHARMACOKINETICS

- In order to administer drugs optimally, knowledge is needed not only of the mechanisms of drug absorption, distribution, metabolism and excretion (*ADME*) but also of the rate (kinetics) at which they occur i.e. pharmacokinetics.

- After a drug is released from its dosage form, the drug is absorbed into the surrounding tissue, the body, or both.

- The distribution through and elimination of the drug in the body varies for each patient but can be characterized using mathematical models and statistics.

- **PHARMACOKINETICS** is defined as the study of time course of drug ADME and their relationship with its therapeutic and toxic effects of the drug. Simply speaking, pharmacokinetics is the kinetics of **ADME** or **KADME**.

- *Pharmacokinetics* is the science of the kinetics of drug absorption, distribution, and elimination (ie, excretion and metabolism).

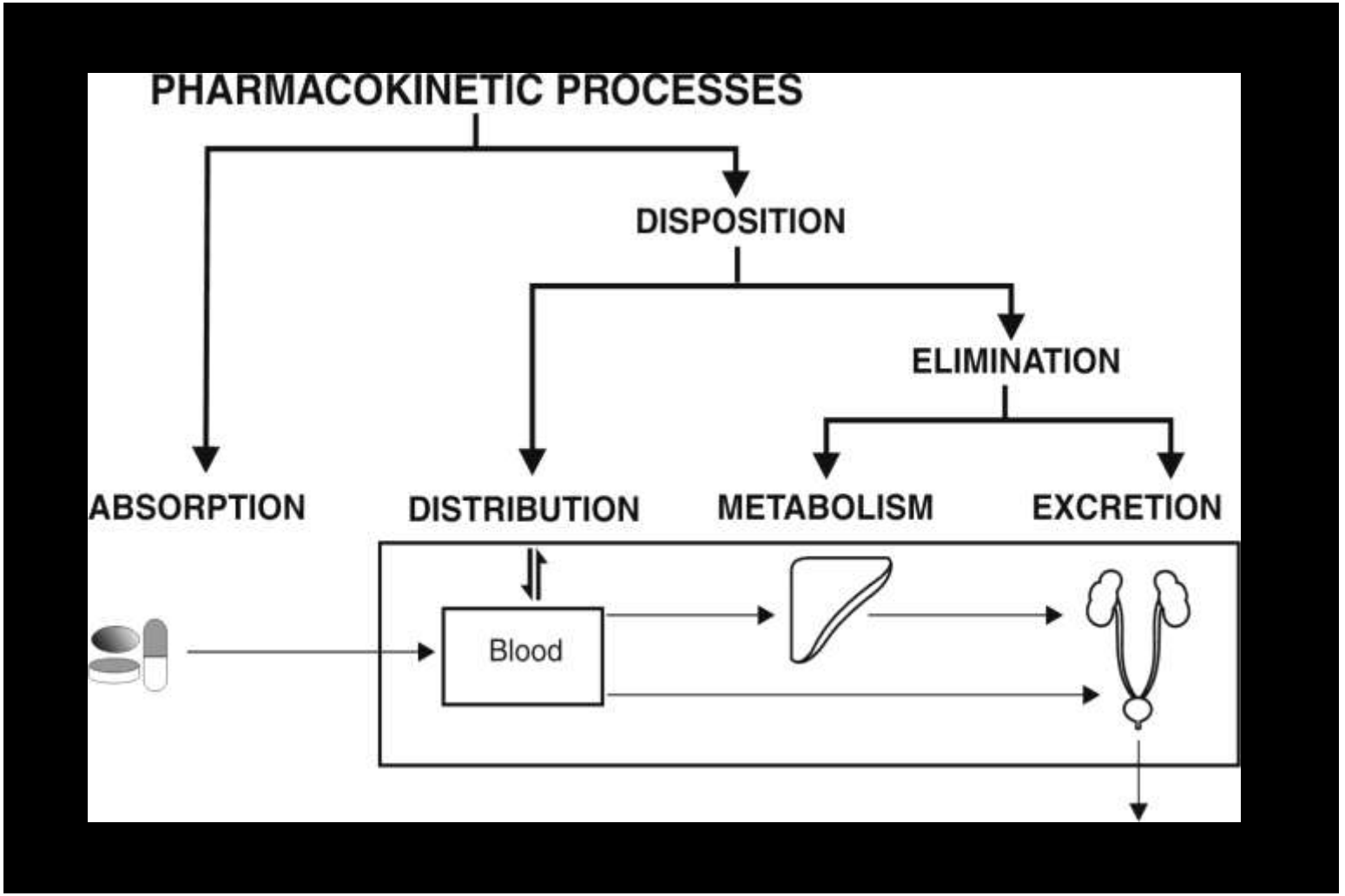
- The description of drug distribution and elimination is often termed **DRUG DISPOSITION**.

- Characterization of drug disposition is an important prerequisite for determination or modification of dosing regimens for individuals and groups of patients.

- The study of pharmacokinetics involves both experimental and theoretical approaches.

- The experimental aspect of pharmacokinetics involves the development of biologic sampling techniques, analytical methods for the measurement of drugs and metabolites, and procedures that facilitate data collection and manipulation.
- The theoretical aspect of pharmacokinetics involves the development of pharmacokinetic models that predict drug disposition after drug administration.
- The application of statistics is an integral part of pharmacokinetic studies.
- Statistical methods are used for pharmacokinetic parameter estimation and data interpretation ultimately for the purpose of designing and predicting optimal dosing regimens for individuals or groups of patients.

- Statistical methods are applied to pharmacokinetic models to determine data error and structural model deviations.
- Mathematics and computer techniques form the theoretical basis of many pharmacokinetic methods.
- Classical pharmacokinetics is a study of theoretical models focusing mostly on model development and parameterization.

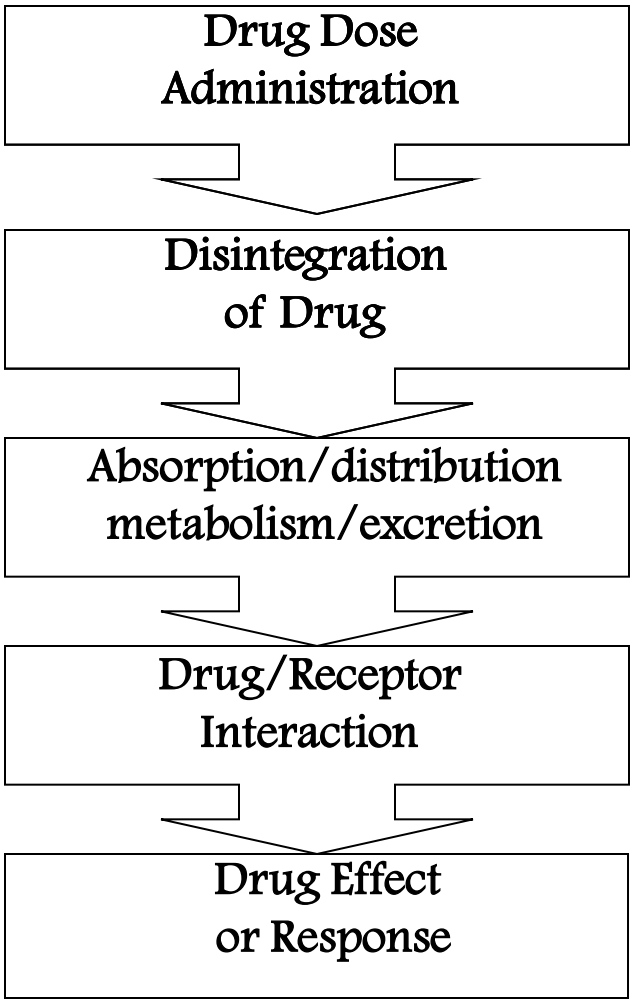

PHARMACOKINETIC PROCESSES
DISPOSITION
ELIMINATION
ABSORPTION
DISTRIBUTION
METABOLISM
EXCRETION
Blood

Pharmaceutical

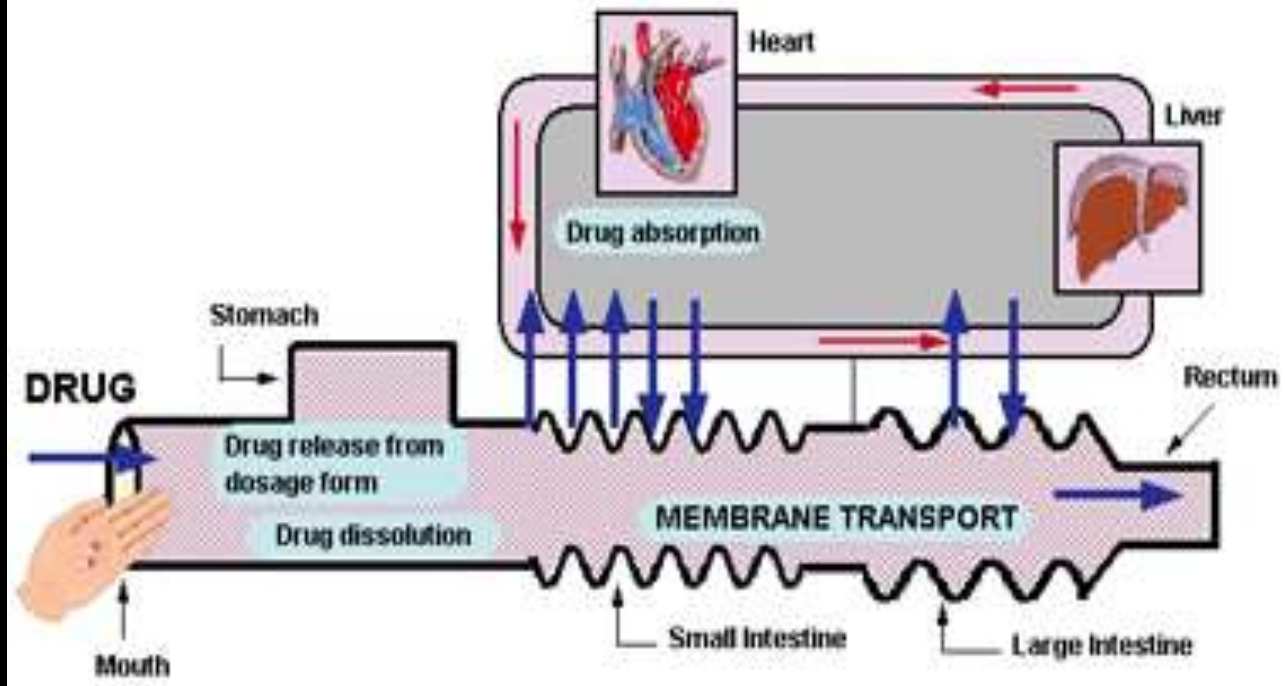
Pharmacokinetics

Pharmacodynamics

Pharmacotherapeutics



Movement of drug through the GI tract:



APPLICATIONS OF PHARMACOKINETIC STUDIES

- Bioavailability measurements
- Effects of body physiology on drug absorption and disposition
- Dosage adjustments in disease states
- Correlation of pharmacologic response with dose
- Evaluation of drug interactions

CLINICAL PHARMACOKINETICS

- During the drug development process, large numbers of patients are tested to determine optimum dosing regimens, which are then recommended by the manufacturer to produce the desired pharmacologic response in the majority of the anticipated patient population.

- The use of pharmacokinetic principles in optimising the drug dosage to suit individual patient needs and achieving maximum therapeutic utility is called as **CLINICAL PHARMACOKINETICS**.

- ***Clinical pharmacokinetics*** is the application of pharmacokinetic methods to drug therapy.

- Clinical pharmacokinetics involves a multidisciplinary approach to individually optimized dosing strategies based on the patient's disease state and patient-specific considerations.

- The influence of many diseases on drug disposition is not adequately studied. Age, gender, genetic, and ethnic differences can also result in pharmacokinetic differences that may affect the outcome of drug therapy.

- The study of pharmacokinetic differences of drugs in various population groups is termed ***Population Pharmacokinetics*** .

- The physicochemical characteristics of the active pharmaceutical ingredient (API, or drug substance), the dosage form or the drug, and the route of administration are critical determinants of the *in-vivo* performance, safety and efficacy of the drug product.

CLINICAL PHARMACOKINETICS INVOLVES

- Initial design of drug dosage regimen, including dose, dose interval, route of administration and dosage form.
- Diagnostic works up to determine the reason for unusual drug response
- Extent of patient compliance
- Bioavailability problems
- Medication errors
- Drug interactions
- Unusual distribution
- Elimination kinetics
- Certain pharmacogenetic effects such as unusual receptor site sensitivity or abnormal levels of metabolic enzymes

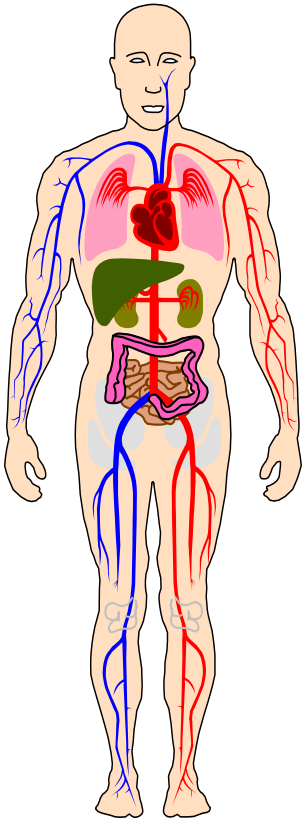
PHARMACODYNAMICS

- Pharmacodynamics refers to the relationship between the drug concentration at the site of action (receptor) and pharmacologic response, including biochemical and physiologic effects that influence the interaction of drug with the receptor.

- The interaction of a drug molecule with a receptor causes the initiation of a sequence of molecular events resulting in a pharmacologic or toxic response. Pharmacokinetic-pharmacodynamic models are constructed to relate plasma drug level to drug concentration in the site of action and establish the intensity and time course of the drug.

- **Pharmacokinetics**
  - "what the body does to the drug"
    - Absorption
    - Distribution
    - Metabolism
    - Elimination

Disposition



- **Pharmacodynamics**
  - "what the drug does to the body"
    - wanted effects - efficacy
    - unwanted effects - toxicity

- Drug administration and therapy can now be conveniently divided into four phases or processes:
  - **The Pharmaceutical Phase**
  - **The Pharmacokinetic Phase**
  - **The Pharmacodynamic Phase**
  - **The Therapeutic Phase**

- **The Pharmaceutical Phase:**

It is concerned with –

  - Physicochemical properties of the drug, and
  - Design and manufacture of an effective drug product for administration by a suitable route.

- **The Pharmacokinetic Phase:**

It is concerned with the ADME of drugs as elicited by the plasma drug concentration-time profile and its relationship with the dose, dosage form and frequency and route of administration. In short, it is the sum of all the processes inflicted by the body on the drug.

- **The Pharmacodynamic Phase:** It is concerned with the biochemical and physiologic effects of the drug and its mechanism of action. It is characterized by the concentration of drug at the site of action and its relation to the magnitude of effects observed. Thus, in comparison –
  - ***Pharmacokinetics*** *is a study of what the body does to the drug, whereas*
  - ***Pharmacodynamics*** *is a study of what the drug does to the body.*
  - ***Pharmacokinetics*** *relates changes in concentration of drug within the body with time after its administration, whereas*
  - ***Pharmacodynamics*** *relates response to concentration of drug in the body.*

- **The Therapeutic Phase:** It is concerned with the translation of pharmacological effect into clinical benefit.

Drug + Excipients
FORMULATION
Drug in Dosage Form
Drug not Released
Oral Administration
Drug Release and Dissolution
Drug Decomposed, Metabolized, Bound or Excreted
Absorption Site in the GIT
ABSORPTION
Drug in Systemic Circulation
DISPOSITION
DISTRIBUTION
ELIMINATION
Extravascular Tissues
Tissues at the Site of Action
Metabolism and Excretion
Pharmacologic Response
Therapeutic / Toxic Effects
Parenteral Administration
PHARMACEUTICS
PHARMACOKINETICS
PHARMACO-DYNAMICS
THERA-PEUTICS
BIOPHARMACEUTICS
CLINICAL PHARMACOKINETICS

TOXICOKINETICS AND CLINICAL TOXICOLOGY

- *Toxicokinetics* is the application of pharmacokinetic principles to the design, conduct, and interpretation of drug safety evaluation studies and in validating dose-related exposure in animals.
- Toxicokinetic data aids in the interpretation of toxicologic findings in animals and extrapolation of the resulting data to humans.
- Toxicokinetic studies are performed in animals during preclinical drug development and may continue after the drug has been tested in clinical trials.
- *Clinical toxicology* is the study of adverse effects of drugs and toxic substances (poisons) in the body.

- The pharmacokinetics of a drug in an overmedicated (intoxicated) patient may be very different from the pharmacokinetics of the same drug given in lower therapeutic doses.

- At very high doses, the drug concentration in the body may saturate enzymes involved in the absorption, biotransformation, or active renal secretion mechanisms, thereby changing the pharmacokinetics from linear to nonlinear pharmacokinetics..

- Drugs frequently involved in toxicity cases include acetaminophen, salicylates, morphine, and the tricylic antidepressants (TCAs). Many of these drugs can be assayed conveniently by fluorescence immunoassay (FIA) kits.

MEASUREMENT OF DRUG CONCENTRATIONS

- Because drug concentrations are an important element in determining individual or population pharmacokinetics, drug concentrations are measured in biologic samples, such as milk, saliva, plasma, and urine.
- Sensitive, accurate, and precise analytical methods are available for the direct measurement of drugs in biologic matrices.
- Such measurements are generally validated so that accurate information is generated for pharmacokinetic and clinical monitoring.
- In general, chromatographic methods are most frequently employed for drug concentration measurement, because chromatography separates the drug from other related materials that may cause assay interference.

SAMPLING OF BIOLOGIC SPECIMENS

- Only a few biologic specimens may be obtained safely from the patient to gain information as to the drug concentration in the body.
- *Invasive methods* include sampling blood, spinal fluid, synovial fluid, tissue biopsy, or any biologic material that requires parenteral or surgical intervention in the patient.
- In contrast, *noninvasive methods* include sampling of urine, saliva, feces, expired air, or any biologic material that can be obtained without parenteral or surgical intervention.
- The measurement of drug and metabolite concentration in each of these biologic materials yields important information, such as the amount of drug retained in, or transported into, that region of the tissue or fluid, the likely pharmacologic or toxicologic outcome of drug dosing, and drug metabolite formation or transport.

DRUG CONCENTRATIONS IN BLOOD, PLASMA, OR SERUM

- Measurement of drug concentration (levels) in the blood, serum, or plasma is the most direct approach to assessing the pharmacokinetics of the drug in the body.
- Whole blood contains cellular elements including red blood cells, white blood cells, platelets, and various other proteins, such as albumin and globulins.
- In general, serum or plasma is most commonly used for drug measurement.
- To obtain serum, whole blood is allowed to clot and the serum is collected from the supernatant after centrifugation. Plasma is obtained from the supernatant of centrifuged whole blood to which an anticoagulant, such as heparin, has been added.

- Therefore, the protein content of serum and plasma is not the same.

- Plasma perfuses all the tissues of the body, including the cellular elements in the blood. Assuming that a drug in the plasma is in dynamic equilibrium with the tissues, then changes in the drug concentration in plasma will reflect changes in tissue drug concentrations.

DRUG CONCENTRATIONS IN TISSUES

- Tissue biopsies are occasionally removed for diagnostic purposes, such as the verification of a malignancy.
- Usually, only a small sample of tissue is removed, making drug concentration measurement difficult.
- Drug concentrations in tissue biopsies may not reflect drug concentration in other tissues nor the drug concentration in all parts of the tissue from which the biopsy material was removed.
- In fact, for many tissues, blood flow to one part of the tissues need not be the same as the blood flow to another part of the same tissue.
- The measurement of the drug concentration in tissue biopsy material may be used to ascertain if the drug reached the tissues and reached the proper concentration within the tissue.

DRUG CONCENTRATIONS IN URINE AND FECES

- Measurement of drug in urine is an indirect method to ascertain the bioavailability of a drug.
- The rate and extent of drug excreted in the urine reflects the rate and extent of systemic drug absorption.
- Measurement of drug in feces may reflect drug that has not been absorbed after an oral dose or may reflect drug that has been expelled by biliary secretion after systemic absorption.
- Fecal drug excretion is often performed in mass balance studies, in which the investigator attempts to account for the entire dose given to the patient.

DRUG CONCENTRATIONS IN SALIVA

- Saliva drug concentrations have been reviewed for many drugs for therapeutic drug monitoring .
- Because only free drug diffuses into the saliva, saliva drug levels tend to approximate free drug rather than total plasma drug concentration.
- The saliva/plasma drug concentration ratio is less than 1 for many drugs. The saliva/plasma drug concentration ratio is mostly influenced by the pKa of the drug and the pH of the saliva.
- Weak acid drugs and weak base drugs with pKa significantly different than pH 7.4 (plasma pH) generally have better correlation to plasma drug levels.
- The saliva drug concentrations taken after equilibrium with the plasma drug concentration generally provide more stable indication of drug levels in the body.

SIGNIFICANCE OF MEASURING PLASMA DRUG CONCENTRATIONS

- The intensity of the pharmacologic or toxic effect of a drug is often related to the concentration of the drug at the receptor site, usually located in the tissue cells.
- Because most of the tissue cells are richly perfused with tissue fluids or plasma, measuring the plasma drug level is a responsive method of monitoring the course of therapy.
- Clinically, individual variations in the pharmacokinetics of drugs are quite common. Monitoring the concentration of drugs in the blood or plasma ascertains that the calculated dose actually delivers the plasma level required for therapeutic effect.
- With some drugs, receptor expression and/or sensitivity in individuals varies, so monitoring of plasma levels is needed to distinguish the patient who is receiving too much of a drug from the patient who is supersensitive to the drug.

- Moreover, the patient's physiologic functions may be affected by disease, nutrition, environment, concurrent drug therapy, and other factors. Pharmacokinetic models allow more accurate interpretation of the relationship between plasma drug levels and pharmacologic response.

- In the absence of pharmacokinetic information, plasma drug levels are relatively useless for dosage adjustment.

- In order to apply this information properly, it is important to know when the blood sample was drawn, what dose of the drug was given, and the route of administration.

- If the proper information is available, the use of pharmacokinetic equations and models may describe the blood level–time curve accurately.

- Monitoring of plasma drug concentrations allows for the adjustment of the drug dosage in order to individualize and optimize therapeutic drug regimens. In the presence of alteration in physiologic functions due to disease, monitoring plasma drug concentrations may provide a guide to the progress of the disease state and enable the investigator to modify the drug dosage accordingly.

- Clinically, sound medical judgment and observation are most important. Therapeutic decisions should not be based solely on plasma drug concentrations.

- In many cases, the *pharmacodynamic response* to the drug may be more important to measure than just the plasma drug concentration.

- For drugs that act irreversibly at the receptor site, plasma drug concentrations may not accurately predict pharmacodynamic response.
- Drugs used in cancer chemotherapy often interfere with nucleic acid or protein biosynthesis to destroy tumor cells.
- For these drugs, the plasma drug concentration does not relate directly to the pharmacodynamic response. In this case, other pathophysiologic parameters and side effects are monitored in the patient to prevent adverse toxicity.

Drugs that have to enter the systemic circulation to exert their effect can be administered by three major routes:

- **The Enteral Route:** includes *peroral* i.e. gastrointestinal, sublingual/buccal and rectal routes. The GI route is the most common for administration of majority of drugs.

- **The Parenteral Route:** includes all routes of administration through or under one or more layers of skin. While no absorption is required when the drug is administered i.v., it is necessary for extravascular parenteral routes like the subcutaneous and the intramuscular routes.

- **The Topical Route:** includes skin, eyes or other specific membranes. The intranasal, inhalation, intravaginal and transdermal routes may be considered enteral or topical according to different definitions.

BIOAVAILABILITY/ABSORPTION OF DRUG FROM COMMON ROUTES OF DRUG ADMINISTRATION

PARENTERAL ROUTE

ROUTE	BIOAVAILABILITY	ADVANTAGES	DISADVANTAGES
Intravenous (IV)	· Complete (100%) systemic drug absorption.	· Drug is given for immediate or controlled effect. · May inject large fluid volumes. · Suitable for irritating drugs	· Increased chance for adverse reaction. · Possible anaphylaxis. · Requires skill in insertion of infusion set. · Tissue damage at site of injection (infiltration, necrosis, or sterile abscess).
Intramuscular injection (IM)	· Rapid absorption from aqueous solutions. · Slow absorption from non-aqueous (oily) solutions.	· Easier to inject than intravenous injection. · Larger volumes may be used compared to subcutaneous solution.	· Irritating drugs may be very painful. · Variable rates of absorption depending upon muscle group injected and blood flow.
Subcutaneous injection (SC)	· Rapid absorption from aqueous solution. · Slow absorption from depot formulations.	· Generally, used for vaccines and drugs not absorbed orally e.g. insulin.	· Rate of drug absorption depends upon blood flow and injection volume.

ENTERAL ROUTE

ROUTE	BIOAVAILABILITY	ADVANTAGES	DISADVANTAGES
Buccal or sublingual (SL)	· Rapid absorption of lipid-soluble drugs.	No presystemic metabolism.	· Some drug may be swallowed. Not for most drugs or drugs with high doses.
Oral (PO)	· Absorption may vary. Generally slower absorption rate compared to IV bolus or IM injection.	· Safest and easiest route of drug administration. · Suitable for both immediate-release and modified-release drug products.	· Some drugs are unstable in GIT, or undergo presystemic metabolism or show erratic absorption.
Rectal (PR)	· Absorption may vary from suppository. · More reliable absorption from enema (solution).	· Useful when patient cannot swallow medication. · Used for local and systemic effects.	· Absorption may be erratic. Suppository may migrate to different position. · Some patient discomfort.

OTHER ROUTES

ROUTE	BIOAVAILABILITY	ADVANTAGES	DISADVANTAGES
Transdermal	· Slow absorption, rate may vary. · Increased absorption with occlusive dressings.	· Transdermal delivery system (patch) is easy to use and withdraw. · Continuous release for a specified period. · Used for lipid-soluble drugs with low dose and low MW. · Low presystemic metabolism.	· Some irritation by patch or drug. · Permeability of skin variable with condition, anatomic site, age, and gender. · Type of cream or ointment base affects drug release and absorption.
Inhalation	· Rapid absorption.	· May be used for local or systemic effects.	· Particle size of drug determines anatomic placement in respiratory tract.

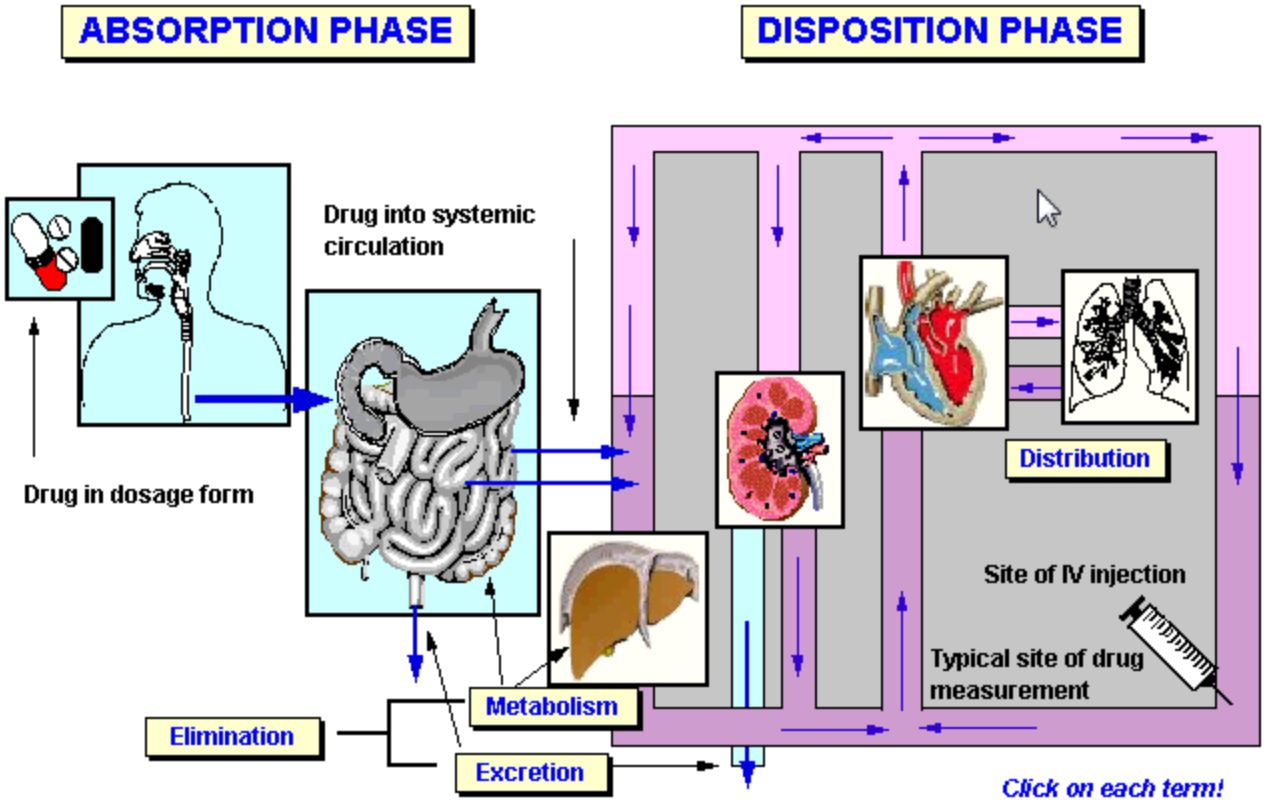
ROUTES OF DRUG ADMINISTRATION

ROUTE	APPROXIMATE ONSET OF ACTION	INDICATIONS	EXAMPLES
Oral (PO, p.o.)	30 - 60 minutes	whenever possible, safest and most convenient route	most medications, e.g. analgesics, sedatives, hypnotics, antibiotics
Sublingual (S.l.)	several minutes	when rapid effect is desired	NTG (nitroglycerin) in angina pectoris
Buccal (bucc.)	several minutes	convenient dosage form for certain drugs; may be used in unconscious patients	androgenic drugs

ROUTE	APPROXIMATE ONSET OF ACTION	INDICATIONS	EXAMPLES
Rectal (p.r.)	15 - 30 minutes	when patients are unable to take oral medications and parenteral route is not indicated, also for local effect	analgesics, antiemetics, laxatives
Transdermal	30 - 60 minutes	convenient dosage form, provides continuous absorption and systemic effects over extended time (hours, days, etc.)	Nitroglycerin, estrogen, morphine
Subcutaneous (sq, s.c., subq., subcu)	several minutes	for drugs that are inactivated in gastrointestinal tract	insulin
Intramuscular (i.m., IM)	several minutes	for drugs with poor oral absorption, when high blood levels are required, when rapid effect is desired	narcotic analgesics antibiotics

ROUTE	APPROXIMATE ONSET OF ACTION	INDICATIONS	EXAMPLES
Intravenous (i.v., IV)	within 1 minute	in emergency situations, when immediate effect is desired, when large volumes need to be administered, e.g. infusion	IV fluids nutrient supplementation antibiotics resuscitative drugs
Intraarterial (i.a.)	within 1 minute	for local effects within specific target organ	cancer drugs
Intrathecal	several minutes	for local effects within the spinal cord	spinal anesthesia

ROUTE	APPROXIMATE ONSET OF ACTION	INDICATIONS	EXAMPLES
Inhalation	within 1 minute	for local effects within respiratory tract	Antiasthmatics, Bronchodialtors
Topical	within 1 hour	for local effects on skin and mucous membrane of eye, ear, nose, mouth	creams, ointments, sprays, tinctures, lozenges
Vaginal	15 - 30 minutes	for local effect	creams, foams, suppositories


ABSORPTION PHASE
DISPOSITION PHASE
Drug into systemic circulation
Drug in dosage form
Distribution
Site of IV injection
Typical site of drug measurement
Metabolism
Elimination
Excretion
Click on each term!