UNIT

I

INTRODUCTION OF BIOPHARMACEUTICS

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Drugs are molecules that are used to diagnose, cure, mitigate, treat, or prevent illness. For systemic or local therapeutic action, drugs are administered in a range of dosage forms or drug products such as solids (tablets, capsules), semisolids (ointments, creams), liquids, suspensions, emulsions, and so on. For the preparation of suitable dosage formulations, active pharmaceutical ingredients are frequently mixed with a number of inert substances (excipients/adjuvants). To get the desired effects, these dosage formulations should be delivered through the appropriate route of administration.

When the same drug is administered through different routes of administration, they show different dose-response relationships. The rate and degree of systemic drug absorption are affected by various factors such as the physicochemical properties of the drug, the type of dosage form, and the route of administration. The study of these factors and apply knowledge this to enhance the effectiveness of a drugs is called biopharmaceutics.

BIOPHARMACEUTICS

Biopharmaceutics studies the impact of a drug's physicochemical properties, dosage form (drug product), and route of administration on the rate and extent of systemic drug absorption. The impact of the drug substance and formulation on absorption and in vivo distribution of the drug to the site of action is described as a series of events that occur before the therapeutic effect of the drug is elicited. Figure 1.1 depicts a general strategy for describing this dynamic interaction after administration.

The study of the drug's physicochemical properties, dosage form, and mode of administration and their effects on the rate and amount of systemic drug absorption is called ***biopharmaceutics***.

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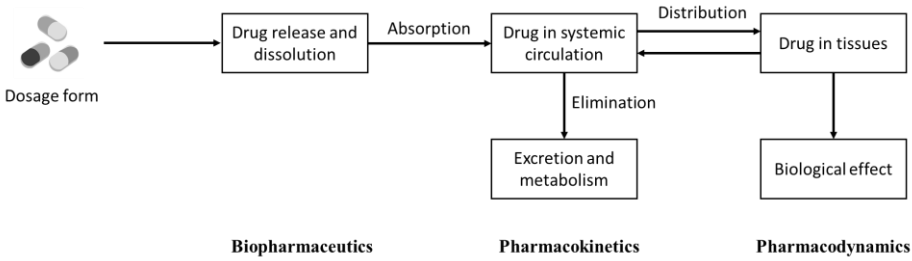

Figure 1.1: Schematic illustration of dynamic interaction after administration

The dosing regimen affects drug efficacy and safety. Varying medications have different recommended dosages and dosing periods. Furthermore, the appropriate dosage for a particular medicine can vary greatly amongst patients.

Patients can take the medication in its dosage form by oral, intravenous, subcutaneous, transdermal, or by any other method of administration that is appropriate for them. After that, the drug is discharged from the dosage form in a method that is predictable and distinguishable. The drug is then absorbed from the site of administration, either into the surrounding tissue for local action or into the body (as is the case with oral dosage forms), or both. At long last, the drug makes its way to the site of action. When the concentration of the drug at the site of action reaches or exceeds the minimum effective concentration, a pharmacodynamic response occurs (MEC). Clinical trials are conducted to determine the optimal dosing regimen in order to provide drug concentrations that are therapeutically effective in the majority of patients. This dosing regimen includes the starting dose, the maintenance dose, the dosage form, and the dosing interval. This sequence of occurrences is strongly influenced by the design of the dosage form and the physicochemical properties of the medication that is being taken.

PHARMACOKINETICS

A drug is absorbed into the surrounding tissue, the body, or both after being released from its dosage form. The distribution and elimination of the drug in the body vary from patient to patient, but can be described using mathematical models and statistical analysis. The science of the kinetics of medication absorption, distribution, and elimination called

pharmacokinetics (metabolism and excretion). Drug disposition commonly refers to the distribution and elimination of drugs. Important requirement for the selection or modification of dosage regimens for individuals or groups of patients is the characterization of drug disposition. Figure 1.2 depicts a general strategy for describing pharmacokinetic processes.

Study of how the body affects a drug after administration, through the processes of absorption, distribution, metabolism, and excretion (ADME) is called ***pharmacokinetics****.*

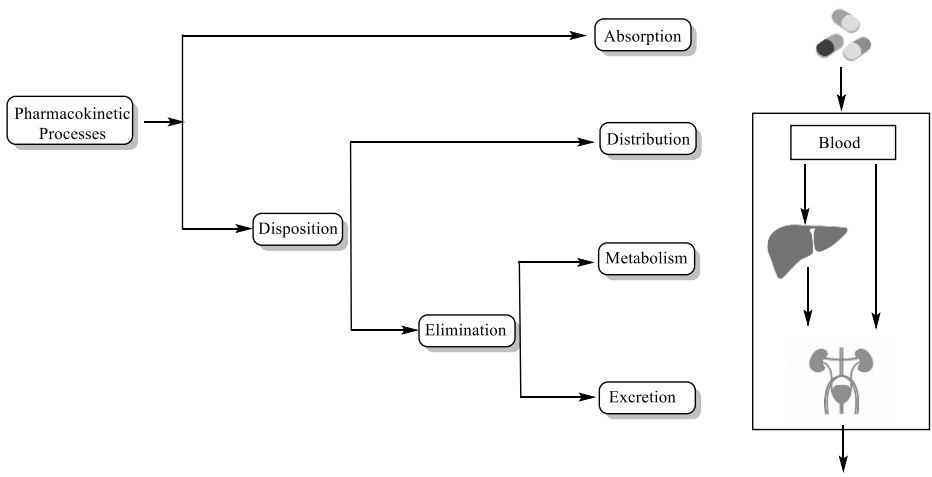

Figure 1.2: Schematic illustration of pharmacokinetic processes

Absorption is the process of a drug moving from its delivery site to the systemic circulation. The bioavailability of a medication from its dose form determines its concentration in plasma, and thus the beginning of effect, as well as the strength and duration of response.

The **bioavailability** of a medication from its dose form determines its concentration in plasma, and thus the beginning of effect, as well as the strength and duration of response. They are referred to together as **drug disposition**. **Drug distribution** refers to the flow of a drug from one compartment to another (usually blood and extravascular tissues).

Elimination is defined as the process by which a medication is removed from the body and its activity is terminated. Elimination is accomplished through two processes: biotransformation (metabolism), which normally inactivates the drug, and excretion, which is responsible for drug/metabolite departure from the body.

To distribute pharmaceuticals ideally, knowledge of the processes of drug absorption, distribution, metabolism, and excretion (ADME) as well as the rate (kinetics) at which they occur, i.e. pharmacokinetics, is essential. The study of the time course of a drug's ADME and its relationship to the drug's therapeutic and detrimental effects is known as **pharmacokinetics (**Figure 1.2).

PHARMACODYNAMICS

This includes drug action mechanisms and the relationship between drug concentration and effect. A basic example of pharmacodynamics is the quantitative interaction between a drug and a drug receptor that produces a reaction. Receptors are the molecules that interact with medications to cause a pharmacological effect within the body. Figure 1.3 demonstrates a general pharmacodynamics concept.

*Study of how drug affect the body (pharmacologic or toxicologic effect) through drug-target interaction is called **pharmacodynamics**. It includes study of biochemical, physiologic, and molecular effects of drugs on the body*

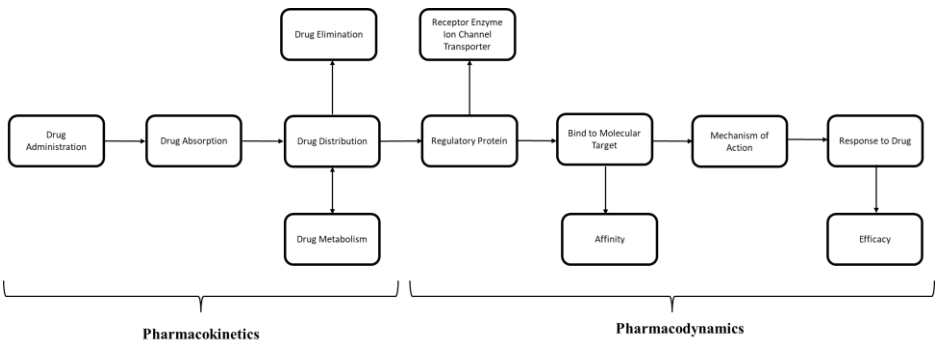

Figure 1.3: Schematic illustration of pharmacodynamics processes

The pharmacodynamic effect, which is also referred to as the pharmacologic effect at times, has the potential to either be therapeutic or induce toxicity. Drugs frequently have multiple effects, including the therapeutic response that is desired as well as side effects that patients do not want. The pharmacodynamic effect is related to the dose and the concentration of the drug for many different medications; the higher the dose, the higher the drug concentrations in the body, and the more intense the pharmacodynamic effect, all the way up to a maximum effect. It is

preferable for the toxic effects and/or side effects of drugs to occur at higher drug concentrations than the minimum required drug concentrations for the desired therapeutic effect. Unfortunately, unwelcome side effects frequently occur at the same time as the therapeutic doses.

PHASES INVOLVED IN DRUG ADMINISTRATION AND THERAPY

Drug administration and therapy may currently be divided into four separate parts or procedures (Figure 1.4):

1. **The Pharmaceutical Phase:** This phase is concerned with
   a) the physicochemical properties of the medication, as well as
   b) the design and production of a safe and effective pharmacological product for administration via an acceptable route.
2. **The Pharmacokinetic Phase** is concerned with pharmaceutical ADME as shown by the plasma drug concentration-time profile, as well as the relationship between dose, dosage form, frequency, and mode of administration. In a word, it is the sum of all the processes imposed on the medication by the body.
3. **The Pharmacodynamic Phase** is concerned with the drug's biochemical and physiologic effects, as well as its mode of action. The drug concentration at the site of action and its connection to the magnitude of the observed effects characterise it.
4. **The Therapeutic Phase** is concerned with converting pharmacological impact into therapeutic benefit.

To provide appropriate therapy, the medicine product must be designed to distribute the active principle at the right pace and amount based on the patient's needs. Knowing what factors impact a drug's bioavailability assists in developing the optimal formulation feasible. A greater understanding of the drug's pharmacokinetics (together with its pharmacodynamics) can assist in the formulation of an appropriate dosing regimen (the way the drug should be taken). This eliminates the need for the empirical method, which involves a great deal of trial and error to establish the correct balance between desired therapeutic and undesirable harmful effects.

Biopharmaceutics and pharmacokinetics knowledge and ideas are critical in the design and development of new pharmaceuticals and dosage formulations, as well as in improving the therapeutic efficacy of current treatments.

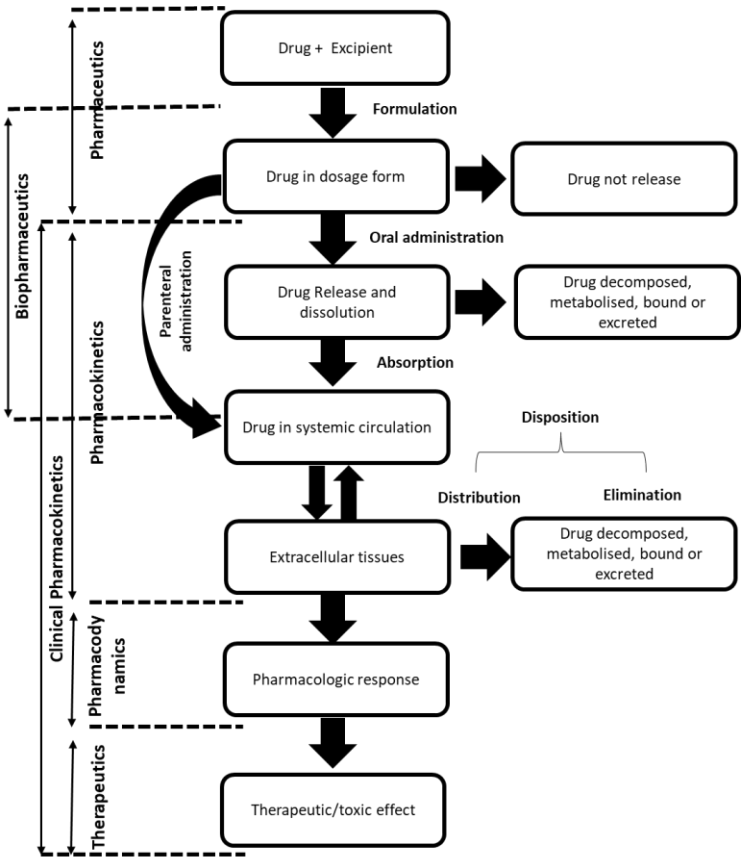

Figure 1.4: The procedures involved in drug treatments are depicted in a diagram.

WHAT ROLE DO BIOPHARMACEUTICS, PHARMACOKINETICS, AND PHARMACOLOGICAL RESPONSES PLAY?

In general, a pharmacologic response will occur when drug molecules engage in a certain manner with drug target molecules. This interaction is necessary for the medicine to have its desired effect. Although it is usual practise to refer to the drug target as a receptor, this does not

mean that each and every drug target in fact falls into the category of receptor.

Although we now know that neither the drug nor the targets are rigid entities and when viewed from the perspective of systems biology, drug responses can hardly ever be explained by a single and punctual interaction event, but rather by the diversity of events triggered by the interaction of the drug with bodily elements, the key and lock analogy is still used to explain the typically specific recognition event that occurs between the drug and the drug target.

Alternatively, we can say, drugs work either by preventing the interaction of a drug target with an endogenous ligand or by inducing a conformational change in the drug target that leads to a pharmacologic response.

The magnitude of the pharmacological effect will essentially be determined by two factors: on the one hand, the number of drug molecules that, at any given moment, are interacting (binding) with the correspondent target copies, and on the other hand, how favourable such an interaction is from a thermodynamic point of view. This conclusion can be drawn from the comments that came before it. The medicine's inherent potency increases in direct proportion to the magnitude of the affinity between the drug and its intended recipient. It is important to keep in mind that the optimal response may be anticipated if, at any one time, all of the free copies of the target are taken up by drug molecules. Take into account, as well, that the living system may resort to a variety of techniques in order to stop the activity of the medicine or compensate for its effects (e.g., inactivating the drug target, upregulating or downregulating the drug target).

It is noteworthy to point out that the meeting of a drug molecule and a target molecule is a probabilistic occurrence that is determined by the collision probability between both partners of the drug-target complex. This is something that has to be taken into consideration. Therefore, it is dependent not only on the number of drug molecules that are located in close proximity to the molecular target, but also on the number of copies of the drug target that are located in close proximity to the drug molecules.

If we give it some thought, we can see how this explains the importance of biopharmaceutics and pharmacokinetics. Not only does the magnitude of the pharmacological reaction depend on the inherent potency of the drug, but it also depends on the number of drug molecules that are occupied by drug target molecules at any particular point in time. This, in turn, is directly dependent on the number of drug molecules that are accessible to the molecules that are being targeted at the site of action. Even if a drug has a high intrinsic potency, there will be no pharmacological reaction if it is unable to enter the biophase in sufficient quantities to occupy a pharmacologically significant proportion of the drug target copies. This holds true even if the drug is available in large quantities.

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