DOSAGE FORM DESIGN

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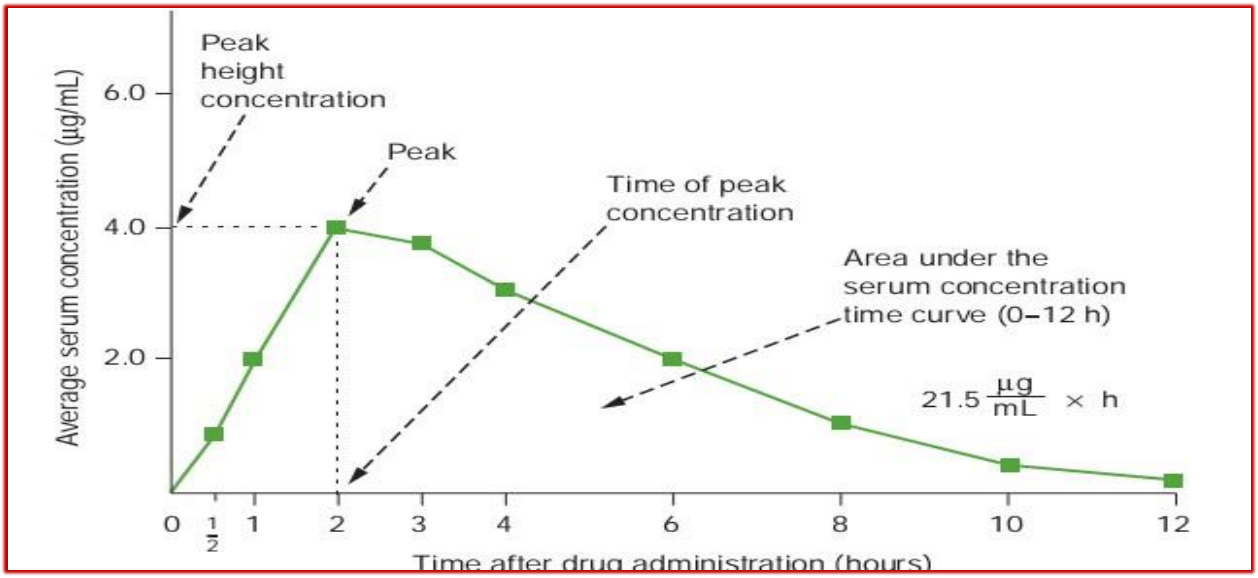
Bioavailability and bioequivalence:

Bioavailability: is the **rate** and **extent** of **drug absorption** from site of administration to the general circulation.

Bioequivalence: refers to a **comparison of bioavailabilities** of **different formulations**, **drug products**, or **batches** of the **same drug product**.



Bioavailability used to determine:

1. **Amount of drug absorbed** from a formulation or dosage form,
2. **Rate at which the drug was absorbed**,
3. **Duration of the drug's presence in biologic fluid** or tissue correlated with the patient's response, and
4. Relationship between **drug blood levels** and **clinical efficacy and toxicity**.

During product development stage:

1. Studies bioavailability to **compare** **different formulations of the drug substance** to ascertain which one allows the most **desirable absorption** pattern.

2. Later **bioavailability studies used to compare the availability of the drug substance in** **different production batches**.

3. They may also be used to **compare the availability** of the drug substance in **different dosage forms (e.g., tablets, capsules, elixirs)**,

4. or in the **same dosage form produced by different (companies) manufacturers**.

 The **absolute bioavailability** following **oral dosing** is generally compared to **intravenous dosing.**

Bioavailability—Absolute versus Relative:

When the systemic availability of a drug administered **orally** is determined in comparison to its **intravenous administration**, it is called as **absolute bioavailability**. It is denoted by symbol **F**.

When the systemic availability of a drug after **oral** administration is compared with that of an **oral standard of the same drug** (such as an **aqueous or non-aqueous solution or a suspension**), it is referred to as **relative or comparative bioavailability**. It is denoted by symbol **Fr**. In contrast to absolute bioavailability, it is used to characterize absorption of a drug from its formulation. F and Fr are generally expressed in percentages.

$$F = \frac{[AUC]_{oral}\ D_{iv}}{[AUC]_{iv}\ D_{oral}}$$

$$F_r = \frac{[AUC]_{test}\ D_{std}}{[AUC]_{std}\ D_{test}}$$

Where:
F: absolute bioavailability
Fr: relative bioavailability

Where: **D** stands for dose administered and subscripts **iv** and **oral** indicate the route of administration

Example: A drug was administered orally at 50 mg, resulting in an AUC of 200 µg·h/mL. The same drug was administered intravenously at 10 mg, with an AUC of 250 µg·h/mL. Calculate the absolute bioavailability.
Answer:

$$F = \frac{AUC_{oral} \cdot Dose_{IV}}{AUC_{IV} \cdot Dose_{oral}}$$

$$F = \frac{200 \cdot 10}{250 \cdot 50} = \frac{2000}{12500} = 0.16\ (16\%)$$

The absolute bioavailability is 16%.

Blood, serum or plasma concentration – time curve:

- Following **oral administration of drug**, **blood samples** are withdrawn at **specific time intervals** and analyzed for **drug content**.
- The **vertical** presents the **concentration** of drug in blood, and **horizontal axis** presents **time** the samples were obtained following drug administration.
- Time zero, the blood concentration of drug should be zero.
- As the drug passes into the stomach and/or intestine, dissolves, and absorbed. As the sampling and analysis continue, the **blood samples reveal increasing concentrations of drug until maximum (peak) concentration (Cmax) is reached. Then the blood level of the drug decreases.**
- **Absorption does not terminate** after the **peak blood level is reached**; it may continue for some time.
- process of drug elimination is continuous. **It begins as soon as the drug first appears in the blood stream** and continues until all the drug has been eliminated.