Module 06

Absolute bioavailability and Relative bioavailability

Absolute bioavailability = $\dfrac{[AUC]_{oral} / Dose_{oral}}{[AUC]_{IV} / Dose_{IV}}$	**Relative bioavailability =** $\dfrac{[AUC]_{A} / Dose_{A}}{[AUC]_{B} / Dose_{B}}$

Pharmaceutical equivalents- Drug products that contain identical amounts of the same active drug ingredients i.e. the same salt or ester of the same therapeutic moiety in identical dosage form, but not necessarily containing the same inactive ingredients.

Bioequivalent drug product- Pharmaceutical equivalent whose rate and extent of absorption may not show a significant difference when administered at the same dose under similar experimental conditions.

MEC and MTC/ MSC

MEC- Minimum effective concentration

MTC- Minimum toxic concentration

MSC- Maximum safe concentration

Methods to determine bioavailability

Pharmacokinetic methods

A. Plasma data

i. The time of peak plasma concentration (t_{max})
ii. The peak plasma concentration (C_{max})

iii. The area under the plasma level- time curve (AUC)

B. Urine data

i. The cumulative amount of drug excreted in the urine (Du)
ii. The rate of drug excretion in the urine (dDu/dt)
iii. The time for maximum urinary excretion (t)

Evaluation and design of a single dose bioequivalency study-

A single dose bioequivalency study is usually performed in normal, healthy human volunteers. The volunteers are used in complete, open label cross over fashion design such as Latin square cross over design. The Latin square design plans the clinical trial so that each subject receives each drug product only once with adequate time between medications for the elimination of drug from the body. Example of Latin square crossover design for a bioequivalency study of three different drug formulations in six human volunteers are given in table.

After each patient receives a drug product, blood samples are collected at appropriate time intervals so that a valid blood drug level-time curve may be obtained.

	Study Period		
Subject	**1**	**2**	**3**
1	A	B	C
2	B	C	A
3	C	A	B
4	A	C	B
5	C	B	A
6	B	A	C

Proper statistical evaluation should be performed on the estimated pharmacokinetic parameters. An analysis of variance (ANOVA) is needed to determine the statistical difference between pharmacokinetic parameters. A statistical difference between pharmacokinetic parameter obtained from two or more drug products is considered significant if there is a probability of less than 1 in 20 times or 0.05 probability ($P<0.05$). The term probability or P is used to indicate the level of statistical significance. If $P>0.05$, the difference between two drug products are not considered significant