Bioavailability and Bioequivalence

Bioavailability is a measurement of the rate and extent of the active drug which reaches the general circulation.

1-Absolute bioavailability

2-Relative bioavailability

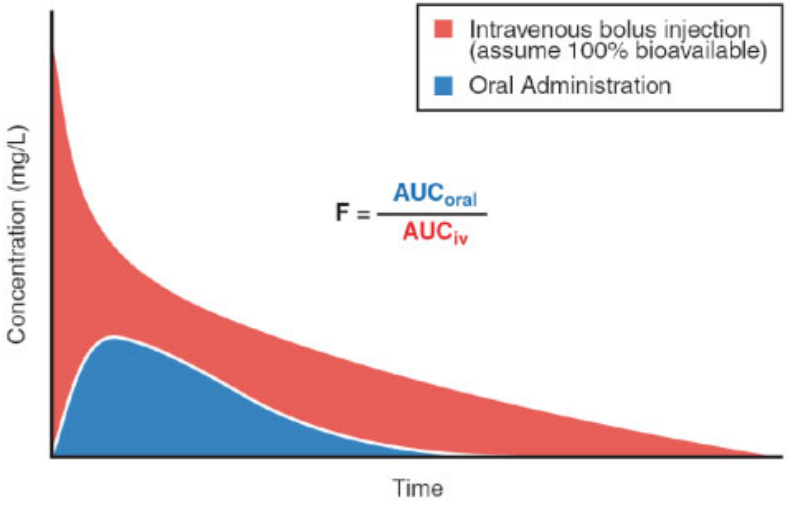
Absolute Bioavailability

Absolute bioavailability=F= $\frac{[AUC]_{po} \div dose_{po}}{[AUC]_{IV} \div dose_{IV}}$

Using urinary data:

Absolute bioavailability=F= $\frac{[Du]_{po}^{\infty} \div dose_{po}}{[Du]_{IV}^{\infty} \div dose_{IV}}$

- F is the absolute bioavailability and also it is the fraction of the dose absorbed.
- After IV administration F is equal to unity or 100%.
- After oral administration of the drug F may vary from a value of F=0 to F=1.


Intravenous bolus injection
(assume 100% bioavailable)
Oral Administration
$F = \frac{AUC_{oral}}{AUC_{iv}}$
Concentration (mg/L)
Time

Methods of Assessing Bioequivalence

- 1-Plasma data
- T_{max} ,
- C_{pmax},
- AUC

$$\left[AUC \right]_o^{\infty} = \int_0^{\infty} Cp \ .dt$$

.

2-Urine Data

$$1-D_u^{\infty}$$

$$2-\frac{dD_u}{dt}$$

$$3-t^{\infty}$$

3-Acute Pharmacological Effect

- Effect on pupil diameter
- Heart rate
- Blood pressure
- Can be useful as an index of drug bioavailability.
- Measurements of the pharmacological effect should be made with sufficient frequency to permit a reasonable estimate of the area under the curve for a time period at least three times the half life of drug.

The Use Of Human Volunteers in Bioavailability Studies

The ***Helsenki declaration*** has set certain scientific standards for the selection and treatment of the participating volunteers, which are intended to protect their safety.

1-the number of participants should be kept to the ***minimum required*** for carrying out a reliable, well designed study.

2-preliminary information from prior animal studies and ***in vitro dissolution and permeability*** tests.

3-the **prior consent** of each participating volunteer should be obtained in writing and each one must be informed of the scope of the experiment, the dangers involved and the conditions to be maintained during the study.

4-children and pregnant or breast-feeding women must not be included in the study.

5-indiviual with certain enzyme deficiency or abnormal metabolism should be avoided.

- 6-The study protocol has to define the range of **age**, **weight**, and the **clinical parameters** that should characterize a normal healthy adult.

- The **guidelines** for Biopharmaceutical Studies in Man, published by the APhS, Academy of Pharmaceutical Science recommends that the test volunteers should be normal healthy adult males, except where not applicable, such as in case of antifertility drugs where female volunteers have to be used.

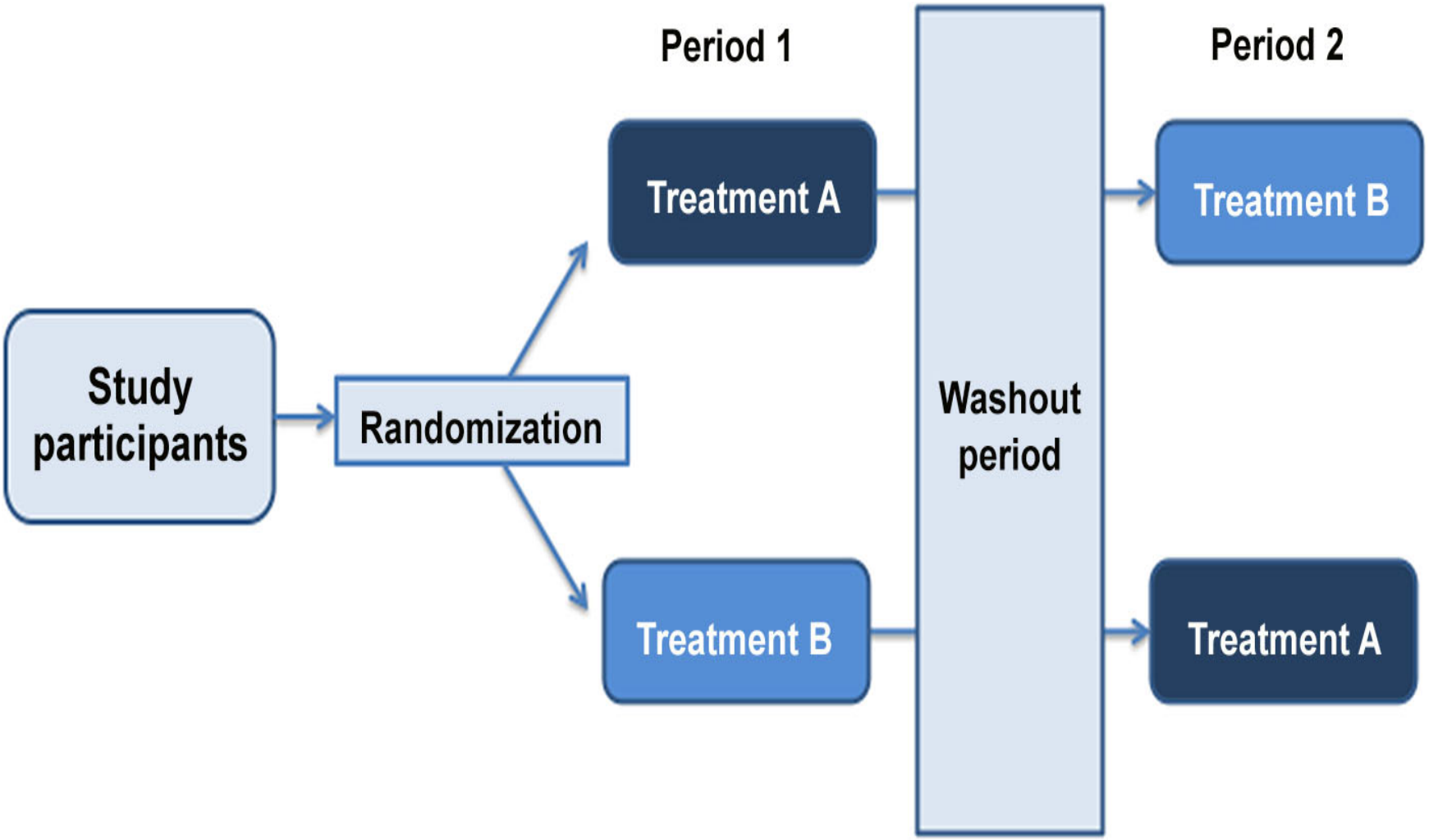
- Generally , the test volunteers range in age from 20-40 year and in weight from 140-200lb, preferably, they should be within a narrow range≈10% of their ideal weight and of similar height .

- All participants should be subjected to a thorough physical examination and the following hematological and clinical chemistry tests:
- Hematology: hemoglobin, hematocrit, WBC, platelets.
- Blood chemistry: BUN (blood urea nitrogen), serum alkaline phosphatase, serum bilurbin, SGPT.
- Urinalysis: specific gravity, albumin, sugar, bile, RBC, WBC.

- No smoking
- No alcoholic drinking
- No medicines (a week before) specially those who have enzyme inducing effect (a month prior the study)
- No sever excercises
- Fasting all over the night
- Standard breakfast after 4 hours.

Cross over Design

Sequence	Period	
	Period 1	Period 2
Group I: AB	Treatment A	Treatment B
Group II: BA	Treatment B	Treatment A


Period 1
Period 2
Treatment A
Treatment B
Study participants
Randomization
Washout period
Treatment B
Treatment A