

Bioavailability

Definition: Bioavailability refers to the extent and rate at which the active moiety (drug or metabolite) enters systemic circulation

The route of administration (ROA) and the dose of a drug have a significant impact on both the rate and extent of bioavailability

Absolute bioavailability: It compares the bioavailability of the active drug in systemic circulation following non-intravenous administration (i.e., after oral, buccal, ocular, nasal, rectal, transdermal, subcutaneous, or sublingual administration), with the bioavailability of the same drug following intravenous administration.

Relative bioavailability: It measures the bioavailability of a formulation (A) of a certain drug when compared with another formulation (B) of the same drug, usually an established standard, or through administration via a different route.

Factors affecting bioavailability

- ✓ Physical properties of the drug (hydrophobicity, pKa, solubility)
- ✓ The drug formulation (immediate release, excipients used, manufacturing methods, modified release – delayed release, extended release, sustained release, etc.)
- ✓ Whether the formulation is administered in a fed or fasted state
- ✓ Gastric emptying rate
- ✓ Circadian differences
- ✓ Interactions with other drugs/foods:
- ✓ Interactions with other drugs (e.g., antacids, alcohol, nicotine)
- ✓ Interactions with other foods (e.g., grapefruit juice, pomello, cranberry juice, brassica vegetables)
- ✓ Transporters: Substrate of efflux transporters (e.g. P-glycoprotein)
- ✓ Health of the gastrointestinal tract
- ✓ Enzyme induction/inhibition by other drugs/foods:
- ✓ Enzyme induction (increased rate of metabolism), e.g., Phenytoin induces CYP1A2, CYP2C9, CYP2C19, and CYP3A4
- ✓ Enzyme inhibition (decreased rate of metabolism), e.g., grapefruit juice inhibits CYP3A → higher nifedipine concentrations

- ✓ Individual variation in metabolic differences
- ✓ Age: In general, drugs are metabolized more slowly in fetal, neonatal, and geriatric populations
- ✓ Phenotypic differences, enterohepatic circulation, diet, gender
- ✓ Disease state
- ✓ E.g., hepatic insufficiency, poor renal function