Factor Affecting Bioavailability

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Reference- P. C. Dandiya and Solution-Pharmacy
Bioavailability - “The rate and extent of absorption of drug from its dosage form”. Bioavailability is very important for any drug for its action point of view. The more bioavailability will be more drug action and less bioavailability means less availability of drug thus less action. Bioavailability of drug which is given by oral route will never be 100% but the drug given by systemic route is considered to be 100%

Bio = Living organism (Body) Availability = To be provided for Action

Bioavailability = \[
\frac{\text{AUC (Area Under Curve) of orally administered drug}}{\text{AUC (Area Under Curve) of Intravenously administered drug}}
\]
Image: Bioavailability - Plasma drug concentration Vs Time Graph, along with various indications

Diagram made by: Solution Pharmacy www.facebook.com/pharmavideo/ E-Mail: solutionpharmacy@gmail.com

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1. **Oral Route**- Any drug given by mouth taken with water is called oral route of drug administration.

2. **Serum drug concentration**- Serum drug concentration means at any specific time the amount of drug available to the blood serum.

3. **Intravenous route**- In this route the drug is directly administered into the venous blood. (Vein)

4. **Time of maximum drug concentration** ($T_{\text{max}}$) Time at which the concentration of drug is at its maximum level.

5. **AUC (Area under curve)** This shows complete time from administration to elimination.

6. **MEC (Minimum effective concentration)** this is the minimum concentration of drug required by the body to produce any of effects.

7. **Therapeutic dose or therapeutic range**- The concentration of drug at which it provides maximum therapeutic response and minimum undesirable effects. Or it’s a range between the MEC and MSE.

8. **Maximum safe concentration** (MSC) this is the concentration of drug at which it exceed the therapeutic window and started to show unerivable or toxic response.

9. **Duration of action**- The total time till any drug gives its action

10. **Onset of action**- The time at which drug started to give its action.
Blood consists of: Plasma in 55%, RBC about 45%, and WBC is also found.

Plasma is the medium for transport of various materials in blood.

- **Platelets** are important for blood clotting.
- **White Blood Cells** (WBC) provide immunity.
- **Red Blood Cells** (RBC) transport oxygen.

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Factors Affecting Bioavailability

There are many factors which affect bioavailability of drugs. For the better understanding we have classified them into two main class.

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Pharmaceutical Factors
Affecting Bioavailability

Partial Size
Smaller the partial size the greater will be surface area and greater surface area will have more dissolution, and more dissolution will result in more bioavailability. For this reason poorly soluble or slowly dissolving drugs are marketed in microfine or finely particle form to facilitate their absorption and this bioavailability.
Example- Microfined Aspirin, Spironolactone, Griseofulvin and digoxin

Salt Form
The dissolution rate of a particular salt is usually different from its parent compound. Salt of weekly acidic drugs are water soluble. Free acidic drug is precipitated from these salts in a micro crystalline form which has faster dissolution rate and hence enhanced bioavailability.
Example- Sodium tolbutamide and sodium secobarbital have better bioavailability than tolbutamide and secobarbital.

Crystal Form
The absorption rate and bioavailability of a drug depends upon its crystalline form also. Mostly amorphous drug are more soluble than crystal form of the drug. Example- Amorphous chloramphenicol palmitate and amorphous novobiocin have faster dissolution rate and better bioavailability as compared to their crystalline form.
Water of Hydration
Many drug can associate with water to produce crystalline form called hydrates. Anhydrous form of caffeine, Theophylline and ampicillin have faster dissolution rate and better bioavailability as compare to Hydrus form.

Nature of Excipients
Excipients are the pharmacologically inert substance like- lactose, calcium sulphate, gum etc. these are added as a filling materials to increase the size of preparation. Binding agents have more effect on the bioavailability of drug such as- Phenytoin, digoxin, levodopa, and warfarin. Some of excipients are wetting gents also, like- lactose and polysorbate 80, which enhance solvent penetration in the drug particles and increase dissolution and absorption.

Degree of Ionization
Non Ionized lipid soluble drugs are better absorbed while strongly acidic and basic drugs or highly ionised drugs are reduced bioavailability.
Example- streptomycin, sulphaguanidine, neostigmine and d-tubocurarine.
Diagram made by Solution Pharmacy. Idea- KD Tripathi

Passive diffusion and filtration across the lipidoid biological membrane.

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Image- Factor that affect the absorption of drug from site of administration to systemic circulation

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Pharmacological Factors
Affecting Bioavailability

Gastric empty and gastric motility
In general those factors which increase the gastric emptying, permit the drug to reach the large absorptive surface of small intestine and increase the bioavailability. Prompt gastric emptying is also important for drug that are unstable in gastric fluids. Gastric emptying is promoted by fasting, anxiety, lying on right side, hyperthyroidism.

Gastric disease
There are several other factor associated with gastrointestinal tract may affect the bioavailability of the drug. Example- (1) In case of achlorhydria, gastric acid secretion is decreased with a increase in gastric pH. This increase the absorption of weakly acidic drugs like aspirin because at higher pH it dissolve faster. (2)In gastroenteritis there is decrease in absorption of drug given orally like- Nalidixic acid, Ampicillin and metoclopramide.

Food and other substance
In general gastrointestinal absorption is favoured by an empty stomach, while the absorption rate (Not extent) is reduced after the eating food. However both the rate and extent of certain antibiotics (Rifampin) is reduced after meal. Absorption of tetracycline is also reduced after taking milk or milk product. Absorption of certain antifungal drugs (Griseofulvin) is enhanced by the administration of fatty diet.
First pass Effects
All drug taken orally, first passes through the GIT wall and then through portal vein system before reaching to the Systemic circulation. First pass effects means the drug degradation occurring before the drug reaches the systemic circulation. The net result is in decrease in bioavailability and reduction in therapeutic response.
Example- Bioavailability of L-dopa, Morphine, Nitro-glycerine, Isosorbide dinitrate, and propranololol is less if given orally.

Drug- Drug Interaction
Difference in bioavailability can also be observed due to drug-drug interaction.
Example- Liquid paraffine decrease the bioavailability of vitamin- A, Antacid containing Aluminium, calcium, magnesium and haematinics containing iron may reduce bioavailability of tetracycline. Probenecid blocks penicillin excretion and thus enhance bioavailability.

Other factors
(1) Route of drug administration
(2) Area of absorbing surface
(3) State of the circulation of blood to the site of administration