Factor Affecting

Bioavailability

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Reference- P. C. Dandiya and Solution-Pharmacy

Bioavailability

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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

$$\text{Bioavailability} = \frac{\text{AUC (Area Under Curve) of orally administered drug}}{\text{AUC (Area Under Curve) of Intravenously administered drug}}$$

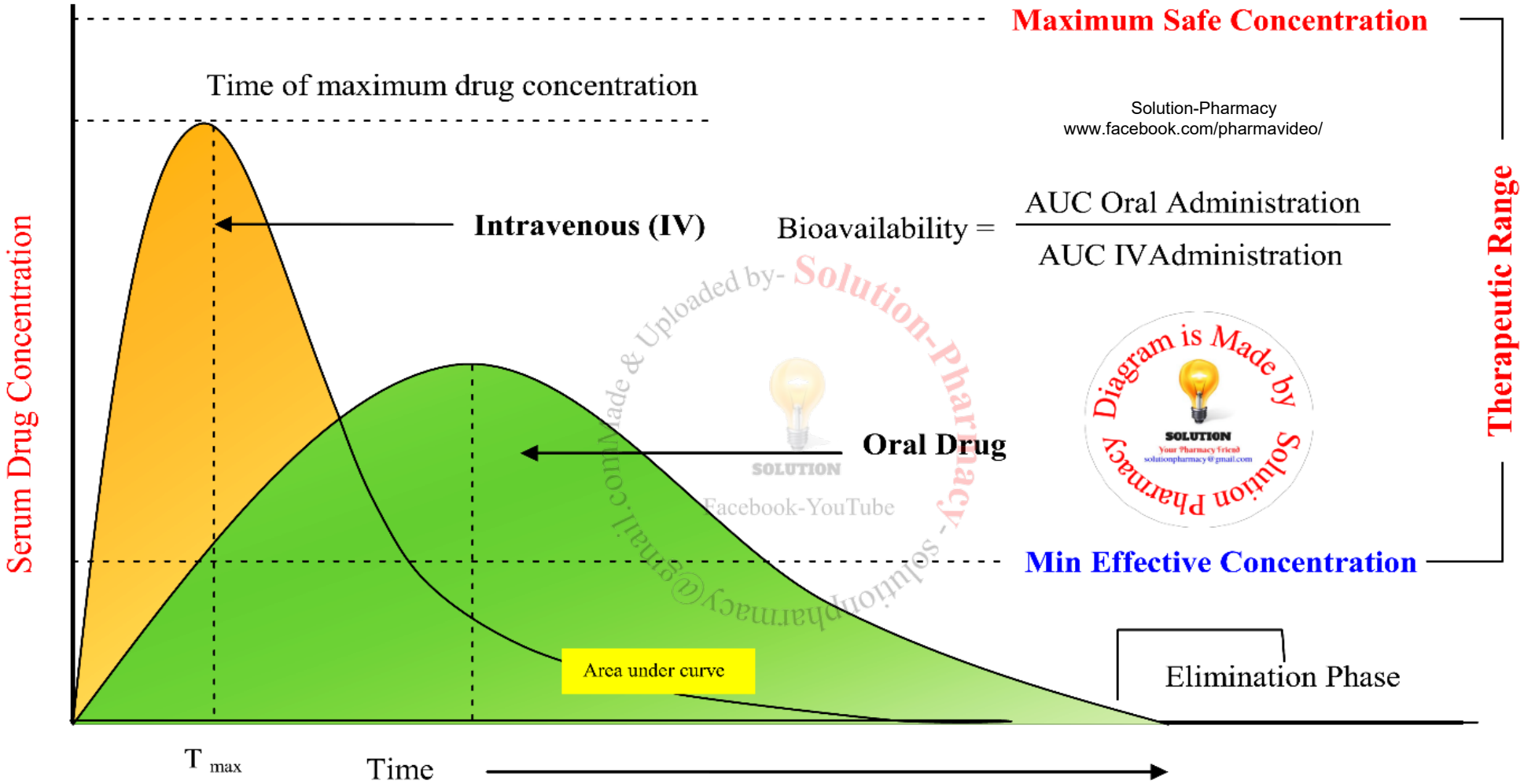

Image- Bioavailability- Plasma drug concentration Vs Time Graph, along with various indications

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

Basic terms and definition used in bioavailability curve

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_{max})** Time at which the concentration of drug is at it's 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 underivable 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.

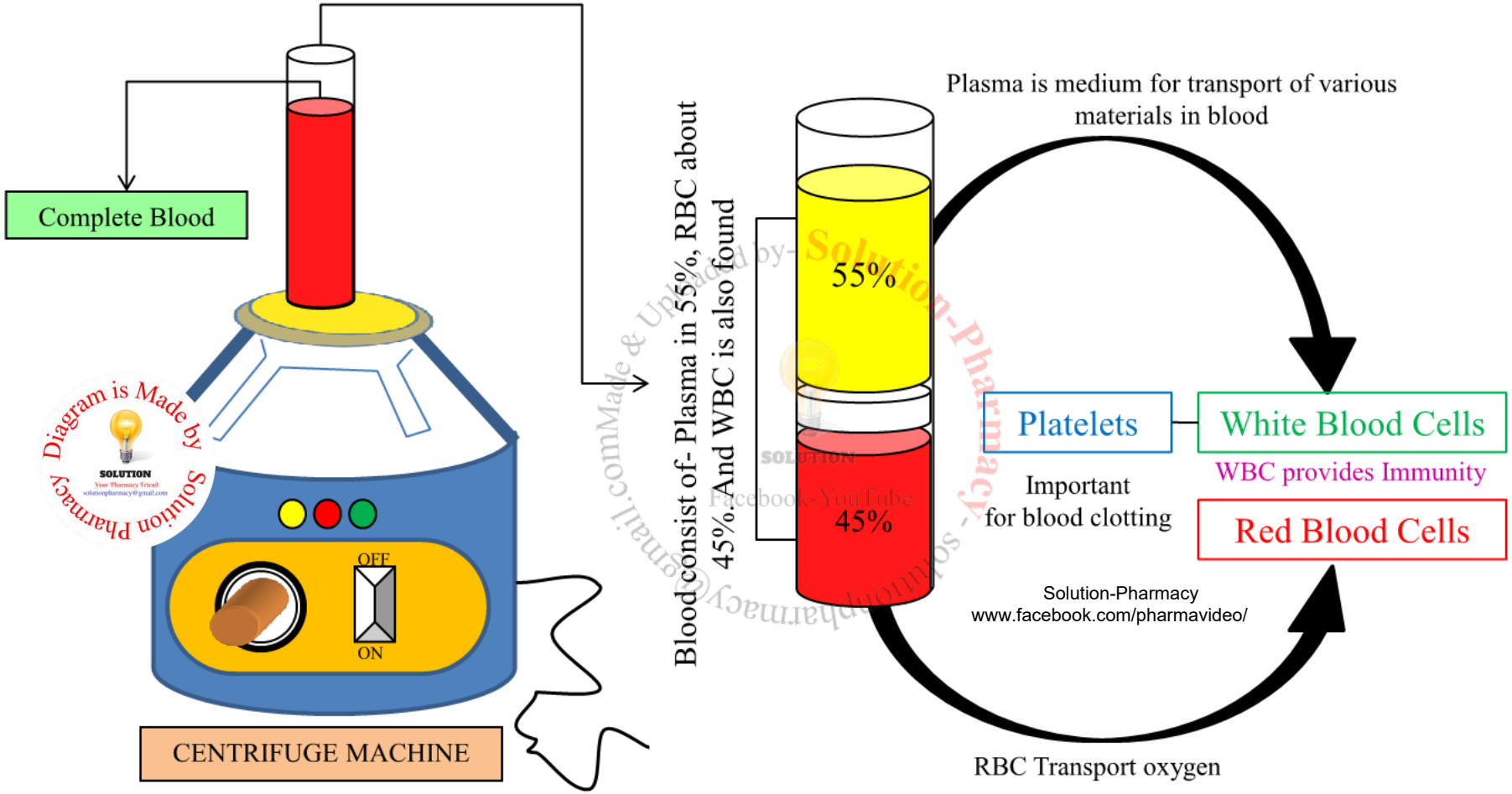

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Image- Component f blood wit special reference to plasma protein

Factors Affecting Bioavailability

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

S.N.	Pharmaceutical Factors	Pharmacological Factors
01	Partial Size	Gastric emptying and gastric motility
02	Salt form	Gastrointestinal disease
03	Crystal forms	Food and other substances
04	Water of hydration	First pass effects
05	Nature of Excipients	Drug-drug interaction
06	Degree of Ionization	Pharmacogenetic Factors
07	Formulation Factors	Emotional Factor (Psychological Factors)

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 dissoluting 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, sulpha guanidine, neostigmine and d-tubocurarine.

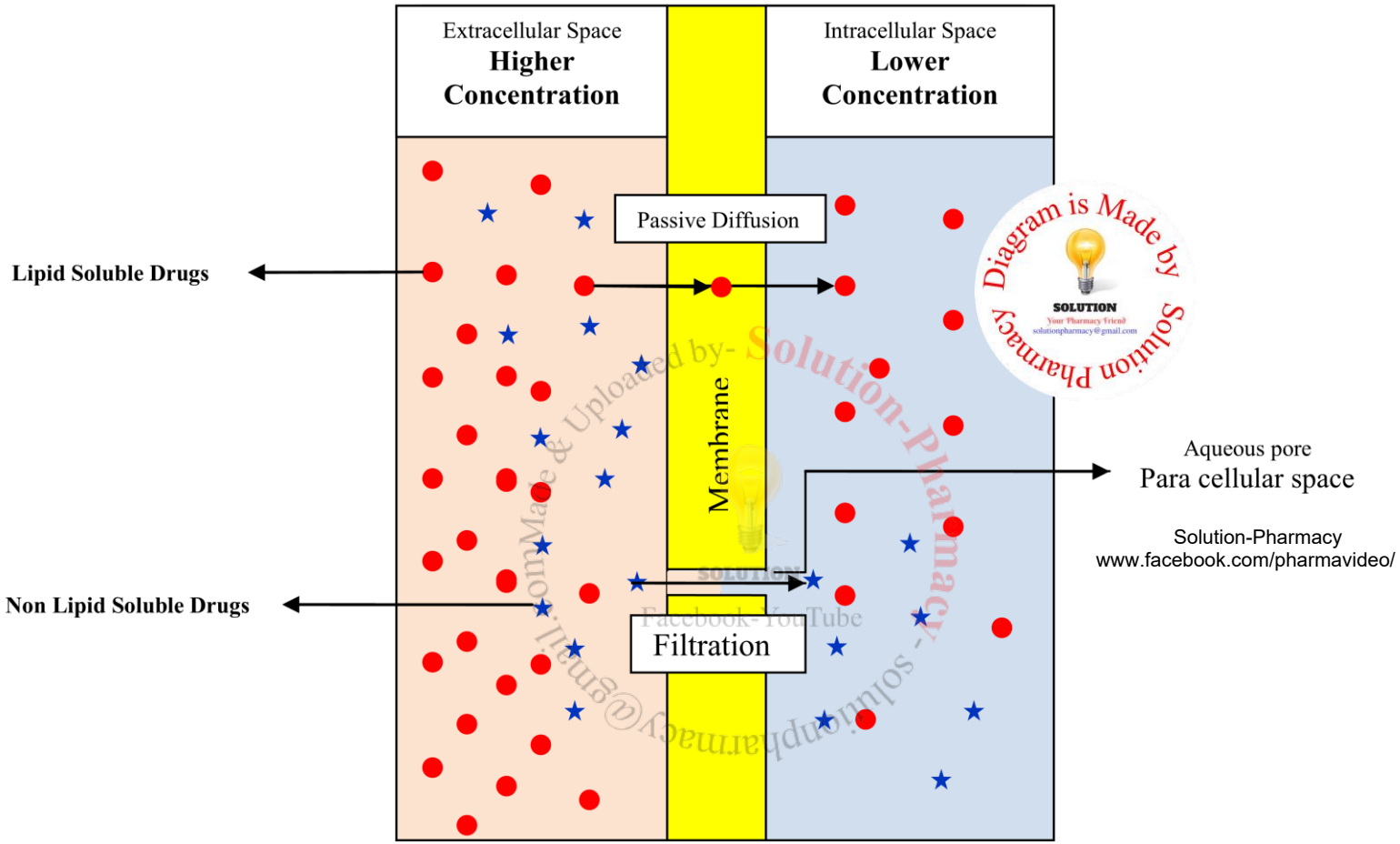

Diagram made by Solution Pharmacy. Idea- KD Tripathi

Passive diffusion and filtration across the lipoid biological membrane.

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

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 gastro intestinal 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 propranolol 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