GPAT/NIPER 2025 CRASH COURSE

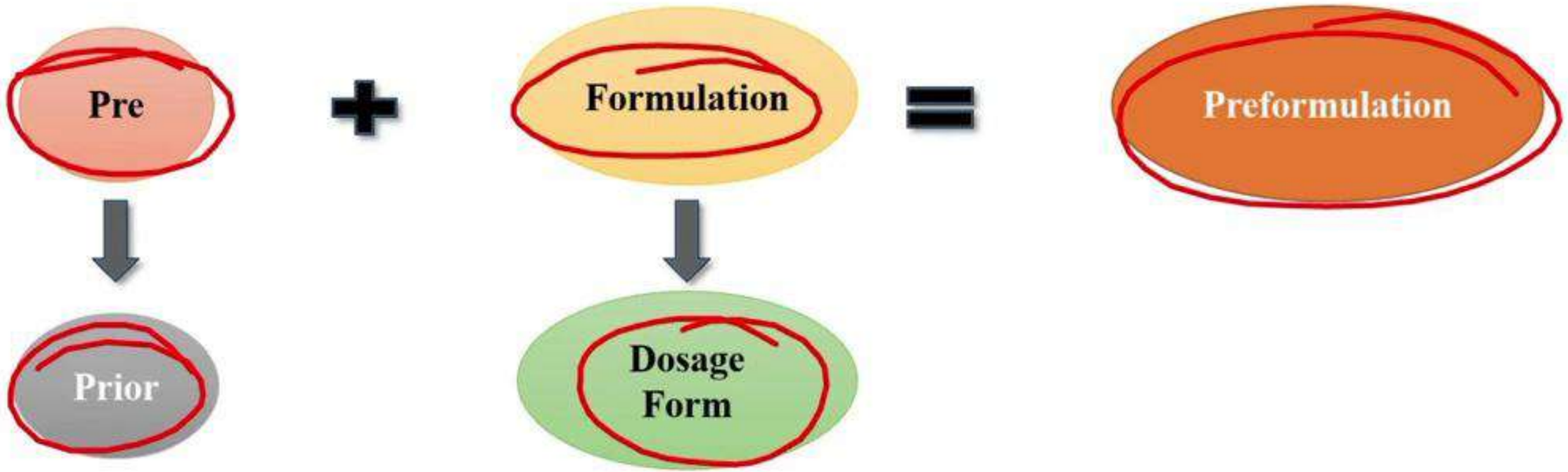
SUBJECT - PHARMACEUTICS

TOPIC - PREFORMULATION

LECTURE- 1

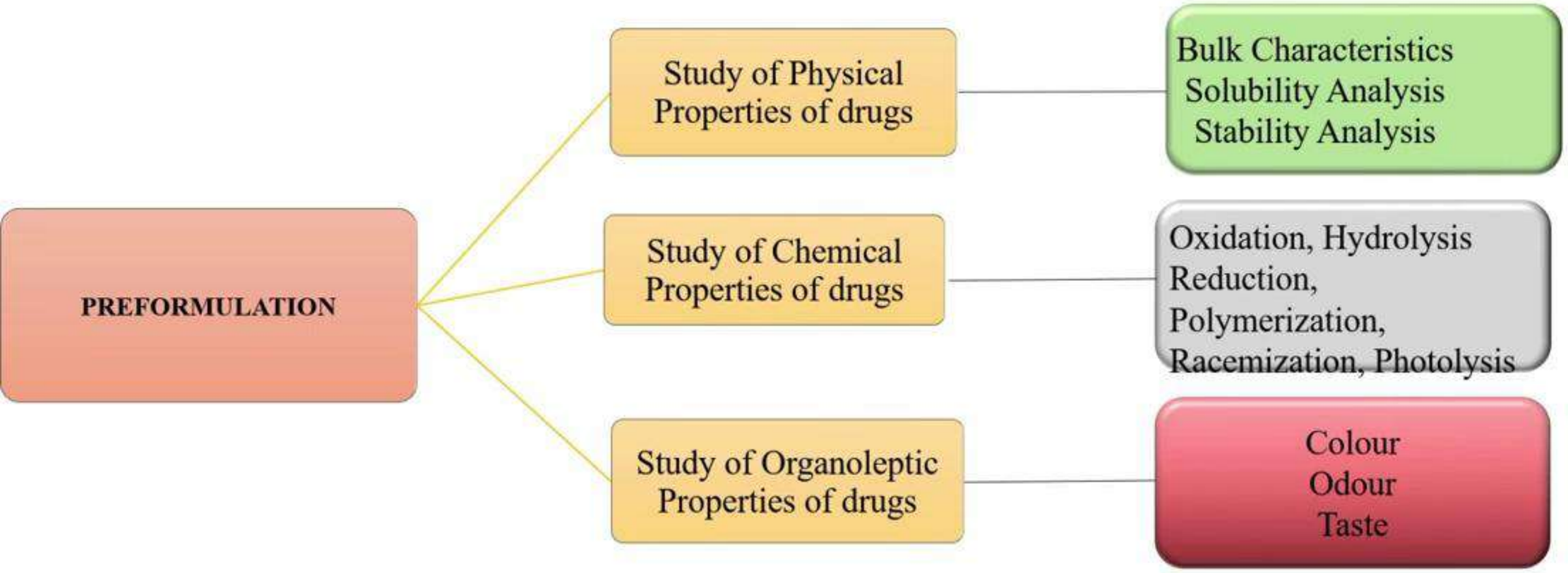
4

INTRODUCTION



- Preformulation studies are the preleminary studies before the preparation of any dosage form.
- It can also be defined as “The phase of research and development in which preformulation studies characterize physical and chemical properties of a drug molecule in order to develop the safe, effective and stable dosage form.

INTRODUCTION



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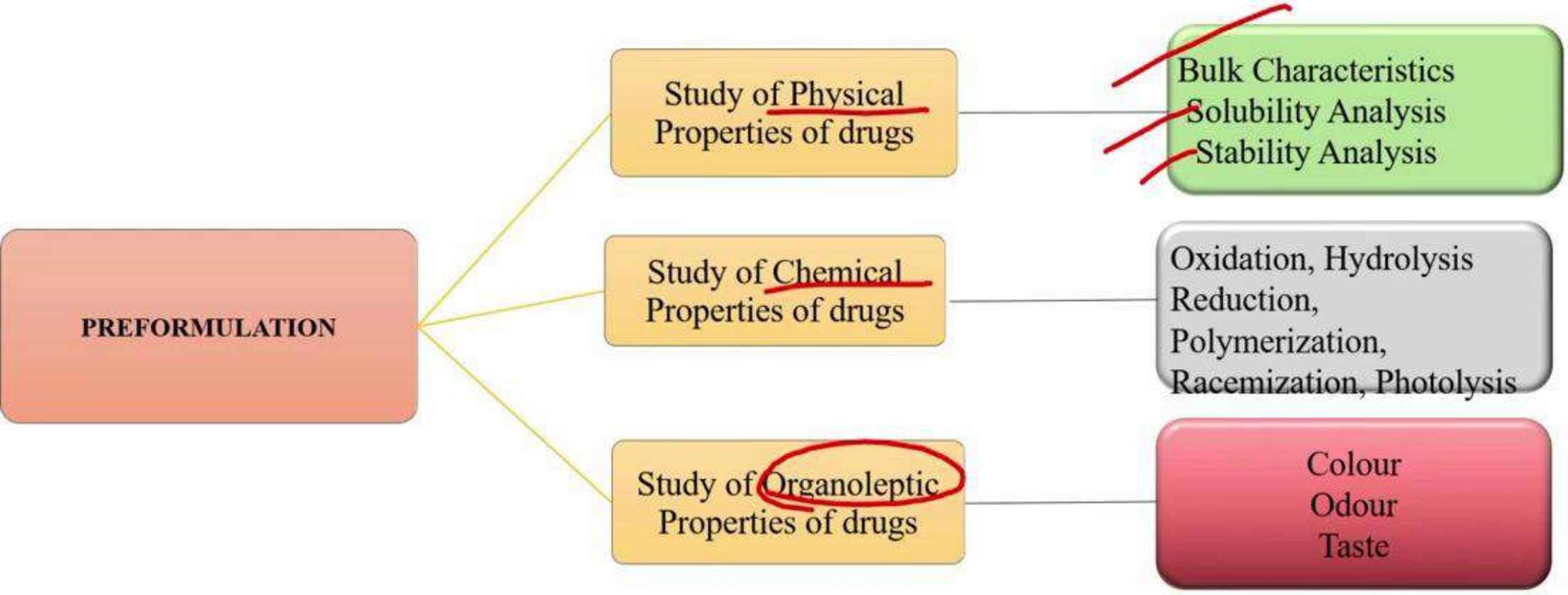

OBJECTIVES

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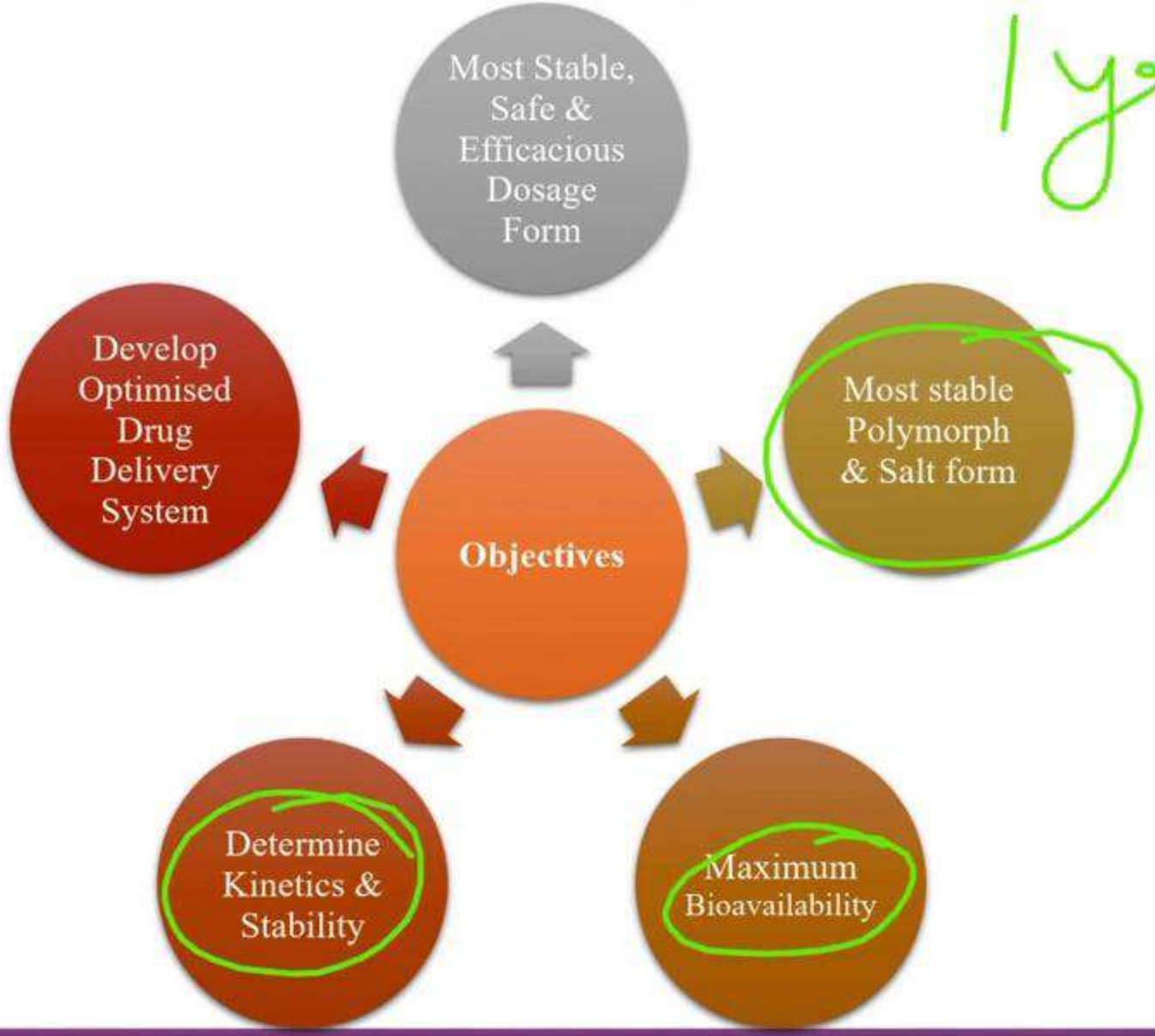
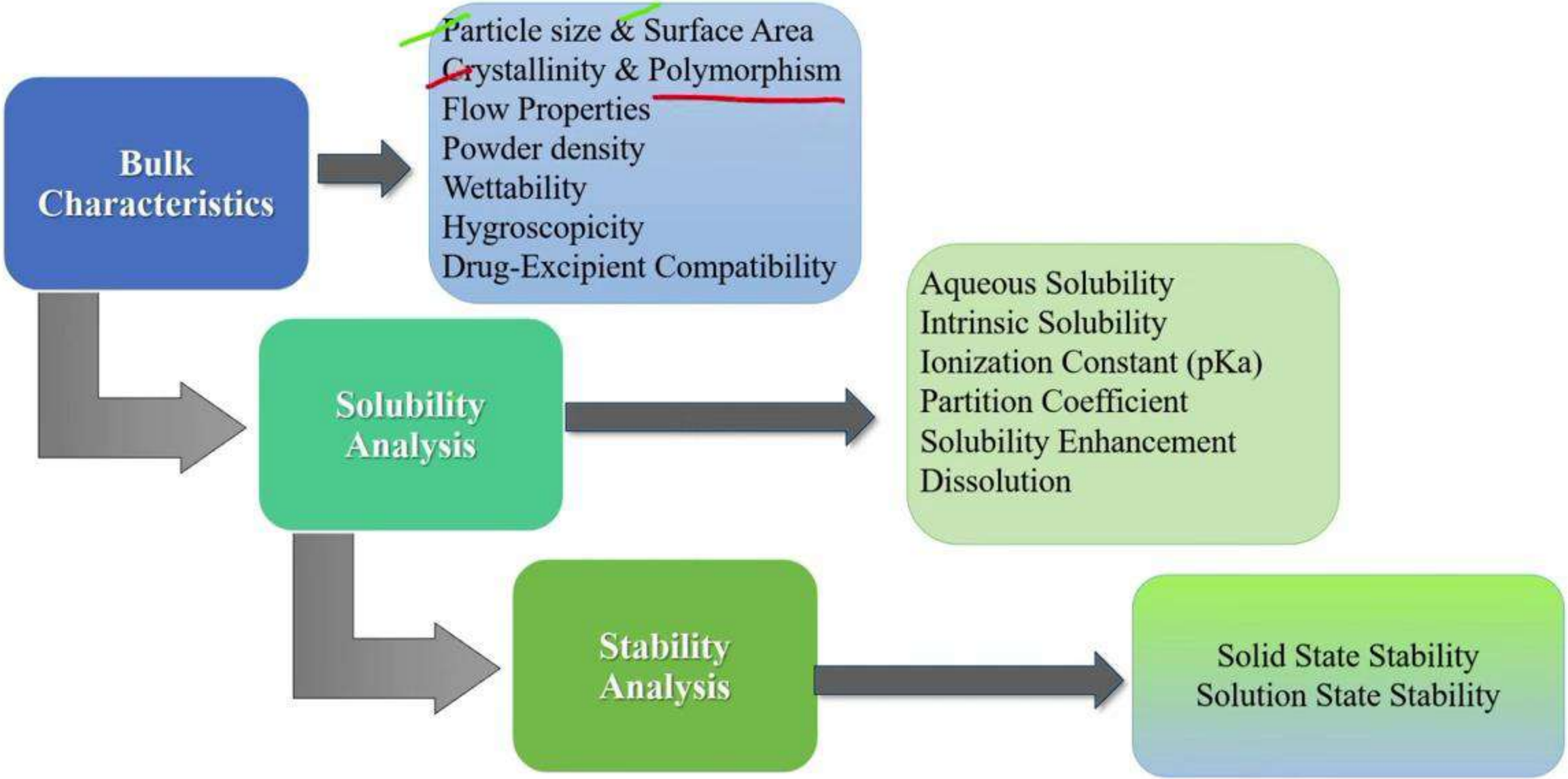


PHYSICAL CHARACTERISTICS



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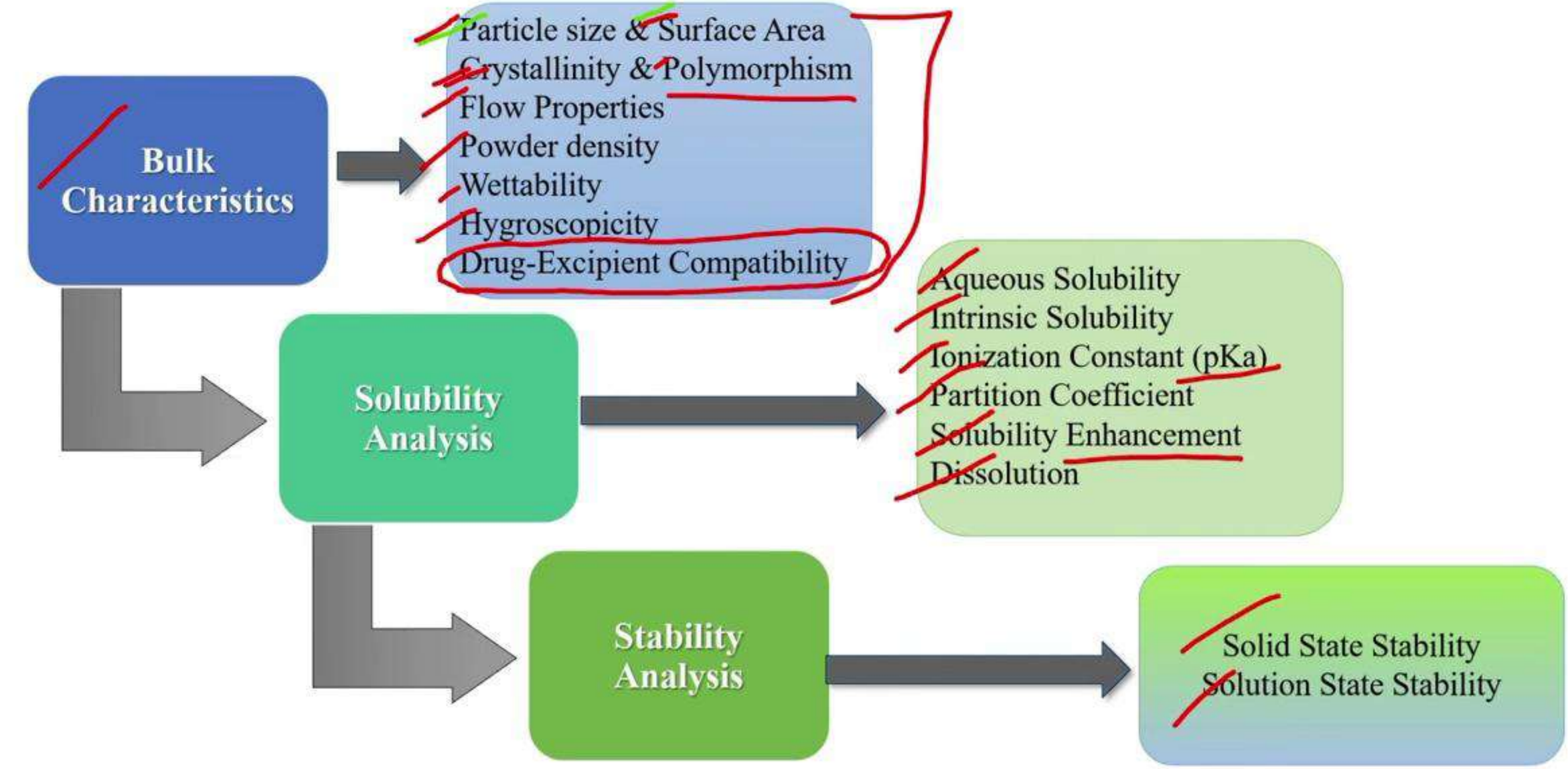

BULK CHARACTERISTICS

1. Particle Size and Surface Area

Particle size is important in following aspects :

- Stability of formulation
- Solubility profile of the formulation
- Flow property

Method	Size Range	Instrument	Description
Microscopy	0.2-100µm	Light Microscope (Transmission Electron Microscope)	Feret, Martin and Projected diameter is measured
Sieving Method	50-1500µm	Mechanical Shaker	Sieve diameter is measured
Sedimentation Method	1-200µm	Anderson Pipette	Stokes diameter is measured
Conductivity Method	0.5-500µm	Coulter Counter HIAC liquid paricle counter	Particle volume distribution is measured

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SURFACE AREA

Surface Area Determination

As the particle size decreases , surface area of the particle increases

FEATURES	ADSORPTION METHOD	AIR PERMEABILITY METHOD
Surface area is measured by	Volume of Nitrogen adsorbed to form a monolayer	Rate at which gas or liquid permeates a bed of powder
Equation	BET (Brunauer; Emmett;Teller) Equation	Poiseuill's Equation & Kozency-Carman Equation
Instrument	Quantasorb	Fisher Subsieve Sizer
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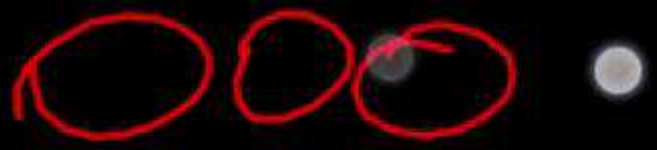

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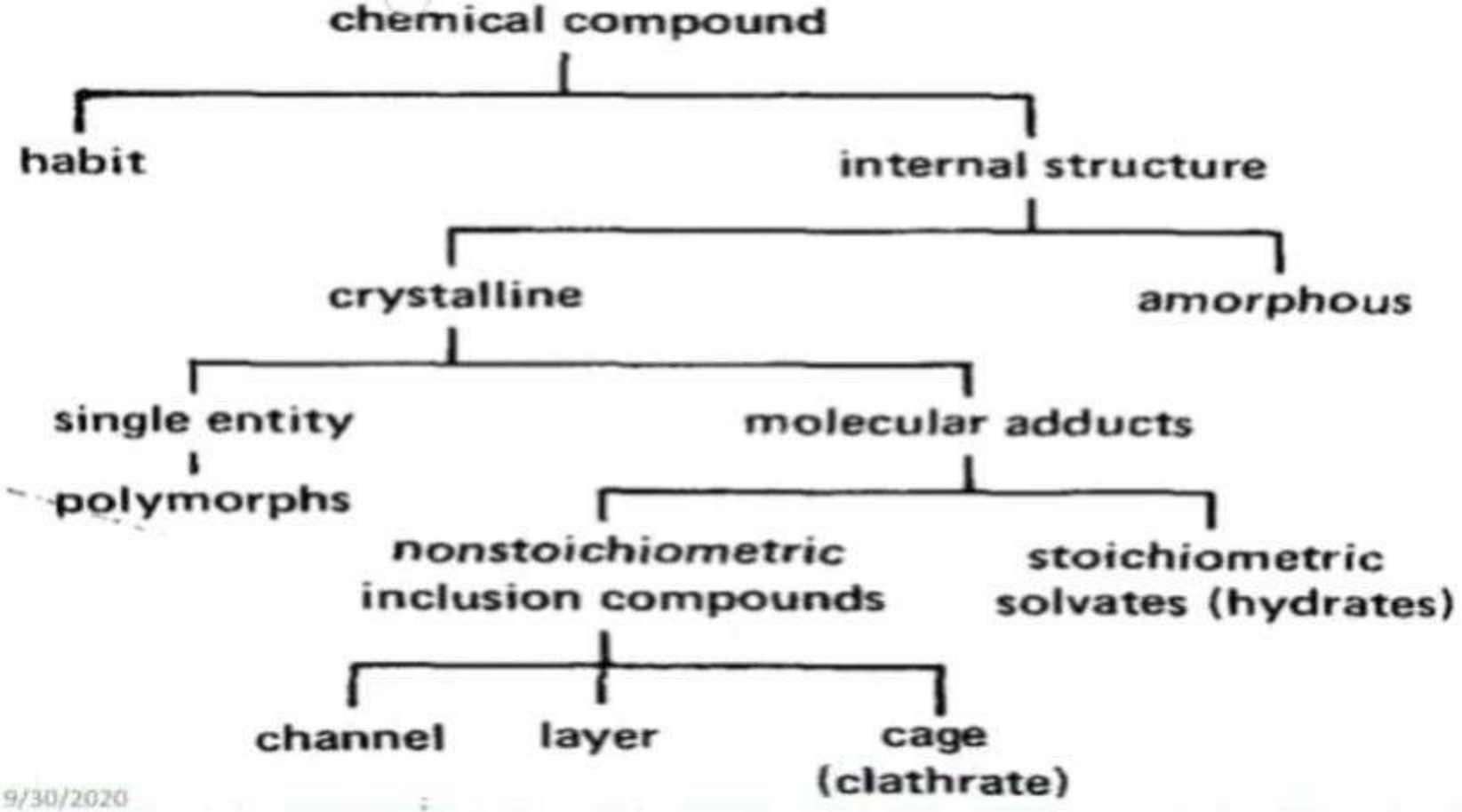
CRYSTALLINITY

2. Crystallinity & Polymorphism

As the particle size decreases , surface area of the particle increases

The degree of crystallinity has a big influence on hardness, transparency, density and dissolution etc.



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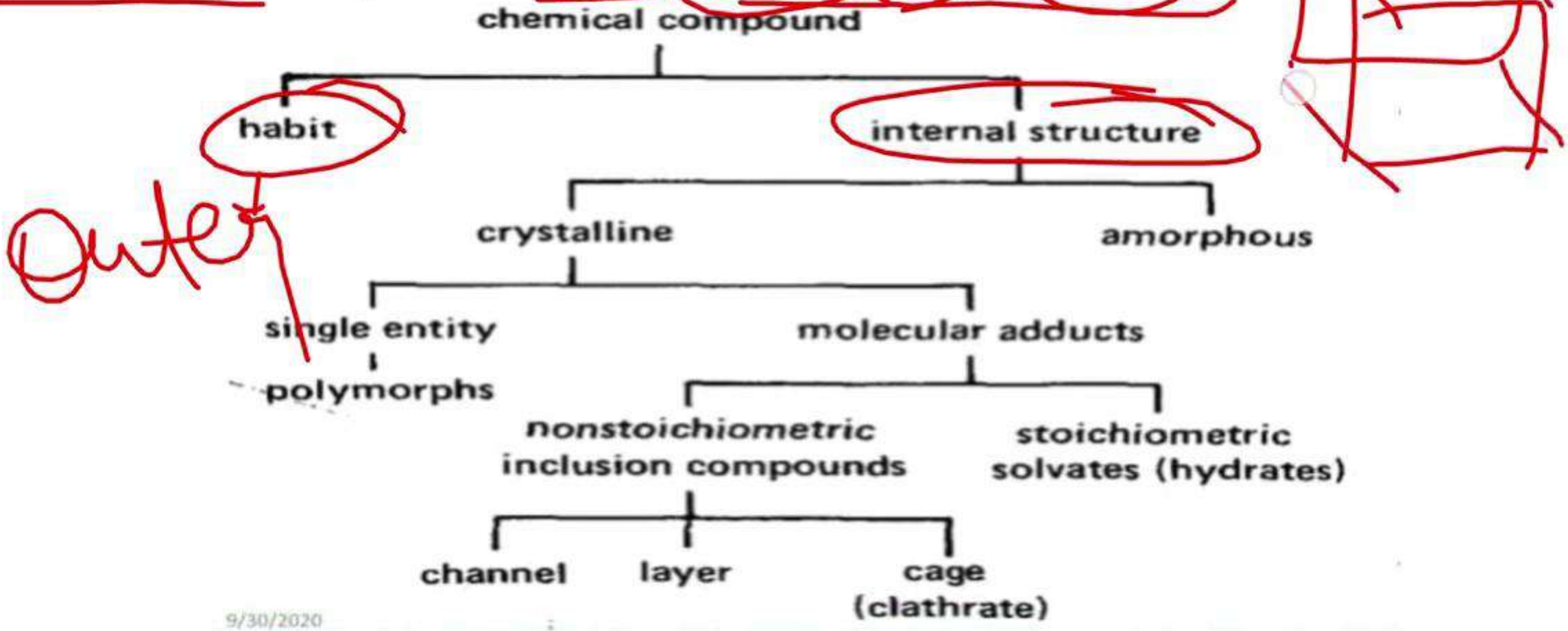

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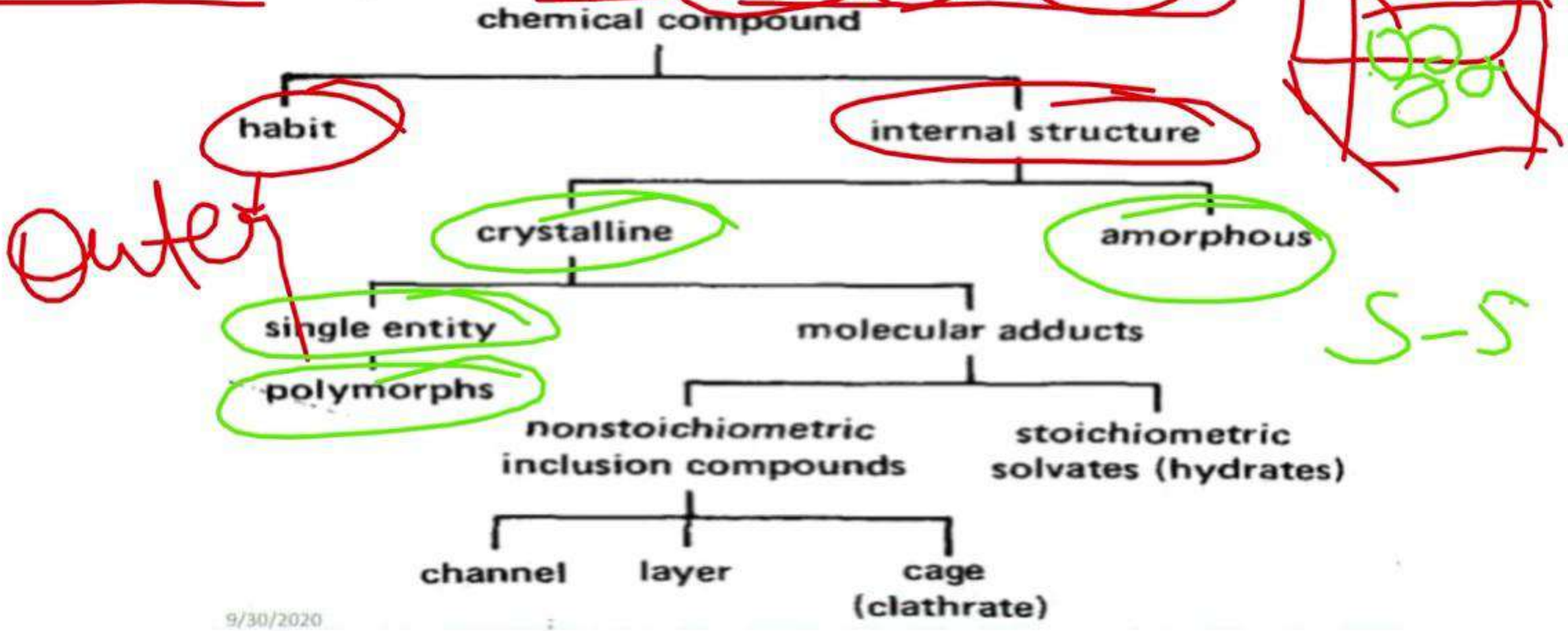

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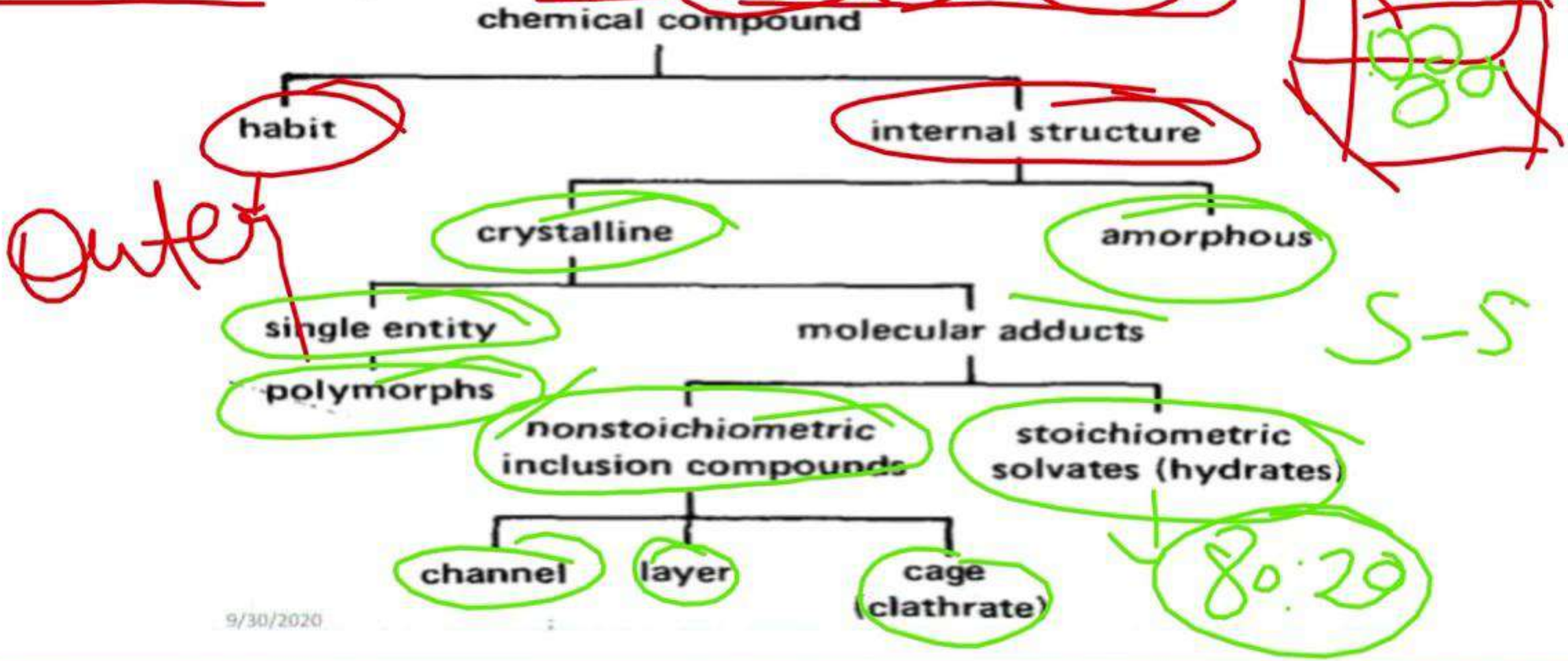
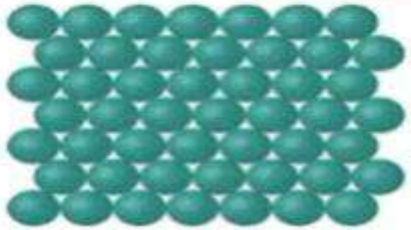


CRYSTALLINITY

Difference between Crystalline and Amorphous Solids



Crystalline	Amorphous
Crystalline form have fixed internal structure.	Amorphous forms do not have any fixed internal structure
Crystalline form has lesser thermodynamic energy as compared to its amorphous form.	Amorphous form has higher thermodynamics energy than its crystalline form
Crystalline forms are more stable than its amorphous forms.	Amorphous forms are less stable than its crystalline forms
Crystalline forms has lesser solubility than its amorphous form	Amorphous forms have a greater solubility than its crystalline forms
Crystalline forms has less tendancy to change its form during storage	Amorphous tends to the word to more stable form during storage

POLYMORPHISM

Polymorphism

Arrangement of a drug substance in more than one crystal forms is known as polymorphism and structures are known as polymorphs.

It is the ability of the compound to crystallize as more than one distinct crystalline species with different internal lattice.

Different crystalline forms are called polymorphs but their chemical composition remain same whereas polymorphs differ from each other with respect to their physical property such as:

- Solubility
- Melting point
- Density
- Hardness
- Compression characteristic

Polymorphs are of 2 types

- **Enatiotropic**
- **Monotropic**

The polymorph which can be changed from one form into another by varying temp or pressure is called as **Enantiotropic polymorph.**

- Eg. Sulphur

One polymorph which is unstable at all temp. & pressure is called as **Monotropic polymorph.**

- Eg. Glyceryl stearate

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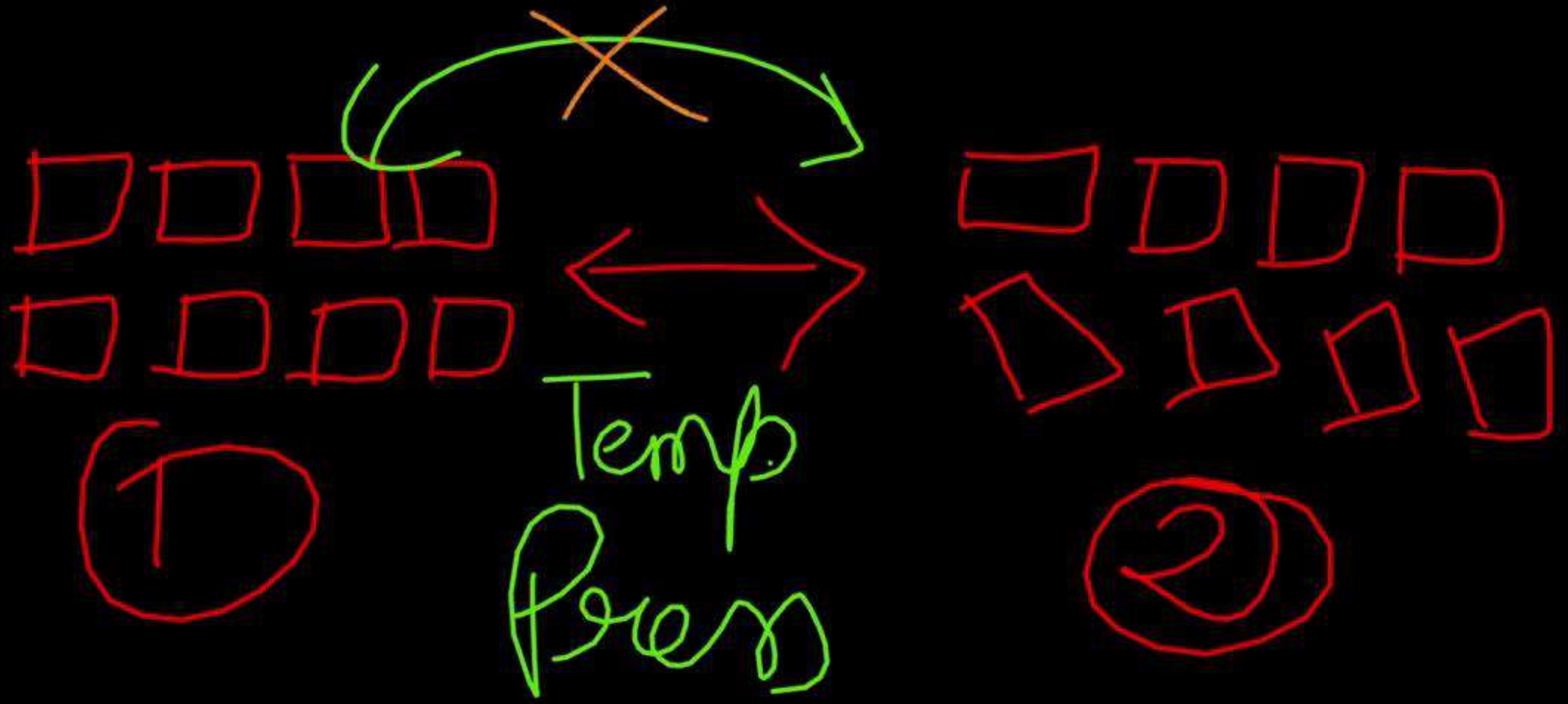

POLYMORPHISM

Characteristics	Stable polymorph	Metastable polymorph	Unstable polymorph
Packing of molecules in crystal lattice	Tightly packed	Less tightly packed	Loosely packed
Melting point	Highest	Moderate	Lowest
Rate of dissolution	Lowest	Moderate	Highest

Many drugs are hydrophobic and have very limited solubility in water. If the drug remains in several polymorphic forms then the stable one will produce the slowest rate of dissolution and it may show minimum bioavailability.
For highly water soluble drugs polymorphism does not show any problem in dissolution rate
Example: **Chloramphenicol palmitate** has three polymorphs α(stable), β(metastable) and γ (unstable). When chloramphenicol palmitate suspension is prepared from α or β polymorph it is found that bioavailabilty is higher with the metastable form.

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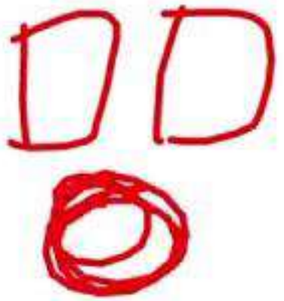
POLYMORPHISM

Methods of Characterization of Polymorphs

1. Hot stage microscopy,
2. Differential Thermal Analysis,
3. Differential Scanning Calorimetry
4. Thermogravimetric Analysis (TGA)
5. X-ray powder diffraction
6. IR-Spectroscopy
7. FTIR Technique
8. NMR Technique



Pseuopolymorphism

Pseudopolymorphism is the phenomenon wherein a compound is obtained in crystalline forms that differ in the nature or stoichiometry of included solvent molecules

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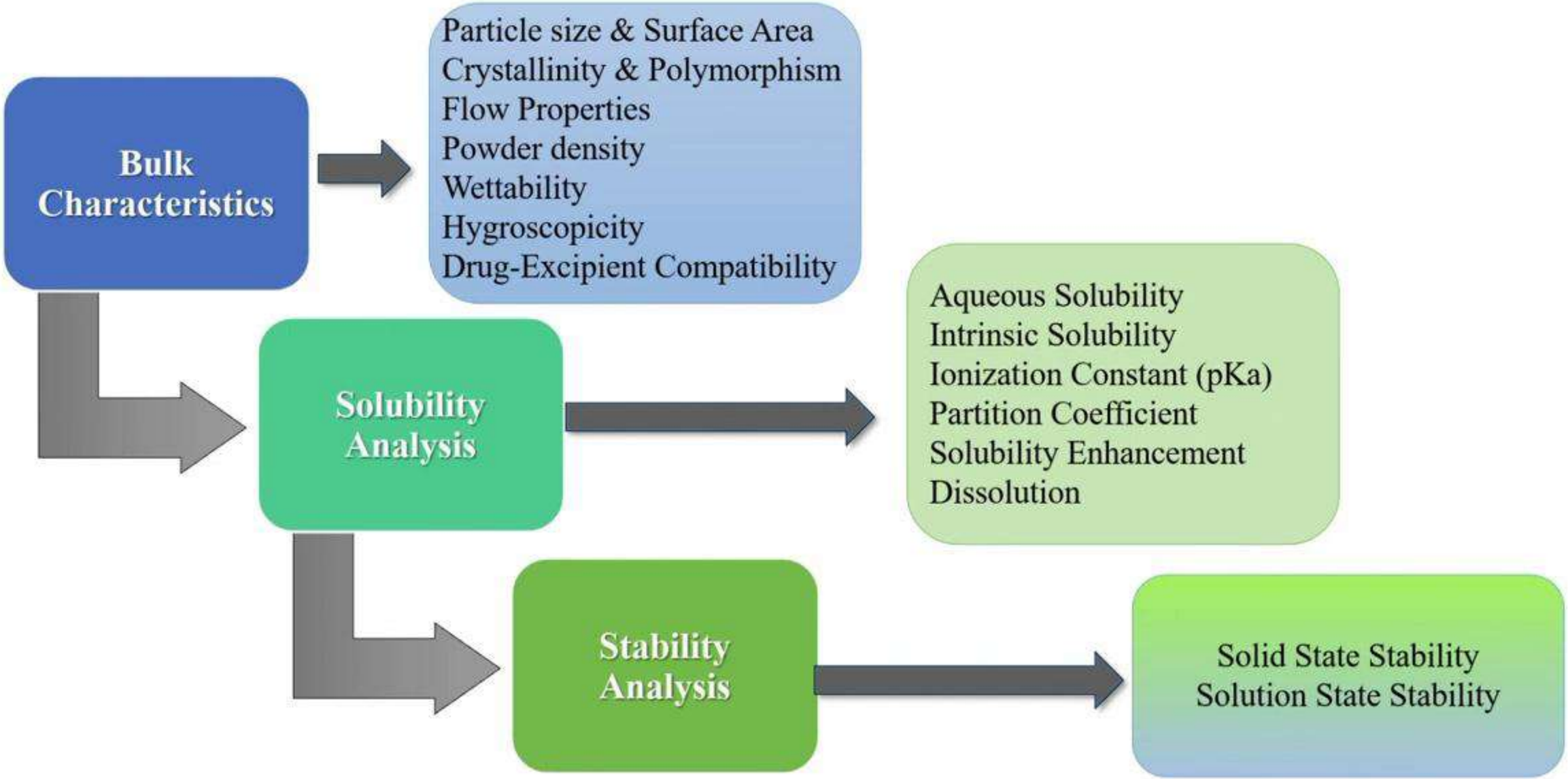
LECTURE- 2

JOIN WITH US ON

@GROWUPPHARMA

PHYSICAL CHARACTERISTICS



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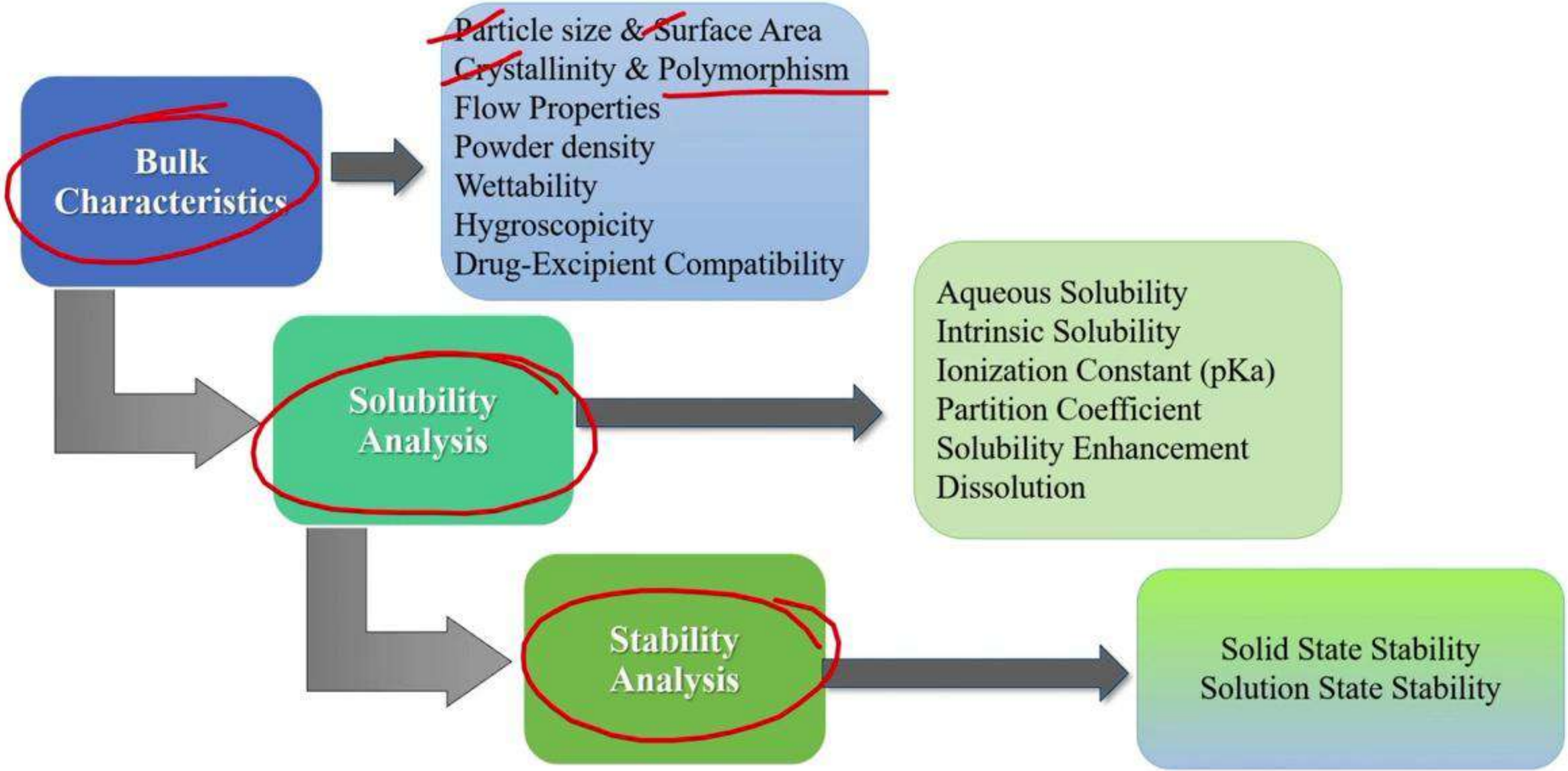
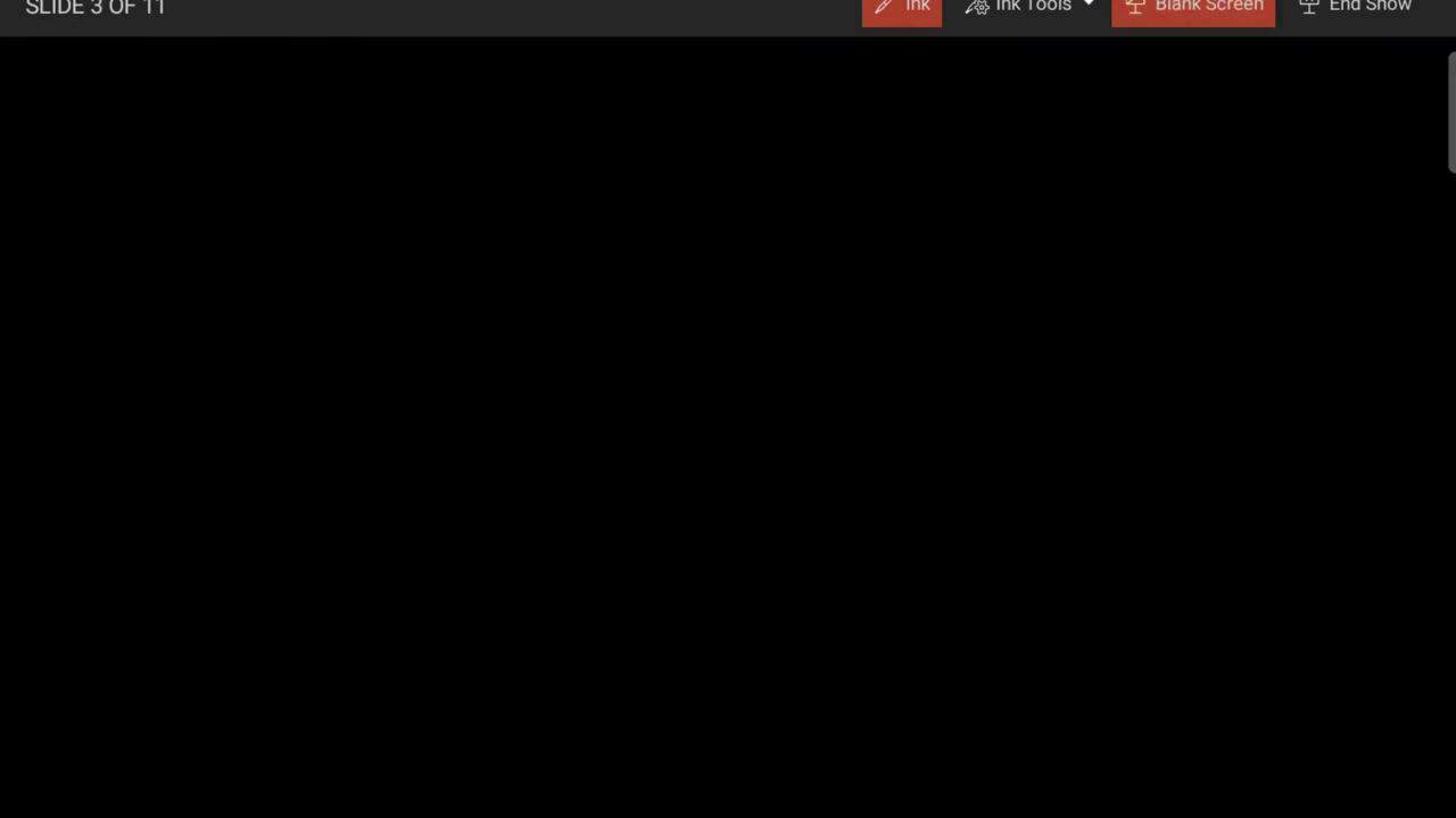
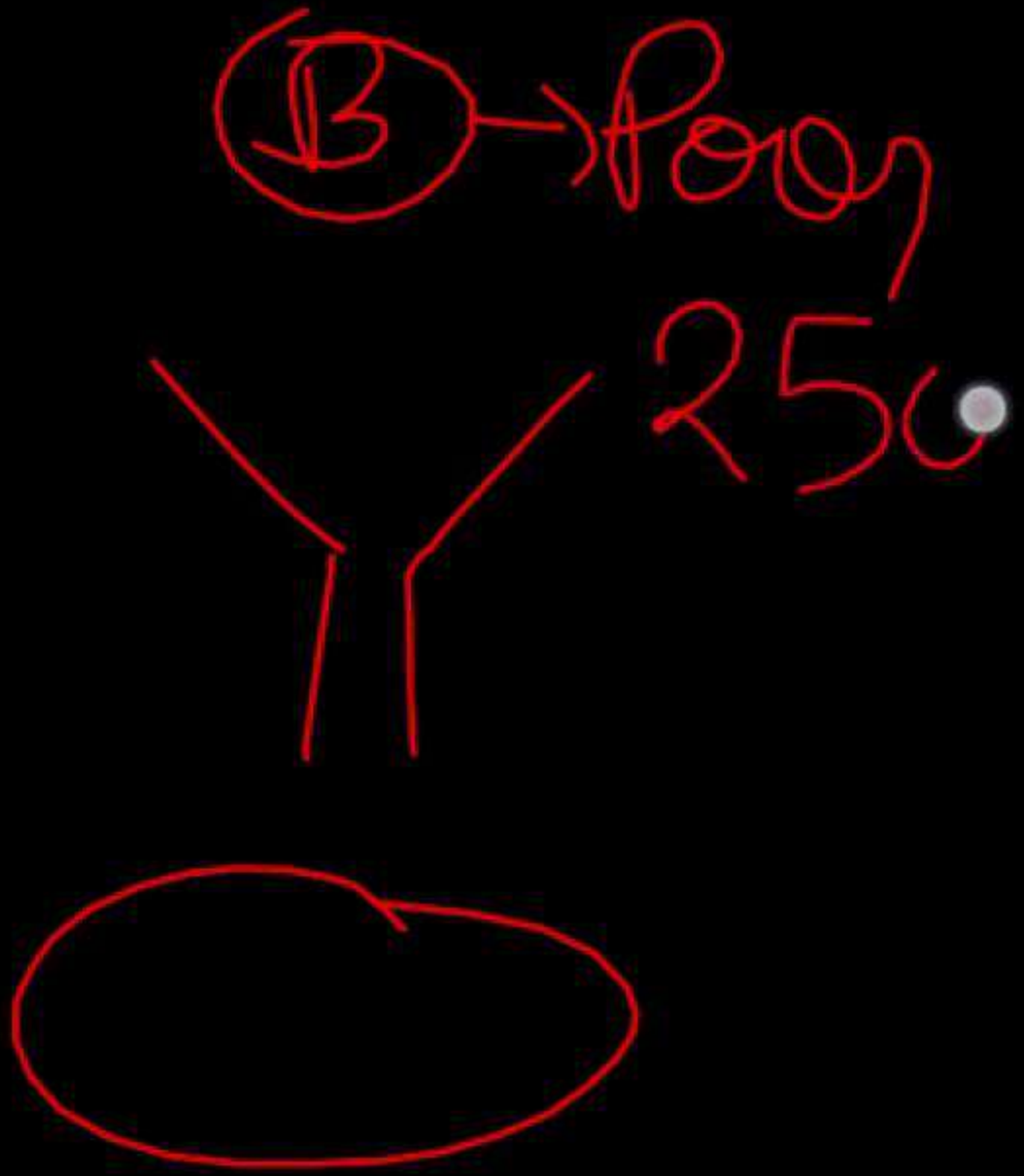



SLIDE 3 OF 11
Ink
Ink Tools
Blank Screen
End Show



FLOW PROPERTIES

- Capacity of any substance to flow is known as flowability
- The flow properties of powders play a major role in tableting and encapsulation process because many common manufacturing problems are attributes to powder flow when powder transfer through large equipment such as hopper
- Uneven powder flow increase particle's friction with die wall causing lubrication problems and increase dust contamination risks during powder transfer and it also affect the weight uniformity of the dose (under or over dosage)

Parameters to Evaluate the Flowability of a Powder

- Carr's compressibility index
- Hausner ratio
- The angle of repose(Θ)

Carr's Compressibility Index

$$\textbf{Carr's index (\%)} = 100 \left(\frac{(\text{Tapped Density} - \text{Bulk Density})}{(\text{Tapped Density})} \right)$$

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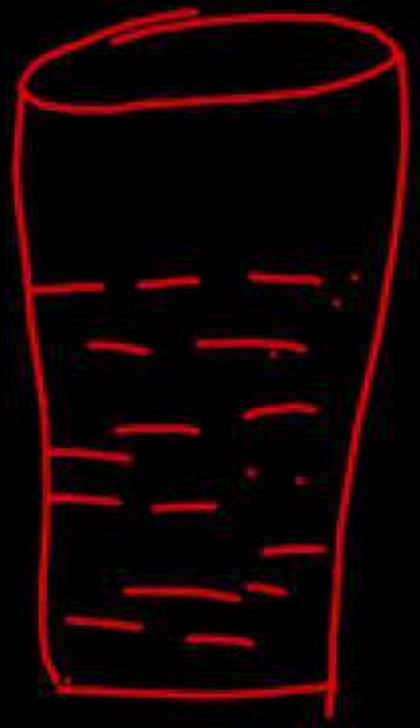

FLOW PROPERTIES

$$\text{Bulk density} = \frac{\text{Weight}}{\text{Bulk volume}}$$

$$D = \frac{M}{V}$$

$$\text{Tapped density} = \frac{\text{Weight}}{\text{Tapped volume}}$$

Hausner's Ratio:

$$\text{Hausner ratio} = \frac{\text{Tapped density}}{\text{Poured or bulk density}}$$

- It is related to interparticle friction. So it can be used to predict powder flow properties. For coarse, free flowing powders the Hausner ratio is approximately 1.2
- Greater the Hausner ratio more cohesive will be the powder and flowability will be reduced

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FLOW PROPERTIES

% Compressibility	Flow description	Hausner's Ratio
5 – 15	Excellent flow	1.0-1.11
12 – 16	Good	1.12-1.18
18 – 21	Fair to Passable	1.19-1.34
23 – 35	Poor	1.35-1.45
33 -38	Very Poor	1.46-1.59
> 40	Extremely poor	>1.60

The Angle of Repose(Θ)

- It is the maximum angle possible between the surface of pile of the powder and hrizontal plane
- It shows interparticle cohesion
- It increases as particle size decreases and moisture content increases
- The rougher and more irregular the surface of the particles, the higher will be the angle of repose

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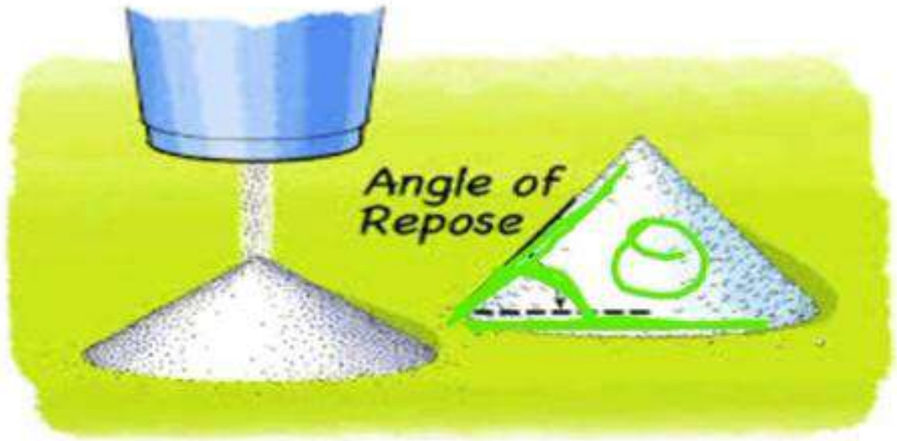

Angle of Repose	Powder Flow
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41-45	Passable
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56-65	Very Poor
>66	Very-Very Poor

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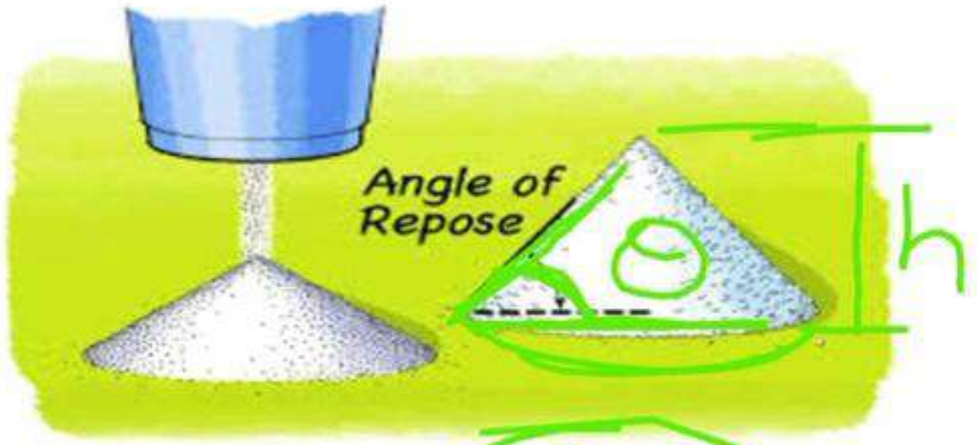

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>66	Very-Very Poor

FLOW PROPERTIES

Factors affecting the flow properties of powder

1. Particle's size & Distribution
2. Particle shape & texture
3. Surface Forces

How flow properties can be improved

1. Alteration of Particle's size & Distribution
2. Alteration of Particle shape & texture
3. Alteration of Surface Forces
4. Formulation additives (Flow activators)

Spherical

Shape factor - ⊙

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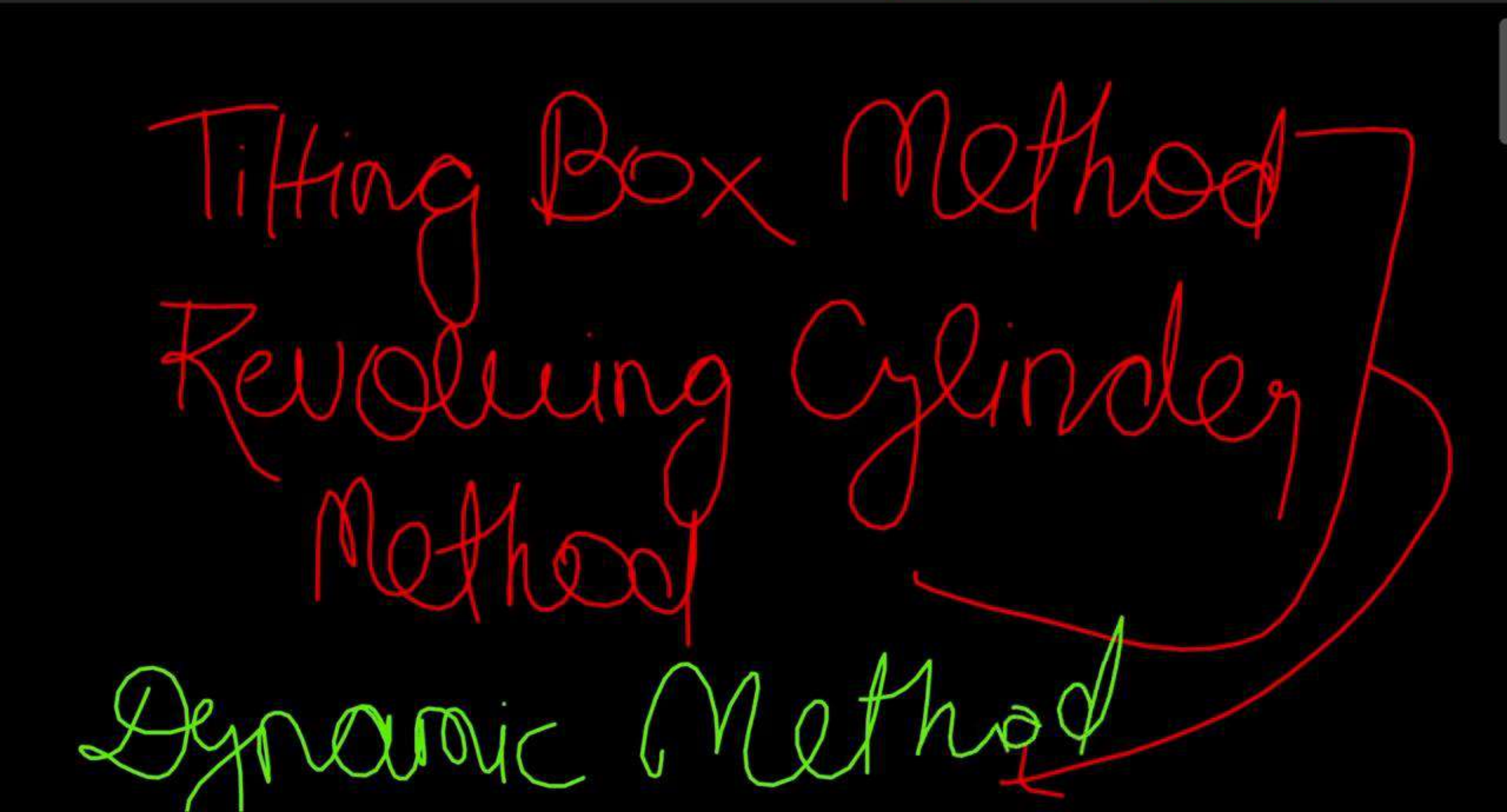
↓
les interparticle
friction



WETTABILITY

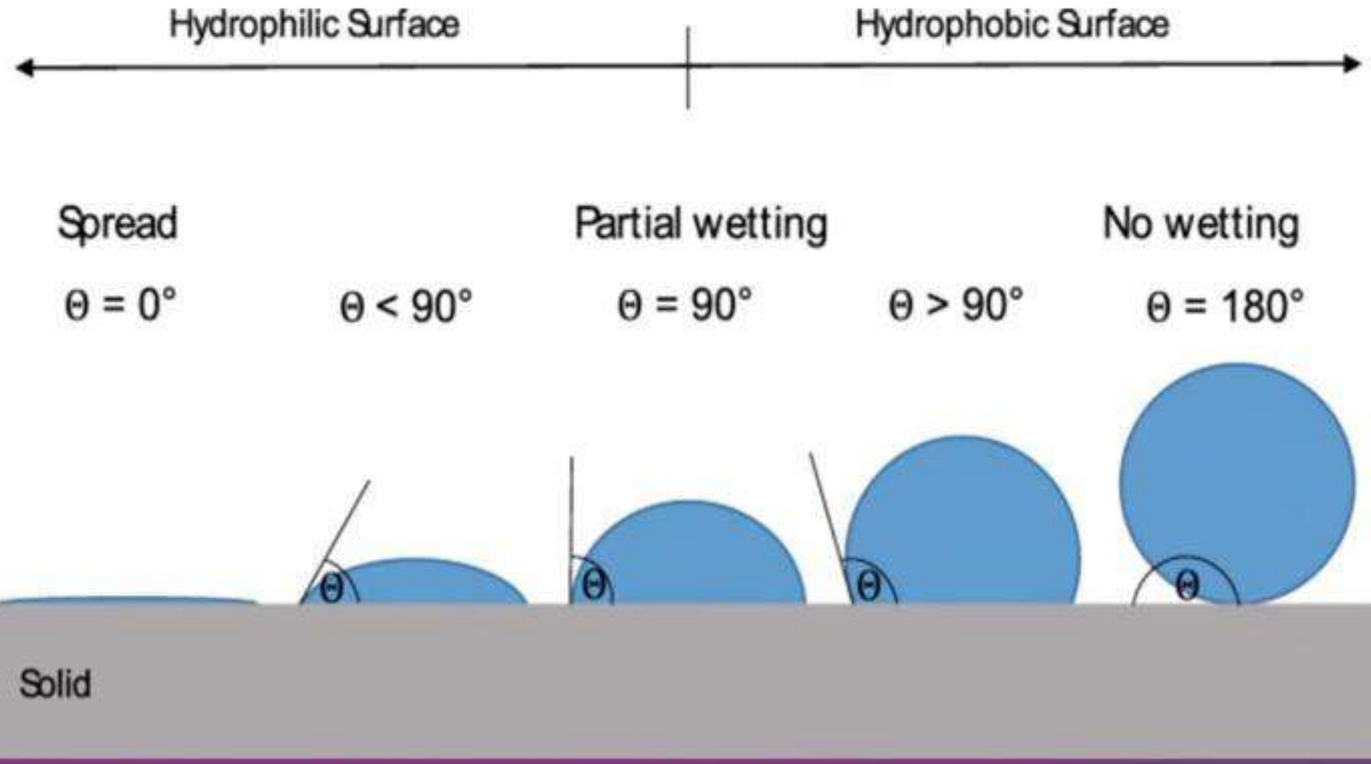
It can be defined as the ability of a liquid to maintain contact with a solid surface

Wetting

- It is the extent of contact between a liquid and a solid surface, when two are brought in contact with each other. This phenomenon is known as wetting and the agents used in wetting is called wetting agent.
- Weting agents act by decreasing interfacial tension which results in decrease in contact angle between the surfaces.
- Wetting agents h HLB value from 7-9

Wetting Agent Tests

- Drave Test
- Emperical Test
- Trough Test
- Contact Angle Method



WETTABILITY

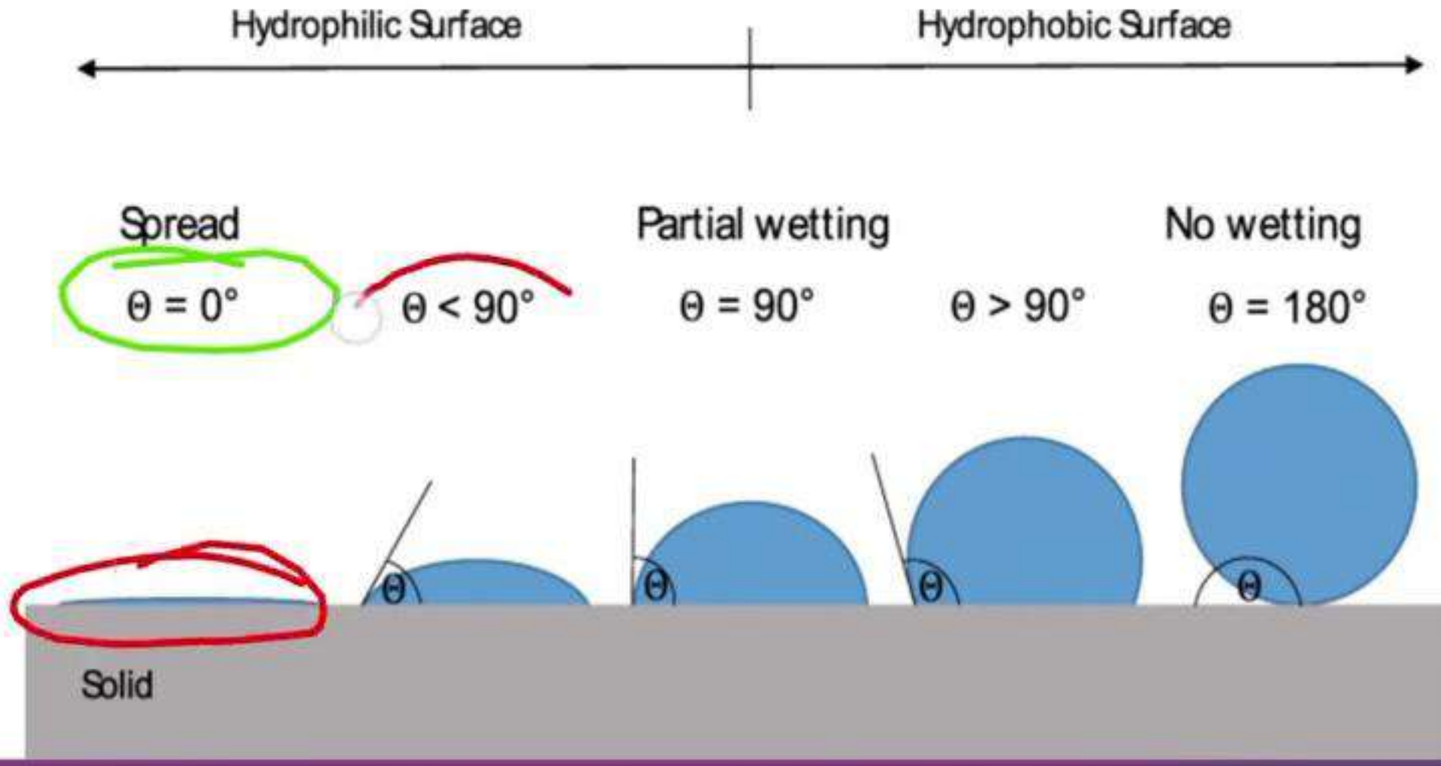
It can be defined as the ability of a liquid to maintain contact with a solid surface

Wetting

- It is the extent of contact between a liquid and a solid surface, when two are brought in contact with each other. This phenomenon is known as wetting and the agents used in wetting is called wetting agent.
- Weting agents act by decreasing interfacial tension which results in decrease in contact angle between the surfaces.
- Wetting agents h HLB value from 7-9

Wetting Agent Tests

- Drave Test
- Emperical Test
- Trough Test
- Contact Angle Method



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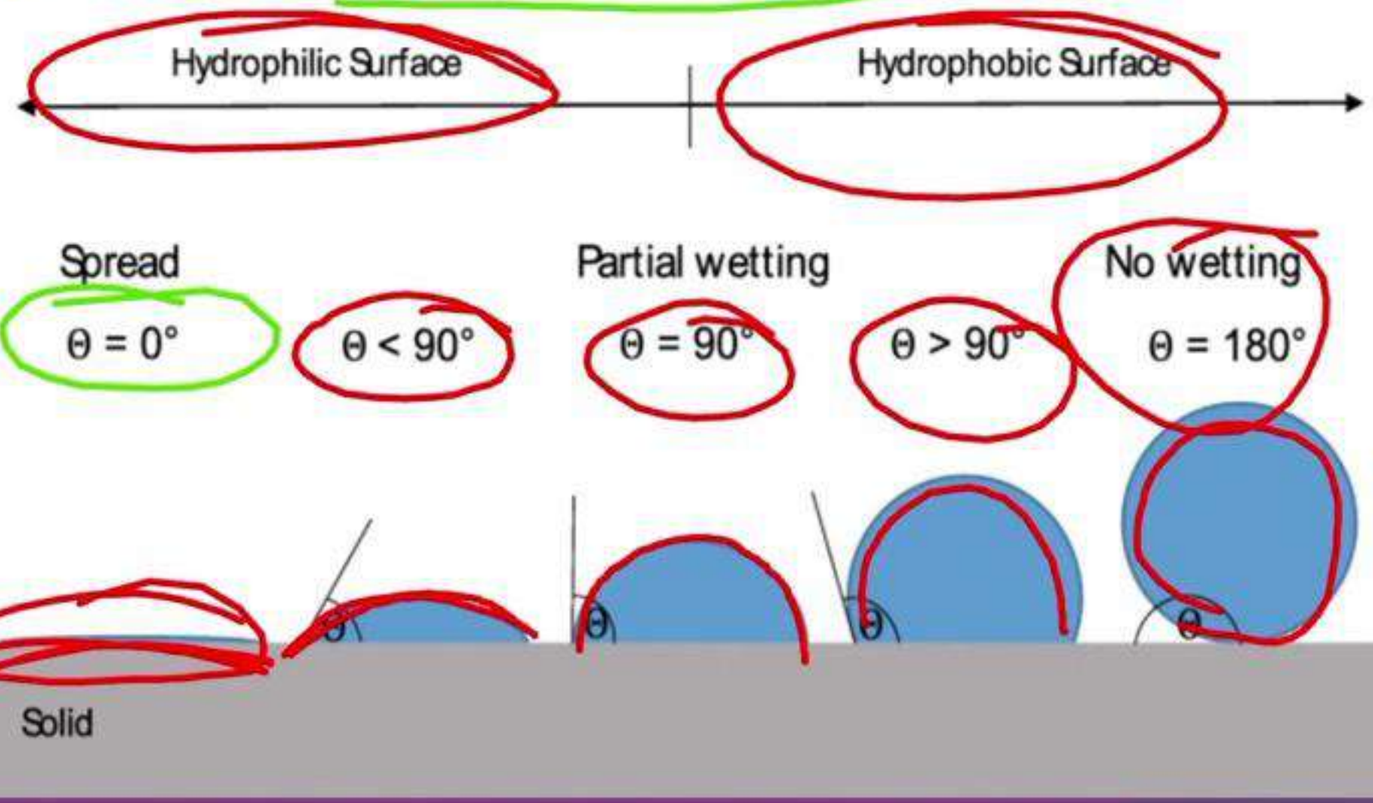

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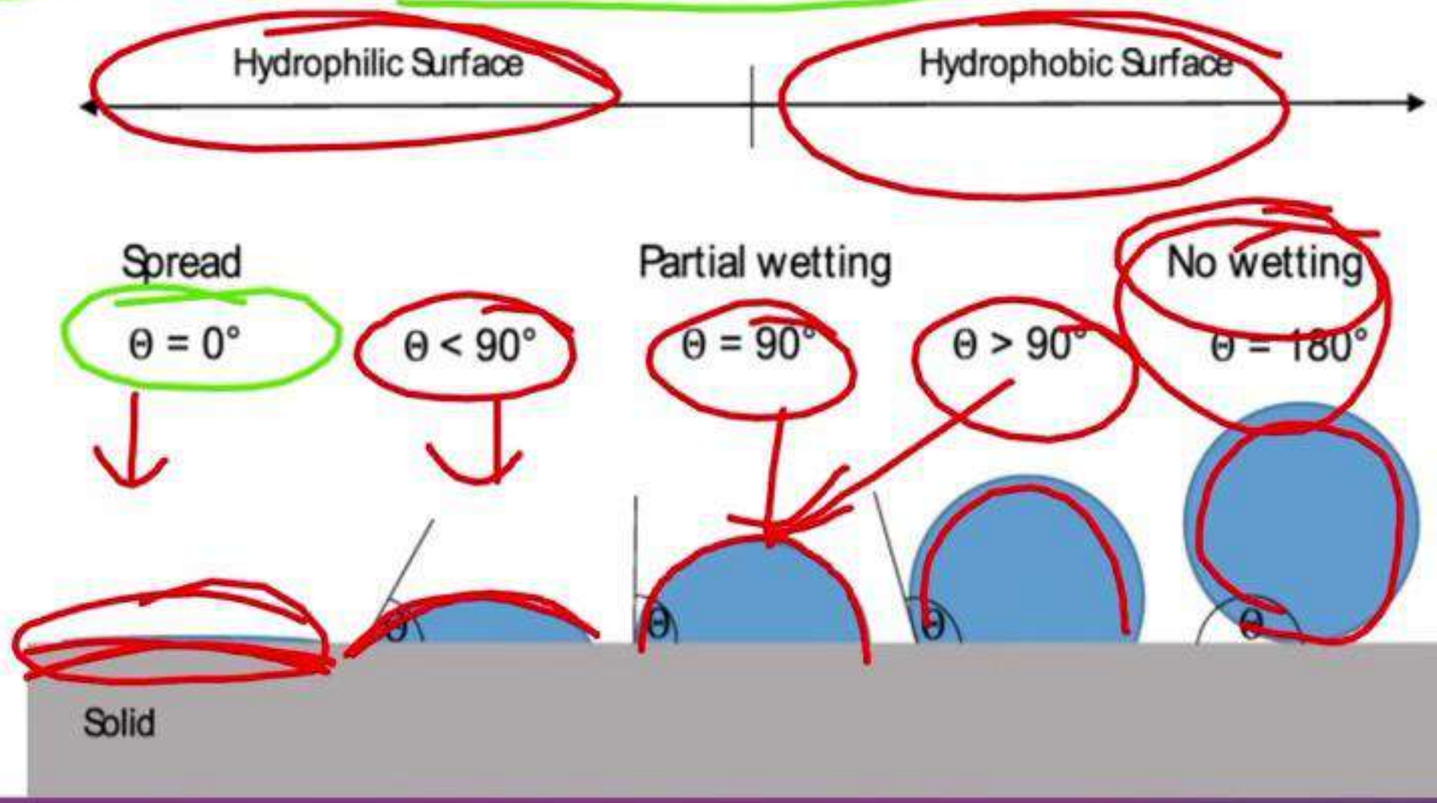

HYGROSCOPICITY

- Many pharmaceutical substances (especially water-soluble salt forms) have tendency to adsorb atmosperic moisture, they are called hygroscopic and this phenomenon is known as hygroscopicity.
- Adsorption and equllibrium moisture content can depend upon the atmospheric humidity, temperature, surface area, exposure and the mechanism of moisture uptake

Classification	% water uptake at 25^{0}C for 24h at 80% RH
Non-Hygroscopic	Increase in weight betwwen 0 - 0.12% W/W
Slightly Hgroscopic	Increase in weight is ≥0.2% - <2% w/w
Hygroscopic	Increase in weight is ≥2.0% - <15% w/w
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Deliquescent	Sufficient amount of water is absorbed freom a solution

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HYGROSCOPICITY

Methods to Measure Hygroscopicity

- Gravimetry
- Thermogravimetry Analysis
- Karl Fischer Titration
- Gas Chromatography

Effect of Hygroscopicity on Pharmaceutical Parameters

- Flow Property
- Chemical Stability
- Surface Property
- Compaction Property
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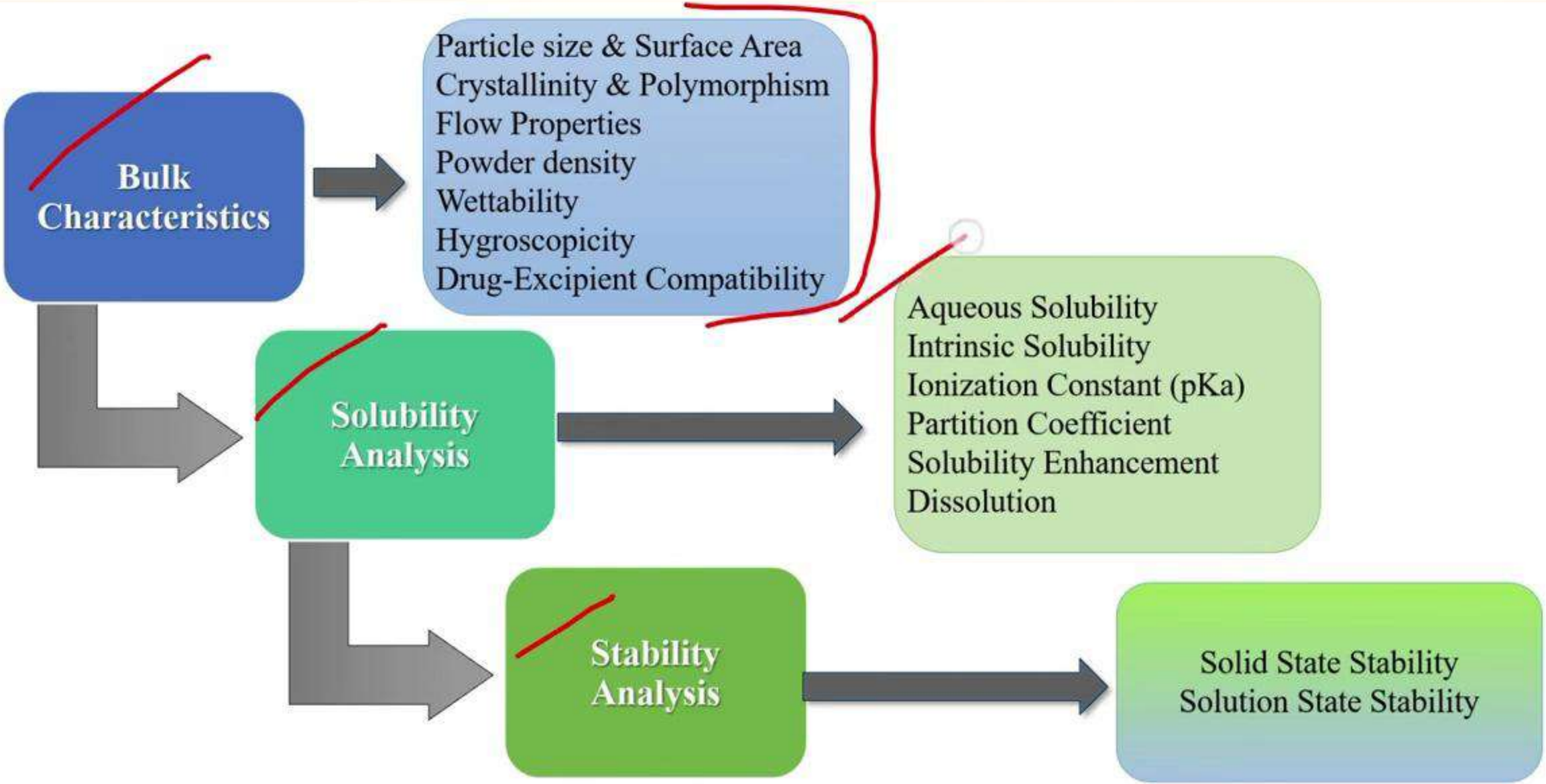
PHYSICAL CHARACTERISTICS



SOLUBILITY ANALYSIS

Aqueous Solubility

The amount of drug that dissolves in a given volume of solvent at specified temperature and pressure to form a saturated solution

$$\text{Solubility} = \left(\frac{\text{Max. Amount of Drug}}{\text{Volume of Solvent}} \right) \times 100$$

100ml

Ideally solubility is measured at two different temperatures :

At 4^0C - To ensure physical stability of the drug

At 37^0C - To support biopharmaceutical evaluation

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Body

Unsaturated $\xrightarrow{+}$ Saturat.

$\xrightarrow{+}$ Temp/ Press

$\propto$ Temp/ Temp

Crystallize $\xleftarrow{\text{Temp}}$ Supersat.

SOLUBILITY ANALYSIS

Solubility Expression

Descriptive Term	Approx. Quantities of Solvent in Per Gram of Solute
Very Soluble	Less than 1 part
Freely Soluble	1-10 parts
Soluble	10-30 parts
Sparingly Soluble	30-100 parts
Slightly Soluble	100-1000 parts
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PARTITION COEFFICIENT

- The lipophilicity of an organic compound is usually described in terms of a partition coefficient, log P, which can be defined as the ratio of the concentration of the unionized compound, at equilibrium, between organic and aqueous phases.
- Partition coefficient is the measurement of a drug's lipophilicity and an indication of its ability to cross cell membranes is the oil/water partition coefficient.

$$P = \frac{(\text{Conc. of drug in octanol})}{(\text{Conc. of drug in water})}$$

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PARTITION COEFFICIENT

If the value of Partition Coefficient -

>1 = Lipophilic Drug

<1 = Hydrophilic Drug

Compounds with log P values between 1 and 3 show good absorption

- log P greater than 6 or less than 3 often have poor transport characteristics.
- Highly non-polar molecules have a preference to reside in the lipophilic regions of membranes, and very polar compounds show poor bioavailability because of their inability to penetrate membrane barriers.
- Thus, there is a parabolic relationship between log P and transport, i.e., candidate drugs that exhibit a balance between these two properties will probably show the best oral bioavailability.

Methods to determine P

- Shake flask method
- Chromatographic method (TLC, HPTLC)
- Counter current and filter probe method

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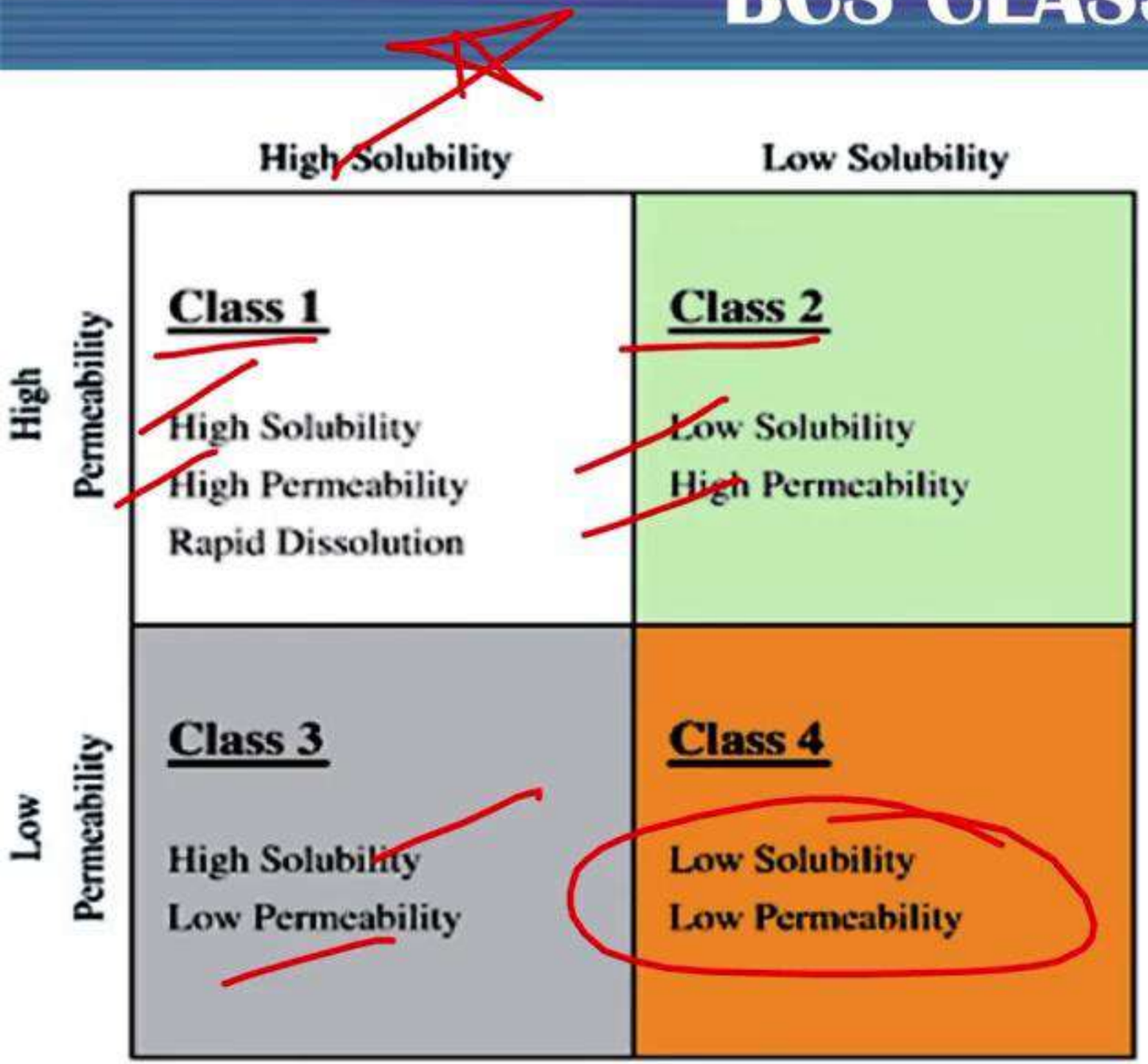

Examples of some drugs as per biopharmaceutical classification system

Class I	Class II	Class III	Class IV
Chloroquine	Carbamazepine	Acyclovir	Coenzyme Q_{10}
Diltiazem	Danazol	Atenolol	Cyclosporin A
Metoprolol	Glibenclamide	Captopril	Ellagic acid
Paracetamol	Ketoconazole	Cimetidine	Furosemide
Propranolol	Nifedipine	Metformin	Ritonavir
Theophylline	Phenytoin	Neomycin B	Saquinavir
Verapamil	Troglitazone	Ranitidine	Taxol

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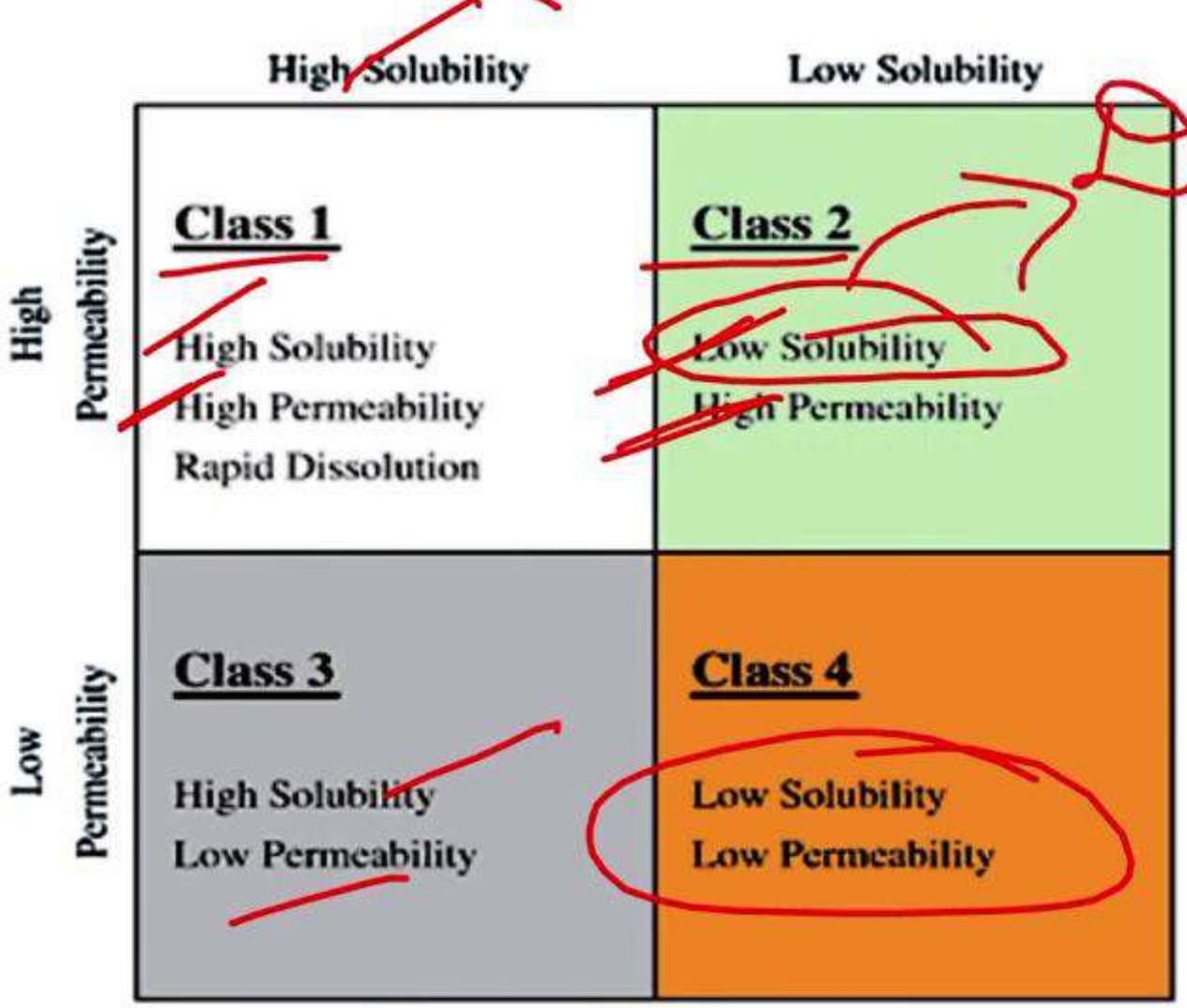

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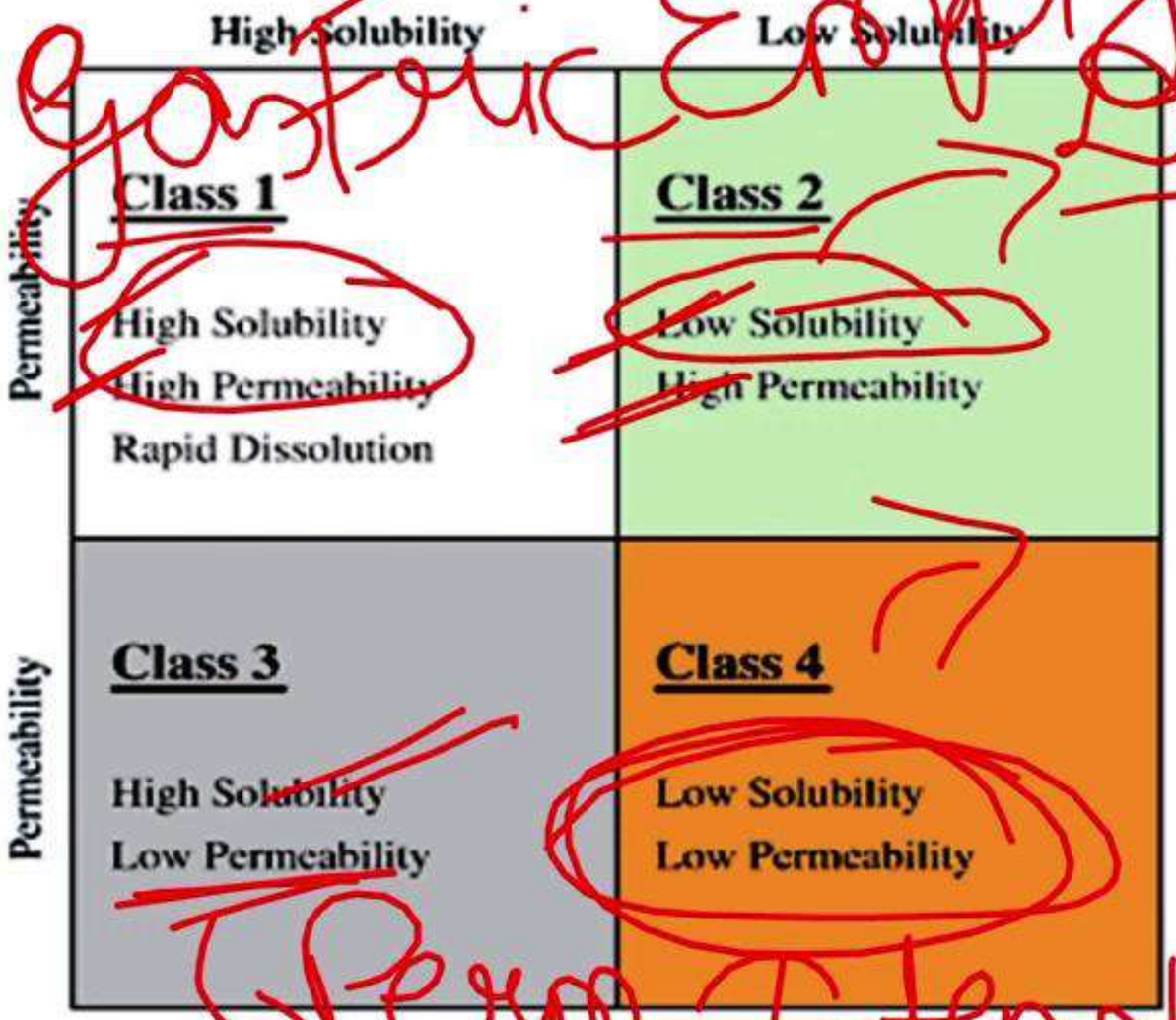

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IONIZATION CONSTANT

Ionization constant or dissociation constant (pKa) ia a negative logarithm of the equlibrium coefficient (Ka) of the neutral and charged forms of a compound .

The concept of pKa is derived from the Henderson–Hasselbalch equation

Acid dissociation constants are sometimes expressed by

$$pKa = -\log_{10} Ka$$

The Henderson–Hassel Balch equation provides an estimate of the ionized and unionized drug concentration at a particular pH

$$HA = H^+ + A^-$$

For acidic compounds

$$pH = pKa + log \frac{(\text{ionized drug})}{(\text{un ionized drug})} = pKa + log \frac{(A^-)}{(HA)}$$

For basic compounds

$$pH = pKa + log \frac{(\text{unionized drug})}{(\text{ionized drug})} = pKa + log \frac{(HA)}{(A^-)}$$

IONIZATION CONSTANT

Methods to Determine Ionization Constant

- Potentiometric (pH) method
- Spectrophotometric method
- Partition-coefficient method
- Conductometric method
- Solubility method

Significance of pKa

From the pKa of a weak acid or weak base the unionized fraction of a drug can be determined at a certain pH

Absorption of Drug :

Unionised Lipophilic > Ionised Lipophilic > Unionised Hydrophilic > Ionised Hydrophilic

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Sorbitol, e.

SOLUBILITY ENHANCEMENT

Techniques	Description
Co-Solvency	Technique to enhance the solubility by using co-solvents.
Hydrotrophy	It indiactes the increase in solubility in water of various substances due to presence of large amount of additives.
Complexation	It increases the solubility by forming the complex between drug and complexing agent (ligand)
Solubilisation	It refers to the process of increasing solubility of poorly soluble drugs by using surfactants.

Caffine → Sodium Benzoate

Riboflavin → Procaine HCl

↓

Dg

→ cyclodextrin

→

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DISSOLUTION

Dissolution is the process by which a solute (solid, liquid or gas) disperses and forms a homogeneous solution when mixed with a solvent.

It involves breaking of intermolecular bonds in the solute and forming new interactions between the solute and solvent molecules.

Rate of dissolution is governed by Noyes-Whitney equation :

$$\frac{dm}{dt} = A \cdot \left[\frac{D}{h}\right] \cdot (C_S - C)$$

where m = mass (mol), t = time (s), C = concentration of solute dissolved at a particular time ($mol \cdot cm^{-3}$), C_s = equilibrium solubility ($mol \cdot cm^{-3}$), D = diffusivity ($cm^2 \cdot s^{-1}$), h = apparent thickness (cm) of the aqueous boundary layer (depends on rate of stirring and the temperature), and A = surface area available for dissolution (cm^2).

Small particle size - greater surface area

↓

Fast rate of dissolution

↓

Rapid drug absorption

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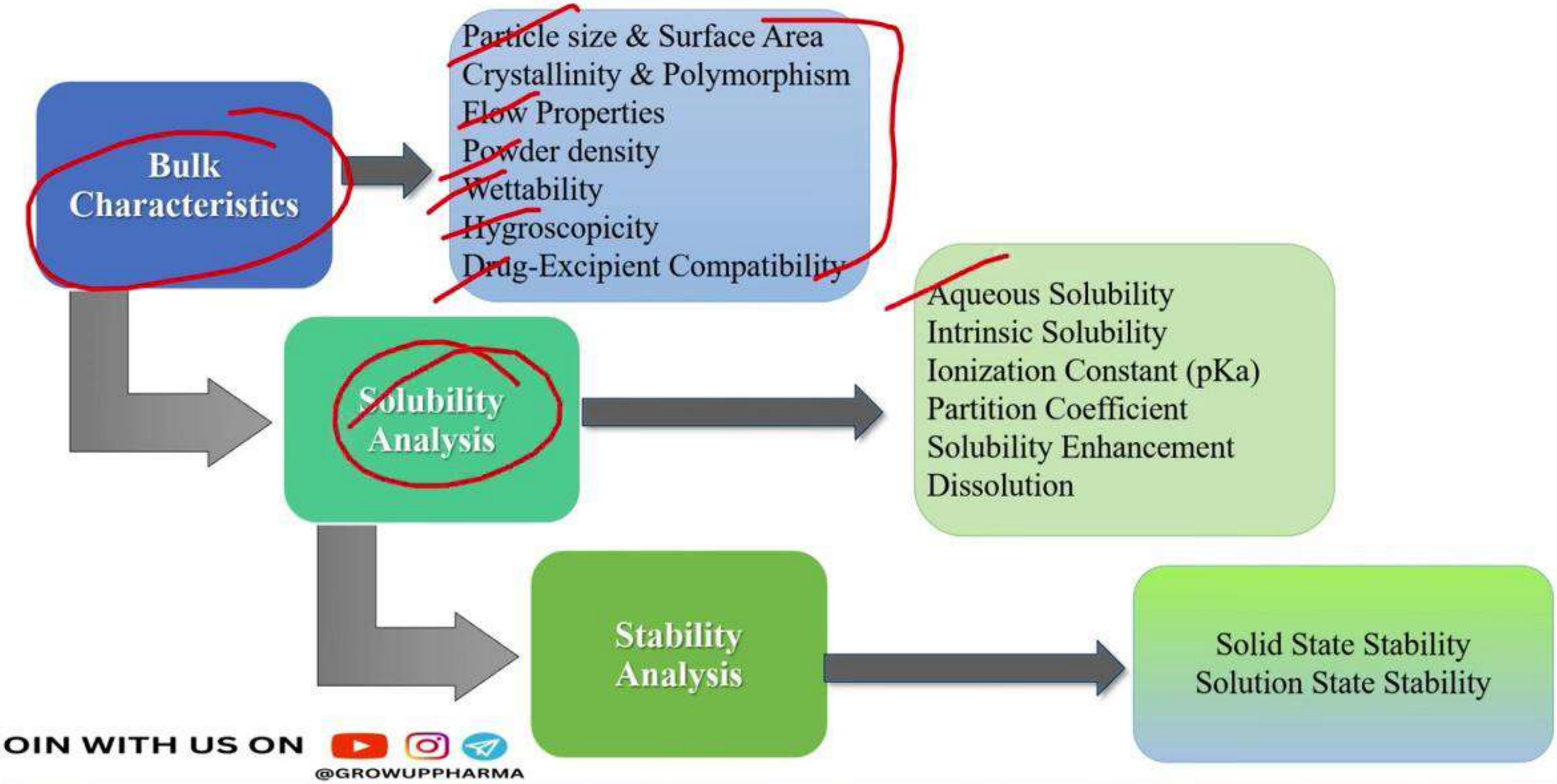
Characteristics
ility Analysis
lity Analysis

ion, Hydrolysis
ion,
erization,
ization, Photolysis

Colour
Odour
Taste

GP
GROWUP PHARMA

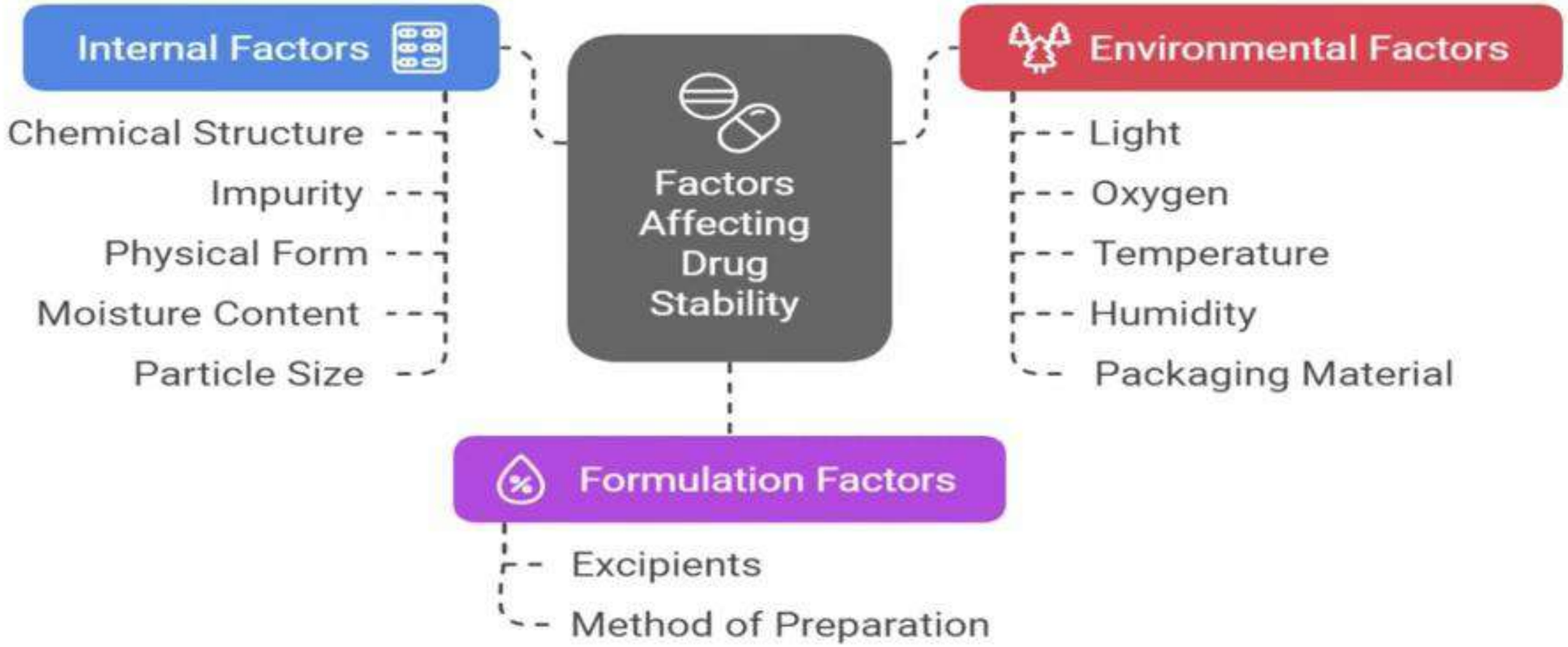
PHYSICAL CHARACTERISTICS



STABILITY ANALYSIS

Stability

The capability of particular formulation to remain within its physical, chemical, microbiological, therapeutic and toxicological specification throughout its shelf life.



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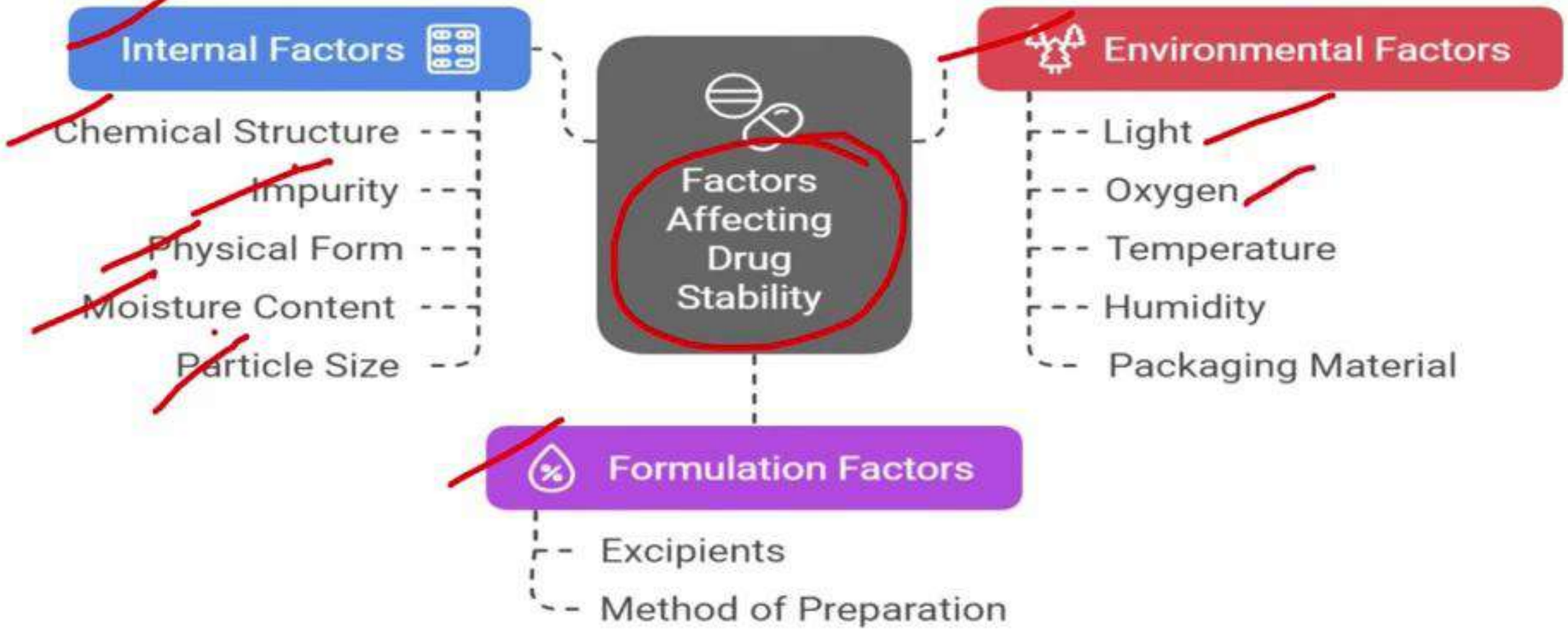

TYPES OF STABILITY

Toxicological Stability

No significance increase in toxicological effect

Chemical Stability

Stability related to the chemical composition of the active ingredient

Physical Stability

Involves the physical properties like appearance , palatability, texture and dissolution

Therapeutical Stability

Ensures the drug maintains its intended therapeutic effect

Microbiological Stability

Should not contain any microbial contamination and growth

STABILITY ANALYSIS

Solution Stability :

Solution stability is studied to identify the best combination of solvent, pH, buffer and ionic strength that gives slowes drug decomposition in solution .

Solid State Stability :

Identify physical and chemical changes which decreases potency of the drug and increase its toxicity on long term sto

Methods of Stability Testing

1. Real Time Stability Testing
2. Accelerated Stability Testing
3. Retained Sample Stability Testing

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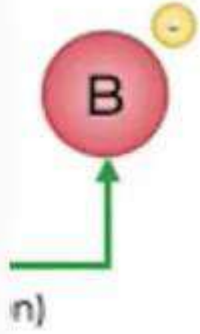


OXIDATION

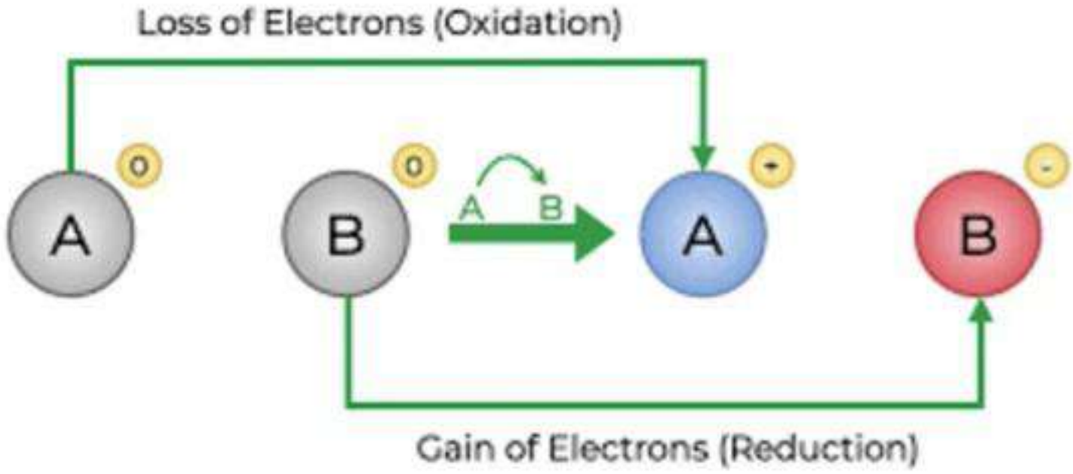
It is very common pathway for drug degradation in both liquid and solid formulation.
It can be defined as the addition of oxygen to the substance or the removal of hydrogen from the substance.

Functional group having high susceptibility towards oxidation

- Substituted aromatic group (Toluene, Phenols, Anisole)
- Alkenes
- Ethers
- Thioethers
- Amines

Factors affecting oxidation process

- Oxygen concentration
- Light
- Heavy metals particularly those having two or more valence state
- Hydrogen & Hydroxyl Ion
- Temperature



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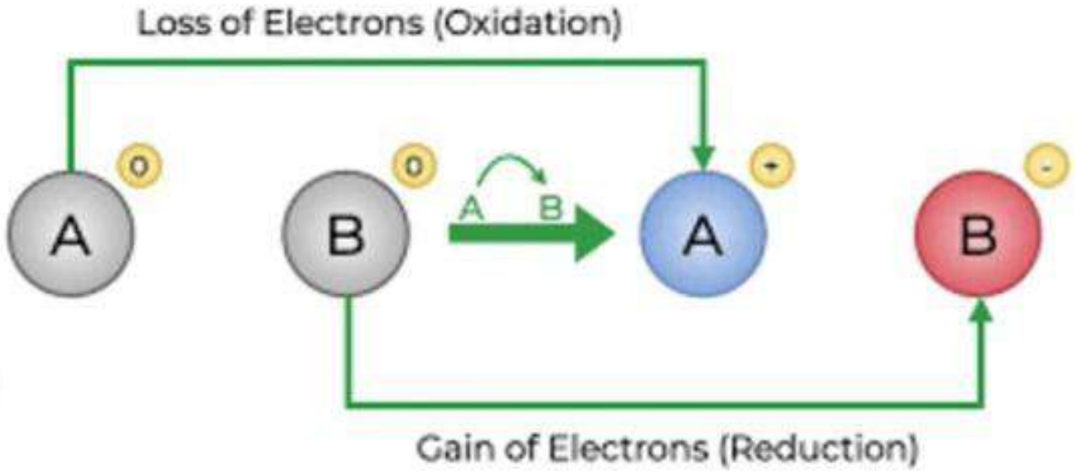


HYDROLYSIS

It is the cleavage of chemical bonds by the addition of water.

The reaction of water with another chemical compound to form two or more products, involving ionization of the water molecule usually splitting the other compound.

Hydrolysis

$$A\text{-}B + H_2O \longrightarrow A\text{-}H + B\text{-}OH$$

Prevention of hydrolysis:

1) pH Adjustment

- Formulate the drug solution close to its pH of optimum stability.
- Optimum buffer concentration.

2) Addition of surfactant

- Nonionic, cationic, and anionic surfactant stabilizes the drug against base catalysis.

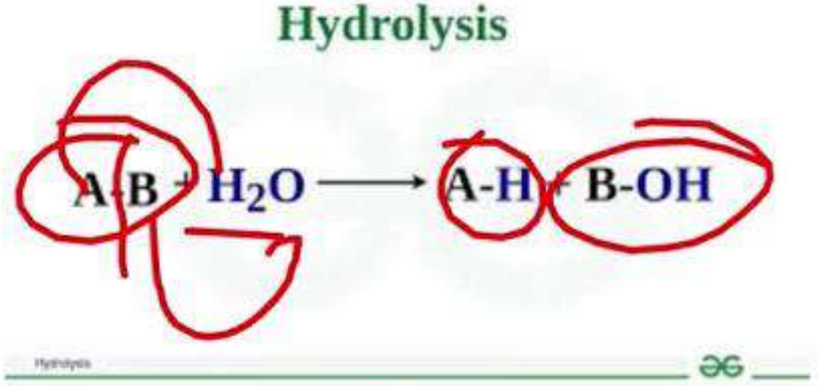
3) Salts and Esters

- The solubility of pharmaceuticals undergoing ester hydrolysis can be reduced by forming less soluble salts.
- By use of complexing agent

Eg. Phosphate esters of clindamycine

HYDROLYSIS

It is the cleavage of chemical bonds by the addition of water.
The reaction of water with another chemical compound to form two or more products, involving ionization of the water molecule usually splitting the other compound.



Prevention of hydrolysis:

1) pH Adjustment

- Formulate the drug solution close to its pH of optimum stability.
- Optimum buffer concentration.

2) Addition of surfactant

- Nonionic, cationic, and anionic surfactant stabilizes the drug against base catalysis.

3) Salts and Esters

- The solubility of pharmaceuticals undergoing ester hydrolysis can be reduced by forming less soluble salts.
- By use of complexing agent

Eg. Phosphate esters of clindamycine

PHOTOLYSIS

Photo dissociation, photolysis, or photodecomposition is a chemical reaction in which a chemical compound is broken down by photons(light).

Prevention of Photolysis

- **Suitable Packing**

Yellow-green glass gives the best protection in U.V. region while Amber gives considerable protection against U.V. radiation but little from I.R.

- **Protection of Drug from Light**

Nifedipine is manufactured under Na light.

- **Avoiding Sunbath**

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RACEMIZATION

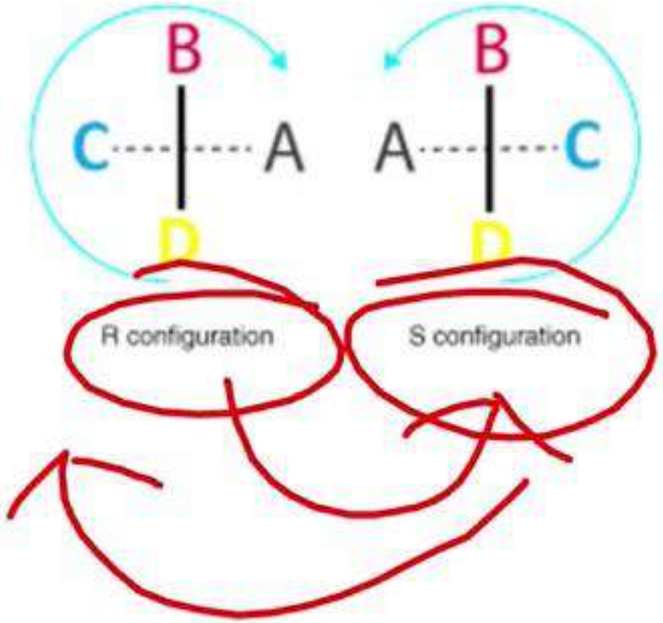
- It is the process in which one enantiomer of a compound, converts to the other enantiomer.
- In this phenomenon optically active ompound loses its optical activity without changing its chemical composition and converted into its inactive form i.e. racemic mixture.
- The inter-conversion from one isomer to another can lead to different pharmacokinetic properties (ADME) as well as different pharmacological & toxicological effect.

Example: L-epinephrine is 15 to 20 times more active than D-form, while activity of racemic mixture is just one half of the L-form.

Factors Affecting Racemization

- Temperature
- Solvent
- Catalyst &
- Presence or absence of light

50 : 50



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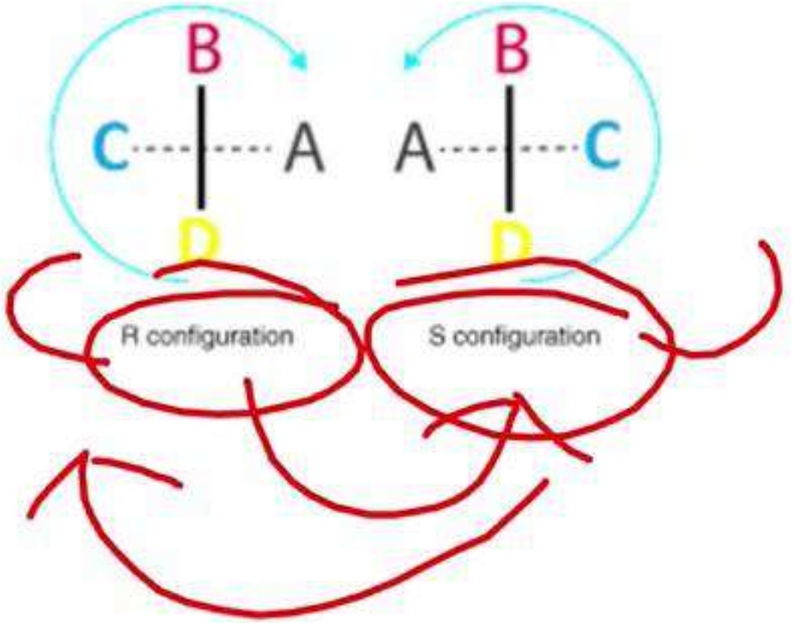
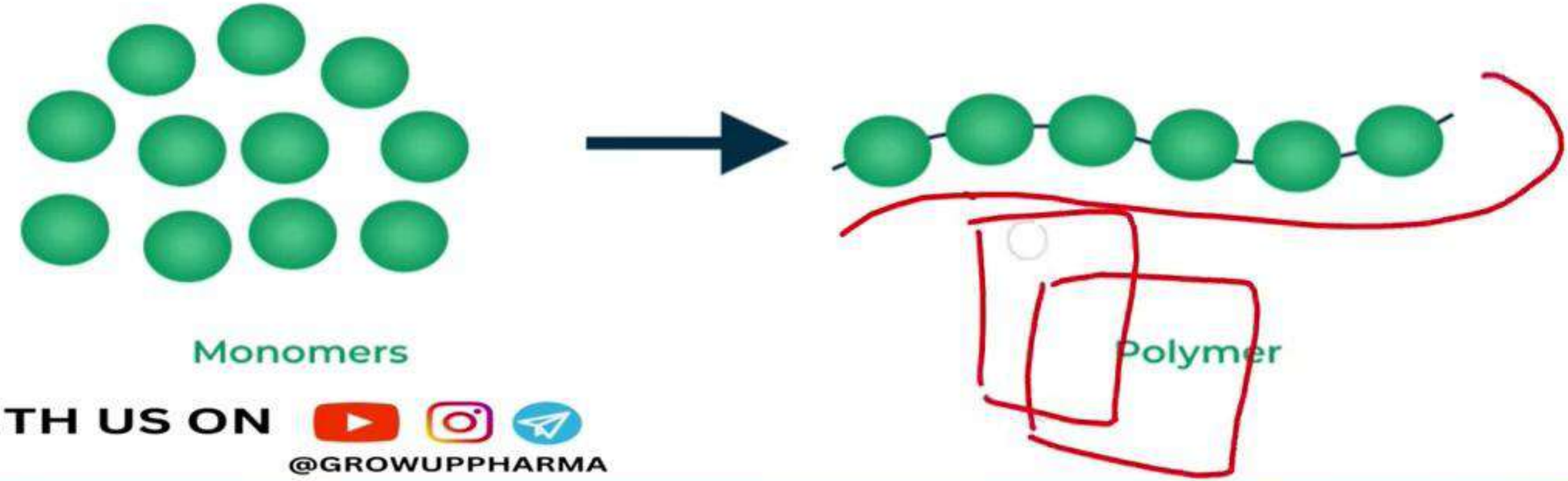


POLYMERIZATION

- Polymerization is a process of reacting monomer molecules together in a chemical reaction to form polymer chains or three-dimensional networks.
- It is a continuous reaction between molecules.
- More than one monomer reacts to form a polymer.

Eg. Darkening of glucose solution is due to polymerization of breakdown product [5- (hydroxyl methyl) furfural. (a colorless liquid used in synthetic resin manufacture).

- ❖ Shellac on aging undergoes polymerization & hence prolongs disintegration time & dissolution time.



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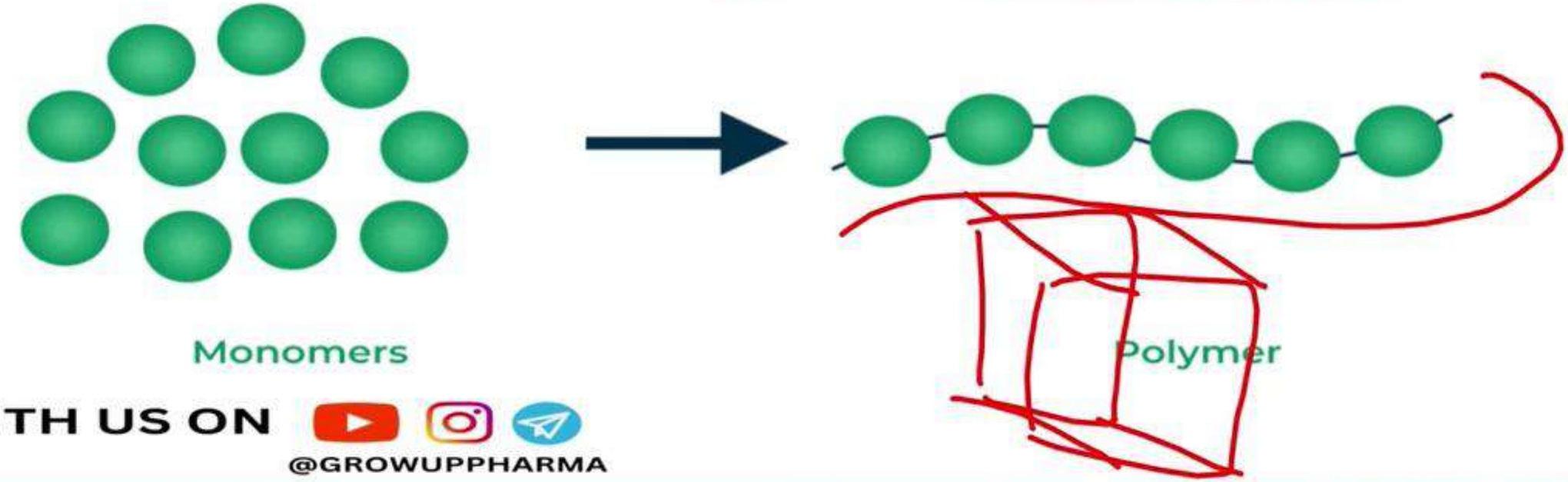


ISOMERISATION

Is the process by which one molecule is transformed into another molecule which has exactly the same atoms, but the atoms have a different arrangement.

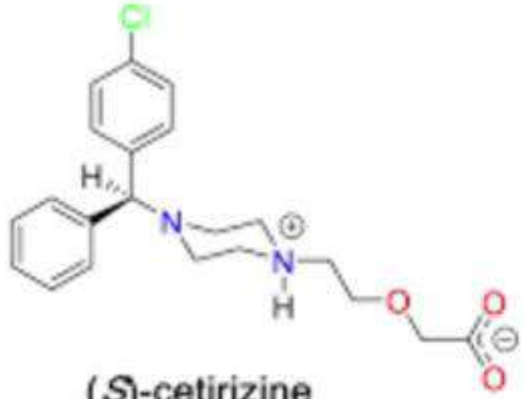
e.g. A-B-C → B-A-C (these related molecules are known as isomers).

Examples:-

- ❖ Tetracycline & its derivatives can undergo reversible Isomerization at pH range 2-6.
- ❖ Trans-cis Isomerization of Amphotericin B
- ❖ Levocetrizine has smaller volume of distribution than its dextroisomer.
- ❖ Esomeprazole is more bioavailable than racemic omeprazole;

ABC →
ABC

(*R*)-cetirizine
(levocetirizine)



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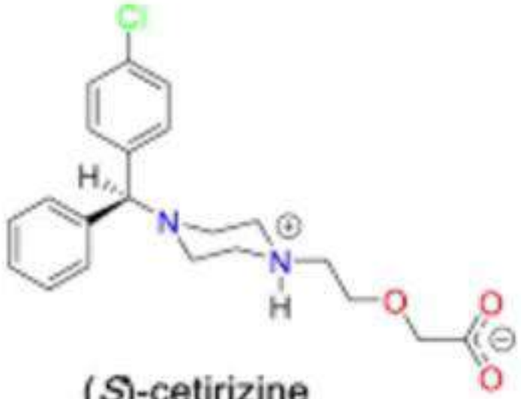

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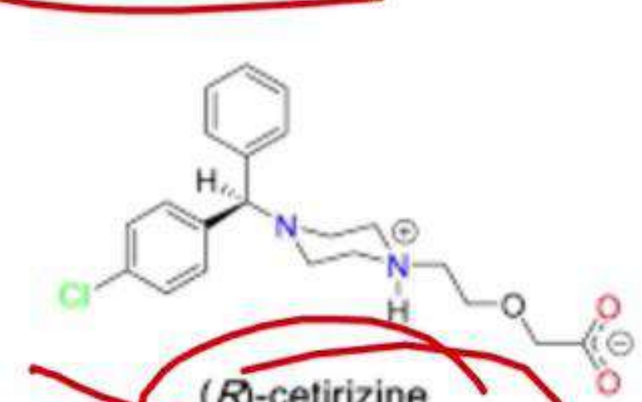

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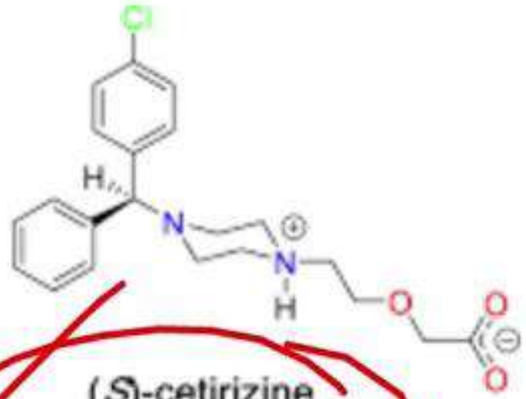

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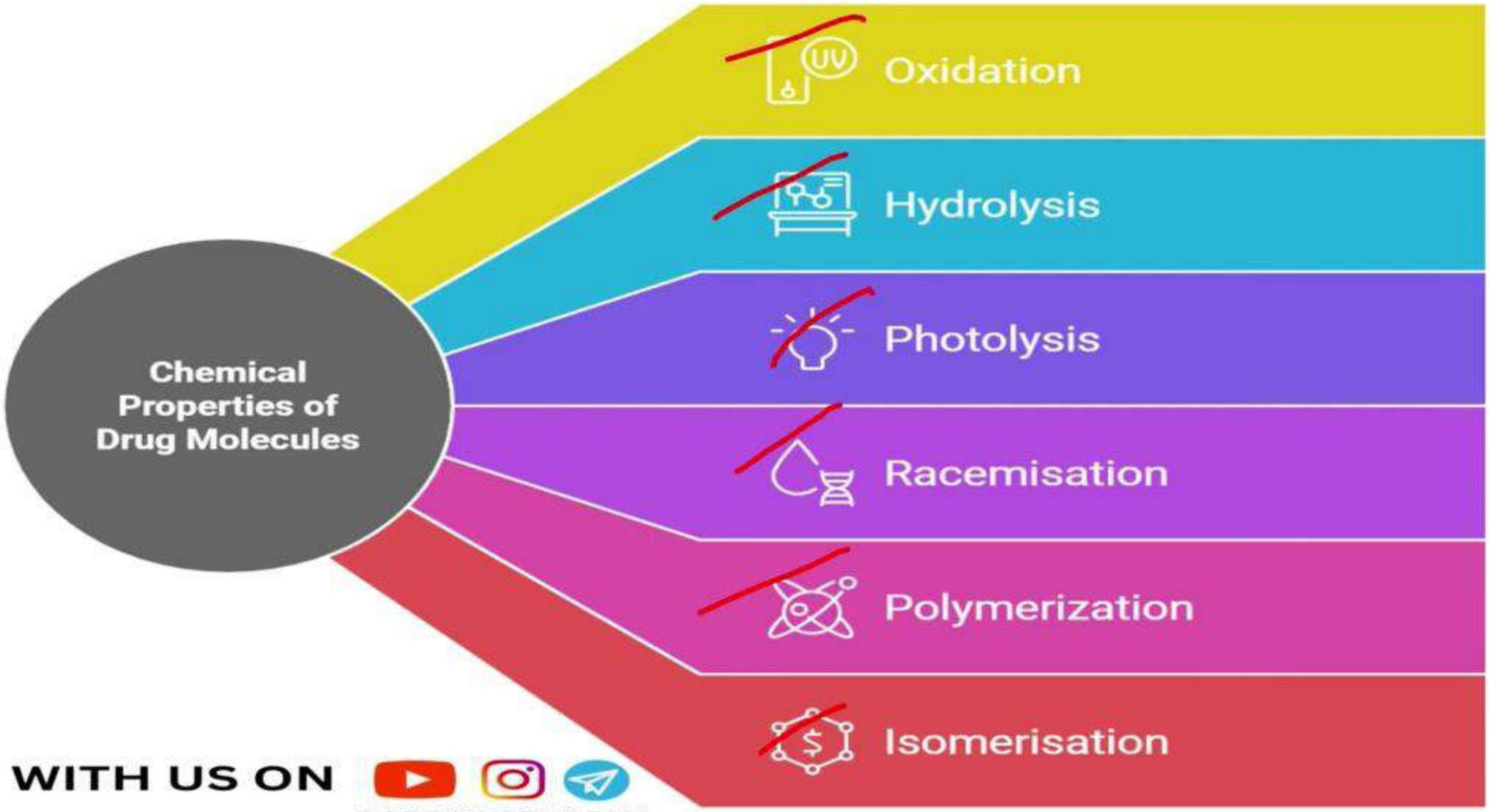
CHEMICAL CHARACTERISTICS



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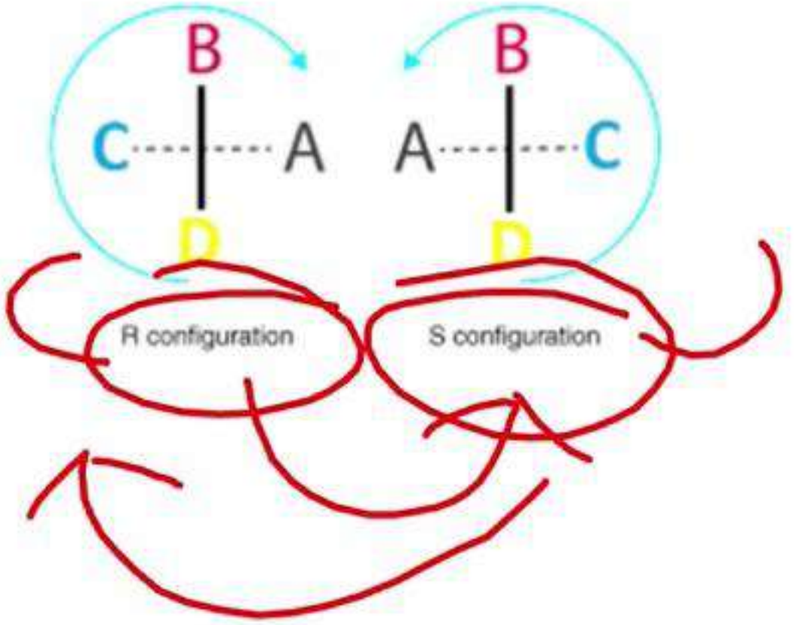

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TOPIC - DOSAGE FORMS

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LECTURE- 1

DOSAGE FORMS

DRUG + EXCIPIENTS

Definition:

Dosage forms are the means by which drug molecules are delivered to the sites of action within the body to produce optimum desired effects & minimum adverse effects.

Excipients - Inactive substance that serves as the vehicle or medium for a drug or other active substance.

DOSAGE FORMS

Gaseous Dosage Form

Consists of aerosols and inhalers

Solid Dosage Form

Includes tablets, capsules, Powder and other solid forms

Semisolid Dosage Form

Comprises ointments, creams, and gels

Liquid Dosage Form

Encompasses syrups, injections, and liquid medications

SOLID DOSAGE FORMS

Pills	A small, round solid preparation for oral administration
Powder	Solid dosage form meant for external & internal purpose & is available in amorphous or crystalline form
Tablet	It is a unit solid dosage form ofdifferentweight ,size & shape containing single or multiple drugs. Other specialized types of tablets are: ➢ Chewable tablets ➢ Dispersible tablets ➢ Sublingual tablets ➢ Enteric coated tablet ➢ Sustained / Extended release tablets ➢ Controlled release tablet
Capsule	A solid unit dosage form containing one or more substances enclosed within a hard or soft gelatin
Lozenges	A disc shaped solid preparation intended to be slowly dissolved in the oral cavity for local action
Suppository	A solid dosage form intended for insertion into the body cavities like rectum or vagina , where they melt , soften or dissolve and exert local or systemic effects

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LIQUID DOSAGE FORMS

Syrups	Concentrated sugar solution in water , it can be medicated & non-medicated
Elixirs	A clear , sweetened hydroalcoholic liquid containing medicaments
Injections	Sterile aqueous or oily suspension , solution meant for parenteral administration
Suspensions	Biphasic liquid dosage form containing finely divided drug particles uniformly distributed in the vehicle
Drops	Medicated oil or water intended to be inserted into ear , eye or nasal cavity
Lotion	Liquid preparation meant for external application to the skin

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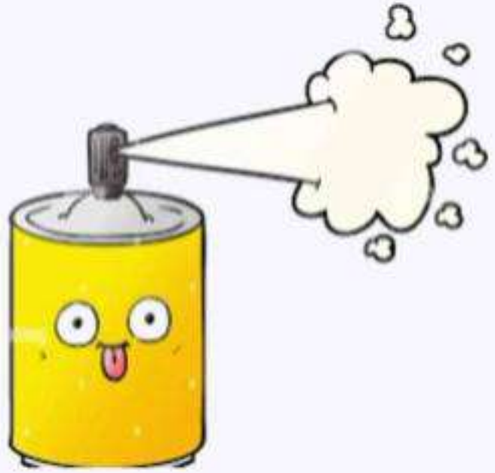
SEMISOLID DOSAGE FORMS

Ointment	These are greasy semisolid dosage form meant for external application to the skin or mucous membrane .
Cream	A water-soluble medication preparation applied to the skin .
Gel	A gel is a semisolid that can have properties ranging from soft and weak to hard & tough .
Paste	Paste are homogenous , semisolid preparation concentrated of insoluble powdered substances (usually not 20%) dispersed in a suitable base.

GASEOUS DOSAGE FORM

Aerosols	Suspension of fine solid or liquid particles withgas used to apply drug to respiratory tract having atomizer with in device
Inhalations	Internal liquid preparations containing medicaments dissolved in suitable solvent or if insoluble suspended in the propellent
Sprays	Gaseous preparations of drugs containing alcohol applied to mucous membrane of nose or throat with atomizer or nebulizer



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Question 1 -

Coulter counter is used in determination of :

(a) Particle surface area

(b) Particle size

(c) Particle volume

(d) All of the above

[GATE- 2010]

Question 2 -

Read the following statements:

[P] : The surface area measurement using BET approach utilizes argon gas for adsorption

[Q]: Full form of BET is Brunauer, Emmett and Teller

Choose the correct answer:

(a) P&Q both are correct

(b) P is correct but Q is incorrect

(c) Q is correct but P is incorrect

(d) Both P & Q are incorrect

[GPAT- 2012]

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[GPAT- 2012]

SURFACE AREA

Surface Area Determination

As the particle size decreases , surface area of the particle increases

FEATURES	ADSORPTION METHOD	AIR PERMEABILITY METHOD
Surface area is measured by	Volume of Nitrogen adsorbed to form a monolayer	Rate at which gas or liquid permeates a bed of powder
Equation	BET (Brunauer; Emmett;Teller) Equation	Poiseuill's Equation & Kozency-Carman Equation
Instrument	Quantasorb	Fisher Subsieve Sizer
Detector	Thermal Conductivity	Water Monometer

Question 3 -

When the angle of repose exceeds… , the powder flow is rarely acceptable for pharmaceutical manufacturing purpose

(a) 25

(b) 30

(c) 50

(d) 60

[GPAT- 2013]

Question 3 -

When the angle of repose exceeds… , the powder flow is rarely acceptable for pharmaceutical manufacturing purpose

(a) 25
(b) 30
(c) 50
(d) 60

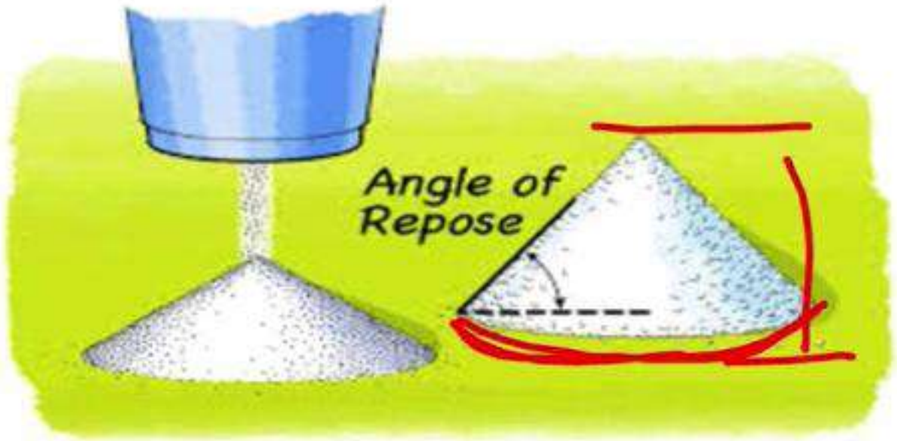
25-30
31-35
36-40
41-45

46

[GPAT- 2013]

FLOW PROPERTIES

$$\theta = tan^{-1}\left(\frac{h}{r}\right)$$



Angle of Repose	Powder Flow
25-30	Excellent
31-35	Good
36-40	Fair
41-45	Passable
46-55	Poor
56-65	Very Poor
>66	Very-Very Poor

Question 4 -

What is the Carr's index of good flow powder property

(a) 5-15

(b) 12-16

(c) 18-21

(d) 28-35

5-15

12-16

33-38

[GPAT- 2016]

% Compressibility	Flow description	Hausner's Ratio
5 – 15	Excellent flow	1.0-1.11
12 – 16	Good	1.12-1.18
18 – 21	Fair to Passable	1.19-1.34
23 – 35	Poor	1.35-1.45
33 -38	Very Poor	1.46-1.59
> 40	Extremely poor	>1.60

13

Question 5 -

The type of particle diameter obtained by microscopic method of evaluation is

(a) Projected diameter

(b) Surface –volume diameter

(c) Volume - surface diameter

(d) Stokes diameter

[GPAT- 2017]

Method	Size Range	Instrument	Description
Microscopy	0.2-100µm	Light Microscope (Transmission Electron Microscope)	Feret, Martin and Projected diameter is measured
Sieving Method	50-1500µm	Mechanical Shaker	Sieve diameter is measured
Sedimentation Method	1-200µm	Anderson Pipette	Stokes diameter is measured
Conductivity Method	0.5-500µm	Coulter Counter HIAC liquid paricle counter	Particle volume distribution is measured

Question 6 -

As per I.P. if the solubility range of a solute is 30 to 100 parts, it will be

(a) Soluble

(b) Freely soluble

(c) Sparingly soluble

(d) Slightly soluble

[GPAT- 2017]

SOLUBILITY ANALYSIS

Solubility Expression

Descriptive Term	Approx. Quantities of Solvent in Per Gram of Solute
Very Soluble	Less than 1 part
Freely Soluble	1-10 parts
Soluble	10-30 parts
Sparingly Soluble	30-100 parts
Slightly Soluble	100-1000 parts
Very Slightly Soluble	1000-10,000 parts
Practically Insoluble	More than 10,000 parts

Question 7 -

In a free-flowing powder, the bulk density and tapped density would be close in value, therefore, the Carr index would be:-

(a) Small

(b) Medium

(c) Large

(d) None

[GPAT- 2018]

POLYMORPHISM

Methods of Characterization of Polymorphs

1. Hot stage microscopy,
2. Differential Thermal Analysis
3. Differential Scanning Calorimetry
4. Thermogravimetric Analysis (TGA)
5. X-ray powder diffraction
6. IR-Spectroscopy
7. FTIR Technique
8. NMR Technique

Pseuopolymorphism

Pseudopolymorphism is the phenomenon wherein a compound is obtained in crystalline forms that differ in the nature or stoichiometry of included solvent molecules

Question 9 -

As per European Pharmacopoeia technical guide, substance stored at 25°C for 24 hours at 80% RH, called very hygroscopic when increase in weight is

(a) 0.2% w/w and <15% w/w

(b) > 0.2% w/w and < 20% w/w

(c) > 15% w/w

(d) 0.2% w/w and < 2% w/w

0 - 0.2% w/w

[GPAT- 2020]

HYGROSCOPICITY

- Many pharmaceutical substances (especially water-soluble salt forms) have tendency to adsorb atmosperic moisture, they are called hygroscopic and this phenomenon is known as hygroscopicity.
- Adsorption and equllibrium moisture content can depend upon the atmospheric humidity, temperature, surface area, exposure and the mechanism of moisture uptake

Classification	% water uptake at 25^0C for 24h at 80% RH
Non-Hygroscopic	Increase in weight betwwen 0 - 0.12% W/W
Slightly Hgroscopic	Increase in weight is ≥0.2% - <2% w/w
Hygroscopic	Increase in weight is ≥2.0% - <15% w/w
Very Hygroscopic	Increase in weight is ≥ 15%w/w
Deliquescent	Sufficient amount of water is absorbed freom a solution

Question 10 -

Choose the wrong statement from the following with regard to Amorphous solids

(a) Usually they are anisotropic

(b) They tend to flow when subjected to sufficient pressure

(c) Considered as super cooled fluids

(d) They do not have definite melting point

[GPAT- 2020]

Question 11 -

The polymorphs exhibit the following different properties Except :

(a) X-ray crystal and diffraction patterns

(b) Melting points

(c) Solubilities

(d) Chemical structures

same

[GPAT- 2020]

Method	Size Range	Instrument	Description
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Conductivity Method	0.5-500µm	Coulter Counter HIAC liquid paricle counter	Particle volume distribution is measured

Question 13 -

Which of the following instrument is used to determine surface area and pore structure of pharmaceutical powders

(a) Coulter counter

(b) Andrerson apparatus

(c) Quantasorb

(d) Optical microscopy

[GPAT- 2022]

Question 14 -

Kozeny Carmen equation is used to determine the

1. Surface area of the powder
2. Viscosity of a liquid
3. Surface tension of a liquid
4. Density of a liquid

[GPAT- 2023(Shift1)]

Question 16 -

Which of the following is the correct choice of particle size measurement technique in scoring order of size?

a. Sieve

b. Anderson Pipette

c. Coulter counter

d. Light scattering

1. a. b. c, d

2. b, d, c, a

3. a, c, b. d

4. d, a. c, b

[GPAT- 2023(Shift-2)]

Question 16 -

Which of the following is the correct choice of particle size m ing order of size?

- 50 - 1500 µm

a. Sieve

b. Anderson Pipette -

c. Coulter counter

d. Light scattering

1. a. b. c, d
2. b, d, c, a
3. a, c, b. d
4. d, a. c, b

[GPAT- 2023(Shift-2)]

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3. a, c, b. d

4. d, a. c, b

[GPAT- 2023(Shift-2)]

SOLUBILITY ENHANCEMENT

Techniques	Description
Co-Solvency	Technique to enhance the solubility by using co-solvents.
Hydrotrophy	It indiactes the increase in solubility in water of various substances due to presence of large amount of additives.
Complexation	It increases the solubility by forming the complex between drug and complexing agent (ligand)
Solubilisation	It refers to the process of increasing solubility of poorly soluble drugs by using surfactants.

Question 19 -

The ability of a substance dissolves in a given solvent system is depends on

(a) Nature and intensity of the forces present in the solute

(b) Nature and intensity of the forces present in the solvent

(c) Interactions between solute and solvent

(d) All the above

Question 20 -

How co-solvents increase the solubility of poorly soluble drugs?

(a) By reducing the interfacial tension between the predominant aqueous solution and hydrophobic solute

(b) By reducing the interfacial tension between solute and solvent

(c) Both

(d) None

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TOPIC – PHARMACEUTICAL TECHNOLOGY

TABLETS LECTURE-1(CLASSIFICATION & EXCIPIENTS)

GPAT/NIPER 2025 CRASH COURSE

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Introduction

- Tablet is a unit dosage form intended to be administered generally orally (not necessarily) to give an desired response
- Prepared either by compression or molding methods
- Pharmaceutical tablets are solid, flat or biconvex discs, unit dosage form, prepared by compressing a drug or a mixture of drugs with or without diluents
- Tablets are now most popular dosage form (70%) of all ethical pharmaceutical preparations produced

Irregular

Round

Coating tablets

Two-color tablets

Various types of tablets

Effervescent tablets

Printed film tablets

Chewable tablets

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Types of Tablets

Tablet ingested orally

- Compressed tablets
- Multiple compressed tablets
- Enteric coated tablets
- Chewable tablets
- Film coated tablets
- Sugar coated tablets
- Controlled released Tablets

Tablet Administered by Other Routes

- Implantation and depots tablets
- Vaginal tablets

Tablets

Tablet used in oral cavity

- Buccal tablets
- Sublingual tablets
- Troches and lozenges
- Dental cone

Tablet used to Prepare Solution

- Effervescent tablets
- Dispensing tablets
- Hypodermic tablets
- Tablets triturate

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Tablets Ingested Orally

Compressed Tablets

Formed by compression and contain no special coating

DT: IP-15 minute or less, USP-30 minutes or less

Eg: Aspirin (Disprin)

Multiple compressed (MCT)

Prepared by more than one compression cycle

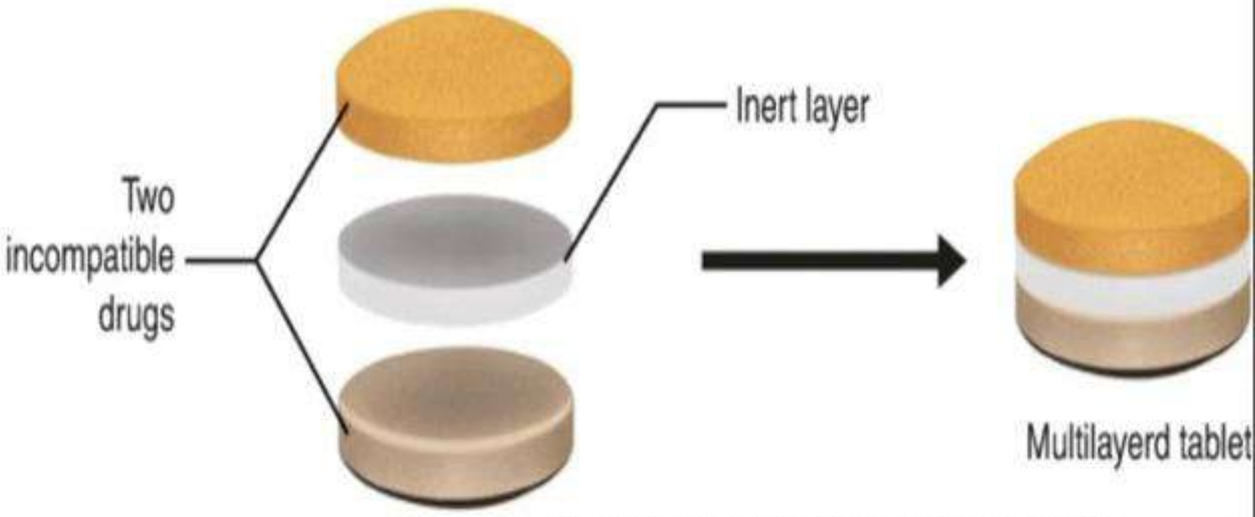
This type is prepared to:

- To formulate 2 or more drugs in a single dosage form
- To formulate two types of dose in single formulation

Are of two class:

Layered Tablets: Two layered or three-layered

Compression coated tablets: tablet within a tablet



Combination of different release profile

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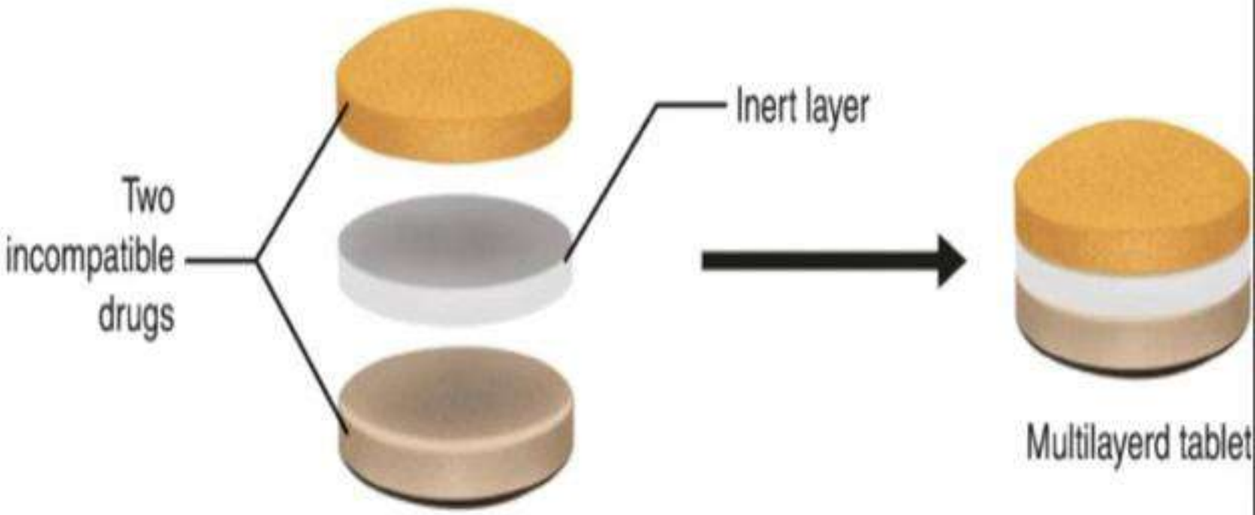

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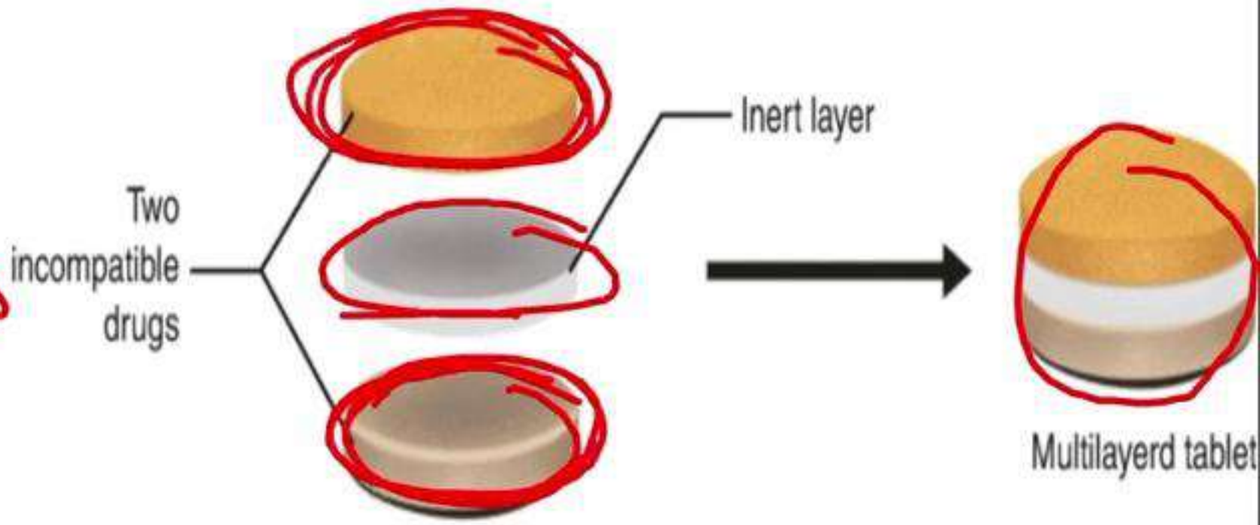

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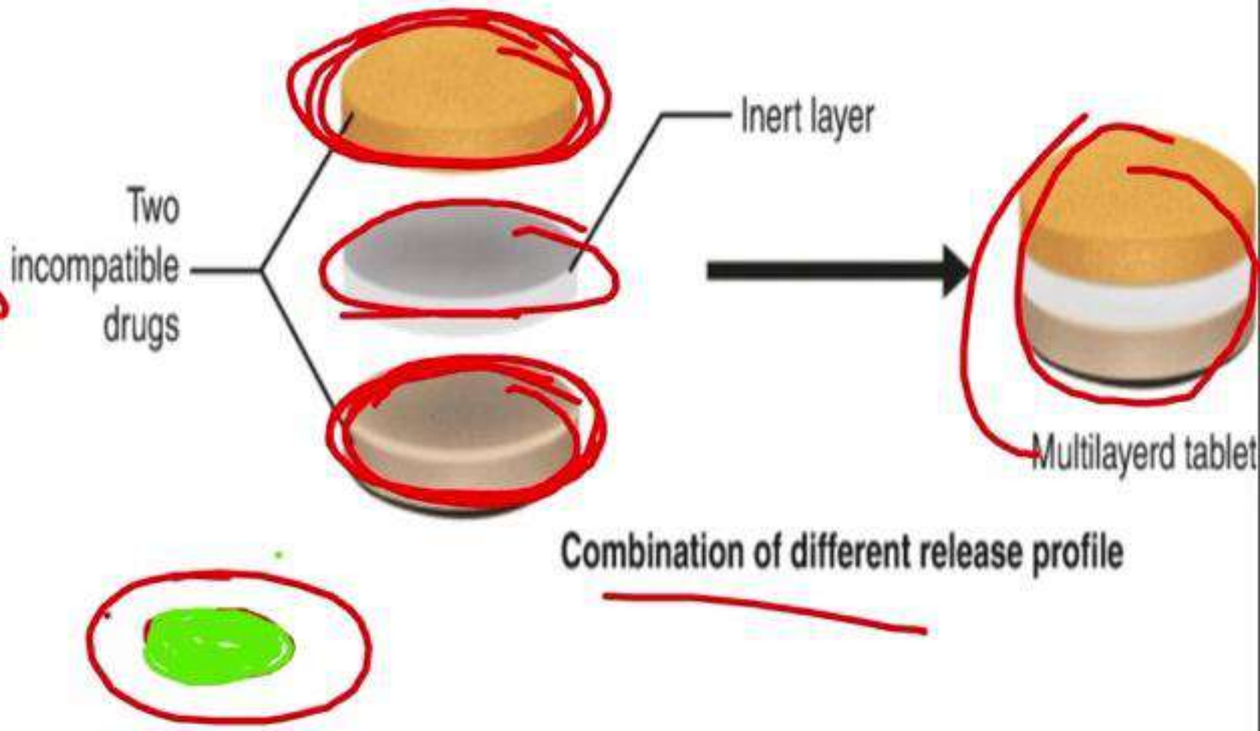

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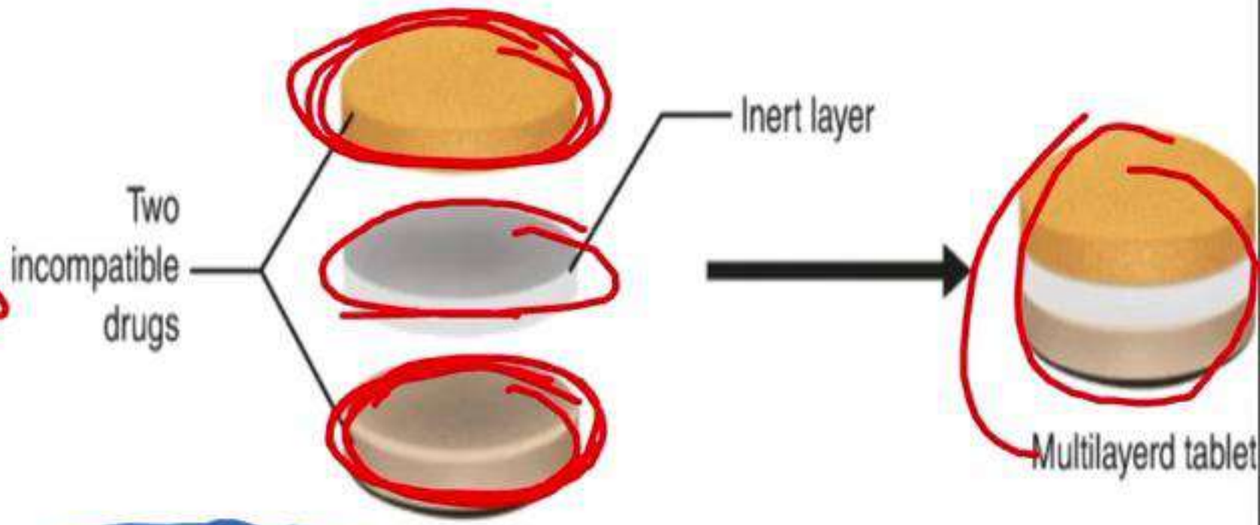

Tablets Ingested Orally

Film-Coated Tablets

- Coated with a thin layer of a polymer
- Tasteless, having little increase in the tablet weight

Polymers: Hydroxy propyl cellulose, Hydroxy propyl methyl cellulose and ethyl cellulose.

DT: 30 minutes or less

Sugar Coated Tablets

Tablet + sugar coating

- Mask bitter and unpleasant odor and thetaste of drug.
- ↑ weight upto 30-50%.

DT: 60 minutes or less

Ex. Ibuprofen tablets and primaquine tablets

Chewable Tablets

- Tablets are chewed in the mouth before swallowing
- Mannitol is used as a base, not contains disintegrating agents
- Given to children or elderly who are having difficulty in swallowing

Ex. Antacid(digene) , aluminium hydroxide, vitamin C tablets

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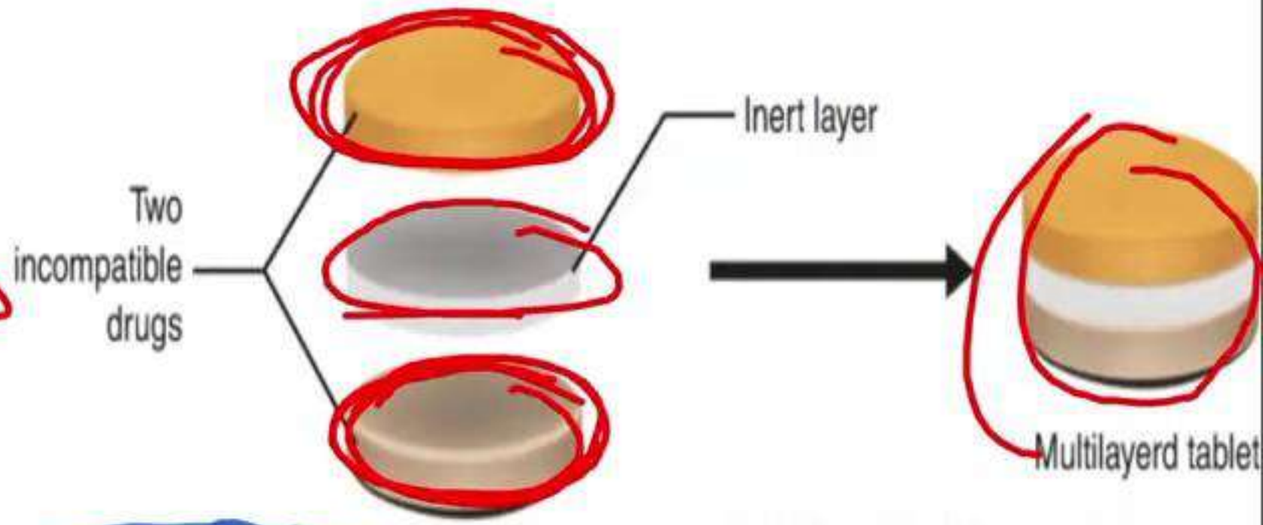


Tablets Ingested Orally

Delayed/ Enteric Coated Tablets

Release drug in SI

Coating agents : CAP, HMP phthalate, PAVP, Eudragit®

DT: 180 min

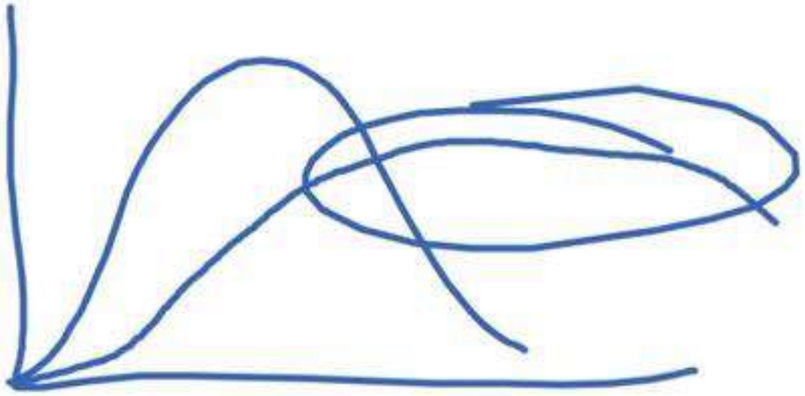
Ex. Enteric coated Bisacodyl, Diclofenac sodium dehyed-release tablet

Controlled Release Tablets

Maintain a drug concentration for extended period of time with minimum side effects

Release the drug at a desired time and provide prolong effect

Ex. Paroxetine Controlled-Release Tablets



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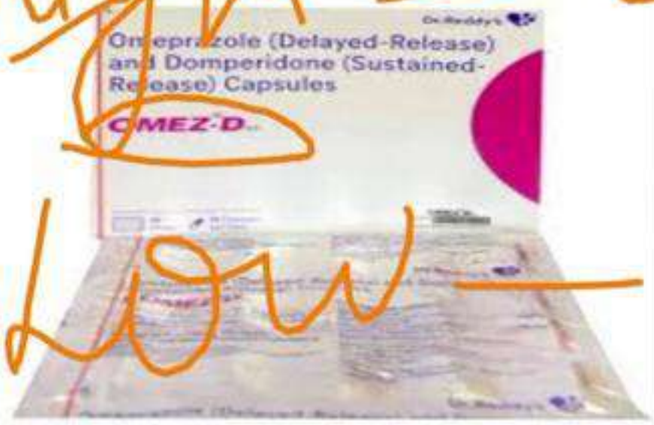
Half life [high / low

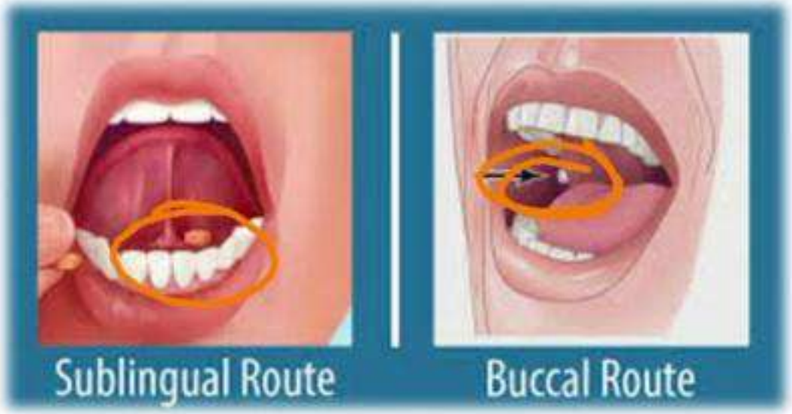


Tablets Used in the Oral Cavity

Buccal Tablet

- Placed between cheek and teeth or cheek/buccal pouch
- Provides sustained action
- Bypass first pass metabolism

e.g. - Progesterone tablet



Sublingual Tablet

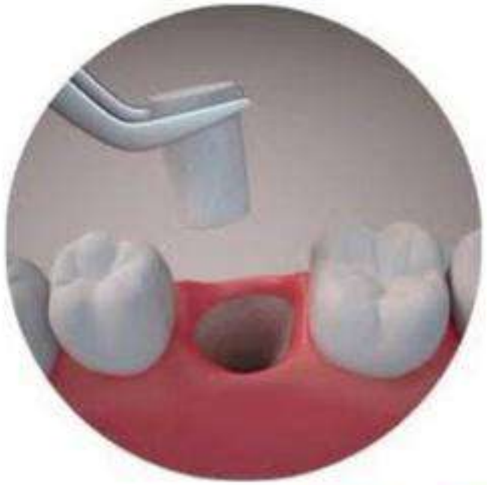
Placed beneath the tongue

e.g. - Nitroglycine

Troches and Lozenge

Produce local effect in the mouth/throat and dissolve slowly in mouth

E.g. - Local anesthetic, Antiseptic, Antibacterial agent



Dental Cones

Placed in empty Socket after tooth extraction.

Vehicle - Sodium bicarbonate, sodium chloride and amino acid

Dissolve in 20-40 minutes

Tablets Administered by Other Routes

Implantation or Depot Tablets

- Inserted subcutaneously using kern injector (Hollow needle and plunger)
- Not more than 8 mm in length
- Must be sterile
- **Time duration** - 1 month to 1 year.

E.g. - Administration of hormones

Vaginal Tablets

- Slow dissolution and drug release vaginal cavity
- Lactose used as diluent

E.g. - Steroids, Antibiotics, antiseptics, asffingents

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Tablets Used to Prepare Solution

Effervescent Tablets

Produce a solution rapidly with release of carbon dioxide

Active ingredient + citric acid / tartaric acid /sodium bicarbonate

Dispensing Tablets (DT)

- Added to a given volume of water t) produce a solution of a given drug concentration
- Preferred for pediatric patients
- Should never be dispensed as a dosage form, toxic orally

E.g. - Silver compounds , Bichloride of Mercury, Merbromin, Quaternary ammonium compounds

Hypodermic Tablets (H T)

One or more drugs with other readily water-soluble and are intended to be added to sterile water or WFI

Administered by parenteral route

Tablet in vial + Sterile water --------injectable solution

Tablet triturates (TT)

- Containing a potent substance mixed with lactose, sucrose and dextrose.
- Disintegrate very quickly in contact with moisture /water
- Small, usually cylindric, molded, or compressed

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Tablet Ingredients

API/DRUG + **ADDITIVES/ EXCIPIENT** = **TABLETS**

Group 1

Impart satisfactory processing and compression characteristics

1. Diluent
2. Granulating Agents
3. Binders and Adhasives
4. Disintegrating Agents
5. Lubricant Antiadherant and Glidant

Group 2

Gives additional physical property

1. Colouring Agent
2. Flavours
3. Sweetening Agents

Group 3

Used solubility retarding materials

1. Polymers
2. Waxes

Diluents

- Diluents are fillers used to make required bulk of the tablet when the drug itself inadequate to produce the bulk.
- It provides better tablet properties such as improve cohesion, permit use of direct compression manufacturing or promote flow.
- Dose of some drug is high, no filler required e.g. - Aspirin, antibiotics

DILUENTS

SUGAR
- Dextrose
- Lactose
- Sucrose
- Mannitol
- Sorbitol
- Amylose
- Inositol

POLYSACCHARIDES
- Starch
- Cellulose and its derivatives
- Modified starch

INORGANIC COMPOUNDS
- Ca. carbonate
- Ca. phosphate
- Ca. sulphate
- Mg. carbonate
- Mg. oxide

Miscellaneous
- Kaolin
- Bentonite
- Silicon derivatives
- Polyvinyl pyrrolidone

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Diluents

Lactose

Most commonly used, But causes Maillard reaction [Reducing sugars(glucose, maltose and lactose) with amine containing drugs]

Good compressibility

Two grades:

(i) 60 to 80 mesh - **coarse grade**

(ii) 80 to 100 mesh **regular grade**

Types

- **α- lactose monohydrate:**
  Containing 5% moisture, poor flow and used in wet granulation & Show Maillard reaction
- **β- lactose anhydrous (DCL-30):**
  Not show maillard reaction, moisture content 0.55%
- **Spray-dried lactose (Zeparox)**:
  Mixture of crystalline α_x0002_monohydrate (80-90%) and amorphous lactose
  Show Maillard reaction

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Diluents

Starch

Directly compressible starch: starex-1500

Emdex, cellutab: hydrolysed starch, 90-92% dextrose and 3-5% maltose

Sucrose

- Also serves as binder or as a bulking agent and sweetener in chewable tablets
- Used in direct compression, Hygroscopic
- Sucrose is called an invert sugar

Sugartab: 90-93% sucrose and 7-10% invert sugar

Dipac: 97% sucrose and 3% modified dextrin

Nutab: 95% sucrose, 4% invert sugar, magnesium stearate and corn starch.

Mannitol

- Provides Cooling sensation due to negative heat of solution
- Used in vitamin and Chewable tablets
- Nonhygroscopic

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Sorbitol

- Optical isomer of Mannitol.
- Sorbitol is hygroscopic at humidities above 65%.
- Low caloric and non-carcinogenic

Dextrose

- Trade Name- Cerelose 2001 & 2401
- Two forms - Hydrous and Anhydrous form
- Directly compressible_x0002_

Cellulose

Microcrystalline Cellulose : a diluent, a disintegrant, a glidant , a lubricant and a pore/channel former

Directly compressible,

Grade: Avicel PH 101(powder) and Avicel PH 102(granules)

Calcium Salts

Not used with tetracycline due to complex formation.

Example: Calcium phosphate, calcium carbonate.

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TABLETS

LECTURE-3 (INSTRUMENTATION, TABLET DEFECTS & EVALUATION TESTS)

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LECTURE-3 (INSTRUMENTATION, TABLET DEFECTS & EVALUATION TESTS)

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GPAT/NIPER 2025 CRASH COURSE

SUBJECT - PHARMACEUTICS

TOPIC – PHARMACEUTICAL TECHNOLOGY

TABLETS

LECTURE-3 (INSTRUMENTATION, TABLET DEFECTS & EVALUATION TESTS)

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Components of the Tablet Punching machine

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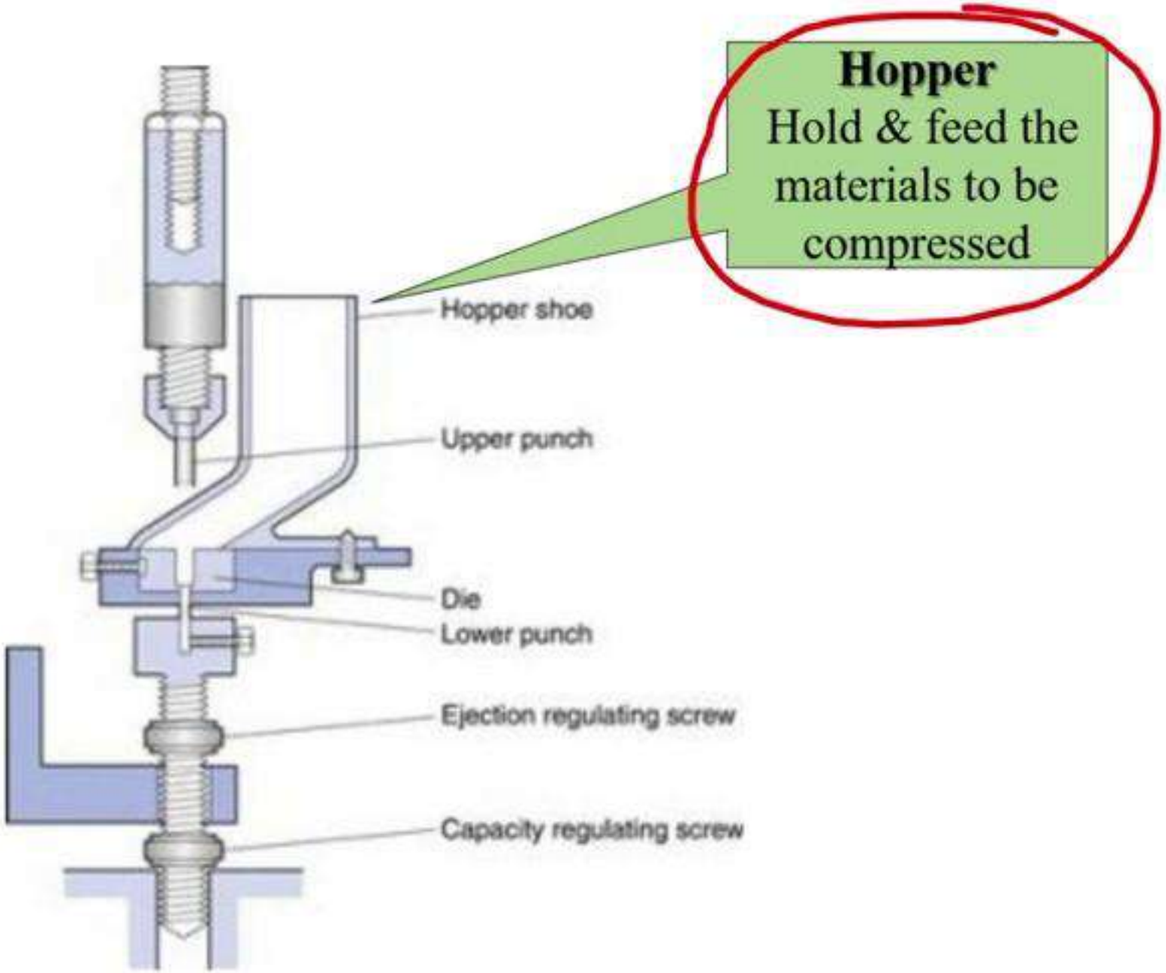
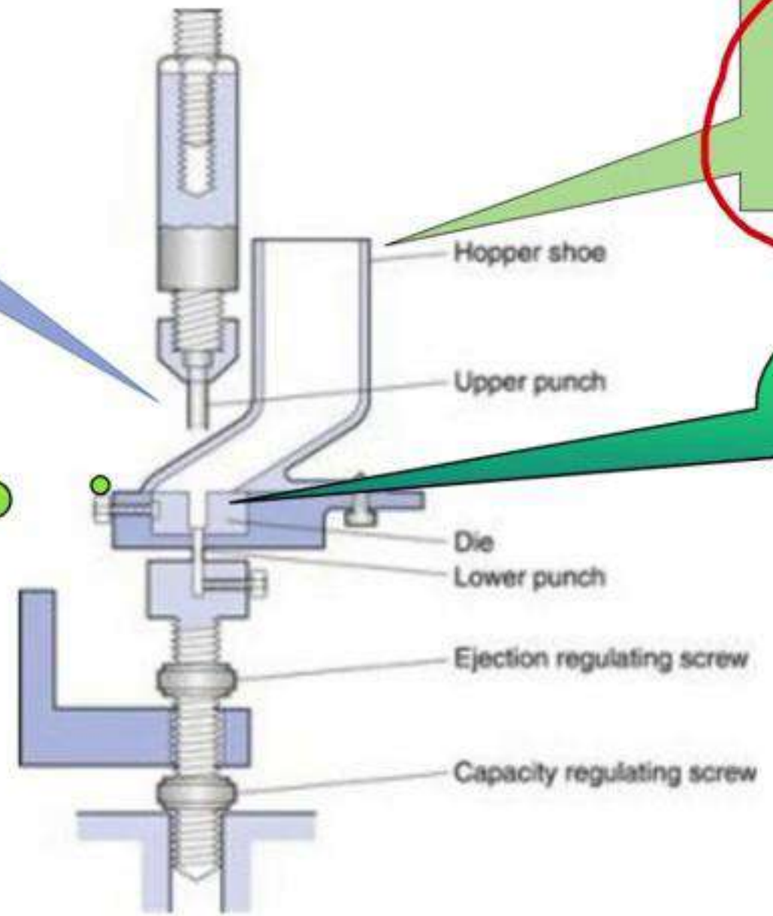


Components of the Tablet Punching machine

Punches
Compress the materials within the dies

Hopper
Hold & feed the materials to be compressed

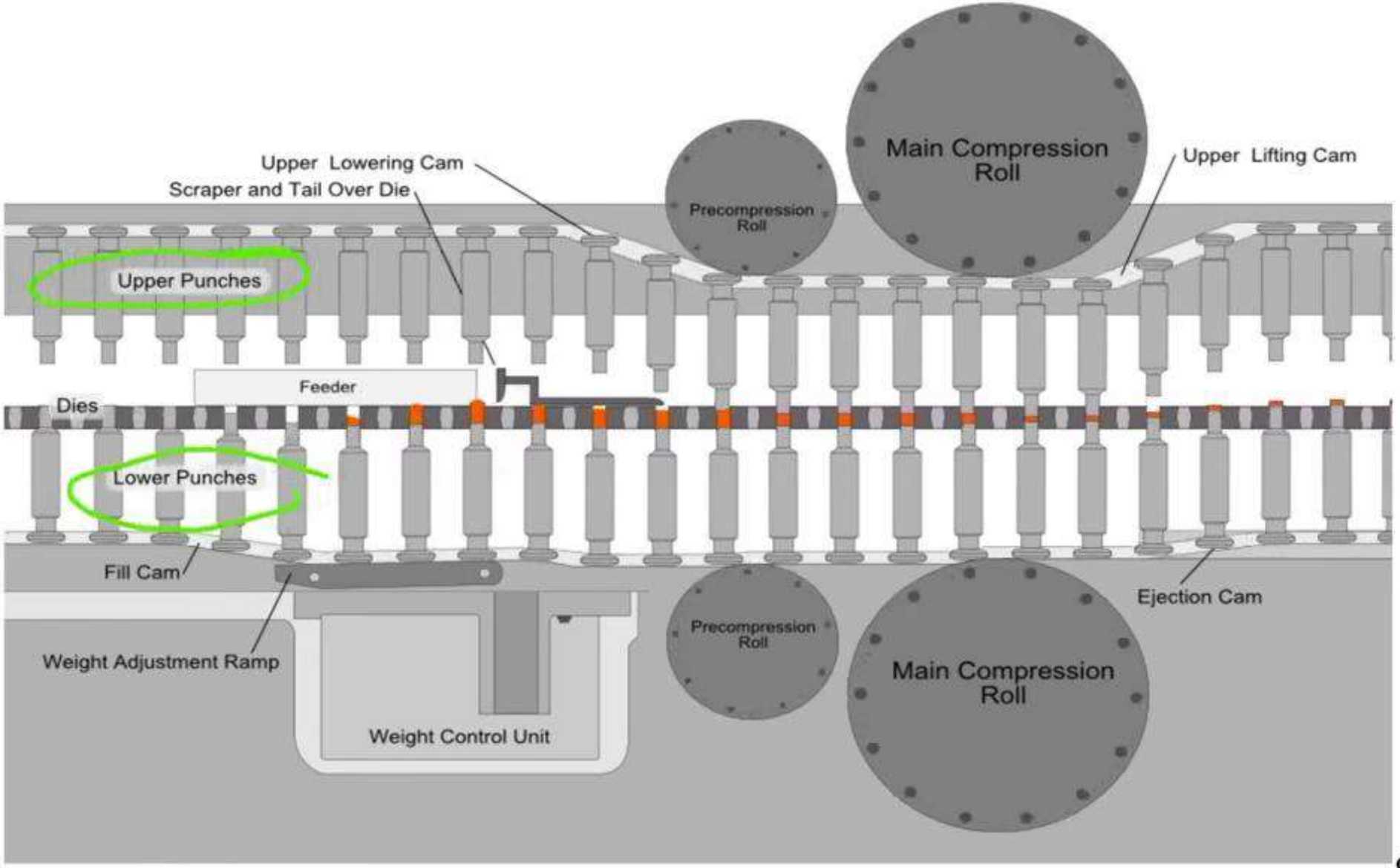


Dies
Defines the shape and size of the tablet.

Die Table
Portion holding the dies

Cam Track
Guides the movement of the punches

Components of the Tablet Punching machine



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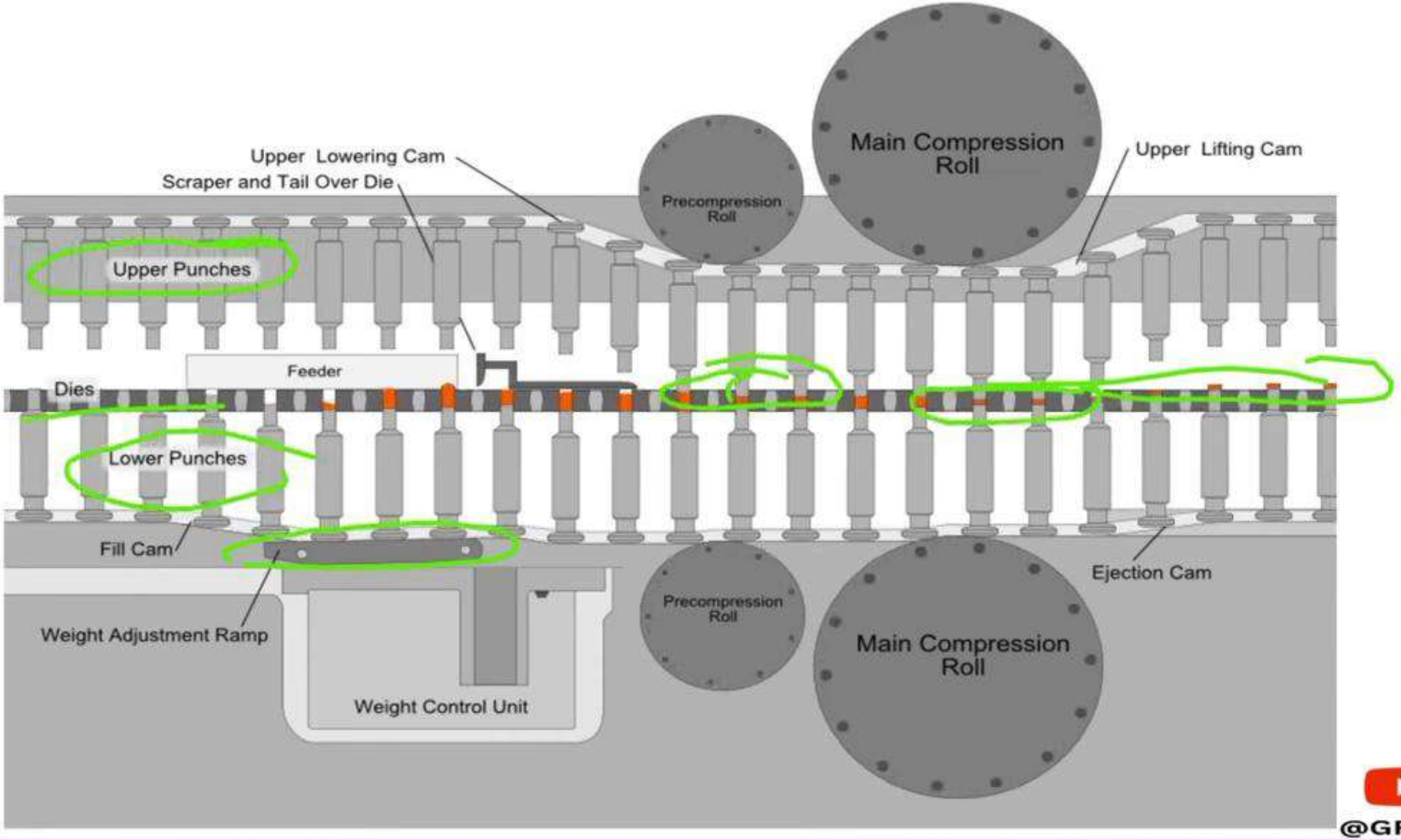

Tablet Defects

Capping

Tablet Defects

Capping
Partial or complete separation of the top or bottom crowns

Causes
Air entrapment
Deep Concave punches

Tablet Defects

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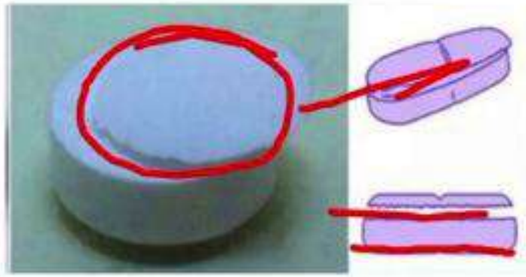
Partial or complete separation of the top or bottom crowns

Causes
Air entrapment
Deep Concave punches
Dry Granulation

Remedies
Pre-compression
Flat Punches
Add certain % of moisture by Sorbitol , PEG



Lamination
Separation of tablet into two or more distinct layers

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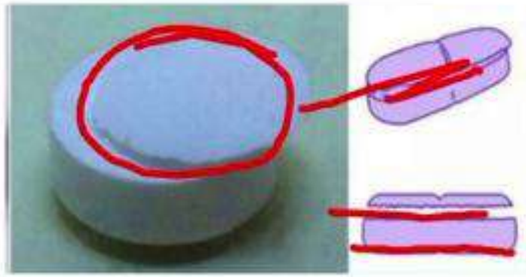

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Deep Concave punches
Dry Granulation

Remedies
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Add certain % of moisture by Sorbitol , PEG

Weight Variation
Tablet forms with different weight

Causes
Poor flow

Tablet Defects

Picking
Tablet material adhere to punch face

Tablet Defects

Picking
Tablet material adhere to punch face

Causes
Excessive moisture in granules
Too little or improper lubrication

Remedies
Proper drying of granules

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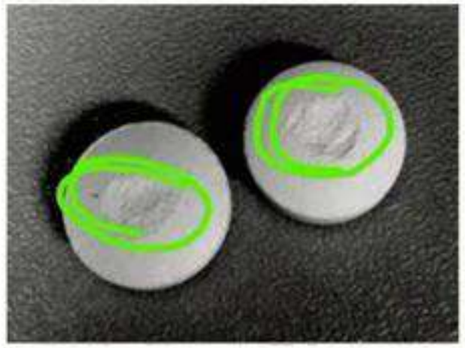
Proper drying of granules
Coating of punch face by Chromium



Sticking
Tablet material adhering to the die walls

Tablet Defects

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Tablet material adhere to punch face

Causes
Excessive moisture in granules
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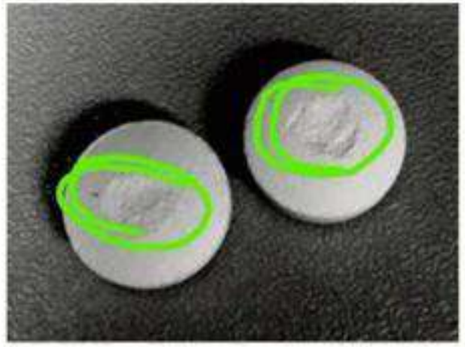

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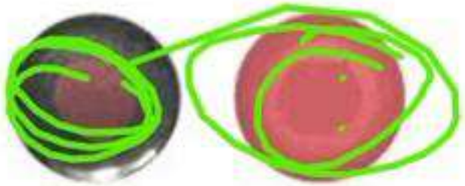

Double Impression

Tablet Defects

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Remedies
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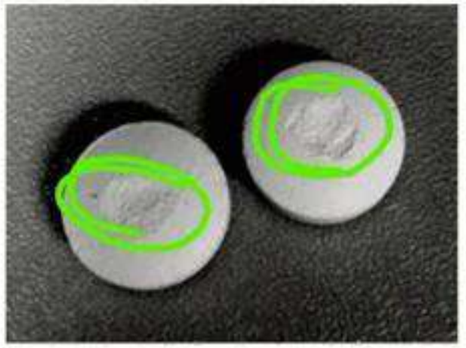


Sticking
Tablet material adhering to the die walls

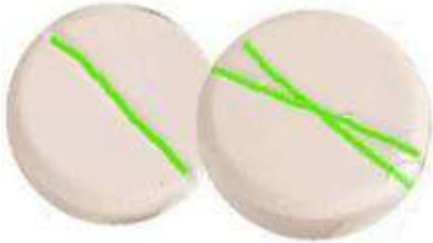
Causes
Excessive moisture in granules
Too little or improper lubrication

Remedies
Proper drying of granules

Double Impression
Punches, have monogram or other engraving

Causes
Due to uncontrolled movement of punch

Remedies
Use anti-turning device



Chipping

Mottling —

Evaluation of Tablets

NON-OFFICIAL TESTS

General Appearance
- Size & shape
- Organoleptic

Hardness

OFFICIAL TESTS

Weight variation test
Content uniformity test
Friability test
Disintegration test
Dissolution test

NON-OFFICIAL TESTS

Shape and Size

- Crown thickness of the tablet is measured in micrometer by Vernier Callipers
- Thickness should be within ±5% of standard value

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Colour of tablet can be evaluated by :

- Reflectance spectrophotometry
- Micro-reflectance phtometer

Hardness/Crushing Strength

Force required to break the tablet

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Instruments :

- Monsanto or stokes hardness taster
- Strong-cobb Tester
- Pfizer Tester
- Erweka Tester

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Tablets and Hardness Limit

Soft	2 kg
Sustained release	8 kg
General	4 kg
Hard	6 kg
Effervescent	1.3 kg

OFFICIAL TESTS

Friability

Instrument: Roche friabilator

RPM: 25

OFFICIAL TESTS

Friability

Instrument: Roche friabilator
RPM: 25
Time: 4 minutes
Total Revolution : 100
Tablet fall: From 6 inches or 15 cm
Limit: 0.5-1% (USP) and NMT 1% (IP).

$$\text{Friability (\%)} = \frac{\text{Initial Weight (W1)} - \text{Final Weight (W2)}}{\text{Initial Weight (W1)}} \times 100$$

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- Select 20 tablets and weighing
- Calculate Average weight
- NMT 2 of the individual weights deviate from average weight

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Weight Variation Test

- Select 20 tablets and weighing
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IP	USP	% Deviation (±)
80 mg or less	130 mg or less	10%
More than 80 mg but less than 250 mg	More than 130 mg but less than 324 mg	7.5%
250 mg or more	324 mg or more	5%

OFFICIAL TESTS

Content Uniformity Test
Total Tablets - 30
First Assay - 10

Test Will Pass if :	
9 Tablets	Contain 85-115% content
10 Tablets	Contain 75-125% content
If not then remaining 20 Tablets	No one should fall outside 85%-115%

OFFICIAL TESTS

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Disintegration Test

±15%

±25%

OFFICIAL TESTS

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Disintegration Test

Tablets : 6
Glass Tube : 6 (3 inches)
Mesh size : USP- 10 mesh (1.7mm)
IP- 8 mesh (2mm)
Temperature : 37±2 ^{0}C
Speed : 28-32 RPM
Up and Down Distance : 5-6 cm
Media: 900 ml Simulated Gastric Fluid (0.1 N HCl)

OFFICIAL TESTS

Type of Tablet	Disintegration Media	Disintegration Time (Min)	
		IP	USP
Dispersible tablet	Water	Less than 3 min	Less than 3 min
Effervescent tablet	Water	Less than 5 min	Less than 5 min
Uncoated tablet	Water	Less than 15 min	Less than 30 min
Film coated tablet	Water or 0.1 N HCl	Less than 30 min	Less than 30 min
Sugar coated tablet	Water	Less than 1 hr	Less than 1 hr
Enteric coated tablet	0.1 M HCl	120 min or less	60 min or less
	Phosphate Buffer	60 min or less	120 min or less

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.....THANKS FOR WATCHING.....

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TABLETS

LECTURE-4 (TABLET COATING & COATING DEFECTS)

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LECTURE-4 (TABLET COATING & COATING DEFECTS)

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Dissolution test

Dissolution Medium- 900ml

Dissolution test

Dissolution Medium- 900ml
Tablets- 6
Time - Conventional Tablets: 1hr
Sustained Release: 8 hr
Sampling Interval -
Conventional Tablets: 10 min
Sustained Release: 1 hr
Temperature - 37±0.5^{0}C

Type	Description	Dosage form
Type I	Rotating Basket	Conventional Tablets, Modified release tablets, Capsules
Type II	Paddle	Orally disintegrating tablets, Chewable tablets, Modified release
Type III	Reciprocating cylinder	Modified release, Chewable tablets
Type IV	Flow through cell apparatus	Modified released, microparticles, granules
Type V	Paddle over disk	Transdermal patches
Type VI	Cylinder	Trandermal Patches
Type VII	Reciprocating disc	Non-disintegrating oral modified D.F

Dissolution test

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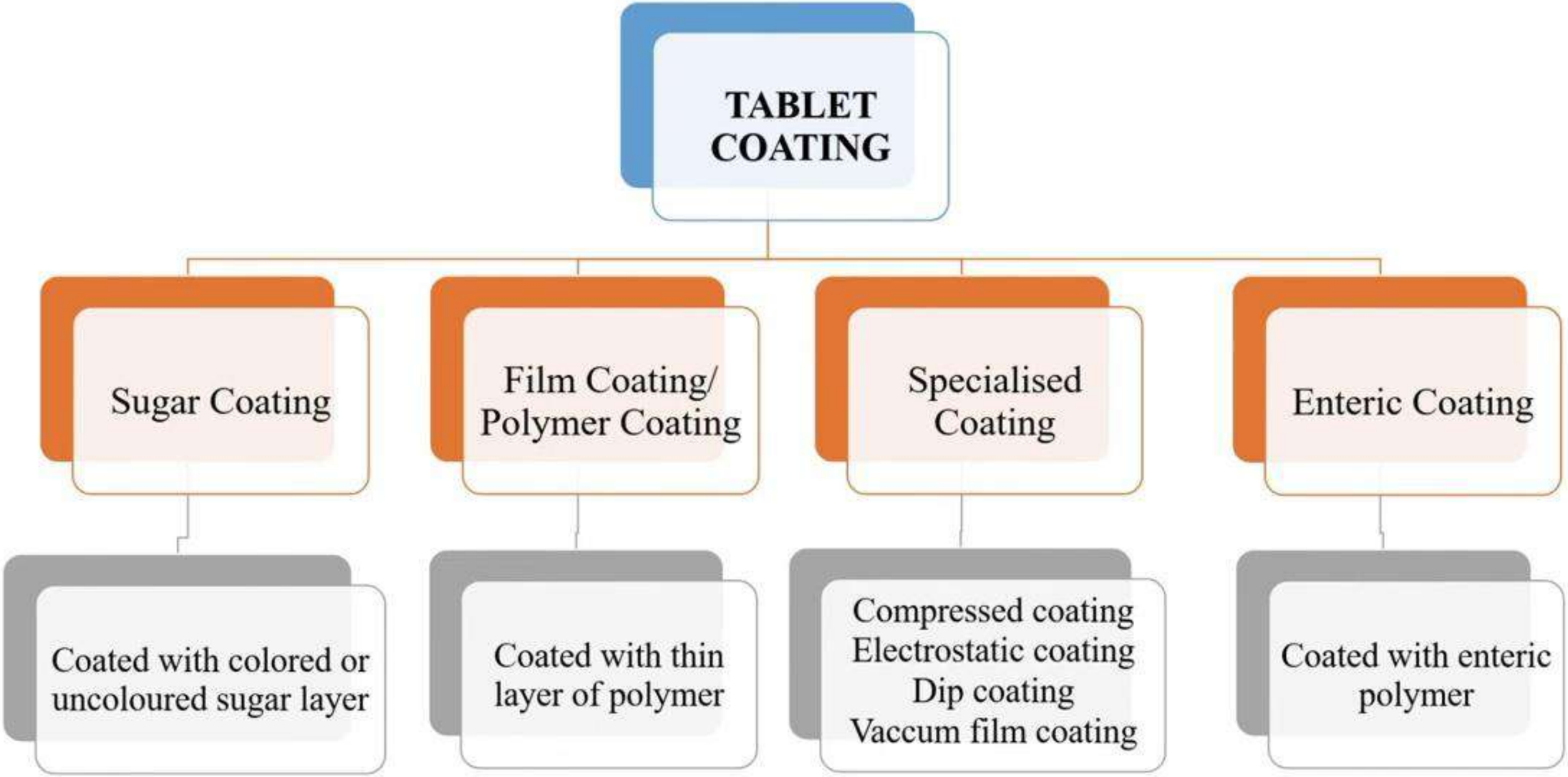
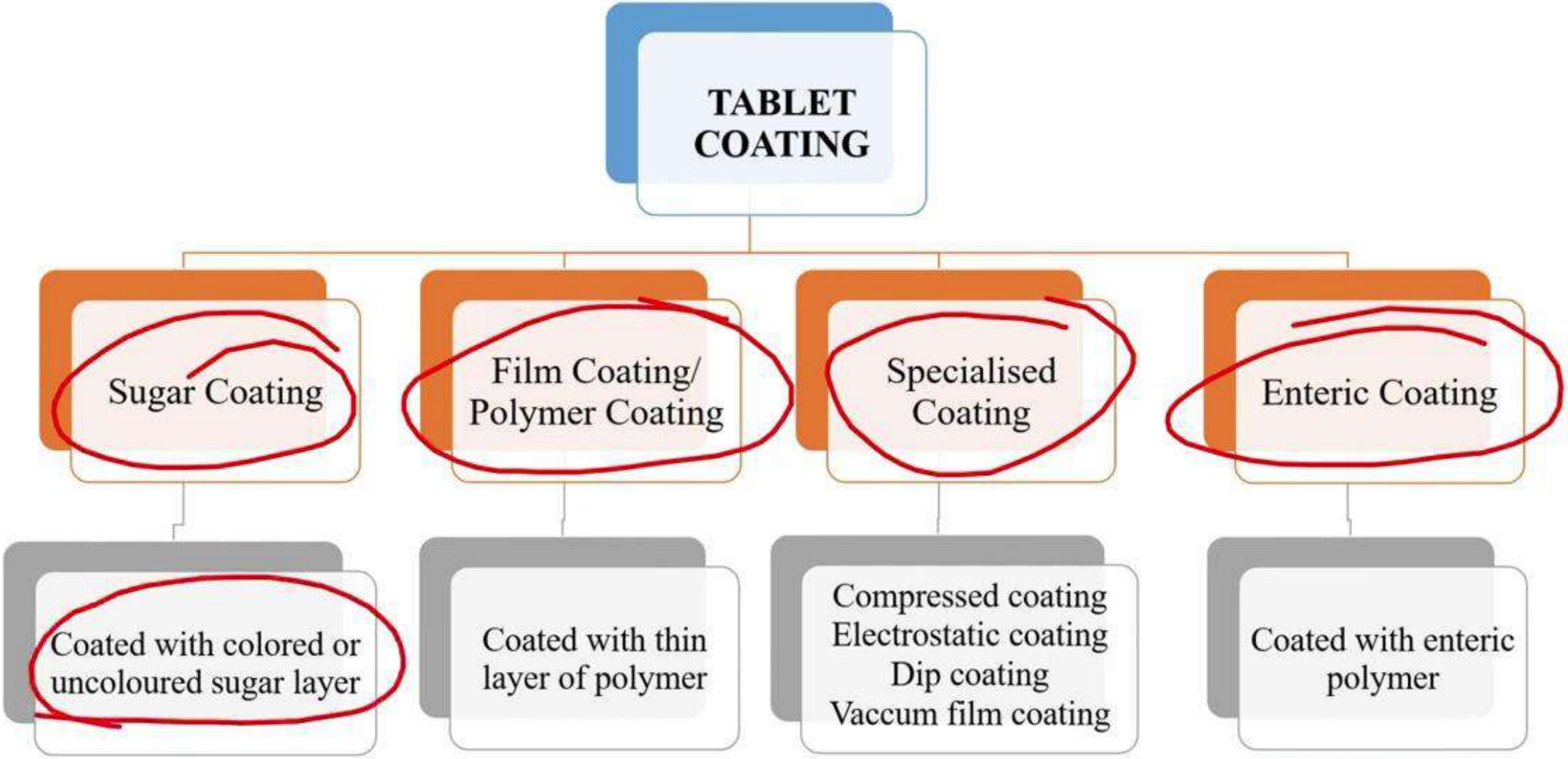
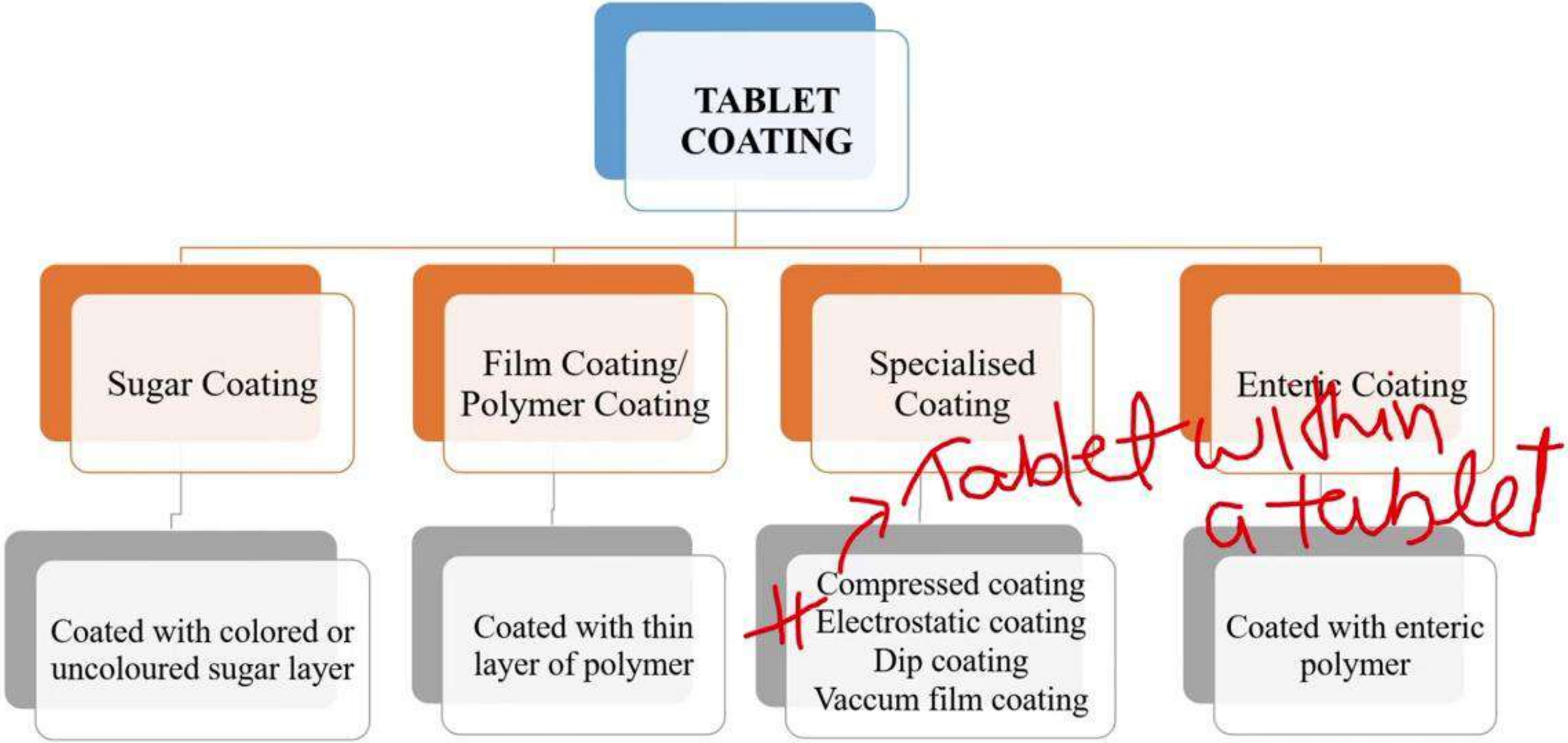
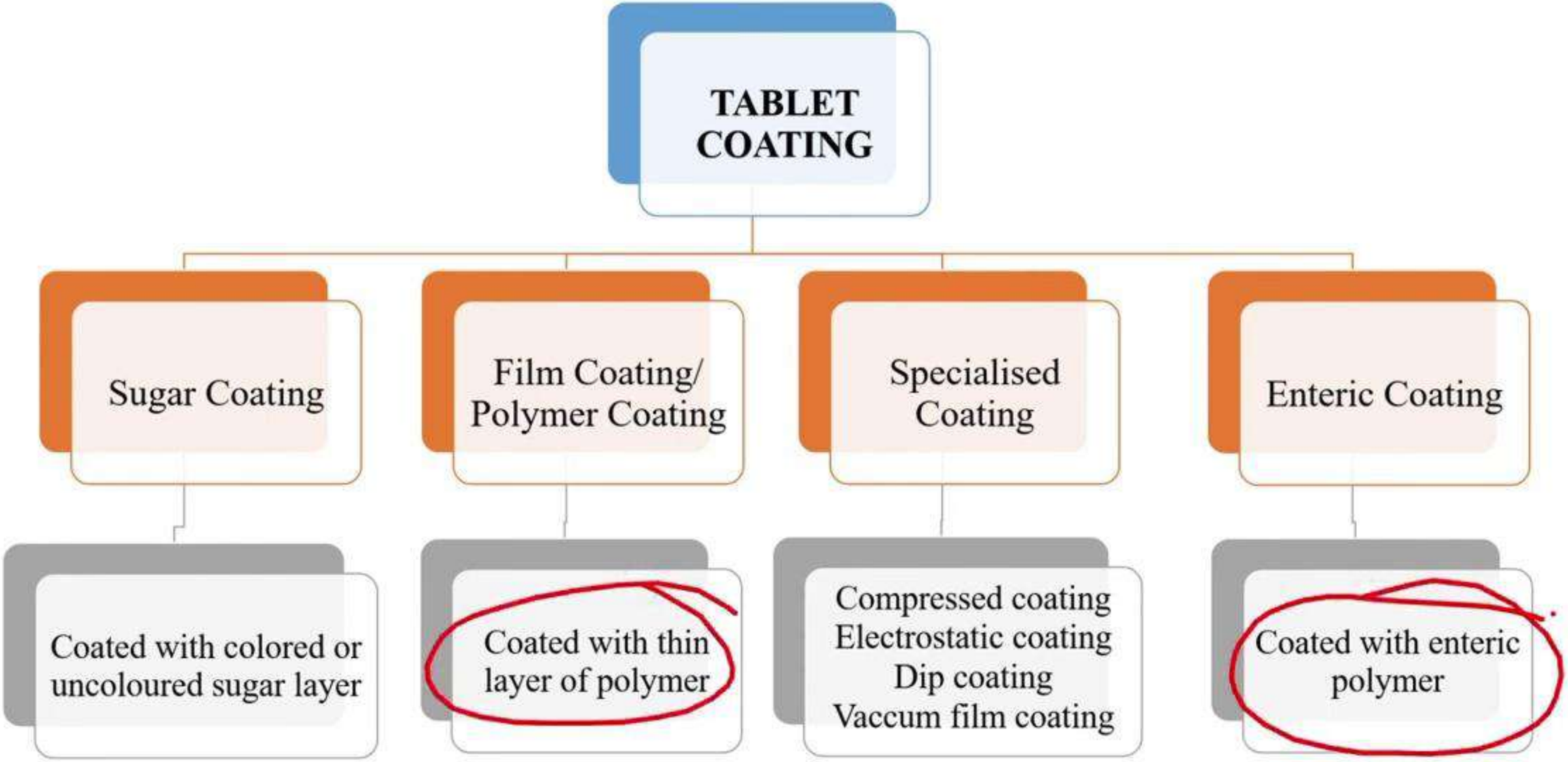
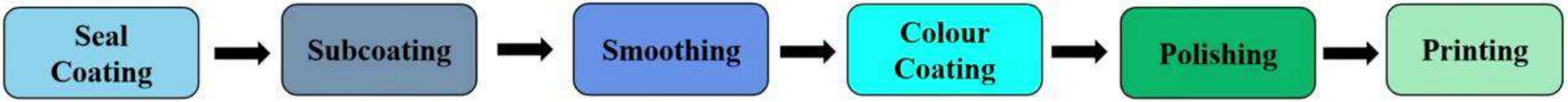





TABLET COATING
Sugar Coating
Film Coating/ Polymer Coating
Specialised Coating
Enteric Coating
Coated with colored or uncoloured sugar layer
Coated with thin layer of polymer
Compressed coating
Electrostatic coating
Dip coating
Vaccum film coating
Coated with enteric polymer
Tablet within a tablet
JOIN WITH US ON
@GROWUPPHARMA



SUGAR COATING



SUGAR COATING

Seal Coating → Subcoating → Smoothing → Colour Coating → Polishing → Printing

SEALING

To prevent the moisture penetration into tablet core

Eg : Shellac, zein, CAP, PVAP

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Seal Coating → Subcoating → Smoothing → Colour Coating → Polishing → Printing

SEALING

To prevent the moisture penetration into tablet core

Eg : Shellac, zein, CAP, PVAP

→ Moisture

↓

Disintegra.

Maize

Alcoholic

SUGAR COATING

Seal Coating → Subcoating → Smoothing → Colour Coating → Polishing → Printing

SEALING

To prevent the moisture penetration into tablet core

Eg : Shellac, zein, CAP, PVAP

SUB COATING

SUGAR COATING

Seal Coating → Subcoating → Smoothing → Colour Coating → Polishing → Printing

SEALING

To prevent the moisture penetration into tablet core

Eg : Shellac, zein, CAP, PVAP

SUB COATING

- Round the edges and build up the tablet size
- Increase weight by 50-100%
- Binding solution - Gelatin, sugarcane, PEG, Acacia
- Dusting Powder - $CaCO_3$, Talc, TiO_2

SUGAR COATING

COLOR COATING
To impart elegancy and uniform colour

SUGAR COATING

COLOR COATING
To impart elegancy and uniform colour

POLISHING
Provide desired luster on the surface of tablet
Eg: Beeswax, Paraffin, Carnuba Wax

PRINTING

TABLET COATING

TABLET COATING

FILM COATING

Adds 2-5% to the tablet weight
Produce smooth, thin films
Methods :

- Pan Pour Method
- Pan Spray Method
- Fluidized bed press (Air Suspension Coating)

COATING MATERIAL

Hydroxypropyl Methylcellulose (HPMC)
Methyl Hydroxyethyl cellulose
Ethyl cellulose (EC)
PVP
PEG
Acrylated Polymers (Eudragit)

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PEG
Acrylated Polymers (Eudragit)

ENTERIC COATING

To provide acid resistance
Release drug into intestine

COATING MATERIAL

Hydroxypropyl Methylcellulose Phthalate (HPMCP)

TABLET COATING DEFECTS

TABLET COATING DEFECTS

PICKING & STICKING
Tablets stick to each other or to coating pan

Causes
Overwetting
Excessive film thickness
Inefficient drying
Higher amount of coating solution

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Remedies
Reduce liquid application rate
Increase in drying rate and temperture

Roughness
Rough surface , when coating is done by spray

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Sticking or Picking

Roughness
Rough surface , when coating is done by spray

Causes
Some droplets of spray dry before reaching to tablet surface causing roughness

Remedies
Keep nozzle closer to the tablet bed
Decrease in degree of atomization

ORANGE PEEL EFFECT

Rough and non-glossy appearance of tablet similar to that of orange

Causes

Improper spreading of coating material before drying

ORANGE PEEL EFFECT

Rough and non-glossy appearance of tablet similar to that of orange

Causes

Improper spreading of coating material before drying

Too rapid drying

High solution viscosity

Remedies

Use mild drying condition

Decrease solution viscosity

BRIDGING

During drying film may shrink and pull away from the sharp corners as bisect

Causes

sity of coating solution

h % of solid content

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During drying film may shrink and pull away from the sharp corners as bisect

Causes
High viscosity of coating solution and high % of solid content
Improper pressure of atomizer

Remedies
Increase plasticizer content
Reduce the viscosity of solution

FILLING
Monograph or bisect of tablet is filled with coating solution

Causes
Applying too much solution resulting in thick film formation

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Causes

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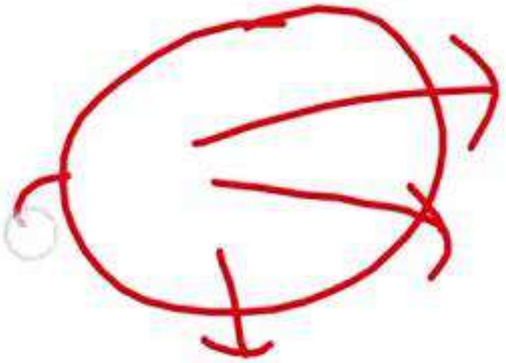
Remedies

Control fluid application rate

BLISTERING
Local detachment of film from the surface forming blister

Causes
Too rapid evaporation of solvent from the core
High temperature
Overheating during spraing



BLISTERING
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High temperature
Overheating during spraing

Remedies
Use mild drying condition

HAZING/BLOOMING/DULL FILM
Coating become dull immediately or after proonged storage at high temperature

Causes
Too high processing temperature
High concentration and low molecular weight of plasticizer

Remedies
Decrease plasticizer content & increase the molecular weight

BLISTERING
Local detachment of film from the surface forming blister

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Too rapid evaporation of solvent from the core
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Overheating during spraing

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Internal stress in the film exceeds tensile strength of the film

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Minimize internal stress in film by adjusting plasticizer

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.....THANKS FOR WATCHING.....

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SUBJECT - PHARMACEUTICS

TOPIC – PHARMACEUTICAL TECHNOLOGY

TABLETS

LECTURE-2 (EXCIPIENTS & METHOD OF PREPARATION)

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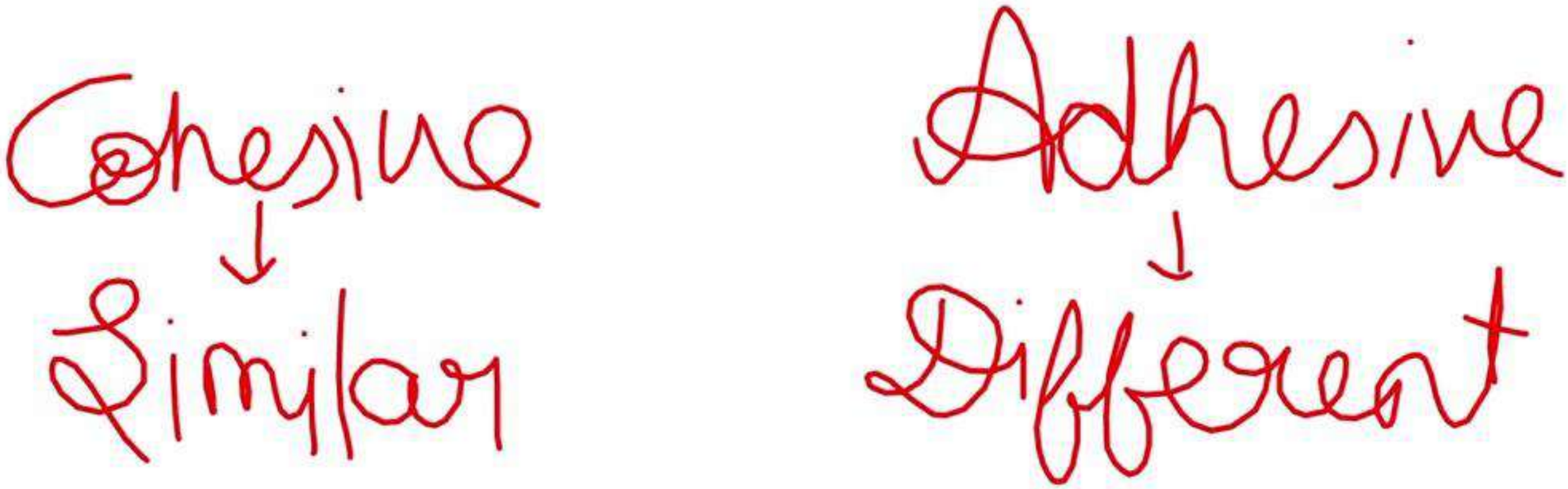
Binder or Tablet Adhesive

Impart cohesiveness to the tablet formulation and helps in holding compressed tablet material after compression.

More the binder, harder the tablet

More effective when they are used in solution form



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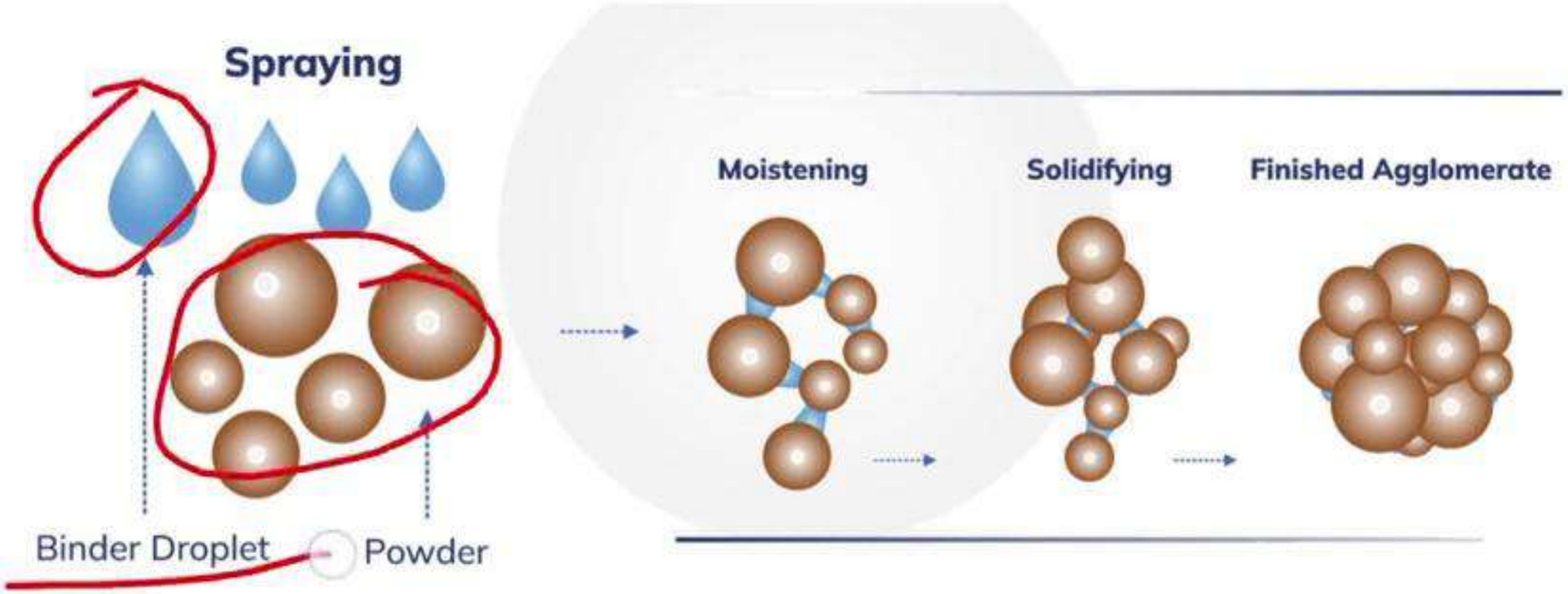

Solution Binder	Dry Binder
Starch	**Cellulose Derivatives** (Ethyl cellulose, Hydroxypropyl cellulose, Hydroxypropylmethyl cellulose)
Sucrose	
Gelatin	**Cross Linked PVP** (Macrogol 4000)
Acacia mucilage	
Tragacanth	

10-25%

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Granulating Agents

Used to convert the fine powders into granules

Provide moisture to convert powders into granules

Liquid glucose, which is a 50% solution in water is a fairly common wet granulating agent

Eg: Starch Mucilage, Water, Alcohol, Acetone etc .

Lubricants

Reduce the friction during tablet ejection between the walls of the tablet and the wall of the die.

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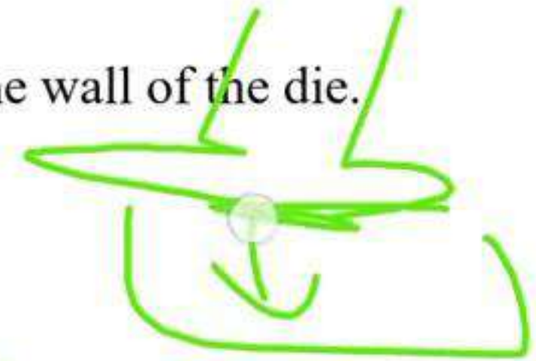
Eg: Stearic acid, Calcium or Magnesium stearate, High melting waxes



Antiadherents

Reducing the sticking or adhesion of tablet to the faces of the punches or to the die wall.

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Eg: Calcium or Magnesium stearate, talc, Corn starch

Glidants

Promote flow of the tablet granulation or powder materials by reducing the friction between the particles

Eg: Corn starch (5-10%), Talc (5%), Magnesium carbonate, Magnesium oxide and Magnesium silicate

Bolting

GoJ

Disintegrant

Facilitates tablet breakup or disintegration when it comes in the contact with GIT fluid.

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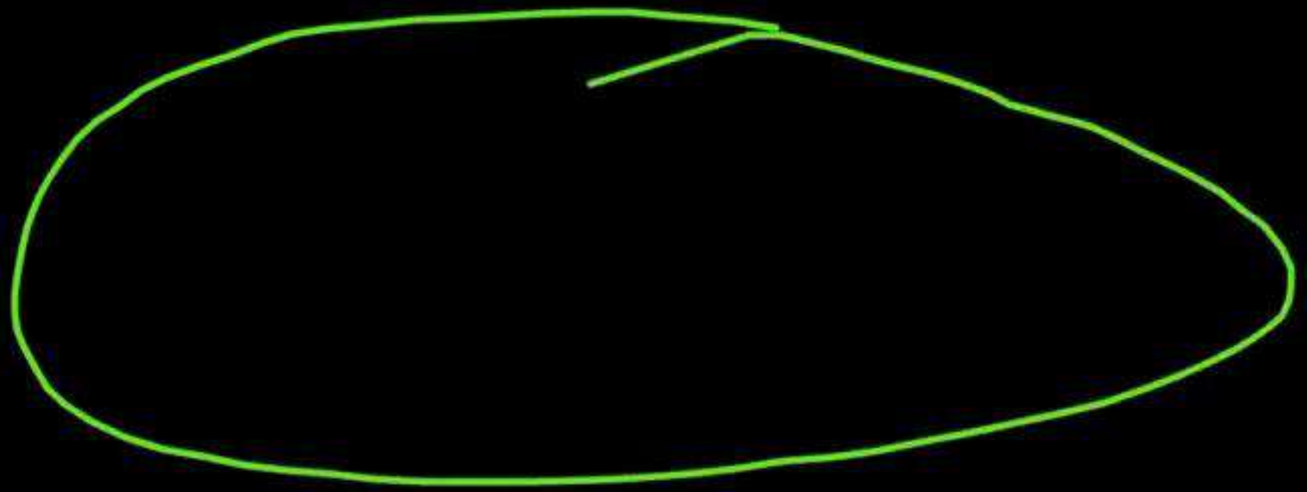
Facilitate water uptake into the pores of tablet

Eg: Starch, MCC, Cationic resins, Sodium starch glycolate.



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Eg: Sodium Bicarbonate, Citric acid, Tartaric acid

Facilitate rupture of tablet by swelling during water sorption

Eg: Acacia, Tragacanth, Alginate

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Recovery of deformed particles to their original shape in contact with water

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Super Disintegrant

Substances or mixture of substances that facilitate the breakup or disintegration of tablet quickly into smaller particles that dissolve more rapidly.

Modified Cellulose

Croscarmellose (2-8%)

Marketed- Ac-di-Sol, Solutab

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Marketed- Ac-di-Sol, Solutab

Modified Starch

Sodium starch glycolate (2-5%)

Marketed- Primojel, Explotab

Cross linked PVP

Crospovidone (0.5-5%%)

Marketed- Kollidon CL, Polyplasdone XL

...ner Disinteg...

...facilitate the breakup or disinteg...

...dified Starch

...arch glycolate (2-5%)

...- Primojel, Explotab

Colouring Agents

Colouring agents are used either to improve the appearance or to identify the finished product uniquely.

These are of two forms - Lakes and Dyes

Lakes

They are dyes that has been absorbed on hydrous oxide ($Al(OH)_3$) and usually employed as dry powder for colouring.

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They contain 10-30% of pure dye & maximum upto 50%

2020

Dyes

These are the colouring agents in solution form

Flavouring Agents

nhance the acceptability of tablets

Sweetening Agents

Sweetening agents (sweeteners) are used to impart sweetness to a preparation.
Mask and change the taste

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Mask and change the taste

Saccharin

250 – 500 times more-sweet than sugar but may leave bitter after taste and may be carcinogenic.

Aspartame

200 time more-sweet than sucrose but have no bitter after taste

Nutra Sweet

Neotame

Structurally related to aspartame and 7000–13000 times sweeter than sucrose , non-caloric

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Mask and change the taste

Saccharin
250 – 500 times more-sweet than sugar but may leave bitter after taste and may be carcinogenic.

Alitame
Approximately 2000 times sweeter than sucrose

Aspartame
200 time more-sweet than sucrose but have no bitter after taste

Neotame
Structurally related to aspartame and 7000–13000 times sweeter than sucrose, non-caloric

Cyclamates
30 times as sweet as sucrose.
banned because of carcinogenic properties

Marketed Co-Processed Excipients

TRADE NAME	CO-PROCESSED EXCIPIENTS
Avicel CE-15	MCC and guar gum
Cal Carb	Calcium carbonate 95% and maltodextrins 5%
Calcium 90	Calcium Carbonate 90-91% and starch 9-10%
Cellactose 80	α-Lactose monohydrate (75%) and cellulose powder (25%)
Emdex	Dextrose 93-99% and maltose 1-7%
Formaxx $CaCO_3$70	Calcium carbonate (70%) and sorbitol (30%)
Ludipress	Lactose monohydrate (93%), Kollidon 30 (3.5%), and Kollidon CL (3.5%)
Microcellac	75% lactose and 25% MCC
StarLac	α-Lactose monohydrate (85%) and maize starch (15%)
Vitacel VE-650	MCC (65%) and calcium carbonate (35%)

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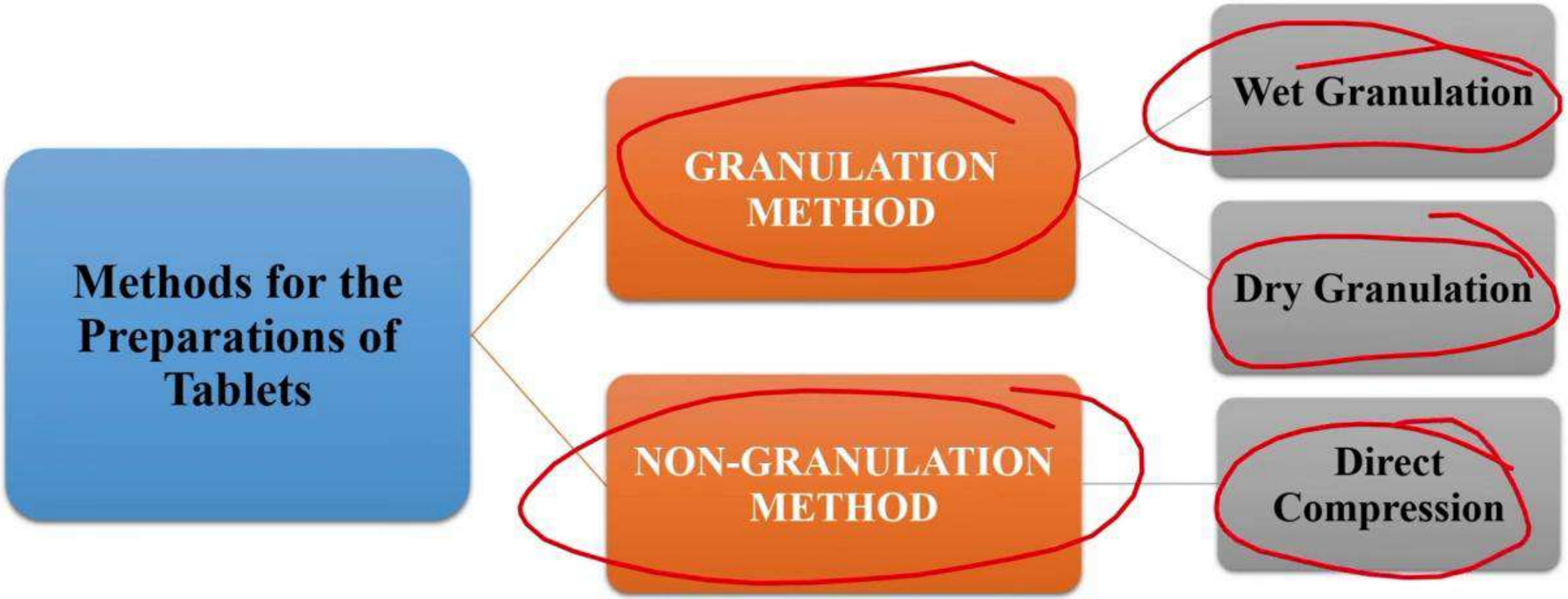
Methods of Tablet Preparation



Manufacturing of Tablet

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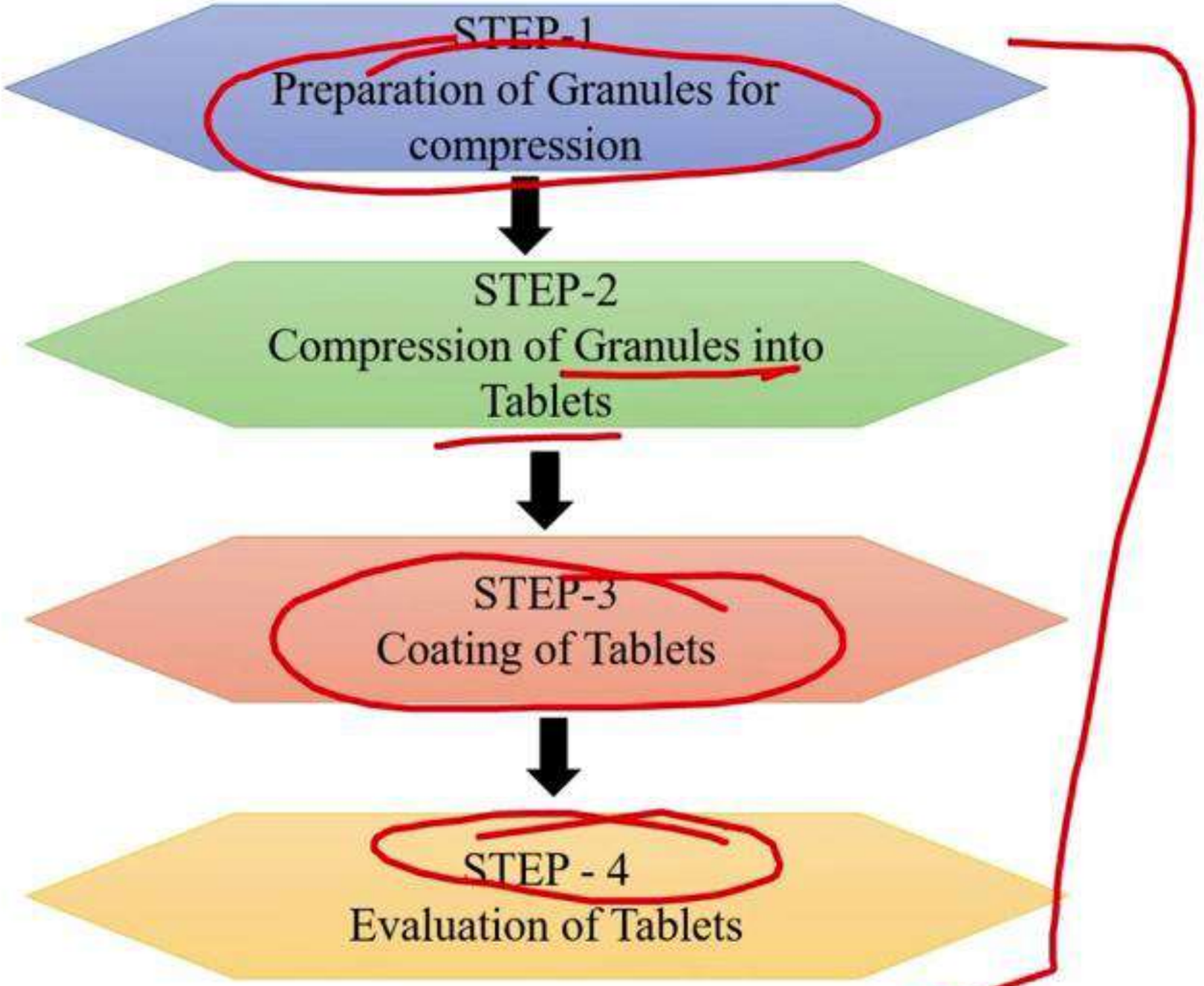
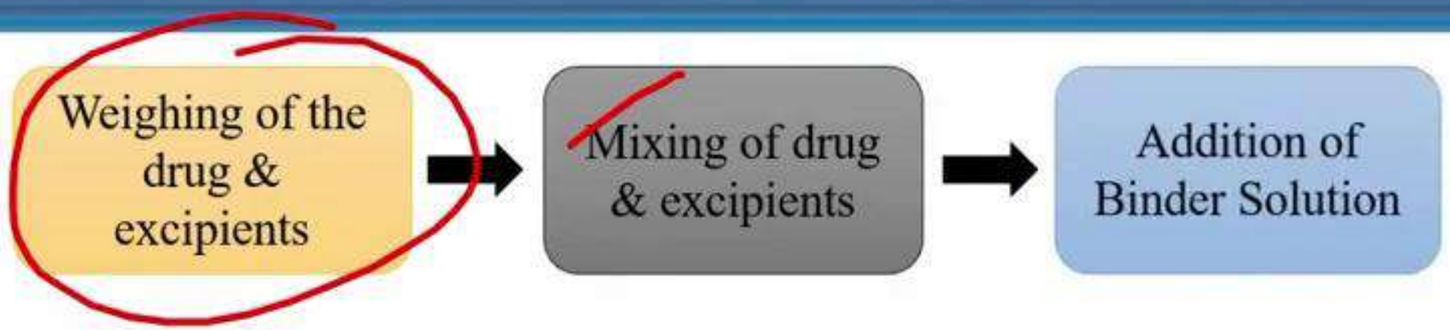


Wet Granulation



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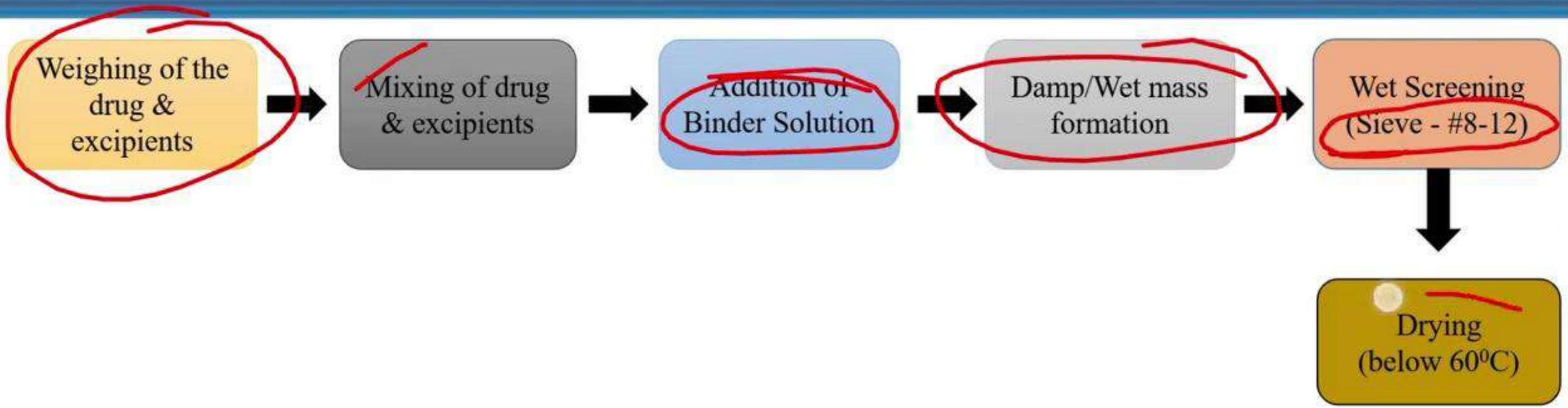

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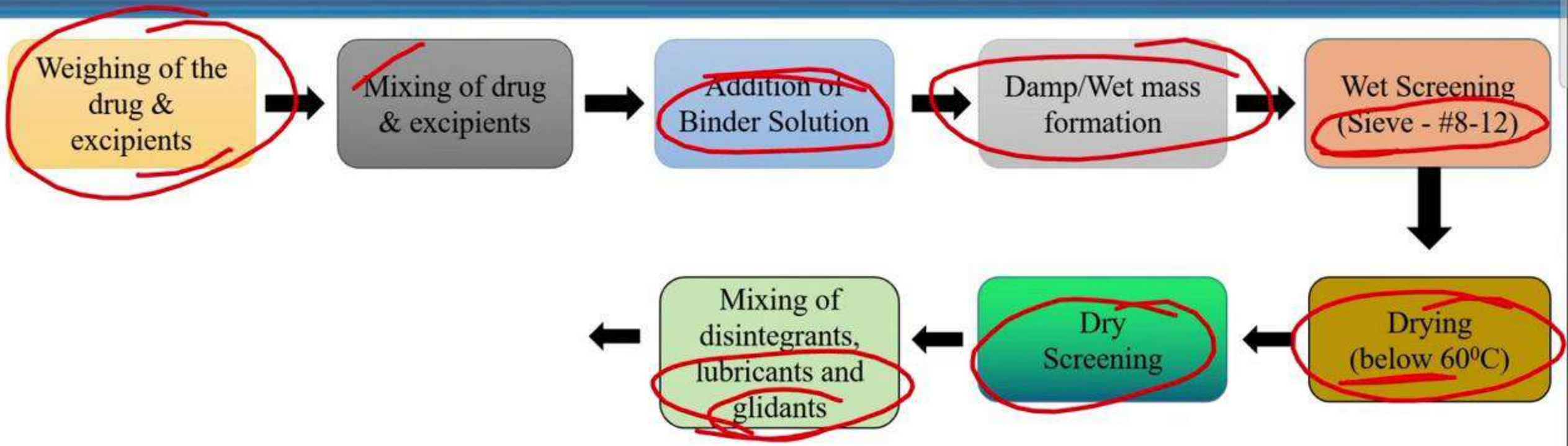

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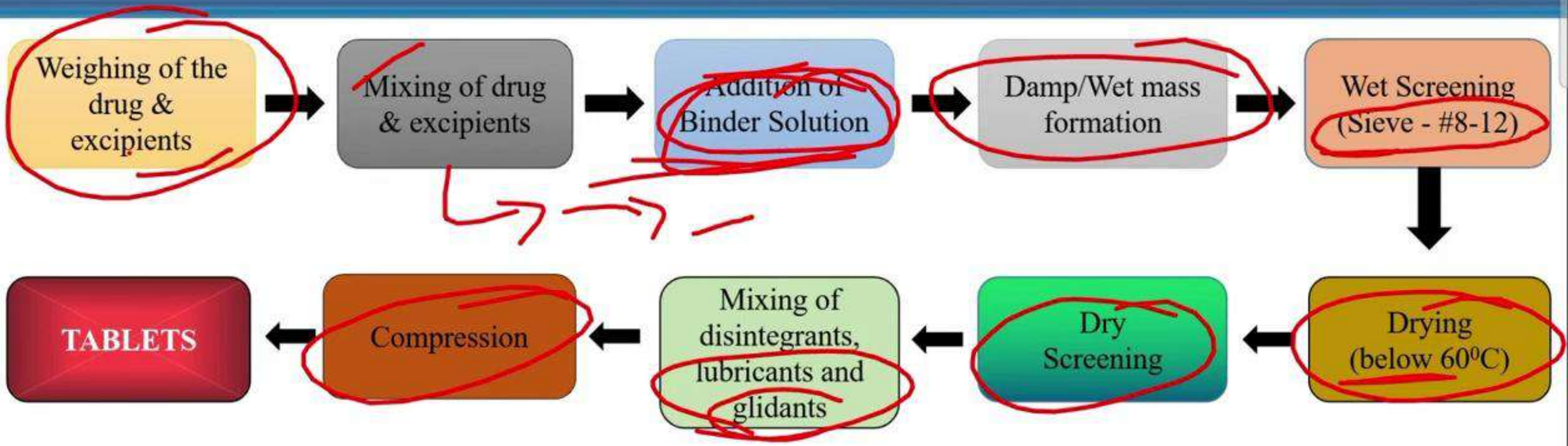

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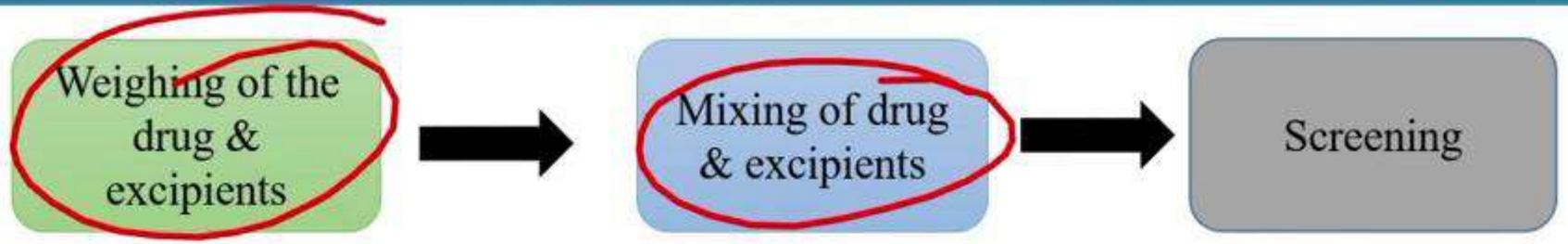

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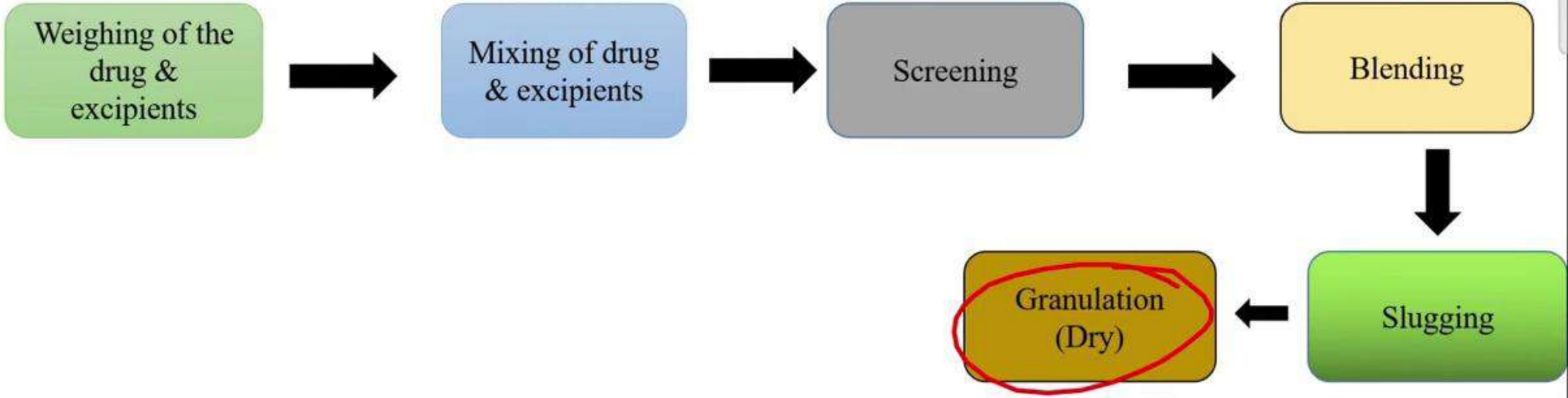

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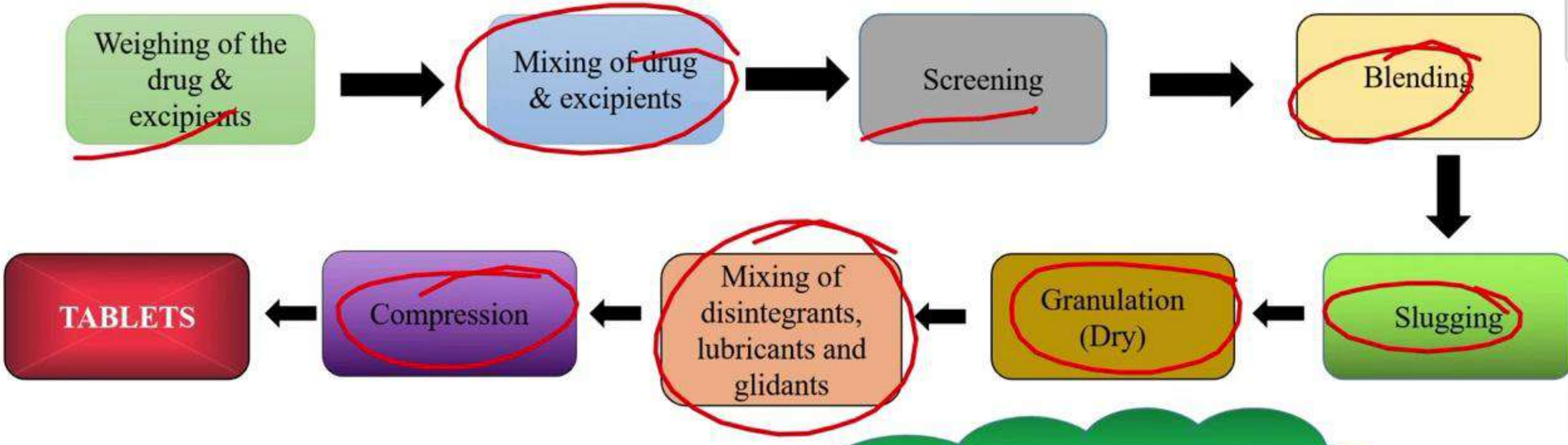

Equipments

High-capacity heavy duty tablet press

Chilsonator roller compactor

Direct Compression

Powders for direct compression has following properties

- Fluidity or flowability , Compressibility
- Easily mixed with other particles
- Homogenous colouring etc.
- Friction and adhesion properties

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Eg: NaCl, KCl

Binder – HPMC

Diluent → Avicel

Weighing of the drug & excipients → Screening (Sieve - #20-25)

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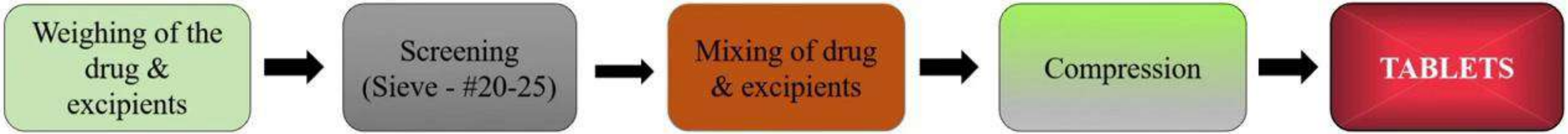

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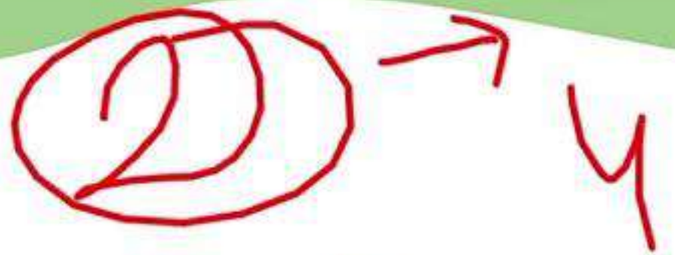

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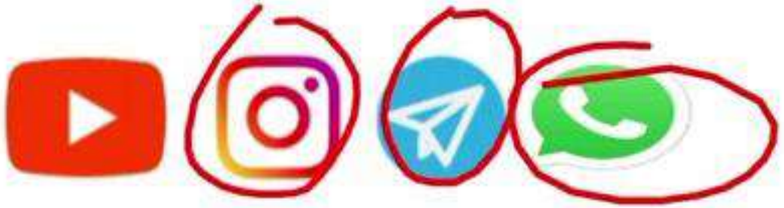

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GPAT/NIPER 2025 CRASH COURSE

SUBJECT - PHARMACEUTICS

TOPIC - TABLETS

GPAT PREVIOUS YEAR QUESTIONS

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GPAT/NIPER 2025 CRASH COURSE

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GPAT PREVIOUS YEAR QUESTIONS

66

Question 1 -

Which filler can NOT be used for the preparation of tablets for amine containing basic drugs to avoid discoloration of the tablets?

(a) Dicalcium phosphate

(b) Microcrystalline cellulose

(c) Starch

(d) Lactose

[GATE- 2010]

Diluents

Lactose

Most commonly used, But causes Maillard reaction [Reducing sugars(glucose, maltose and lactose) with amine containing drugs]

Good compressibility

Two grades:

(i) 60 to 80 mesh - **coarse grade**

(ii) 80 to 100 mesh **regular grade**

Types

- **α- lactose monohydrate:**
  Containing 5% moisture, poor flow and used in wet granulation & Show Maillard reaction
- **β- lactose anhydrous (DCL-30):**
  Not show maillard reaction, moisture content 0.55%
- **Spray-dried lactose (Zeparox)**:
  Mixture of crystalline α_x0002_monohydrate (80-90%) and amorphous lactose
  Show Maillard reaction

Question 2 -

Larger values of Ky in the Heckel Plot indicate formation of what quality of tablets?

(a) Harder tablets

(b) Softer tablets

(c) Fluffy tablets

(d) Brittle tablets

90-95%

[GATE- 2011]

Question 4 -

The thickness Gold coating on a USP Dissolution apparatus - I basket should be:

(a) Not more than 2.5 μ in thickness

(b) Not more than 0.001 mm in thickness

(c) Not more than 0.025 μ in thickness

(d) Not more than 0.1 mm in thickness

[GATE- 2012]

Question 5-

Which of the following would cause increase in the binding strength at the dry granulation process in significant degree :

(a) Carboxymethylamylopectiglycolate

(b) Magnesium Stearate

(c) Macrogol 4000

(d) Lactose

[GATE- 2013]

Question 6 -

Which of the following in not added to chewing tablet

(a) Gildant

(b) Disintegrant

(c) Anitadhesive

(d) Lubricant

[GATE- 2014]

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(d) Lubricant

[GATE- 2014]

Question 7 -

The disintegration time of the effervescent tablets is

(a) 2 minutes

(b) 2.4 minutes

(c) 3.5 minutes

(d) 5 minutes

GPAT

[GATE- 2014]

Type of Tablet	Disintegration Media	Disintegration Time (Min)	
		IP	USP
Dispersible tablet	Water	Less than 3 min	Less than 3 min
Effervescent tablet	Water	Less than 5 min	Less than 5 min
Uncoated tablet	Water	Less than 15 min	Less than 30 min
Film coated tablet	Water or 0.1 N HCl	Less than 30 min	Less than 30 min
Sugar coated tablet	Water	Less than 1 hr	Less than 1 hr
Enteric coated tablet	0.1 M HCl	120 min or less	60 min or less
	Phosphate Buffer	60 min or less	120 min or less

Question 8 -

Evaluation of colour is tablets is done by

(a) Reflectance spectrophotometer

(b) Tristimulus colorimeter

(c) Microreflectance photometer

(d) All of the above

GPAT

[GATE- 2014]

Question 9 -

Delayed disintegration in tablet is a result of:

(a) Large force of compression

(b) Small force of compression

(c) Higher amount of granule

(d) Low amount of granule

GPAT

[GATE- 2015]

Question 10 -

Inadequate drying during coating of tablet leads to which coating defect:

(a) Chipping

(b) Lamination

(c) Mottling

(d) Lamination

[GATE- 2015]

Question 12-

Which problem can arise if the material to be compressed into tablet tends to adhere to die walls:

(a) Picking

(b) Sticking

(c) Capping

(d) Marbling

GPAT
[GATE- 2016]

Question 13-

Which one of the following is a solid dosage form excipient which can play the role of a diluent, a disintegrant, a glidant, a lubricant and a pore/ channel former.

(a) Lactose

(b) Microcrystalline cellulose

(c) Ethyl cellulose

(d) Eudragit RL 100

GPAT

[GATE- 2016]

Dissolution test

Dissolution Medium- 900ml
Tablets- 6
Time - Conventional Tablets: 1hr
Sustained Release: 8 hr
Sampling Interval -
Conventional Tablets: 10 min
Sustained Release: 1 hr
Temperature - 37±0.5^{0}C

Type	Description	Dosage form
Type I	Rotating Basket	Conventional Tablets, Modified release tablets, Capsules
Type II	Paddle	Orally disintegrating tablets, Chewable tablets, Modified release
Type III	Reciprocating cylinder	Modified release, Chewable tablets
Type IV	Flow through cell apparatus	Modified released, microparticles, granules
Type V	Paddle over disk	Transdermal patches
Type VI	Cylinder	Trandermal Patches
Type VII	Reciprocating disc	Non-disintegrating oral modified D.F

Question 15-

The friability issue of the tablet can be solved by different ways except:

(a) Increasing the upper punch pressure of tablet machine

(b) Addition of more tablet binder to granules

(c) Increasing the moisture content of granules

(d) Adjusting the lower punch pressure of tablet machine

GPAT

[GATE- 2018]

Question 16-

A material which is insoluble and inert and used in matrix tablet formulation is:

(a) Polyethylene

(b) Stearyl alcohol

(c) Polyethylene glycol

(d) Triglycerides

[GATE- 2018]

Question 17-

Substance used to reduce friction during tablet compression and facilitate ejection of tablets from the die cavity is called as:

(a) Lubricant

(b) Glidant

(c) Anti-adherent

(d) Humectant

[GATE- 2018]

Question 18-

Purpose of seal coating step of sugar coating is :

(a) Gives smooth surface to the tablet

(b) Enhance weight of the tablet for coating

(c) Gives sweet taste to the tablet

(d) Prevent moisture penetration in the tablet

[GATE- 2021]

SUGAR COATING

Seal Coating → Subcoating → Smoothing → Colour Coating → Polishing → Printing

SEALING

To prevent the moisture penetration into tablet core

Eg : Shellac, zein, CAP, PVAP

SUB COATING

- Round the edges and build up the tablet size
- Increase weight by 50-100%
- Binding solution - Gelatin, sugarcane, PEG, Acacia
- Dusting Powder - $CaCO_3$, Talc, TiO_2

SMOOTHING (SYRUPING)

Cover & fill imperfection in the tablet surface caused by subcoating

Eg: Simple syrup solution , corn starch, sugar cane

Equation, Formula

Instruments

Syndrome

Drug of

Question 21-

A component of film coating solution to make film more pliable , enhance spread over tablet , beds and granules is called :

(a) Adsorbent

(b) Humectant

(c) Stiffening Agent

(d) Plasticizer

[GPAT 2023(1st Shift)]

Question 22-

A tablet excipient , whose function is to ensure that tablet formulation and ejection can occur with low friction between the solid and the die wall is called :

(a) Glidant

(b) Lubricant

(c) Anti-adhesive

(d) Binder

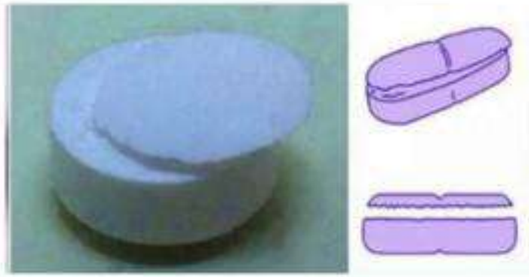
[GPAT 2023(1st Shift)]

Tablet Defects

Capping
Partial or complete separation of the top or bottom crowns

Causes
Air entrapment
Deep Concave punches
Dry Granulation

Remedies
Pre-compression
Flat Punches
Add certain % of moisture by Sorbitol , PEG



Lamination
Separation of tablet into two or more distinct layers

Causes
Air entrapment
Deep Concave punches
Dry Granulation

Remedies
Pre-compression
Flat Punches
Add certain % of moisture by Sorbitol , PEG

Weight Variation
Tablet forms with different weight

Causes
Poor flow
Lack of glidant and lubricants

Remedies
Improve flow properties
Add sufficient amount of glidants and lubricants

Question 24-

"Picking" , is a term used to describe :

(a) Separation of tablet into two or more layers

(b) The situation when the surface material from the tablet is sticking to and being removed from the tablet's surface by a punch

(c) Unequal distribution of the colour on tablet

(d) Partial or complete separation of the top and bottom crown of the tablet from the main body of the tablet

[GPAT 2023(2nd Shift)]

Question 25-

List 1 (Dissolution Apparatus)		List 2 (Name)	
A	Type 1	1.	Reciprocating Holder
B.	Type 5	2.	Paddled Overdisk
C.	USP App 6	3.	Basket Type
D.	USP App 7	4.	Cylinder Apparatus

1. A-(3); B-(2); C-(4); D-(1)
2. A-(4); B-(1); C-(2); D-(3)
3. A-(2); B-(3); C-(1); D-(2)
4. A-(1); B-(2); C-(3); D-(4)

[GPAT 2023(2nd Shift)]

Question 26-

Which of the following is/are in-process QC test(s) for tablets:

A. Drug content, Puncture Test

B. Zeta-sizing Test

C. Dissolution Test

D. Hardness, Friability, Average weight

[GPAT 2024]

Question 27-

During compression of tablets, dwell time is:

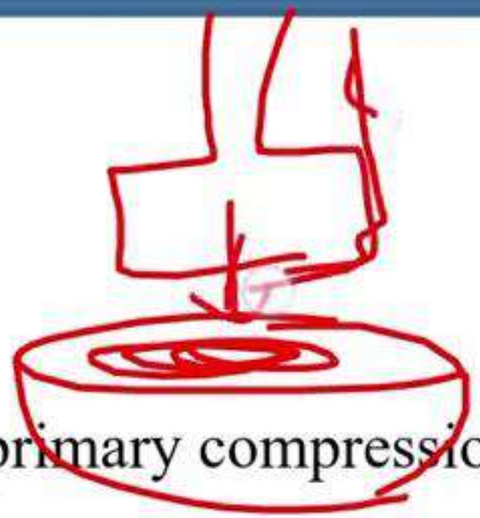
A. Time it takes for the punches to eject the tablets

B. Time it takes for the punches to eject tablet under the primary compression rollers

C. Time it takes for the punches to punch tablet

D. Time it takes for the punches to stop moving vertically and to achieve maximum penetration in the die under the primary compression rollers

[GPAT 2024]



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[GPAT 2024]

TABLET COATING

FILM COATING

Adds 2-5% to the tablet weight
Produce smooth, thin films
Methods :

- Pan Pour Method
- Pan Spray Method
- Fluidized bed press (Air Suspension Coating)

COATING MATERIAL

Hydroxypropyl Methylcellulose (HPMC)
Methyl Hydroxyethyl cellulose
Ethyl cellulose (EC)
PVP
PEG
Acrylated Polymers (Eudragit)

ENTERIC COATING

To provide acid resistance
Release drug into intestine

COATING MATERIAL

Hydroxypropyl Methylcellulose Phthalate (HPMCP)
Ethyl Cellulose Phthalate
Polyvinyl acetate phthalate
Acrylated Polymers (Eudragit L, Eudragit S)

Question 30-

The rate limiting step for the absorption of controlled release tablet is the:

A. Metabolism of the drug

B. Excretion of the drug

C. Dissolution of the drug

D. Distribution of the drug

[GPAT 2024]

Tablet

Dissolu

Ink Tools

Eraser

Erase All


Fast
Low
Absorb
Tablet
Dissolu
Absor
RDS
Slow
Absorn
Fun
Ab
CR

.....THANKS FOR WATCHING.....

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TOPIC- CAPSULE

LECTURE - 1

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Latin → Capsula

↓

Small Container

Gelatin →

Introduction to Capsules

- ✓ Capsules are solid dosage forms in which the drug substance is enclosed within a soluble shell, typically made of gelatin or other suitable materials.
- ✓ They are widely used for oral administration of drugs, providing an easy-to-swallow and tasteless option for patients.
- ✓ Capsules can be classified into two main types:

Hard Gelatin Capsules
Intended for the capsulation of particulate solids (such as powders, granules, and pellets)

Soft Gelatin Capsules
Encloses the medicaments in the form of powders, pastes, or non-aqueous liquids.

Advantages of Capsules

- ✓ Easy to swallow, especially for patients who have difficulty with tablets.
- ✓ Mask the taste and odor of unpleasant drugs.
- ✓ Faster disintegration and drug release compared to tablets.
- ✓ Flexible dosing as capsules can be opened and mixed with food (for certain types).
- ✓ Suitable for both solid and liquid drug formulations.

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Disadvantages of Capsules

Not Suitable for :

- **Efflorescent material** : Shell beomes too soft
- **Deliquescent Material** : Shell become excessive brittle
- Extremely soluble materials such as KCl, KBr, NH4Cl : Sudden release cause irritation in stomach

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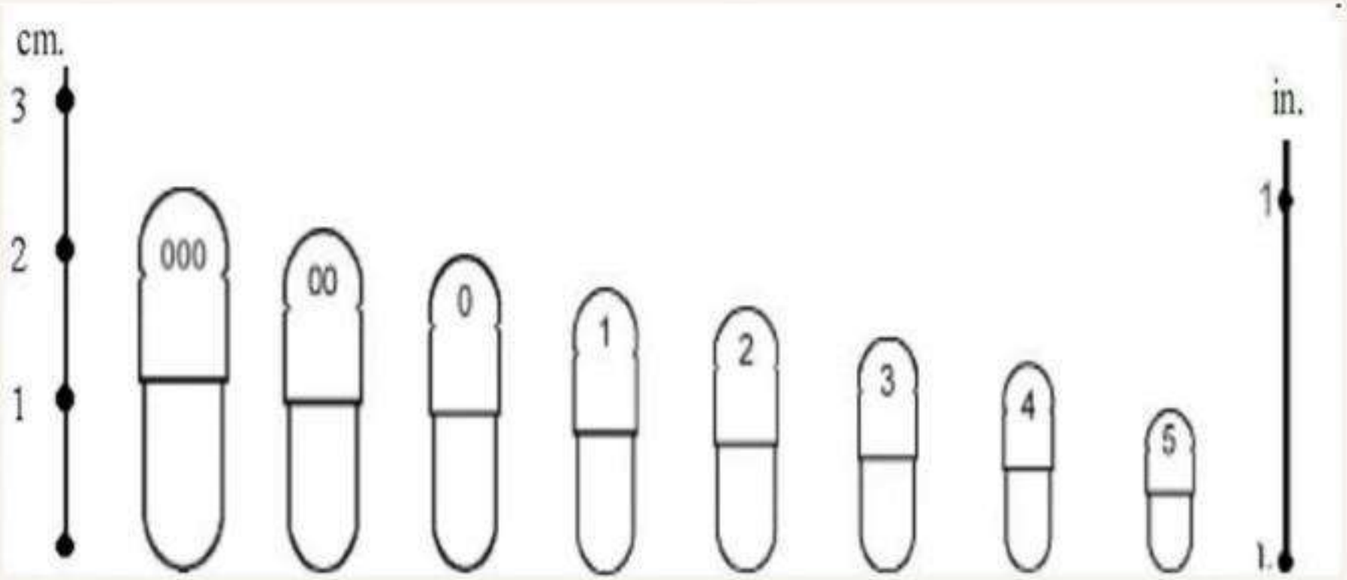
Capsules Size Distribution

Capsule Size	Volume (ml)	Weight (mg)
000	1.35	950
00	0.95	650
0	0.75	450
1	0.55	300
2	0.40	250
3	0.30	200
4	0.25	150
5	0.15	100



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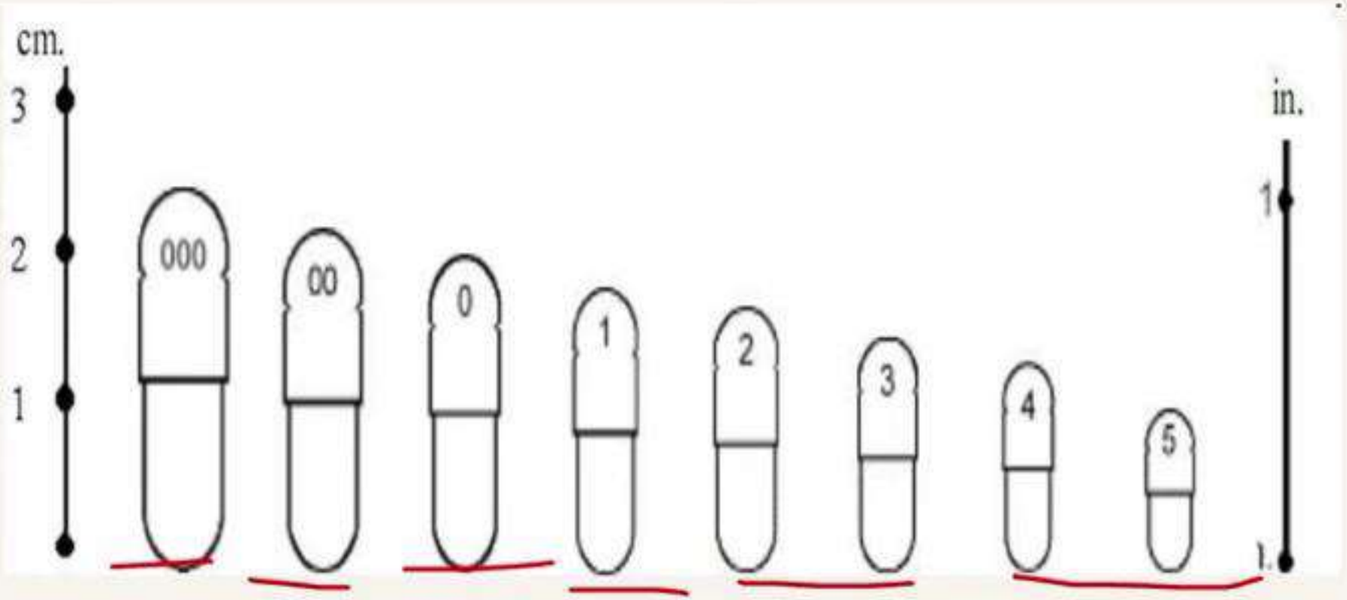

Excipients Used in Capsules

Pharmaceutical excipients play a crucial role in capsule formulation, affecting stability, dissolution, and bioavailability.

Common Excipients in Capsules

Excipient Type	Examples	Function
Diluents	Lactose, Microcrystalline Cellulose (MCC), Mannitol	Adjusts capsule weight, improves flow properties
Disintegrants	Croscarmellose Sodium, Sodium Starch Glycolate	Facilitates capsule rupture for drug release
Lubricants/Glidants	Magnesium Stearate, Colloidal Silicon Dioxide	Reduces friction, enhances flow properties
Wetting Agents	Sodium Lauryl Sulfate (SLS), Polysorbates	Improves dissolution of hydrophobic drugs

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Excipients Used in Capsules

1. **Diluents (Fillers)**
   - **Function** : Adjust capsule weight and bulk, improve powder flow, and aid in uniform drug distribution.
   - **Examples** :
     a. **Lactose Monohydrate** : Common, compatible with most drugs.
     b. **Microcrystalline Cellulose (MCC) :** Improves flow and compressibility.
     c. **Mannitol** : Used in chewable capsules due to its sweet taste.
   - **Selection Criteria**: Must be non-reactive, inert, and compatible with API.

Excipients Used in Capsules

2. **Disintegrants**:
   - **Function**: Helps break down the capsule in gastrointestinal fluids, facilitating drug release.
   - **Examples**:
     1. **Croscarmellose Sodium** – Superdisintegrant, swells rapidly.
     2. **Sodium Starch Glycolate (SSG)** – Enhances water penetration into capsules.
     3. **Pregelatinized Starch** – Mild disintegrant, also improves binding.
   - **Consideration**: Hard gelatin capsules typically dissolve in gastric fluids, but for modified-release formulations, disintegrants play a crucial role.

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Excipients Used in Capsules

3. Lubricants & Glidants:

- **Function**: Reduce powder adhesion to capsule-filling machines and improve powder flow.
- **Examples**:
  a. **Magnesium Stearate –** Common lubricant, prevents sticking.
  b. **Talc –** Improves powder flow but may delay dissolution.
  c. **Colloidal Silicon Dioxide –** Enhances flowability by reducing interparticle friction.
- **Consideration**: Hard gelatin capsules typically dissolve in gastric fluids, but for modified-release formulations, disintegrants play a crucial role.

Excipients Used in Capsules

4. Wetting Agents:

- **Function**: Enhance solubility of poorly water-soluble drugs.
- **Examples**:
  a. **Sodium Lauryl Sulfate (SLS) –** Improves wettability and dispersion.
  b. **Polysorbates (Tween 80) –** Common surfactant for lipophilic drugs.

- **Key Benefit:** Improves bioavailability of BCS Class II & IV drugs.

Capsule Shell Formation

Gelatin

Gelatin is a natural, water-soluble protein derived from collagen, which is found in animal skin, bones, and connective tissues. It is widely used in pharmaceutical, food, and cosmetic industries due to its gel-forming, film-forming, and binding properties.

Key Components:

1. Gelatin is the most common material used for capsule shells.
2. It is derived from collagen, usually sourced from animal bones or skin.
3. Gelatin is biocompatible, biodegradable, and forms a clear, flexible film.

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Irreversible Hydrolytic

Key Components:

1. Gelatin is the most common material used for capsule shells.
2. It is derived from collagen, usually sourced from animal bones or skin.
3. Gelatin is biocompatible, biodegradable, and forms a clear, flexible film.

Types of Gelatin

Gelatin is classified based on its source and method of extraction. The two main types of gelatin used in pharmaceuticals are Type A and Type B.

1. Type A Gelatin (Acid-Processed Gelatin):

- ✓ **Source**: Derived from porcine (pig) skin using acid treatment.
- ✓ **Isoelectric Point**: pH 7 – 9 (higher than Type B).
- ✓ **Properties**:
  a. Produces soft and flexible capsules.
  b. More soluble in acidic conditions.
  c. Lower gel strength compared to Type B.

Types of Gelatin

2. **Type B Gelatin (Alkaline-Processed Gelatin):**

- ✓ **Source**: Derived from bovine (cow) bones and hides using alkali treatment.
- ✓ **Isoelectric** Point: pH ~4.7 – 5.3 (lower than Type A).
- ✓ **Properties**:
    a. Higher gel strength than Type A.
    b. More stable in neutral to basic conditions.
    c. Takes longer to dissolve than Type A gelatin.

Types of Gelatin

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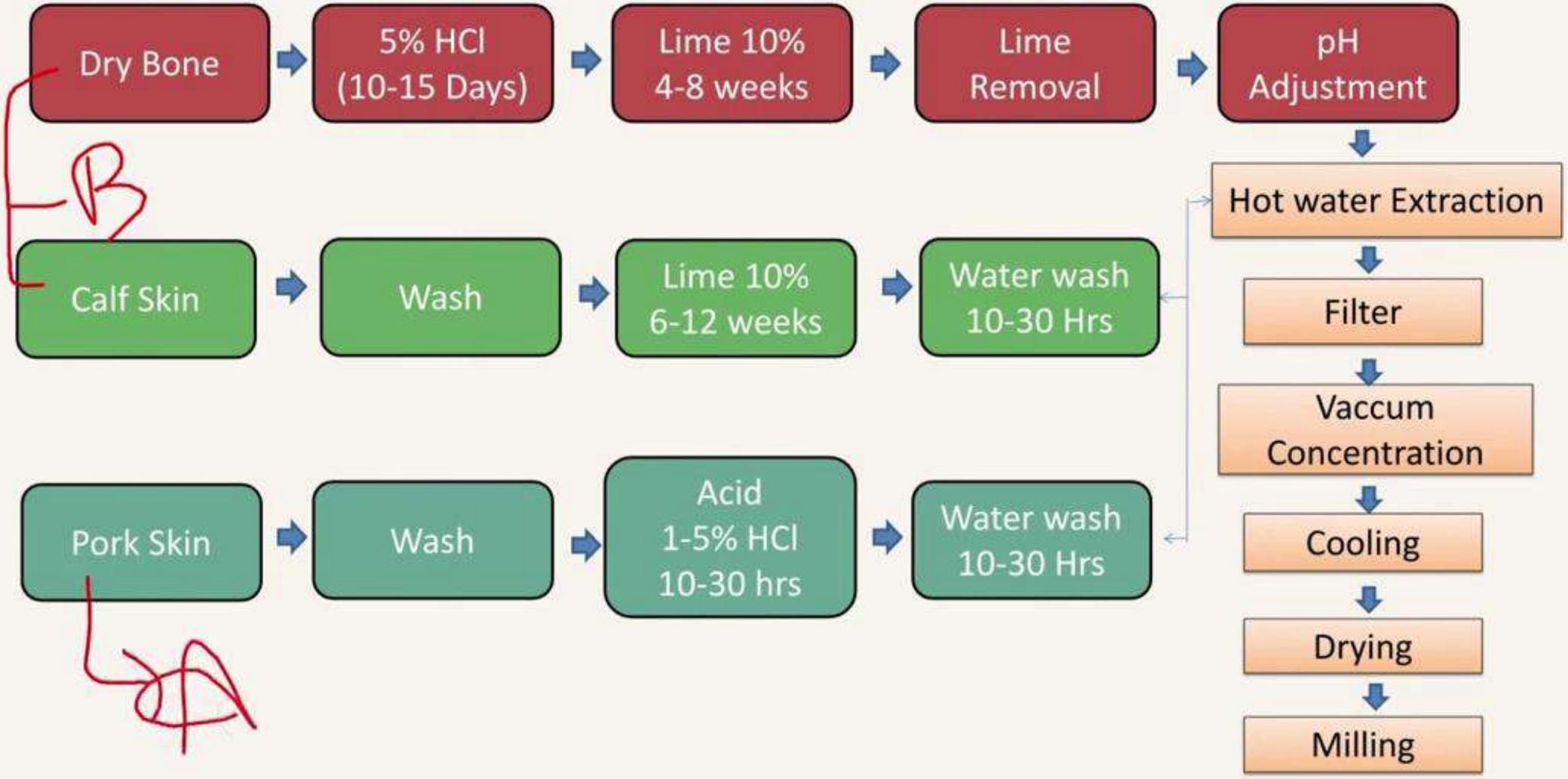
Pharma Gel B →

Gelatin Preparation



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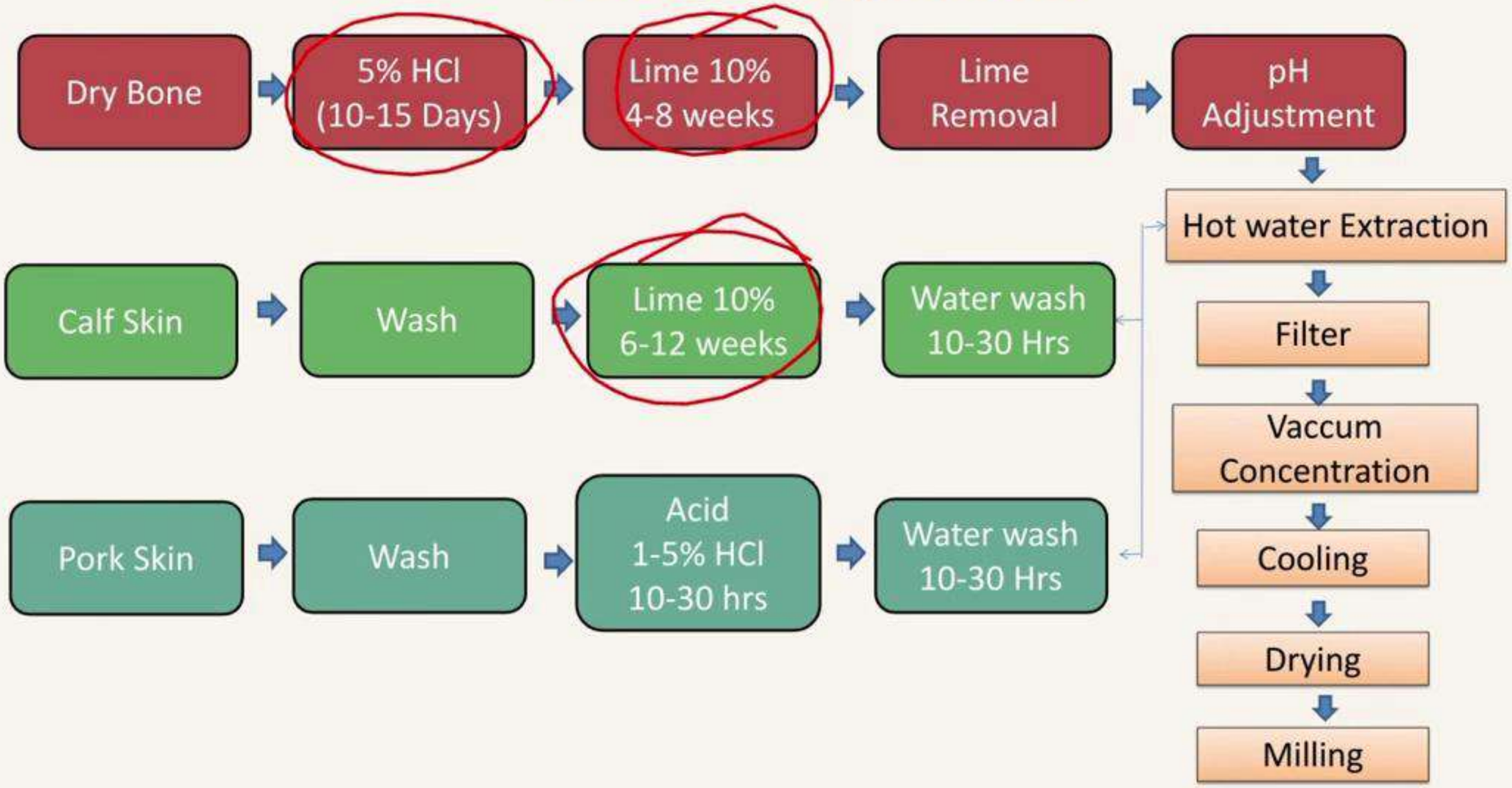

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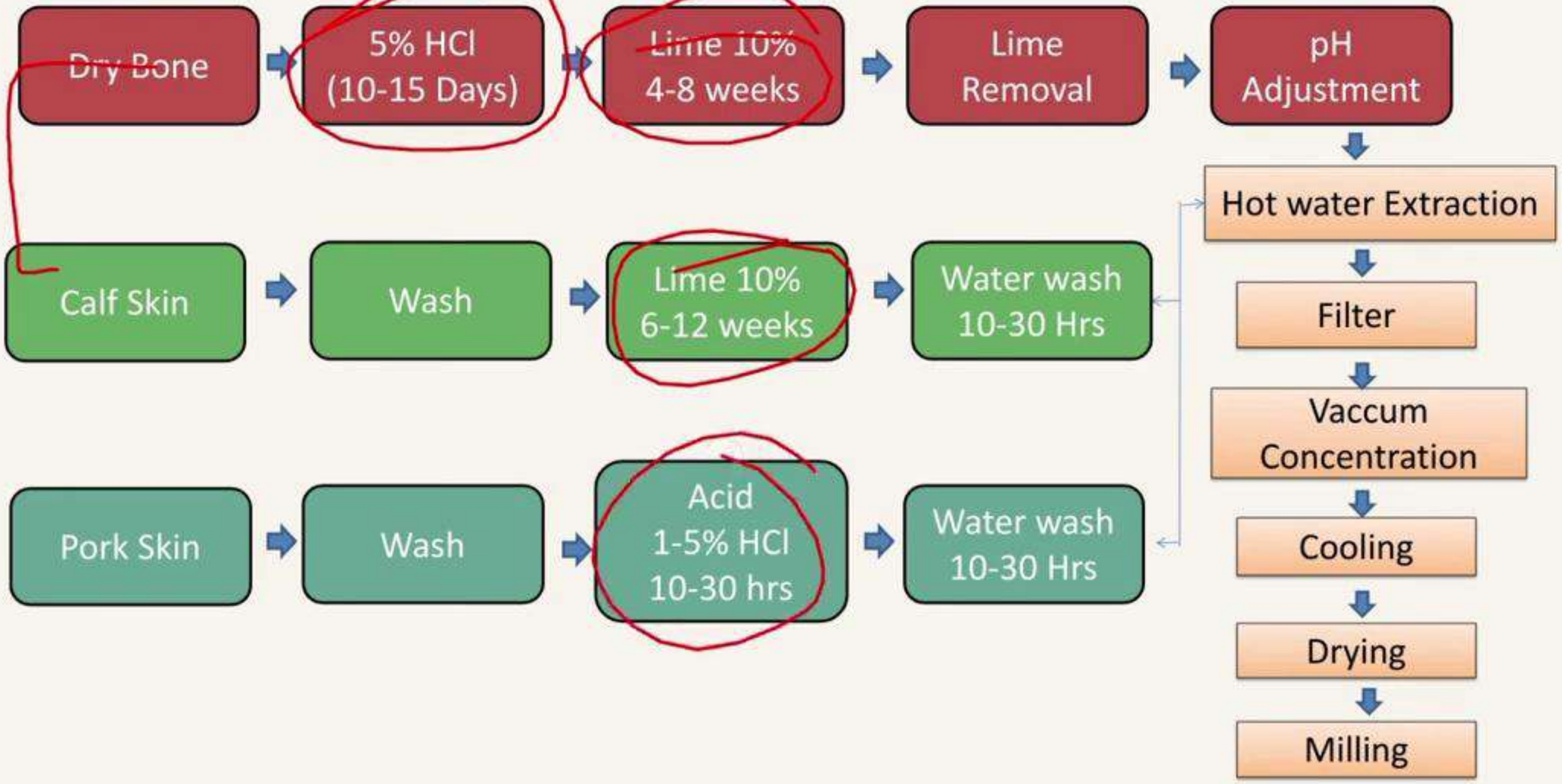

Bloom Strength

- ✓ Bloom strength is a measure of the gel strength or firmness of gelatin.
- ✓ It is the measurement of cohesive strength of cross linking that occur between gelatin molecule and is determined by the gelometer.
- ✓ Bloom strength is directly proportional to molecular weight of gelatin.
- ✓ Higher Bloom strength indicates a stronger, more rigid gel.
- ✓ Typical range for capsule gelatin: 150–250 .
- ✓ Bloom strength is determined by measuring the weight in gram required to move a plastic plunger that is 0.5 inches in dia, 4mm into 6 $\frac{2}{3}$% gelatin gel that has been 10^0C for 17hrs

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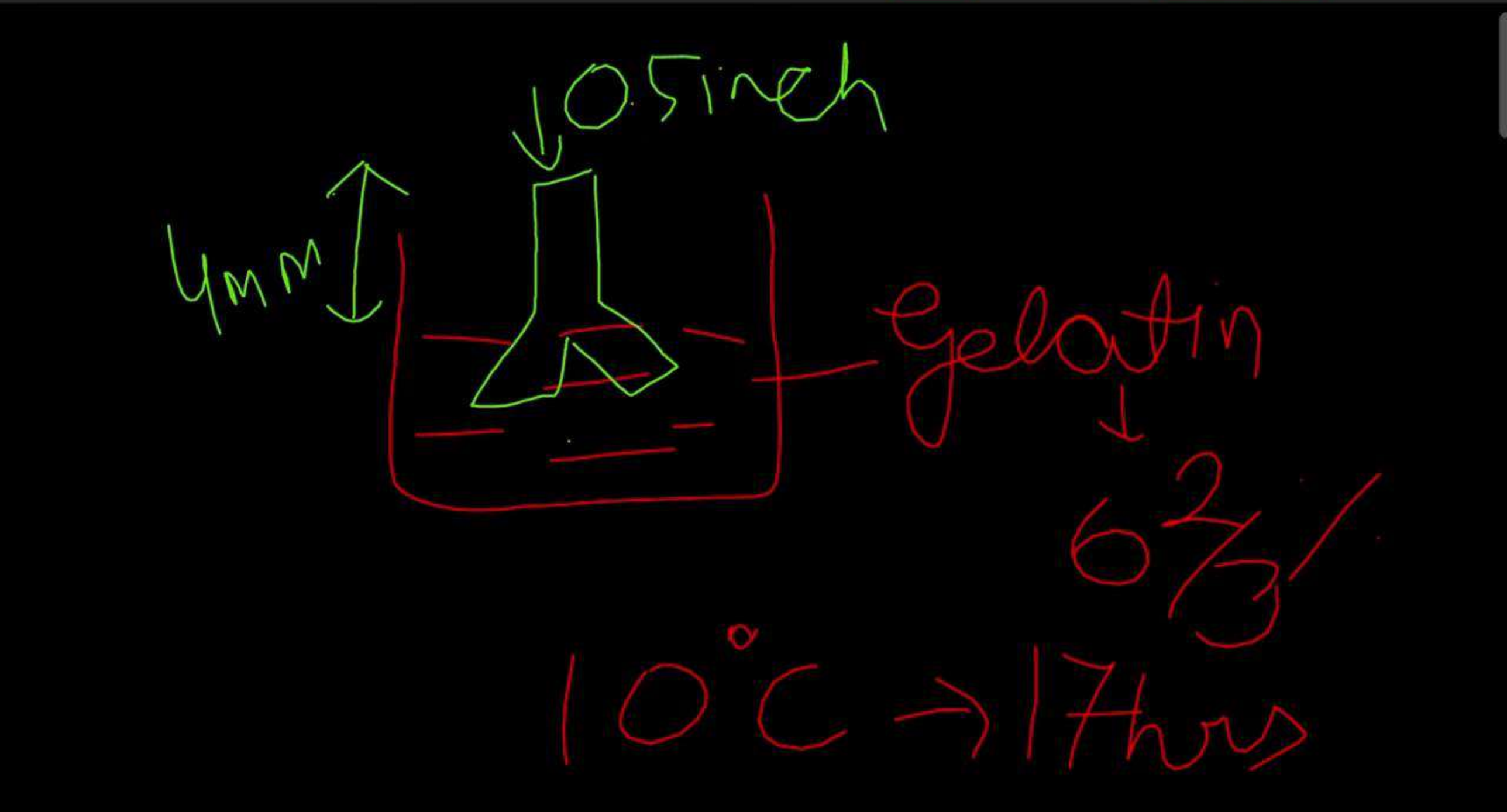

Viscosity

- ✓ It is a measure of molecular chain length of gelatin and determined by 6% of gelatin water at 60^0C
- ✓ It ranges from 25 to 45 millipoise
- ✓ Viscosity is a measure of the resistance of gelatin solution to flow.
- ✓ It is influenced by the molecular weight and concentration of gelatin.
- ✓ Viscosity is critical for capsule manufacturing as it affects the thickness and uniformity of the capsule shell.
- ✓ Controlled viscosity ensures proper dipping and film formation during capsule production.

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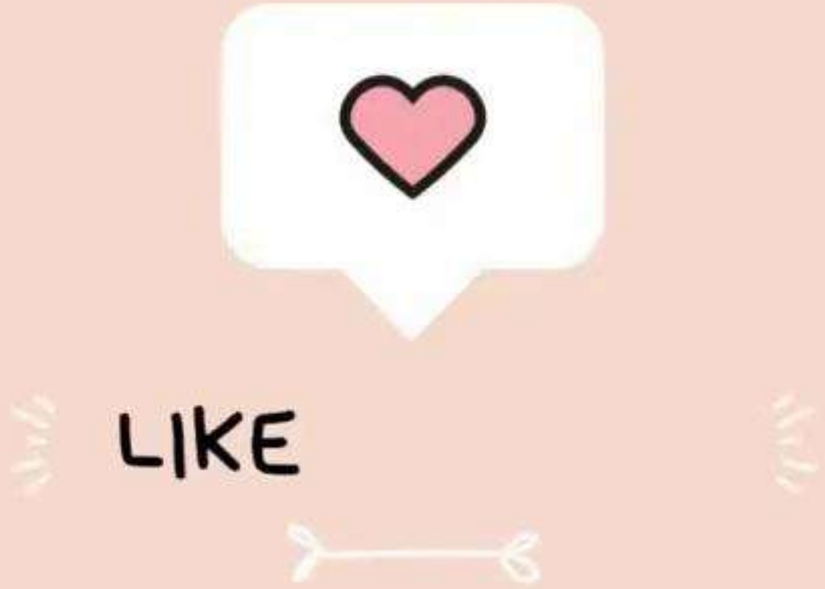
Lecture 1 Capsule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Introduction to Hard Gelatin Capsules (HGC)

- Hard Gelatin Capsules are a common dosage form made of a two-piece capsule shell: a body and a cap
- They are typically used for solid oral medications, including powders, granules, and pellets.

Shorter Piece - Cap
Longer Piece - Body

Relative Humidity - 30-45%
Moisture Content - 13-16%
Below 10% - Become brittle and suffer dimensional changes
Above 16% - Problems in filling and loss of mechanical strength

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Above 16% - Problems in filling and loss of mechanical strength

PREPARATION OF EMPTY CAPSULE SHELLS

1. DIPPING

150 Pairs of the stainless steel pins are dipped into the dipping solution(Gelatin solution)

Temperature - 22^{0}C (Pins)
50^{0}C (Solution)

Time - 12 Seconds

2. SPINNING

The pinsare rotated to distribute the gelatin over the pins uniformly

3. DRYING

By the use of dry air

4. STRIPPING

A series of bronze jaws strip the cap and body portions of the capsules from the pins

5. TRIMMING

The cap and body lengths are precisely trimmed to a ±0.15 mm tolerance by stationary knives

6. JOINING

After trimming to the right length, the cap and body portion are joined.

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50^{0}C (Solution)

Time - 12 Seconds

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3. DRYING

By the use of dry air

45min.

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Equipments Used

Capsule Filling achine

Feeding	Machine of capsule filling	Material to be filled
Augur type	Eli Lilly	Pallets
	Holfiger and Karg	Powders, pallets and Thixotropic material
Dosator type	Farmatic	Slugs
	Macofar	Cohesive powder
	mG_2	Powder, capsule and pallets
	Zanasi	Powder, pallets, paste, liquid, small capsules and tablets
Vibrator fill	Osaka	Powder and granules
ACCOFIL	Perry	Powder

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Equipments Used In Capsule Manufacturing

Name of equipment	Application
Rotosort	It removes loose powder, removes unfilled joined capsules and capsules with loose caps, new filled capsule sorting machine
Rotofill	Fill Pellet in Hard Gelatin Capsule
Accofill	Fill Powder in Hard Gelatin Capsule
Accogel	Fill Powder in Soft Gelatin Capsule
Erweka KEA	Dedusting and polishing
Scidenader PM60	Cleaning and polishing
Roto weigh	It is capsule weighing machine. It measures the reflected energy (backscatter) of low power X-ray beam
Vericap 1200	It measures the change in dielectric constant or capacitance variation.

SEALING

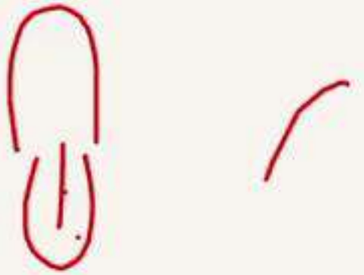
The capsules filled by manual or hand filling machines are sealed in order to prevent the detachment of caps from the bodies during packaging, handling or storage.

1.Banding:

In this method capsules are sealed by placing gelatin color bands at the meeting point of caps and the bodies.

2.Moistening

In this method , inner surface of caps is moistened with warm gelatin solution and these are then quickly slipped over the filled bodies.



3.Spot Welding

Capsules are sealed by welding process in which causes the cap and body to fuse.

The joints which leaves a ring like appearance at the point of sealing

4.Thermal welding

In this method, Applying wetting sol. At the meeting points of cap and body which causes lowering of M.P at applied area.

Finally they are sealed at a temp. 40-45ºc.

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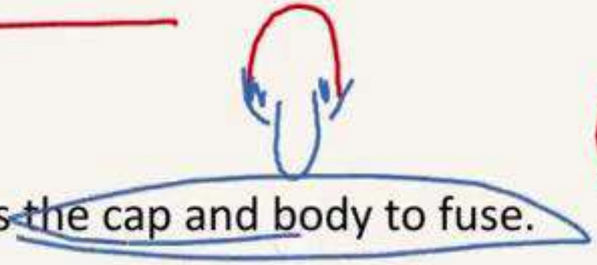

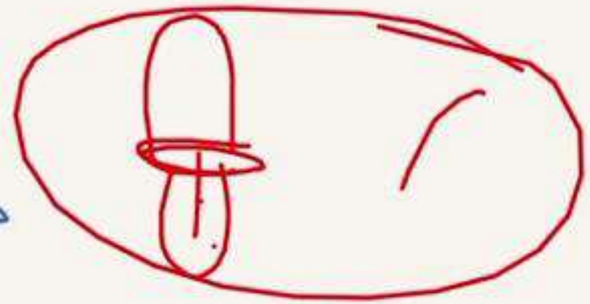

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4.Thermal welding

In this method, Applying wetting sol. At the meeting points of cap and body which causes lowering of M.P at applied area.

Finally they are sealed at a temp. 40-45ºc.

POLISHING

Before final packaging the filled and sealed capsules are subjected to dusting and polishing to remove a particles and to make them glossy.

Cloth dusting

It is a manual method in this small number of capsules are rubbed with a cloth.

Pan polishing

Accela- cota tablet coating pans may be used for polishing the filled capsules.

These pans are lined with cheese cloth or polyurethane which captures the dust and other powders adhering to the capsule

Ink Blank Screen

Plasticizer : Gelatin

Hard — 04 : 1

Medium — 06 : 1

Soft — 08 : 1

Introduction to Soft Gelatin Capsules (Softgels)

- **Soft Gelatin Capsules** (Softgels) are a type of capsule that is made from a single-piece, flexible gelatin shell, and are often filled with liquids, oils, or semi-solid substances.
- **Softgels** are often used for drugs that require better absorption, like oily or hydrophobic substances.
- **Advantages**:

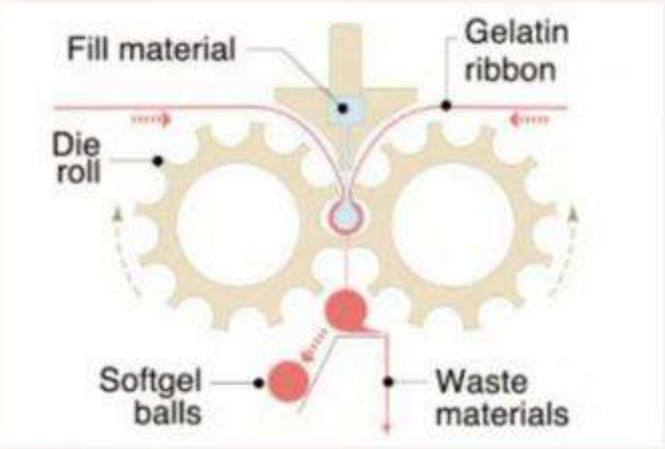
a. Higher bioavailability: Faster absorption into the bloodstream due to the liquid form.

b. Ideal for liquid or semi-solid drugs that cannot be effectively encapsulated in hard capsules.

SHAPE	CAPACITY(ml)
Spherical	0.05-5
Ovoid	0.05-7
Cylindrical	0.15-25
Pear-like	0.3-5

Manufacture of Soft Gelatin Capsules

- Rotary Die Process
- Plate Process
- Reciprocating Process
- Accogel Machine
- Seamless Process (Bubble Method)



Difference Between Hard Gelatin and Soft Gelatin Capsules

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Ratio of Plasticizer - 0.8:1	**Ratio of Plasticizer** - 0.4:1

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200-250

100gm

Evaluation Tests of Capsules

1. Content Uniformity

- 30 capsules selected and 10 of these are assayed individually
- At least 9 contain 85 – 115% of drug and none contain below 75 to 125 % of drug.
- If 1 to 3 of them fall outside of 85 – 115 % limits, the reaming 20 capsules are individually assayed and the requirement are met if at least 27 contain 85 – 115 % of drug and none contain less than 75 – 125 % of drug.
- This test is ensuring uniform distribution of medicament and important in case of potent drug

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±15% ±25%

Evaluation Tests of Capsules

2. Weight uniformity

- This test applies to all types of capsules and it is performed by 20 capsules
- Determine the average weight for capsule and finding out weight variation of each capsule.
- Weight of each capsule should fall within 90 to 110%

3. Disintegration test

Official test

SGC: 60 minutes

HGC: 30 minutes

Evaluation Tests of Capsules

Dissolution Test

- Place 1000 ml of water free from dissolved air having temperature of 36.5ºC to 37.5ºC
- Place specified number of capsules in each basket.
- Start motor and adjust speed 100 rpm as per monograph. Withdraw the required volume of solution after 45 minutes or as specified in the monograph. Filter and weigh the amount of active ingredients by the method specified in the monograph.
- The test is said to pass if the amount of active ingredient is not less than 70% or the stated amount in monograph

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Base Adsorption

- Number of grams of liquid base required to produce a capsulable mixture when mixed with one gm of solid (s)
- For determination the solid must be completely wetted with the liquid base
- Base Adsorption is used to determine the minim per gram factor (M/g) of the solid.
- M/g defined as the volume in minims that is occupied by one gm of the solid (s) plus the weight of liquid base (BA)

$$B.A. = \frac{Weight\ of\ Base}{Weight\ of\ Solid}$$

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Ink Blank Screen

$BA \Rightarrow (B$

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Lecture Based Quiz

uestion 3: Which of the following is an important evaluation test for capsules to ensure proper drug release

A) Uniformity of weight

B) Dissolution test

C) Microbial testing

D) All of the above

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CAPSULE

PYQ DISCUSSION

Pharmaceutics

Growup Pharma

Youtube: @growup pharma

Lecture 3

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Lecture 3

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Question 1 -

Green bone is a source of

(a) Type A Gelatin

(b) Type B Gelatin

(c) Both

(d) None

[GPAT 2010]

Bloom Strength

- ✓ Bloom strength is a measure of the gel strength or firmness of gelatin.
- ✓ It is the measurement of cohesive strength of cross linking that occur between gelatin molecule and is determined by the gelometer.
- ✓ Bloom strength is directly proportional to molecular weight of gelatin.
- ✓ Higher Bloom strength indicates a stronger, more rigid gel.
- ✓ Typical range for capsule gelatin: 150–250 .
- ✓ Bloom strength is determined by measuring the weight in gram required to move a plastic plunger that is 0.5 inches in dia, 4mm into 6 $\frac{2}{3}$% gelatin gel that has been 10^0C for 17hrs

Question 3 -

Which one of the following drying methods is commonly used in Pharma industry for dryingof soft shell capsules?

(a) Truck drying.
(b) Fluid bed drying
(c) Vacuum drying
(d) Microwave drying

[GPAT 2011]

Question 4 -

Plasticizers

By addition of which of the followings the shells of soft gelatin capsules may be made elastic:

(a) Polyethylene glycol

(b) Sorbitol

(c) Propylene glycol

(d) Dibutyl phthalate

[GPAT 2011]

Question 5 -

Statement [P] : Soft gelatin capsules contain 12-15 % moisture.

Statement [Q] : Hard gelatin capsule shells contain 6-10 % moisture.

Choose the correct statement?

(a) Both of the above statements P & Q are true

(b) Both of the above statements P & Q are false

(c) Statement P is true and Q is false

(d) Statement P is false and Q is true

[GPAT 2013]

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Question 6 -

The correct statements concerning concertation microencapsulation

(1) Concertation always leads to monophasic microcapsule

(2) When the gelatin is used for microcapsule's wall material, the concertation is bound to happen

(3) Only gelatin can be used for microcapsule's wall

(4) Simple or compound concertation can be distinguished according to the number of macromolecular colloids taking part in the process

(5) The pH conditions of the system and the solubility of the auxiliary materials do not have any effect of the preparation of the microcapsule

(a) Only 1 and 4 are correct

(b) Only 2 and 3 are correct

(c) Only 1 and 5 are correct

(d) Only 2 and 4 are correct

[GPAT 2013]

Question 7 -

Isoelectric point of Type A gelatin is _____.

(a) pH 7.0

(b) pH 4.7

(c) pH 9.0

(d) pH 7.4

[GPAT 2018]

Types of Gelatin

Gelatin is classified based on its source and method of extraction. The two main types of gelatin used in pharmaceuticals are Type A and Type B.

1. Type A Gelatin (Acid-Processed Gelatin):

- ✓ **Source**: Derived from porcine (pig) skin using acid treatment.
- ✓ **Isoelectric Point**: pH 9 (higher than Type B).
- ✓ **Properties**:
  a. Produces soft and flexible capsules.
  b. More soluble in acidic conditions.
  c. Lower gel strength compared to Type B.

Question 8 -

In Capsule making the Bloom Strength of gelatin is proportional to molecular weight of the gelatin and is a measure of the :

(a) Cohesive Strength of the solvent molecule

(b) Cohesive strength of the cross linking that occurs between gelatin molecules .

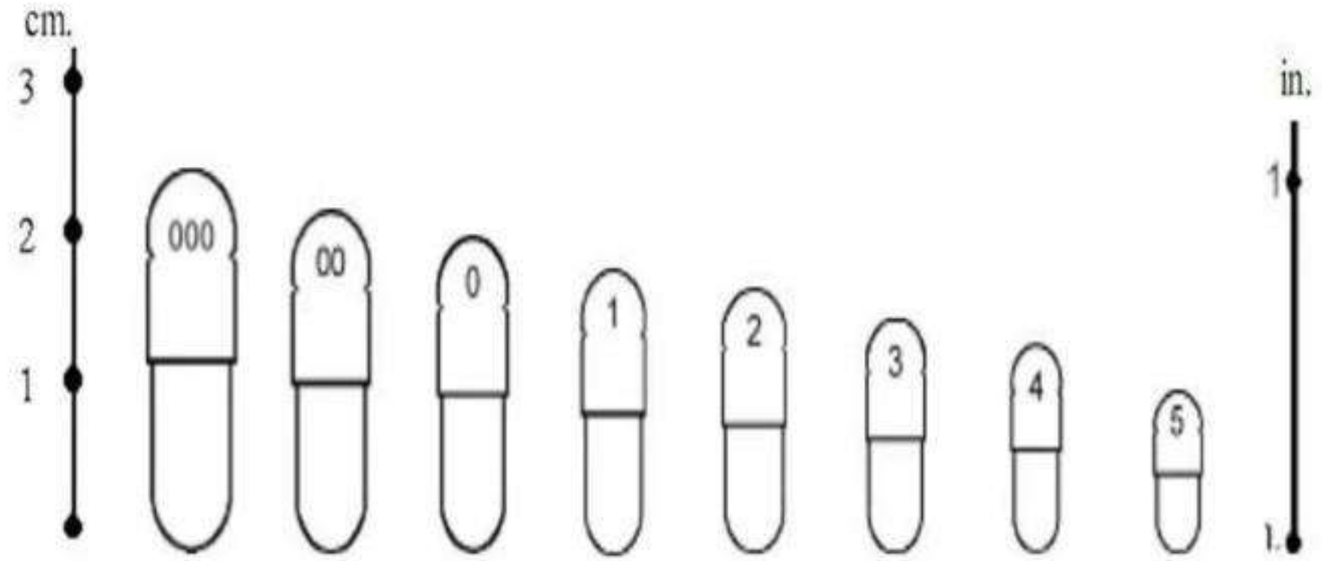
(c) Adhesive strength of Gelatin with dipping pins .

(d) Adhesive strength of gelatin with other polymer

[GPAT 2020]

Capsules Size Distribution

Capsule Size	Volume (ml)	Weight (mg)
000	1.35	950
00	0.95	650
0	0.75	450
1	0.55	300
2	0.40	250
3	0.30	200
4	0.25	150
5	0.15	100



Question 9 -

What is the approximate amount of powder (in mg) that can be filled in empty gelatin capsule of size 00 ?

(a) 1040 mg

(b) 650 mg

(c) 325 mg

(d) 162 mg

[GPAT 2023 1st Shift]

Question 11 -

The bloom strength is directly proportional to:

A. Viscosity

B. Density

C. Molecular weight

D. Measure of the strength and stiffness of the gelatin

[GPAT 2024]

Question 11 -

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[GPAT 2024]

Question 13 -

Which of the following one is used as opacifier :

(a) TiO2

(b) Mgo

(c) Siliactes

(d) All of the above

Equipments Used In Capsule Manufacturing

Name of equipment	Application
Rotosort	It removes loose powder, removes unfilled joined capsules and capsules with loose caps, new filled capsule sorting machine
Rotofill	Fill Pellet in Hard Gelatin Capsule
Accofill	Fill Powder in Hard Gelatin Capsule
Accogel	Fill Powder in Soft Gelatin Capsule
Erweka KEA	Dedusting and polishing
Scidenader PM60	Cleaning and polishing
Roto weigh	It is capsule weighing machine. It measures the reflected energy (backscatter) of low power X-ray beam
Vericap 1200	It measures the change in dielectric constant or capacitance variation.

Question 16 -

Filling of liquid in capsules is done by :

(a) Rotofil

(b) Qualiseal

(c) mG2

(d) Liquiseal

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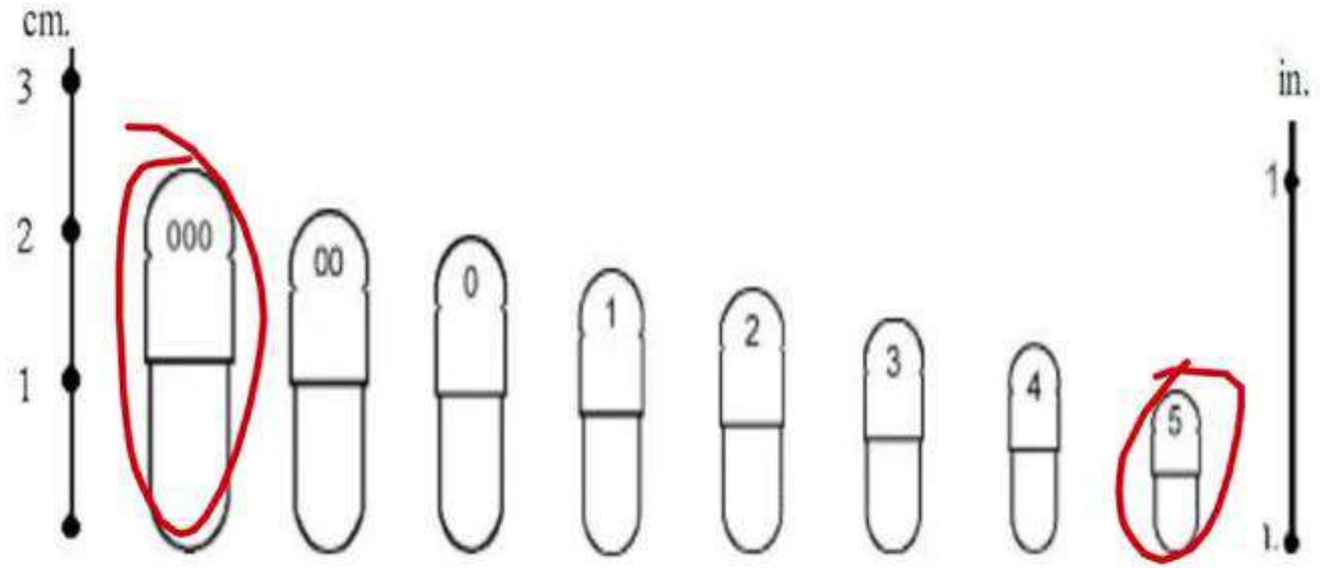

Question 20 -

Gelatin used for soft gel manufacturing should not contain more than _____ ppm of iron.

(a) 5

(b) 15

(c) 25

(d) 35

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Lecture 3 Capsule

GPAT/NIPER 2025 CRASH COURSE

Microencapsulation

Pharmaceutics

Growup Pharma

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Microencapsulation

Introduction

- Microencapsulation refers to the process of enclosing a core material (such as a liquid, solid, or gas) within a coating material to form microcapsules.
- These microcapsules are typically in the size range of **1 to 1000 micrometers** and are designed to control the release of the core material, protect it from external factors, or mask its taste or odor.
- Common applications include the pharmaceutical industry (for drug delivery), food industry (for f avoring or preservatives), and agriculture (for controlled release of fertilizers or pesticides).

Morphology of Microcapsules

Core Material:

The inner substance or active ingredient that is being encapsulated. This can be a drug, nutrient, or any other material.

Coating:

The outer shell of the microcapsule, made from various materials. It determines the release characteristics and protects the core material.

Shape and Size:

Microcapsules generally have a spherical shape, though other shapes like irregular or elongated can also be made. Their size ranges from 1 micron to a few millimeters.

Shell Structure:

The shell can be smooth, porous, or dense, depending on the method used for preparation and the desired release profile.

Morphology of Microcapsules

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Purpose of Microencapsulation

3. **Taste Masking:** Microencapsulation helps mask the unpleasant taste or odor of certain drugs or food additives.

4. **Improved Stability:** The core material is shielded from physical, chemical, or microbial damage, enhancing its shelf-life.

5. **Taste or Odor Improvement:** Encapsulating substances like vitamins or f avors prevents unwanted taste or smell during consumption.

Classification of Microcapsules

Microcapsules can be classified based on several factors:

1. **By Type of Core Material:**

   a. **Liquid Core Microcapsules:**

      Encapsulate liquids, often oils, in a solid shell.

   b. **Solid Core Microcapsules:**

      Encapsulate solids, including powders or granules.

Classification of Microcapsules

Microsphere

Microcapsule

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Classification of Microcapsules

2. **By Release Mechanism:**

a. **Time-Controlled**:

Release is governed by time (e.g., sustained-release capsules).

b. **Environment-Controlled**:

Release is triggered by external factors like pH, temperature, or enzymes.

c. **Targeted Release**:

Designed to release the core material at a specif ic site within the body (e.g., for targeted drug delivery).

Classification of Microcapsules

3. **By Coating Material:**

a. **Polymeric Microcapsules**

Made from natural or synthetic polymers (e.g., polylactic acid, gelatin).

b. **Lipid-Based Microcapsules**:

Made from lipids or surfactants, often used in drug delivery for lipophilic drugs.

Classification of Microcapsules

1. Mononuclear
2. Polynuclear
3. Matrix

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Coating Materials Used in Microencapsulation

2. **Lipids**:

   Used to create lipid-based microcapsules that are stable and have controlled release properties, often in food and pharmaceutical industries.

3. **Carbohydrates**:

   Starch and cyclodextrins are sometimes used as coating agents for food and pharmaceutical applications.

Techniques of Microencapsulation

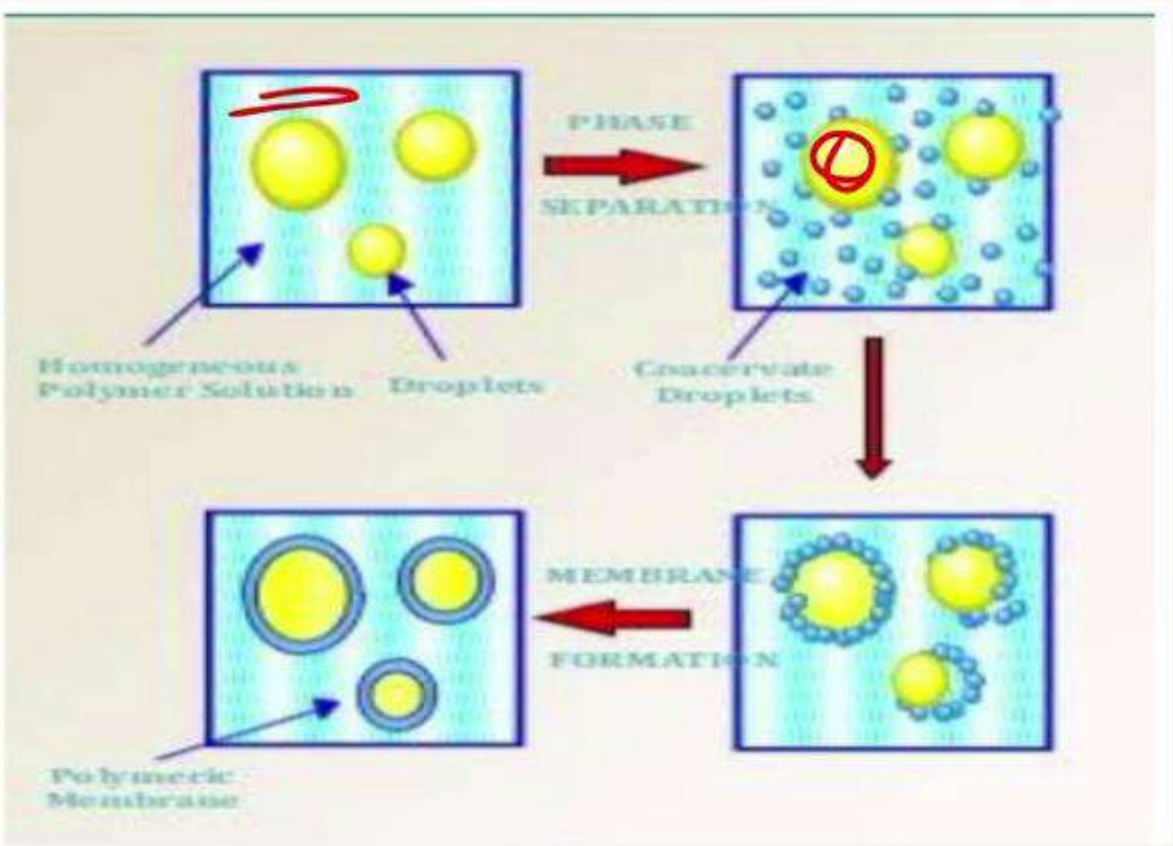
Various techniques are used to create microcapsules. Some of the most common methods include:

1. Coacervation (Phase Separation) Method:
   This technique involves creating a liquid-liquid phase separation, where the coating material is mixed with the core material and a solvent. The coating material undergoes phase separation and forms a membrane around the core.

   Steps:
   a. Dissolve coating material in a solvent.
   b. Add the core material to the solution.
   c. Allow the phase separation to form a coacervate (a gel-like substance).
   d. Solidify the coacervate to form microcapsules.

Techniques of Microencapsulation

1.Coacervation (Phase Separation) Method:



Techniques of Microencapsulation

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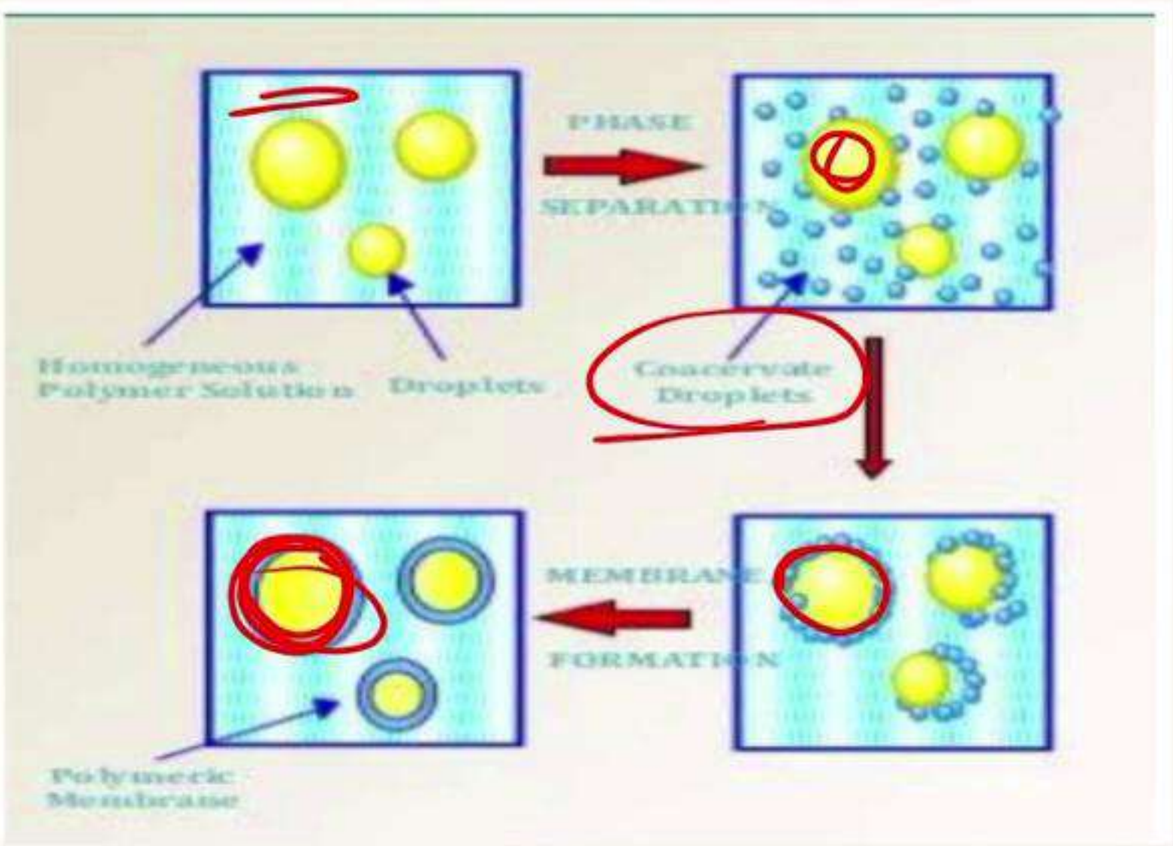

Techniques of Microencapsulation

2. Spray Drying:

A core material is sprayed in the form of a fine mist into a hot air stream, where the solvent evaporates, leaving the encapsulated material.

Steps:

a. Core material and coating are dissolved in a solvent.

b. The mixture is sprayed into a heated chamber.

c. As the solvent evaporates, the coating material solidifies around the core, forming microcapsules.

Techniques of Microencapsulation

3. Solvent Evaporation:

   A core material is sprayed in the form of a f ne mist into a hot air stream, where the solvent evaporates, leaving the encapsulated material.

Steps:

a. Dissolve polymer in a solvent.
b. Add core material (liquid or solid).
c. Evaporate the solvent under controlled conditions to form solid microcapsules.

Techniques of Microencapsulation

Microencapsulation Method		Particle Size (μm)
Air Suspension (Wurster Process)	Used for encapsulation of solid only	35-5000
Pan Coating		600-5000
Multiorifice centrifugal process	Both for Solid & Liquid	1-5000
Coacervation phase separation		2-5000
Solvent evaporation		5-5000
Spray drying & Congealing		600

Techniques of Microencapsulation

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Spray drying & Congealing		600

Techniques of Microencapsulation

4. Extrusion:

   The core material is mixed with the coating solution and extruded through a nozzle into a bath containing a hardening solution.

Steps:

a. Prepare a mixture of core and coating material.
b. Extrude through a nozzle into a hardening solution (e.g., calcium chloride for alginate).
c. The extruded material forms microcapsules as it hardens..

Techniques of Microencapsulation

4. Extrusion:

   The core material is mixed with the coating solution and extruded through a nozzle into a bath containing a hardening solution.

Anti tack Agent →

Steps:

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Channeling Agent ->

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c. The extruded material forms microcapsules as it hardens..

Lecture Based Quiz

Answer 1:

B) To protect the core material and control its release

Explanation:

Microencapsulation is primarily used to protect sensitive active ingredients from environmental factors (e.g., light, moisture, oxygen) and to control the release of the core material. It allows for sustained, delayed, or targeted release of drugs, improving their efficacy and safety.

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Microencapsulation

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Microencapsulation

GPAT & NIPER 2025 CRASH COURSE

Physical Pharmacy
Lecture -01
States of Matter

GPAT & NIPER 2025 CRASH COURSE

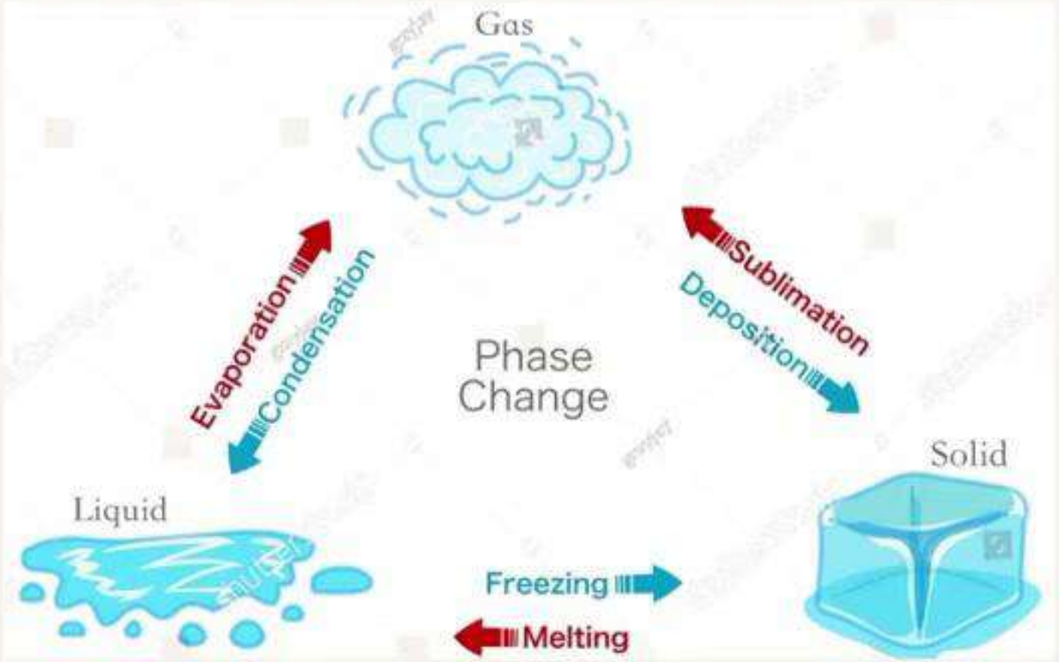
Physical Pharmacy
Lecture -01
States of Matter

States of Matter

Matter is a substance which occupies space and possess rest mass, especially as distinct from energy.

Matters can be classified as

- Solid:(Ex-Tablet, capsule)
- Liquid:(Ex-Syrup, solution)
- Gas:(Ex-Aerosol)



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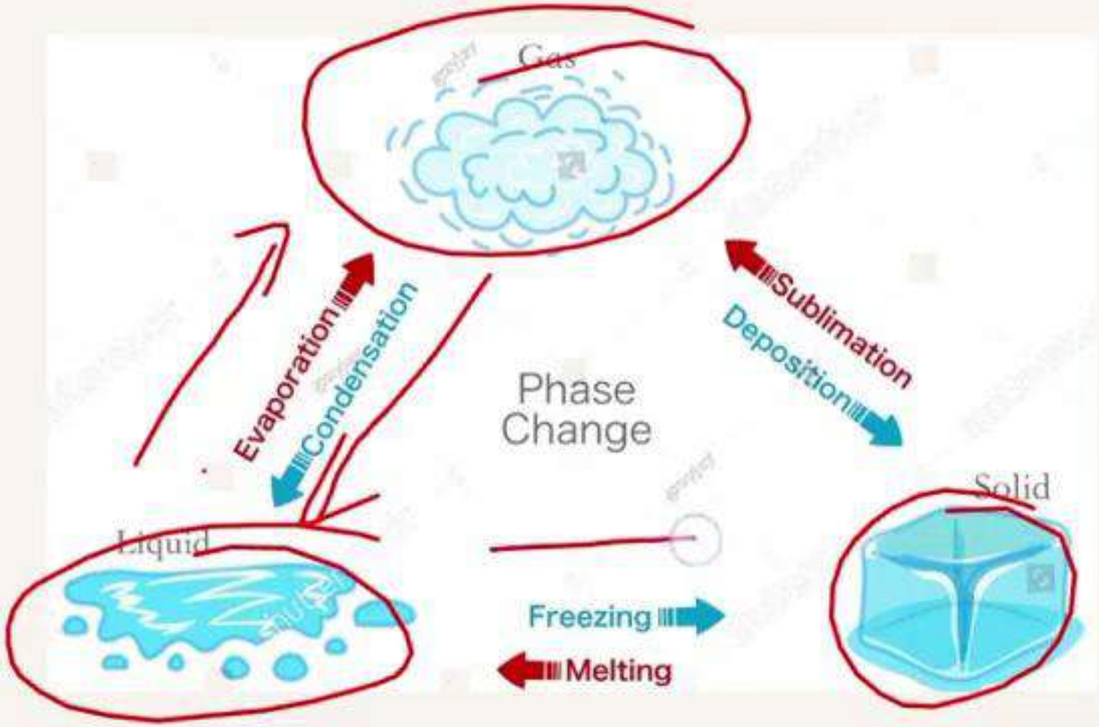


Ink

Blank Screen

Solid ⟷ Liquid ⟷ Gas

Ink

Blank Screen

Solid ↔ Liquid ↔ Gas ↔ Plasma/ionise

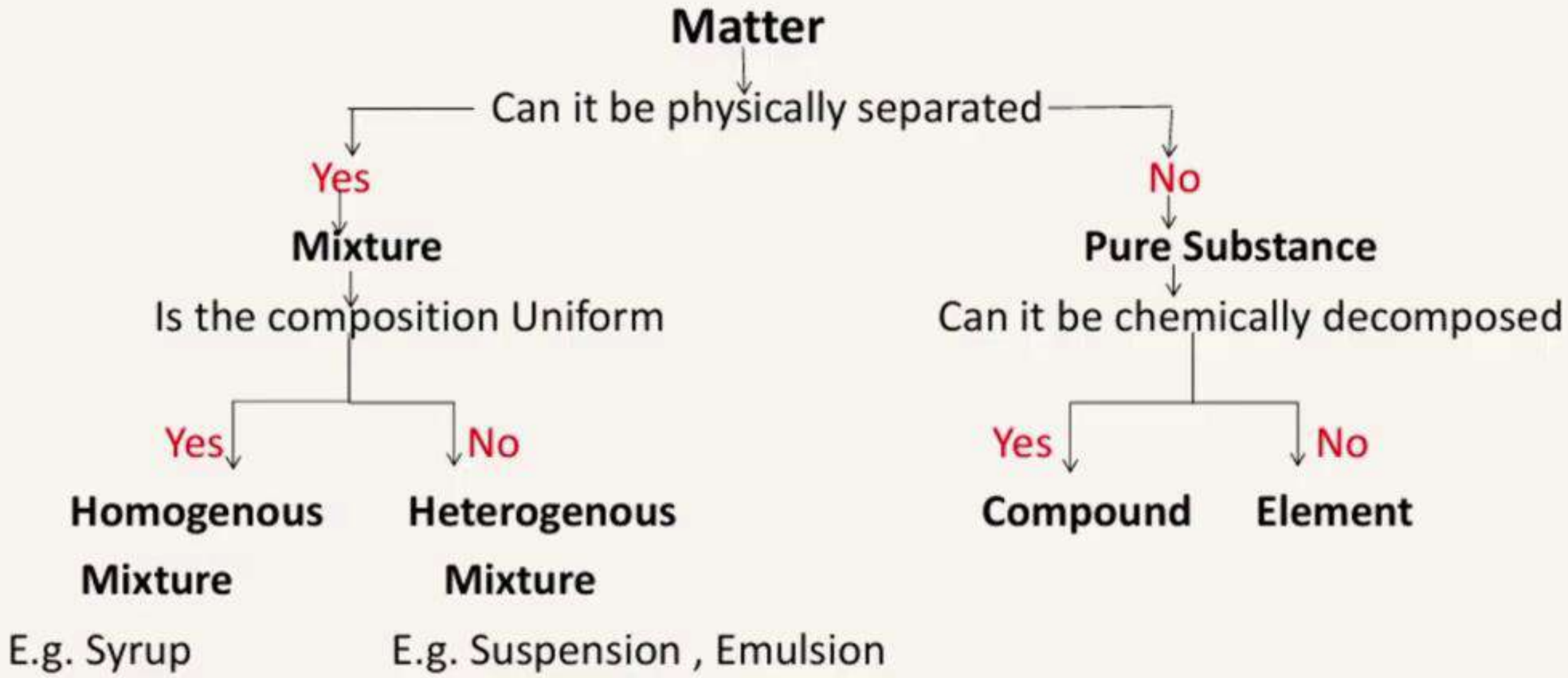
Liquid

Form of gas

0K/-273 C

Bose Einstein Condensate (BEC)

States of Matter



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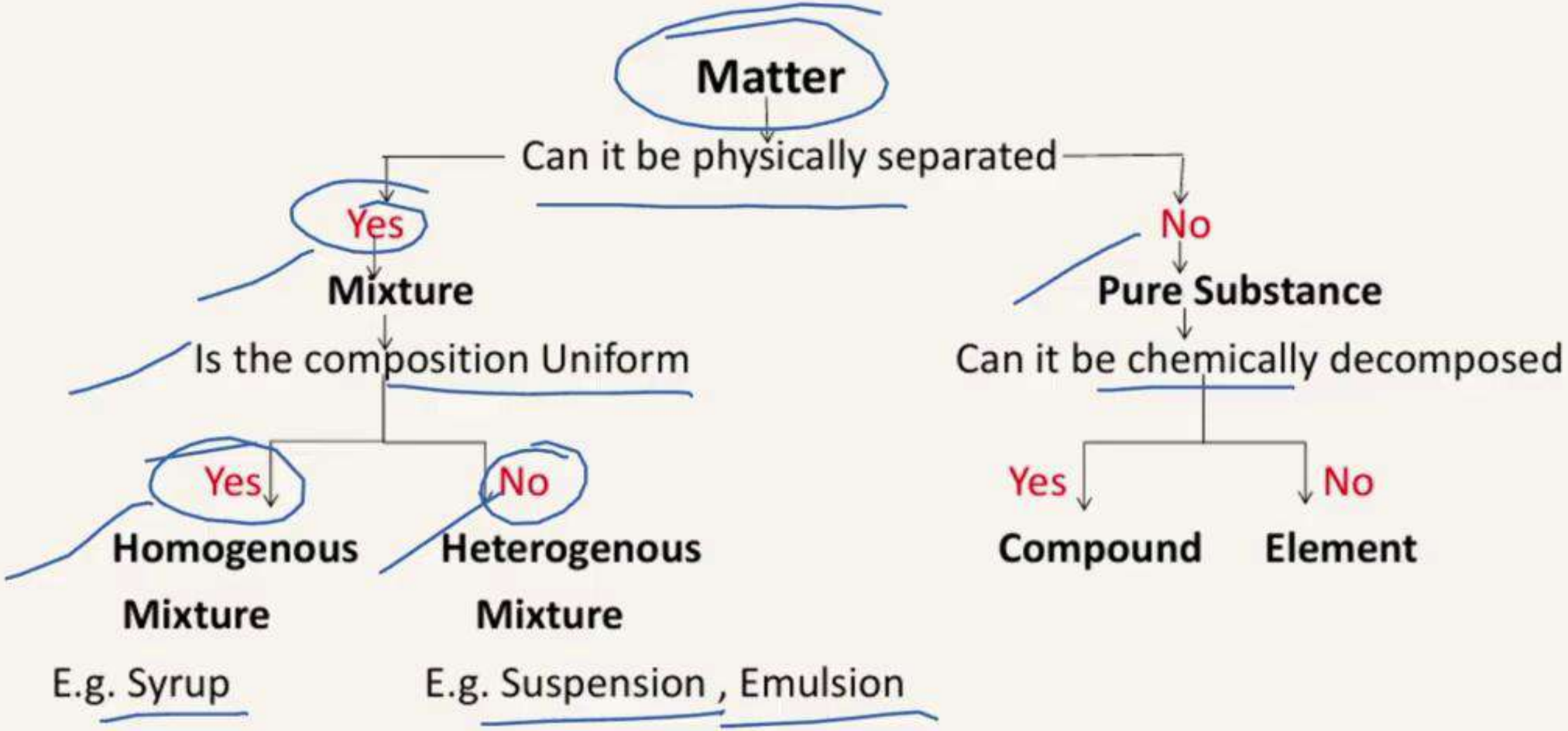


States of Matter

Properties	Solids	Liquids	Gases
Volume	Fixed Volume	Fixed Volume	No fixed volume
Shape	Fixed definite shape	No fixed defnite shape takes shape of container	No fixed definite shape
Intermolecular space	Least	Less but more than solid	Maximum
Force of Attraction	Maximum	Less than solid	Least
Fluidity	Cannot flow	Can flow	Can flow
Compressibility	No compressibility	Slight compressiility	High compressibility
Diffusion	No diffusibility	Slight diffusibility	High diffusibility

Properties of Matter

1. Additive Property

Properties depends on the total contribution of atoms in the molecules.

E.g. - Molecular weight, Mass

2. Constitutive Property

Properties depend on the arrangement of number and kind of atoms within a molecule .

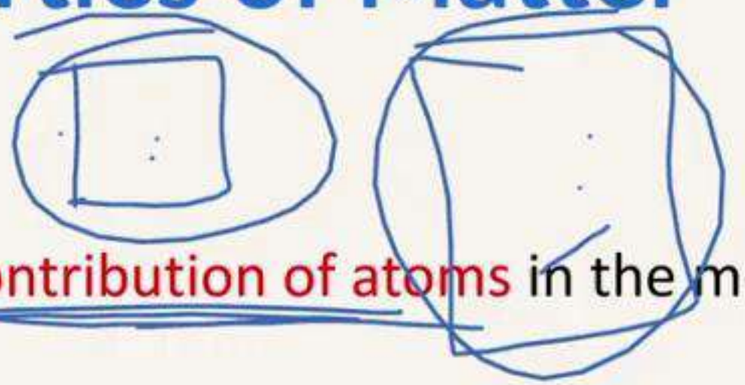
E.g.- Refractive index , Optical rotation

3. Colligative Properties

Properties depend on the number of species or particles present in a given solution .

E.g.- Osmotic Pressure , Lowering of vapour pressure , Freezing point depression , Elevation in boiling point .

Properties of Matter



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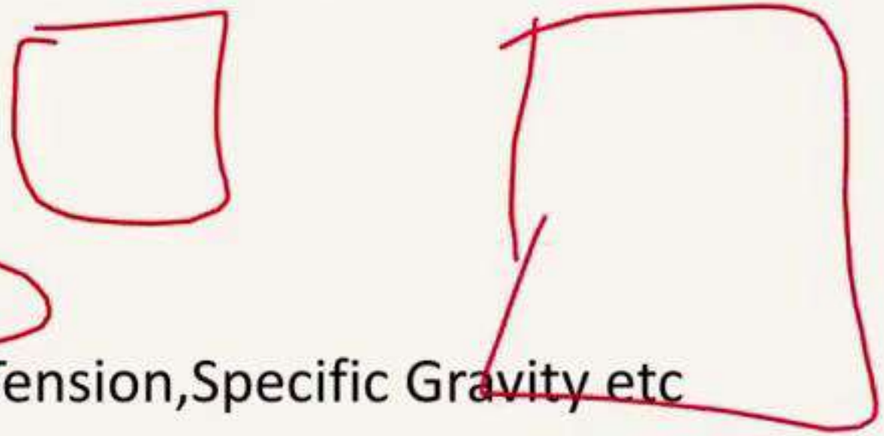

Types of Properties -

1. Intensive Properties

Properties that do not depend upon volume .

E.g.- Temperature, Density, Viscosity,Surface Tension,Specific Gravity etc

2. Extensive Properties

Properties that depend upon volume (quantity) of substance .

E.g.- Mass, Length, Volume .

THE GASEOUS STATE

- A gas is a substance that has no fixed size or shape.
- The physical behavior of gases is independent of the chemical nature of the molecules.
- The Barometer is used for pressure measurement.
- Molecules in a gas are always in a state of vigorous & rapid motion and travel in random paths.
- Gases have a lower density than other states of matter, such as solids and liquids

Ink

Blank Screen

$16^{\circ}C$

$K = C + 273.15$

$\Rightarrow 16 + 273.15$

$\Rightarrow$

IDEAL GAS LAW

The laws that describe ideal gases are collectively called **Ideal Gas Laws**.
Refer to ideal situation where no intermolecular interaction exist and no energy is exchanged upon collision.

PV = nRT

Where,

P = Pressure
V = Volume
R = Gas constant (1.987 calories/mole)
T = Absolute temperature

- The conditions 0 ^{0}C and 1 atm are called standard temperature and pressure (STP).
- Experiments show that at STP, 1 mole of an ideal gas occupies 22.414 L

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2021

IMPORTANT LAWS & EQUATIONS

1) Boyle 's law :

This law states that the pressure of a fixed amount of gas at a constant temperature is inversely proportional to the volume of the gas.

$$P_1V_1 = P_2V_2$$

Charles Law: This law states that the pressure of a fixed amount of gas at a constant

"At a fixed pressure, the volume of a gas is proportional to the temperature of the gas."

$$V \propto T$$

3) Gay-Lussac's law: This law is a special case of ideal gas law. This law applies to ideal gases held at a constant volume allowing only the pressure and temperature to change.

$$P_1/T_1 = P_2/T_2$$

IMPORTANT LAWS & EQUATIONS

4) Avogadro law:

This law states that the volume of a sample gas is directly proportional the number of moles in the sample at constant temperature and pressure.

$$V \propto n$$

$$V_1/n_1 = V_2/n_2$$

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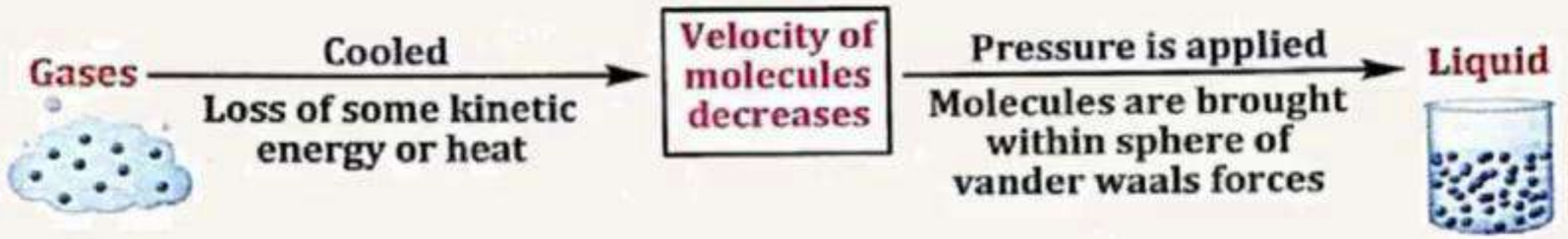
LIQUIFACTION OF GASES

When pressure on a gas is increased, its molecules closer together, and its temperature is reduced, which removes enough energy to make it change from the gaseous to the liquid state.



PRINCIPLES OF LIQUIFACTION

Cooling Effect:

Reducing the temperature lowers the kinetic energy of gas molecules, making them more likely to condense into a liquid.

Application of Pressure:

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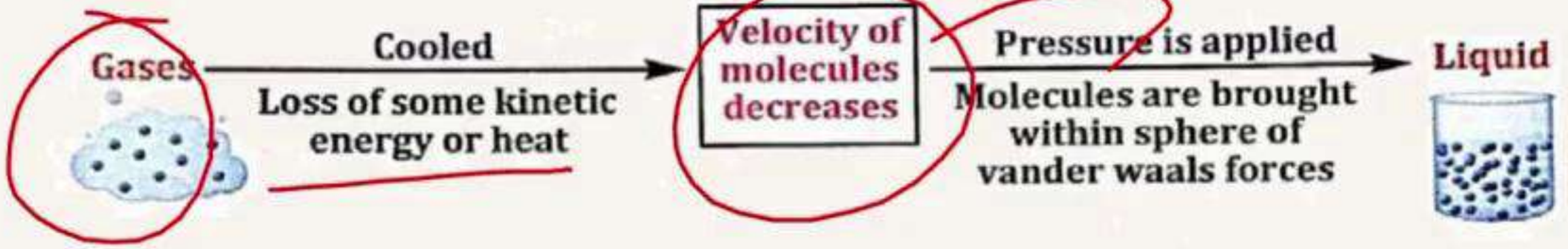

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LIQUID STATE

Vapour Pressure of Liquid:

- The rate of condensation equals the rate of vaporization at a definite temperature, the vapor becomes saturated, and a dynamic equilibrium is established.
- The pressure of the saturated vapor above the liquid is then known as the equilibrium vapor pressure.

Clausius-Clapeyron Equation:

The relationship between the vapor pressure and the absolute temperature of a liquid is expressed by the Clausius-Clapeyron equation

$$\log \frac{P_1}{P_2} = \frac{\Delta H_v}{2.303R}\left(\frac{1}{T_2} - \frac{1}{T_1}\right)$$

Where ,P_1 and P_2 are the vapor pressures at absolute temperatures T_1 and T_2 & ΔH_v is the molar heat of vaporization.

LIQUID COMPLEXES

Complex fluids are binary mixtures that have coexistence between two phases:

1. Solid- liquid (suspension and solution of macromolecules such as polymers)
2. Solid-gas (granular)
3. Liquid-gas (foams) or
4. Liquid-liquid (emulsions).

They exhibit usual mechanical responses to applied stress or strain due to the geometrical constraints that the phases coexistence imposes.

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Liquid Crystal (Mesophase) Phase

- When heated, solids do not directly convert into the isotropic liquid phase but assume an intermediate phase known as the liquid crystal phase.
- This phase exists between the solid and liquid states.
- It possess characteristics of both liquids & crystalline solids.
- A fourth state of matter is called liquid crystal state or mesophase or (mesomorphic phases). Liquid crystals retain their dual liquid and solid nature only over a certain range of temperatures and pressure.
- **At high temperature or low pressure -** It transforms into an ordinary liquid .
- **At low temperature and high pressure -** It freezes into an ordinary solid .
- Properties of liquid crystals like solids - Orderly arrangement of particles , optical activity etc.
- Properties of liquid crystal like liquids - Fluidity , Viscosity , Surface tension .

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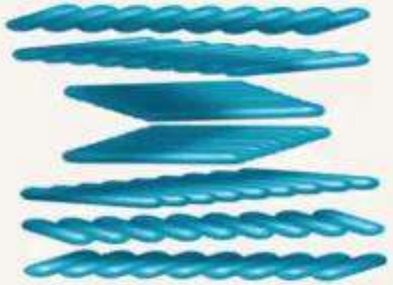
Types of Liquid Crystals

Type	Description
Nematic Liquid Crystals (Thread-like)	Molecules are parallel but mobile in three directions; rotation is restricted.
Smectic Liquid Crystals (Soap-like/Grease-like)	Molecules are layered and mobile in two directions but rotate in one axis.
Cholesteric Liquid Crystals (Crystal type)	Molecules make a **180° turn**, forming a **helix structure**. Involved in **atherosclerosis**. *(GPAT - 2011)*

Nematic phase

Smectic phase



Cholesteric phase

Solids

- Solid is a state of matter that has a fixed shape and volume. In solids, particles are tightly or closely packed.
- The gaps between the particles are tiny and hence it is tough to compress them.
- The molecules of a solid are held together by strong bonds which imparts a high melting point to these substances. In order to their decreasing strengths, these include metallic bonds, ionic bonds, valence bonds and molecular bonds.
- There are two types of solid Crystalline Solid and Amorphous Solid

1. Crystalline solid: In crystalline solids the particles are arranged in a 3 dimensional order. The particles have equal intermolecular forces.

- They have sharp melting point and are anisotropic.
- They are called true solids.

Example: Benzoic acid, Diamond.

Solids

Amorphous solids:

Word amorphous is derived from greek word which means shapeless.

It has an irregular arrangement of solid particles. The intermolecular forces are not equal. Also, the distance between particles varies.

They have an undefined geometric shape.

They are also called supercooled liquids.

They are isotropic in nature

Example: Naphthalene, glass

The smallest geometrical portion of the crystal, which repeats to build the entire structure, is called a unit cell.

A three-dimensional arrangement is called a crystal lattice or space lattice

Binding Forces Between Molecules

- Repulsive and attractive forces
- Intramolecular forces
- Intermolecular forces
- Bond energy

Repulsive and Attractive Forces

- **Attractive Forces:**
  a. These forces pull molecules or atoms together.
  b. They include van der Waals attractions, hydrogen bonds, dipole-dipole interactions, and ion-dipole attractions.

- **Repulsive Forces:**
  a. When molecules get too close, their electron clouds overlap, leading to strong repulsive forces (as dictated by the Pauli exclusion principle).
  a. These forces prevent the collapse of matter into an overly compact state.

- **Balance:**
  The equilibrium distance between atoms or molecules in any material is determined by the balance between these attractive and repulsive forces.

Intramolecular Forces (IMFs)

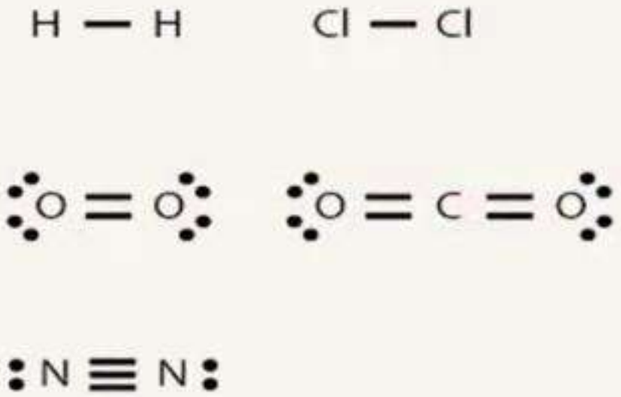
Ionic bond:

This bond is formed by the complete transfer of valence electron(s) between atoms.

Covalent bond:

This bond is formed between atoms that have similar electronegativities—the affinity or desire for electrons.

They share electrons in order to achieve octet configuration and become more stable ; (three type single ,double & triple bond)



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This type of covalent bonding specifically occurs between atoms of metals

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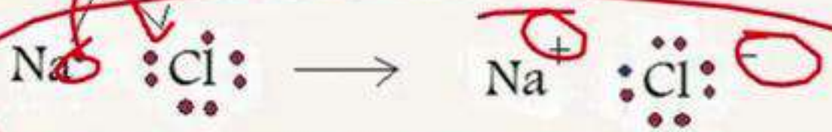

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Van der Waals Forces

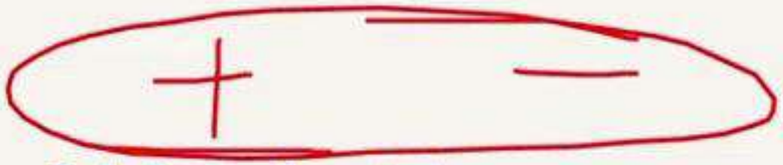
VanderWaal interactions are weak forces that involve the dispersion of charge across a molecule called a dipole

VanderWaal interactions can be classified into:

A. Dipole–dipole interaction ,orientation effect ,or Keesom force

B. Dipole-induced dipole interaction ,induction effect ,or Debye force

C. Induced dipole-induced dipole interaction ,dispersion effect or London force



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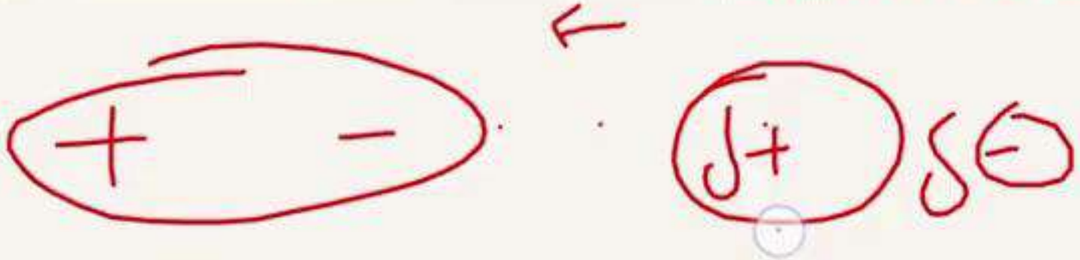

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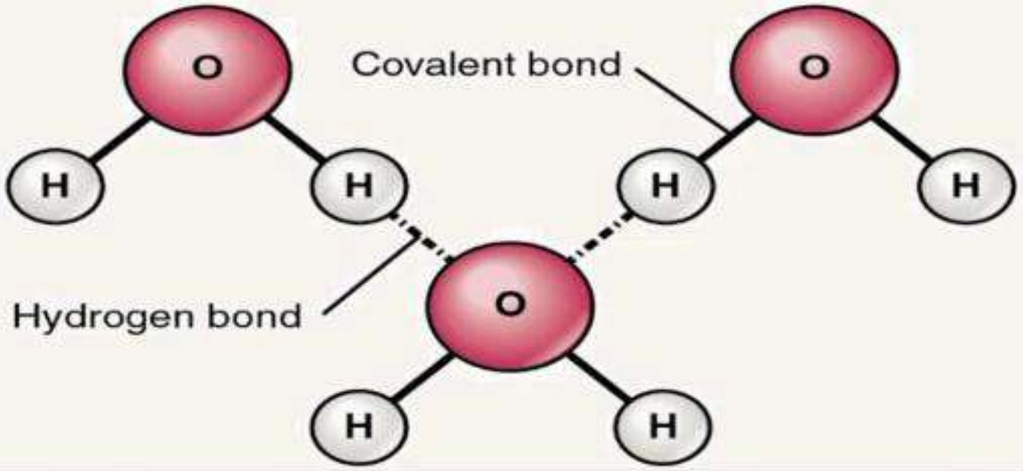
Hydrogen bond

Hydrogen bond is a strong type of dipole-dipole interaction hydrogen that occurs between a molecule containing a and a strongly electronegative atom such as fluorine atom ,oxygen ,or nitrogen

In order to create the bond ,the hydrogen atom must be covalently attached to another electronegative atom



Intermolecular Forces (IMFs)

Ion-Dipole Interactions:

An ion-dipole interaction is the result of an electrostatic interaction between a charged ion and a molecule that has a dipole

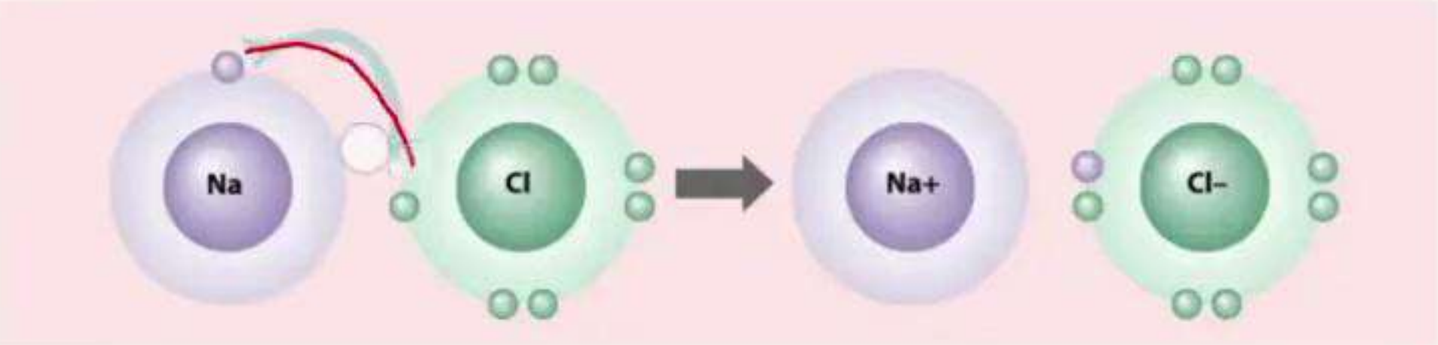
They play a crucial role in the dissolution of ionic compounds in polar solvents (e.g., salt in water).

Ion-Induced Dipole Interactions:

Ion Induced dipole forces occur between a charged ion and a non polar molecule. Though generally weaker than ion-dipole interactions, they are important in many solvation processes.

BOND ENERGY

- Bond energy is a measure of bond strength.
- It is the heat required to break one mole of molecules to their individual atoms



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Physical Pharmaceutics

Lecture 2

Micromeritics and Powder Rheology

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Micromeritics and Powder Rheology

INTRODUCTION

- The Science and Technology of small particles is known as Micromeritics
- Micromeritics involve the study of small particles and of a few microns size.
- The term was coined by Joseph Marius DallaValk.
- 1micrometer = 10^{3} mm(millimeters) or 10^{-6} m (meter), 10^{-4} cm(centimeter), 1000 nm (nanometer)
- It is the study of various characteristics like Particle size and size distribution,Particle shape and surface area, Porosity, Density, Flow property etc

APPLICATIONS OF MICROMERITICS

Release and Dissolution	Particle size and surface area influences the release of drug from dosage form.
Absorption and Drug action	Particle size and surface area influences the drug absorption and subsequently the therapeutic action. Reduction of particles size can increase the rate of absorption of and consequently

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Physical stability	The particle size in a formulation influences the physical stability of the suspension and emulsion.
Dose Uniformity	Good flow properties of granules and powders are important in the manufacturing of tablet and capsules.

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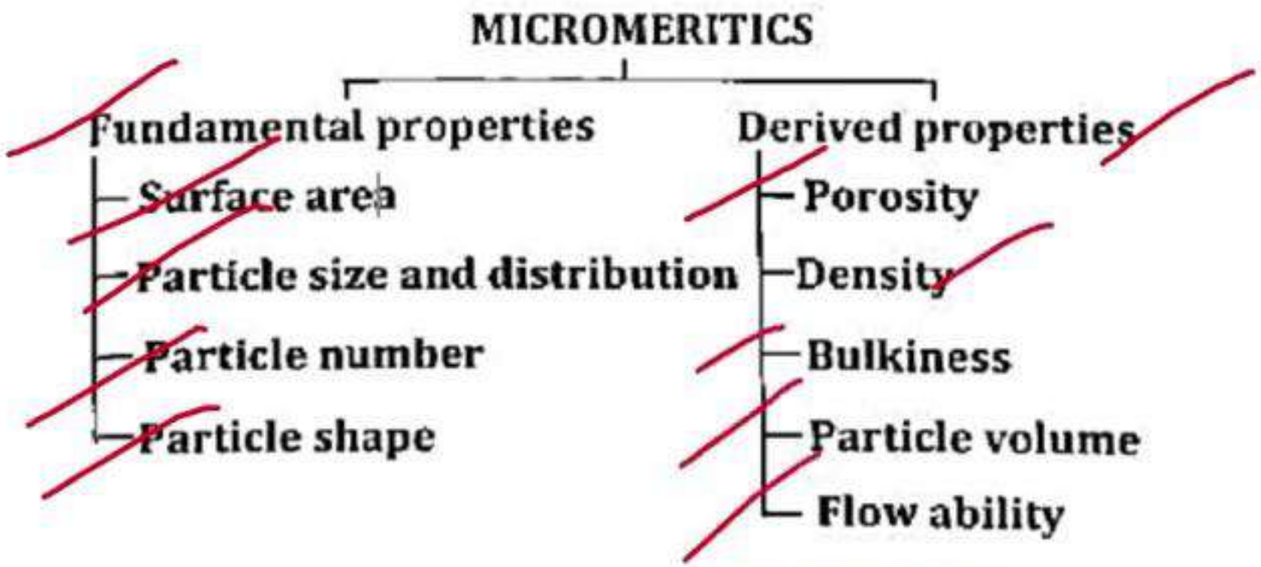

PARTICLE SIZE

- It is expressed by radius or diameter.
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Flow ability

PARTICLE SIZE

- It is expressed by radius or diameter.
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- One micrometer is equal to 10^{-3} mm or 10^{-6} m
- One millimicrometer is called one nanometer (nm)
- One nanometer = 10^{-9} m or 10^{-6} mm or 10^{-3} µm
- 1 m = 1000 mm
- 1 mm = 1000 µm
- 1 µm = 1000 nm
- Size of the particles may be expressed as follows:

DIAMETER	DESCRIPTION
Surface diameter, d_s	It is the diameter of a sphere having the same surface area as that of an asymmetric particle.
Volume diameter, d_v	It is the diameter of a sphere having the same volume as that of an asymmetric particle.
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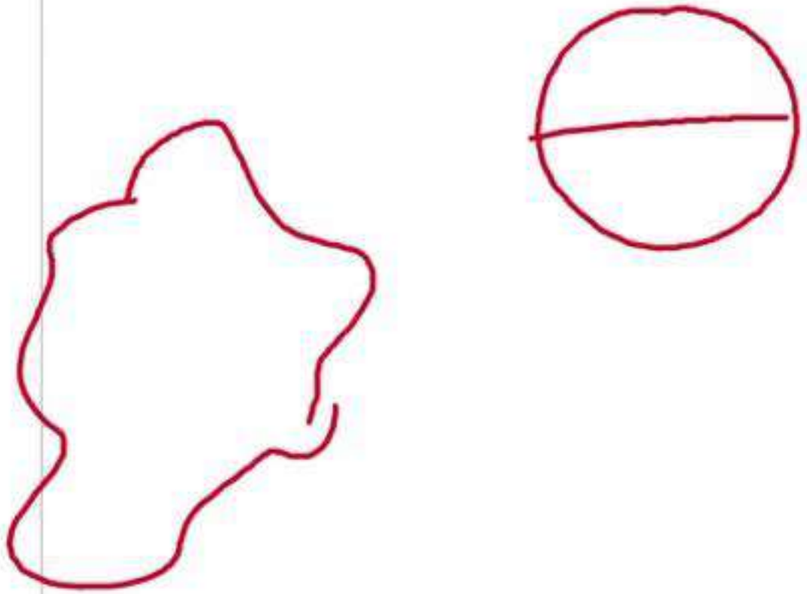

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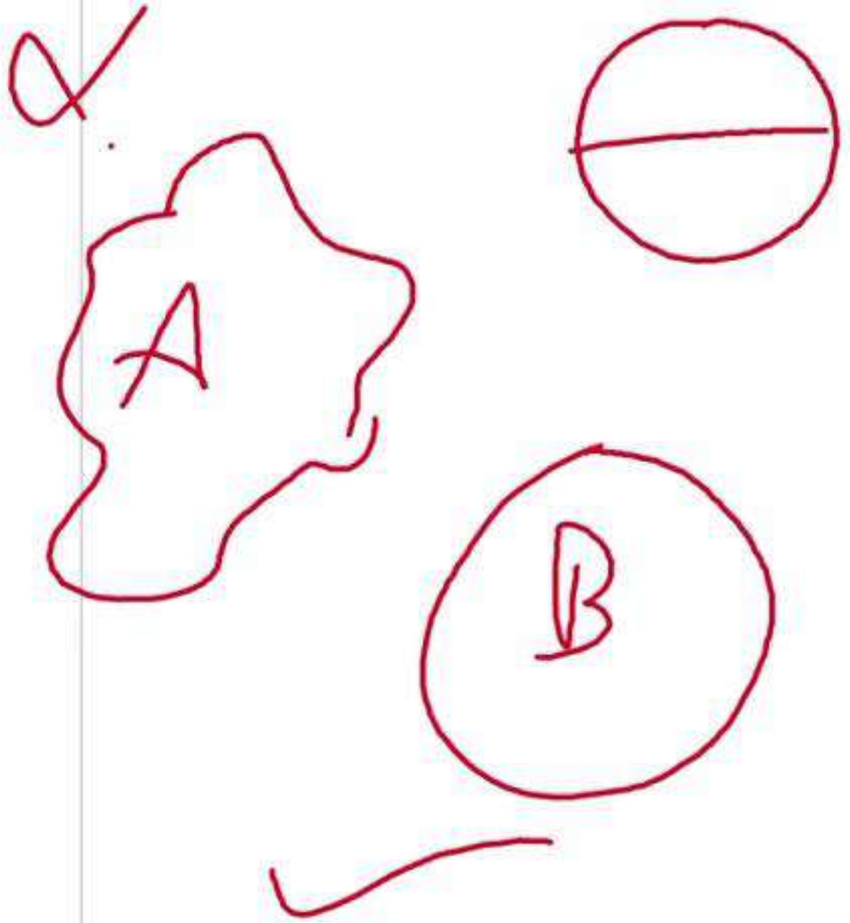

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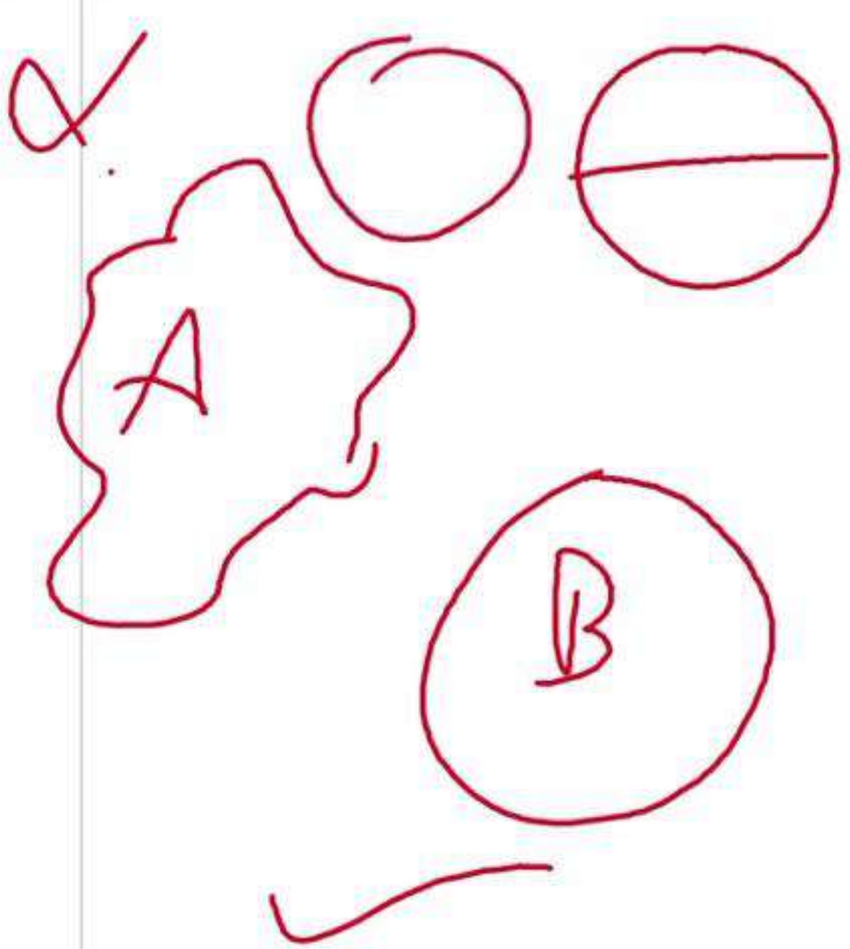

- One nanometer = 10^{-9} m or 10^{-6} mm or 10^{-3} µm
- 1 m = 1000 mm
- 1 mm = 1000 µm
- 1 µm = 1000 nm
- Size of the particles may be expressed as follows:

DIAMETER	DESCRIPTION
Surface diameter, d_s	It is the diameter of a sphere having the same surface area as that of an asymmetric particle.
Volume diameter, d_v	It is the diameter of a sphere having the same volume as that of an asymmetric particle.
Projected diameter, d_p	It is the diameter of a sphere having the same area as the asymmetric particle as observed under a microscope.
Stoke's diameter, d_{st}	It is the diameter of an equivalent sphere undergoing sedimentation at the same rate as the asymmetric particle.
Sieve diameter, d_{sieve}	Diameter of a sphere that passes through the same sieve aperture as the asymmetric particle.
Volume surface diameter, d_{vs}	Diameter of a sphere that has the same volume-to-surface area ratio as the asymmetric particle.
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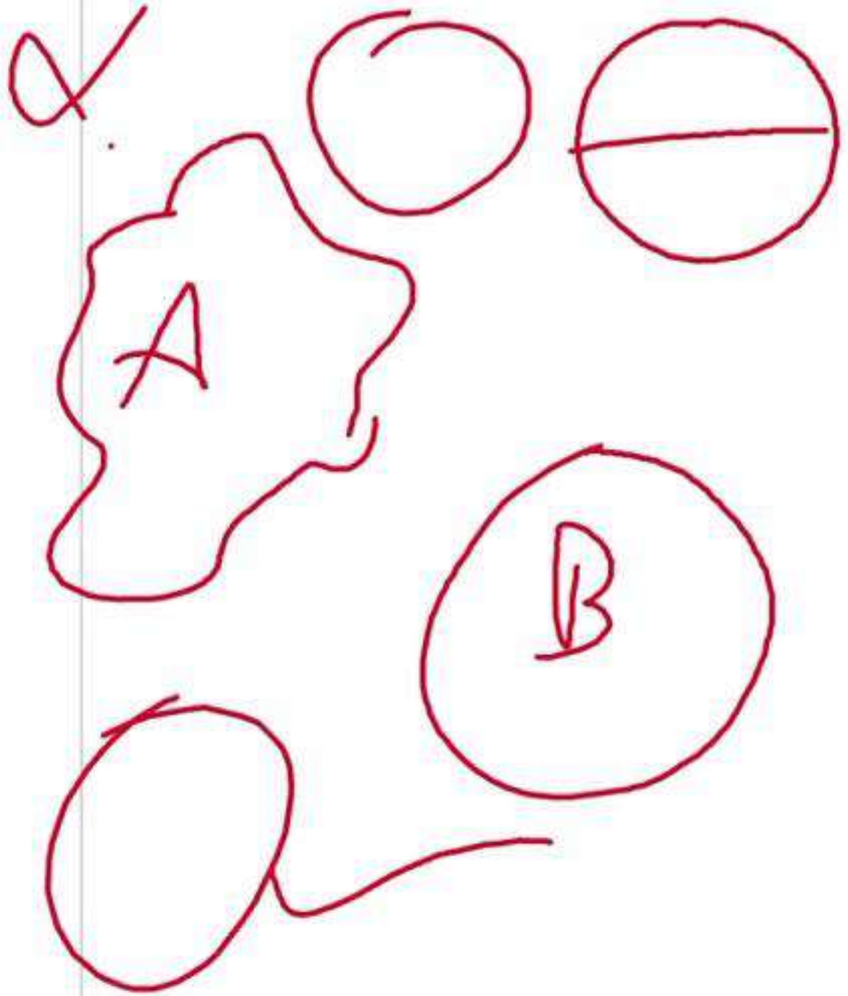

PARTICLE NUMBER

- The number of particles per unit weight, **N**, which is expressed in terms of $d_v n$.
- The volume of a single particle is $\pi d_v n^3/6$.
- The mass (Volume × Density) is $\pi d_v n^3 \rho/6$.
- The number of particles per gram is then obtained from the proportion:

$$N = \frac{6}{\pi d_{vn}^3 \rho}$$

METHODS OF PARTICLE SIZE DETERMINATION

METHOD	SIZE RANGE	INSTRUMENT	COMMENT
	0.2-100 μm	Optical microscope	✓ Popular measurements are the Feret diameter, Martin diameter,

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TERMINATION

$d_{vn} \Rightarrow 2.41\ \mu m$

$\rho = 3\ g/cm^3$

$N \Rightarrow \frac{6}{3.14 \times (2.41$

METHODS OF PARTICLE SIZE DETERMINATION

METHOD	SIZE RANGE	INSTRUMENT	COMMENT
Microscopy	0.2-100 µm	Optical microscope	✓ Popular measurements are the Feret diameter, Martin diameter, and Projected area diameter. ✓ It can detect the presence of particles of more than one component. ✓ **Disadvantage**: The diameter is obtained from only 2 dimensions of the particle (length and breadth). No estimation of the depth.
	0.001-0.1 µm	Transmission Electron Microscope (TEM)	
	0.1-1000 µm	Scanning Electron Microscope	
Scanning Electron Microscopy (SEM) **Sieving**	50-1500 µm	Mechanical shaker	Standard sieves are used, calibrated by the National Bureau of Standards.
Sedimentation	1-200 µm	Anderson Pipette Gravity sedimentation	The application of ultracentrifugation to determine the molecular weight of high polymers. Expressed in Stoke's diameter
Conductivity Method			Also known as stream scanning

Stop

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Sedimentation Formula

$$V = \frac{2r^2 g(d_s - d_c)}{9\eta}$$

Where:

- V = Velocity of separation (cm/sec)
- g = Acceleration due to gravity
- r = Droplet radius (cm)
- d_s = Density of disperse phase (g/cm^3)
- d_c = Density of continuous phase (g/cm^3)
- η = Viscosity of the continuous phase (g/cm.sec)

The Particle Diameter by Microscopy Method

Diameter Type	Description

- η = Viscosity of the continuous phase (g/cm.sec)

The Particle Diameter by Microscopy Method

Diameter Type	Description
Projected area diameter	It is the diameter of a circle with the same area as that of the particle observed on the surface. Microscopic method of evaluation is Projected diameter
Martin diameter	The length of the line bisecting the image of the particle. The bisecting line is taken parallel to a fixed direction, irrespective of the orientation of the particle.
Feret diameter	It is the distance between two tangents on opposite sides of the particle parallel to a fixed direction

Physical Pharmacy HOME INSERT DRAW VIEW

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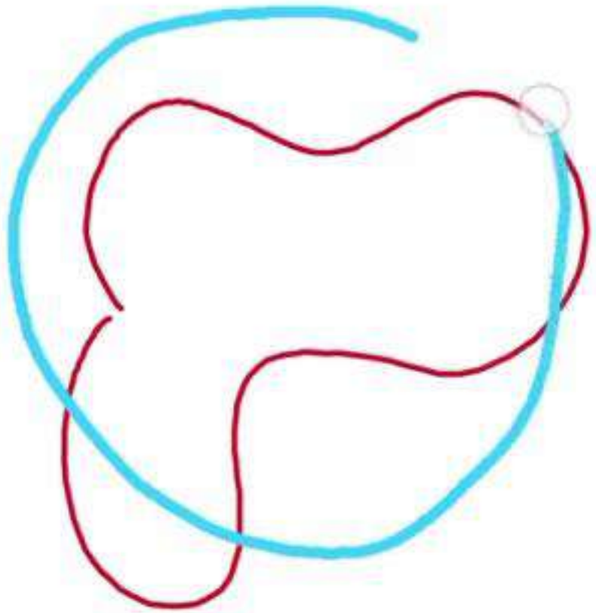
g the image of the particle. allel to a fixed direction, irrespective cle.
tangents on opposite sides of the



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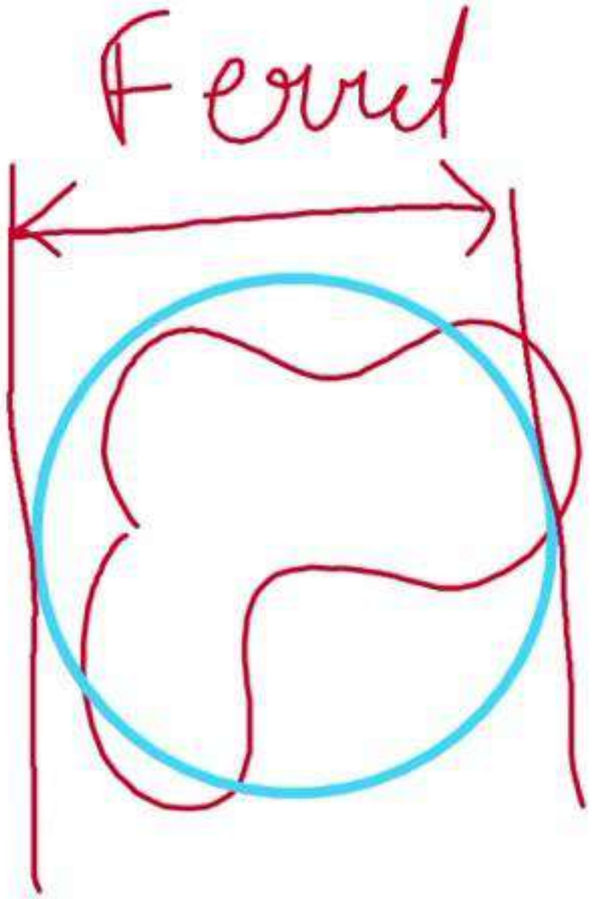

n.sec)

hod

Description
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secting the image of the particle. n parallel to a fixed direction, irrespective particle.
en two tangents on opposite sides of the d direction

Surface Area

- As particle size decreases, surface area increases.
- Two primary methods for surface area calculation:
  1. **Adsorption method**
  2. **Air permeability method**

DETERMINATION OF SURFACE AREA

FEATURES	ADSORPTION METHOD	AIR PERMEABILITY METHOD
Surface area measured by	Nitrogen adsorption using BET equation.	Air resistance through packed powder.
Equation	$\log \frac{P_2}{P_1} = \frac{\Delta H_v (T_2 - T_1)}{2.303 R T_1 T_2}$	$V = \frac{A}{\eta S_w^2} \cdot \frac{\Delta P t}{K l} \cdot \frac{\varepsilon}{(1-\varepsilon)^2}$
Instrument	Quantasorb [GPAT - 2022]	Fisher subsieve sizer

DERIVED PROPERTIES OF POWDERS

1. **Adsorption method**
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DERIVED PROPERTIES OF POWDERS

- ✓ Size or diameter is a fundamental property of a particle.
- ✓ Volume, density, porosity etc., are the properties derived from fundamental properties. e.g. Volume can be calculated from the diameter of the particle (4/3 πr 3).

Density

True Density:

Stop

eases.
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BET → Brunauer Emmett Teller

→ Por

Stop

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→ Poiseuille

→ Kozeny-

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True Density:

Material itself (excludes voids). Measured via gas displacement (He pycnometer)

$$\frac{\text{Weight of powder}}{\text{True volume of powder}}$$

Stop

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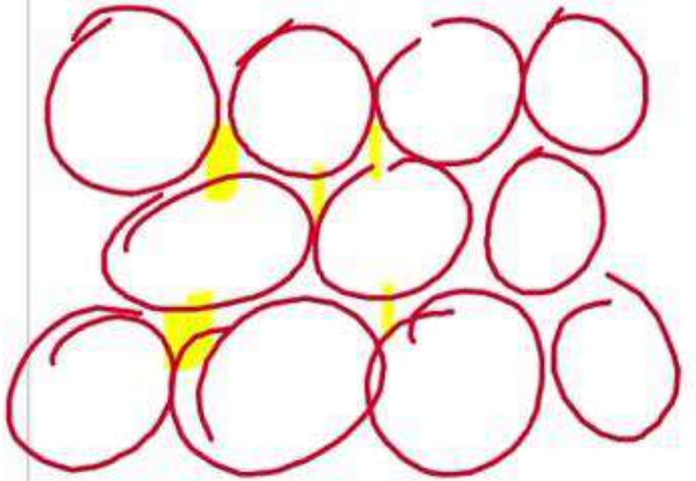

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Material itself (excludes voids). Measured via gas displacement (He pycnometer)

$$\frac{\text{Weight of powder}}{\text{True volume of powder}}$$

Granule Density:

Includes intraparticle pores. Measured via mercury displacement

$$\frac{\text{Granule weight}}{\text{Granule volume}}$$

Physical Pharmaceutics **Lecture 2** **GPAT 2025 FREE CRASH COURSE**

Bulk Density:

Includes all voids. Measured via bulk density apparatus.

$$\frac{\text{Mass of powder (m)}}{\text{Bulk volume } (V_b)}$$

BULKINESS

- ✓ The reciprocal of bulk density, is often called bulkiness or bulk.
- ✓ Bulkiness increases with a decrease in particle size.
- ✓ In a mixture of materials of different sizes, however, the smaller particles shift between the larger ones and tend to reduce the bulkiness

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POROSITY

- The porosity or voids Ɛ of the powder is defined as the ratio of the void volume to the bulk volume of the packing.
- Porosity is a dimensionless quantity.
- **Void volume**

  V = Bulk volume(V_b) - True volume(V_p)

$$\varepsilon = \frac{V_b - V_p}{V_b}$$

- The higher the porosity, the faster the rate of dissolution.

PACKING ARRANGEMENTS

The arrangement of particles in a powder influences the volume occupied by it.

Packing Arrangements	Porosity

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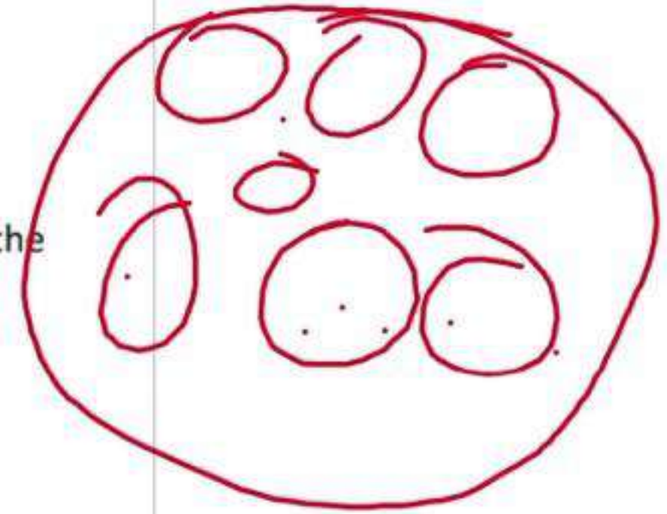
POROSITY



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Packing Arrangements	Porosity
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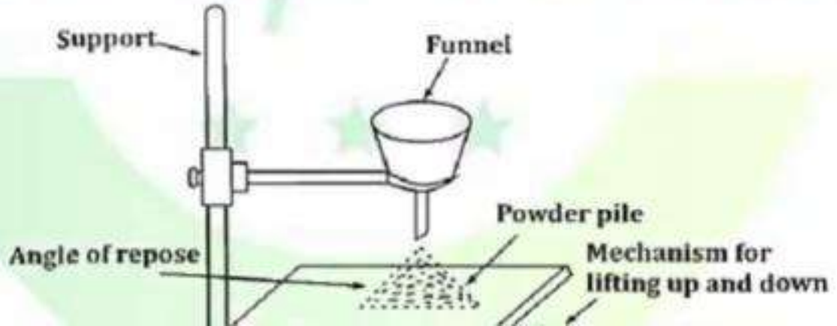
PACKING ARRANGEMENTS

The arrangement of particles in a powder influences the volume occupied by it.

Packing Arrangements	Porosity
Close packing (Rhombohedral Packing)	26%
Loose Packing (Cubic Packing)	48%
Very Closely	Less than 30%
Aggregation & flocculation	Greater than 50%

ANGLE OF REPOSE

- It is usually determined by fixed funnel method and is the measure of the flow ability of powder/granules.
- The maximum angle possible between the surface of a pile of the powder and horizontal plane.
- The rougher and more irregular the surface of the particles, the higher will be the angle of repose.
- For an API of approximately same particle size, the angle of repose will increase with departure from spherical shape.
- Free flowing powders show a flatter cone and have smaller angle of repose.The angle of repose exceeds 50, the powder flow is rarely acceptable for pharmaceutical manufacturing purpose



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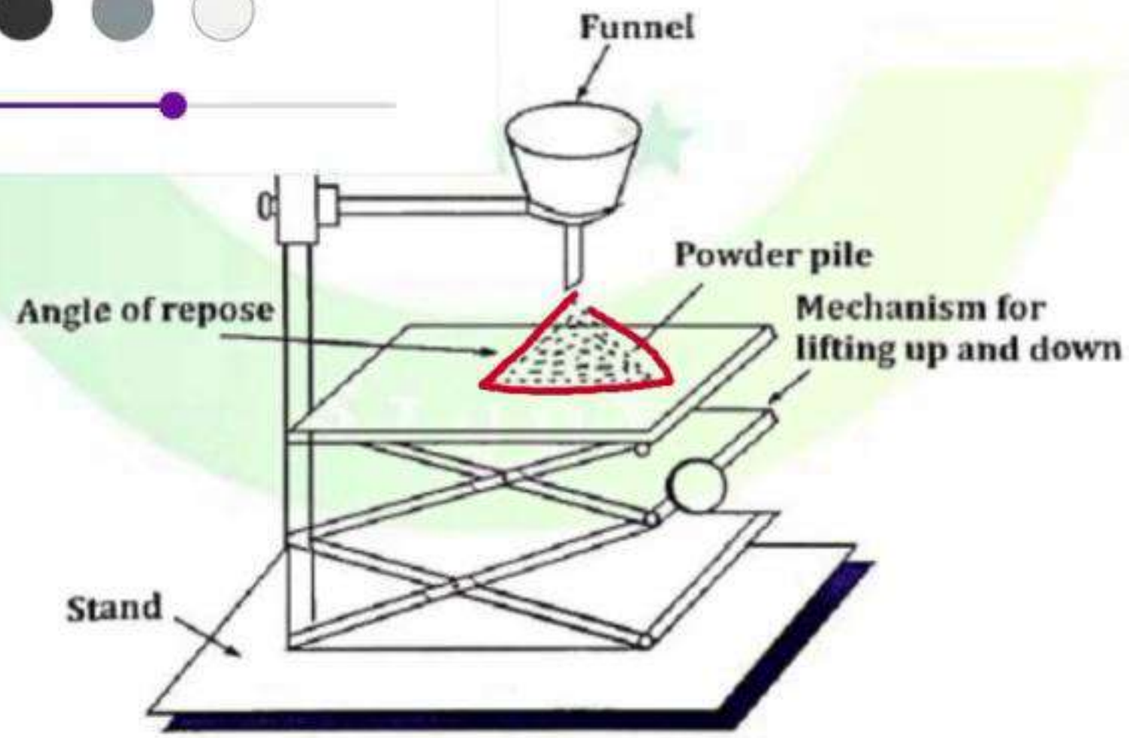

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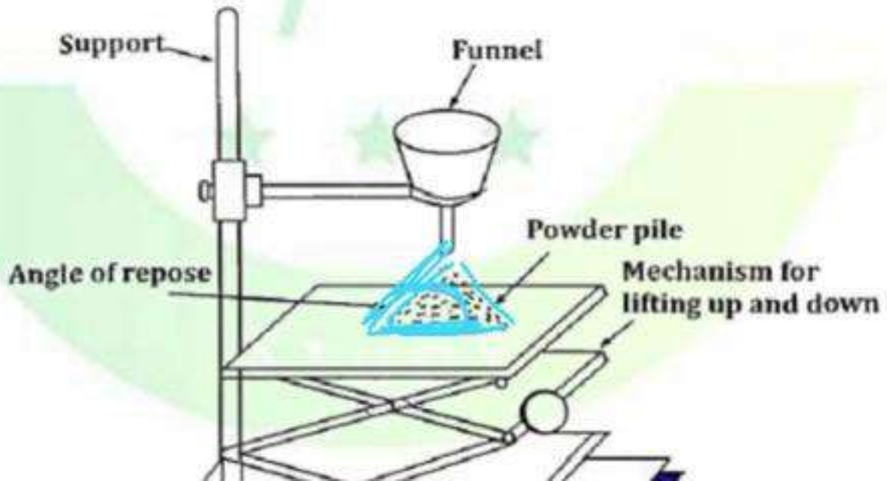

θ, angle of repose, h & r are height and radius of the powder, respectively

Angle of Repose	Powder Flow
25-30	Excellent
31-35	Good
36-40	Fair
41-45	Passable
46-55	Poor
56-65	Very Poor
>66	Very-Very Poor

DISPERSIBILITY

56-65	Very Poor
>66	Very-Very Poor

DISPERSIBILITY

The ability of a material to flow or pour easily over a plane.

$$\text{Dispersibility} = \frac{\text{Weight of powder in watch glass}}{\text{Initial weight of the sample}} \times 100$$

CARR'S CONSOLIDATION INDEX (COMPRESSIBILITY)

- It is indirectly related to the relative low rate, cohesiveness, particle size, shape an moisture content.
- In a free-flowing powder, the bulk density and tapped density would be close in value therefore, the Carr's index would be small

$$\text{Carr's index (\%)} = 100 \left[\frac{(\text{Tapped Density} - \text{Bulk Density})}{(\text{Tapped Density})} \right.$$

reduced

$$\text{Hausner ratio} = \frac{\text{Tapped density}}{\text{Poured or bulk density}}$$

Scale of Compressibility

% Compressibility	Flow description	Hausner's Ratio
5 – 15	Excellent flow	1.0-1.11
12 – 16	Good	1.12-1.18
18 – 21	Fair to Passable	1.19-1.34
23 – 35	Poor	1.35-1.45
33 -38	Very Poor	1.46-1.59

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> 40	Extremely poor	>1.60

Thanks for Watching

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