SOLID DOSAGE FORMS

PHARMACEUTICAL POWDER

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•**Powder** is solid dosage from which contains mixture of finely divided drug and / or chemicals in a dry form that may be intended **for internal use (oral powders) or external use (topical or dusting powder).**

• **Powders** are intimate mixtures of dry, finely divided **drugs with or without excipients** and can be used either internally or externally.

Advantages of Powders

1- More convenient to swallow than tablet or capsules.

2- Powders have increased stability compared to solutions.

3- A large dose that cannot be administered in other forms can be administered as powder.

4- A rapid dispersion of drugs occurs in the stomach when given in powder forms rather than in compressed form.

5- A powder can be dispersed in water or another liquid and more easily swallowed.

6- Can be prepared into granules for use in preparing tablets and or reconstituted to liquid form

7- Used in blending with medicated application as ointments, suppositories and pastes.

Disadvantages of powder:

1-Inaccurate dose.

2- Due to unpleasant taste, drug powders are not the dosage form of choice.

3- Powders are bulky and inconvenient to carry.

4- It is difficult to protect powders containing hygroscopic, deliquescent.

5- Time and expenses require in the preparation of uniform powders are great.

6- Powders and granules are not a suitable method for the administration of drugs that are inactivated in the stomach; these should be presented as enteric-coated tablets.

CLASSIFICATION OF POWDERS

Classification of powders according to:

A- The manner of their dispensing:

1- Divided powders.

a - Simple and compound powders for internal use.

b- Powders for reconstitution.

2- Bulk powder.

a- Bulk powders for internal use:

Oral bulk powders for internal use.

Example: Antacid Oral bulk powders for reconstitution for internal use.

b- Bulk powders for external use:

- Dust.
- Douches.
- Dental
- Insufflations
- Snuff
- Effervescent granules.

Talc powder
(Perforated can)

Dental powder

1- Divided Powders

- Divided powders are similar formulations to bulk powders but individual doses are separately wrapped.
- These are powders **used for potent drugs** (drugs that are effective in low concentrations), it was used before in old days but after development of other dosage forms it became obsolete.
- They are intended for internal use only.
- Traditionally in papers (unsatisfactory for most products, specially if the ingredients are hygroscopic, volatile or deliquescent). Volatile or hygroscopic drugs are wrapped in aluminum foil or plastic bags.
- They also may be dispensed in metal foil, small heat- sealed plastic bags or other containers.

A- Simple and compound powders for internal use:

- **Simple powder:** it consists of only one active ingredient and suitable excipient. If powder is in crystalline form, then it is reduced to fine.
- **Compound powder:** it consists of mixture of more than one active ingredient and other constituents

B- Powders for reconstitution:

These powders are intended to be reconstituted just before use. They are used to protect drugs against hydrolysis and enhance stability of the active constituents.

2- Bulk powders

- These are powders used for **less potent drugs.**
- These are powders supplied in bulk or large quantities.
- They are intended for internal or external use.

a- Bulk powder for internal use :

They are non-potent substances such as antacid. They are dispensed in a wide mouth container so that the teaspoon can easily remove the powder.

- Practically limits the use of orally administered bulk Powders to antacids, dietary supplements, laxatives.

b- Bulk powders for external use:

External bulk powder contain non-potent substance for external application .these powders are dispensed in glass, plastic wide mouth bottles and also in cardboard with specific method of application.

1- Dust bulk powders:

- These are used externally on the skin.
- They consist of protective, antiseptic, antipruritic, and absorbent agent.
- Very fine state of subdivision (to avoid irritation).
- Flow easily, spread uniformly and stick to the skin when applied.

- Dusting powders usually contain substance such as zinc oxide, starch and boric acid and as natural mineral substance such as kaolin or talc.
- These are used externally for local application not intended for systemic action. They are employed chiefly as lubricant, protective, absorbent, antiseptics, antipruritic, astringent, antiperspirants.

2- Douche powder:

These powders are intended to be used as antiseptics or cleansing agents for a body cavity; most commonly for vaginal use although they may be formulated for nasal, otic or ophthalmic use also .

These powders dissolved first in specific amount of water and then applied to the intended body cavities.

They contain antiseptic, cleansing, and, antiparasitic e.g. Applied in vaginal cavity for trichomoniasis.

They are generally dispensed in wide-mouth bottles which are tightly closed to protect the ingredients from moisture.

3- Dental powder (Dentifrices):

- Fine powders that are used to clean teeth are called dentifrices.
- Cleaning properties of these powders are achieved through incorporation of detergents. Besides the detergent, a small amount of mild abrasive (precipitated calcium carbonate or hydrous dibasic calcium phosphate) is also included.
- Dentists usually use dentifrices with high abrasive properties that are not suitable for daily use.

4- Insufflations:

Insufflations are a class of powders meant for application to the body cavities e.g., ear, nose, vagina etc.

- An insufflator (powder blower) usually is employed to administer these products.

5- Snuffs:

These are finely divided solid dosage forms of medicaments dispensed in flat metal boxes with hinged lid. These powders are inhaled into nostrils for decongestion, and bronchodilator action.

❖ Special powder:

1- Effervescent Granules:

- Effervescent powders contain materials which react in presence of water evolving carbon dioxide.
- This class of preparations can be supplied either by compounding the ingredients as granules or dispensed in the form of salts.
- For evolution of the gas two constituents are essential, a soluble carbonate such as sodium bicarbonate and an organic acid such as citric or tartaric acid.
- The preparation can be supplied either as a bulk powder or distributed in individual powders.

2- Eutectic Mixtures:

Are defined as mixtures of low melting point ingredients which on mixing together turn to liquid form due to depression in melting point of the mixture below room temperature.

- They are mixtures of substances, that liquefy when mixed, rubbed or triturated together.
- The melting points of many eutectic mixtures are below room temperature.
- This problem during formulation of powders of such material can be solved by using inert adsorbent such as starch, talc, lactose to prevent dampness of the powder and dispensing the components of the eutectic mixture separately.

Size Classification Of Powders

In order to characterize the particle size of a given powder, the United States Pharmacopeia (USP) uses these descriptive terms:

1. very coarse.
2. Coarse.
3. moderately coarse.
4. Fine.
5. very fine.

• These terms are related to the proportion of powder that is capable of passing through the openings of standard sieves of varying fineness in a specified period while being shaken, generally in a mechanical sieve shaker.

• **Powders are subdivided solids which are classified in the BP according to the size of their constituent particles ranged from 1.25 mm to 1.7 mm in diameter.**


THE
SIEVE

Table 6.1 OPENING OF STANDARD SIEVES

SIEVE NUMBER	SIEVE OPENING
2.0	9.50 mm
3.5	5.60 mm
4.0	4.75 mm
8.0	2.36 mm
10.0	2.00 mm
20.0	850.00 μm
30.0	600.00 μm
40.0	425.00 μm
50.0	300.00 μm
60.0	250.00 μm
70.0	212.00 μm
80.0	180.00 μm
100.0	150.00 μm
120.0	125.00 μm
200.0	75.00 μm
230.0	63.00 μm
270.0	53.00 μm
325.0	45.00 μm
400.0	38.00 μm

Size Classification Of Powders

Powders of vegetable and animal origin drugs are officially defined as follows:

1-Very coarse (No. 8) powder:

All particles pass through a No. 8 sieve (2.36 mm) and not more than 20% pass through a No. 60 sieve.

2- Coarse (No. 20) powder:

All particles pass through a No. 20 sieve (0.85 mm) and not more than 40% pass through a No. 60 sieve.

3- Moderately coarse (No. 40) powder:

All particles pass through a No. 40 sieve (0.42 mm) and not more than 40 % pass through a No. 80 sieve.

4- Fine (No. 60) powder:

All particles pass through a No. 60 sieve (0.25 mm) and not more than 40% pass through a No. 100 sieve.

5- Very fine (No. 80) powder:

All particles pass through a No. 80 sieve (0.18 mm). There is no limit to greater fineness.

❖ **Particle size can influence a variety of important factors, including the following:**

1- Dissolution rate of particles intended to dissolve; drug micronization can increase the rate of drug dissolution and its bioavailability.

2. Suspendability of particles intended to remain undissolved but uniformly dispersed in a liquid vehicle (e.g., fine dispersions have particles approximately 0.5 to 10 μm).

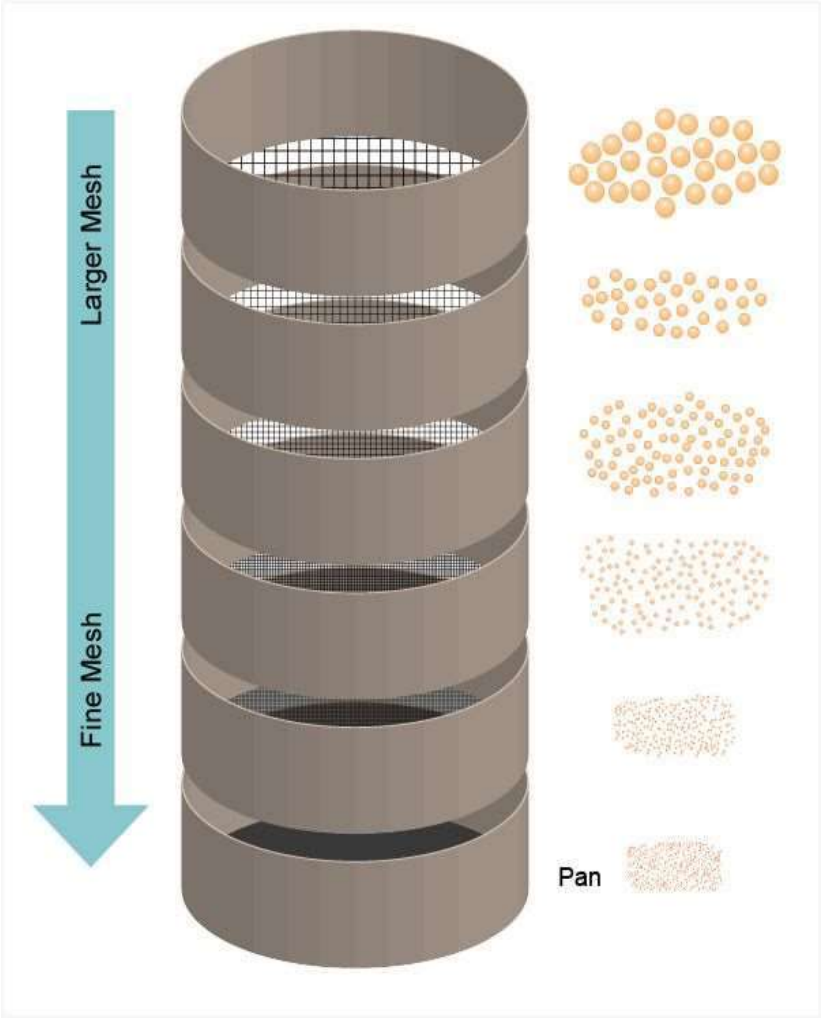
3. Uniform distribution of a drug substance in a powder mixture or solid dosage form to ensure dose-to-dose content uniformity.

4. Penetrability of particles intended to be inhaled for deposition deep in the respiratory tract (e.g., 1 to 5 μm).

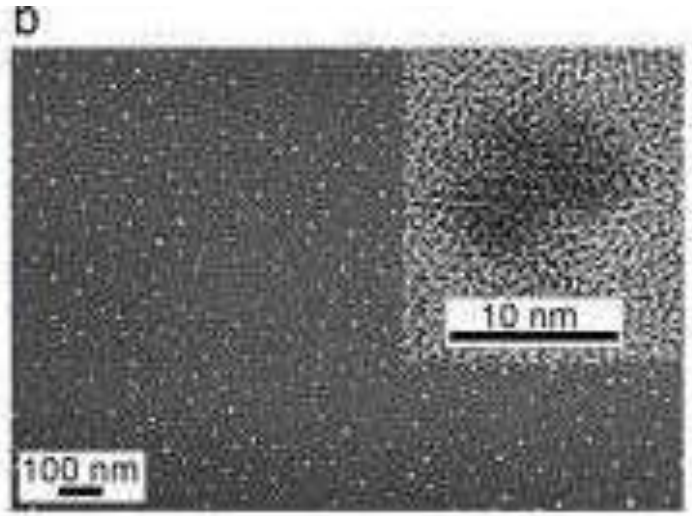
5. Lack of grittiness of solid particles in dermal ointments, creams, and ophthalmic preparations (e.g., fine powders may be 50 to 100 μm in size)

Methods for the determination of particle size

1- Sieving: in which particles are passed by mechanical shaking through a series of sieves of known and successively smaller size and the proportion of powder passing through or being withheld on each sieve is determined.



2- Microscopy: particles are sized through the use of calibrated grid background or other measuring device.



3- SEDIMENTATION RATE: in which particles is determined by measuring the terminal settling velocity of particles through a liquid medium in gravitational or centrifugal environment .

Sedimentation rate may be calculated from Stokes' law.

$$V = \frac{2r^2 g(\rho - \rho_0)}{9\eta}$$

r: is the radius of the sphere that has a volume equal to the particle.

P: is the particle density.

P: is the density of the dispersion medium or vehicle.

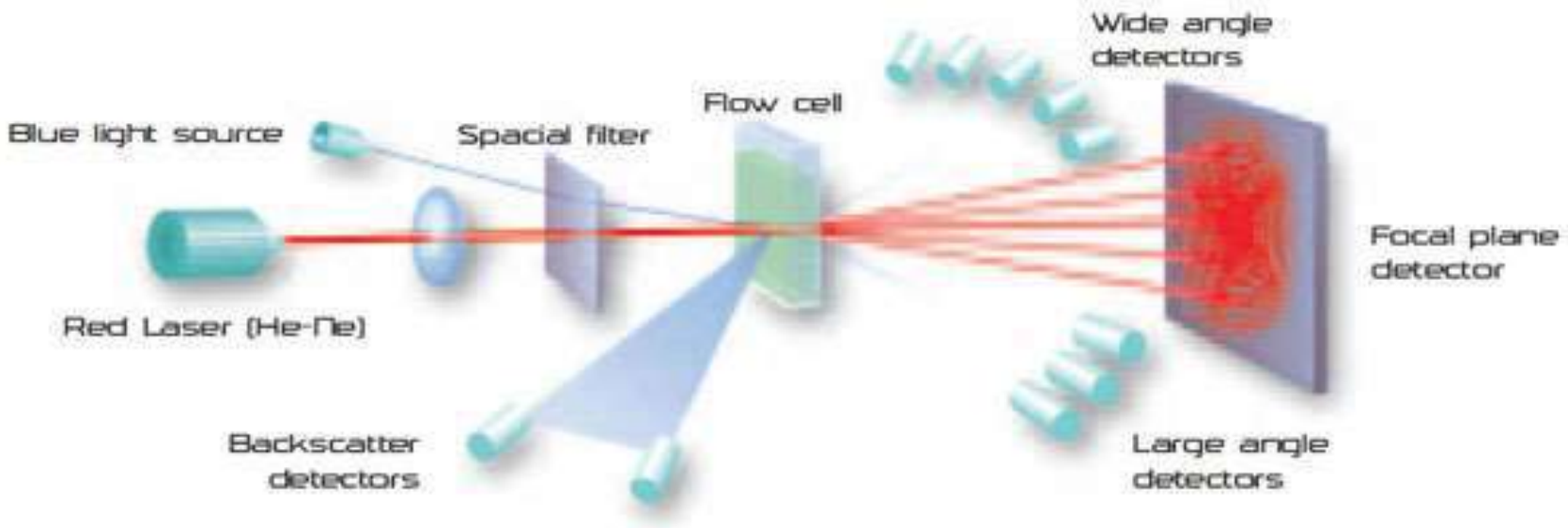
η: is the vehicle viscosity.

g: is the gravity acceleration.

- Sedimentation is not a preferred method for the assessment of particle size and size distribution. It is more commonly used for the quality assessment of colloidal systems, such as suspensions and emulsions

4- Light energy diffraction or light scattering: in which particle size is determined by the reduction in light reaching the sensor as the particle, dispersed in a liquid or gas, passes through the sensing.

A suspension is pumped through a measuring cell and is subsequently illuminated by a laser beam. When particles of different sizes pass a laser beam, they cause the laser light to be scattered at angles that are inversely proportional to the particle size



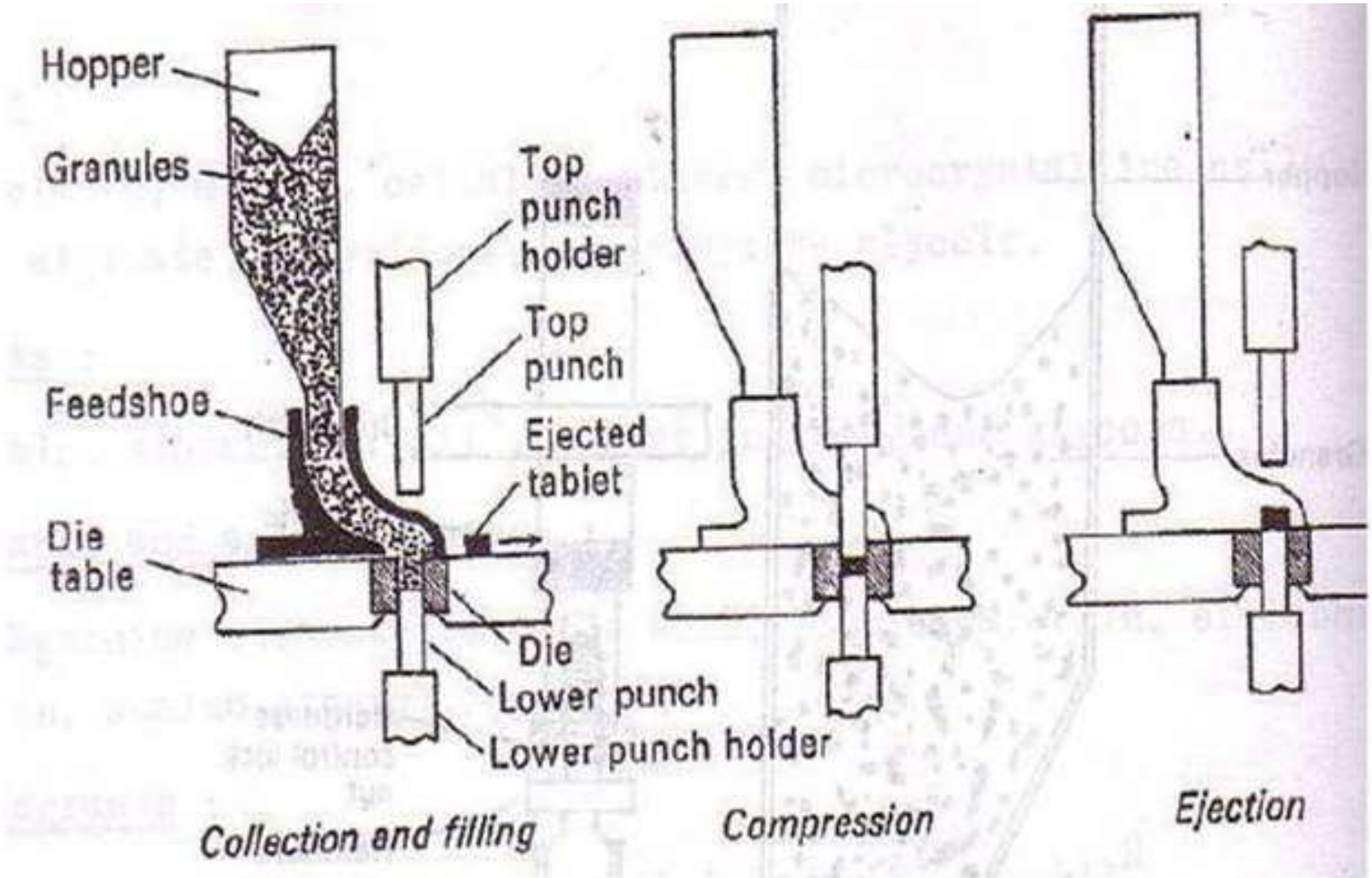
Properties of Powders

1- Flowability

- Powder flowability is the ability of a powder to flow in a desired manner in a specific piece of equipment**.**
- **Flow rate**: Mass of a substance that passes through a given surface per unit time. Represented by g/sec.
- Pharmaceutical powders may be classified as free-flowing or cohesive (non-free-flowing).
- Flow properties are significantly affected by changes in particle size, density, shape, electrostatic charge, and adsorbed moisture, which may arise from processing or formulation.

Flowability of a powder is critical to most pharmaceutical unit operations. For example, adequate flow is important for ensuring:

- Mixing and blend homogeneity during blending of two or more powders
- Adequate control of dosage form weight variation during tablet and capsule filling unit operations
- Uniformity of roller compaction of the powder
- Transfer of powders between different unit operations through bins.


Hopper
Granules
Top punch holder
Top punch
Feedshoe
Ejected tablet
Die table
Die
Lower punch
Lower punch holder
Collection and filling
Compression
Ejection

❖ Factors affecting Powder Flowability:

1- **Particle size**:

Frictional and cohesive forces (resistance to flow) are increased as the particle size is reduced . Very fine particles do not flow as large particles.

- In general, particles in the size range of 250 to 2,000 mm flow freely if the shape is amenable.
- Particles in the size range of 75 to 250 mm may flow freely or cause problems, depending on shape and other factors.
- With most particles smaller than 100 mm, flow is a problem.

2-Particle shape:

Rough irregular particles presents more points of contact than smooth spherical particles thus Spherical particles flow better than needles.

3- **Moisture content:** Drying the powders will reduce the cohesiveness.

4- **Density and porosity:** Particles with high density and low porosity tend to posses free flowing properties.

Factors affecting the flow properties of powder:

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

1- Alteration of Particle's size & Distribution:

There is certain particle size at which powder's flow ability is optimum.

Coarse particles are more preferred than fine ones as they are less cohesive. .The size distribution can also be altered to improve flow ability by removing a proportion of the fine particle fraction or by increasing the proportion of coarser particles, such as occurs in granulation .

2- Alteration of Particle Shape & texture Particle's Shape:

Generally, more spherical particles have better flow properties than more irregular particles.

Spherical particles are obtained by spray.

Particle's texture : particles with very rough surfaces will be more cohesive and have a greater tendency to interlock than smooth surfaced particles.

3- Alteration of Surface Forces:

- Reduction of electrostatic charges can improve powder flow ability. Electrostatic charges can be reduced by altering process conditions to reduce frictional contacts.
- Moisture content of particle greatly affects powder's flow ability.

Adsorbed surface moisture films tend to increase bulk density and reduce porosity .

Drying the particles will reduce the cohesiveness and improve the flow.

- Hygroscopic powders, stored and processed under low humidity conditions .

4- Formulation additives (Flow activators) -Flow activators are commonly referred as glidants.

Flow activators improve the flow ability of powders by reducing adhesion and cohesion .

e.g. talc , maize starch and magnesium stearate

The flowability of powder can be determined by :

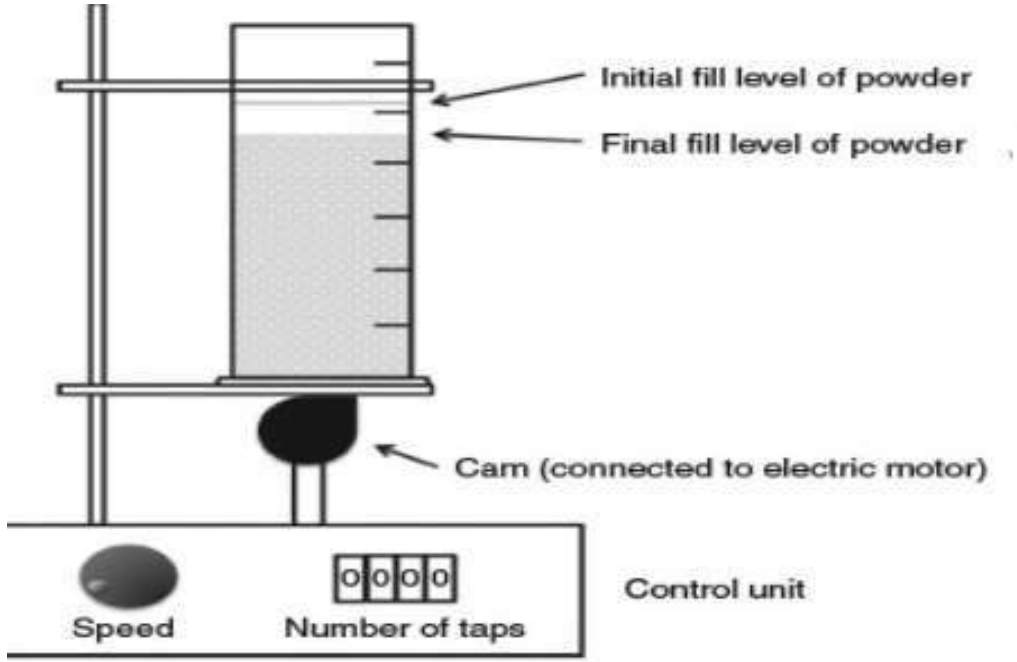
1- Carr’s compressibility index (I):

• A volume of powder is filled into a graduated glass cylinder and repeatedly tapped for a known duration. The volume of powder after tapping is measured.

• **Carr’s index (%) =Tapped density – Poured or bulk density x 100/Tapped density**

• Bulk density = weight / bulk volume.

• Tapped density = weight / tapped volume.



$$I = \left[1 - \frac{V}{V_o}\right] \cdot 100$$

Where:

V: is the volume occupied by a sample of the powder after being subjected to a standardized tapping procedure.

V_0: is the volume before tapping.

- Values of I below 15% usually rise to good flow characteristics, but reading above25% indicate poor flowability.

Relationship between powder flowability and % compressibility

Flow description	% Compressibility
Excellent flow	5 – 15
Good	16 – 18
Fair	19 – 21
Poor	22 – 35
Very Poor	36 -40
Extremely poor	> 40

2- Angle of repose

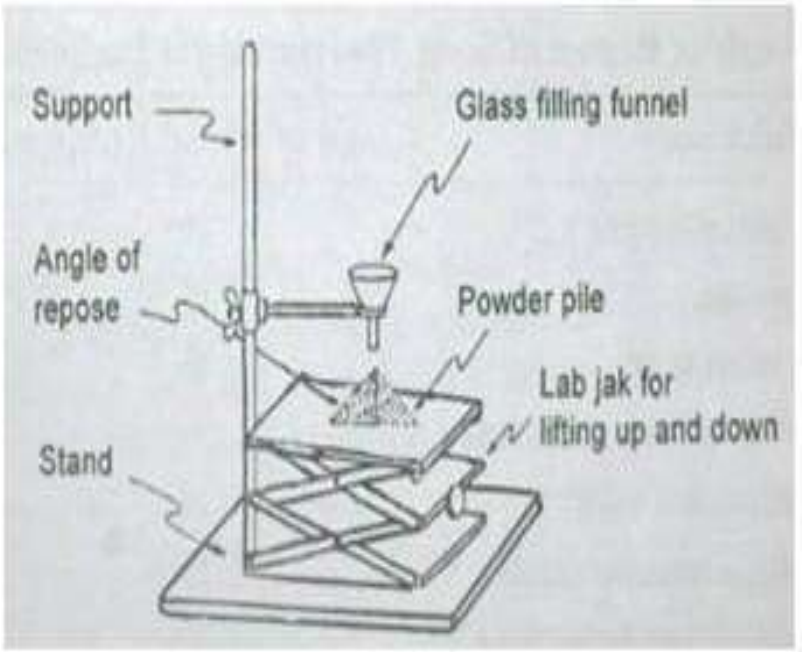
• The angle of repose is a relatively simple technique for estimating the flow properties of a powder.

•φ = the maximum angle possible between the surface of a pile of powder and horizontal plane

• It can easily be determined by allowing a powder to flow through a funnel and fall freely onto a surface.

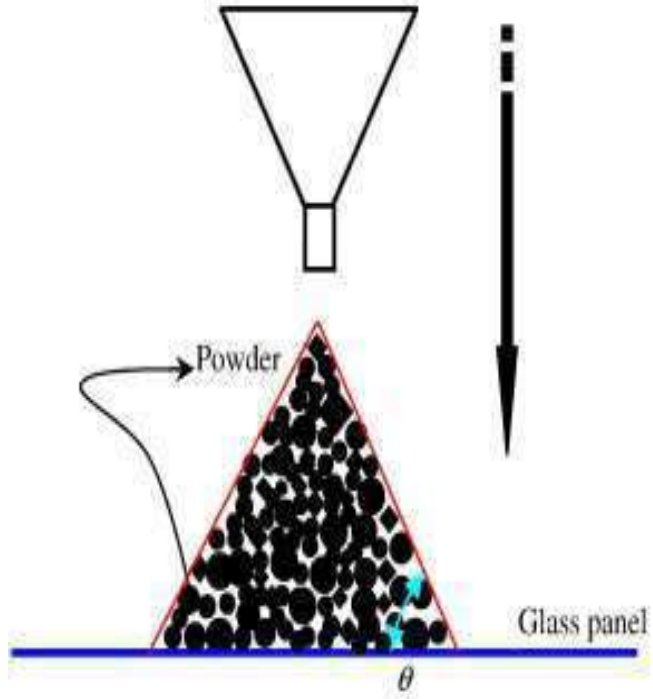
• The height and diameter of the resulting cone are measured, and the angle of repose is calculated from this equation:

$$\tan \theta = h/r$$

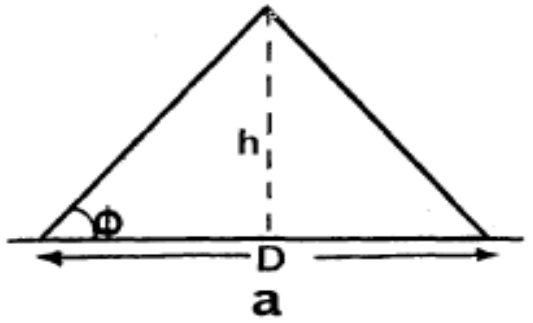


$$\tan \theta = h/r$$

h : is the height of the powder cone.
r : is the radius of the powder cone.



Excellent flowability	if $\theta < 25^{o}$
Good flowability	if $25^{o} < \theta < 30^{o}$
Passable flowability	if $30^{o} < \theta < 40^{o}$
Very poor flowability	if $\theta > 40^{o}$



Mass-Volume Relationships

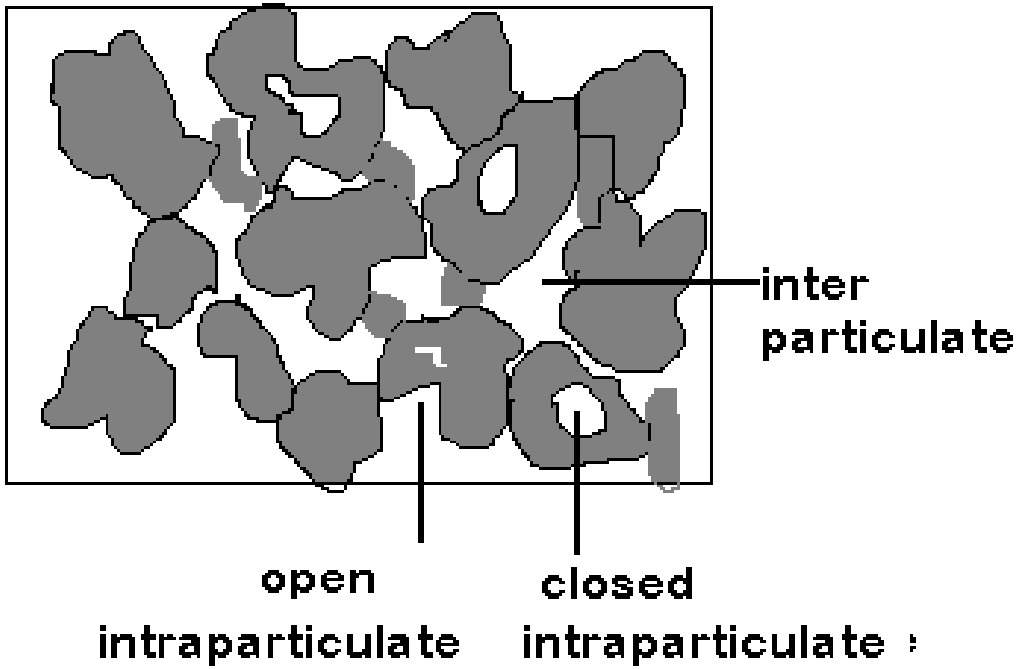
The mass of a bulk powder can be accuracy determined but measurement of the volume is more complicated.

The main problem arises in measuring the volume of bulk powders is the presence of three types of air spaces or voids between particles.

1- **Open intraparticulate voids:-** Those within a single particle but open to the external environment.

2**. Closed intraparticulate voids:-** Those within a single particle but closed to the external

3**. Interparticulate voids:-** The air spaces between individual particles.



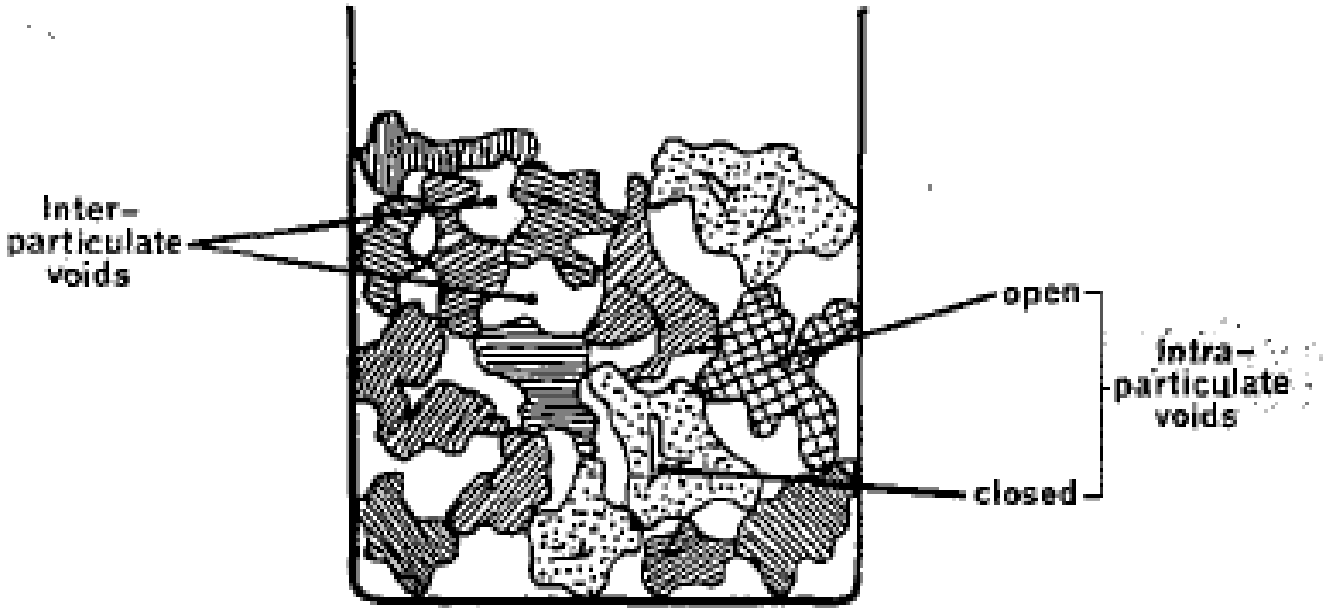


FIG. 4-4. *Diagram of various intraparticulate and inter-particulate air spaces in a bed of powder.*

Therefore, at least three interpretations of "powder volume may be proposed:

- **The true volume (Vt):** The total volume of the solid particles, which excludes all spaces greater than molecular dimensions, and which has a characteristic value for each material. Or it is volume of powder itself .
- **Granular volume of the powder (Vg): (Tapped or particle volume)**

It is the cumulative volume occupied by the particles, including all intraparticulate (but not interparticulate) voids. Or it is the volume of powder itself and volume of intraparticulate spaces.

- **The bulk volume (Vb):** The total volume occupied by the entire powder mass under the particular packing achieved during the measurement.

It comprises the true volume and inter and intra particulate voids (porosity) .

2- Porosity : the porosity or voids of powder is defined as the ratio of the void volume to the bulk volume of packing.

$$\text{Porosity} = (V_{bulk} - V / V_{bulk}) * 100$$

OR

$$\frac{V_{bulk} - V}{V_{bulk}} \times 100$$

V : true volume

➢ Packing arrangements :

powder beds of uniform sized spheres can assume two ideal packing arrangement.

Closest or rhombohedral most open ,**loosest or cubic packing.**

The theoretical porosity of powder of uniform spheres in closest packing is 26% and for loosest packing is 48%.

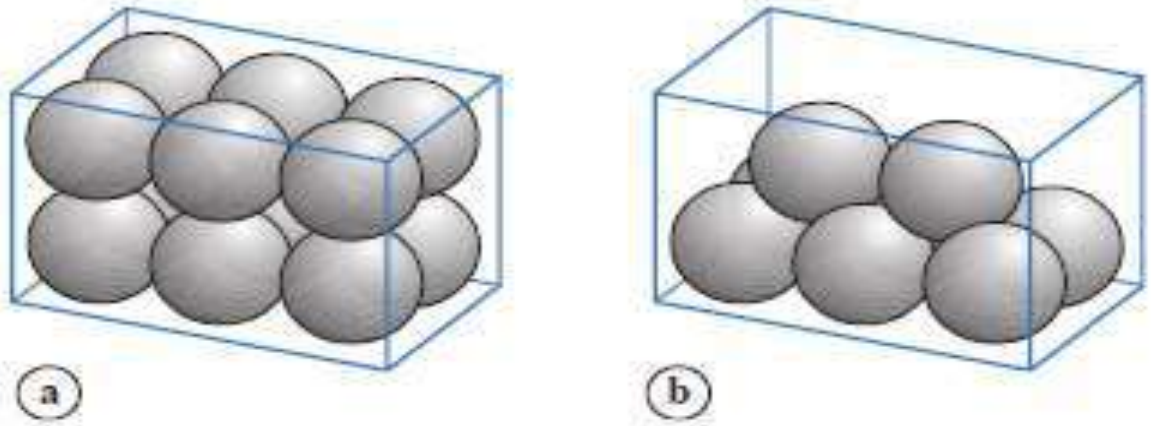
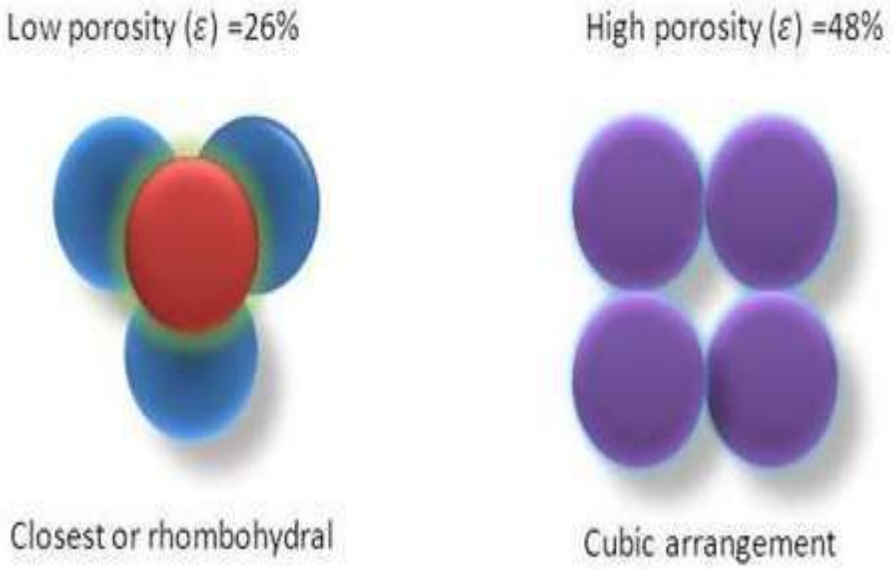


Fig. 12.2 • Different geometric packings of spherical particles, (a) Cubic packing. (b) Rhombohedral packing.



3-Density

The ratio of mass to volume is known as the density (ρ) of the material.

By considering the three types of volume of powders, we can define the respective densities as:

- **True density (ρt):** Mass of the powder/ True volume of the powder .

True density, ρt = M / Vt

- **Granular density (ρg): (Tapped density)** Mass of the powder/ granule volume of the powder.

Granular density, ρg = M / Vg

- **Bulk density (ρ_b):** It is the ratio of total mass of the powder to the bulk Volume of the powder. $\rho_b = M / V_b$

Where , M is the total mass of the powder

V_b is the Bulk Volume of the powder

It is measured by pouring the weighed powder into a measuring cylinder and the volume is noted.

- Bulk density is of great importance for capsule filling, tablet compressibility and for the homogeneity of formulation in which there are large difference in drug and excipient densities.
- Powders with low apparent density (bulk density) and large bulk volume are light powders, and those with high apparent density and small bulk volume are heavy powders.

COMMINUTION OF DRUGS

- Size reduction or comminution or pulverization is the process of reducing large substance into smaller particles.

Advantages of Size Reduction:

1- For effective mixing particles of uniform are desirable. As content uniformity is important in case of potent and low drug formulations.

2- Extraction : the time required for extraction is shortened by the increased area of contact between the solvent and solid and the reduced distance the solvent has to penetrate the material.

3- Dissolution : the time required for dissolution of solid chemicals is shortened by the use of smaller particles.

4- Increased S.A. affects the therapeutic efficiency of medicinal compounds that possess a low solubility in body fluids by increasing the area of contact between the solid and the dissolving fluid. Thus compound dissolves in a shorter time.

5- Drying will be effective when small sized granules or powder are used.

6- During compression of tablet, particle size should be small so that powder can easily flow into dies.

Disadvantages of size reduction:

1- Thermolabile substance get decomposed during size reduction. This due heat produced during milling.

2- There are chances of contamination during milling and grinding.

In extemporaneous compounding, there are three methods of comminution:

➢ **Trituration**:- Trituration is the continuous rubbing or grinding of the powder in a mortar with a pestle.

This method is used when working with hard, fracturable powders.

- A finer grinding action is accomplished by using a mortar with a rough surface (as a porcelain mortar) than one with a smooth surface (as a glass mortar).
- The trituration method is used for both pulverization and mixing.

➢ Pulverization by intervention:-

Pulverization by intervention **method is used with hard crystalline powders that do not crush or triturate easily, or gummy-type substances**.

- The first step is to use an "intervening" volatile solvent (such as alcohol or acetone) that will dissolve the compound.

The dissolved powder is then mixed in a mortar or spread on an ointment slab to enhance the evaporation of the solvent.

As the solvent evaporates, the powder will recrystallize out of solution as fine particles.

Example:

✓Camphor which cannot be pulverized easily by trituration because of its gummy properties, can be reduced to a fine powder by the addition of a small amount of alcohol or other volatile solvent.

✓Iodine crystals can be triturated with the aid of a small quantity of ether.

➢ **Levigation**:-

Levigation: reduces the particle size by triturating it in a mortar or spatulating it on an ointment slab or pad with a small amount of a liquid in which the solid is not soluble.

A paste is formed by combining the powder and a small amount of liquid (the levigating agent) in which the powder is insoluble.

The paste is then triturated, reducing the particle size.

The levigated paste may then be added to the ointment base and the mixture made uniform and smooth by rubbing them together with a spatula on the ointment tile.

The solvent should be somewhat viscous such as mineral oil or glycerin.

This method is also used to reduce the particle size of insoluble materials when compounding ointments and suspensions.

BLENDING POWDERS

• When two or more powdered substances are to be combined to form a uniform mixture, it is best to reduce the particle size of each powder individually before weighing and blending.

There are four main methods of mixing powders in small-scale operations:

- **Trituration**
- **Spatulation**
- **Sifting**
- **Tumbling**

Spatulation

• Spatulation is blending small amounts of powders by movement of a spatula through them on a sheet of paper or an ointment tile.

This method is adequate for mixing small amounts of powders and combinations of powders having the same densities

• It is not suitable for large quantities of powders or for powders containing potent substances, because homogeneous blending is not as certain as other methods.

Trituration

Trituration may be employed both to comminute and to mix powders. If simple admixture is desired without the special need for comminution, the glass mortar is usually preferred.

- When a small amount of a potent substance is to be mixed with a large amount of diluent, the geometric dilution method is used to ensure the uniform distribution of the potent drug.

Geometric dilution:

Geometric dilution is the process by which a homogenous mixture or even distribution of two or more substances is achieved.

This method is used when potent substances must be mixed with a large amount of diluent.

The potent drug and an approximately equal volume of diluent are placed in a mortar and thoroughly mixed by trituration.

A second portion of diluent, equal in volume to the powder mixture in the mortar is added, and trituration is repeated.

The process is continued; equal volumes of diluent are added to the powder mixture in the mortar until all of the diluent is incorporated.

Sifting

Powders may also be mixed by passing them through sifters like those used in the kitchen to sift flour.

- The sifting method is helpful for powders that resist mixing by trituration
- Sifting results in a light, fluffy product.
- Very light powders, such as magnesium oxide and charcoal, can be completely mixed by shaking them through a sieve.

- Standardized prescription sieves are available, but an ordinary household flour sifter can be used effectively for this purpose.
- This process allows the removal of any large foreign bodies and agglomerates from the powder mix.
- This process is not acceptable for the incorporation of potent drugs into a diluent powder.

Tumbling

Tumbling is a process of mixing powders by shaking or rotating them in a closed container.

This method is used when two or more powders have considerable density differences.

- Special small-scale and large-scale motorized powder blenders mix powders by tumbling them.
- Mixing by this process is thorough but time consuming.
- Such blenders are widely employed in industry, as are mixers that use motorized blades to blend powders in a large vessel.

Double Cone Tumbling Mixer

V Type Pharmaceutical Mixer

FIGURE 6.4 Laboratory-scale V-blender. (Courtesy of GlobePharma.)

Planetary Mixers

Problems in Powder Manufacture

1- Hygroscopic and Deliquescent Powder Problem:

Absorption of moisture from air leading to partial or complete liquefaction.

Solution:

- ✓ Applied in a granular form to decrease the exposed surface to air.
- ✓ Packed in aluminum foil or in plastic film packets Addition of light magnesium oxide to reduce the tendency to damp.
- ✓ Addition of adsorbent materials such as starch

2- Efflorescent powders Problem:

Crystalline substances which during storage loose their water of crystallization and change to powder (to be efflorescent).

The liberated water convert the powder to a paste or to a liquid.

Examples: Alum, atropine sulfate, citric acid, codeine phosphate.

Solution:

Using the anhydrous form, and treating it in a manner similar to hygroscopic powders

3- Eutectic Mixtures Problem:

mixture of substances that liquefy when mixed, rubbed or triturated together.

The melting points of many eutectic mixtures are below room temperature.

Examples: menthol- thymol- phenol-camphor.

Solution:

- ✓ Using inert adsorbent such as starch, talc, lactose to prevent dampness of the powder
- ✓ Dispensing the components of the eutectic mixture separately.

4- Incorporation of Liquids Solution:

The liquid is triturated with an equal weight of the powder and the remaining powder is added in several portions with trituration.

Adsorbent is incorporated, usually light kaolin.