

Micromeritics

- Micromeritics is the science of small particles; a particle is any unit of matter having defined physical dimensions. Micromeritics is the study of several characteristics, including:
 - a. particle size
 - b. size distribution,
 - c. shape,
 - d. angle of repose,
 - e. porosity,
 - f. true volume,
 - g. bulk volume,
 - h. apparent density,
 - i. bulkiness

- **Angle of Repose**

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

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

- Where **h** is the height of the powder cone and **r** is the radius of the powder cone.

- **Example:** A powder was poured through the funnel, forming a cone 3.3 cm high and 9 cm in diameter. What is the angle of repose?

$$\tan \theta = h/r = 3.3/4.5 = 0.73$$

$$\arctan 0.73 = 36.25^\circ$$

- Powders with a low angle of repose flow freely, and powders with a high angle of repose flow poorly.

Angel of repose as an indication of powder flow properties

Angel of repose (degrees)	Types of flow
< 20	Excellent
20-30	Good
30-40	Passable
>40	Very poor

Flowability:

- Several factors determine the flow properties of powders, including:
 - Shape: Spherical particles flow better than needles.
 - Size: Very fine particles do not flow as freely as large particles.
- In general, particles in the size range of 250 to 2,000 μm flow freely if the shape is amenable.
- Particles in the size range of 75 to 250 μm may flow freely or cause problems, depending on shape and other factors.
- With most particles smaller than 100 μm , flow is a problem.

Particle Size Reduction

- Comminution, the reduction of the particle size of a solid substance to a finer state, is used to facilitate:
 - Crude drug extraction,
 - Increase the dissolution rates of a drug,
 - Aid in the formulation of pharmaceutically acceptable dosage forms, and
 - Enhance the absorption of drugs.
- The reduction in the particle size of a solid is accompanied by a great increase in the specific surface area of that substance.

Comminution of drugs

- On a small scale, the pharmacist reduces the size of chemical substances by grinding with a mortar and pestle.
- A finer grinding action is accomplished using a mortar with a rough surface (as a porcelain mortar) than one with a smooth surface (as a glass mortar).
- Grinding a drug in a mortar to reduce its particle size is termed *trituration or comminution*.
- On a large scale, various types of mills and pulverizers may be used to reduce particle size.

Manual methods include

1. Trituration It is the principle method of comminution in pharmacy.

- It is the process of reduction of particle size by rubbing in mortar and pestle. The size reduction results from both pressure and attrition as the pestle is firmly pressed down and given a circular motion over the inner surface of the mortar. Care must be taken to scraping the side down with spatula frequently

2. Levigation is commonly used in small-scale preparation of ointments and suspensions to reduce the particle size and grittiness of the added powders.

- A mortar and pestle or an ointment tile may be used.
- 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 is made uniform and smooth by rubbing them together with a spatula on the ointment tile.
- Mineral oil and glycerin are commonly used levigating agents.

- **3. Pulverization by intervention:** This method includes reduction of particle size with the aid of a second agent, which can readily remove from the pulverized product.
- This method usually used to reduce the particle size of camphour which otherwise difficult to triturate. When a few drops of alcohol or other volatile solvent are added, a camphour is readily triturated and the pulverized camphor is readily recovered as soon as solvent evaporated.
- *On a large scale, various types of mills and pulverizers may be used to reduce particle size.*
- Fitz Mill comminuting machine with a product containment system. Through the grinding action of rapidly moving blades in the comminuting chamber, particles are reduced in size and passed through a screen of desired dimension to the collection container.
- The collection and containment system has the following advantages:
 1. Protects the environment from chemical dust,
 2. Reduces product loss, and
 3. Prevents product contamination.

Special processes of particle size reduction

- These processes may be used to prepare powders for dosage forms including freeze-drying and spray drying.
- **Freeze Drying :(Drying by sublimation, lyophilization):** It refers to the removal of water by sublimation from frozen products at low temperatures.
- Freeze drying is usually carried out in a temperature range of -10 to -40°C . It is used to dry biological products such as blood serum, plasma, certain antibiotics such as penicillin, and other substances that are heat-labile and cannot be dried by the usual application of heat.
- ***Spray drying:*** This process converts solution or suspensions into dry, free-flowing powders in a single drying step. The solution or suspension is atomized or sprayed into an enclosed chamber into which heated air is also introduced. The atomization process produces very fine, generally spherical droplets with large surface areas that dry almost instantaneously.

Blending Powders

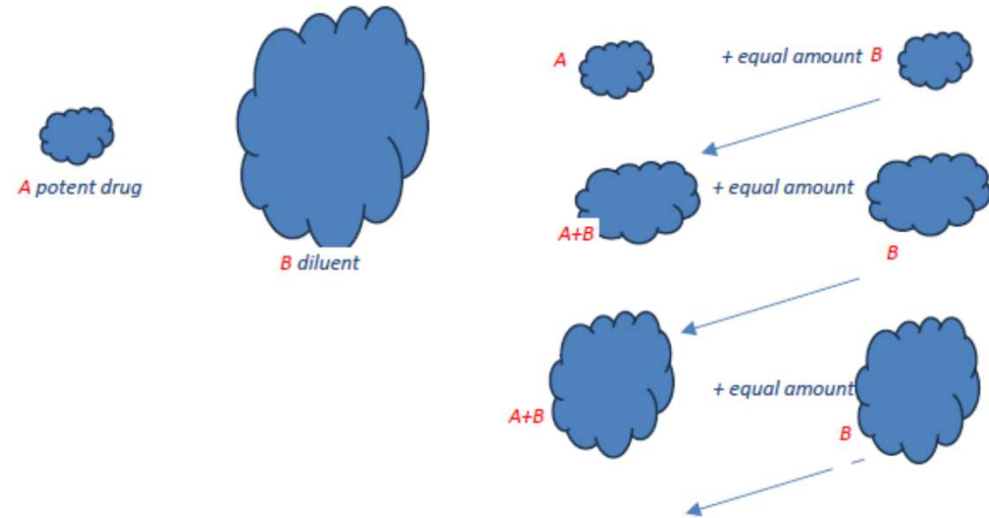
- When two or more powdered substances are to be combined to form a uniform mixture, it is best to reduce the particle size of each powder individually before weighing and blending.
- Depending on the nature of the ingredients, the amount of powder, and the equipment, powders may be blended by
 1. Spatulation,
 2. Trituration,
 3. Sifting, and
 4. Tumbling

Spatulation

- Spatulation is blending small amounts of powders by moving a spatula through them on a sheet of paper or an ointment tile.
- It is unsuitable for large quantities of powders or powders containing potent substances because homogeneous blending is not as certain as other methods.
- Very little compression or compacting of the powder results from spatulation, which is especially suited to mixing solid substances that form eutectic mixtures (or liquefy) when in close and prolonged contact with one another.
- Substances that form eutectic mixtures when combined include phenol, camphor, menthol, thymol, aspirin, phenyl salicylate, and other similar chemicals. To diminish contact, a powder prepared from such substances is commonly mixed in the presence of an inert diluent, such as light magnesium oxide or magnesium carbonate, to separate the troublesome agents physically

Trituration

- Trituration may be employed both to triturate and to mix powders. The glass mortar is usually preferred if simple mixing is desired without comminution.
- When a small amount of a potent substance is mixed with a large amount of diluent, geometric dilution is used to ensure the uniform distribution of the potent drug.



- This method is especially indicated when the potent substance and other ingredients are the same color and a visible sign of mixing is lacking.
- By this method, the potent drug is placed with an approximately equal volume of the diluent in a mortar and is mixed thoroughly by trituration. Then, a second portion of the diluent equal in volume to the mixture is added, and the trituration is repeated.
- This process is continued by adding an equal volume of diluent to the powder mixture and repeating this until all of the diluent is incorporated.
- Some pharmacists add an inert colored powder to the diluent before mixing to permit visual inspection of the mixing process. (to ensure uniform distribution)

Sifting (sieving)

- Powders may also be mixed by passing them through sifters like those used in the kitchen to sift flour.
- Sifting results in a light, fluffy product. This process is not acceptable for incorporating potent drugs into a diluent powder.

Tumbling

- Another method of mixing powders is tumbling the powder in a rotating chamber.
- Special small-scale and large-scale motorized powder blenders mix powders by tumbling them
- Mixing by this process is thorough but time-consuming.
- Blenders, such as mixers that use motorized blades to blend powders in a large vessel, are widely employed in the industry.

Problems associated with particle size reduction

- **Segregation:** an undesirable separation of the different components of the powder mixture (blend) due to differences in density and size.

- **Segregation may occur by:**

- 1- Sifting or percolation

Fine particles tend to sift or percolate through coarse particles and end up at the bottom of the container, which actually “lifts” the larger particles to the surface.

- 2- Air entrapment (fluidization),

Fine, aerated powders with differences in particle size or density may result in a striation pattern and may occur during powder transfer.

- 3- Particle entrapment (dusting).

Dusting occurs when the finer, lighter particles remain suspended in the air longer and do not settle as quickly as the larger or denser particles.

