17. POWDERS, POWDER TECHNOLOGY AND MICROMERITICS

Powders are pharmaceutical solid dosage forms consisting of a homogeneous mixture of one or more powdered solid substances. Powders are prepared for use internally or externally and can be packaged in the form of cachets, packets, hard gelatin capsules, pouches, etc.

Smaller particulate powdering of solid materials is made by grinding machines based on different action mechanisms such as impact, compression, rubbing - sliding and stretching. Depending on these mechanisms, the particles become smaller particles as a result of fragmentation, breaking, shearing and rupture respectively. The effectiveness of the milling process depends on the type of milling equipment and the nature of the solid material. Generally, three groups of equipment are classified according to the size of the milled product:

1. Coarse milling (eg, jaw, gyratory, roll, impact crushers, etc.),
2. Intermediate milling (eg rotary cutters, disk, hammer, roller and chaser mills),
3. Fine Grinding milling (eg, ball, rod, hammer, colloid and fluid energy mills).

These mills consist of three basic parts: a feed hopper, a grinding chamber and a collecting container for the milled product. In Figure 1, some grinders of different types are shown schematically.

The mortar and pestle are used for powdering of small amounts of solids and for the preparation of homogeneous mixtures. Different mortars are selected according to the color and erosive nature of the powders. Glass mortar is used for colored powders and porcelain mortar for white powders. Powders are added to the mortar by geometrical dilution method and homogenized by pestling and mixing. Each dose is weighed from this mixture and placed in the package.

Although the use of powders as a dosage form is reduced, the behavior and properties of finely powdered solid materials are important in pharmacy. Successful formulations of suspensions, emulsions, tablets, capsules and powders, both in terms of physical stability and therapeutic efficacy, depend on the particle size achieved in the product.

The properties of powders are examined individually and in the bulk form. Powders have two important properties: One of these is the individual particle shape and surface area, the other is the size range in number or weight and hence the total surface area of the particles. Other important features derived from these two basic features are porosity, flow properties, consolidation, and compressibility.

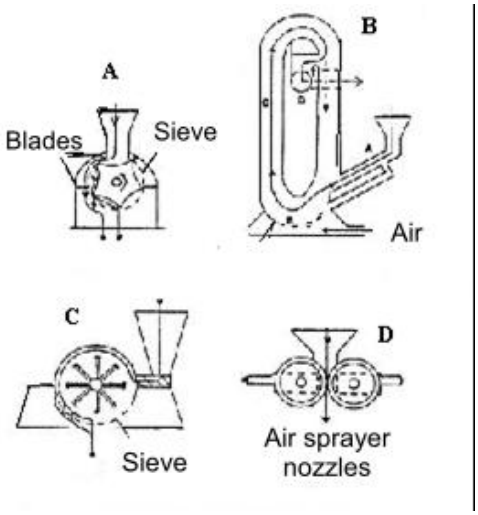


Figure 17.1. Schematic representation of the four types of mills used in pharmaceutical processes. (A) Cutter, (B) Fluid energy mill, (C) Hammer mill, (D) Rotating mill *[Lachman, L., et al., The Theory and Practice of Industrial Pharmacy, 3rd Ed., Lea Febiger, Philadelphia, 21-46, 1986]*.

17.1. Investigation of Particle Size and Size Distribution in Powders and Granules
Particle size and size distribution can be determined using different methods:

• Sieve method
• Microscopy method
• Sedimentation method
• Coulter counter method
• HIAC / Royco particle counter method
• Laser diffraction method

In Experiment 17.1, sieve method and vibration operated sieve set (vibrating sieve set) will be used.

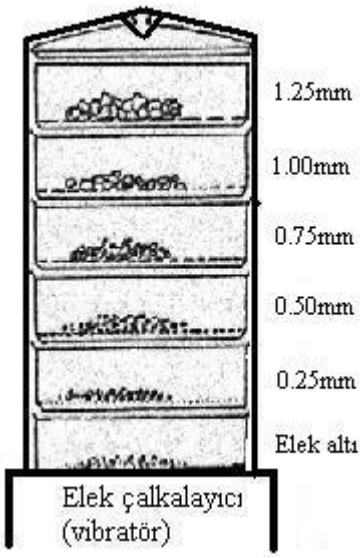


Figure 17.2. Schematic representation of sieve analysis.

Practice 17.1.

I- Investigation of Particle Size and Size Distribution

Granule formula	
Potato starch	70 g
Lactose	30 g
Binder solution	q.s.

Binder solution	
Gelatin	6 g
Glycerin	2 g
Water	92 g

Preparation:
Lactose and starch are thoroughly mixed in the mortar. 25 g of binding solution is weighed in a small beaker and the amount is recorded. The binder solution is added dropwise to the mixture in the mortar and mixed until the proper consistency. The beaker containing the binder solution is weighed again and the amount of binder solution consumed is calculated and recorded. The obtained paste is passed through a 1.6 mm sieve. It is dried at 40-50 ° C in an air stream drying cabinet and passed through a 1.2 mm mesh diameter sieve. The resulting granule mass is weighed (m) and the amount is recorded.

Sieve analysis:
Vibrating sieve tool (Figure 17.2) is used. The openings of the sieves are 1.25 mm, 1.00 mm, 0.75 mm, 0.50 mm and 0.25 mm. The sieves are placed on the vibrator from largest to smallest, with the largest porosity at the top and the smallest porosity at the bottom. The prepared granule or powder mixture is placed on the topmost sieve, the closure is closed and the device is operated intermittently for 10 minutes at a vibration amplitude of approximately 1 mm of the vibrator. At the end of the process, the amount of powder or granules on each sieve is weighed accurately and recorded in Table 17.1.

Table 17.1. Sieve analysis data.

Sieve openings (mm)	Arithmetic mean size of openings (mm)	Amount of powder on the smaller sieve		% Cumulative amount
		(g)	(%)*	
(I)	*(II)*	*(III)*	*(IV)*	*(V)*
1.50-1.25				
1.25-1.00				
1.00-0.75				
0.75-0.50				
0.50-0.25				
0.25-0				

* *% the sum of quantities as g in column 3 is used.*

I.1. Show percentage distributions of granules according to their diameters in the form of a column graph; use column I on the x axis and column IV on the y axis. Combine the midpoints of each column to form the bell curve of the % dispersion curve and record the particle diameter (d_{mod}) corresponding to the peak of this curve.

I.2. Draw the cumulative particle distribution curve (use column II on the x-axis and column V on the y-axis). Record the corresponding particle diameter (d_{median}) at 50% accumulated value.

I.3. Draw the graph using logarithmic-probability paper by adding the cumulative amount % (column V) on the probability scale, and particle diameter (column II) on the logarithmic scale. Calculate the geometric mean diameter (d_{geo}) and standard deviation from this plot.

NOTE: The slope of the graph obtained on the logarithmic-probability paper gives the standard deviation and is calculated by the following formula. The geometric mean diameter is the diameter corresponding to the 50% cumulative amount.

$$\text{Slope} = \frac{\text{Size corresponding to 84\%}}{\text{Size corresponding to 50\%}}$$

or

$$\text{Slope} = \frac{\text{Size corresponding to 50\%}}{\text{Size corresponding to 16\%}}$$

I.4. Show different average diameters you find in a table.

II- Investigation of Bulk Density and Volume Consolidation Properties of Powder and Granules

Determination of bulk density:
The weight of a 10 ml graduated cylinder is recorded. Approximately 10 ml of powder or granules is placed into it and the full volume (Vk) is read. The weight of the powder or granule (m_k) is calculated by re-weighing with the mass in the graduated cylinder. m_k / V_k gives the bulk density (ρ_k) of the powder or granule.

Determination of tapped density:
The weight of a10 ml graduated cylinder is recorded. Approximately 10 ml of powder or granules is placed into it and the full volume (Vk) is read. The weight of the powder or granule (m_k) is calculated by re-weighing with the mass in the graduated cylinder. The graduated cylinder is left on a wooden surface at a height of 2.5 cm and the volume is read. This volume is the volume after a tap. In the same way, 5, 25, 50, 75, 100, 125, 150, 175, 200 taps are made for 2 seconds intervals and counting on each other; the volume (V_v) is determined after each tap. The tapping process continues until there is no reduction in powder volume. In figure 17.3, an apparatus for the determination of tapped volumes of powder or granules is shown schematically.

$$\text{Tapped density } (\rho_v) = \frac{\text{Weight of powder / granule}}{\text{Tapped volume of powder / granule}}$$

II.1. Draw the table of experimental data of the tapped powder / granule.

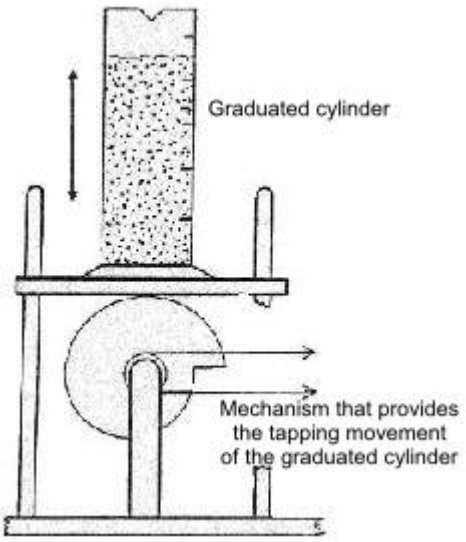


Figure 17.3. Schematic representation of the apparatus used for the determination of tapped volumes of powder or granules. *[Lachman, L., et al., The Theory and Practice of Industrial Pharmacy, 3rd Ed., Lea Febiger, Philadelphia, 21-46, 1986].*

III- Investigation of the Effect of Particle Size on Bulk Density

III.1. Mix the granules over 1.25 mm and over 1.00 mm sieves (greater than 1.00 mm) and place approximately 10 ml granules in a 10 ml graduated cylinder. Record the volume (V_k). Weigh the powder/granule in the graduated cylinder and find bulk density (ρ_k). Record the new volume (V_v) by performing the tapping process until there is no reduction in the volume of the powder and calculate the

tapped density (ρ_v). Calculate Hausner index (HI) and% compressibility (Carr Index) values using the following equations:

$HI = \rho_v / \rho_k$

$\%\ \text{compressibility} = [\ (\rho_v - \rho_k) / \rho_v] \times 100$

III.2. Mix granules under 1.00 mm sieve (less than 1.00 mm) and repeat the above procedure to calculate the bulk volume (V_k), bulk density (ρ_k) and tapped density (ρ_v) HI and compressibility % values using the above equations.

III.3. Show your results in the table below.

Table 17.2. Effect of particle size on bulk density and compressibility.

Powder / granule particle size (mm)	Weight (g)	Bulk volume (cm^3)	Bulk density ρ_k (g/cm^3)	Number of taps	Tapped volume V_v (cm^3)	Tapped density ρ_v (g/cm^3)	Hausner index (HI)

Questions

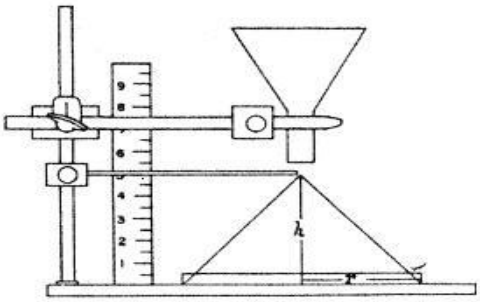
1. What kind of result do you get in terms of particle size, from Table 17.1 and the graphs you draw?
2. Compare the bulk densities of powders / granules with particle size greater than 1.00 mm and the bulk densities of powders / granules smaller than 1.00 mm. If you found them different, explain why.
3. Calculate the amount and % of powder or granules lost during the process.
4. Examine whether the amount of binder solution you use affects particle size distribution, taking into account the amount of binder solution used by the other batch.
5. What do you think about the HI and % compressibility values you calculate?
6. How is bulk density determined according to EP?

17.2. Investigation of Flow Properties of Powder and Granules

Examination of flow properties of powders can be done by a specification of the angle of repose and flow rate.

The Angle of Repose and Flow Rate Determination

Angle of repose is the angle between the side surface of a conical heap on a flat surface and the plane it is sitting on. (Figure 17.4). This angle gives information about the powder flow characteristics. The flow rate is defined as the amount of powder that flows per unit time.



Şekil 17.4. Determination of angle of repose *[Parrott, E., L., Experimental Therapeutics, 4th Ed., Burgess Publishing Co., Minneapolis, 17-89, 1977]*.

Angle of repose	*Flow characteristics*
$\alpha \leq 30^o$	Excellent
$\alpha \geq 40^o$	Poor
$\alpha \geq 60^o$	Very, very poor

1. Place a funnel with a certain length of the drain pipe on a support. Adjust the end of the funnel to a height of 5 cm from the ground. Place a millimeter paper directly under the funnel. Take 25 ml of powder or granules with a particle size greater than 1.00 mm, weigh the amount (m) and place it by closing the tip of the funnel with your finger. Pull your finger while pressing the chronometer and look at the chronometer when the discharge of powder is finished and determine the flow time (t). Determine the length of the diameter of the resulting pile from several points. Measure the height of the pile (h). Calculate the angle of repose (α) and flow rate (ν) from the following equations.

$$\tan\alpha = h / r \qquad \nu = m / t$$

2. Repeat this test with a powder or granule with a particle size smaller than 1.00 mm.
3. Repeat the first experiment by adding 2% (w / w) glidant (eg talc) to the powder or granule.

Questions:

1. Fill the table through experimental findings.

Table 17.3. Experimental findings.

Test sequence	Particle size		Angle of repose (degree)	Flow rate (g/s)
	>1mm	<1mm		
1				
2				
3				

2. What is the relationship between the angle of repose and flow properties?
3. Write the effect of particle size on the angle of repose and flow rate.
4. Describe the effect of the added glidant on the flow characteristics of the powder or granule.

17.3. Investigation of Compressibility Properties of Powder and Granules

Compressibility properties of powders and granules can be determined with the Heckel and Kawakita equations. For this, the powder or granule masses are pressed in tablet form at various pressure values. The volume of the mass in the pressed cylindrical form is determined.

Heckel equation:

$$\ln \frac{v_p}{v_p - v_\infty} = kP + \ln \frac{v_o}{v_o - v_\infty}$$

vo : Volume powder or granule (volume filling the die)
vp : Volume of cylindrical mass after application of pressure P
v∞ : Actual volume of the cylindrical mass (pore-free, volume unchanged by Pn application)
k : Slope; k= 1 / Py; Py : Yield value.
P : Applied pressure

Kawakita equation:

$$\frac{v_o - v_p}{v_o} = \frac{abp}{1+bp}$$

$$\frac{P}{C} = \frac{1}{ab} + \frac{1}{a}P$$

v_o : Volume powder or granule (volume filling the die)
v_p : Volume of the tablet after application of pressure P
C : Volume reduction = $(v_o - v_p) / v_o$
a : Coefficient related to the initial porosity of the powder
b : Compression factor is related to the elastic deformation of the system.