

Powders and Granules

PHAR 632
Dr. Elkeeb

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Objectives

- Understand the definitions, uses, characterization and preparation of different powders and granules.
- Distinguish between different particle size determination methods.

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Powders and Granules

- **Powders:** mixture of dry, finely divided drug and/or chemicals that is intended for internal or external use. Fine particles result from the comminution of any dry substance.
- **Granules:** Dry aggregates of powder particles, 4-12 sieve (will discuss more details later).

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Advantages of powders

1. Flexibility of compounding
2. Good chemical stability
3. Rapid dispersion of ingredients
4. Little or no disintegration required
5. Rapid onset of action
6. Easy to administer to elderly and children
7. Can be mixed with food or liquids
8. A better choice if drug is too bulky to be prepared as tablet or capsule
9. Prepare as individualized doses

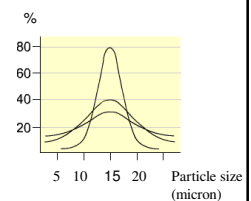
Disadvantages of Powder

1. Time consuming preparation
2. Inaccuracy of dose
3. Unpleasant tasting, hygroscopic and deliquescent
4. Patient has to measure the amount taken

Powder Characterization

Important parameters in describing powders

- Mean particle size
- Distribution
- Shape
- Crystal form



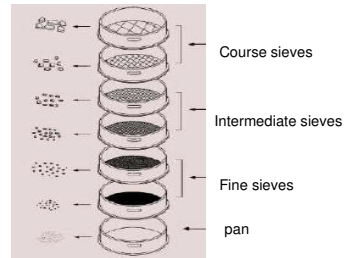
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Mean Particle Size

- Is an important parameter.
- According to USP, a powder ranges from **very coarse** to **very fine approaching colloidal dimension** 1 micron or less.
 - Very coarse, coarse, moderate, fine and very fine
- Depending on the proportion of the powder capable of **passing through** the openings of standard **sieves** after being shaken.
- Particle size is described in terms of sieve number or mesh fraction.

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Sieving



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Particle Size

Power (size category)	Specification
Very Coarse (No 8)	All particles pass through sieve 8, not more than 20% pass through Sieve 60.
Coarse (No 20)	All pass through sieve 20 and not more than 40% pass through sieve 60.
Moderate (No 40)	All pass through sieve 40 and not more than 40% pass through sieve 80.
Fine (No 60)	All pass through sieve 60 and not more than 40% pass through sieve 100.
Very Fine (No 80)	All particles pass through sieve 80.

Large sieve number= smaller sieve opening

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Particle Size

- Particle size of a powder can influence the following:
 - **Dissolution rate**
 - **Grittiness**: what does it affect?
 - **Suspendability of particles**: (suspension) need uniform dispersion in liquid vehicle (1-50 μm)
 - **Uniform distribution**: ensures dose to dose content uniformity
 - **Penetrability (respiratory track)** 5-20 μm

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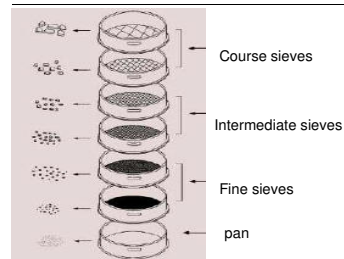
Powders Particle Size Determination

Methods of determining particle size:

1. Sieving
2. Microscopy
3. Sedimentation
4. laser scattering
5. laser holography
6. Cascade impaction

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Sieving



This method is used for powders with particles between 40-9500 micron.

Used for large particle sized

<http://www.itapt2.org/images>

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Microscopy



Accurate and direct method.

**Particle size range
1– 3000 micron**

**Allows determination
of size and shape**

<http://www.microphotonics.com/Particles-image.html> 13

Sedimentation rate

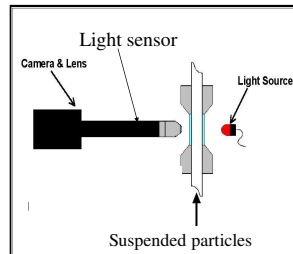
- Particle size measurement is done through determination of the sedimentation (*settling*) velocity of the particles.
- Using Andreasen pipet.
- Sedimentation rate (Stokes' law)
- 0.8-300 micron

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Laser Scattering

Scattering the laser light by the particles dispersed in air or liquid reduces the light reaching the sensor.

The method is very fast, allows determination of small particle size particles 0.02-2,000 micron and allows for shape determination.



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<http://www.jorin.co.uk>

Laser Holography

- Individual imaging particles. Using 3D laser beams, i.e. allows shape determination.
- A pulsed laser is fired through an aerosolized particle spray and photographed using 3D laser beam allowing the particle to be individually imaged and sized.
- 1.4-100 micron (small range).

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Cascade Impaction

- Based on the fact that powder carried by air stream will resist settling and stay flowing depending on its size.
- Particles are separated into different size range by collecting the particles at increasing air stream.

□ <http://www.skccinc.com/instructions/40086.pdf>

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Particle Size Reduction

Comminution	
Small scale	Large scale
Using mortar: <u>Trituration</u> mortars. 	<u>Levigation</u>: Using liquid mortar or ointment tile (slab) and spatula. 
<u>Pulverization by intervention?</u>	
Mills 	

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Powders Blending



1. Trituration:
 - Blending powders on small scale by using mortars? **What type of mortar?**
2. Spatulation: Small scale. 
3. Sifting: Using sieves, create a fluffy powder.
4. Tumbling: Rotating chamber 

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Geometric dilution

5. If small amount of potent drug is to be mixed with large amount of diluent, geometric dilution should be used to ensure uniform distribution. It is done by mixing equal amounts of the drug and the diluent, then dilution with diluent that is equal to the total drug mixture.

x g of drug x g of diluent

 Mix then and add 2x g of diluent


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Eutectic mixture

- Definition
A mixture of 2 or more solids that has a melting point lower than any of its ingredients.
- Examples: Menthol, camphor, aspirin, thymol, phenol, phenylsalicylate and other chemicals
- To overcome this problem while compounding solid dosage forms a third powder is added to act as adsorbent
 - Magnesium oxide
 - Magnesium carbonate
 - Calcium carbonate
 - Kaolin

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Hygroscopic and Deliquescent Powders

- Hygroscopic are powders absorb moisture from the air.
- Deliquescent powders absorb moisture from the air until they will partially or wholly _____? _____
- Store in tight container and incorporate a desiccant packet or capsule. ???
- Patient should be instructed to store in dry place and in a tightly closed container.

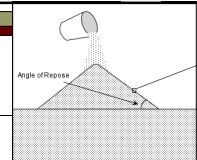
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Efflorescent Powders

- A crystalline powder that contains water of hydration or crystallization.
- Water can be liberated in low humidity environment or from manipulation.
- Causes powder to become sticky, past or even liquefy.
- So how do you compound this????
- Use an anhydrous salt of the drug. Or a drying bulky powder.

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Flow properties



- Angle of repose is a simple technique to estimate the flow properties of a powder.
- Allow the powder to flow freely from a funnel and create a cone.
- Determine the height (h) and the radius of the cone (r).
- Determine the angle of repose by $\tan \theta = h/r$

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Flow properties

- Flow properties are affected by a number of factors include the shape and size of the particles.

The spherical particle and granules are better than needle shape crystals.

Particles with size less than 100 micron have flow problems.

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Porosity

- Briefly read the porosity from the textbook Ansel's.

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Medicated Powder

Medicated Powder use

- Externally used
- Inhaled (local, systemic)
- Vaginal douches
- Orally after mixing with water by patient.
- Dry powder constituted by the pharmacist for oral or parenteral use.

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Medicated Powder

Advantages

- Easiness of swallowing.
- Fast therapeutic effect.
- How ?????
- Dose size

Disadvantages

- Undesirable Taste
- Dose accuracy

Stability

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Powder as Dosage Form

Bulk (antacids, laxatives)
Patient has to measure the dose
Non-potent drugs

Divided (chart) in folded papers or packets.
Prepackaged
Potent drugs/ convenience



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Bulk Powder

Examples

- Douche powder
- Anti-infective, Anti-fungal. (local)
- Antacids
- Mild laxatives

Packed in

- Wide mouth glass or plastic container.
- Topical powder in sifter-top container



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Divided (chart) Powders

Examples:

Laxative

Douche powder



Packed:

1. Zipper bag
2. Plastic tube
3. Powder papers (chart):
 1. Simple bond paper. (not moisture resistant)
 2. Vegetable parchment. (not moisture resistant)
 3. Glassine paper (limited moisture resistance).
 4. Waxed paper a transparent (water proof)

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Granules

- Agglomerates of smaller particles of powders
- Spherical or irregular
- 4-12 sieve size
- Advantages:
 - Good flowability, compressibility, stability
 - Less likely to cake or harden by storage and easily wetted.

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Granules

Common example is antibiotics.

- Prepared by wet or dry granulation
- **Wet:**
 - Wet the powder to create paste, pass through screen, then dry.
- **Dry:** roll compactor to compact powder into sheets or slugs, then granulated to required size. *Results in a lots of fines.*

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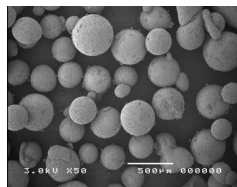
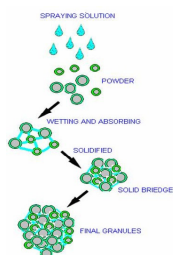
Wet Granulation

- Widely used method
 1. Weighing and blending ingredients
 2. Prepare damp mass
 3. Screening into pellets or granules
 4. Drying the granules
 5. Sizing the granulation by dry screening

<http://www.samedanltd.com>

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Wet Granulation



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Dry granulation

- The powder mixture is compacted in large pieces and subsequently broken down into granules.
- Either the active ingredient or the diluent must have cohesive properties.
- Dry granulation is used when wet granulation is not possible due to heat sensitivity.

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Dry granulation

1. Weighing the ingredient mixture.
2. Slugging or compressing into flat tablets or pellets 1 inch diameter.
3. Pass through screen.

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Effervescent Granules

- Granules or coarse powder.
- Medication in dry mixture (Na bicarbonate, citric, tartaric acid)
- When mixed with water, acid and base react, it liberates CO_2 (Why is CO_2 important?).
- Why granules and not fine particles?
- Mixture of tartaric acid and/or citric acid (to avoid crumbling and sticking).

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Effervescent Granules preparation

1-Fusion :

The source of water to create the paste: One molecule of H_2O present in each molecule of citric acid acts as a binder.

Process:

Size reduction

Heating

Sieving

Drying

- Process is done at low humidity

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Effervescent Granules preparation

2- Wet method:

- Hydroalcoholic solution is used to create a dough, granulation , drying.

□ Any Questions?

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Patient Consultation !

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Reference

- The Ansel's book chapter 6.

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