POWDERS AND GRANULES

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POWDERS

-pulvis-

Powders are mixtures of finely divided drugs and/or chemicals used externally or internally in dry form.

Advantages & Disadvantages

-More stable than liquid

- More convenient to swallow than tablet or capsules

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

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

- Rapid therapeutic effect due to large surface area

- Undesirability of taking bitter or unpleasant tasting of drugs

- Difficulty of protecting from decomposition those powders containing hygroscopic, deliquescent or aromatic materials

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

- Inaccuracy of bulk powders

Characteristics

- Chemical & physical features
  - morphology
  - purity
  - solubility
  - flowability
  - stability
  - particle size
  - uniformity
  - compatibility

PRECAUTIONS IN PREPARING POWDERS TO BE OF HIGH EFFICACY

1. The powders must be homogenous blend of all the components

2. Must be of the most advantageous particle size

STEPS in PREPARING POWDERS

Particle size reduction



Mixing of Powders

Packaging of Powders

Particle Size Reduction

Comminution or grinding may be defined as the process of particle size reduction

METHODS OF COMMINUTION IN SMALL SCALE

Trituration - Is the process of grinding a powder in a mortar and pestle to reduce its particle size.

Pulverization by Intervention - Is the reduction of particle size with the aid of a second agent which can be readily removed from the pulverized product

Example: applies to camphor where it is readily triturated when a few drops of alcohol or other volatile solvent is added. The pulverized camphor is readily recovered as the solvent evaporates.

Levigation - Is the process of reducing particle size by first forming a paste of the solid with a minimum amount of a levigating agent and then triturating the paste in a mortar or on slab with a spatula.



The Basis of Choice of Levigating Agent is:

1. **Its ability to form a smooth paste with the substance**
2. **Its compatibility in the product so water cannot be used for levigating a substance for oleaginous ointment base**



OPENING OF STANDARD SIEVES

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

Medicated Powders

@ Some medicated powders are intended to be used internally; others externally

@ Most powders for internal use are taken orally after mixing with water

@ Some powders are intended to be inhaled for local or systemic effects

@ Medicated powders for external use are dusted on the affected area from **sifter-type container or applied from powder aerosol**

@ External use should bear a label marked EXTERNAL USE ONLY

@ Medicated for oral use may be intended for local effects (laxatives) or systemic effect (analgesic)



AEROSOL POWDERS

administered by inhalation with the aid of dry-powder inhalers, which deliver micronized particles of medication in metered quantities (range of 1 to 6 um)

example: Alupent; each dose is delivered through the mouthpiece upon activation of the aerosol unit's valve it use in the treatment of asthma and other bronchial disorders

Particle Size Analysis

Powders of vegetable and animal drugs

- Very coarse (No.8)
- Coarse (no. 20)
- Moderately coarse (No. 40)
- Fine (No. 60)
- Very Fine (No. 80)



Particle Size Analysis

The powders fineness for chemicals

- Coarse (No. 20)
- Moderately coarse (No. 40)
- Fine (No. 80)
- Very Fine (No. 120)



PACKAGING of POWDERS

BULK POWDERS

1. **Antacid or laxative powders**, which the patient generally takes by mixing the directed amount of powder
2. **Douche powder** usually dissolved in warm water by the patient for vaginal use
3. Dusting powders
4. Medicated or non medicated powders
5. Dentifrices or dental cleansing powders
6. Insufflations
7. Triturations

After the powders have been properly mixed by the geometric dilution, it may be divided into individual units based upon the dose. Method used is called "block and divide"

Powder papers:

2 3/4 x 3 3/4 inches,

3 x 4 1/2 inches,

3 3/4 x 5 inches and

4 1/2 x 6 inches

SELECTION OF PAPER

1. Hygroscopic or deliquescent - use water proof or waxed paper

2. Powders containing volatile components - should be wrapped in waxed or in glassine papers

3. Powders containing neither volatile components nor ingredients adversely affected by air or moisture are usually be wrapped in white papers

Papers may be:

1. Simple bond papers
2. Vegetable parchment
3. Glassine, a glazed, transparent paper
4. Waxed paper, a transparent waterproof paper







Examples Of Finely Divided Powders

1. Oral powders are supplied as finely divided powders or as effervescent granules
2. Douche powders, generally dissolved in warm water for vaginal use
3. Medicated or non medicated powders for external application usually dispensed in sifter cans for convenient application to the skin
4. Dentifrices or dental cleansing powder
5. Denture powders, for dentifrices or for adhesive to hold dentures



Advantages Of Divided Powders

1. Flexibility
2. Rapid therapeutic effect
3. Stability
4. Ease of administration

Disadvantages Of Divided Powders

1. Time consuming to prepare

2. Not well suited for dispensing of many unpleasant tasting hygroscopic drug

3. Inaccuracy

GRANULES

---→ prepared agglomerates of smaller particles. They are generally irregularly shaped and behave as single larger particles. They are usually in the 4 to 12 sieve size range.



Examples:

1. Pricipen (Ampicillin) for oral suspension (for reconstitution)
2. Senokot Granules - for laxative
3. Effervescent products as Bromo Seltzer
4. K-lyte - Granulations of effervescent products - compressed into tablet



EFFERVESCENT GRANULATED SALTS

Effervescent salts are granules or coarse to very coarse powders containing a soluble medicinal agent in a dry mixture

Composition: Sodium bicarbonate, citric acid, and tartaric acid

Note: When added to water, the acids and base react to **liberate CO2 resulting in effervescence**

Example: Sodium Phosphate - cathartic

Reasons why effervescent salts are usually prepared from a combination of **citric acid and tartaric acid rather** than a single acid because of difficulties presented as follows:

1. When tartaric acid is the sole acid, resulting granules lose their firmness readily and crumble
2. Citric acid alone results in a sticky mixture difficult to granulate

So combination will give a **balance** and obtain a **satisfactory product.**

Method Of Preparation

1. Dry or Fusion method
2. Wet method

Objectives Of Using The Methods

1. To determine the proper formula for the preparation that will result in effective effervescence and effect of the product
2. Efficient use of the acids and base present
3. Stable granulation
4. Pleasant taste

Preparation of Granules

1. **Dry Granulation**

= the dry powder is passed through a roll compactor and then through a granulating machine

= a roll compactor, also called a roll press or roller compactor, processes a fine powder into dense sheets

= the surface of the compacting rolls may be smooth or may have pocket indentations or corrugations that allow compaction of different forms and textures

= the compacted powder is granulated to uniform particle size in mechanical granulator

= or dry method also termed slugging

2. **Wet Granulation**

Examples: **Zantac EFFERdose tablets**

Lactinex Granules = mixed culture of Lactobacillus acidophilus and Lactobacillus bulgaricus in 1 g packets used in the treatment of uncomplicated diarrhea; mixed with water, beverages, sprinkled on food, or eaten plain

Official Effervescent Salt: Sodium Phosphate NF

Dried Sodium Phosphate (Dried and Powdered)	200 g
Sodium Bicarbonate (Dry Powder)	477 g
Tartaric acid (Dry Powder)	252 g
Citric acid, (Uneffluorescence crystals)	162 g
to make	1000 g

A good working formula

Citric acid	15%
Tartaric acid	28%
Sodium bicarbonate	53%

NOTE: Dose is assumed to be a heaping teaspoon (5g). Granules should be packaged in tight, dry wide mouth glass jars in cool place

Reactions:

1. $H_3C_6H_5O_7.H_2O + 3NaHCO_3 \rightarrow Na_3C_6H_5O_7 + 4H_2O + 3CO_2$

citric acid — sodium citrate

2. $H_2C_4H_4O_6 + 2NaHCO_3 \rightarrow Na_2C_4H_4O_6 + 2H_2O + 2CO_2$

tartaric acid

It should be noted that it requires 3 molecules of $NaHCO_3$ to neutralize 1 molecule of citric acid (1) and 2 molecules of $NaHCO_3$ to neutralize 1 molecule of tartaric acid (2)

THE PROCEDURE: FUSION OR DRY METHOD

1. Powder citric acid crystals
2. Mix with other powders previously sieved through #60 to ensure uniformity
3. Place in a suitable dish in an oven previously heated between 93-104^oC
4. During the heating, turn the powder with an acid resistant spatula.
5. It is removed from the oven and rubbed through an acid resistant sieve to produce granules of desired size

no. 4 sieve produce large granules ,no. 8 sieve produced medium size granules, no. 10 sieve produced small granules

6. After sieving the granules are immediately dried at a temperature not exceeding 54^oC the transfer immediately to a container and promptly and tightly sealed.

WET METHOD

This differs from the fusion method in that the source of binding agent is not necessarily the water crystallization of citric acid but may be **water added to the nonsolvent** (such as alcohol) which is employed as the moistening agent to form the pliable mass of material for granulation.

This granules may **be compressed into tablets form** (Bromo Seltzer by Warner Lambert)

DENTIFRICES

Form of bulk powder, generally containing flavors, soap or detergent, mild abrasive, and an polishing agent.

Forms: paste, powder, liquid, and block or solid

Use: used with a tooth brush for the purpose of cleansing the accessible surfaces of the teeth.

These contain abrasives such as Calcium carbonate, calcium phosphate, calcium sulfate, insoluble sodium metaphosphate, hydrated $Al_2 O_3$, $MgCO_3$ and phosphates, $NaHCO_3$ and NaCl

Dentifrices contain **non-carbohydrates sweetening agents** but a few contain sugar.

Toothpaste contain liquids such as glycerin, propylene glycol, sorbitol solution, water and thickeners such as starch, tragacanth, alginate and cellulose derivatives.

Block form consist the following:

1. **Polishing agents** - calcium carbonate, dibasic calcium phosphate dihydrate or anhydrous, tricalcium phosphate, calcium pyrophosphate, insoluble sodium metaphosphate and hydrated alumina
2. Massed with 20% to 30% of hard soap and sufficient glycerol and flavoring oils to retain an **attractive appearance and flavor**
3. Tooth powders contain an **abrasive**, a surface active detergent e.g. sodium lauryl sulfate
4. **Flavoring oils** - spearmint, peppermint, wintergreen, and cinnamon mint
5. **Sweetening agents** - saccharin
6. Water 7. **Humectant** - glycerol, sorbitol, propylene glycol
8. **Binder** - gums, karaya and tragacanth, seaweed colloids: sodium alginate and Irish moss extract, and synthetic derivatives of cellulose: methylcellulose and carboxymethylcellulose
9. **Preservatives** - dichlorophene, benzoates, and esters
10. **Fluoride compounds** - stannous and sodium fluoride

Example Formula Of Dentifrices

CMC 120 H	0.9 g
Glycerin	1.0 g
Propylene Glycol	18.0 g
Purified water	13.5 g
Methyl paraben	0.1 g
Saccharin sodium solution 50%	0.1 g
Peppermint oil	0.3 g
Mineral oil	1.0 g
Sodium Lauryl Sulfate	2.5 g
Dicalcium Phosphate in very fine powder	54.0 g









DOUCHE POWDERS

Are products which are completely soluble and are intended to be dissolved in water prior to use as antiseptic or cleansing agent for a body cavity





Components:

1. Boric acid or Borax
2. Astringents as K alum, ammonium alum, $ZnSO_4$
3. Antimicrobial as oxyquinoline sulfate or povidone iodine
4. Quaternary ammonium compounds as benzethonium chloride
5. Detergents as sodium lauryl sulfate
6. Oxidizing agents as sodium perborate
7. Salts, as sodium citrate, sodium chloride
8. Aromatic as menthol, thymol, eucalyptol, methyl salicylate, and phenol

Packaging: may be in a wide mouth glass jars to protect from volatile constituents and by bulk powder boxes

DUSTING POWDERS

Are non-toxic preparations for local application and therefore no systemic effect.

Dispensing: should be dispensed in a very fine state of subdivision to enhance effectiveness and minimized irritation

Packaging: available in sifter-type containers or pressure aerosols, the latter more expensive but protects content from air, moisture and contamination

Uses: lubricants, absorbents, antiseptics, antipruritics, astringents, and antiperspirant

TRITURATIONS

Are dilution of potent powdered drugs prepared by intimately mixing them with a suitable diluents in a definite proportion by weight. They were at one time official as 1-10 dilutions.

Preparation: in making trituration, geometric dilution is used to assure thorough mixing. The active ingredient is placed in a clean smooth, dry mortar. An equal bulk (by estimation) of the weight diluents is added. It is mixed quickly and twice as much diluents, not equal to the amount in the mortar is added and mixed.

Examples: Strychnine sulfate, arsenic, mercury bichloride, atropine in convenient concentration using lactose as the diluents for use at the Rx counter.







INSUFFLATIONS

Are finely divided powders introduced into the body cavities such as the ears, nose, throat, tooth sockets and vagina.

Administration: Insufflator (powder blower) is usually used, pressure aerosols are being employed especially for potent drugs.

Examples:

1. Norisodrine Sulfate Aerohaler Cartridge (Abbott) - specialized equipment or inhalation
2. Cromolyn Sodium Powder - relieve bronchial asthma