Granules Dosage Forms

- One disadvantage of bulk powders is that, because of particle size differences, the ingredients may segregate, either on storage in the final container or in the hoppers of packaging machines. If this happens the product will be nonuniform and the patient will not receive the same dose of the ingredients on each occasion. This can be prevented by granulating the mixed powders.
- **Granules** are aggregates of a group of particles to form larger particles sufficiently robust to withstand handling. They are irregular or spherical in shape. They are usually in the 4-12-mesh size range, although granules of various mesh sizes may be prepared depending upon their application.

Advantage of granulation

1) Granules **flow better** than powders. The easy flow characteristics are important in supplying drug materials from the hopper or feeding container into the tableting presses. For this reason powder mixtures are usually granulated if they are intended to be compressed into tablets. Granules also eliminate or control dust.

2) Granules increase compressibility.

3) Granules have a **smaller surface area** than a comparable volume of powders. This makes granules **more stable** physically and chemically than the corresponding powders. Granules are less likely to cake or harden upon standing than are powders.

4) Granules are **more easily wetted** by a solvent than are certain powders (which tend to float on the surface), so that granules are also preferred in making solutions. Example: Principen® (ampicillin) for Oral Suspension (Squibb). Ampicillin is unstable in aqueous solution, so it is usually prepared as granules and reconstituted by a pharmacist with purified water just prior to dispensing. The granules also contain colorants, flavorants, and other pharmaceutical ingredients, so the resulting solution or suspension has all the desired medicinal and pharmaceutical features of a liquid pharmaceutical.

5) Granules produce particle-size uniformity, thus content uniformity.

- Examples of granules
- A number of commercial products containing antibiotic drugs that are Examples include:

➢ KLACID granules for oral suspension (clarithromycin, Abbot),

➢ Augmentin ES-600 (amoxicillin/ clavulanate potassium, GSK) Uricol granules.

- The granules are prepared to contain not only the medicinal agent but also colorants, flavorings, and other pharmaceutical ingredients. The granules are measured and mixed with water or other beverages, sprinkled on food, or eaten plain. Granulations of effervescent products may be compressed into tablet form, as Zantac EFFER dose tablets (Glaxo Wellcome). Also, (Multivitamins) effervescent granules and tablets are dissolved in water before use.

Preparation of granules

- Granules are prepared by wet methods and dry methods.
- Wet method:

1) Moisten the powder or powder mixture with a fluid (with or without a binder).

2) Pass the resulting paste through a screen of the mesh size to produce the desired size of granules.

3) The resultant granules are placed on drying trays and are dried by air or under heat. The granules are periodically moved about on the drying trays to prevent adhesion into a large mass.

4) Screening stage.

- Another type of wet method is fluid bed processing, in which particles are placed in a conical piece of equipment and are vigorously dispersed and suspended while a liquid excipient is sprayed on the particles and the product dried, forming granules or pellets of defined particle size

Dry method*:*

- The dry granulation method may be performed in a couple of ways. By one method, the dry powder is passed through a roll compactor and then through a granulating machine. An alternative dry method, termed slugging, is the compression of a powder or powder mixture into large tablets or slugs on a compressing machine under 8,000 to 12,000 lb of pressure, depending on the physical characteristics of the powder. The slugs are generally flat-faced and are about 2.5 cm (1 in.) in diameter. The slugs are granulated into the desired particle size, generally for use in the production of tablets.
- The dry process often results in the production of fines, that is, powder that has not agglomerated into granules. These fines are separated, collected, and reprocessed.

Effervescent granulated salts:

- An effervescent dosage form, frequently tablets or granules, contains ingredients that, when in contact with water, rapidly release carbon dioxide. The dosage form is dissolved or dispersed in water to initiate the effervescence prior to ingestion.
- Effervescent salts are granules or coarse to very coarse powders containing a medicinal agent in a dry mixture usually composed of sodium bicarbonate, citric acid, and tartaric acid. When added to water, the acids and the base react to liberate carbon dioxide, resulting in effervescence. The resulting carbonated solution masks the undesirable taste of any medicinal agent.
- Using granules or coarse particles of the mixed powders rather than small powder particles decreases the rate of solution and prevents violent and uncontrollable effervescence. Sudden and rapid effervescence could overflow the glass and leave little residual carbonation in the solution.
- Using a combination of citric and tartaric acids rather than either acid alone avoids certain difficulties. When tartaric acid is used as the sole acid, the resulting granules readily lose their firmness and crumble. Citric acid alone results in a sticky mixture that is difficult to granulate.

Effervescence

➢ A good effervescent blend consists of both citric acid and tartaric acid (1:2 ratio).

➢ The ratio of the effervescent ingredients is 1:2:3.4 for the citric acid: tartaric acid: sodium bicarbonate.

- Effervescent granules are prepared by two general methods: (a) the dry or fusion method and (b) the wet method

Fusion or dry method

- In the fusion method, the one molecule of water present in each molecule of citric acid acts as the binding agent for the powder mixture. Before mixing the powders, the citric acid crystals are powdered and then mixed with the other powders of the same sieve size to ensure uniformity of the mixture. The sieves and the mixing equipment should be made of stainless steel or other material resistant to the effect of the acids.
- The mixing of the powders is performed as rapidly as is practical, preferably in an environment of low humidity to avoid absorption of moisture and a premature chemical reaction.
- After mixing, the powder is placed on a suitable dish in an oven at 34°C to 40°C. During the heating process, an acid-resistant spatula is used to turn the powder. The heat releases the water of crystallization from the citric acid, which in turn dissolves a portion of the powder mixture, setting the chemical reaction and consequently releasing some carbon dioxide.
- This causes the softened mass of powder to become somewhat spongy, and when it has reached the proper consistency (as bread dough), it is removed from the oven and rubbed through a sieve to produce granules of the desired size.

➢ A no. 4 sieve produces large granules,

➢ A no. 8 sieve prepares medium size granules, and

➢ A no. 10 sieve prepares small granules.

- The granules are dried at a temperature not exceeding 54°C and are immediately placed in containers and tightly sealed.

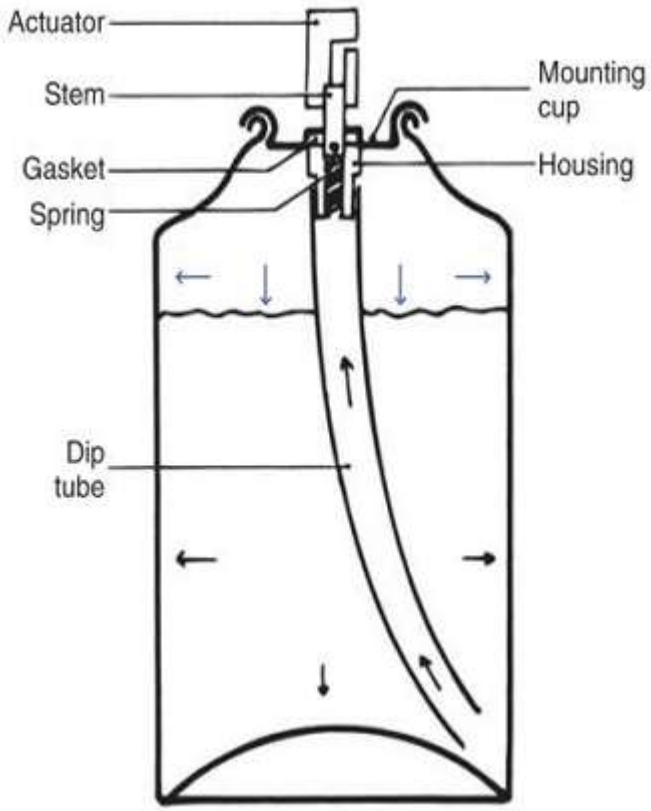
- Wet Method
- The wet method differs from the fusion method in that the source of the binding agent is not the water of crystallization from the citric acid but the water added to alcohol as the moistening agent, forming the pliable mass for granulation.
- In this method, all of the powders may be anhydrous as long as water is added to the moistening liquid. Just enough liquid is added (in portions) to prepare a mass of proper consistency; then, the granules are prepared and dried in the same manner as described.

Aerosols and Foams
Chapter 14
ANSEL'S Pharmaceutical Dosage Forms and Drug Delivery Systems
Eleventh Edition

Objectives:
After reading this topic, the student will be able to:
- Define aerosols
- Understand the types and applications of aerosols
- Identify the main advantage of aerosols
- Define foams
- Explore the types and applications of foams
- Identify the main advantage of foams
- Differentiate between aerosols and foams

- Pharmaceutical aerosols are pressurized systems that, upon valve actuation, emit a fine dispersion (either continuous or metered) of liquid and/ or solid materials containing one or more active ingredients in a gaseous medium.
- Pharmaceutical aerosols are similar to other dosage forms because they require the same types of considerations with respect to formulation, product stability, and therapeutic efficacy. However, pharmaceutical aerosols unlike other dosage forms differ in their dependence upon the function of the container, its valve assembly, and an added component the propellant-for the physical delivery of the medication in proper form.

- The term pressurized product.
- Pressure is applied to the aerosol system through the use of one or more liquefied or gaseous propellants.
- Upon activation of the valve assembly of the aerosol, the pressure exerted by the propellant forces the contents of the package out through the opening of the valve.
- The physical form in which the contents are emitted depends on the formulation of the product and the type of valve.



- Aerosol products may be designed to expel their contents as a fine mist; a coarse, wet, or dry spray; a steady stream; or a stable or a fast-breaking foam. The physical form selected for a given aerosol is based on intended use. There are two types of aerosols.

1. Space sprays Aerosols used to provide an airborne mist. For example, inhalation therapy, as in the treatment of asthma or emphysema, must present particles in the form of a fine liquid mist or as finely divided solid particles. Particles less than 6 μm will reach the respiratory bronchioles, and those less than 2 μm will reach the alveolar ducts and alveoli, also, room disinfectant's, room deodorizers fall in this list The particle size of the released product is generally quite small, usually below 50 μm, and must be carefully controlled so that the dispersed droplets or particles remain airborne for a long time. The valve opening is small, so the particle released are of small size. The formulation is either solution or suspension.

2. Surface sprays or surface coatings. Aerosols intended to carry the active ingredient to a surface of the body (dermatologic aerosols). Included in this group many cosmetic preparations like personal deodorant sprays, By contrast, the particle size for a dermatologic spray intended for deposition on the skin is coarser and generally less critical to the therapeutic efficacy of the product. Some dermatologic aerosols present the medication in the form of a powder. a wet spray, a stream of liquid (usually a local anaesthetic), or an ointment-like product.