Aerosols

They are pressurized dosage forms that upon actuation emit a fine dispersion of a liquid and/or solid materials containing one or more active ingredients in a gaseous medium.

Consideration required in aerosols:

1. Proper function of the container and valve assembly.
2. The propellant.
3. Physical delivery of the medication in proper form.

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 fast breaking foam.

The physical form of aerosol is depend on the intended use:

- For inhalation therapy (like in treatment of asthma or emphysema) the product must be fine liquid mist or as finely divided solid particles (< 6µm for respiratory bronchioles) and (< 2µm reach alveolar ducts and alveoli).
- For dermatological purpose the particle size is coarser and less critical in therapeutic efficacy.

Space sprays: are aerosols used to provide an airborne mist, the particle size of the released product quite small below 50 µm.

Surface sprays: are aerosols which are intended to carry the active ingredients to a surface such as to the skin.

Types of aerosols:

- *Inhalation aerosols*: commonly known as metered dose inhalers (MDSIs), are intended to produce fine particles or droplets for inhalation through the mouth and deposition in the pulmonary tree. The design of system intended to release measured quantities of API with each actuation.
- *Nasal aerosols*: commonly known as nasal MDIs, produce fine particles or droplets for delivery through nasal vestibule and deposition in the nasal cavity.
- *Lingual aerosols*: they are intended to produce fine particles or droplets for deposition on the surface of the tongue.
- *Topical aerosols*: produce fine particles or droplets for application to the skin.

Advantages of aerosols:

1. A portion of medication easily withdrawn from the package without contamination or exposure to the remaining material.

2. Aerosol container protects medicinal agents from atmospheric oxygen , moisture and from light.

3. Topical medication may be applied in a uniform thin layer to the skin without touching the affected area.

4. Physical form and P.S of the emitted product may be controlled by proper formulation and valve control.

5. Aerosol process is a clean process requiring little or no wash up by the user.

The aerosol principle:

Aerosol formulation consist of two components:

- Product concentrate: is the active ingredient of the aerosol combined with the required additives such as antioxidants, surfactants, and solvents to prepare a stable and effective product.

- Propellant : it is of two types:
  -A liquefied gas or mixture of liquefied gasses that serve as a dual role the propellant and solvent or vehicle for the product concentrate mostly used are chlorofluorocarbons (CFCs) such as dichlorodifluoromethane, dichlorotetrafluoroethane and trichloromonofluoromethane.
  -Compressed gas propellants such as nitrogen, nitrous oxide and carbon dioxide.

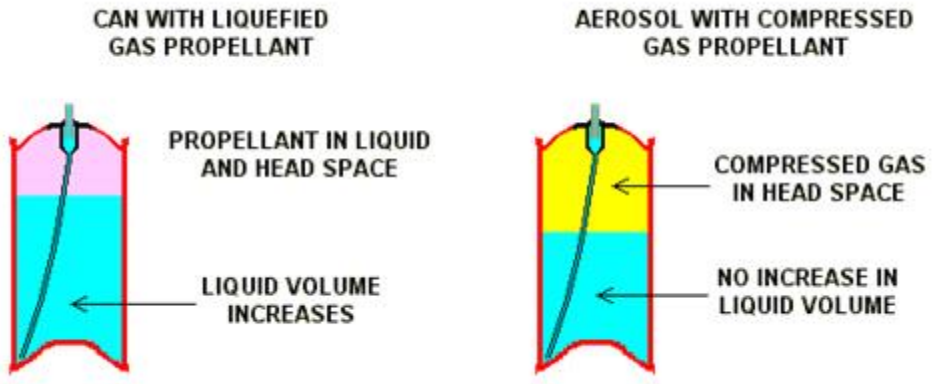
Fluorinated hydrocarbons are gases at room temperature, they may be liquefied by cooling below their boiling point or by compression at room temperature.

When a liquefied gas propellant is sealed within an aerosol container with the product concentrate, equilibrium is quickly established between portion of the propellant that remains liquefied and that which vaporizes and occupies the upper portion of the aerosol container.

The vapor phase exerts pressure in all directions against the walls of the container, the valve assembly and the surface of the liquid gas which is composed of the liquefied gas and the product concentrate. It is the pressure that upon actuation of the aerosol valve, forces the liquid phase up the dip tube and out of the orifice of the valve into the atmosphere.

As the propellant meets the air, it expands and evaporates because of the drop in pressure, leaving the product concentrate as airborne liquid droplets or dry particles depending on the formulation.

As the liquid phase is removed from the container, equilibrium between the propellant remaining liquefied and that in the vapor state is reestablished.



Aerosol system:

The pressure of an aerosol is critical to its performance and it can be controlled by:

a. The type and amount of propellant.

b. The nature and amount of product concentrate.

Space sprays generally contain a greater proportion of propellant than do aerosols intended for surface coating.

1.Two-phase system aerosol: it consists of the liquid phase containing the liquefied propellant and product concentrate and the vapor phase.

2.Three-phase system: it consist of a layer of water immiscible liquid propellant, a layer of highly aqueous product concentrate and the vapor phase. Because the liquefied propellant usually has a greater density than the aqueous layer , it generally resides at the bottom of the container with the aqueous phase floating above it.

To avoid expulsion of the reservoir of liquefied propellant, the dip tube must extend only with in the aqueous phase (product concentrate) and not down into the layer of liquefied propellant.

3. *Compressed gas system:* compressed rather than liquefied gases used to prepare aerosols, the pressure of the compressed gas in the headspace of the container forces the product concentrate up the dip tube and out of the valve e.g is nitrogen gas, carbon dioxide and nitros oxide which is insoluble in the product concentrate.

Advantages of nitrogen gas:

- Inert behavior toward other formulative components.
- Protective influence on products subject to oxidation.
- Odorless and tasteless gas.

Unlike aerosols prepared with liquefied gas propellants, compressed gas filled aerosols have no reservoir of propellant, thus higher gas pressure are required in these systems and the pressure in these aerosols diminishes as the product is used.

Aerosol container and valve assembly:

The effectiveness of aerosol depends on achieving the proper combination of formulation, container and valve assembly.

- The formulation must not chemically interact with the container or valve components to ensure stability.
- The container and the valve must be capable of withstanding the pressure required by the product.
- The container must resist corrosion and the valve must contribute to the form of the product to be emitted.

Containers:

Various materials have been used, including:

a. Glass uncoated or plastic coated.

b. Metal including tin-plated steel, aluminum and stainless steel.

c. Plastic containers.

Glass presents fewer problems with respect to chemical compatibility with the formula than do metal containers and it is not subject to corrosion. Plastic containers are commonly applied to the outer surface of glass containers to render them more resistant to accidental breakage.

Tin-plated steel containers are the most widely used metal containers for aerosols, when required special protective coatings are employed within the container to prevent corrosion and interaction between the container and formulation.

Valve assembly:

Its function is to permit expulsion of the contents of the can in the desired form, at the desired rate, and in the case of metered valves in the proper amount or dose.

Materials used must be inert to the formulations and must be approved by FDA, among materials used in valve are plastic, rubber, aluminum and stainless steel.

The usual aerosol valve assembly is composed of the following parts:

1.*Actuator:* it is the button that the user presses to activate the valve assembly for emission of the product. The actuator permits easy opening and closing of the valve.

The design of the inner chamber and size of the emission orifice of the actuator contribute to the physical form(mist, coarse spray, solid stream or foam) in which the product is discharged.

Particle size of the emitted product depend on:

- Type and quantity of propellant used.
- Actuator design and dimensions.

Large orifices and less propellant are used for products to be emitted as foams and solid streams than for those intended to be sprays or mists.

2. *Stem:* supports the actuator and delivers the formulation in the proper form to the chamber of the actuator.

3. *Gasket:* placed snugly with the stem and prevents leakage of the formulation when the valve is closed.

4. *Spring:* holds the gasket in place and is the mechanism by which the actuator retracts when pressure is released, returning the valve to the closed position.

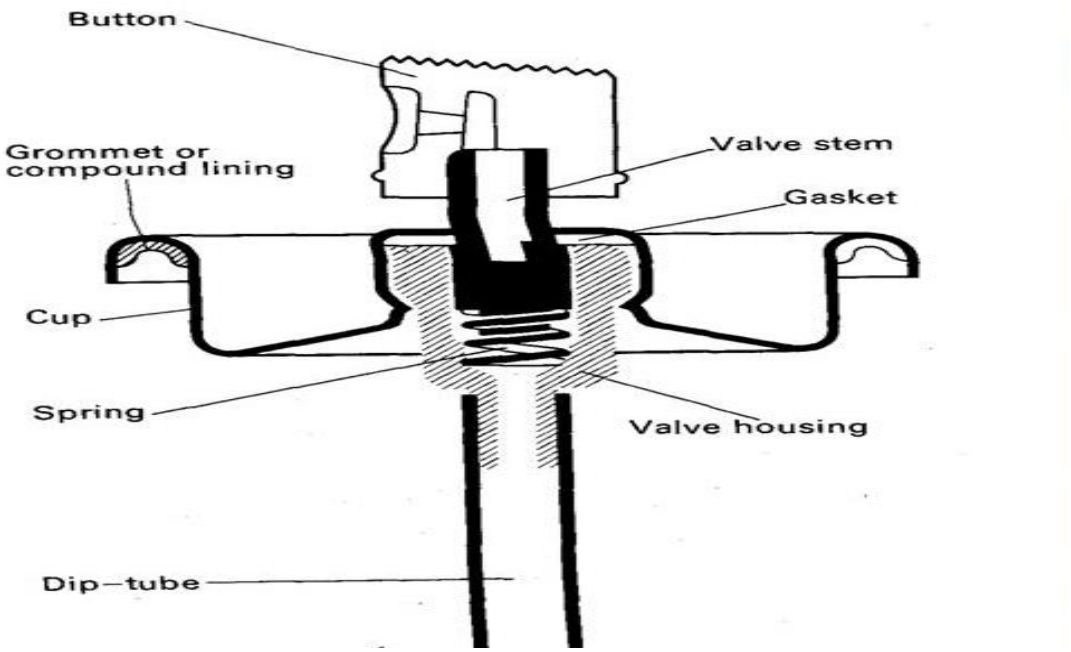
5. *Mounting cup:* attached to aerosol container to hold valve in place, because the underside of mounting cup is exposed to the formulation, it may be coated with an inert material (e.g epoxy or vinyl) to prevent undesirable interactions.

6. *Housing:* directly below the mounting cup, it links the dip tube and the stem and actuator. With the stem, its orifice helps to determine the delivery rate and the form in which the product is emitted.

7. *Dip tube:* extends from the housing down into the product, bring the formulation from the container to the valve.

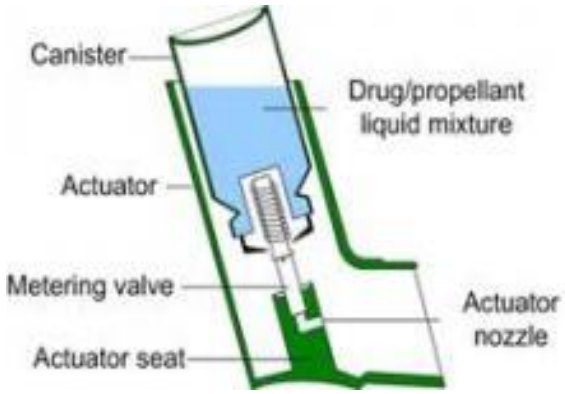
The viscosity of the product and its intended delivery rate determine the inner dimensions of the dip tube and housing for a particular product.

The actuator, stem, housing and dip tubes are generally made of plastic, the mounting cup and spring of metal and the gasket of rubber or plastic resistant to formulations.



Metered-Dose inhalers:

Metering valves are employed when the formulation is a potent medication, as in the inhalation therapy.



The amount of material discharged is regulated by an auxiliary valve chamber, a single depression of the actuator causes evacuation of this chamber and delivery of its contents, the integrity of the chamber is controlled by a dual valve mechanism.

When the actuator valve is closed the chamber is sealed from the atmosphere. However in this position the chamber is permitted to fill with the contents of the container to which it is open.

Depression of actuator causes reversal of positions, the chamber becomes open to atmosphere releasing its contents at the same time becoming sealed from the contents of the container. Upon release of the actuator, the system is restored for the next dose.

Filling operations:

Fluorinated hydrocarbons may be filled:

- ❖ Cold filling

In this method both the product concentrate and the propellant must be cooled to -35^{o}C to -40^{o}C, this temperature is necessary to liquefy the propellant gas. The cooling system composed of dry ice and acetone, after the chilled product concentrate transfer to container, the liquefied gas is added.

The heavy vapors of the cold liquid propellant generally displace the air in the container, when sufficient propellant has been added the valve assembly is inserted and crimped into place.

Because of the low temperatures required aqueous systems cannot be filled by this process because the water turns to ice.

- ❖ Pressure filling

In this process the product concentrate is quantitatively placed in the aerosol container, the valve assembly is inserted and the liquefied gas under pressure is metered into the valve stem from a pressure burette.

When the pressure in the container equals that in the burette the propellant stop flowing.

Pressure filling is preferred over cold filling due to:

1. There is less danger of moisture contamination of the product.

2. Less propellant is lost in this process.

Packaging, labeling and storage:

Most aerosol containers have a protective cap or cover that fits over the valve and mounting cup, this protects the valve against contamination with dust and dirt.

Should advice consumer not to use or store them near heat or an open flame and not to puncture pressurized containers.

Proper administration and use:

The patient should be told whether the inhaler requires shaking before use and how to hold it between the index finger and thumb so that the aerosol canister is upside down.

The patient should be instructed to hold the breath for several seconds or as long as possible to gain the maximum benefit from the medication, then remove the inhaler from the mouth and exhale slowly through lips