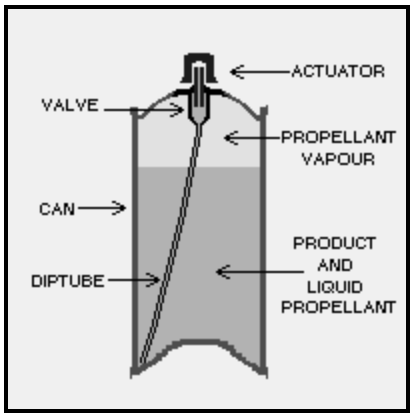
# PHARMACEUTICAL AEROSOLS

**DEFINITION:-**

"A system that depends on the power of a compressed gas to expel the contents from the container".




**COMPONENTS:-**

1. Propellant
2. Container
3. Valve and actuator (valve assembly)
4. Product Concentrate

**PROPELLANT:-**The propellant is responsible for developing the proper pressure within the container,and it expels the product when the valve is opened and aids in the atomization or foam production of the product.

**CLASSIFICATION OF PROPELLANT:-**

1. LIQUEFIED GASES:

(a) Halogenated Hydrocarbons: (Chlorofluro Carbons), Hydrofluoro carbons

Examples: Fluorinated chlorinated Hydrocarbons, Trichloromonofluoro methane (11), Dichlorodifluro methane (12), Dichloro tetra fluoro ethane (114)

(b) Hydrocarbons: Examples: Propane Butane Isobutane

2. COMPRESSED GASES:

(a) Soluble gases:

Examples: Carbon dioxide Nitrous oxide

(b) Insoluble gases:

**2. CONTAINER:-**

"The containers used for manufacture of aerosol must withstand pressures as high as 140 to 180 psig at 130o F". The following aerosol containers have been used to package aerosol products.

Fig:-Tin Plated

Fig:-Aluminium

(A) Metal Containers:

1. Tin plated steel:

(a) Side-seam (Three-piece)

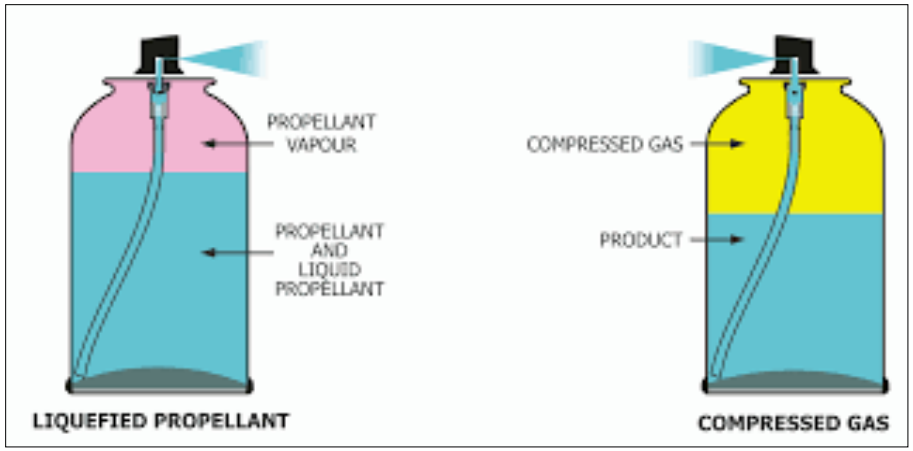
(b) Two-piece or drawn

(c) Tin free steel

2. Aluminium:

(a) Two-piece(b) One-piece (extruded or drawn)

3. Stainless steel

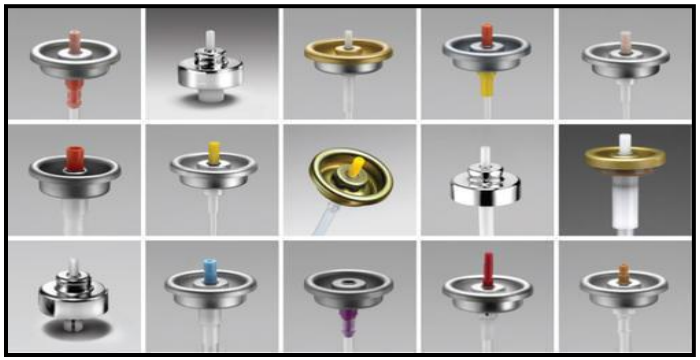


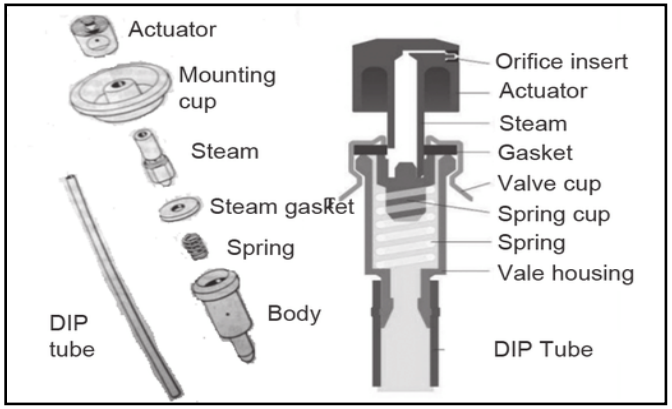
(B) Glass Containers:

1. Uncoated glass 2. Plastic-coated glass

Fig:-Glass Container

**3. VALVE AND ACTUATOER:-**Capable of delivering the content in the desired form such as spray, foam, solid stream etc.Easy to open and close.






Types of aerosol:-

1) Continuous spray valves

2) Metering valves.

An aerosol valve contains the following components:-

1) Actuator

2) Stem,
3) Stem gasket,
4) Spring,
5) Housing,
6) Dip tube
7) Ferrule or mounting cup.

**ACTUATOR:-**Actuator is a specially designed button fitted to the valve stem. This is used to ensure that the product is delivered properly in the desired form. The actuator allows for easy opening and closing of the valve.

Types of actuators:-

a. Spray actuators
b. Foam actuators
c. Solid stream actuators
d. Special actuators

**TYPES OF AEROSOLS SYSTEMS**

The aerosol systems are of the following types:

1) Solution system.
2) Water based system.
3) Suspension or dispersion system.
4) Foam systems: i) Aqueous stable foams,
ii) Non-aqueous stable foams,
iii) Quick breaking foams, and iv) Thermal foams.
5) Intranasal aerosols.

**1) Solution System:-**

Size of particles:-

- Metered dose inhalers : < 8 µm
- Nasal aqueous aerosols : 50 - 75 µm
- Topical sprays : 100 µm
- Space sprays : < 1 µm - 50 µm
- Surface coating sprays : 50 µm - 200 µm

Applications: Space insecticides, room deodorants, vaporizer sprays, hair dyes, perfumes, paints, and protective coatings.

Example:-

- Isoproterenol HCl : 0.25 % w/w
- Ascorbic acid : 0.10 % w/w
- Ethanol : 35.75 % w/w
- Propellant 12 : 63.90 % w/w

**3) Suspension or dispersion system:-**

Examples: • Ephedrine bitartratte : 0.50 % w/w • Sorbitan trioleate : 0.50 % w/w

• Propellant 114 : 49.50 % w/w • Propellant 12 : 49.50 % w/w

**4) Foam systems**

Foam aerosols consists of the following in emulsion form:

- Active ingredient
- Aqueous / non aqueous vehicle
- Surfactant
- Propellants

## Manufacture of Aerosols

The following apparatus are used for manufacturing aerosols:

1) Cold filling apparatus,

2) Pressure filling apparatus, and

3) Compressed gas filling apparatus.

### 1) Cold filling apparatus:-

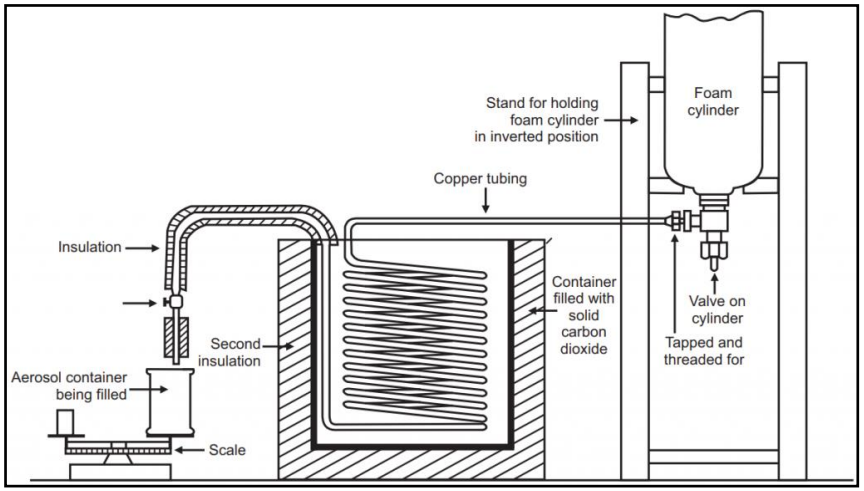



Fig:Apparatus for Cold Filling

Procedure:-

1) This method is used to fill non-aqueous products and products that can withstand low temperature (-40°F).

2) The product concentrate is chilled to –40°Ftemperature and filled in already chilled container.

3) This chilled propellant is completely added in 1 or 2 stages depending on its amount.

4) In another method, the product concentrate and propellant are chilled in a separate vessel to -40°F and then filled into a container.

5) The valve is placed and crimped over the container.

6) The leakage and strength of container can be tested by passing it into a heated water bath, where the container contents are heated at 130°F temperature.

7) Then the containers are dried, capped, and labelled.

2) Pressure filling apparatus:-

Procedure

1) This method is used to fill the concentrate into the container at room temperature.

2) The valve is placed in the container and crimped.

3) The propellant is added either through the valve opening or “under the cap”.

4) The valve opening is smaller in size (0.018 -0.030 inches), thus the product ion is limited and the process is slow.

5) The production rate can be increased by using rotary filling machines and newer filling heads where the propellants are filled through valve stem.

6) The air entrapped in the container and the air in head space is removed before the propellant is filled to protect the products from getting affected.

3) Compressed gas filling apparatus:-

Procedure

1) In this method, the product concentrate is filled in the container.

2) Valve is placed and crimped on the container.

3) Vacuum is applied to remove the air from the container.

4) Filling head is put in the valve opening and gas is allowed to flow into the container.

5) The valve is depressed and gas is allowed to flow into the container.

6) When the delivery pressure and the pressure within the container equalises, the gas stops flowing.

7) If more amount of gas is required, carbon dioxide and nitrous oxide is used.

8) By shaking the container either manually or with mechanical shakers, high solubility of the gas in the product can be achieved.

**EVALUTION OF AEROSOLS**

Pharmaceutical aerosols are evaluated for the following parameters:-

1) Flammability and combustibility:

The effect of an aerosol on extension of an open flame can be evaluated by the following two tests:

i) Flame extension or projection test:-In this test, the aerosol product is sprayed for 4 seconds into the flame. Depending on the formulation nature, the flame extends and its length is measured with ruler.

ii) Flash point test:-In this test, the aerosol product is chilled to -25°F temperture and transferred to a standard tag open cap apparatus.

2) Physicochemical characteristics:-The following physicochemical characteristics of aerosol are tested as follows:-

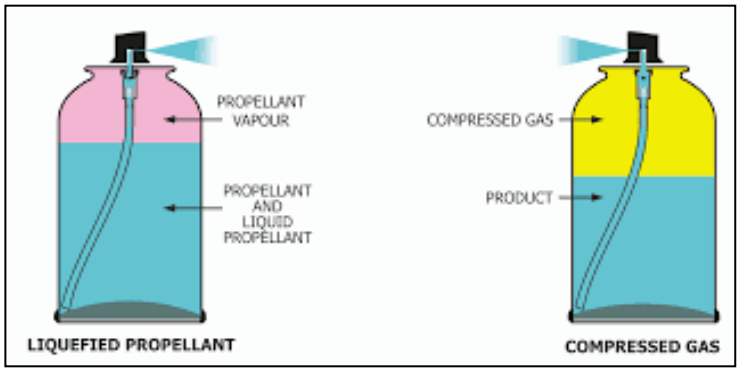
i) Vapour pressure:-A pressure gauge is used to dertermine the vapour pressure of aerosol product.

ii) Density:-A hydrometer or a pycnometer is modified and used to dertermine the density of aerosol product and the liquefied gas propellant.

iii) Moisture content:-Karl Fischer apparatus or gas chromatography is used to dertermine the moisture contain of aerosol product.

v) Qualitative and quantitative tests for propellants:-IR spectroscopy and gas chromatography are used for the qualitative and quantitative tests for propellant; these method also indicate the proportion of each propellant in the blend.

3) Performance characteristics




The container and valve design influences the dosing, performance, and clinical efficacy of aerosol product. The following tests are performedto determinethe efficiency and performance of the valve:

i) Aerosol valve discharge rate ii) Spray pattern

iii) Dosage with metered valves iv) Net contents

v) Foam stability vi) Particle size determination

4) Biological testing:-

i) Therapeutic efficiency Fig:-Particle Sizedetermination The inhalation aerolsols or MDIs are tested for their dose uniformity and particle size distribution along with their pharmacokinetics and pharmacodynamic studies. Topical aerosols are applied to the test area and absorption of therapeutic ingredients is determined.

ii) Toxicity:- The topical as well as inhalation aerosol product are tested for toxicity.The toxicity of inhalation aerosols is determined by exposing the test animals to the sprayed vapours.

**FORMULATION OF AEROSOLS**

The formulation of an aerosol consists of the following two essential components:

1) Propellant, and 2) Product concentrate.

Propellant

A propellant develops pressure within the aerosol container, and forces out the product in the desired physical form (spray, mist, or foam) with the help of other components. Propellants are classified into:

| Liquefied Gases | Compressed Gases |
|---|---|
| Propellant is an integral part of the formation. | Propellant forms a separate phase on product surface. |
| Spray consists of smaller and finer particles. | Spray consists of larger and wet particles. |
| Pressure is maintained throughout the product life. | A pressure drops occurs throughout the product life. |
| Large temperature changes affects the pressure inside the container. | Change in temperature do not affect the pressure exerted by the gases in the container. |
| Pressure exerted does not depend on propellant concentration, hence no pressure drops is seen. | Pressure exerted depends on the propellant concentration, hence presence drops is seen. |
| Cost varies with the nature of propellant andgenerally of higher cost. | Low cost. |

## Product Concentrate

Concentrate is either the active ingredient or is a mixture of active ingredients and other required agents (like solvents, antioxidants, and surfactants). Propellants and the active ingredients can be combined in many ways to obtain products having variable characteristics.

## Quality Control:-

Quality control of pharmaceutical aerosol includes the following tests:

1)Propellant 2)Valves, Actuators, and Dip Tubes 3)Containers

4)Weight Checking 5)Leak Test 6)Spray Testing

**Stability Studies:-**

An entire aerosol package is made up of the product and the container. Therefore, the product effect on the container and vice versa should be studied while studying the stability aspects of aerosols..The pharmaceutical aerosols are tested for their stability based on the following components:

1) The product concentrates

2) The container

3) The valve assembly

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