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Definition

Packaging of therapeutic active ingredients in a pressurized system.

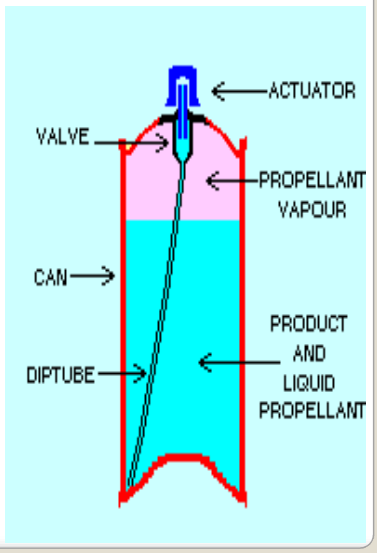
Aerosols are depends on the power of compressed or liquefied gas to expel the contents from containers.

Advantages

- A dose can be removed with out contamination of materials. Stability is enhanced for these substances adversely affected by oxygen and or moisture. When sterility is an important factor, it can be maintained while a dose is being dispensed.
- The medication can be delivered directly to the affected area in a desired form, such as spray, steam, quick breaking foam or stable foam.
- Irritation produced by the mechanical application of topical medication is reduced or eliminated.
- Ease of convenience of application.
- Application of medication in thin layer

Components of aerosols

- *Propellant*
- *Container*
- *Valve and actuator*
- *Product concentrate*



Propellant

It is responsible for developing the power pressure with in the container and also expel the product when the valve is opened and in the atomization or foam production of the product.

For oral and inhalation eg.

Fluorinated hydrocarbons
Dichlorodifluromethane (propellent 12)
Dichlorotetrafluromethane (propellent 114)

Topical preparation

Propane
Butane
Isobutane

Compound gases

Nitrogen
Carbon di oxide
Nitrous oxide

Containers

They must be stand at pressure as high as 140 to 180 psig (pounds per sq. inch gauge) at 130^0 F.

A. Metals

1. Tinplated steel
(a) Side-seam (three pieces)
(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

1. Uncoated glass
2. Plastic coated glass

METAL CONTAINERS

GLASS CONTAINERS

Physiochemical properties of propellants

- *Vapor pressure*
- *Boiling points*
- *Liquid density*

Valves

- ✓ To delivered the drug in desired form.
- ✓ To give proper amount of medication.
- ✓ Not differ from valve to valve of medication in pharmaceutical preparation.

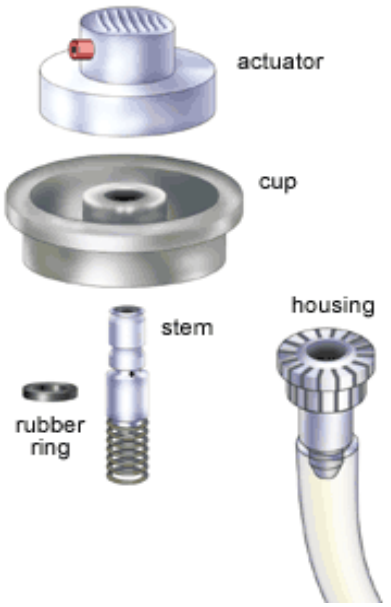
Types

- Continuous spray valve
- High speed production technique.
- Metering valves

Dispersing of potent medication at proper dispersion/ spray approximately 50 to 150 mg ±10 % of liquid materials at one time use of same valve.

Valve components

- Ferrul or mount cap
- Valve body or housing
- Stem
- Gasket
- Spring
- Dip tube

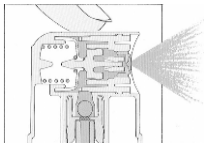


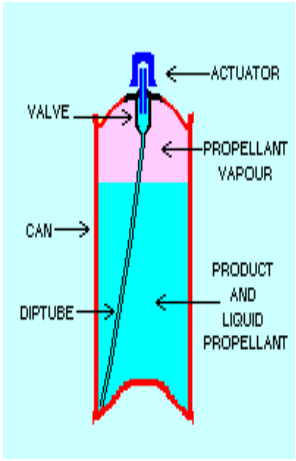
Actuator

To ensure that aerosol product is delivered in the proper and desired form.

Different types of actuators

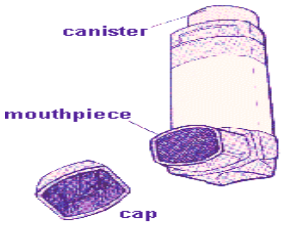
- *Spray actuators*
- *Foam actuators*
- *Solid steam actuators*
- *Special actuators*





Metered dose inhaler

To increased interest in modifying metered dose inhalers (MDIs) to minimize the number of administration error and to improve the drug delivery of aerosols particles into the drug delivery system of the nasal passageways and respiratory tract.



Metered Dose Inhaler

Formulation of aerosols

Contains two essential components

- Product concentrate
- Propellant

Product concentrate

Product concentrate contains ingredients or mixture of active ingredients and other such as solvents, antioxidants and surfactants.

Propellant

May be single or blend of various propellants

❖ Blends of propellant used in a p'ceutical formulation to achieve desired solubility characteristics or various surfactants are mixed to give the proper HLB value for emulsion system.

❖ To give the desired vapor pressure, solubility & particle size.

Parameters consideration

- *Physical, chemical and p'ceutical properties of active ingredients.*
- *Site of application*

Types of system

- *Solution system*
- *Water based system*
- *Suspension or Dispersion systems*
- *Foam systems*
  1. *Aqueous stable foams*
  2. *Nonaqueous stable foams*
  3. *Quick-breaking foams*
  4. *Thermal foams*
- *Intranasal aerosols*

Manufacturing of Pharmaceutical Aerosols

Apparatus

- *Pressure filling apparatus*
- *Cold filling apparatus*
- *Compressed gas filling apparatus*

Large scale equipment

- *Concentrate filler*
- *Valve placer*
- *Purger and crimper*
- *Pressure filler*
- *Leak test tank*

QUALITY CONTROL TESTS

It Includes the testing of :

- 1. Propellents
- 2. Valves, Actuator, Dip Tubes
- 3. Containers
- 4. Weight Checking
- 5. Leak Testing
- 6. Spray Testing

1.Propellents:

- All Propellents are accompanied by Specification sheet.

Parameter	Tested By
Identification ⟶	Gas Chromatography
Purity ⟶	Moisture, Halogen, Non-Volatile Residue Determination

2.Valves, Actuator, Dip-tubes

- Sampling is done according to standard procedure as found in Military Standards "MIL-STD-105D".
- For metered dose aerosols test methods was developed by
  - → 'Aerosol Specification Committee'
  - → 'Industrial Pharmaceutical Technical Section
  - → 'Academy Of Pharmaceutical Sciences.
- The object of this test is to determine magnitude of valve delivery & degree of uniformity between individual valves.
- Standard test solutions were proposed to rule out variation in valve delivery.

Test Solutions

Ingredients % w/w	Test Solutions 'A'	Test Solutions 'B'	Test Solutions 'C'
Iso Propyl Myristate	0.10%	0.10%	0.10%
Dichloro Difluoro methane	49.95%	25.0%	50.25%
Dichloro tetrafluoro ethane	49.95%	25.0%	24.75%
Trichloro monofluoro methane	-	-	24.9%
Alcohol USP	-	49.9%	-
Specific Gravity @ 25℃	1.384	1.092	1.388

Testing Procedure:

- Take 25 valves & placed on containers,
- Filled with specific test solution
- Actuator with 0.020 inch orifice is attached.
- Valve is actuated to fullest extent for 2 sec.
- Repeat this for total 2 individual delivery from each 25 test units.

$$\text{Valve delivery per actuation in } \mu L = \frac{\text{Individual delivery wt in mg.}}{\text{Specific gravity of test sol}^n}$$

Valve Acceptance:

Deliveries	Limit's
54µL or less	± 15%
55 to 200 µL	± 10%

Contd..

- If 4 or more are outside limits : valves are rejected
- If 3 delivery are outside limits : another 25 valves are tested
  : lot is rejected if more than 1 delivery outside specification
- If 2 delivery from 1 valve are beyond limits
  : another 25 valves are tested
  : lot is rejected if more than 1 delivery outside specification

3.Containers

- Containers are examined for defects in lining.
- Q.C aspects includes degree of conductivity of electric current as measure of exposed metals.
- Glass containers examined for Flaws.

4.Weight Checking

- Is done by periodically adding tared empty aerosol container to filling lines which after filling with concentrate are removed & weighed.
- Same procedure is used for checking weight of Propellents.

5.Leak Test

- Is done by measuring the Crimp's dimension & comparing.
- Final testing of valve closure is done by passing filled containers through water bath.

6.Spray Testing

- It is done for
  - »To clear dip tube of pure propellant & concentrate,
  - »To check for defects in valves & spray pattern.

Evaluation Tests:

A. Flammability & combustibility:

1. Flash point
2. Flash Projection

B. Physicochemical characteristics:

1. Vapour pressure
2. Density
3. Moisture content
4. Identification of Propellents

Contnd...

C. Performance:

1. Aerosol valve discharge rate
2. Spray pattern
3. Dosage with metered valves
4. Net contents
5. Foam stability
6. Particle size determination

D. Biological testing:

1. Therapeutic activity
2. Toxicity studies

A. Flammability & combustibility:

» 1.Flash point:

Apparatus : Open Cup Tag Apparatus →

Test liquids temp. is allowed to increase slowly & temp. at which vapors Ignite is called as Flash Point .

» 2.Flame Projection: ⟶

Product is sprayed for 4 sec onto flame & exact length is measured with ruler.

B. Physicochemical characteristics:

Property	Method
1. Vapor Pressure	» Can Puncturing Device.
2. Density	» Hydrometer, » Pycnometer.
3. Moisture	» Karl Fisher Method, » Gas Chromatography.
4. Identification	» Gas Chromatography, » IR Spectroscopy.

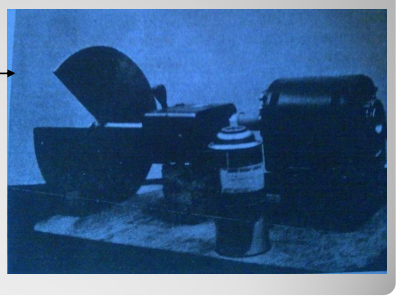
C. Performance:

1.Aerosol valve discharge rate :

- Aerosol product of known weight is discharged for specific time.
- By reweighing the container, the change in the wt. per time dispensed is the Discharge rate in gm/sec.

2. Spray pattern :

- The method is based on the impingement of spray on piece of paper that has treated with Dye-Talc mixture.



3. Dosage with metered valves :

- Reproducibility of dosage determined by:
  - »Assay
  - »Accurate weighing of filled container followed by dispensing several dosage. containers again reweighed & diff. in wt. divided by no. of dosage dispensed gives average dose.

4. Net Contents :

- Tared cans placed on filling lines are reweighed & then difference in wt. is equal to net content.
- In Destructive method : opening the container & removing as much of product possible.

5. Foam stability :

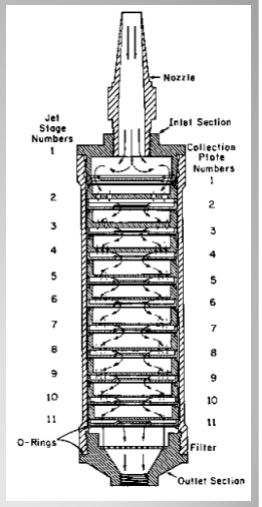
Various Methods : » Visual Evaluation,
» Time for given mass to penetrate the foam,
» Time for given rod to fall which is inserted into the foam,
» Rotational Viscometer.

6.Partical Size Determination :

Methods : » Cascade Impactor,
» Light Scattering Decay.

a). Cascade Impactor :

Principle :
Stream of particle projected through a series of nozzle & glass slides at high velocity, larger particle are impacted on low velocity stage , & smaller on higher velocity stage.



b). Light Scattering Decay :

Principal :
As aerosol settles under turbulent condition, the changes in the light of a Tyndall beam is measured.

D. Biological testing:

1.Therapeutic Activity :

» For Inhalation Aerosols : is depends on the particle size.

» For Topical Aerosols : is applied to test areas & adsorption of therapeutic ingredient is determined.

2.Toxicity :

» For Inhalation Aerosols : exposing test animals to vapor sprayed from Aerosol container.

» For Topical Aerosols : Irritation & Chilling effects are determined.

References:

- "The Theory & Practice Of Industrial Pharmacy" by Leon Lachman, H.A.Liberman, Joseph Kanig, 3rd Edition, Varghese Pub., page no. 613-618.
- Remington's "The Science & Practice Of Pharmacy" 3rd Edition, Volume-I, page no.1014-1015.

Thank You....!