



A Review on Pharmaceutical Aerosols and Their Commercial Application

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ABSTRACT:

The desired application area and purpose of use determine the formulation of aerosol cans. Compared to Oral Solid Dosage (OSD) forms, aerosol formulations are thought to be the most efficient Novel Drug Delivery Systems (NDDS) for delivering Active Pharmaceutical Ingredients (APIs) either systemically or for quicker local action. Aerosols are applied topically, therefore they have little effect on the body's major organs and rarely cause hypersensitive reactions where they are applied. When compared to OSD, they provide better bioavailability and the intended pharmacological effects. In order to increase patient compliance and formulation efficacy, novel excipients are being used these days. The selection of certain excipients ought to be guided by the formulation specifications described in the corresponding pharmacopoeia or formulary. Different dosage forms are produced to achieve specific goals and bioavailability by combining different excipients, including glidants, sorbents, anti-adherents, lubricants, sweeteners, binders, flavoring agents, and vehicles. The excipients and their variants utilized in topical medicinal aerosols are the main theme of this review.

Key words: Aerosol, types, metered dose inhaler, dry powder inhaler, nebulizers, commercial applications.

Introduction:

Aerosol:

Aerosol systems (AS) (also termed pressurised packages or pressurised dosage forms) are a type of novel-delivery drug system (NDDS). They achieve very efficient active pharmaceutical ingredient(s) bioavailability inside the organism, thus for systemic circulation as for efficacy on the specific local site. In simpler words, an aerosol is a colloidal solution composed of solid drug substance particles and/or liquid droplets that are dispersed in a gas (propellant), the latter acting as a continuous phase.

OR

Aerosols emit or operate the composition from a pressurized or liquefied gas by pressure that is produced within the container. (1) A new technology for a drug delivery to the respiratory system is an important application of pharmaceutical inhalation aerosols. These aerosols produce a high dose when used as inhaled medicinal oral products of medication in Broncho-alveolar fluids and other lung tissues.

Advantages over other dosages forms:

Aerosol	Other dosage forms
1. Convenient to apply and administer without the help of others.	1. Not so much convenient (Exception ODTs) and help and guide are needed.
2. The onset of action is very faster.	2. Comparably not so much faster in OSD and Other dosage forms.
3. Due to its closed packaging of aerosols, there is no direct contact with the apis.	3. In this case it's not so as its packaging is thin and blistered.
4. A specific amount of calculated dose or drug can be actuated from the container without contamination.	4. No specificity and shows contamination.

5. Hydrolysis of APIs and used excipients can be prevented since propellants do not contain any moisture.	5. High moisture contact is high as it is exposed to environment leads to hydrolysis of drug excipients and APIs.
6. Aerosol formulation, maintaining valve assembly control, the physical form and particle size of the emitted product may increase efficacy of a drug.	6. Efficacy can be increased in case of Parenteral not in case of solids.
7. Avoids the first pass metabolism (Presystemic metabolism)[17] & Hepatic metabolism leads to high drug absorption.	7. High first pass metabolism so less drug is going through ADME process.(55)

Components of aerosol:

- 1] Propellant
- 2] Container
- 3] Valve
- 4] Actuator

1] Propellant:

The vessel undergoes a pressure procedure to use propellants in the form of high-pressure gas, such as compressed carbon dioxide or nitrogen, or treated liquid gas, such as methane or ethane. NB: Compressed gases are a rarity. Pharmaceutical aerosols in modern times use propellants such as trichlorofluoromethane; dichlorodifluoromethane; dichlorotetrafluoroethane; difluoroethane. The propellant substances are normally solid or liquid. They may dissolve in the propellant or they may not fully dissolve. The formulation also contains additional additives such as solvents, antioxidants, surface active agents, etc. All these constituents, along with propellants, drugs and excipients, are packed in a pressurized aerosol canister.

2) Container:

Material Pharmaceutical aerosol packaging manufacturers make containers from numerous materials, such as metal (e.g., tin-plated steel, aluminum, and stainless steel), glass, and plastic. These vessels are made to endure high pressures.

3) Valve:

The valves should open and close easily. Besides, make sure the content is sent as described. Right now are the three sorts of valves used.

- 1) The medication is being released constantly via the valve disinhibits itself.
- 2) Compressor rod pushing is the way triggering the actuator and then only releasing through metering valve from the device.
- 3) A foam valve releases the necessary substance as foam balls.

4] Actuator:

To make it simple to open and close the valve as needed, the actuator is mounted on the valve stem. Actuators come in a variety of varieties and can create spray, fine mist, or foam. Aerosols can be given in three liquid forms (emulsion, solution, or semisolid) depending on the product concentration. These formulations include the appropriate excipients in addition to the active component. (2)

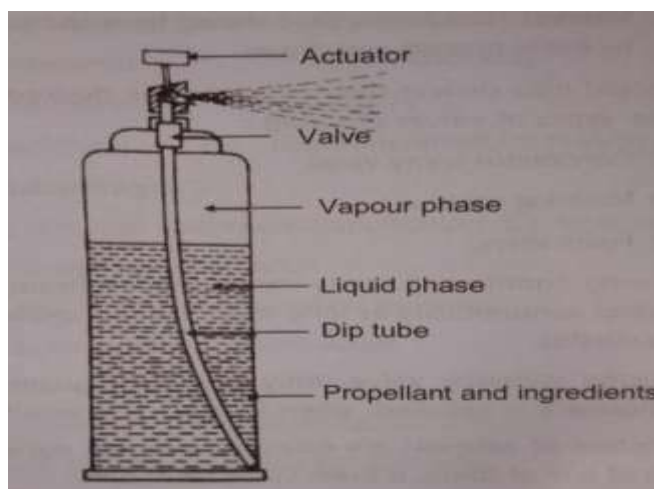


Fig: Actuator

Aerosol Drug Delivery System:

Type:

1. Metered dose inhaler (MDI):

Metered dosage inhalers, or MDIs for short, are portable medical devices that are used to precisely administer a dose of medication to the lungs. A propellant holds either a suspended or dissolved form of the drug.⁽³⁾ Localized respiratory diseases including asthma and COPD are frequently treated with these inhalers. A pressurized propellant spray is used by MDIs to dispense medication, ensuring that only a small amount of the dosage enters the respiratory system. Usually, the lungs only absorb 10–20% of the dosage that is released.⁽⁴⁾ Riker Laboratories, which is now a branch of the 3M firm, created the first MDI back in 1956. It combines two cutting-edge technologies: the Mesh Burg metering valve and the chlorofluorocarbon (CFC) propellant.⁽⁵⁾ The use of spacer devices in the late 1970s significantly improved medication administration by MDIs. These devices were created expressly to lessen esophageal deposition and improve medication absorption into the lungs.⁽⁶⁾ Metered dose inhalers provide a number of benefits, including as being portable, not requiring external power sources, and having the capacity to administer a fixed dosage formulation.⁽⁷⁾

Instructions for Using the MDI:

Use the MDI as directed by these steps:

- 1] Make sure you give the inhaler three or four good shakes before using it.
- 2] Remove the top.
- 3] Release the breath, being careful to keep it away from the inhaler.
- 4] Close your mouth around the inhaler, place it close to your lips, and slide it between your teeth.
- 5] Take a slow breath in and hold it there until you've taken a full breath, all the while pressing the top of the inhaler once.
- 6] Take the inhaler out of your mouth, hold your breath for ten or so seconds, and then release the air. (8,9,10,11)

Advantages:

- 1 It administers a prescribed dose.
- 2) Advantages of its small size are its portability and convenience of use. In general, it provides a more cost-effective choice when compared to nebulizers and dry powder inhalers.
- 3) Rapid and simple to use
- 4) The contents are still protected against microbial contamination.
- 5) It has a multi-dose capacity with more than 100 doses at its disposal.

Disadvantages:

- 1] It is difficult to deliver large doses of pmdi.
- 2] Accurate timing between inhalation and dose actuation is required.
- 3] A patient's method influences the way a medication is administered. (12)

Components of pMDI:

The propellant, metering valve, actuator, and container are components of the pMDI formulation and are all essential to the process. Other additives such as co-solvents, surfactants, stabilizers, lubricants, and bulking agents are also used in addition to these components. The MDI aerosol's active component needs to be therapeutically effective at low dosages without irritating the respiratory system. It should also exhibit compatibility and stability.

Propellant:

An MDI's propellant, a liquefied gas with a vapor pressure greater than atmospheric pressure (14.7 Psia) at 105°F, is an essential component. It plays an essential part in building up the pressure inside the container and releasing the product when the valve is opened. The aerosol system needs propellants to provide the necessary pressure, which makes it easier for the material to be ejected from the container. A variety of propellants are frequently employed in combination to provide aerosols the appropriate spray and delivery properties. Propeller properties have a greater impact than any other aspect, as they typically account for over 99% of the administered dose in MDIs.

Depending upon their chemical nature there are different types of liquefied gas propellant as follow:

- Fluorinated Hydrocarbon

- Hydrofluoroalkane
- Hydrocarbon
- Semifluorinated alkane. (13,14,15,16)

➤ **Fluorinated Hydrocarbon:**

These compounds are referred to as chlorofluorocarbons (cfc's), and they are frequently utilized as nasal aerosol and oral inhalation propellants. Dichlorodifluoromethane (P-12), dichloro-tetrafluoroethene (P-114), and trichloromonofluoromethane (P-11) are notable propellants in this category. (17)

➤ **Hydro fluoroalkane:**

The alternative propellants known as non-chlorofluorocarbons (non-cfc's), such as HFA-134a, HFA-152a, and HFA-227, don't contain chlorine and don't threaten the ozone layer.

➤ **Hydrocarbon:**

Hydrocarbons including propane, butane, and isobutane are used as propellants in topical medicinal aerosols due to their affordability and eco-friendliness. Despite the benefits they provide, their flammability and explosiveness pose a possible risk. (18 and 19)

➤ **Container:**

Glass, stainless steel, and aluminum canisters have been used for pharmaceutical aerosols because of their attractive look and excellent drug compatibility. At 130°F, these containers need to be able to withstand pressures of up to 180 Psig. Canisters composed of aluminum are used to hold most PMDI formulations. (20)

➤ **Metering valve:**

The metering valve plays a crucial role in regulating the propellant and active ingredient flow out of the container, which in turn determines how the aerosol sprays. It is imperative that the valve be constructed from materials that won't react with the contents of the aerosol. Its primary function is to measure and distribute liquid medications precisely while keeping a tight seal to stop unintentional propellant leaks. This valve is made up of an intricate assembly consisting of at least seven different parts made of different materials. (21)

➤ **Actuator:**

An essential component of MDI, the actuator allows the valve to open and close smoothly. The actuator (adaptor), which is designed for oral inhalation, has a spray nozzle as its discharge orifice and a socket that seals and connects to the stem of the metering valve. By ensuring that the active components are administered within the specified particle size range, the expansion chamber plays a crucial role in determining the physical features of the spray. Furthermore, in order to lessen the strain on the valve stem—which could lead to imprecise metering or leakage between the valve stem and actuator—the actuator must successfully stop the container from moving sideways during activation. Furthermore, the actuator needs to provide sufficient airflow to the mouthpiece in order to minimize airflow resistance.

Technological advances of pressurized metered dose inhalers (pMDIs):

Coordination devices or breath-actuated devices are the two categories into which new pmdis fall. Breath-actuated PMDis, like as the Airbreather, were developed expressly to address the issue of inadequate synchronization between the patient's breathing and inhaler actuation. The patient's breath activates these mechanical devices, which then distribute the required dosage.(24, 25) Coordinated PMDis, on the other hand, were made to synchronize the patient's inhalation with the inhaler's dose release. By synchronizing the inhalation flow rate, the actuator makes sure that the patient has enough time to reliably trigger the pmdi during inhalation.(26)

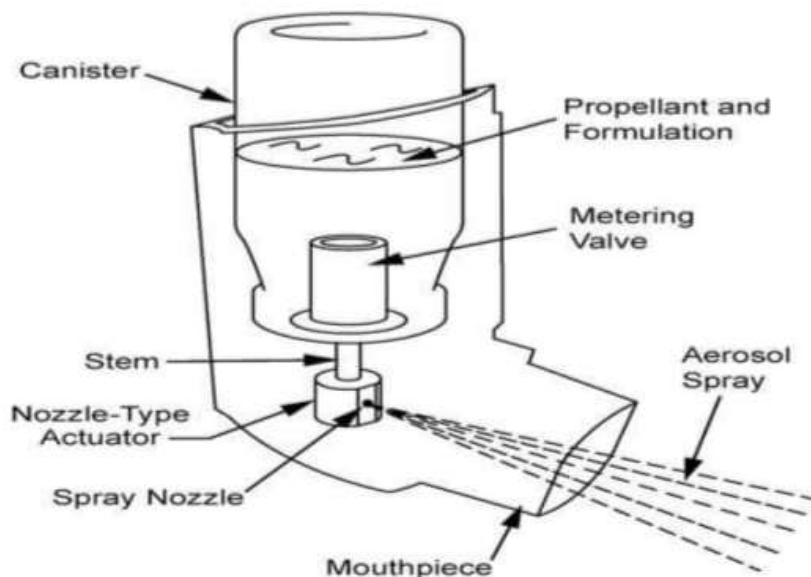


Fig: Metered Dose Inhaler

A novel method was presented by Kelkar and Dalby with the goal of decreasing the size of droplets that were distributed from pmdis. This process involves adding dissolved CO₂ to a concoction of ethanol and HFA-134. When the dosage was activated, the CO₂ bubbles burst, causing the released HFA/ethanol droplet to react effervescently. As a result, the raindrops break apart into smaller pieces. This strategy's main objective is to increase the respirable part that is released from a typical PMDi. (27) The particles' size, which varies from 1 to 7 μm , dictates which lung regions they target. (28) When opposed to subcutaneous and intravenous injections, pulmonary medication delivery offers a non-invasive alternative. (29) Clinical research shows that these devices are useful for treating outpatient cases and exacerbations. (30) Both the environment and the unique characteristics of each patient should be taken into account when selecting a device. (31, 32) For asthma and COPD maintenance therapy, pressurized metered dose inhalers (18.9%–35.3% of patients) and dry powder inhalers (62.8%–88.5% of patients) are frequently prescribed. (33) Flovent HFA, which contains the usable inhaled corticosteroid fluticasone, is an illustration of a pressurized metered dose inhaler. (34)

2. Dry powder Inhaler (DPIs):

Using bolus drug delivery devices, dry powder inhalation is a technique for administering medication in a powder form through the pulmonary route. There are systemic and local repercussions to this method. (38) Dry powder inhalers do not require propellants, in contrast to other inhalers, also referred to as DPIs. Rather, the right dosage of medication is determined by the patient's rate of inhalation. The first DPI, known as the spin inhaler, was released in 1967 and was successful in the market when it came to delivering the mast cell stabilizer sodium cromoglycate. (39) In contrast, the turbo inhaler was the first contemporary multidose DPI to control the dosage by means of a dosing disc. (40) There are several different kinds of DPI devices on the market right now, such as breath-activated, power-driven, single- or multiple-dose devices. (41, 44) Nevertheless, these devices have drawbacks, including poor respirable percentage, flow dependency rate for breath-actuated devices, inadequate drug deagglomeration, and excessive complexity for power-driven DPIs. More sophisticated DPIs have therefore been created to address these issues. (45)

Based upon dosage form of drug the DPI are classified into two types:

1] Single dose DPI:

Powder inhalers for single doses are made up of a holder into which a powder capsule is placed. The powder is breathed from the capsule after the device is opened. We have updated this system.

It includes,

A] Spinhaler

B] Rotahaler

A) Spinhaler:

The working process is the same as for a rotahaler, with the exception that the outer sleeves are moved down to puncture the capsule and allow the propellant to release the drug.

Advantages:

1) Using this equipment is extremely safe.

2) The Spinhaler made it easier for patients to use and gave producers the chance to create powders that last longer on the shelf. This achievement was made possible by reducing the need for exact synchronization on the part of the patient.

Disadvantages:

1) Because the device is meant to administer a single dose, it must be loaded before each usage.

2) Some patients may find it difficult to administer Spinhaler formulations, and they may become intolerant to using them.

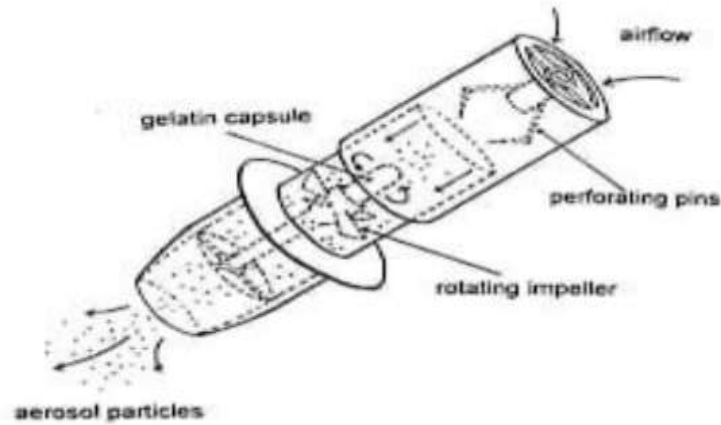


Fig: Spinhaler

B) Rotahaler:

With the colored end facing inward, place the capsule inside the rotahaler. Rotate the device to rupture the capsule. In order to allow the powder to enter the airway, take a deep breath. It's not necessary to time it with the aerosol, but it can take many breaths.

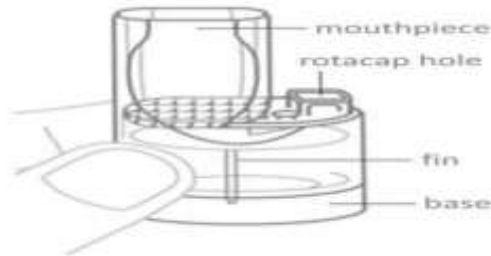


Fig: Rotahaler

Advantages:

1) Its design is user-friendly and compact, making it appropriate for most patients.

2) You do not need to coordinate your breaths.

Disadvantages:

1) Every time, a dose needs to be loaded.

2) For those with restricted finger or hand motion, loading the rotahaler can be difficult.

3) Humidity can sometimes affect how effective the pills are.

2] Multidose DPI:

Multidose devices work with a circular disk that holds four to eight powder doses, which is sufficient for one to two days of treatment. Until the time comes for inhalation, the doses are kept in separate aluminum blister reservoirs for storage. This specific device, which contains 60 doses in a foil-foil aluminum strip that is accessed just before the user inhales, is regarded as a true multidose device.

Advantages:

- 1) Unlike PMDI, shaking before use is not required.
- 2) After the patient inhales the first 200 milliliters of air, the gadget will discharge all of the powder.
- 3) The gadget is little and easy to use; it should be used in accordance with the guidelines that come with it.
- 4) You do not need to coordinate your breaths.
- 5) The apparatus is capable of storing several dosages.
- 6) The evaluation of sufficient inspiratory flow is made possible by the whistle adapter that is attached.

Disadvantages:

- 1] There is no clear manual for the inhaler's total emptiness. Second, it is inappropriate for people of all ages.
- 3] Incorrect administration of the recommended dosage could occur from not keeping an upright posture when the turbobaler is being loaded.(46-48)

3)Nebulizer:

A mouthpiece or mask can be used to inhale medication into the lungs in the form of a mist with a nebulizer, a medical equipment. Nebulization is a widely used aerosol production technique that is used by adults and children worldwide for both long-term management of respiratory disorders like asthma and COPD as well as emergency treatment of acute illnesses.(57) The Latin word "nebula," which means "mist," is where the name "nebulizer" comes from. It was first used in 1872. These gadgets produce a thin mist that swiftly releases tension in the bronchial muscles by penetrating deep into the respiratory system (58). Nebulizers transform medicine from a solution into an aerosol by using pressurized gas or an electric/battery-operated compressor, resulting in tiny droplets that can efficiently enter the alveoli. A gas flow of roughly 6–8 L/min is normally needed to run the nebulizer. The nebulizer uses oxygen, compressed gas, or ultrasonic power to spread the medication solution and administer the therapeutic dose straight to the lungs.(59) Nebulization is frequently used to deliver bronchodilators, but it can also be used to deliver a number of other drugs, such as steroids and antibiotics. Nebulizer usage is decreasing, while some patients still favor them. Nebulizer solutions are made up of medication solutions and excipients mixed together to provide the intended result. Sodium citrate serves as a buffer and is a frequently used excipient in nebulizer compositions. Disodium edetate improves stability by acting as a chelating agent for cations and works as a surfactant in combination with polysorbate 80. While sodium hydroxide, hydrochloric acid, and sulfuric acid are used to change pH or improve drug absorption, sodium chloride is utilized to adjust isotonicity. Nitrogen is used for headspace sparging to decrease oxidation and achieve stability. Moreover, calcium chloride is added to increase DNase's biological activity. The nebulizer solutions that are now on the market are sterile and sealed in vials that resemble unit doses to ensure that no antimicrobial agents enter. (60)

Types of Nebulizers:

- A) Jet nebulizer
- B) Ultrasonic nebulizer

Excipients Used in Pharma Aerosols:

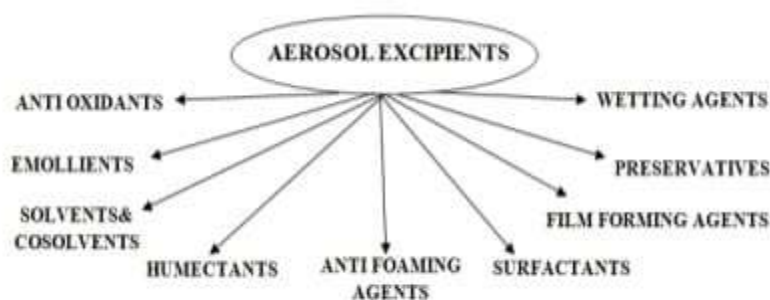


Figure 1. Excipients used in Pharma aerosols

1.Solvents/Co-Solvents:

A solvent is a material that has the capacity to dissolve a solute, which can be any kind of liquid, solid, or gas with a different chemical makeup, to create a solution. Although they are most often found in liquid form, solvents can also exist as solids or gasses. Examples of solvents are inorganic solvents like sulfur dioxide and liquid ammonia, as well as organic solvents like benzene, acetone, and acetic acid. In contrast, water-miscible organic solvents known as co-solvents are added to liquid medicine formulations to increase the solubility of poorly soluble compounds and to improve the chemical stability of active pharmaceutical ingredients. (52)

2.Buffering Agents:

Weak acids or bases are known as buffering agents, and they are used to control a solution's acidity (pH) even in the presence of new acids or bases. A number of factors depend on the formulation's pH, such as maintaining or improving the chemical's stability, guaranteeing physiological compatibility and incompatibility, boosting the formulation's antimicrobial efficacy, and maximizing solubility (or insolubility if taste is an issue).

3.Preservatives:

Preservatives are chemicals used to prevent food, wood, medicine formulations, and other materials from deteriorating. They are used in a variety of pharmaceutical and cosmetic products, where they successfully reduce the danger of contamination and microbial growth. It is significant to remember that sterile, single-dose products do not require preservatives. These kinds of excipients are advantageous since they mainly target microbiological cells and do not harm or irritate mammalian cells. It is noteworthy to note, nonetheless, that there is a restricted number of approved preservatives available for oral solid dosage forms (OSDs) and multiuse aerosols, and the possibilities are even more constrained for other routes of administration. It is imperative to refrain from using them in parenteral infusions.

4.Anti-Oxidants:

Oxidative stress on fluorescence photoproducts (FPPs) can be mitigated by antioxidants. These days, antioxidants are frequently created using enzymes and other substances. Antioxidants such as beta carotene, vitamin C, and vitamin E can mitigate the deleterious consequences of oxidation. Antioxidants are routinely added to prepared foods and vegetable oils in the food industry to stop or minimize the deterioration that occurs from exposure to air. They are also used to regulate API oxidation. For this aim, common ingredients include colorants (aging discolouration) and oils or fats that are prone to oxidation (rancidification), as well as preservatives such potassium sorbate.(53)

5.Anti-Foaming Agents:

Defoamers, another name for anti-foaming agents, are chemicals that are used in liquid dosage formulations to reduce the amount of foam that forms. This problem, which is unwanted and disruptive, frequently occurs during the production process or when reconstituting liquid dosages. By lowering the liquid phase's cohesive binding and surface tension, anti-foaming chemicals successfully diminish foam. Antifoaming agents include insoluble oils, polydimethylsiloxanes and other silicones, stearates, and glycols, as well as certain alcohols. Polydimethylsiloxane-silicon dioxide, or methicone, is one example. It is usually employed in quantities ranging from 1 to 50 parts per million. Furthermore, wet granulation—the process of using foam in place of aqueous granulation fluid—is gaining popularity.

6.Humectants:

These compounds are vital components of medications and cosmetics because they prevent moisture loss from the skin, which is crucial for maintaining the skin's natural moisture content. For external usage, hygroscopic excipients are usually added at a concentration of around 5% to aqueous suspensions and emulsions. Their main purpose is to keep the product from drying out after it has been applied to the skin. They also stop cap-locking, which is the result of condensation building up on the container closure's neck after the first opening. Among these excipients are well-known brands including PEG, glycerol, and propylene glycol. (54)

Quality control test in Aerosol:

1.Spray testing:

This inspection's primary goal is to extract any pure propellant and concentrate from the dip tube. It also looks for valve issues and abnormalities in the spray pattern. with order to conduct this test, test sprays are directed onto treated paper that has been covered with a dye-talc mixture. A dye that is either oil- or water-soluble is used, depending on the type of aerosol. The sprayed particles and the paper's dye combine to create a solution that the paper absorbs. The test's outcomes offer a thorough record that can be compared and utilized to create a profile of the spray pattern. A 100% batch inspection, in which every aerosol in a batch is subjected to spray testing and the outcomes are compared between batches, is the standard procedure used in the pharmaceutical sector. When it comes to metered dose aerosols, the patient's drug dosage can be greatly affected by the spray pattern.

2.Leak testing:

The purpose of the leak test is to make sure the aerosol dispenser valve is correctly crimped, preventing any faulty containers. This is accomplished by evaluating the crimp's measures and confirming that they adhere to the necessary requirements. In order to evaluate the filled containers, a water bath is used, and the valve closure is tested one last time. This test defines leakage as the difference in weight between the same container before and after it has been stored upright for at least three days at a temperature of $25^{\circ}\text{C} \pm 2^{\circ}\text{C}$. In accordance with USP-NF rules, twelve pressurized containers are chosen at random, and the aerosol dispensers are weighed in milligrams as the starting weight prior to placement (W1). After that, the filled containers must stay upright at room temperature for at least three days. Following this time frame, each container's weight needs to be measured once more to get the weight in milligrams (W2). The testing period (T) has a length expressed in hours.

$$\text{Ratio of leakage} = \frac{W2 - W1}{W1} \times \frac{100}{T}$$

The average annual leakage rate of the 12 sample containers needs to be less than 3.5% of the net filled weight in order to meet standard criteria. Furthermore, it is imperative that the leakage rate of all tested containers not surpass 5% of the net loaded weight annually. Should one of the twelve containers exceed the 5% threshold, but none of them above the 7% annual leakage rate, it becomes imperative to evaluate the leakage rate for an extra

twenty-four containers. Finally, as per the specifications, no more than two of the thirty-six containers should have a leakage rate higher than 7% of the net fill weight annually.

3.Weight checking:

Through this evaluation method, the accuracy of the filling process will be evaluated, and the final product weight will be guaranteed to be consistent. To concentrate them, tared empty containers are inserted into the filling lines. These containers are subsequently taken out of the batch and weighed to see if they fit the specifications (USP-NF, 2014). Empty aerosol containers are periodically added to the filling lines for weight verification. Once they are filled with product concentration and weighed, they are withdrawn. Usually, the same technique is used to confirm the propellants' weight. To confirm the correctness of the filling process, the completed product's filled container is also weighed.

4.Valve acceptance:

To make sure that valves are purchased from technically sound sources, valve acceptance testing is crucial. The correct running of operational units depends on valves, and any problems with valves might result in a reduction in manufacturing output. A 2003 study discovered that poor design and inferior materials accounted for a sizable portion of valve failures. As a result, acceptance testing is required to evaluate the functioning of valves under various pressure and temperature scenarios. There are two types of metered aerosol valves with distinct delivery limits that are subject to the acceptance test method. If a specific number of valves fall beyond the set limits, they are rejected, and further testing is necessary to assess the acceptability of the batch.

5.Containers:

Containers are made of a variety of materials, such as aluminum, stainless steel, tin-plate, and some kinds of glass. The aerosol container's resistance to internal pressure of up to 140–180 psi at 130 degrees Fahrenheit is an important consideration (Remington and Allen, 2015). Containers that are coated or uncoated are inspected to find any internal flaws. Various parts of quality control and evaluation criteria are used according to the kind of container being utilized. As a quantitative indicator of the exposed metal, the degree of electrical current conductivity in metal containers is one of the quality control concerns to be considered. Glass containers are examined to look for flaws and cracks. Furthermore, standard criteria like weight and measures are assessed to make sure they meet required standards.

It is necessary to verify that the neckline dimensions and other structural elements of the containers meet the required standards. In addition, evaluations are conducted on dip tubes, actuators, and valves. (51)

Technological Advances in Aerosol Drug Delivery:

In recent years, pressurized metered dosage inhalers (pmdis) and dry powder inhalers (dpis) have dominated the market. Although pulmonary delivery techniques have yielded notable results, technological breakthroughs have spurred a renewed interest in aqueous aerosol drug delivery. This is especially true for compact devices intended for ambulatory patients in the home health field (Lange & Finlay, 2006; Smaldone, 2006). The most recent advancements in liquid aerosolization technology have mostly addressed the well-known requirement for devices that can deliver systemic medications through the pulmonary route (Sanjar & Matthews, 2001) by providing a precisely metered dose to the deep lung (Schuster et al., 1998). Aqueous aerosol delivery systems simplify the formulation procedure and make it easier to provide novel pulmonary treatments. Currently available products for aqueous aerosol generation can be categorized into four main types:

- 1)Air-jet nebulizers
- 2)Vibrating nebulizers
- 3)Smart nebulizers
- 4)Metered dose liquid inhalers (mdlis).

1) Air-jet nebulizers:

In the past, the standard technique for giving pulmonary medication to immobile patients in acute care or home care settings was jet nebulization. Patients experiencing acute respiratory distress can benefit most from this method since they may find it difficult to synchronize device activation with their breathing patterns or may need greater doses in order to target the lungs properly. However, because of their bulkiness, the necessity for expert help, and the need for extra tubing, mouthpieces, compressed air or oxygen sources, these nebulizers frequently provide difficulties.

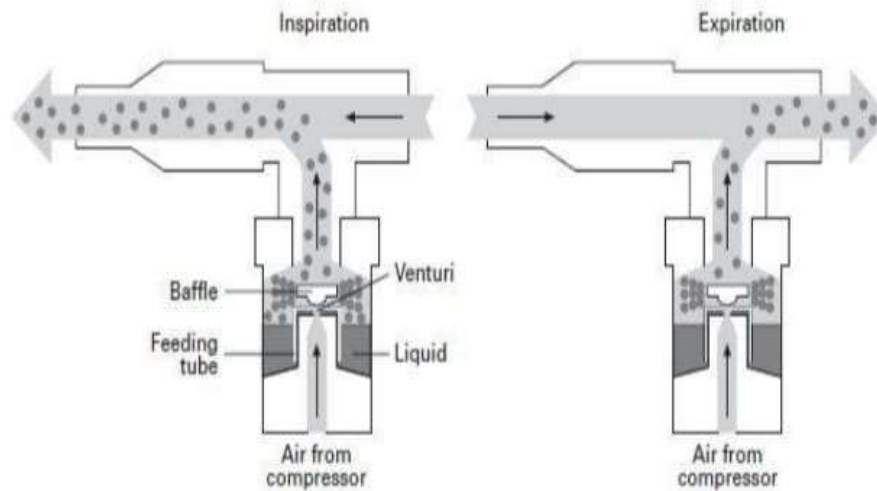


Fig: Air-Jet nebulizer

Advantages:

- Cheap
- Easy to use
- Effective than pMDI and DPIs for administering medication.

Disadvantage:

- Inefficient
- Difficult to clean
- Need to compress gas

How to use jet nebulizer?

Kids can treat themselves with a jet nebulizer because it's so simple to use. Perform these actions:

- 1) Wash your hands to prevent contamination of the drug. Ensure that the air compressor and line are securely fastened.
- 2) Fill the medicine cup with the required prescription; make sure the medication is accurate every time.
- 3) Attach the mouthpiece and hose to the medication cup, making sure the connection is snug.
- 4) Insert the mouthpiece into your upper lip.
- 5) Breathe deeply to ensure that all of the medication that has been misted reaches your lungs. Continue treating the patient until the medicine in the medicine cup is completely gone.
- 6) Switch off the machine after using it.(50)

2.Vibrating mesh nebulizers:

Apart from jet nebulization, aerosols can also be produced by ultrasonic equipment. These gadgets create a therapeutic aerosol mist of respirable droplets by vibrating a piezoelectric crystal at high frequencies (1-3 mhz). Both cavitation theory and capillary wave theory (Mercer, 1981) explain the conventional process of producing ultrasonic aerosols. However, new developments in ultrasonic technology have paved the way for the creation of vibrating mesh nebulization, or micropump technology, for pulmonary administration. This method creates high rf, low velocity aerosols by attaching a vibrating piezoelectric crystal to a mesh plate that has been laser-bored. Primary aerosol droplets within the respirable range (1-5 μm in diameter) are created when fluid is fed from a small volume reservoir through many tapered holes caused by the oscillation of the mesh plate. The aeroneb® pro (aerogen inc., Galway, Ireland) is one vibrating mesh nebulizer that is now on the market and has been tested for a number of formulations and treatments.

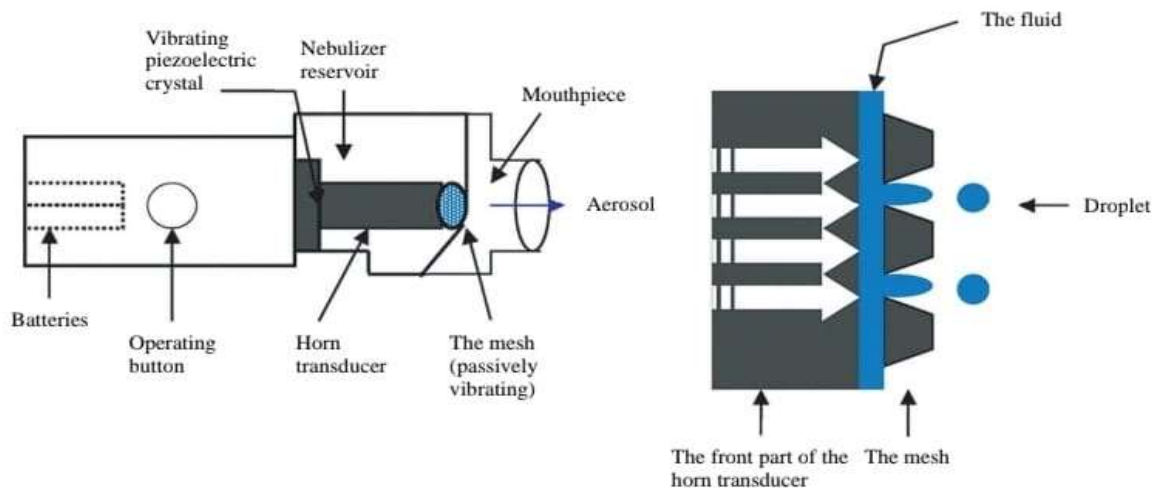


Fig: Vibrating mesh nebulizers

3. Smart nebulizers:

The rise in the number of novel pulmonary delivery formulations underscores the growing need for more precise dosing control, especially with expensive or potentially hazardous drugs. Because of dosing during exhalation, air-jet nebulizers that run continuously have been found to waste between 60 and 70% of the formulation. Even though breath-assisted nebulizers produce less waste, nebulization may not reach the lungs efficiently at the end of inhalation. Prior to clinical trials, a great deal of research has been done using simulated lung models to predict human lung deposition. The respiratory patterns, such as minute volume, are important in determining drug deposition in the lungs.

4. Metered dose liquid inhalers:

With the integration of cutting-edge aerosol generation technology utilizing both mechanical and electromechanical approaches, a new age of single-dose aerosol delivery devices is presently undergoing research and clinical trials (Hindle, 2004). Only 20% and 50% deposition were accomplished in half-propelled and cfc-propelled pmdis, respectively, demonstrating the ineffectiveness of the delivery mechanisms used by pmdis for metered dose (Dalby et al., 2004). Due to fast speeds and inadequate breath-actuation coordination, most of the drug-containing aerosol is lost, causing impaction in the oropharynx (Newman, Pavia, Moren, Sheahan, & Clarke, 1981). mdlis provide more formulation freedom and yield precisely dosed aerosols at lower velocities by doing away with the need for a volatile propellant. Mdlis show tremendous promise for local pulmonary delivery as well as

Application of Aerosol:

- Automobile (Starter Motors, Drive Chains, Car locks, Spark plugs, Door Hinges, Push back and tilting systems)
- Industrial (Overhauling machinery, crane hook bearings, and wheels, Lubricates and opens jammed bearings, Loosens jammed nuts and bolts, Power tools, Jigs & fixtures).
- Ordnance (Guns, Precision fitting, Linkages)
- Electrical Equipment (Alternators, Motors, Relays, Circuit Breakers, Fuses, Potentiometer Relays, Switch gears, etc.)
- Pneumatic Systems (Sticky solenoid valves, Clogged needle valves, Automatic valves & cylinders)
- Household (Drawers, Hinges, Pins, Sliding Contact at Windows, Sewing Machines, etc.)
- Domestic (Mixers and Grinders, Hand Tools, Washing Machines, Collapsible Grills, Folding Chairs and Tables, TV, Radio, and Tape recorder tuners, etc.)
- General Purpose (Sliding Windows and door channels, Locks, Switches, Bicycle chains and sprockets, rolling shutters, elevator doors, etc.)(56)

Marketed Aerosol product:

1. Aerocort Rotocaps:

Asthma is treated with Aerocort Rotacap (wheezing and shortness of breath). Breathing becomes easier as a result of the air passage muscles being relaxed.



Fig: Aerocort Rotacaps

Use:

- Treatment of Asthma

Side Effect:

- Oral thrush
- Dry mouth
- Mouth Infection
- Hoarseness of voice

2. Fullform Rotocaps:

Complete form 200 Rotacap is used to treat chronic obstructive pulmonary disease (a lung condition in which the airflow to the lungs is impeded) and asthma, which causes wheezing and shortness of breath. Breathing becomes easier as a result of the air passage muscles being relaxed.



Fig: Fullform Rotocaps

Use:

- Chronic obstructive pulmonary disease (COPD)

Side Effect:

- Headache
- Pneumonia
- Voice change

- Tremors

3. Foracort Inhaler:

Two medications are combined into one inhaler with the Foracort Inhaler 200. It facilitates breathing by easing the chronic symptoms of COPD and asthma. It functions by relaxing the muscles in the airways and preventing the production of specific chemical messengers that lead to inflammation (swelling).



Fig: Foracort Inhaler

Use:

- Treatment of Asthma.
- Chronic obstructive pulmonary disease (COPD).

Side Effect:

- Nausea
- Vomiting
- Headache
- Stomach discomfort
- Cough

4. Duolin Inhaler:

Chronic obstructive pulmonary disease (a lung condition in which the airflow to the lungs is impeded) is treated using a duolin inhaler. Breathing becomes easier as a result of its assistance in relaxing the muscles of the airways. It eases breathing difficulties, wheezing, and coughing.



Fig: Duolin Inhaler

Use:

- [Treatment and prevention of Asthma](#)
- Treatment and prevention of Bronchitis

Side Effect:

- Dryness in mouth
- Cough
- Tremors
- Palpitations
- Muscle cramp

5. Budecort 200 Inhaler:

The purpose of the Budecort 200 Inhaler is to stop asthma attacks, such as wheezing and dyspnea. It is referred to as a "preventer" and is a steroid. This medication won't halt an asthma attack that has already begun, so you'll also need a fast-acting "reliever."



Fig: Budecort Inhaler.

Use:

- Asthma

Side Effect:

- Difficulty in swallowing
- Fungal infection of mouth
- Fungal infection of oropharynx
- Headache
- Abdominal pain
- Depression
- Joint pain

Future & Perspectives

- (1) Establish a network of observatories throughout India and the surrounding seas to conduct in-situ measurements of cloud characteristics, size, shape, mixing state, and aerosol chemical composition.
- (2) Perform in-depth analyses of aerosol types, aerosol dispersion both vertically and horizontally, dust and black carbon mixing, and annual variations.
- (3) Satellites are used to measure aerosol dispersion, investigate the chemical composition of clouds, assess cloud microphysical properties, track solar radiation, and track longwave radiation from Earth.
- (4) Conduct broad campaigns to evaluate aerosols and cloud properties, particularly the aerosol indirect effect, in different regions of India and the adjacent maritime areas. These campaigns should make use of airplanes, ships, and ground-based observations.(63)

Conclusion:

Technology has made major strides in the manufacturing of aerosols for inhalation therapy. From conventional nebulizers to more advanced technologies like electrohydrodynamic atomization, surface acoustic waves, and capillary aerosol generation, it has changed over time. The use of smart monitoring systems in conjunction with these new technologies has increased patient adherence to treatment. The physicochemical characteristics of the formulations, in addition to the nebulizer's design and operation, determine how well aerosolization works. Standardized testing for nebulization goods will make it easier to compare devices in vitro, which will increase the efficiency of the device in vivo. The state of the disease, the device's availability and cost, medication interactions, and the effectiveness of the treatment all play a role in the ultimate decision about whether or not to prescribe a device.

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