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AEROSOLS & IT'S USES IN COPD

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ABSTRACT

When treating patients with respiratory diseases, aerosols are frequently used. The right aerosol delivery system must be picked by the doctor. The metered dose inhaler is typically the first option of a device for patients who are mechanically ventilated as well as those who breathe on their own. There are significant differences between the devices in the dosage that is delivered to the lungs; for the average prescription, nebulizers provide more medicine to the lungs than metered dose inhalers, which may be especially relevant for patients who are critically unwell.

Keywords: Aerosols, Inhaler, Nebulizers, Propellant, Valves.

INTRODUCTION

Pressurized dosage forms are included in aerosols, which are dispersion phase systems in which extremely small solid drug particles are scattered in the propellants, which serve as a continuous phase.containing one or more active ingredients that, when activated, release a fine dispersion of liquid or solid material in a gaseous atmosphere. Aerosol is also known as a pressurized package becauseit is typically used to describe a medicine with therapeutic activity [1]. The name "aerosol" alludes to the fine mist of spray that is produced by the majority of pressured systems.

The following are some benefits of aerosols:

- They have both local and systemic effects, are sterile, and are devoid of any contamination.
- Sterility may be preserved throughout the product's shelf life if it is packaged in sterile circumstances.
- When applied immediately to the area that is hurt, they have a cooling and refreshing effect.
- Without assistance from others, using and applying them is simple.
- Compared to other dose types, their action is quicker.
- Some medications are sensitive to light; thus, their containers shield the medication from light [2].

The aerosol's valve assembly, container, actuators, and propellant all play a role in how the contents are delivered. Product concentration and propellant are the two elements that make up an aerosol. The therapeutically effective Ingredients are in the product concentrate. The creation of proper pressure inside the container to release the product concentrate in the required form, such as spray, mist, solid, foam, stream, etc., depends on the propellant having a vapour pressure greater than atmospheric pressure at 400 degrees Celsius [16]

Principle of Aerosol

A high-velocity gas flow is directed through a tube that is submerged in a water reservoir in this system. It is powered by a compressed gas. The product concentration and the propellant shown in Figure 1 are the two ingredients that make up an aerosol formulation.

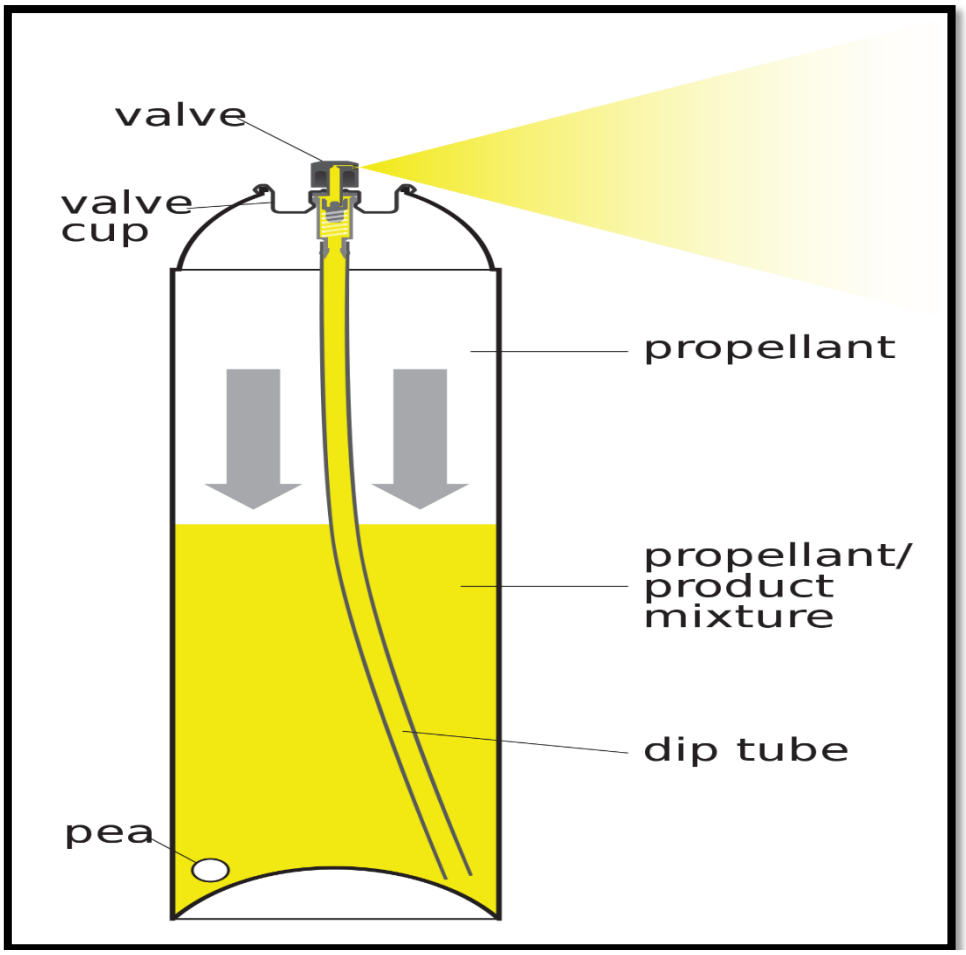


Figure 1: Principle of Aerosol

Working principle: Water is drawn up between the surfaces of the tube as gas flows through it, coming in contact with the path of the gas flow through tiny spores. Aerosol is created when a gas stream interacts with a fluid's surface and spreads liquid [3-6].

Aerosols are categorized

Space Sprays: Space spray is the term used to describe how these products are distributed. It has 30–40 psi of pressure and is pressurized at 700°F with 85% propellant. There are no particles larger than 50 m in it. In order to retain air. Deodorizers and disinfectants, for instance [17].

Foam: Foam spray refers to aerosols that are designed to transport active substances to the surface. These are created by propellants expanding quickly through an emulsion. Products are discharged as foam. such as shaving cream[18].

They come in two different kinds:
1) Water-based stable foams
2) Foams that are not aqueous
Surface coatings: When they are sprayed on a surface, a moist coating results. Between 22 and 55 PSIG and 700 °F, it comprises 30 to 70% propellant. for instance, hairspray and powder spray[19].

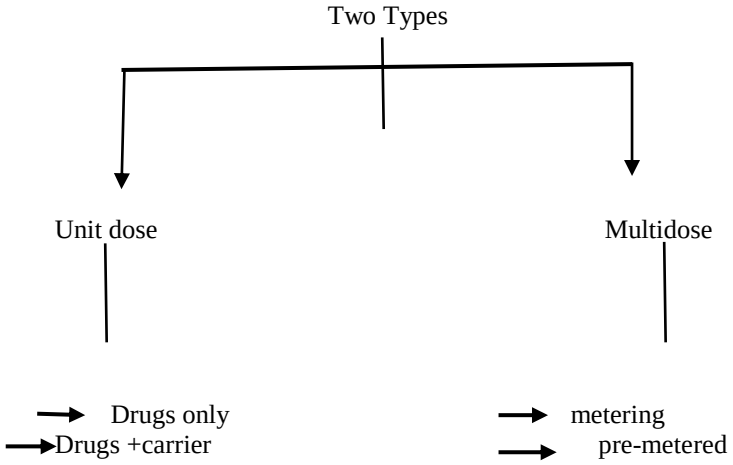
Inhaler: Any dry medicine or drug solution given by the nose or oral respiratory route is considered to be inhaled. It is frequently used to treat respiratory issues including asthma[20].
There are three different kinds of them:
1) Pressurized metered dose inhalers (pMDIs)
2) Inhalers with dry powder (DPIs)
3) Nebulizers

1) Pressurized metered dose inhalers (pMDIs)

It is made up of a spacer, an actuator, and a canister. The active ingredients, which are the medication, a liquefied gas propellant, and stabilizers, are contained in the canister's metering dose valve formulation. A single metered dose is released when the actuator opens the metre dose valve. Cavitation is the name of this procedure [7-10].The liquefied gas propellant is very flammable and breaks down into liquid droplets that quickly evaporate. The following are some disadvantages of metered dosage delivery:

A) When pMDIs are compressed, the dose is released at a high rate and is deposited in the oropharynx.
B) It's important to carefully coordinate your actuation and inhalation.
C)High probability of pharyngeal depositions.

2) Inhalers with dry powder (DPIs)



Unit dose:
Dry powder inhalers with a single dose can be used again and again. They are simple to use and appropriate for many ailments that call for an immediate effect. In this dosage, the capsule must be opened and the user must inhale the powder. Their benefit is that a big dose cannot be given by the unit dose in the event of an asthma attack. For instance, the Innova TM (inhale therapeutic systems: San Carlos, U.S.A.) is a dry powder unit dose that has been around for a while. An inhaleris positioned in a clear holding chamber with a stored bolus of compressed air-producing aerosol.

Multi-dose:
A.S. Draco created the original Turbuhaler multi-dose DPIs that could deliver carrier-free particles at moderate flow rates. Dishaler, a drug created by Glaxo Smith, took the place of Turbuhaler. Salbutamol and betamethasone, among other medications, were delivered through DISHALER. This method makes use of a circular disc holding four or eight dosages of powder, each of which is stored in a separate aluminium blister container.

3) Nebulizers
A drug is given using a nebulizer so that it can be inhaled as a mist through the lungs. To disperse dosage solution and suspension into tiny aerosol droplets known as mists, they are powered by oxygen, compressed air, or ultrasonic energy. Through the mouth, they are immediately inhaled [11].

The following are nebulizers' benefits:

- Possibility of high dose
- Utilization is simple
- There is no CFC (chlorofluorocarbon) release
- They distribute more quickly and are more portable, smaller, and lighter

The following are some drawbacks of nebulizers:

- They cost a lot
- Contamination is a possibility
- They are unable to be successfully aerosolized
- Pressurized gas is needed for jet nebulizers

Aerosol Components
A. Propellant
B. Container

C. Valve and actuator
D. Product concentrate

A. Propellant

is in charge of generating the necessary pressure inside the container. They supply the energy needed to propel the product out of the container. It frequently performs the combined functions of propellant and solvent or vehicle for the product concentration when the propellant is a liquefied gas or a combination of liquefied gases. Nitrogen is used as the propellant in some aerosol systems instead of carbon dioxide or other liquefied compressed gases [12–13].

There are two kinds of them.
a)Liquefied gases propellant
b)Compressed gases propellant
Liquefied gases propellants

They are gases that turn into liquids when under pressure. As the valve is opened, the product is consumed; some of the liquid propellants converts to gas, maintaining a gaseous atmosphere in the head space.

Kinds of propellants:

Chlorofluorocarbon Propellants

Propellants are flammable, non-toxic, and chemically inert. They used to be used somewhat frequently in earlier times, but less so these days. Because they are non-flammable and toxic-free, they have these advantages [21].

Hydrocarbons propellants

As a result of their low toxicity and lack of reactivity, hydrocarbon propellants can be utilized as a propellant. Because there is no chlorine present, hydrocarbons are employed to make water-based aerosols because they are resistant to hydrolysis. Water cannot mix with them. Their benefits include being great solvents, while their drawbacks include being explosive and flammable. By using a vapour tap valve, flammability is decreased [14].

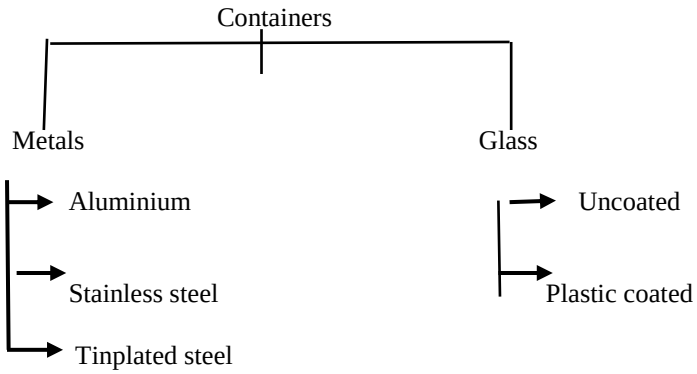
Compressed gas propellants

The product is released as a thin mist, foam, or semisolid using compressed gas as the propellant, such as nitrogen or carbon dioxide. The forms it creates are less stable than those made by the liquefied gas propellant, and it creates rather moist sprays. When the aerosol valve is opened, the gas from these propellants' "pushes" the liquid out of the can by occupying the headspace above it in the can [22].

B. Containers

The chosen aerosol container must be capable of withstanding high pressure between 140 and 180 psig (per square inch gauge) at 130 °F. Cost and material compatibility with the formulation should also be taken into account [23].

There are two types of containers, and they are as follows:



Aluminium: Compared to other metals, aluminium containers are lighter and less corrosive. Metered dosage inhalers (MDIs) and many topical aerosol products contain aluminum. Aluminium containers are coated with vinyl or phenolic resins to lessen the aluminum's interaction with the formulation. From 10 ml to 1,000 ml, the container is offered in various sizes.

Stainless steel: Although they are quite expensive or costly, they are extremely sturdy containers that are resistant to various materials and do not require inside coating.

Tinplated steel: Tin-plated steel consists of a steel plate sheet that has been tin-coated. The coated sheet is divided into three parts: the top, bottom, and body, which are soldered together. Coating ingredients include oleoresin, phenol, and vinyl. Topical aerosols are packaged in steel with a tin coating.
Glass containers: These containers have a lot of aesthetic value, but they can only be used for goods with pressures of up to 33 PSIG. They are also only used when a little amount of propellant is being used, as when the pressure is under 25 PSIG. Glass containers must have two layers of plastic coating applied to them in order to protect them from breaking under high pressure. [15]

C. Valve and actuator
Valves: Controlling the passage of the propellant and medicinal substance out of the container is the valve's main duty. As demonstrated in Figure 2, valves are simple to open and close. The content can be delivered by them in the desired format, such as a spray or foam stream, for example [24].
There are two types of valves:
1. Metering valves
2. Constant spray valves

Figure 2: Components of aerosol valves

Actuators: These are buttons with specific designs that aid in dispensing medication in the desired form, such as a spray, wet stream, foam, or solid stream. In addition to the expansion chamber, which affects the kind and amount of propellant utilized, the actuator also has orifices of various sizes and shapes [25].

Stems: The stem supports the actuator and delivers the formulation in the right form to the actuator's chamber. Stainless steel and nylon are the materials that make it up [26].

Gasket: The gasket prevents formulation leakage and secures the stem and valve firmly in place [27].

Spring: The spring secures the gasket in position and aids in keeping the valve closed when the formulation is activated, releasing pressure [28].

Mounting cup: Aluminium is typically used for the mounting cup, which is used to mount the aerosol can and position the valve. It may have a covering made of an inert substance, such as vinyl, to stop any contact with the contents and to stop aluminium from corroding [12–15].

APPARATUS USED IN PHARMACEUTICAL AEROSOL:

Pressure filling apparatus
Cold filling apparatus
Compressed gas filling apparatus

Pressure filling apparatus

An aerosol container must be filled with the appropriate amount of propellant, which is measured by a metering burette in the pressure-filling device. The input valve, which is located at the valve's base and is under its own vapour pressure, is where the propellant is to be injected.
The valve's top is attached to a cylinder of compressed gas or nitrogen, and when the nitrogen pressure is applied, the propellant flows into the container through the measuring burette.

Cold filling apparatus
It is made up of a copper tube-equipped insulated box. Copper acetone dry ice is placed within the insulated tubing. It cools more quickly because the copper tubing has more surface area[29].

Compressed gas filling apparatus
Propeller fuel is a compressed gas. A pressure reduction valve lowers the pressure of the compressed gas as it is under high pressure. Filling the aerosol container with compressed gas propellant requires a pressure of 150 pounds per square inch gauge[2, 8].

EVALUATION PARAMETERS OF PHARMACEUTICAL AEROSOLS:

Combustibility and flammability
Flame projection is also a part of it.
1) Flashpoint: The typical test device is the tag open cup instrument. The aerosol product is transported to the testing equipment after being refrigerated to a temperature of roughly 250F. The test liquid's temperature is gradually raised [30].
2) Flame extension and flame projection: An open flame is sprayed with the aerosol product for roughly 4 seconds, and the length of the flame is measured using a ruler [30].

Physical and Chemical Features
- ❖ Atmospheric pressure
- ❖ Specific gravity
- ❖ Content of moisture
- ❖ Identifying the various propellants
- ❖ Ratio of concentrate to propellant

Performance
- Aerosol valve discharge rate: An aerosol product of known weight is taken and its content is discharged using standard apparatus for a given period of time. The container www.bjmhr.com 9 Kumar et. al., Br J Med Health Res. 2018;5(11) ISSN: 2394-2967 is reweighted. Then the change in weight per time dispensed is the discharged rate. The discharge rate can also be expressed as grams per second.
- Spray pattern: The technique entails the application of sprays to paper that has been coated with a dye-talc mixture. The spray pattern was recorded.
- Metered valve dosage: The doses are delivered into the active material's absorbents or into the solvents. The amount of the active component is determined by the solution's assay. The average dosages are then determined by reweighing the container and dividing the weight difference by the number of doses administered. The steps are repeated, and the outcomes are contrasted.
- Net contents: After the tared cans are weighed after being placed on the filling line, the net contents are determined by the weight differential.
- Foam stability: Depending on the formulation, a foam's lifespan can be anywhere between a few seconds and an hour or more. Various techniques are used to assess a foam's stability, including rotational viscometer, visual inspection, the amount of time it takes for a given mass to penetrate it, the length of time it takes for a given rod to fall into the foam, and time for the mass to exit the foam.
- Quantifying the size of the particles.
- Leakage.

Biologic features: Biologic testing takes both therapeutic activity and toxicity into account [8].

PHARMACEUTICAL AEROSOL QUALITY CONTROL:
Pharmaceutical aerosol quality control comprises inspecting and testing the propellant, valves, actuator and dip tubes, container, weight, and leak and spray tests.

Propellant: These tests include
1) Using gas chromatography to distinguish between two or more propellant mixtures.
2) Moisture, halogen, and non-volatile residue determination is used to determine the propellants' purity.

Actuators, valves, and dip tubes:
It is examined physically and chemically. Their test protocols are as follows:

- Select a container that is suitable and add 25 valves.
- A specified test solution is put inside the container.
- The valves are connected to a button actuator that has a 0.02-inch orifice.
- At a temperature of 25–10 C, the filled container is placed in an environment that is suitable.
- The filled containers are triggered fully for 2 seconds after the product reaches a temperature of 25 10C.
- Repeating this process results in final delivery of 2 out of every 25 test units [19].

Containers: The linings of containers are checked for flaws. Electric current conductivity is used as a metric for exposed metals in quality control. legislation compliance checks on glass containers [31].

Weight measurement: It is accomplished by intermittently inserting empty tarte containers into filling lines, which are then removed and reweighted after being filled with product concentrate [32].

Leak test: This is carried out by comparing and measuring the dimensions of the crimps valve. By running filled containers through the water bath, the valve is finally tested [8].

CONCLUSION

Aerosols are excellent for treating respiratory and asthma-like conditions since they may be applied directly to the affected area and are completely contaminant-free. Hydrofluorocarbon (HFC) propellants are being used in their stead since chlorofluorocarbon (CFC) propellants destroy ozone. They are employed for a variety of applications in the treatment of asthma and chronic obstructive lung disorders due to their benefits, which include the ability to direct the medicine to the site of action and also a reduction in systemic adverse effects, among others (COPD).

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