**AEROSOLS**

DEFINITION OF AEROSOLS.

•COMPONENTS OF AEROSOLS

–(1) Drug product concentrate [solution, emulsion, dry powder]

–(2) Propellant [compressed gas (co2, N2, NO) & liquified gas ( HC, CFC, HFC)

–(3) Container [ Aluminium, steel, tin, glass)

–(4) Valve and actuator [Metering, Spray , foam]

•MANUFACTURING (COLD FILL PROCESS and PRESSURE FILL PROCESS)

•MECHANISMS OF AEROSOL DEPOSITION AND PARTICLE SIZES.

•ADVANTAGES OF AEROSOL: *RATIONALE OF USE*

•DISADVANTAGES.

•METHOD OF USE THERAPEUTIC INHALATION AEROSOLS.

•**TYPES OF AEROSOLS [INHALERS (MDI, DPI) & NEBULIZERS].**

•USES / APPLICATIONS OF PHARMACEUTICAL AEROSOLS.

**AEROSOLS**

•An aerosol is a suspension of fine solid particles or liquid droplets in a gas.

•NATURAL AIROSOLS: clouds, fog and smoke.

•WHAT ARE PHARMACEUTICAL AEROSOLS?

•Pharmaceutical aerosol is a suspension of fine solid drug particles or liquid drug droplets in a carrier gas/propellant.

•Also known as pressurized dosage form as carrier gas/propellant is compressed or liquefied under pressure to expel the contents from the container as a fine solid particles or liquid mists.

•Also known as Inhalational Drug Delivery systems (IDDS) or inhalants as drug is inhaled through nose / mouth to the lungs.

•Commonly used for respiratory disease (asthma) and lung disease (emphysema).

•They are intended for **local action** in the nasal / throat area, and **systemic action** also when drugs are absorbed from the lungs in to the blood stream.

•***ALL PHARMACEUTICAL AEROSOLS ARE NOT INHALATIONAL.***

•***E.g Topical aerosol sprays: Local anesthetics, pain reliever spay.***

**COMPONENTS OF AEROSOL PACKAGE**

 

(1) Drug Product Concentrates

(2) Propellant.

(3) Container.

(4) Valve and actuator.



1-PRODUCT CONCENTRATES

•Based on the drug product formulation as solution, emulsion, suspension or powder we can have Solutions aerosol, emulsion aerosol or Suspensions aerosols .

•Foams are produced when the product concentrate is dispersed throughout the propellant and the propellant is in the internal phase; i.e., the emulsion behaves like o/w emulsion

2-PROPELLANTS

•Propellants are chemicals with a vapor pressure greater than atmospheric pressure at a temperature of 40˚C.

•Propellants are simply compressed gas or liquid under pressure that can readily be vaporized into the desired pressurized gas.

•It is one of the most important components of the aerosol package (It is said to be the heart of the aerosol).

•It also serves as a solvent for certain active ingredient.

•It provides the necessary force to expel the contents; it causes the product to be dispensed as foam or mist/spray, depending on the formulation and the type of valve employed.

**Compressed Gas Propellant**



Compressed gas propellants really only occupy the head space above the liquid product in the can. When the aerosol valve is opened the gas 'pushes' the liquid out of the can. The amount of gas in headspace remains the same but it has more *pressure* space, and as a result the *drop during the life of the can.*

 Examples

Carbon dioxide

Nitrous oxide

Nitrogen

**Liquefied Gas Propellant**



As the product is used up, some of the liquid propellant turns to gas and keeps the head space full of gas, pressure in the can remains essentially constant and the spray performance is maintained throughout the life of Aerosols.

Hydrocarbons: [Liquefied Petroleum Gas

(eg. propane, butane, & isobutane)

Halocarbons: (CFC) CloroFhloroCarbons

Trichloro-monofluoro-methane (propellant 11)

Dichloro-difluoro-methane (propellant 12)

Dichloro-tetrafluoro-ethane

Compressed gas; pros and cons:

–Pressure falls during use;

–doesn't have any environmental problems

•Hydrocarbon propellants ; pros and cons:

•Most common

•Cheap,

•Good solvent

•Doesn't have any environmental problems (no ozone depletion).

•Bad taste,

•Flammable

•Chlorofluorocarbons ; pros and cons:

•Most common

•Cheap,

•Good solvent

•Environmental problems (depletes ozone layer)

•FDA banned use of CFC

•Hydrofluorocarbons (HFA

•Replaced CFC

•No Environmental problems (does not depletes ozone layer).

•Very costly.

**4-VALVES**

•Aerosol valve is multifunctional in that:

•It is capable of being easily opened and closed.

•It regulate the flow of product concentrate.

•It regulate the amount of emitted material.

•It is capable of delivering the content in the desired form (mist spray, or foam).

•Mist is a phenomenon of small droplets suspended in air.

•A spray is a dynamic collection of drops dispersed in a gas.

•The process of forming a spray is known as atomization/nebulization.

1.Continuous Spray valve is the most common used valve.

2.Metering valves are used to accurately deliver a dose of medication. applicable to the dispensing of potent medication. These operate on the principle of a chamber whose size determines the amount of medication dispensed.

3.Foam valves have only one orifice that leads to a single expansion chamber of appropriate volume to allow the product concentrate to expand into a ball of foam.

**Components of Valves**



**ACTUATORS**

•A specially designed button to activate the valve assembly.

•The actuator allows for easy opening and closing of the valve and is an integral part of almost every aerosol package.

•It is actuator design and dimensions that determine the physical form of the emitted product concentrate (spray or foam).

•Actuators types:

1.Spray. (Various openings 1-3)

2.Foam. (Large orifices)

3.Solid stream. (Large opining – as ointment)

4.Special applications. (They are designed to deliver the medication to the appropriate site of action - throat, nose, eye, or vaginal tract).

**MANUFACTURE OF PHARMACEUTICAL AEROSOLS**

•Two methods are used to manufacture aerosols

•**COLD FILL PROCESS and the PRESSURE FILL PROCESS.**

•In the cold fill process, both the product concentrate and the propellant must be cooled to temperatures below 0°C where they will remain liquefied.

•The chilled product concentrate is quantitatively added to the equally cold aerosol container and then the liquefied gas is added.

•The heavy vapors of the cold liquid propellant will generally displace the air present in the container.

•When filling is complete, the valve assembly is inserted into the container and crimped into place.

•The container is then passed through a water bath of about 55°C to check for leaks or distortion in the container.

•The cold fill process takes advantage of the property that some ingredients will liquefy when cooled.

•Aqueous solutions cannot be filled by this process since the water will turn to ice in the low temperatures.

**PRESSURE FILL PROCESS**: more common than cold filling

•Pressure filling is carried out essentially at room temperature.

•The product concentrate is placed in the container, the valve assembly is inserted and crimped into place.

•Then the liquefied gas, under pressure, is added through the valve.

•The entrapped air in the package might be ignored if it does not interfere with the stability of the product, or it may be evacuated prior to filling or during filling.

•After the filling operation is complete, the valve is tested for proper function.

•It has the advantage that there is less danger of moisture contamination of the product and also less propellant is lost in the process.

**ADVANTAGES OF AEROSOL: *RATIONALE OF USE***

•Drug is delivered directly to the target organ (lung),

•**Less dose required so less systemic exposure so less toxic.**

•**Fast action, no decomposition of drug.**

•Aerosol doses are generally smaller than systemic doses; for example: oral albuterol is 2 to 4 mg; inhaled albuterol is 0.2 mg

•Systemic side effects are less frequent and severe with inhalation compared to systemic delivery (injection, oral).

•Onset of effect with inhaled drugs is faster than with oral dosing; eg, oral albuterol is ≤ 30 min; inhaled albuterol is ~ 5 min.

•Since the drugs are absorbed directly into the blood stream via the lungs, there is no decomposition or loss of drug in the gastrointestinal tract such as occurs when the drug is administered orally.

•Since the medication is sealed in a container, there is no danger of contamination of the product with foreign materials.

**DISADVANTAGES OF AEROSOL**

•**Loss of Drugs: 10-20% drugs goes to lungs.**

•**Where Does remaining Aerosol Drug Go?**

•The remaining drug is lost in the *device*, the *exhaled breath*, the *oropharynx*, and the *environment*.

•**Reasons of drug loss** or dose variability

•The number and variability of device types confuses patients and clinicians.

•Lack of standardized technical information on inhalers for clinicians.

•Lack of knowledge of correct or optimal use of aerosol devices by patients and clinicians.

•Difficulty in coordinating hand action and inhalation with MDIs.

•Correct breathing pattern, is difficult.

•NOTE: ***Drug loss may lead to dose variability.***









**TYPES OF AEROSOLS INHALATION DELIVERY SYSTEMS**

•There are currently two main types of aerosol generating devices.

•**1-Inhalers 2-Nebulizers**

**•INHALERS** are portable, handheld devices that are available in two types: Metered dose inhalers (MDI) and Dry Powder Inhaler DPI.

•**MDI are the most commonly prescribed**. These devices push out a pre-measured spray of medicine. When the person squeezes the inhaler, a measured "puff" of medicine is released.

•ADVANTAGES: Short treatment time, Reproducible dose emitted.

•DISADVANTAGES:

•Fixed drug concentrations

•Failure to shake can alter drug dose causing variability

•Limited range of drugs

•Hand–breathing coordination is difficult for many patients

•Proper inhalation pattern (slow inspiration to total lung capacity) and breath-hold can be difficult

**NEBULIZERS: D**istinctly different from both pMDIs and DPIs, in that the drug is dissolved or suspended in a polar liquid, usually water.

•Used for drugs that cannot be conveniently formulated into MDIs or DPIs, or where the therapeutic dose is too large.

•Nebulizers are electric- or battery-powered machines that turn liquid drugs into a fine mist that's inhaled into the lungs. The user breathes in the mist through a mouthpiece or facemask.

•Nebulizers are used mostly in hospital and ambulatory care settings and are not typically used for chronic-disease management because they are larger and less convenient, and the aerosol is delivered continuously over an extended period of time.

•ADVANTAGES: Nebulizers deliver relatively **large volumes of drug.**

•Drug concentrations can be modified.

•Normal breathing patterns can be used.

•Useful in very young, very old, debilitated, or distressed patients

•An inspiratory pause (breath-hold) is not required for efficacy