AEROSOLS

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Aerosols are colloidal systems consisting of very finely subdivided liquid or solid particles dispersed in and surrounded by a gas.

Pharmaceutical aerosols are defined as systems that are prepared by the solution, suspension or emulsion of therapeutically active substances in the propellant or solvent gas mixture. The content of package is expelled by the pressure generated by the propellant in the container.

Advantages of Aerosols

- ☺ Rapid onset of action.
- ☺Circumvention of the first-pass effect.
- ☺Avoidance of degradation in the GI tract.
- ☺Lower dosage that will minimize adverse reactions.
- ☺Dose titration to individual needs and ideal for medication.
- ☺Alternate route when therapeutic agent may interact chemically or physically with other medicinals needed concurrently.
- ☺Viable alternative when the drug entity exhibits erratic pharmacokinetics upon oral or parenteral administration.
- ☺Container and valve closure are tamperproof.

Disadvantages of Aerosols

☹ **Lung deposition is a relatively low fraction of the total dose.**

☹ **A number of variables (correct breathing pattern, use of device) can affect lung deposition and dose reproducibility.**

☹ **The difficulty of coordinating hand action and inhalation with the pMDIs reduces effectiveness.**

☹**The lack of knowledge of correct or optimal use of aerosol devices by patients and clinicians decreases effectiveness.**

☹**The number and variability of device types confuses patients and clinicians.**

☹**The lack of standardized technical information on inhalers for clinicians reduces effectiveness.**

Components of the Aerosol System

An aerosol system consists of four main parts:

1) Container
2) Propellant
3) Valve
4) Active substance concentrate (Solvent)

Propellants

Propellants are the most important part of aerosols. In addition to supplying the necessary force to expel the product, the propellant must also act as a solvent and diluent.

Compounds useful as propellants can be classified as:

1) Liquefied gases
2) Compressed gases

Properties of CFCs

Özelliği		Trikloromonoflorometan (CFC-11)	Diklorodifloromethan (CFC-12)	Diklorotetrafloroetan (CFC-114)
Molekül formülü		CCl_3F	CCl_3F_2	$CClF_2CClF_2$
Sayısal Numarası		11	12	114
Molekül Ağırlığı		137.28	120.93	170.93
Kaynama Noktası (1 atm)	° C	23.7	-29.8	3.55
Buhar basıncı (psia)	21° C	13.4	84.9	27.6
Yoğunluk (g/ml)	21° C	1.485	1.325	1.468
Sudaki çözünürlük (% ağırlık)	23° C	0.11	0.028	0.013

Properties of hydrocarbons

BİLEŞİM (% mol)				
Ticari İsimlendirme	**Basınç (psia, 21 ° C)**	**n-Bütan**	**Propan**	**İzo-Bütan**
A108	108±4	-	99	1
A-31	31 ±2	3	1	96
A-17	17 ±2	98	-	2
A-24	24 ±2	49.2	0.6	50
A-40	40 ±2	2	12	86
A-46	46 ±2	2	20	78
A-52	52 ±2	2	28	70
A-70	70 ±2	1	51	48

Properties of compressed gases

Özelliği		Karbondioksit	Azotmonooksit	Azot
Molekül formülü		CO_2	N_2O	N_2
Molekül Ağırlığı		44	44	28
Kaynama Noktası (1 atm)	° C	-42	-52	-160
Buhar basıncı (psia)	21° C	852	735	492
Yoğunluk (g/ml)	21° C	1.53	1.53	0.967
Sudaki çözünürlük (% ağırlık)	23° C	0.7	0.5	0.014

Valves

The most basic part of any aerosol is the valve mechanism through which the contents of the package are emitted.

There are 3 valve mechanisms:

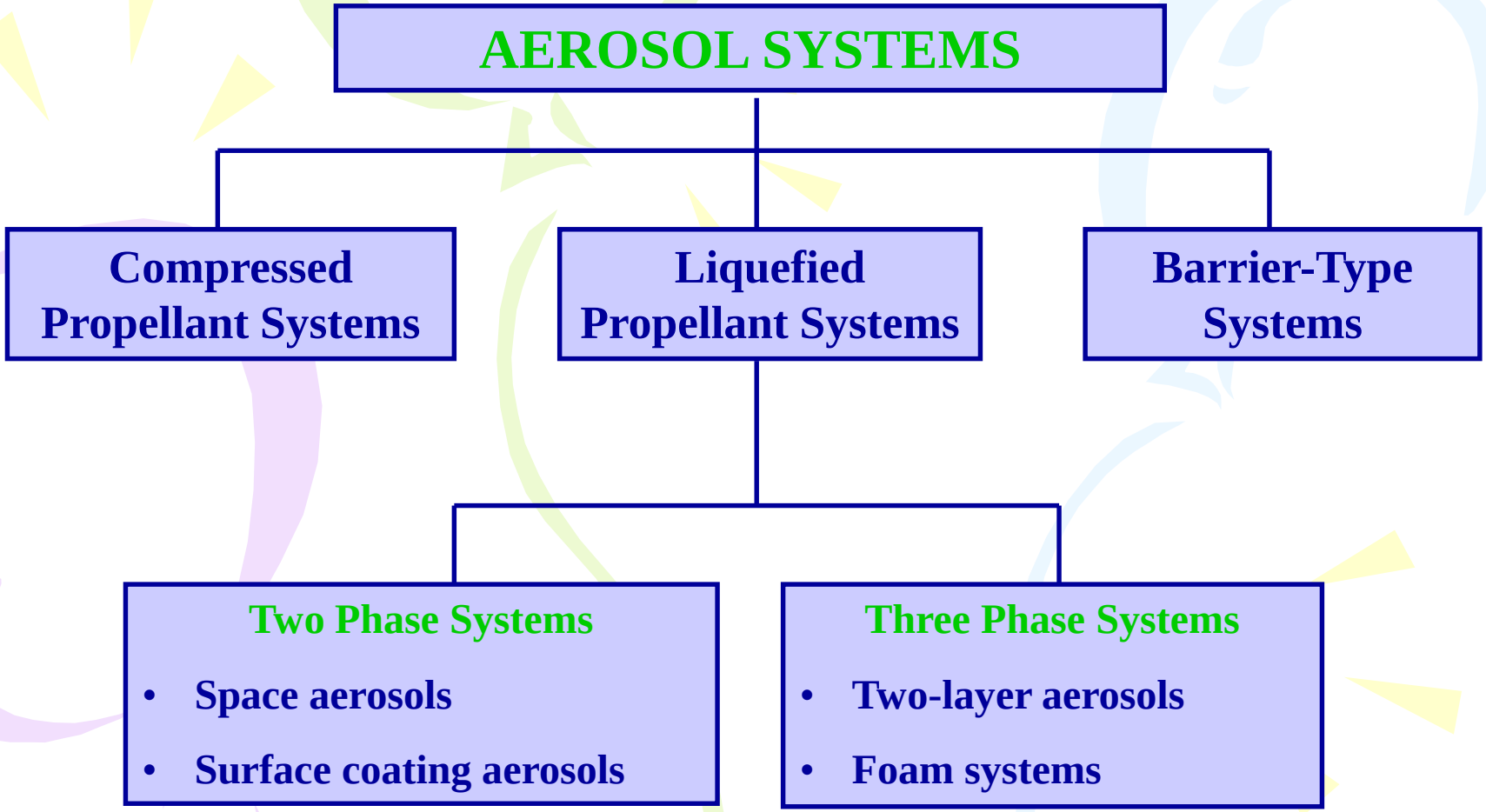
1) Continuous-spray valves
2) Discontinuous-spray valves
3) Foam valves

Active Substance Concentrate (Solvent)

The active substance concentrate is used to dissolve the active substance and forms the aerosol formulation together with the propellant.

Although liquefied propellants are good solvents, they are very expensive and therefore the use of solvents in aerosols where liquefied propellants are used is essential.

The active substance concentrate is present in the aerosol container in solution, suspension, emulsion or semi-solid form.


AEROSOL SYSTEMS
Compressed Propellant Systems
Liquefied Propellant Systems
Barrier-Type Systems
Two Phase Systems
• Space aerosols
• Surface coating aerosols
Three Phase Systems
• Two-layer aerosols
• Foam systems

Space Aerosols

Aerosols used to provide an airborne mist are called *space sprays* and include room disinfectants and deodorizers.

This group of aerosols produce particles that are usually less than 50 µm in size. This will ensure that the dispersed droplets or particles will remain airborne for a prolonged period of time.

Surface Coating Aerosols

Aerosols intended to carry the active drug to a surface are called *surface sprays* or *surface coating sprays*.

This class of sprays includes products such as deodorant sprays, hair sprays, perfume and cologne sprays, shaving lathers, paint sprays, and various household products such as spray starch, waxes, polishes, and cleaners.

This group of aerosols produce particles that are 50-200 μm in size.

Three Phase Systems

A three phase system (i.e., a heterogeneous system) consists of a layer of water immiscible liquefied propellant, a layer of propellant immiscible liquid (usually water) and the vapor phase.

1) Two layer aerosols
2) Foam aerosols

Barrier-Type Systems

These systems separate the propellant from the product itself. The pressure on the outside of the barrier serves to push the contents from the container.

Piston Type Systems

Since it is difficult to empty the contents of a semisolid from an aerosol container completely, a piston-type aerosol system has been developed.

The concentrate is placed into the upper portion of the container. The pressure from nitrogen or a liquefied hydrocarbon gas pushes against the other side of the piston, and when the valve is opened, the product is dispensed.

Pharmaceutical Aerosols

There are 3 types of pharmaceutical aerosols:

1) Pressurized metered dose inhalers (pMDI)
2) Dry powder inhalers (DPI)
3) Nebulizers

Pressurized Metered Dose Inhalers (pMDI)

pMDIs are pharmaceutical drug delivery systems designed for oral or nasal use.

The pMDI consists of a canister, the medication, the propellant/excipient, a metering valve, the mouthpiece, and actuator.

The metering valve acts to prepare a pre-measured dose of medication along with the propellant.

Dry Powder Inhalers (DPIs)

Dry powder inhalers (DPIs) have been developed as an alternative to pMDI systems due to the damage to the ozone layer of CFC propellants.

DPIs contain only the powdered active substance or mixture of powdered active substance with a excipient. Lactose is generally used as excipient in the DPIs.

Types of DPIs

DPIs can be classified into three categories based on the design of their dose containers.

Single-dose inhalers: Each dose is filled in separate hard gelatin capsule and the capsule is placed in the inhaler before use. Spinhaler® and Rotahaler® are examples of single dose inhalers.

Multiple Unit-dose DPIs: The Diskhaler® (GlaxoSmithKline) is an example of the multiple unit-dose DPI. Each blister is mechanically punctured when the cover is lifted, allowing the medication to be inhaled though the mouth.

Multi-dose inhalers: Multi-dose DPIs measure doses from a powder reservoir. Turbuhaler® and Easyhaler® are examples of multi-dose systems.

Nebulizers

Nebulizers were designed to atomize aqueous solutions or suspensions.

There are 3 types of nebulizers:

1) Jet nebulizers
2) Ultrasonic nebulizers
3) Mesh nebulizers

Jet nebulizers are operated by compressed air or oxygen in order to aerosolize liquid medications.

A jet nebulizer delivers compressed gas through a jet, causing a region of negative pressure. The solution is entrained into the gas stream and is sheared into a liquid film. This film is unstable and breaks into droplets due to surface tension forces. A baffle in the aerosol stream produces smaller particles.

Ultrasonic nebulizers incorporate a piezoelectric crystal vibrating at high frequencies (1-3 MHz). These vibrations are transferred to the surface of the solution, creating a standing wave that generates aerosol .

Mesh Nebulizers

Mesh nebulizers use electricity to vibrate a piezo (at approximately ~128 KHz) element that moves liquid formulations through a fine mesh to generate aerosol. The diameter of the mesh or aperture determines the size of the particle generated. Mesh nebulizers are very efficient and result in minimal residual volume (0.1–0.5 mL).

Warnings on Packaging in Aerosols

It is mandatory to include some warnings on the packaging of the products in the form of pressurized spray:

-Pressurized container: protect from sunlight and do not expose to temperatures exceeding 50 ºC. Do not pierce or burn, even after use.

-Do not use near heat, flame or while smoking.

-Keep away from children.

-Do not breathe directly and protect your eyes.