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Aerosols In Pharmaceutical Innovation: An Review

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ABSTRACT:

Aerosols are formulations comprising finely dispersed particles or droplets suspended in a gas, widely utilized in pharmaceutics for their efficiency in drug delivery. These systems are integral in the administration of medications via inhalers, nebulizers, and metered-dose inhalers (MDIs), offering a significant advantage in targeting pulmonary tissues, thereby enhancing drug bioavailability and therapeutic efficacy. include rapid onset of action, minimized systemic side effects, and the convenience of self-administration. Aerosols facilitate precise dosage control and can deliver medications directly to the site of action, improving therapeutic outcomes and patient compliance. However, there are notablesuch as issues with stability and formulation complexity. The propellants used, traditionally chlorofluorocarbons (CFCs), have raised environmental concerns, leading to the development of environmentally friendly alternatives like hydrofluoroalkanes (HFAs). of aerosols in the future are promising, with ongoing advancements in nanotechnology and biomaterials enhancing their efficiency and targeting capabilities. Innovations in inhaler design and formulation science are expected to improve drug delivery systems, potentially expanding their use beyond respiratory disorders to include systemic and localized treatments.In conclusion, aerosols represent a dynamic and evolving domain in pharmaceutics, poised to revolutionize drug delivery and patient care with continued research and technological advancements1,2

KEYWORDS: Pharmaceutical aerosol , preformulation ,MDI , Propellent

INTRODUCTION:

Pharmaceutical aerosols are goods with therapeutically active ingredients which are compressed and released when the right valve system is triggered.This technique involves using pressurised air pressure to expel the contents of the container it is used on. Medicinal aerosols were first started being developed in 1950. They were intended for the management of different skin conditions such as minor injuries, and burns. and infections. Even though the term ‘aerosol’ has been used for a relatively short time only, the inhalation therapies and systems for the treatment of medical diseases have been around for thousands of years,not until 1920. Inhalation treatment was used by the traditional cultures including the Ayurvedic medical practice in early civilization in India around 2000 BC. respiratory ailments . It is believed that the Ancient Egyptians used the vapour of the herb Hyoscyamus muticus which has anticholinergic properties for. medicinal purposes. 3 The Persian physician Ibn Sina or Avicenna had been using in inhalation therapy the essential oils of pine and eucalyptus centuries ago to treat specific respiratory problems. The product concentration, which has the pharmaceutically active ingredient, and the propellant work together in order to produce the

aerosol, which is the delivery system. dose form. additives, co-solvents and any other filler as may be necessary to enhance the stability and performance of the final product. The product concentrate can be dissolved in water, made into a semisol, or suspended, and then used to create aerosol systems which may be pastes, emulsions or dry powders, solutions, or dispersions3,4

TYPES OF AEROSOLS:

Non-Inhalational Aerosols: Non-inhalational aerosols are a suspension of fine solid or liquid particles which are not intended to be inhaled, in contrast to inhalational aerosols. particles in a gas. These are used in applications such as air filtering, dust control, applying pressure, coating among other uses. Other aerosols which are not inhale they are foams, sprays, dust-controlling agents, filters and the like.

Topical aerosols: A topical aerosol is an aerosol type that was designed for use on the skin or other outer surfaces of the body. The goal of topical The approach that is taken with aerosols is to apply their active components directly to the skin. They are mainly used for protection from the sun, as moisturizers, to disinfect wounds, for pain relief and in the treatment of wounds. healing. Topical aerosols include but not limited to hairspray, sunscreen, antibiotic and lidocaine sprays.

Metered dose inhaler (MDI): MDI stands for metered dose inhaler and it is a portable medical device that delivers the required amount of drug into the lungs when in use. This is for allergies, chronic obstructive pulmonary disease, and asthma and other respiratory illnesses. An NMDI is a non-metered dosage inhaler An NMDI is a non-metered dosage inhaler. An NMDI is a device that delivers medicine to the lungs; it is different from an MDI in that it does not. give an amount of medication that has been previously set. Some of the factors that may influence the amount of medication that the user receives include the breathing technique among others. NMDI is available in several types includingrespimat, nebulizers, dry powder inhalers (DPI) and soft moist inhalers (SMI).

Two-phase aerosols: A two-step process that characterizes an aerosol, namely the liquid phase and the vapour phase. One of the liquefied propellants and the product. concentration are dispersed within the liquid phase or in other words are diffused within the liquid phase. The vapour phase of the system is constituted by the evaporated propellant gas from the liquid phase. Hair Some examples of two phase aerosols include spray, deodorant, room freshener and among others.5,6,7

Aerosols with three phases: A three phase aerosol system contains a liquid propellant phase, an aqueous product phase and a vapour phase. Liquid the propellant phase is composed of some product concentrate that has been dissolved or dispersed in the liquefied propellant. The product concentration is emulsified or dispersed in water or another aqueous solution to form the aqueous product phase which is another layer of liquid. Propeller gas that has consists of the vapour phase of the liquid propellant phase which has evaporated.7

IDENTIFICATION AND CHARACTERISATION METHODS

Distribution of Particle Sizes: Size of particles in aerosols varies from nano meter to micro meter. Particles' behavior in the atmosphere, health effects and light-scattering as well as light-absorbing properties are dependent upon the size distribution of aerosols. The tool Particles are sorted with the help of an electrical mobility analyzer on the basis of size, charge, and electrical mobility. After being charged, Particles are transported through a laminar air flow which is non-turbulent and a high voltage electric field. Particles with less mobility take long time to reach the detector as compared to the small particles. whereas larger particles with low motility are deviated by a smaller extent within the airflow. To control the timing of particle arrival, the device measures the time of their arrival. the distribution of the size of those particles. Aerosol particles can be in various shapes such as spherical, irregular and fibrous and these influence the particle's ability and manner in which they interact with surfaces. 8,9

Density: The concentration of aerosol particles determines the density of the particles and thus their rate of settling and their behaviour in the atmosphere. Knowing the density of aerosol during preformulation helps in understanding its behaviour and enhancing its dispersion. The density of the API can be determined by empirical methods such as by using the pycnometer or gas displacement methods or by conducting literature search.

Solubility: The solubility in an aerosol during preformulation is critical to the aerosol's performance, stability and the desired drug delivery. The solubility of API can be determined by shake-flask or UV spectroscopy in some relevant solvents (water, alcohols, propellants, etc.)

Chemical Reactivity: Aerosols also have the capability to undergo a chemical transformation with the atmosphere to produce new chemicals, haze or secondary particles.

Toxicity: The evaluation of toxicity of an aerosol is a key factor in preformulation studies in order to conform to the safety measures and the requirements of the relevant authorities in the market. The The current toxicological information on the active pharmaceutical ingredient, in vivo and in vitro must be evaluated.10,11

EXCIPIENT DRUG COMPATIBILITY STUDY

Compatibility analysis of excipients and drugs is critical in aerosol development's preformulation stage. The stability, effectiveness, and safety of the finished product may be affected by the behavior of the drug substance (API) and the excipients used in formulation, which are known by these investigations. The main goal of this work is to establish the list of excipients that are not compatible with API.

The following categories apply to drug-excipient interactions:The following categories apply to drug-excipient interactions:

• Physical contact

• Interaction between chemicals

• Interaction between physicochemical Compatibility study methodologies:• Interaction between physicochemical Compatibility study methodologies:

• Fourier-transform infrared (FTIR) spectroscopy • Powder X-ray diffraction (PXRD)

• X-ray diffraction (XRD) • Differential scanning calorimeter (DSC) 12,13,14

CRITERIA FOR EXCIPIENT SELECTION:

The pharmaceutical excipients are bare substances or concepts which are incorporated into the formulation of pharmaceutical products that play a crucial role in the preparation,manufacture and dispensing of the active pharmaceutical ingredient(API). Even though they are not functional in the pharmacology aspect, they still addbeneficial aspects to the end product. Some of the parameters that should be considered whenselecting an excipient are as follows. Drug compatibility: The active substance and theexcipients cannot come into any form of reaction which would lead to their deterioration orlosing potency. Solubilization: There are also other excipients like cyclodextrins or cosolvents,which can enhance the release and bioavailability of the drug by enhancing its solubility in thepropellant. Toxicity: The excipient in case of usage through topical or inhalation should be non toxic, safe and adhere to the policies of safety consideration in its application. Regulatory

Compliance: All necessary regulations with pharmaceutical industry particularly aerosols enforcement should be observed in regards of the excipient used. Cost-effectiveness: Performance and beneficial aspects of the excipient should be compared with the cost of using it. Availability: Pretty much, the excipient needs to be available in consistence quantity and quality aimed for reliable production. Handling ease: The excipients should be easy to use and incorporated in the formulation process of aerosols

FORMULATION

A suspension of tiny liquid or solid particles in a gas is called an aerosol usually made under pressure.All this necessitates a careful balancing between substances and methods so as to achieve an aerosol that is safe and performs a useful aeresol types. An aerosol formulation, unlike usual formulations, On the name of the call describes one of the aerosol the most constitutive and vital parts, is . Propellant: Apressurised gas responsible for the excretion of the product from the container. It may be noted that typical propellants consist of the following: Hydrofluoroalkanes (HFA): These low – GWP — non – and –flammable molecules are quite common in respiratory aerosols containing therapeutics because of being environmentally woke.

• **Hydrocarbons**: These have been know in history to be preferred for their sky high efficiency coupled with the low cost. However, they also have limitations as GWP being too high and also being flammable and others which are health hazards. In some areas regulations control their use more and more.

• **Compressed** air: Mostly used for medical and food aerosols when chemical propellants are not acceptable. Though it is not a flammable substance and therefore environmentally safe, its pressure is not very high, and therefore there are instances of poor spraying.

Solvents: Solvents are important to understand when it comes to aerosols because they are quite often disregarded. These multifunctional elements allows for a homogeneous and stable system which can easily be used from the container by dissolving other excipients and active substances. The following types o

• Glycols

• Alcohols

• Solvents with chlorine

Emollients: Emollients in aerosol form are a convenient and speedy way to protect and For the face and neck to tone, soothe & moisturize dry sensitive skin. The key elements, which usually consist of oils, fats, Emollients and waxes create an occlusive barrier to prevepnt water loss in the skin, which helps condition dry skin. Mineral oil, petrolatum, Lanolin, shea butter) Example applications Deodorants are compositions, the main task which is Neutrab or hide ordour). They frequently include20,21

MANUFACTURING OF AEROSOL8.9

There are special methods and techniques by which a wide variety of products is made using aerosols. For the production of aerosols. The type of aerosol, its Which determine the manufacturing processes that will be used for a certain application.

Methods for making Aerosol

1. **Cold filling process**
2. **Pressure filling process**

COLD FILLING PROCESS:

The active ingredients are suspended or dissolved in a propellant vehicle and/or cosolvent. ProductTycoon Concentrate — make the product This is then cooled to -30°C, and the product The container is filled with the Cooled product The support for the cylinder is pressurized to force its propellant.Contains powerful hormones To pass through the chilling unit. The copper tubing in the chilling unit is coiled for better To the cooling side and this entire assembly is fitted in a insulated box. Container with coils Already containing acetone or dry ice, the latter of which is a coolant. Finally, Cold propellant at the top of the container Crimping of the Container and Valve assembly.24,25

Advantages:

This works with fluorocarbon propellants and can be used with both metered and non-metered valves. International Journal of Research Publication and Reviews, Vol 5, no 2, pp 3373-3379 February 2024 3377

• Compared to the pressure filling approach, this is easier

• Compared to pressure filling, this technique is quicker.

Disadvantages:

• Some propellants may vaporize from the container before the crimping valve. Therefore it is not suitable for hydrocarbon propellants.

• An excessive amount of propellant escaping and vaporizing may form an explosive mixture at the floor level26,27,28

PRESSURE FILLING PROCESS:

Prepare the product concentrate at room temperature. Measure the volume of the concentrate and add it to the can. Crimp the valve assembly to the can.

Attach a propellant cylinder to the can's valve assembly. Pressurise the inlet valve at the bottom of the cylinder to add the desired amount of propellant.

Allow trapped air to escape through the upper valve. The propellant will stop flowing when the burette and container's pressure equalise.29,30

Advantages:

• There is a decrease in propellant escaping into space. It is therefore friendly to the environment.

• The process of filling is done at room temperature.

• Successful filling of solutions, emulsions, and suspensions is achievable, which is not achievable with cold filling techniques.31,32

Disadvantages:

• Filling inhalation aerosols with a metered valve is not appropriate for this method; also, the process takes longer than cold filling.

• Rapid production rates are feasible.

PHYSICO-CHEMICAL CHARACTERISTICS VAPOUR PRESSURE:

Differential scanning calorimetry is one method that can be used to find an aerosol's vapour pressure (DSC). By measuring the difference in the amount of heat needed to raise the temperature of a sample and a reference as a function of temperature, differential scanning calorimetry is a thermoanalytical technique.Throughout the experiment, the temperature of the sample and reference are kept almost constant.

DENSITY:

Both a hydrometer and a pycnometer can be used to measure the density of aerosol. Based on the idea of buoyancy, an instrument called a hydrometer or lactometer is used to measure the density or relative density of liquids. Usually, they are graduated and calibrated using one or more scales, like specific gravity.33,34

MOISTURE CONTENT:

The Karl Fischer method can be used to determine the aerosol's moisture content. Iodine and sulphur dioxide undergo an oxidation process, which is the basis of the Karl Fischer titration method. The Karl Fischer method measures moisture content by reacting quantitatively and selectively with water using the Karl

Fischer reagent. Iodine, sulphur dioxide, a base, and a solvent—such as alcohol—make up the Karl Fischer reagent.

STABILITY STUDIES

The ability of a certain formulation in a certain container/closure system to maintain its physical, chemical, microbiological, etc. properties is known as pharmaceutical product stability. Incorporating quality, efficacy, and safety into a medicine formulation requires a sophisticated set of processes that are expensive, time-consuming, and need scientific knowledge.35

STABILITY TESTING METHODS

Real-Time stability testing:

For real-time stability testing, a longer test period is typically used to allow for significant product degradation under advised storage settings. The length of the test depends on the product's stability, which needs to be sufficient to show unequivocally that no detectable deterioration takes place and to allow one to discern degradation from inter-assay variance. Data is gathered during testing at a suitable frequency to enable trend analysis to differentiate between daily ambiguity and instability. By using a single batch of reference material whose stability properties have already been determined, the reliability of data interpretation can be strengthened. The consistency of the performance and the stability of the reagents are also aspects of the reference material's stability.

Accelerated stability testing:

Accelerated stability testing involves stressing a product at multiple high (higher than ambient) temperatures in order to calculate the minimum amount of heat input necessary for the product to fail. This is done in order to put the product in an environment that speeds up deterioration. Next, shelf life is estimated using this data, or it can be used to contrast the relative stability of different formulations. This typically shortens the development schedule by giving an early indication of the product shelf life. During accelerated stability testing, stress factors such as moisture, light, agitation, gravity, pH, and packing are applied in addition to temperature.42

CONCLUSION:

On aerosols, a thorough investigation was done. prescription drugs Products known as aerosols are pressure-packed mixtures of medicinally active substances that release when the proper valve system is activated. We outline the GLP and GMP standards for aerosol in this study. Preformulation investigations were also examined, including drug identification and characterisation procedures, drug compatibility tests including excipients, selection criteria for excipients, formulation and optimisation methods, and formulation. Studies on packaging and labelling specifications, stability studies, SOPs, and evaluation studies were also conducted.

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