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LATEST APPROACHES FOR DRY POWDER & LIQUID INHALATIONS

Govind Narayan*, Rohit Sharma, Deepanshu, Tarun Garg

Seth G.L. Bihani S.D. College of Technical Education, SriGanganagar

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For Correspondence:

Govind Narayan

Seth G.L. Bihani S.D. College of Technical Education, SriGanganagar

E-mail:

sharma.govind46@gmail.com

ABSTRACT

The lung has served as route of drug administration for thousand of year ancient inhalation therapies include the use of leaves and plants vapours from aromatic plants balsam and myrrh. In this article we can summarize the rationale behind and advances of pulmonary drug delivery systems (Dry powder inhaler & liquid inhalations). The pulmonary route has gained increasing importance in recent times due to its unique properties such as large absorptive area of up to 100 m^2. Particularly thin .01micro meter-0.2 micrometer absorptive mucosal membrane and good blood deliver. This article is focusing on the dry powder & liquid inhalational preparations & advancemans of pulmonary route. It can be use in various respiratory diseases.

INTRODUCTION

The advance of inhalation therapy [effective and safe] depends not only on a pharmacologically active molecule, but also on a delivery system and its application. The pulmonary route has gained increasing importance in the recent times due to its unique properties such as large absorptive area of up to 100 m^2, particularly thin [0.1-0.2 micrometer] absorptive mucosal membrane and good blood deliver. The respiratory tract is exposed to a relatively large no of biological and non biological meticulous. These are enclosed in a 20,000 L of air that must be inhaled daily accomplish gas exchange. Devices used to distribute drug by pulmonary route area based on one of three platforms pressurized metered dose inhaler, nebulizer and dry powder inhaler. Pulmonary drug delivered by inhalation by the patent of drug delivery compositions are designed to be delivered by breathing by the patient of drug dispersion can get to the lung. It has been found that certain drugs given by pulmonary route are readily absorbed during the alveolar region directly into blood circulation. May compensation over other routes of management for the treatment of specific disease states, mostly Lung linked large protein molecules which degrade in the gastro intestinal conditions and are eliminated by the first pass metabolism in the liver can be delivered via the pulmonary route if deposited in the respiratory region of the lung. It can give good potency by other route. New dispersible formulation are drug aerosol delivery devices for inhalable peptides ,proteins and various small molecules have in the past decade develop into increase interest for the treatment of systemic and respiratory disease . This advanced technology was initially applied to the systemic delivery of large molecules, such as insulin, interferon –b or a protease inhibitor.[1,2]

ADVANTAGES

- It is a needle free pulmonary drug delivery.
- It needs low and portion of oral dose.
- Pulmonary routes provide a non-persistent method of delivering drugs into the blood stream for those molecules that currently cannot be delivered by injection. These include peptides & proteins.
- Such as insulin for diabetes or interferon beta for multiple sclerosis and most of the drugs developed in recent year for biotechnology companies

- Pulmonary drug delivery having very insignificant side effects since rest of body is not out to drug.
- On set of action is very more rapidly with pulmonary drug delivery I.V. route and quicker than can be achieved with either oral delivery or subcautaneous injection.
- Decrease of dosage i.e. drug content of one 4 mg tablet of salbutamol equals to 40 doses of meter doses.[3,4]

CURRENT APPLICATIONS OF PULMONARY DRUG DELIVERY

Function of pulmonary drug delivery in asthma and COPD. Asthma is a chronic long-standing lung disease that is considered by inflammation and contraction of airways. Asthma origin chronic periods of puffing, chest tension .squatness of breath and coughing Asthma. But it most often starts in children. The influences people of allergen. The skin offers an even a smaller amount naturally porous boundary to macromolecules then the gastrointestinal. Today's inhaled drug delivery market is dominated by the three main category of drug such as bronchodilators, corticosteroids, anticholinergics. For managing of asthma advances dose drugs such levosalbutamol inhaler which having higher value as compare to salbutamol.[5]

Devices:- MDI-Meter Dose Inhaler & DPI-Dry powder inhaler, Nebulizer

1. **MDI-** A metered dose inhaler is a multifaceted system designed to provide a fine mist of medicament generally with an aerodynamic particle size of less than 5 micron for inhalation dose ,to the airways for the treatment of respiratory disease.

TRENDS: Advances in MDI technology and use enatiomer preparation of inhaled drugs.

Their difference in things of enantiomer of many medication and beta agonist adrenergic bronchodilators have inward much consideration. Recently levo salbutamol active anatiomer of salbutamol is present in market which is free from termers And palpitation that seen in salbutamol. In the same way that the (R) enatiomer of albuterol is mainly dependable for bronchodilator while (S) enatiomer may stimulate air way reactivity. One trend has been to the genric MDIs to over the offset availability. They are introduce in literature by comparing them with well acknowledged older devices. New technology to increase patient inhalation coordination. Spacer is used to improve patient coordination with MDIs.

Flow gated technology in spacer

Spacer today in market which is static free with valve mechanism which increases drug dose reaching to lungs.[6]

The autohaler modifications of pMDI: It is the first breath actuated or activated pressurized metered dose inhaler.

Autohaler solve the rationalization problem of the pressurized metered dose inhaler (pMDI) viz. Coordination of actuation efforts to aerosolize the dose of medication different dry powder inhaler. Autohaler is modified form of pressurized metered dose inhaler.

Recent role pulmonary delivery in patient on ventilators Aerosol to patents on ventilators has received much usual by doctors in addition to patient in1990.[7]

Mainly two types of nebulizers

Ultrasonic Jet

Ultrasonic nebulizer: Ultrasound waves are create in an ultrasonic nebulizer chamber by a ceramic piezoelectric crystal that vibrates when electrically excited.

Recent developments in liquid aerosol technology can merge the advantage of MDIs and nebulizers are known metered dose liquid inhaler.

Recently developments to advancement inhalation harmonization of patient devices like baby mask are mainly used. This mask is attached to spacer for small tidal volumes and low inspiratory flow rates infants and young children.

By using baby mask we can easily give medication to child up to 2 years this is recently advancements in specification to child up to two years this is recently advancements in application of pulmonary dry delivery.

The major advantage that all there system aim for is a reduced velocity of the aerosol.

Liquid inhalers applying the concept of a low velocity aerosol are often referred to as soft mist inhaler. This feature is of per amount and increase the lung disposition.

Wet nebulisation: In this main object at the generation of monodisperse aerosol the absence of propellant in the formulation by applying aqueous drug, formulation, a

reduction in the residual volume after nebulisation and an improved portability compound with nebulizer.[8]

1. **DPI**: Dry powder inhaler aerosol are commonly highly soluble and rapidly dissolve in the fluid layer lining the surface of the deep lungs before passing through the thin cytoplasm of the type first alveolar cells the intestinal space and duct endothelium.

Challenges in pulmonary drug delivery

- Low efficiency of inhalation system
- Less drug mass per puff
- Poor formulation stability of drug
- Improper dosing reproducibility

Mainly two types

- Unit dose: Devices single dose powders inhaler are devices in which a powder containing capsule is placed in a holder. The capsule residue must be discarded after use and a new capsule inserted for the next dose.
- Multi dose: Multi dose device uses a circular disk that contain either four or eight powder doses on a single disk. The dose maintained in separate aluminium blister reservoirs until just before in a foil-foil aluminium strip that is opened only at he point just prior to patient inspiration.

New trends in DPI

- Changes in the performance of the DPI can be achieved by either through changes in the design of the device through changes in the powder formulation.[9]
- Smaller porous particle(3-5mm) have been used to improves deagglomeration and drug disposition.
- New developments really aim at an increase of the deagglomeration forces generated during the inhalation. It is well known that if the more efficient the forces is higfer the FPF will be .A main classification parameter in the new device developments is whether or not the powder deagglomeration is power assisted (active devices) or depends on the kinetic energy of the inhalation generated by the patient.[10]

Airclassifier technology in device

The inhaler contain a classifier (cyclone) chamber in which high, internal forces are applied on to the rotating particles. Air classifier technology system one contain a cyclone chamber for particles deagglomeration. Modified form of air classifier technology is multiple air-classifier technology.

Multiple air classifier technology

In this technology multiple classifier chamber are placed in a parallel arrangement which further increases the dose that can be aerosolized. The concept of a disposable inhaler is interesting because it reduces the chance of microbial contamination.

Recent advances in formulation for pulmonary drug delivery

Effective inhalable medication are produced by drug formulation. Formulation stability is another challenge in producing pulmonary drug delivery. Formulation is responsible for keeping drug pharmacological effect occurs. A formulation that is retained in the drugs for the desired length of time and avoids the clearance mechanism of the lung is necessary.[11] Various following techniques:

Lactose carrier system

Recent advances in inhalation therapy have sparked considerable biomedical interest in the development of novel particle technologies for respiratory drug formulation, lactose has an established safety profile and improves the flow. And promoting dosing accuracy.[12]

Liposome's

Liposome's as pulmonary drug delivery vehicle. More recently, they have been investigated as a sustained release therapy in the treatment of lung disease , gene therapy and a method of delivering therapeutic agents to the alveolar surface for the treatment of systemic disease.[13]

Large porous particle

Pulmo spheres are the new type of aerosol formulation is the large hollow particles. They have low particle densities excellent dispersibility and can be used in both MDI and DPI delivery system. These particles can be prepared using polymeric or non polymeric exicipients by solvent evaporation and spray drying techniques.[14]

Biodegradable polymer

Currently used biodegradable polymer micro spheres are currently being studied as sustained release polymer drug carriers. Polymer such as poly lactic acid used in medical applications such as suture orthopaedic implants and medical dressing and poly glycolic acid have been investigated. In this method of delivering therapeutic agents to be alveolar surface for the treatment of systemic disease.[15]

Advances in propellant used in pulmonary drug delivery devices

Recently HFA propellants are a new alteration for CFC propellants in pulmonary drug delivery devices. Advances/Recent Trend in application of pulmonary drug delivery

- Insulin by aerosol
- Aerosol in transplantation
- Acute lung injection
- In cancer chemotherapy
- Amphotericin B
- Gentamycin aerosol
- Pulmonary arterial hypertension
- Pulmonary delivery of drug for bone disorders

CONCLUSION

Given the advances in pulmonary delivery technology, there have been a number of significant achievements in technologies to express and delivery drugs by pulmonary route. Improvements in the aerosol's velocity, particle size or moment of release have been achieved. Pulmonary delivery revolves around economic evaluation, approvals, administration and managed healthcare. Inhalation gives the most direct access to drug target. Pulmonary delivery drug delivery is an important research area which impacts the treatment of illness including asthma, chronic obstructive pulmonary disease and various diseases. It is a needle complimentary technique. In the treatment of obstructive respiratory disease, pulmonary delivery can minimize systemic effects provide response and minimize the required dose since the drug is delivered directly to the conducting zone of lungs. To improve the quality of pulmonary drug delivery system without affecting their integrity because of advancement in application of pulmonary drug delivery it is useful for multiple diseases. The drug delivering drugs to the lungs including targeted delivery which can improve efficacy and reduce unwanted systemic side effects a large

surface area for absorption , thin alveolar epithelium permitting rapid absorption, absence of first pass metabolism rapid onset of action and bioavailability. Due to recent advances in the post genomic era and molecular biology, our understanding of the molecular and biochemical composition of the lung, molecular basis of disease and the barriers to drug delivering has improved.

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