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Review Article

A Review on Pulmonary Drug Delivery System

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ABSTRACT

The lung drug delivery system (PDDS) is a crucial pathway for the administration of many medications. Concerns concerning the scientific and environmental benefits of treating lung ailments have grown in recent years. Drug delivery systems for the treatment of lung disorders are being developed because lung delivery has become one of the most popular ways of the scheduled or local drug rescuer. It is noted in this article that PDSDS improves adherence to suitable patient outcomes. This innovative drug delivery method provides a number of benefits in its conventional version. Drug delivery systems (DDS) are increasingly being used to treat lung disorders due to their potential therapeutic benefits in the area of pulmonary embolism. Additionally, this method makes it easier to place medications in high-intensity regions of the patient's lungs, which lowers the total amount of medication given to patients (10–20% of the peroral volume), increases local drug activity, minimizes systemic side effects, and avoids first-pass metabolism

INTRODUCTION

Lung diseases, often known as pulmonary diseases, are illnesses or conditions that interfere with the lungs' ability to breathe. Environmental causes including bacterial, viral, or fungal diseases could be the reason. According to the WHO Report 2017, lung illness ranks fourth among respiratory disease-related mortality in India, accounting for approximately 10.9% of all deaths. Chronic obstructive pulmonary disease, asthma, bronchitis, emphysema, pneumonia, acute respiratory distress, interstitial lung disease, and lung cancer are among the main illnesses. Devices, systems, or formulations that deliver medications to the lungs for the treatment of respiratory conditions or systemic distribution for other illnesses are referred to as pulmonary drug delivery. Pulmonary drug administration, which can have both local and systemic effects, is currently accomplished by inhaling medications orally or nasally. They have a significant benefit since the medication enters the systemic circulation directly, increasing its bioavailability. It can avoid the first-pass metabolism and offers an efficient non-invasive

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technique. The inhalation system's stability and efficiency, however, continue to be major issues. Because of the distinct physiological characteristics of the lungs, pulmonary administration provides an alternative method of delivering drugs throughout the body. These distinct physiological characteristics include. The alveolar surface area for medication absorption is vast and highly vascularized

- Systemic medication distribution that is non-invasive
- High solute permeability due to a thin epithelial barrier
- A decrease in proteolytic activity
- Avoid hepatic metabolism in the first pass.
- Quick action In contrast to other healthy organs, medications could be administered to the airways of a particular size or infected with a specific illness or injury within the lungs.
- For instance, medication deposition occurs in deeper airways due to the recent introduction of ultrafine therapeutic particles.

[B] Advantages

1. The pulmonary delivery method is needle-free.
2. A small portion of the oral dose is needed
3. Because the drug is not administered to the rest of the body, pulmonary drug delivery has extremely few adverse effects.
4. Pulmonary medication administration has a very rapid commencement of action.
5. Pulmonary medication administration prevents the medicine from being broken down by the liver

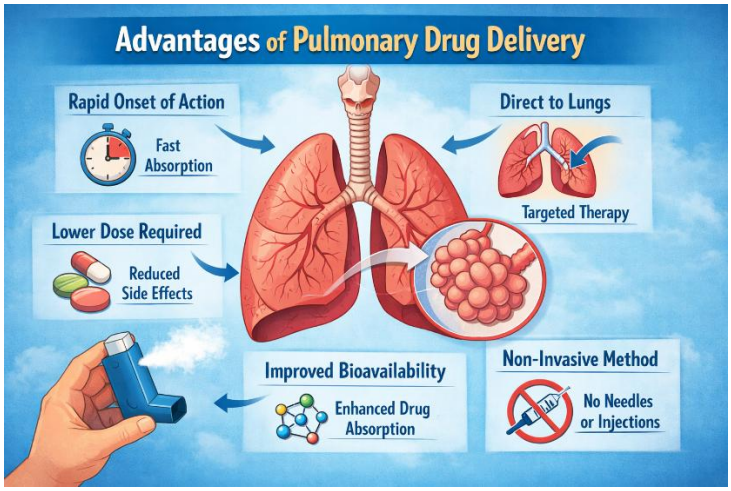

Figure: Image showing some other advantages of Pulmonary drug delivery system

[C] Disadvantages

1. Local side effects are caused by oropharyngeal deposition.
2. Patients could find it challenging to properly use the pulmonary medication devices.
3. The mucus layer's physical barrier may restrict drug absorption.
4. The repeatability of medication distribution in the lungs is influenced by a number of factors, including pharmacological and physiological obstacles.
5. In order to target drug delivery, delivery devices are needed in addition to the lungs being accessible surfaces for drug delivery complexes.
6. Drug stability in vivo.
7. Specificity of targeting.

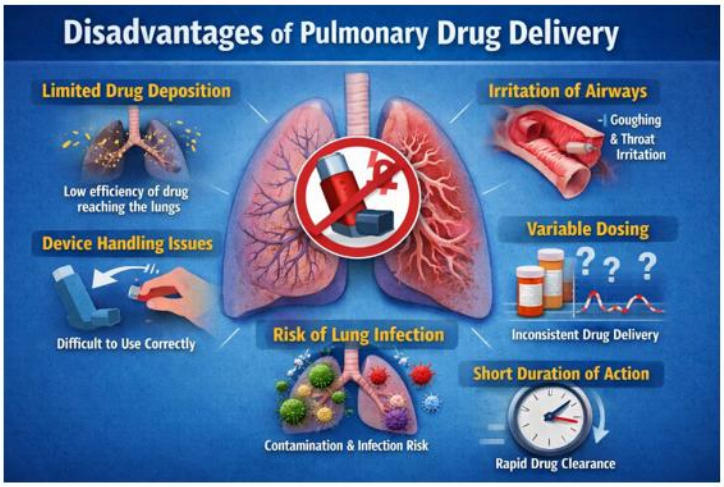

Figure: Image showing some other disadvantages of Pulmonary drug delivery system

[D] Anatomy and Physiology of of Pulmonary Drug Delivery [4-6]

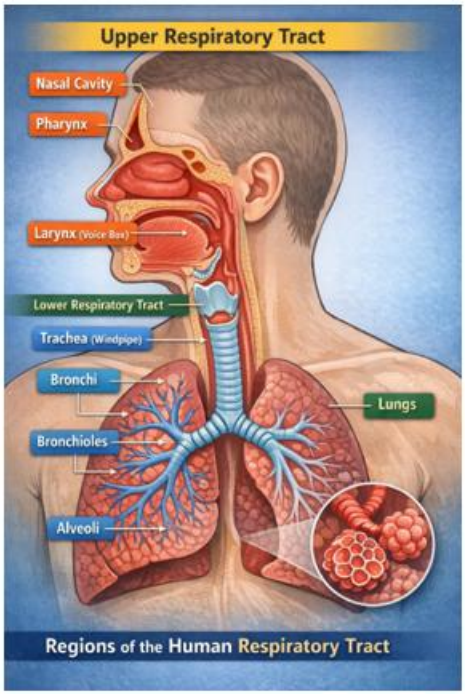

Figure: Different regions of a human respiratory tract

In addition to removing carbon dioxide and returning it to the lungs for exhalation, the respiratory system collaborates with the circulatory system to transport oxygen from the lungs to the cells. Respiration is the exchange of carbon dioxide and oxygen between the blood, bodily tissues, and the air. One pint of air is inhaled by healthy lungs twelve to fifteen times every minute. Every minute, all of the body's blood passes through the lungs.

There were two parts to the human respiratory system:

1. Conducting airway
2. The respiratory area.

The nasal cavity, related sinuses, nasopharynx, oropharynx, larynx, trachea, bronchi, and bronchioles are among the different types of airways. Alveolar sacs, alveolar ducts, and respiratory bronchioles make up the respiratory region.

A series of branching airways makes up the human respiratory tract. The lungs' primary function is gas exchange, which involves taking carbon dioxide out of the blood and supplying oxygen to it as it passes through the pulmonary capillary bed.

1. **Lungs:** The respiratory system begins at the nose and ends at an alveolar sac deep within the lungs.
2. **Nasopharyngeal region:** This "upper airways" area includes the respiratory airways that extend from the nose to the larynx.
3. **Trachea–bronchial region:** Also known as "conducting" or "central airways," these airways begin at the larynx, go through the trachea, bronchi, and bronchioles, and terminate at the terminal bronchioles.
4. **Alveolar areas:** Also known as "pulmonary regions," "respiratory airways," or "peripheral airways," consisting of the alveolar ducts, alveoli, and respiratory bronchioles.
5. **Pulmonary epithelium:** More than six of the more than forty distinct cell types found in the lung line the airways. By analyzing the structure of pulmonary epithelia at three main levels, its diversity may be demonstrated.
6. **The bronchi:** Goblet and ciliated cells make up the majority of their lining. There are a few Kulchitsky cells along with some serous, brush, and Clara cells.
7. **The bronchioles:** Ciliated cuboidal cells make up the majority of their lining. As the airways advance, the amount of Clara cells rises while the frequency of goblet and serous cells falls.

[E] Factors affecting on Pulmonary Drug delivery system

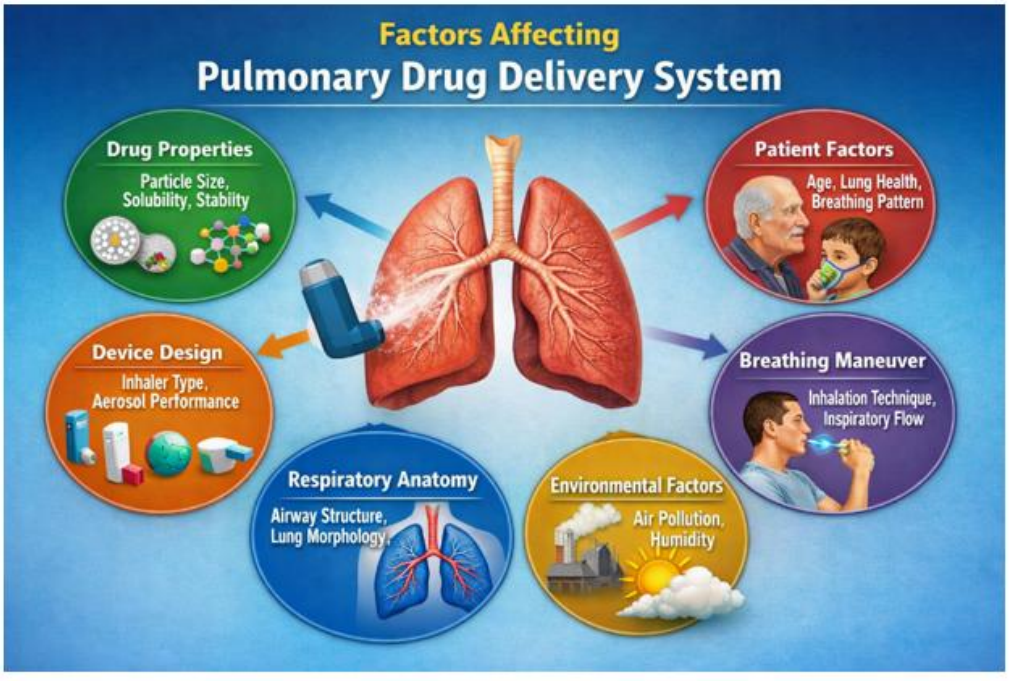

Figure: Showing Different factors affecting Pulmonary Drug Delivery System

[F] Drug Delivery Devices[7-21]

Drug delivery systems are just as critical for the pulmonary route as the formulation itself. Without appropriate drug delivery systems, it is challenging to distribute a formulation via the pulmonary route.

The following list includes the medication delivery devices:

1. Inhaler with metered dosage
2. Inhaler for dry powder
3. Nebulizers: Jet and ultrasonic nebulizers

1. Metered dose inhaler

The metered-dose inhaler called an MDI for brief, may be a pressurized inhaler that delivers medication by employing a propellant spray. It's composed of 4 essential components: the bottom formulation (drug, propellant, excipients, etc) the container, the metering valve, and the actuator (or mouthpiece). It is a drug delivery system that delivers tiny droplets of a medication with a particle size of less than five micrometers. It is used to treat respiratory conditions like COPD and asthma. From suspension or solution, they will tend. The materials that are insoluble in the propellant and solvent are distributed within the appropriate propellant vehicle only in suspension formulations. Particle size and the solubility of active ingredients and surfactants or dispersing agents are the important factors to be considered in formulating MDI suspension formulations. A solution formulation of MDI contains the active ingredient dissolved during a pure or mixture of propellants. Solution aerosol is relatively easy to formulate provided the ingredients are soluble in the propellant-solvent system. MDIs contain the propellant like chlorofluorocarbons and hydrofluroalkanes. They contain a micronized sort of the drug during a propellant struggling with surfactants to stop the clumping of drug crystals. The opposite components are other solvents and lubricants for the valve mechanism. When the device is actuated, the propellant gets exposed to atmospheric pressure, which leads to aerosolization of the drug. As it travels through the air, the aerosol warms up resulting in evaporation of the propellant that reduces the particle size to the desirable range. How to use the MDI, Currently, inhalation therapy is the best option for lung diseases like asthma, cystic fibrosis, and chronic obstructive pulmonary disease (COPD). These local therapies allow the use of smaller doses and reduce systemic side effects. In the last 20 years, an interesting scientific interest in the technology for pulmonary delivery was spiked by the very fact that the lungs are often used as a portal for systemic drug delivery. Because of the rapid absorption via the vast alveolar region, the large vasculature and thin air-blood barrier, and the avoidance of first-pass metabolism, pulmonary delivery is a desirable method for systemic administration. The amount of drug that reaches the intended location of deposition determines how effective an aerosol therapy is (13, 14, 15).

Figure: Metered dose inhaler

2. Dry powder inhaler

It requires a certain level of skill because it is a flexible mechanism. The formulation is in solid form, as the word itself suggests. The solid medication is contained in a dry powder mixture in this bolus drug delivery device, which becomes fluidized when the patient inhales. It either has the active medication by itself or has a carrier powder added to the medication to improve its flow characteristics. Compared to metered dose inhalers, dry powder inhalers are more stable, easier to use, and less expensive. Hazardous propellants like CFCs are not required. They will be made for one or more doses.

Figure: Dry powder inhaler

3. Nebulizer

Nebulizers are frequently used to deliver medications to the respiratory tract by aerosolizing drug solutions or suspensions. They are especially useful when treating hospitalized patients. Asthma, cystic fibrosis, and other respiratory conditions are frequently treated with it.

Two varieties of nebulizers are listed below.

a) Jet nebulizer: A jet nebulizer uses pressurized gas to transform and spray liquid into tiny droplets; baffles are employed to prevent big droplets from escaping the device. Drug waste and time consumption are drawbacks.

Figure: Jet nebulizer

b) **Ultrasonic nebulizer:** This type creates aerosol droplets by vibrating a piezoelectric crystal at a high frequency, which creates ultrasonic waves. Pulmonary drug delivery has benefited greatly from the use of ultrasonic nebulizers. In theory, ultrasonic nebulizers offer the possibility of instantly adjusting the dose given to the particular needs of a patient, taking into account the patient's breathing pattern, physiological profile, and disease state, because the process in which aerosol droplets are generated is independent and does not require breath actuation. However, because of the challenges and constraints of traditional designs and technologies.

Figure: Ultrasonic Nebulizer

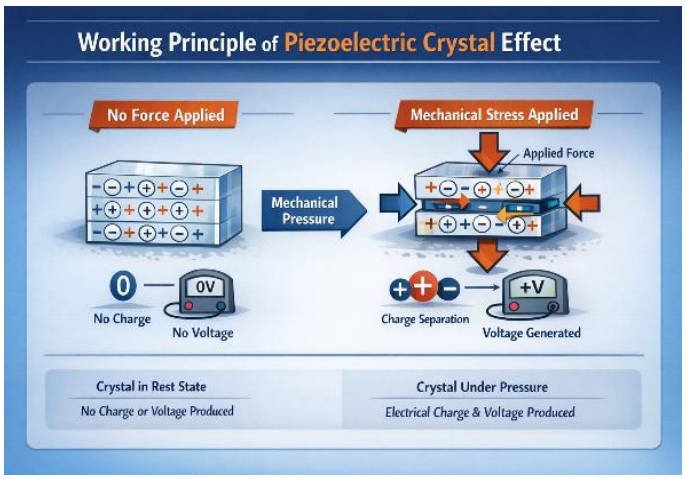

Figure: Piezoelectric crystal effect

[G] Recent Trends in Applications of Pulmonary Drug Delivery[22]

In addition to COPD and asthma, pulmonary medication administration is used for the following conditions:

- Aerosolized insulin
- Management of Migraine
- Nicotine Aerosol for Quitting Smoking
- Angina aerosols.
- Vaccination by aerosol.
- Antitrypsin Alpha 1

- Transplantation Aerosols
- Hypertension of the pulmonary arteries
- Severe Lung Damage
- Aerosol Surfactant
- Aerosol-based Gene Therapy

[F] FUTURE SCOPE:

Protein and peptide medications, such as calcitonin, granulocyte colony-stimulating factor (rhG-CSF), human growth hormone, insulin, and luteinizing hormone-releasing hormone (LHRH) analogs, are currently being studied for possible systemic absorption through the pulmonary system. Despite extensive clinical experience with an aerosolized macromolecule, there haven't been any major safety concerns or issues with coughing or throat irritation.

[G] CONCLUSION:

One of the earliest drug delivery methods is pulmonary distribution. However, because of its potential benefits, it is increasingly frequently used. Asthma, chronic obstructive lung disease, and other ailments are all impacted by this crucial drug delivery mechanism. The pulmonary route can be used to give a medication that causes gastrointestinal distress. The targeted distribution of medications to the lungs is determined by this system's ability to achieve the ideal particle size. Pulmonary drug delivery can make use of carriers such as liposomes, microparticles, and nanoparticles. An efficient pulmonary drug delivery system can be created using a variety of cutting-edge technology. While there are many benefits to using a dry powder inhaler, such as its affordability, ruggedness, and ease of use, one of the main challenges with DPI is that it can deliver a significant amount of powder (around 50 mg) in a single breath. Therefore, when compared to other modes of administration, pulmonary medication delivery is the most effective.

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