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Increased lung exposure to inhaled drugs through pharmaceutical means

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SUMMARY

The pulmonary administration approach has been extensively utilized for the treatment of both local lung diseases like asthma, chronic obstructive pulmonary disease, and respiratory infections as well as systemic disorders like diabetes. The majority of medications taken by inhalation pass quickly through the lungs and have brief therapeutic effects. By reducing the number of times a patient is given a medication, prolonged pulmonary exposure from inhaled medications may not only improve therapeutic outcomes but also clinical benefits for patients. This article provides a comprehensive analysis of the physical and chemical strategies for increasing the pulmonary exposure of inhaled medications. It begins by providing an overview of the numerous physiological and pathophysiological challenges that must be overcome in order to create inhaled medications that are exposed to the lung for an extended period of time. It then moves on to discuss the most recent advancements in a number of methods that can circumvent these challenges. In conclusion, a summary of the uses of inhaled medications that are exposed to the lung for an extended period of time for the treatment of various diseases and the safety concerns associated with various methods of exposing the lungs to inhaled medications are provided.

Keywords: Local lung diseases; Pulmonary drug delivery; Pulmonary clearance pathways

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INTRODUCTION

Due to its unique physiological and anatomical characteristics, including its large absorption area, highly permeable alveolar epithelial membrane, high vascularization, and limited first-pass effects, the lung has emerged as an important route for drug administration. Because it has a number of advantages over other methods of administration, including a faster onset of action, targeted delivery, fewer side effects, and improved bioavailability, this method has received more attention. Pneumonic medication conveyance (PDD) frameworks have been utilized not only for the treatment of a few local illnesses like asthma, COPD, and respiratory tract infections, but also for the achievement of improved bioavailability in order to more easily deal with basic infections like diabetes4 [1].

DESCRIPTON

In most cases, an inhaler device is necessary to aid in the delivery of inhaled medication to the intended lungs5. Nebulizers, metered dose inhalers (MDIs), and dry powder inhalers (DPIs) are the current inhalation devices in use. DPIs are used to deliver dry powder formulations, which typically consist of micronized drug powder and various coarse carrier particles (such as lactose) in contrast to nebulizers and MDIs, which typically deliver drugs in the form of solution or suspension. DPIs are gaining popularity because they are easier to manage and better for drugs' stability. For drugs to be delivered to the lungs in an effective and reproducible manner, it is crucial to choose the right drug formulations and devices with specific design. Mucociliary clearance, macrophage phagocytosis, dissolution, and translocation from the airways to other locations are all possible clearance pathways for drug particles once they are deposited in the lung. As a consequence of this, the local drug concentration in the lungs might rapidly decrease, rendering its therapeutic effects ineffective. Patients must take the medication on a regular basis in order to maintain the effective drug concentration at the action sites, which may lead to low patient compliance. An effective method for achieving a prolonged pharmacological effect is to extend the retention of inhaled particles in the lungs [2].

In this section, we begin by discussing the various physiological and pathophysiological obstacles that must be overcome when designing inhaled medicines that require prolonged lung exposure. Then, we discuss

recent advancements in a variety of physical and chemical strategies that can circumvent these obstacles. In conclusion, a summary of the applications of inhaled medicines with extended lung exposure for the treatment of various diseases and the safety concerns associated with various strategies to extend inhaled medicines' pulmonary exposure are provided [3].

Factors that influence the inhaled medications' pulmonary exposure. Drug delivery and physiology of the lung, as depicted in, the conducing zone and respiratory zone make up the lung's structure, which is shaped like an inverted tree. The trachea splits in two main bronchi, each of which branches off into smaller and smaller bronchioles before reaching sac-like alveoli for gas exchange. There are approximately 23 bifurcations between the trachea and the alveolar sacs in total. Pseudostratified columnar epithelium of ciliated, goblet, or mucus-secreting, and basal, or progenitor, cells make up the proximal conducting airways. A simple cuboidal cell layer gradually replaces the lower to the more distal airways, and the alveoli have a very thin epithelial lining. The location in the lungs where inhaled medications are deposited has a significant impact on their fate. There are three main mechanisms controlling the deposition of inhaled drug particles: inertial impaction, gravitational sedimentation, and Brownian diffusion. For instance, the alveolar region's large surface area, highly permeable bio-membrane, and abundant blood supply are favorable for rapid absorption. On the other hand, the epithelial cells in the conducting airways serve as a strong barrier for systemic absorption. The inertial impaction mechanism is typically used to deposit large drug particles (Da > 5 m) in the upper airways (mouth, trachea, and main bronchi, where air velocity is relatively high) because these particles could not follow the change in airstream flow direction. The aerodynamic diameter (Da) of the particles is the primary factor that determines the location of deposition and the mechanism that is used. The gravitational settling mechanism could deposit drug particles with Da between 1 and 5 m in the central and distal tracts, where air velocity is low. Drug particles with a Da of less than one millimeter may remain suspended in the air and are primarily exhaled. Random Brownian motion could largely deposit the ultrafine particles (100 nm) in the respiratory tract. Due to their high diffusion coefficients, particles with a diameter of less than 10 nm could easily be deposited in the tracheo-bronchial region of the lungs, while particles with a diameter of less than 100 nm could reach the alveolar region [4-8].

The obstacles—pathways for pulmonary clearance It is difficult to create inhaled medications that have a long-lasting pharmacological effect due to their prolonged pulmonary exposure. This is due to the fact that there are numerous routes of elimination, such as coughing, mucociliary transport, macrophage phagocytosis, and translocation into cells, blood, and lymph which enables the drugs inhaled to be quickly expelled from the lungs. By interfering with these pathways, some physiological factors, the pathophysiological conditions of the patients, and the physicochemical properties of the inhaled drugs all have a significant impact on the medication's retention in the lungs. This section goes over a number of clearance pathways that affect how long the inhaled drugs stay in the lungs [9,10].

CONCLUSION

The mucociliary lift (MCE) may be the primary freedom mechanism for the drugs inhaled through the upper and middle aviation routes. This MCE is a self-clearing mechanism of the airways that moves sperm and keeps the airways clear of mucus and dirt by using the cilia in the mucociliary layers. Goblet cells and ciliated columnar cells make up the mucociliary layer, which is covered by fluid from the lung lining. The periciliary sol layer and the mucus gel layer of the lung lining fluid significantly aid in drug clearance. The mucus layer is made up of salts, mucin, proteins, lipids, and water. The cilia and mucus work together to remove foreign substances from the lungs. When the cilia swing rhythmically, particles that are entrapped in the mucus layer can be expelled from the lungs. While larger particles are effectively eliminated by the MCE, smaller particles can pass through mucus and enter the bronchial epithelium, escaping mucociliary clearance. As the diameter of the airways decreases, the fluid that lines the lung becomes thinner. In the alveoli, where the thickness of the lung lining fluid can be less than 0.1 m, the surfactant layer, which is made up of lipids, cholesterol, and proteins, takes the place of the mucus layer.

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CONFLICT OF INTEREST

Author declares that they have no conflict of interest.

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