Archives of Medicine©
14 (08) 2022 : 001-002 • MINI REVIEW

Pharmaceutical methods to increase the lung exposure to inhaled medications

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SUMMARY

For the treatment of systemic disorders like diabetes as well as local lung diseases including asthma, chronic obstructive pulmonary disease, and respiratory infections, the pulmonary administration route has been extensively used. The majority of inhaled medications are quickly removed from the lungs and have transient therapeutic effects. Extended pulmonary exposure from inhaled medications may not only increase patient compliance by lowering drug administration frequency, but also increase clinical benefits for patients through improved therapeutic results. The physical and chemical methods to increase the pulmonary exposure of inhaled medications are systematically reviewed in this article. It begins with an overview of the numerous physiological and pathophysiological obstacles to creating inhaled medications with prolonged lung exposure, and then it moves on to discuss recent developments in a number of techniques to get around these obstacles. Finally, a summary of the uses of inhaled medications with prolonged lung exposure for treating various diseases and the safety issues related to various methods of prolonging pulmonary exposure of inhaled medications is provided.

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

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Word count: 1112 **Tables:** 00 **Figures:** 00 **References:** 10

Received: 01.08.2022, Manuscript No. ipaom-22-13194; **Editor assigned:** 03.08.2022, PreQC No. P-13194; **Reviewed:** 09.08.2022, QC No. Q-13194; **Revised:** 13.08.2022, Manuscript No. R-13194; **Published:** 18. 08.2022

INTRODUCTION

The lung has become an important route for drug administration because of its unique physiological and anatomical characteristics, such as its large absorption area, highly permeable alveolar epithelial membrane, high vascularization, and limited first-pass effects. This method has received more attention because it has a number of advantages over other methods of administration, such as a faster onset of action, targeted delivery, fewer side effects, and improved bioavailability. Pneumonic medication conveyance (PDD) frameworks have been taken advantage of not just for the therapy of a few neighborhood illnesses like asthma, persistent obstructive aspiratory sicknesses (COPD) and respiratory plot contaminations, yet additionally for the accomplishment of upgraded bioavailability to more readily deal with fundamental infections like diabetes 4 [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

For the breathed in drugs kept in the upper and center aviation routes, the mucociliary lift (MCE) might be the predominant freedom mechanism. Through the cilia in the mucociliary layers, this MCE is a self-clearing mechanism of the airways that propels sperm and keeps the airways clear of mucus and dirt. The mucociliary layer is made up of goblet cells and ciliated columnar cells that are covered by fluid from the lining of the lung. The clearance of the inhaled drugs is significantly aided by the periciliary sol layer and the mucus gel layer of the lung lining fluid. Water, mucin, proteins, lipids, and salts make up the mucus layer. For the purpose of removing foreign substances from the lungs, the cilia and mucus collaborate. Particles that are entrapped in the mucus layer can be expelled from the lungs when the cilia swing rhythmically. Smaller particles can pass through mucus and enter the bronchial epithelium, escaping from mucociliary clearance while larger particles are effectively eliminated by the MCE.As the airways' diameter decreases, the fluid that lines the lung becomes thinner. Last but not least, the surfactant layer, which is made up of lipids, cholesterol, and proteins, replaces the mucus layer in the alveoli, where the thickness of the lung lining fluid can be less than 0.1 m.

AKNOWLEDGEMENT

None.

CONFLICT OF INTEREST

Author declares that they have no conflict of interest.

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