Research Article

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CARRIER PARTICLES INFLUENCE ON DRY POWDER INHALATION IN LUNG DISEASE

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Abstract

Dry powder inhalers (DPI) are used to cure various lung diseases such as asthma and chronic obstructive pulmonary disease (COPD). DPI typically consist of either drug alone or drug blended with inert carriers like lactose, lucine or mannitol that are FDA-approved for inhalation as lactose and mannitol in an ordered mixture. The use of carrier particles enhances drug particles flowability and increases the inhalation efficiency. Carrier particles can be chosen according to their median particle size, taking into account the fact that an increase in median particle size increases the adhesion force between drug and carrier particles. Carrier particles also decrease the residual fine drug particles that adhere to inhalation devices and capsules upon inhalation of fine drug particles. Inflammation in asthma is present throughout the lungs, but asthma is associated particularly with lymphocytes and eosinophil cells. The highest numbers of eosinophils were found in the walls of non-respiratory bronchioles. And COPD is characterized by airflow obstruction that is not fully reversible and is usually progressive in the long term. It can result in significant disability and impaired quality of life. Smoking is the main cause of COPD. COPD is of two types, i.e., Chronic bronchitis, which involves a long-term cough with mucus and Emphysema, which involves destruction of the lungs over time.

Keywords: Dry Powder Inhalers (DPIs), Chronic obstructive pulmonary disease (COPD), Metered dose inhaler (MDI), Active pharmaceutical ingredient (API), Cerebrospinal encephalopathy (CSE).

Introduction

The origin of inhalation can be traced back to early civilization where this route of administration was relatively uncommon. Since a few decades the respiratory tract has been used for direct delivery of drugs to the lung via inhalation to treat respiratory diseases such as asthma, cystic fibrosis, obstructive lung disorders and other airways diseases[1]. In recent years, there has been a growing interest in the development of inhalation therapy to address other disease states given the avoidance of first-pass metabolism via delivery to the lungs that the inhalation route affords. A few examples within the literature list antibiotics, diabetes and cystic fibrosis. Inhalers are well known devices for administering pharmaceutical products to the respiratory tract by inhalation[1]. Inhalers are widely

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used particularly in the treatment of the respiratory tract diseases. There are a number of types of inhalers currently available. The most widely used type is the pressurized metered dose inhaler (MDI) which uses a propellant to expel droplets containing the pharmaceutical product[2]. An alternative device to the MDI is the dry powder inhaler (DPI).

Dry powder inhalers

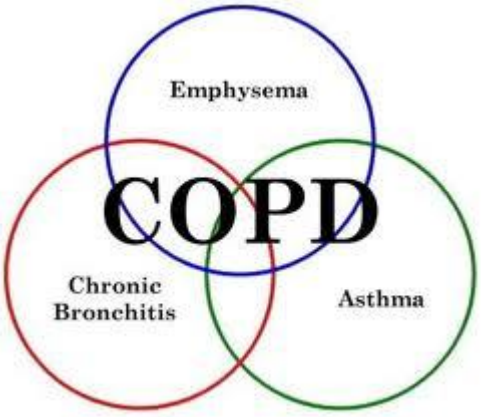
These have many advantages in comparison to MDIs such as lack of stability problems, no need of propellant, no need of coordination, while the DPI disadvantages are flow rate dependence of the delivered dose and the respirable fraction, cost/complexity of formulation use or dose, and moisture sensitivity[3]. The delivery of dry powder particles of pharmaceutical products to the respiratory tract presents certain problems. The inhaler should deliver the maximum possible proportion of the active particles to the lungs, including a significant proportion to the lower lung, preferably at the low inhalation capabilities to which some patients, especially asthmatics, are limited[4]. Dry powder inhaler (DPI) is a device that delivers medication to the lungs in the form of a dry powder. DPI formulations typically consist of either drug alone or drug blended with inert carriers that are FDA-approved for inhalation as lactose and mannitol in an ordered mixture. DPIs are propellant free, portable, easy to prepare and low cost devices with improved stability of the formulation as a result of dry state, less need for patient coordination and less potential for formulation problems[3]. Upon aerosolization the powder formulation must deaggregate into fine drug particles in the 1-5μm range for effective pulmonary delivery. The use of carrier particles enhances drug particles flowability and increases the inhalation efficiency[4].

Formulations for DPIs are especially attractive due to their simplicity, as the formulation usually consists of the API alone or the micronized API and an inert carrier like lactose or mannitol. The amount of formulation is typically less than 40 mg and the trend is for even lower fill weights to be used. As the formulation needs to be quickly and easily evacuated from both container and device, it is important that it remain free-flowing from the point of manufacture to the point of inhalation by the patient[5]. This particular property will sometimes require additional attention, as DPI formulations tend to have a hygroscopic nature and the absorption of moisture can quickly cause a change in powder flow properties. In DPI's, Strong attachment of the drug to the carrier surface may occur within asperities and clefts of the carrier surface, which are highly energetic sites on which the active particles are preferably attracted to and adhere more strongly[6]. Because of such strong interparticle forces, drug particles will be unlikely to leave the surface of the carrier particles and to be deposited in the lower respiratory tract. Surface asperities could be classified into two types macroscopic asperities which entrap drug particles and decrease drug release upon inhalation, and microscopic asperities which could contact drug by one point at the edges of those asperities, this decrease of the contact area between drug particle and carrier particle reduces the interactions[7]. Therefore, the features of the carrier particles should be such as to give sufficient adhesion force to hold the active particles to the surface of the carrier particles during manufacturing and in the delivery device before use[8].

Carrier particles can be chosen according to their median particle size, taking into account the fact that an increase in median particle size increases the adhesion force between drug and carrier particles. Carrier particles also decrease the residual fine drug particles that adhere to inhalation devices and capsules upon inhalation of fine drug particles[8]. With the use of carrier particles, drug particles are emitted from capsules and devices more easily, and the inhalation efficiency increases[9]. In DPI's various carriers are used, Lactose is the predominant carrier in dry powder inhalation, has reducing properties and would not be the appropriate excipient for some drugs such as proteins or peptides[9]. Lactose has been recognized in several earlier studies which clarify that the efficiency of a powder formulation is highly dependent on the lactose quality and source, the size distribution of the used lactose carrier and the content of fine lactose. Lactose mostly has small amorphous parts at the surface and it may cause the CSE (cerebrospinal encephalopathy), so there is a need for safe alternatives. Mannitol can be used as a carrier instead of lactose. Mannitol has no reducing property, is stable, crystalline and causes no cerebrospinal encephalopathy (CSE).

In addition, it provides no toxic effects. Mannitol is a sugar-alcohol which is not absorbed in the gastro-intestinal tract, does not cross the blood brain barrier and is not metabolized to any substantial extent when injected. Mannitol is stable as a powder and resists moisture at relatively high humidities up to 95%RH[7]. The various other used carriers are xylitol, maltodextrins, dextrans, cyclodextrins and amino acids such asglycine, arginine, lysine, aspartic acid and glutamic acid, and peptides such as HAS (human serum albumin) and gelatin. There are many types of inhalers used in the DPI field[8]. Different inhaler devices have different efficacy due to differences in lung deposition. The drug powder itself has to be prepared in the same way as the one used in MDIs, by micronization. Excipients have to be added to enhance the flowability. The drug is often present in low concentration on the coarse carrier surface. Upon inhalation, the carrier should ideally be retained in the inhaler device or deposit in the oropharyngeal region due to its large particle size. Therefore drug detachment from the carrier is thought to be crucial in determining the overall delivery efficiency of drugs from dry powder aerosols[9]. The inhaler design influences the fine particle output which also depends strongly on the patient inspiratory performance, in which the fine particle output is more or less flow dependent. However, a higher resistance to air flow limits the range of possible flow rates[10]. Furthermore reduced particle velocity results in a reduced mouth and throat deposition.

The desired site of deposition should be the starting point for every DPI development[10]. The target area may vary with the disease and drug to be administered. When local effects are desired, receptor densities may be indicative for the preferred site of drug deposition. And when systemic absorption is desired, difference in membrane permeability and clearing mechanism may be decisive. The most important disease for which local effects in the airways are desired are asthma and COPD. Inflammation in asthma is present throughout the lungs, but asthma is associated particularly with lymphocytes and eosinophil cells. The highest number of eosinophils was found in the walls of non- respiratory bronchioles. And COPD is characterized by airflow obstruction that is not fully reversible and is usually progressive in the long term[5].



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References

1. Prevalence of asthma increasing in Africa, www.ginasthma.com, 2004.
2. Anderson S.D.; Brannan J.; Spring J.; Spalding N.; Rodwell L.T.; Chan K.; Gonda I.; Walsh A.; Clark A.R.: A New Method For Bronchial-provocation Testing in Asthmatic Subjects Using a Dry Powder of Mannitol: Am. J. Respir. Crit. Care Med. 156 (1997), pp. 758-765.
3. Arnold k.; Grass P.; Knecht A.; Roos R.; Sluke G.; Thieme H.; Wenzel J.: Inhalation powders and method of manufacturing them: European Patent No. 0663815 B1(1993).
4. Chronic obstructive pulmonary disease (COPD) NICE clinical guideline 2004.
5. NICE. Chronic obstructive pulmonary disease (update):CG101. Full guideline.***1.*** June 2010.
6. Dahl R, et al. Thorax, 2010. 65(6): p. 473-9.
7. MHRA. Drug Safety Update. Volume 4, Issue 4, November 2010.
8. Tiotropium: safety studies of Spiriva Respimatq. Singh S, et al. BMJ, 2011. 342:d3215 - 19.
9. Boehringer Ingelheim. SPC for Spiriva microgram inhalation powder, hard capsule. Last updated 24/08/2010.
10. NICE. Chronic obstructive pulmonary disease rolflumilast: TA244. ***22.*** January 2012.