



Review Article

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The Inhalation of Active Pharmaceutical Ingredients and Its Pharmaceutical Studies

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ABSTRACT

The aerosols such as gas borne suspension of solid or liquid particles are used for therapeutic applications of lung and other systemic diseases. These inhaled pharmaceutical aerosols deliver drug (active pharmaceutical ingredient) to the alveolar region to the blood in the capillaries. The injectable drugs are significantly administered by inhalation. There are so many drug delivery systems of inhaled pharmaceuticals are available. The metered dose inhaler, dry powder inhaler and nebulizers drug delivery systems are most famous. The development of suitable drug delivery system of inhaled pharmaceuticals for new drugs is very simple at this modern times technology. This review deals about inhaled pharmaceutical aerosols and its studies including particle size and adhesive forces of aerosol particles.

Keywords: Dry powder inhaler; Pharmaceutical inhalation; Drug delivery; Lung

INTRODUCTION

The drug delivery of inhaled aerosol pharmaceuticals are difficulty in efficiently producing tiny aerosol particles and difficulty in consistently delivering the indented amount to the respective parts of the respiratory tract [1]. The particle sizes of the inhaled pharmaceuticals are very significant part. The particle size decides where to deposit in the respiratory tract. If particle size is large the inhaled particles deposit in mouth and throat. If particle size is too tiny the inhaled particles exhaled. Both are not desirable. The preferable particle size of the inhaled pharmaceutical is 1-5 μ m [2]. The inhalation flow speed, particle surface properties are affects aerosol generation deposition in the lung. The respiratory system geometry also effective impact on inhaled pharmaceutical aerosol drug delivery. The proper understanding of inhaled pharmaceutical aerosol mechanics very significant to prepare aerosol drug delivery system [3].

Table 1: Advantages and disadvantages of inhaled aerosols

S No	Advantages	Disadvantages
1	Safe	Sometime lesser therapeutic effect
2	Comfortable	Unpredictable and variable dose
3	Onset of action is rapid and predictable	The no or poor absorption for some systemic disease
4	Lower or null adverse reactions	
5	Lesser quantity of drugs used	

PARTICLE SIZE DISTRIBUTION

The particles of different sizes are called polydisperse. The inhaled pharmaceuticals are mostly polydisperse. The monodisperse particles of single size produced with controlled conditions. The particle size is significant attribute of inhaled pharmaceutical aerosols [4]. The distribution of particle sizes calculated are studied as frequency and count distributions, the log normal distribution, cumulative distributions, mass and volume distributions, cumulative mass and volume distribution. The total mass of an aerosol calculated from its mass median diameter and number of particles unit/volume [5].⁵

THE MOVEMENT OF AEROSOL PARTICLES

Aerosol mechanics help us to study the movement of single aerosol particle in a fluid. The forces and equations governs single aerosol particle moving in a fluid. The determination of particle in a fluid flow simplified as the spherical is particle size assumption and the particle density is more than surrounding fluid density. The fluid forces such as buoyancy force, magnus force, lift force, basset force, and pressure force are significant if fluid density is greater than particle density. The drag force, settling velocity, brownian diffusion, particle motion, the concept of aerodynamic diameter, effect of induced electrical charge, space charge and effect of humidity on electrostatic charge research is required to determine the importance of inhaled pharmaceutical aerosols [6].

THE HUMAN RESPIRATORY SYSTEM

The geometry of respiratory tract is not fully understood. The millions of alveoli with diameter of order of 300 μ m. The respiratory tract geometry differs from individual to individual. The basic areas of respiratory tract is the extrathoracic region, tracheo bronchial and the alveolar region. The extrathoracic region is upper airways consists of nose, mouth or throat. This region as oral cavity, nasal cavity, larynx and pharynx. Distal to the extrathoracic region is the tracheobronchial region called lower airways [7]. It starting with the trachea passing through the bronchi and stopping at the terminal bronchioles. Both extrathoracic and tracheobronchial region are called conducting airways. Alveolar region consists of alveoli. The lung model weibel is most known one, it is symmetric model. Haefeli-Bleur is the revised lung model.

The human lungs pump vital oxygen through respiratory region of the body and in to the blood. This procedure makes mans survival on the earth. The respiratory system provides filtration, warm and moistens inhaled air [8]. Air passes from nose, pharynx or throat and passes from the mouth, nose to the larynx or voice box. Then air passes to the top of the windpipe, and lungs. The air canal provide human to speak and keep food not enter in to the lower respiratory tract. The gas exchange area deals that transfer of oxygen to the blood and carbondioxide is removed from blood. The breathing process is controlled by the brain.

PARTICLE DEPOSITION IN THE RESPIRATORY TRACT

The inhaled pharmaceutical aerosol deposit in the respiratory tract. Other factor inhalation flow rate affects particle deposition. The lung model used to predict impaction with reasonable accuracy. The parameters used to determining impaction are flow velocity and linear dimension, particle diameter and cunningham slip correction factor governed by Reynolds number. The modern deposition models of different lung regions typically empirical models, lagrangian dynamic models and eulerian dynamic models. The equations are there to calculate the amount of aerosol deposition in the lung. Emprical model is simple. The equation of empirical model fits with invivo data of lung deposition of aerosols [9].

TARGET OF AEROSOL DEPOSITION

It is not possible to control aerosol deposition in the different regions of respiratory tract. Because of stochastic nature of the lung, dispersion, chaotic mixing and diffusion. If particles settled by sedimentation then those particles deposited in alveolar regions [10]. Intersubject variability is also a factor of lung deposition of inhaled pharmaceutical aerosols. The particle size 1-3 μ m is useful in achieving lung targeting. There is variation of lung deposition of aerosol with diseased lungs and effect of age on deposition.

DRY POWDER INHALERS

Powdered aerosol [11] is the modern drug delivery of inhaled pharmaceutical aerosols. The difficulties are manufacturing powder aerosol and reproducing measured quantity of fine particles. The purpose of orally inhaled pharmaceutical aerosols administered through patient breath. The inhalation of large quantity of inhaled powder causes coughing. The Dunbar *et al.*, described about basic nature of dry powder inhaler. Dry powder inhaler operation classified as an active and passive. Active operation carried out with external mechanical energy. Passive operation carried out with patient's single large breath.

VANDER WAALS ADHESIVE FORCES

The determination of the origin of the adhesive forces helpful to design target drug delivery. It is impossible to find force of adhesion of dry powder particles at this time [12]. The source of the intermolecular potential energy lies in the quantum mechanical electromagnetic interaction between the electrons and protons of the molecules called generically vander waals forces. There are equations in understanding of origin of adhesive forces. The electrostatic forces found on motion of the charged particles. The dry powder inhalers mechanics are complex. There is complicate measurement mechanics involved in initial and final states of the powder. Turbulent aerodynamic forces involved and good research works were involved in the design of dry powder particles.

DRY POWDER INHALER FOR RESPIRATORY MEDICINES

Dry powder inhaler (DPI) devices for inhaled medications are aeroliser, diskus, ellipta, flexhaler, handihaler, neohaler, Pressair, rotahaler, turbuhaler, and twisthaler. The dry powder filled into the capsules and capsules kept into the chamber of the inhaler device [13]. The moving mechanism will split the capsules in to head and body and powder will drawn out of capsules. The powder will be inhaled by deep breath of patient who inhales. The need of the DPI drug delivery is to excel consistent, efficient dose delivery, correct use of device, patient compliance and treatment efficacy. The once daily DPI drug delivery ellipta used to treat asthma and chronic obstructive pulmonary disease.

SUSTAINED RELEASE FORMULATION

Microencapsulation methods are useful to produce sustained release inhalable formulation [14]. The modified solvent evaporation method is most widely used process to produce controlled particle size. Usually sustained release is sustained release of active pharmaceutical ingredient over an extended period of time with unit dose. Sustained release inhaled pharmaceutical provide reduction of dosing frequency, lesser side effects, once daily, economic and patient compliance. The polylactic acid, poly lactide co-glycolide, hydroxyl propyl methyl cellulose, ethyl cellulose, eudragit rs 100 and eudragit rl 100 polymers are useful to produce sustained release microparticles.

CONCLUSION

Dry powder inhaler aerosols contains sustained release microparticle producing effective delivery. At this period of time, there are many achievements of developing sustained release microparticles of inhaled aerosols. The novel drug delivery system fruitful to control local lung disease and systemic diseases.

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