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Review Article

# A Review on Advancement in Inhalation Drug Delivery: "Current Trends and Future Perspectives"

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## ABSTRACT

Inhalation drug delivery system offer a promising approach for treating respiratory and systemic condition by delivering medication directly to the lungs.Pulmonary drug delivery has gathered momentum in the several years with increased interest in using the lungs as a means of delivering drugs systematically advances in devices technology have led to the development of more efficient delivery systems capable of delivering larger doses and finer particles into the lungs.Dry powder inhalers design should provide accurate, reproducible, safe, and efficacious drug delivery the challenges and applications is to develop the device-independent delivery and devices that are easy for patients use. Drug delivery is the method or process of administering a pharmaceutical compound to achieve a therapeutic effect in humans.This targeted delivery method provides several benefits, including rapid onset of action, increased bioavailability and reduced side effects.various inhalation devices such as metered-dose inhalers, dry powder inhalers, and nebulizers have been developed to cater to different patient needs.In future enhancing the efficacy and patient experience of inhalation therapy.This review provides an overview of the current state of inhalation drug delivery system higlighting their applications and exploring the latest development and innovations in this field and has better understanding the potential of inhalation drug delivery.

## INTRODUCTION

Inhalation with different form and for a different purpose, inhalation therapy has been around for thousands of years. As shown by various artifacts in museums that may be the earliest inhalation devices ever used, inhalation therapy was employed by ancient civilizations in Egypt, Greece, India, and the People's Republic of China. Asthma, cystic fibrosis, chronic obstructive pulmonary disease (COPD), and other lung conditions are now best treated with inhalation treatment[1]. There are currently around 250 inhaler devices available to administer

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medications for long-term respiratory conditions. Numerous benefits of inhalation therapy include the ability to utilize small dosages of medication, a quick onset of action, and a decreased risk of side effects because of systemic absorption[2].The last ten years have seen the cutting-edge innovations of the preceding 25 years either mature into commercial goods or be adjusted to satisfy requirements for development, quality, safety, or efficacy. It is necessary to examine each medication separately in order to account for aspects of the lung physiology that are involved in the pharmacokinetics of disposition, such as local dissolution, clearance mechanisms (absorption, mucociliary and cell mediated transport), metabolism, or sequestration (transporters)[3]. Drugs can be delivered by this pathway to particular cell types, including organelles within a cell, endothelial cells, neutrophils, macrophages, lymphocytes, and epithelial cells. In addition to varied formulations, there are a variety of delivery methods, including nebulizers, aerosolizers, dry powder inhalers, and metered dosage inhalers (MDI)[4].This review will focus on this aspect of inhalation system development because the technology utilized to create the aerosol (liquid dispersion or powder deagglomeration) is the essential component of any inhalation system[5].

## HISTORY OF INHALATION DRUG DELIVERY SYSTEM

Inhalation therapy was developed in an effort to treat these illnesses, and it is still evolving today. Since ancient times, people have looked for an efficient way to inhale medications. For more than 3500 years, the primary method of treating respiratory conditions, especially asthma, has been aerosol medicine administration. In the past, smoking or putting herbal concoctions in a heated container and breathing in the fumes were common ways to provide therapeutic aerosols.For more than 3500 years, the primary method of treating respiratory conditions, especially asthma, has been aerosol medicine administration. In the past, smoking or putting herbal concoctions in a heated container and breathing in the fumes were common ways to provide therapeutic aerosols. Plants that contain tropane alkaloids, like opium, Datura stramineum, and Hyoscyamus niger, have been utilized as the primary raw materials since ancient times. Since the 18th century, aerosol therapy technology has advanced quickly. Since it signaled the start of the hunt for tools for efficient pain management, the development of anesthesia surely had an impact on the creation of nebulizers.The development of medicinal aerosols was greatly aided by the 1956 introduction of the first metered-dose aerosol inhaler. In the middle of the 19th century, the first dry powder inhaler was created. It wasn't until the 1990s that it became widely used in clinical settings. The 1987 signing of the Montreal Protocol sparked a wave of inhaler technological innovation that gave rise to the present inhaler business. Inhalation therapy is being used for purposes far beyond pulmonary medicine and the treatment of obstructive lung illnesses(Figure1: Inhalation drug delivery system). Its future development prospects include both the discovery of novel therapeutic compounds and delivery systems using digital technology and the enhancement of current ones[6].

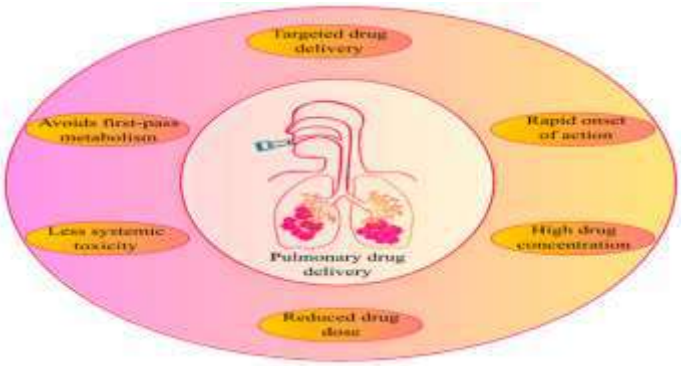


**Figure 1:Inhalation drug delivery**

## DEVICES OF INHALATION DRUG DELIVERY SYSTEM

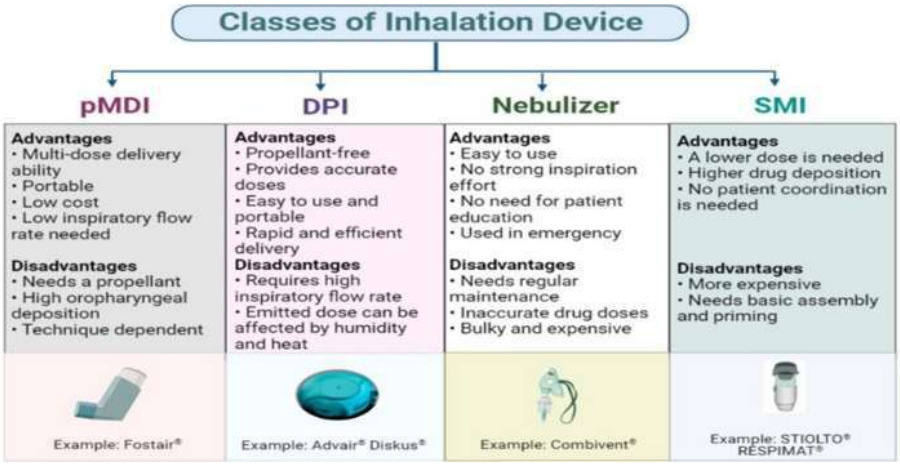


**Figure 2: Classes of inhalation devices**

### 1.METERED DOSE INHALERS(MDI):

The MDI is readily recognized by the majority of patients who have ever received treatement for asthma in developed countries and increasingly so, in developing countries. (Figure 3: Mechanism of metered dose inhalers) These include the general form and the key mechanical subsystem (metering valve, canister, and actuater mouth piece) that make up the device[7].In developing MDI systems, there are two major areas that need to be considered : the device hardware and the formulation . The hardware consists of the vial (aluminium can or plasticized glass vial), metering valve, actuator and for newer MDI usually a dose counter[8] .Climate change carries with it many risks, including catastrophic, weather events, famine, adverse health outcomes and displacement of whole communities[9]. A range of inhaler devices can be used to administer bronchodilators including metered-dose inhalers (MDIs), dry powder inhalers, soft mist inhalers, and nebulizers[10].

### MECHANISM:

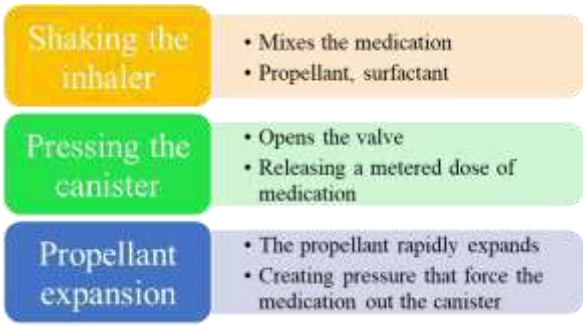


**Figure 3: Mechanism of metered dose inhalers**

## 2.DRY POWDER INHALERS:

Drug inhalation gained interest for the treatement of respiratory disease particularly after Philip stern acknowledged in 1764 the only possible way of applying medicines directly to the lung is through the windpipe.The MDI became rapidly popular because this type of device is small (portable), inexpensive, theoretically easy to use, fast, and silent compared to nebulizer equipment.Dry powder inhalers innovation in the future, breaking with this tradition is necessary.Safer,simpler, cheaper, and yet more effective DPIs are necessary to make high expectations about mass vaccination and TB therapy, particularly in developing countries, come true[11].While the inspiratory flow is variable with the patient's ability and conditions, the turbulence is differently sized within each device because depending of its technical design[12]. Effects of physico-chemical properties of particulate systems such as particle size, density, porosity, surface morphology, inter-particle force, surface morphology, inter particle force, surface energy etc ( Figure 4: Mechanism of dry powder inhalers)[13].

## MECHANISM:

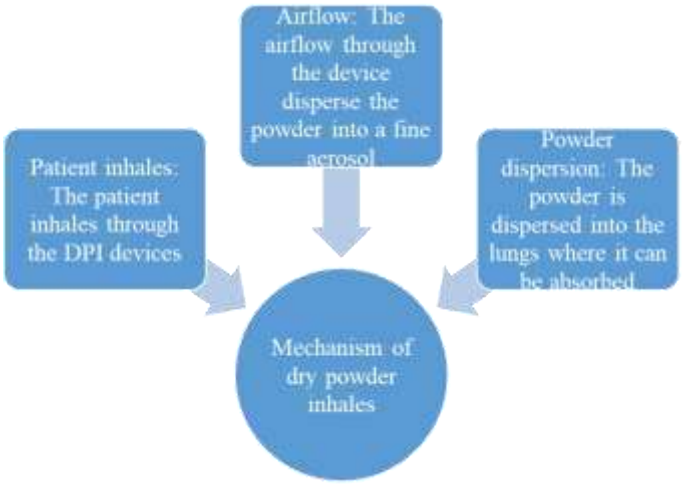


**Figure 4:Mechanism of Dry powder inhalers**

## 3.NEBULIZERS:

The order to properly work ,an inhaled drug must reach an effective distribution in the area to be treated .In this respect, the results of aerosol therapy are deeply influenced not only by the traditional physical, pharmacokinetic and pharmacodynamic properties of the drug , but also by the suitability of the delivery system and its correct use by the patient [14].Nebulizers are also conductive to the formulation of process sensitive proteins, peptides, and biological medication .The handheld respimat device extrudes a liquid formulation through a micronozzle block, forming colliding microjets, using only mechanical energy from a compressed spring[15].Despite the fact that nebulized drug therapy in CF may result in increased survival, improved lung function, fewer exacerbations, and minimal systemic effects and adverse events, variability in aerosol delivery, lung deposition, and clinical response is common(Figure 5: Mechanism of Nebulizers). Furthermore aerosol lung deposition with conventional nebulizers is highly dependent on the pulmonary morphology and ventilatory pattern of the patient[16].

## MECHANISM:

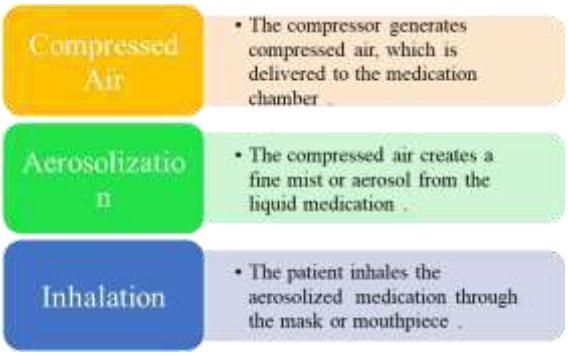


**Figure 5: Mechanism of Nebulizers**

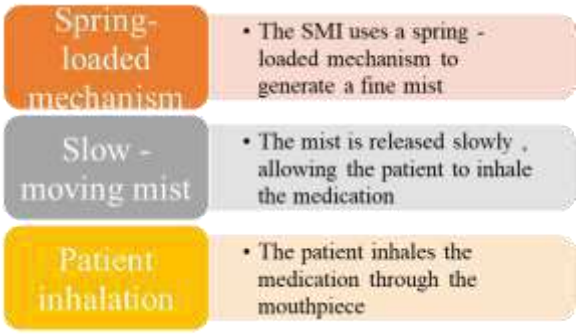


**Figure 6: Mechanism of Soft mist inhalers**

## 4.SOFT MIST INHALERS:

The soft mist inhales is propellant - free multidose inhaler device that does not suffer from the ballistic effect of aerosol created in pMDI, thereby reducing the deposition of aerosol in the mouth throat region.Soft mist inhalers possess advantages of pressurized metered dose inhaler and most of the dry powder inhaler including high drug deposition(up to >50% of the dose) in the lungs, portability, and compactness, without the inconvenience of propellent usage or the necessity to formulate drugs as complicated dry powder formulation[17].Soft mist inhaler, which uses spring power to produce a slow moving liquid aerosol that produces a high fraction of fine particles fraction is important, as regional lung deposition varies according to the aerosol particle size and flow rate particles have smaller than 5µm have greater potential for deposition in the lungs.The model possesses all the basics antaomical features of the real extra-thoracic airway such as the oral cavity, oropharynx, larynx and trachea in order to predict the fate of aerosol particles within lungs, single-path models or even whole-lung simulations have been carried out. Due to limited functional respiratory imaging technology (Figure 6:Mechanism of soft mist inhalers)[18].

**MECHANISM:**

## 5.PROPELLENTS:

Aerosol delivery of formulation can target different region of the airway, such as the upper bronchial airways, such as the upper brochial airways, terminal bronchioles, or the alveolar regions.The non-invasive nature make the strategy application of therapeutic drugs and genes[19].Delivery of medication to the lung in aerosol has a long a major boost to the aerosol therapy field was the insulin formulation developed for diabetic patients compared to oral or intravenous delivery.Increased deposition and adsorption of the drugs and gene, Decreased systemic toxic, Immediate availability of the medication, Non-invasive nature[20].The effectiveness of pulmonary devices is also dependent upon the breathing pattern of the patient.Rapid ispiration is not recommended when using a pressurised metered dose inhalers and nebulizers and increase the deposition by impaction in the upper airways and has rapid inspiratory air flow is required to deagglomerate drug particles for inhalation in dry powder devices (Figure 7: Mechanism of Propellents)[21].

**MECHANISM:**

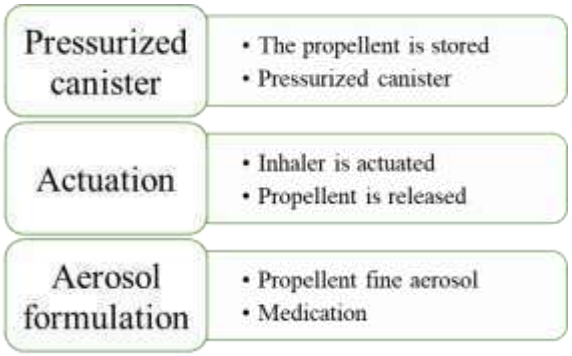


**Figure 7: Mechanism of propellents**

## APPLICATION OF INHALATION DRUG DELIVERY SYSTEM:

**Table 1:Application of Inhalation Drug Delivery System**

| | | |
|---|---|---|
| 1. | Asthma | Inhalation therapy |
| 2. | COPD | Helps to manage symptoms and slow disease progession |
| 3. | Cystic fibrosis | Helps manage respiratory symptoms and improve lungs function |
| 4. | Pulmonary hypertension | Helps to maintain symptoms and improve exercise capacity |
| 5. | Respiratory infections | Inhalation therapy can deliver antibiotics directly to the lungs |
| 6. | Targeted delivery | Inhalation therapy delivers medication directly to the lungs |
| 7. | Rapid onset of action | Inhalation therapy delivers can provide quick relief from symptoms |
| 8. | Reduced side effects | Inhalation therapy can reduce systemic side effects |
| 9. | Metered-dose inhalers | Deliver a specific dose of medication with each actuation |
| 10. | Dry powder inhalers | Deliver medication in dry powder form |

## FLOWCHART OF PHARMACOKINETICS AND PHARMACODYNAMIC:

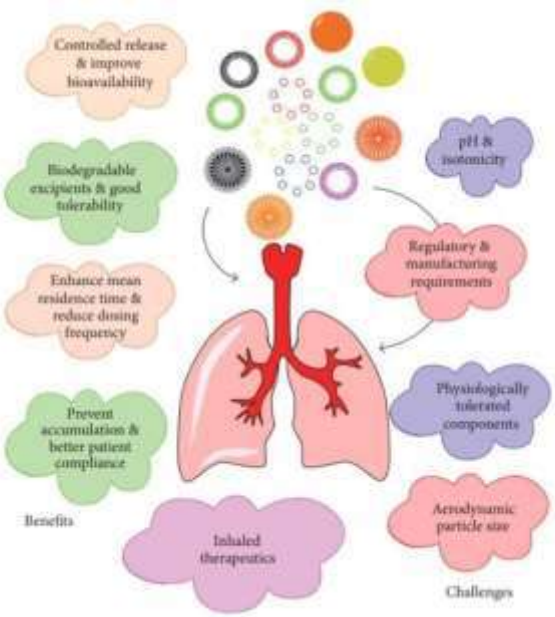


**Figure 8: Pharmacokinetics and pharmacodynamic of IDDS**

## CONCLUSION:

Inhalation drug delivery system offer a targeted and effective way to deliver medication directly to

the lungs, providing rapid relief from symptoms and improving treatment outcomes for respiratory disease such as asthma, COPD, and cystic fibrosis. Various devices such sa metered dose inhalers (MDIs), dry powder inhalers (DPIs), and nebulizers each have distinct advantages depending on the patients' needs and nature of the medication. Despite their benefits, proper device usage and patient adherence remain the crucial for optimal therapeutic outcomes and ongoing innovations continue to improve delivery efficiency patient compliance, and device design highlighting the vital role of inhalation system in modern respiratory therapy. Propellent has come a long way and has ideal of topical delivery of lungs and has the devices and formulations has brought research closer to a therapeutic reality. The successful delivery of any therapeutic agent to the pulmonary region DPI depends on four mutually dependent parameters the formulation the metering system in inhaler device and the patient understanding/training. I hereby conclude that inhalation drug delivery has rapid onset of action and continue to evolve to providing innovative solution for target drug delivery with minimal side effects ensuring the better outcomes.

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