



AMERICAN JOURNAL OF PHARMTECH RESEARCH

Journal home page: <http://www.ajptr.com/>

Comprehensive Review On Dry Powder Inhalations: Mechanisms, Technologies, and Future Directions

Chinna Reddy Palem^{1*}, Venkatasanthosh Paidi¹, Deepthi Battula¹, Sricharan Gumudevelli²

1. Asphar Research Labs Pvt. Ltd., IDA, Balangar, Hyderabad-500037; Telangana, India.

2. ITTS Labs, 2500 Nesconset Hwy, Bldg 19, Unit 72C, Stony Brook NY, 11790.

ABSTRACT

Dry powder inhalers (DPIs) represent a pivotal technology in pulmonary drug delivery, offering advantages such as improved stability, breath-actuated dosing, and enhanced patient convenience. This review presents an in-depth exploration of DPIs, from foundational principles to emerging innovations. Beginning with the historical development and physiological basis for pulmonary delivery, the review delves into the mechanisms of DPI function, highlighting the importance of aerodynamic particle behavior and key physicochemical properties. Critical formulation components such as active pharmaceutical ingredients, carrier particles, and excipients are examined alongside particle engineering and manufacturing technologies essential for scalable, high-quality production. Device design and aerosolization mechanisms are discussed in the context of usability, patient handling, and dose consistency. In vitro and in vivo performance evaluation techniques, including aerosol characterization, deposition studies, and pharmacokinetics, are reviewed. This review also captures recent advances in nanotechnology, biologics delivery, smart inhalers, and vaccine formulations. Regulatory frameworks, market dynamics, and current commercial DPI products are assessed to provide a comprehensive view of the global landscape. Finally, future directions are outlined, including personalized medicine approaches, sustainable inhaler technologies, and opportunities for innovation in systemic and respiratory therapies.

Keywords: Dry powder inhalers; Pulmonary drug delivery; Regulatory Guidelines; future perspectives

*Corresponding Author Email: palemchinnareddy@gmail.com, cpalem@ascentpharm.com

Received 22 May 2025, Accepted 05 June 2025

Please cite this article as: Palem CR *et al.*, Comprehensive Review On Dry Powder Inhalations: Mechanisms, Technologies, and Future Directions . American Journal of PharmTech Research 2025.

INTRODUCTION

Inhalation therapy has emerged as a cornerstone in the treatment of respiratory diseases, offering direct drug delivery to the lungs for rapid onset of action, targeted deposition, and reduced systemic side effects¹. By bypassing hepatic first-pass metabolism and gastrointestinal degradation, inhaled therapies achieve higher local drug concentrations with lower systemic exposure, enhancing both safety and efficacy^{2,3}. This route is particularly advantageous in chronic pulmonary conditions such as asthma, chronic obstructive pulmonary disease (COPD), and cystic fibrosis, as well as in emerging applications for systemic delivery⁴. There are three primary types of inhalation delivery systems for pulmonary drug administration: nebulizers, pressurized metered-dose inhalers (pMDIs), and dry powder inhalers (DPIs). Among these, DPIs delivering micronized drugs as dry powders are increasingly favored for their ability to enhance pulmonary deposition, particularly in the peripheral airways, thereby improving drug bioavailability and therapeutic efficacy⁵⁻⁷.

In a dry powder inhaler (DPI), aerosolization is driven by the patient's own inspiratory effort. To facilitate efficient de-agglomeration of the formulation into respirable particles, a high degree of airflow turbulence is required⁸. This turbulence is achieved through the incorporation of intrinsic airflow resistance within the DPI device, which enhances shear and impaction forces during inhalation⁹. The inspiratory effort required to generate adequate turbulence is therefore directly influenced by the device's resistance profile. Although optimal flow rates vary among DPI designs, an inspiratory flow rate in the range of 60-90 L/min is generally necessary to ensure effective pulmonary deposition and therapeutic efficacy^{10,11}.

DPIs have gained significant traction in pulmonary drug delivery due to their propellant-free design, enhanced formulation stability, dose flexibility, extended patent life, and improved patient adherence¹²⁻¹⁴. Their utility spans both local and systemic therapies, particularly in managing asthma, COPD, cystic fibrosis, and respiratory infections¹⁵. Despite these advantages, DPI performance remains highly dependent on device architecture, powder properties, and the patient's inspiratory effort^{16,17}. Technological advancements such as engineered particles, innovative excipients, and smart inhalers have significantly improved drug dispersion, lung deposition, and clinical outcomes over the last decade^{18,19}. Furthermore, the replacement of chlorofluorocarbon (CFC) propellants with Hydrofluoroalkanes (HFAs) in response to environmental mandates like the Montreal Protocol has enhanced sustainability without compromising efficacy²⁰⁻²².

DPI performance is intrinsically linked to a combination of formulation science, particle engineering, and device mechanics. Innovations in carrier selection, excipient technologies, and

manufacturing processes have expanded the capability of DPIs to deliver high-dose, poorly soluble, and biologic compounds²³. Furthermore, integration with smart technologies and environmental sustainability initiatives positions DPIs as a leading platform in modern pulmonary drug delivery. This review explores the fundamental mechanisms of DPI drug delivery, technological advances in formulation and device design, and emerging trends that will shape the next generation of DPI-based therapies.

FUNDAMENTALS OF DRY POWDER INHALATIONS

Dry powder inhalations (DPIs) are a pulmonary drug delivery approach that relies on the patient's inspiratory effort to disperse and deliver micronized drug particles to the lungs. Unlike aerosol-based systems, DPIs do not require propellants; instead, they utilize the kinetic energy of inhaled air to de-agglomerate and aerosolize the powder formulation. Effective drug delivery via DPIs depends on several fundamental factors. First, an understanding of respiratory tract anatomy and aerodynamic behavior is essential, as the size and shape of particles influence their deposition in specific lung regions. Particles with an aerodynamic diameter of 1–5 μm are ideal for reaching the lower respiratory tract.

Mechanism of Drug Delivery via DPIs

The drug delivery mechanism in DPIs involves several interdependent steps. Upon inhalation, air is drawn through the inhaler device, generating turbulent airflow. This turbulence plays a critical role in de-agglomerating the dry powder formulation, which typically consists of micronized drug particles either alone or blended with larger carrier particles such as lactose or mannitol. The energy generated by the airflow must be sufficient to overcome the cohesive forces between particles, particularly van der Waals interactions and electrostatic charges. Once aerosolized, the resulting cloud of fine particles is carried deep into the respiratory tract (Figure 1). The aerodynamic diameter of these particles generally in the range of 1–5 μm is crucial for effective lung deposition²³. Particles larger than this tend to deposit in the oropharynx, while smaller ones may be exhaled before settling in the alveoli.

The device resistance, along with formulation characteristics such as flowability and dispersibility, significantly affects aerosolization efficiency. Different DPI designs vary in their internal airflow resistance, which in turn influences the inspiratory flow rate needed for optimal performance typically between 30 - 90L/min depending on the device. Ultimately, the efficiency of drug delivery via DPIs depends on the coordinated interaction of device design, powder properties, and patient-specific factors such as inspiratory effort and technique²⁴⁻²⁵.

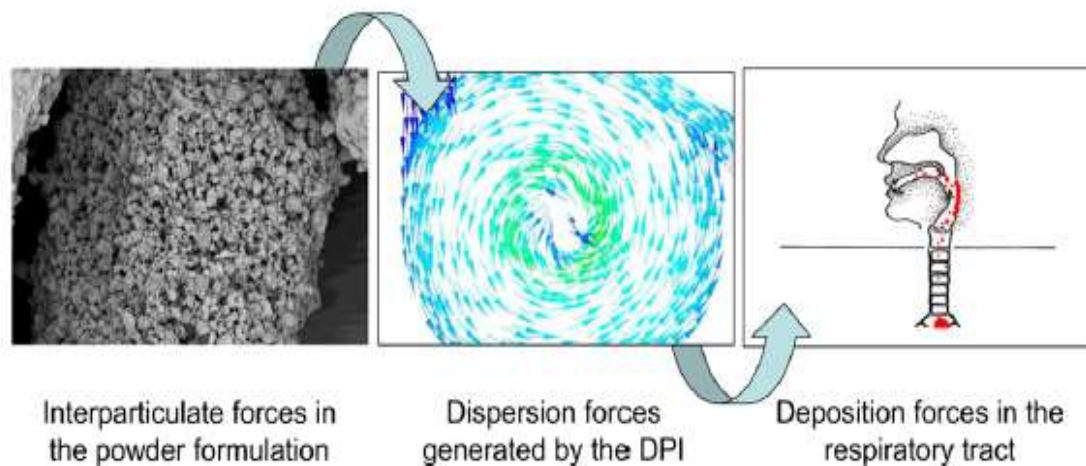


Figure 1: Illustrates the desired balance for optimal DPI therapy between the interparticulate forces in the powder formulation, the dispersion forces generated by the inhaler and the deposition forces in the respiratory tract (Courtesy of M. Hoppentocht, et al. 2014.)

Respiratory Tract Anatomy and Aerodynamic Considerations

The human respiratory tract is anatomically divided into three key regions: the extra-thoracic, tracheobronchial, and alveolar zones (Table 1). The alveolar region, comprising approximately 300 million alveoli, provides a vast surface area of 70-100 m² optimized for gas exchange and drug absorption. Surrounding these alveoli is a dense capillary network with over 280 billion microvessels, making the lungs one of the most vascularized organs. This, combined with a high pulmonary blood flow (~5.7 L/min), enables rapid systemic absorption of inhaled drugs²⁶. Key anatomical features such as the ultra-thin alveolar-capillary membrane (0.1–0.5 µm), minimal diffusion distance, and intimate air blood interface, further enhance drug uptake and support both local and systemic delivery²⁷. The aerodynamic behavior of inhaled particles plays a critical role in deposition (Figure 2), with optimal lung targeting achieved when particles have an aerodynamic diameter between 1–5 µm.

Pulmonary drug delivery offers distinct advantages, including site-specific deposition for respiratory conditions like asthma and COPD, improving therapeutic efficacy while minimizing systemic side effects. Moreover, the lung's physiology makes it a viable route for systemic delivery of drugs with poor oral bioavailability, enabling rapid onset and improved pharmacokinetic profiles^{28, 29}.

Table 1: Classification and typical parameters of human pulmonary airway systems

Parameters	Extra-thoracic region	Tracheobronchial region	Alveolar region
Region includes	Oral–pharyngeal cavity, larynx, and tracheal entrance	Trachea, bronchi, and bronchiole terminals	Bronchioles, alveoli, and alveolar ducts
Particle size	>6 μ m	2–5 μ m	<2 μ m
Drug deposition mechanism	Gravity, and Brownian diffusion	Sedimentation	Brownian diffusion

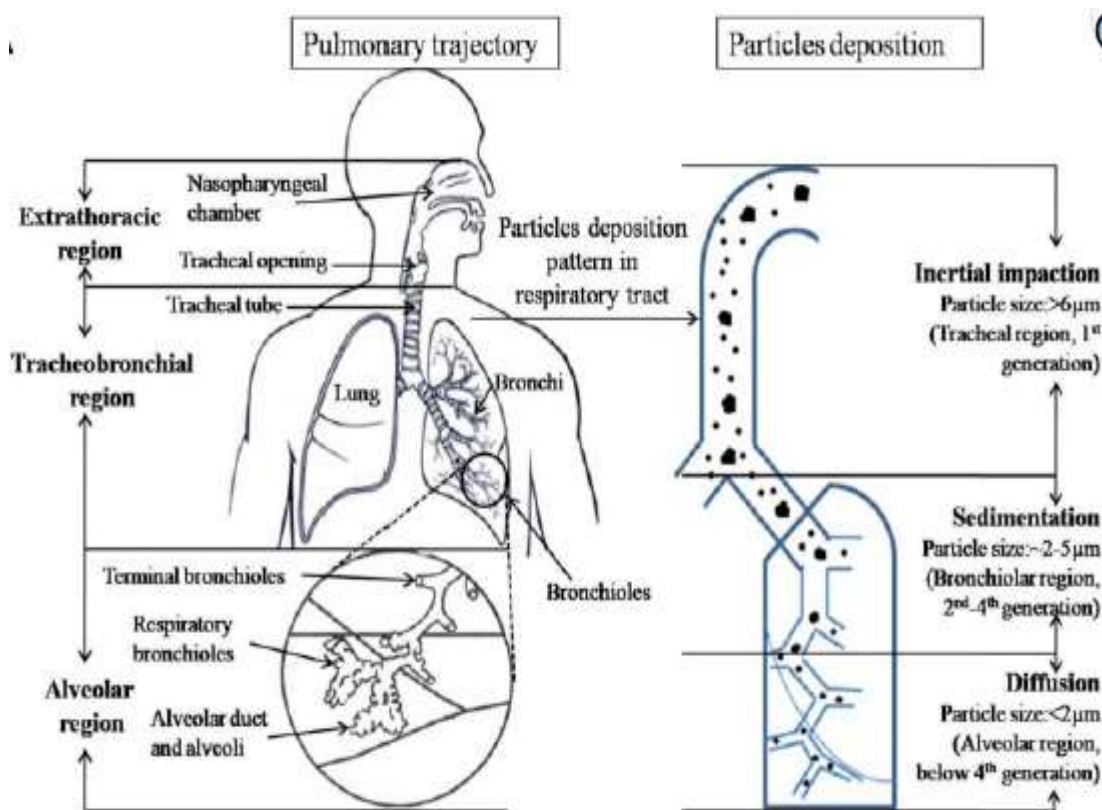


Figure 2: Illustrates the airways system, pulmonary tract, and particle deposition pattern of DPIs (Courtesy of Birendra Chaurasiya et al., 2020.)

Key Physicochemical Properties of DPIs

Performance of DPIs is highly dependent on the physicochemical properties of the powder formulation. These properties influence powder flow, dispersion, aerosolization, and ultimately, drug deposition in the lungs. Aerodynamic particle size is critical for lung deposition. Particles with a mass median aerodynamic diameter (MMAD) between 1–5 μ m are ideal for reaching the lower respiratory tract. Larger particles tend to deposit in the oropharynx, while smaller ones may be exhaled. Particle Shape and Morphology- irregular, porous, or corrugated particles often exhibit better aerosolization due to reduced inter-particulate cohesion. Spherical particles, though more flowable, may agglomerate more easily³⁰⁻³⁴.

Surface Properties - surface energy, roughness, and charge affect particle-particle interactions. High surface energy can lead to increased cohesion and poor dispersion, while engineered surfaces can enhance flow and de-agglomeration. Density – low density particles with high surface area-to-mass ratios can improve suspension in the airflow and promote deep lung deposition. Tapped and bulk density also influence blending and packing behavior during manufacturing. Hygroscopicity - moisture uptake can alter particle size and increase cohesion, adversely affecting powder flow and dispersion. Proper storage conditions and moisture-protective packaging are essential. Flowability - good powder flow is essential for dose uniformity and device compatibility. Flow is influenced by particle size distribution, shape, and external factors like humidity. Optimizing these physicochemical characteristics is crucial for developing effective, stable, and patient-friendly DPI formulations.

FORMULATION STRATEGIES FOR DPIs

The successful development of DPIs involves a systematic formulation approach encompassing the drug substance, excipients, and device compatibility. DPI formulation can generally be divided into three key stages:

1. **Active Pharmaceutical Ingredient (API) Preparation** - This includes the production and micronization of the drug substance to achieve the desired aerodynamic particle size, typically between 1-5 μ m. Particle engineering techniques such as jet milling, spray drying, or supercritical fluid processing are commonly employed to optimize particle morphology, surface properties, and stability.
2. **Formulation with or without Carrier** - DPI formulations can be categorized as carrier-based or carrier-free. Carrier-based systems typically use larger excipients like lactose or mannitol to improve powder flow and facilitate uniform dosing^{33, 34}. The API adheres to the carrier surface and is detached upon inhalation. Carrier-free systems involve engineered particles (e.g., porous or cohesive particles) that are designed for improved dispersion and high-dose delivery without excipients. These require advanced control over particle morphology and surface energy. Excipients may also be added to enhance stability, moisture protection, or dispersibility.
3. **Device-Formulation Integration**-The final formulation must be compatible with the inhaler device, ensuring efficient aerosolization and dose delivery³⁶⁻³⁸. This stage involves optimizing formulation properties to match the deaggregation and dispersion capabilities of the device. All DPIs incorporate following fundamental functional components
 - Dose metering system: Ensures consistent and accurate dose delivery.

- Aerosolization mechanism: Converts powder into an inhalable aerosol upon actuation.
- Deaggregation mechanism: Breaks apart agglomerated particles to produce respirable-size particles.
- Mouthpiece adaptor: Directs the aerosol efficiently into the patient's oropharynx.

Strategic alignment of formulation characteristics with device design is critical to achieving effective lung deposition, dose consistency, and therapeutic efficacy.

DPI Formulation Design

DPIs are designed as either pre-metered or device-metered systems. Pre-metered DPIs contain pre-filled doses of drug formulation in individual containers such as capsules, blisters, or cartridges³⁴. These doses may be inhaled directly from the container or transferred to a chamber within the device prior to use. In contrast, device-metered DPIs store the formulation in a bulk reservoir and meter each dose internally using mechanisms like metering chambers or rotating wheels. Examples include the Turbuhaler® and Flexhaler®, which deliver multiple doses from a single reservoir^{36,37}.

DPI performance is governed by several interdependent factors mentioned in below (Figure 3)

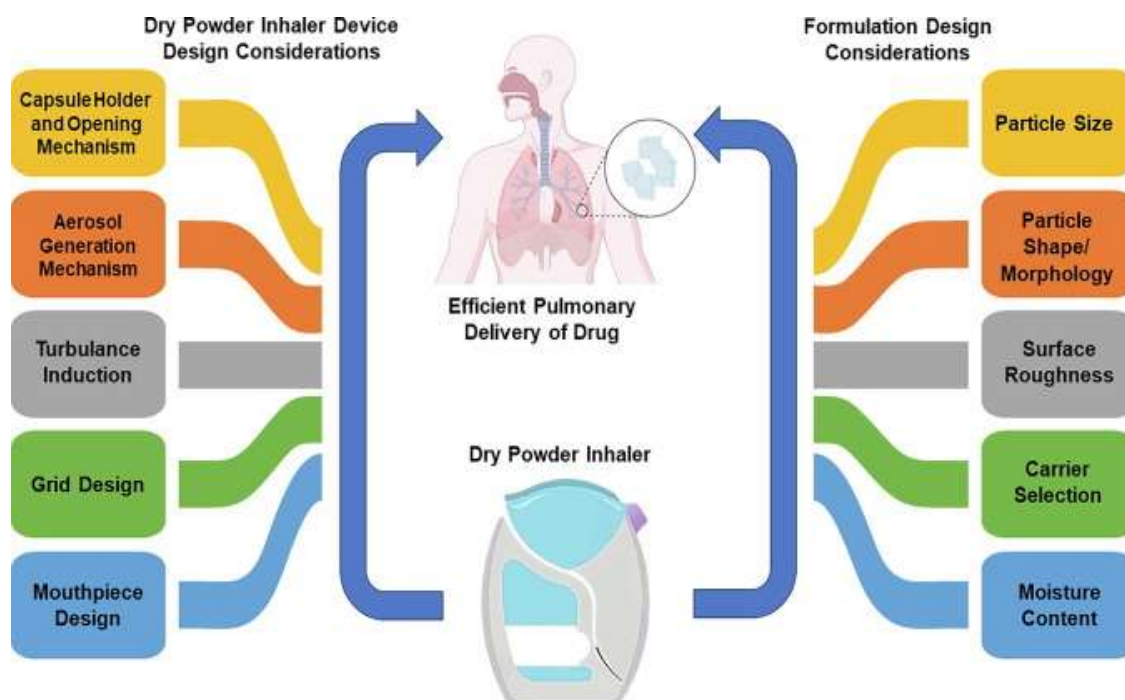


Figure 3: Illustrates the comparative key consideration for formulation design and dry powder inhaler device design (Courtesy of Patravale, V. et al., 2024.)

- Formulation properties such as particle size distribution, flowability, and moisture sensitivity.
- Container closure system integrity, which ensures protection against humidity and dose uniformity across uses.

- Manufacturing robustness, which affects reproducibility and long-term stability.
- Patient-related variables, including inspiratory effort and proper handling, which can significantly impact dose delivery especially in paediatric, geriatric, or respiratory-compromised populations.

Effective aerosolization typically requires blending micronized APIs with larger carrier particles (e.g., lactose monohydrate) to improve flow and dispersion. In both pre- and device-metered systems, device-formulation compatibility is critical to maintaining consistent performance over the product's shelf life³⁸. A comprehensive understanding of formulation science, device engineering, and patient usability is essential not only for initial product development but also for sustaining product quality and enabling innovation across the product life cycle.

MANUFACTURING AND PROCESSING TECHNOLOGIES

DPI manufacturing involves precise powder blending to ensure uniform drug distribution, typically using low-shear mixers. Scale-up challenges include maintaining content uniformity, managing static charge, and ensuring consistent powder flow. Quality control focuses on blend uniformity, moisture content, and aerosol performance metrics such as fine particle fraction (FPF) and mass median aerodynamic diameter (MMAD). Regulatory compliance requires adherence to GMP and ICH guidelines, with stability and performance testing conducted under controlled environmental conditions.

Powder Blending and Homogenization

Achieving uniform distribution of the active pharmaceutical ingredient (API) within a carrier-based DPI formulation is critical for dose uniformity. Typically, low-shear tumble blending (e.g., using a V-blender or Turbula mixer) is employed for mixing micronized APIs (1–5 µm) with larger carrier particles (50–200 µm), such as lactose. Blending times and speeds must be optimized, as over-blending can cause drug-carrier adhesion, reducing dispersibility, while under-blending may result in content uniformity failures⁴⁰⁻⁴⁶. Content uniformity should meet USP <905> criteria, with acceptance values (AV) not exceeding 15.

Scale-Up and Industrial Production Challenges

Scaling DPI production from lab to commercial scale presents several challenges, including maintaining homogeneity, larger batch sizes can lead to segregation of fine and coarse particles, affecting dose consistency. Static charge build-up, common with micronized powders, static can lead to wall adherence and material loss. Powder flow issues, poor flow may lead to inconsistent filling in device-metered systems. To address this, real-time Process Analytical Technology (PAT) tools such as NIR spectroscopy and in-line laser diffraction are increasingly used to monitor blend

uniformity and particle size distribution during production. These support compliance with ICH Q8 - Q10 guidelines on pharmaceutical development and quality systems^{47, 48}.

DEVICE DESIGN AND MECHANISM

DPI device and formulation engineering are the two major arms that play a crucial role in the effectiveness of the DPI delivery. The effectiveness of DPIs relies heavily on the interplay between device design, powder formulation, and patient inhalation effort. This section explores the types of DPI devices, their aerosolization mechanisms, and critical aspects of patient usability.

Types of DPI Devices

DPI devices are classified based on their dosing and powder containment systems. The primary categories include - single-dose devices - These devices deliver one pre-metered dose per capsule or blister. The drug is loaded into the device by the patient before each use (examples: HandiHaler® & Breezhaler®). Advantages of Single dose devices includes accurate dosing, minimal cross-contamination and limitations of manual capsule loading may affect patient adherence.

Multi-Dose Devices are similar to single-dose devices, but contain multiple capsules for several doses. These are still manually inserted but offer more dosing flexibility. Multi-Dose Reservoir-Based Devices contain a bulk reservoir of formulation and meter the dose internally during each actuation (Examples Turbuhaler® and Flexhaler®). Advantages of Multi-Dose Reservoir-Based Devices include convenient, preloaded, fewer steps for patients and limitations of dose uniformity may be affected by powder flow or environmental exposure³⁶. Multi-Dose Blister-Based Devices (Figure 4) - have pre-metered doses sealed in individual blisters on a strip or disc that are punctured upon actuation (examples Diskus® (Accuhaler) & Ellipta®). **Advantages of Multi-Dose Blister-Based Devices** include accurate dose control, protection from moisture and limitations of complex manufacturing, and costlier.

Inhaler Design and Aerosolization Mechanisms

DPI function relies on converting a dry powder into an inhalable aerosol through patient-generated airflow. Key design elements include

Airflow resistance and de-agglomeration –

DPIs incorporate internal resistance to create turbulent energy during inhalation, which facilitates de-agglomeration of cohesive drug particles⁴⁵. Resistance levels are generally classified as low resistance (e.g., Aerolizer®)- requires high inspiratory flow (≥ 60 L/min), medium resistance (e.g., Diskus®) - Moderate inspiratory effort (40–60 L/min) and high resistance (e.g., HandiHaler® - works well at lower flow rates (~ 30 L/min).

Aerosolization Mechanisms includes passive DPIs (Most common, rely solely on patient effort to disperse powder) and active DPIs (incorporate mechanical or electronic assistance (e.g., impellers, vibrating mesh) to aerosolize powders independently of the patient's inspiratory capacity beneficial for paediatric or severely ill patients).

Dose metering and delivery - dosing mechanisms includes Rotating wheels or screw augers (Turbuhaler®) to meter powder from a reservoir and Piercing mechanisms (Diskus®, capsule-based DPIs) to release pre-metered doses^{46,48}. The design must ensure consistent dose emission, low device retention, and minimal throat deposition.

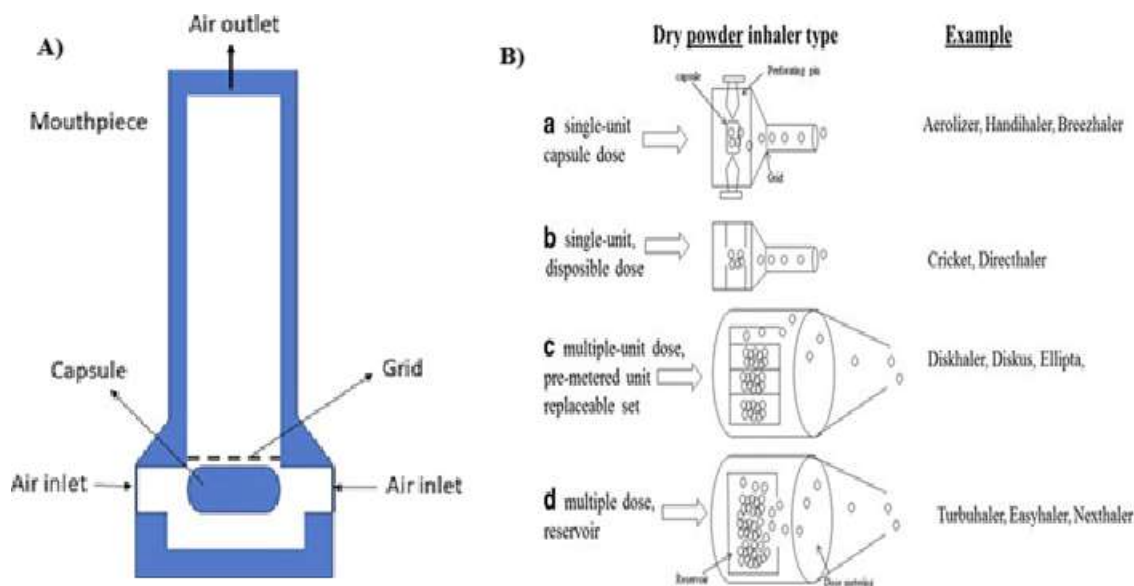


Figure 4: A). Model design for dry powder inhaler device B). Different types of marketed DPI designs (Courtesy of Patravale, V. et al., 2024.)

Despite their technological advantages and potential to improve dose consistency and usability, no active DPIs have yet been successfully commercialized. Challenges in device complexity, cost, regulatory approval, and patient acceptance have limited their widespread adoption⁵⁰.

IN VITRO AND IN VIVO PERFORMANCE TESTING

The development and regulatory approval of inhalation drug products demand a comprehensive evaluation of their performance using both in vitro and in vivo methodologies. These assessments are crucial to ensure product quality, efficacy, safety, and reproducibility. The aerosol characterization, deposition profiling, and bioavailability studies, which collectively provide formulation optimization and clinical success^{51, 52}.

Aerosol Characterization (MMAD & FPF)

Aerosol characterization is a foundational aspect of inhalation product development. The primary goal is to assess the aerodynamic properties of the emitted particles, as these directly influence the

site of deposition in the respiratory tract and, consequently, the therapeutic effect. Two critical parameters used in aerosol characterization are Mass Median Aerodynamic Diameter (MMAD) and Fine Particle Fraction (FPF). MMAD is the particle diameter at which 50% of the aerosol mass is composed of smaller particles and 50% of larger ones. An MMAD of 1–5 μ m is typically considered optimal for pulmonary delivery, allowing deposition in the lower airways and alveolar region. FPF defined as the percentage of the total aerosolized dose that consists of particles below a specific aerodynamic size threshold (commonly 5 μ m), FPF reflects the proportion of the drug likely to reach the deep lung. A high FPF indicates more efficient lung deposition⁵²⁻⁵⁵. Characterization tools such as laser diffraction, aerodynamic particle sizers, and cascade impactors are widely used to determine these parameters under standardized flow conditions⁵⁶. Consistent aerosol performance is essential for batch-to-batch reproducibility and establishing bioequivalence for generic formulations.

In Vitro Deposition Studies (Cascade Impactor, NGI)

In vitro deposition testing simulates the deposition of inhaled drug particles across different regions of the respiratory. The Cascade Impactor, particularly the Next Generation Impactor (NGI), is the most commonly used device in regulatory submissions for assessing aerodynamic particle size distribution⁵⁷. The NGI separates particles based on their inertia and collects them on different stages that correspond to anatomical tract. These studies are critical in assessing lung targeting efficiency and guiding formulation or device modifications regions of the human airways. The Andersen Cascade Impactor (ACI) and NGI differ in design and cut-off diameters but are both recognized by pharmacopeias (e.g., USP, Ph. Eur.) for regulatory testing. Proper calibration, flow rate control, and environmental conditioning are essential to ensure reliable and reproducible data.

Bioavailability and Pharmacokinetic Studies

While in vitro studies are valuable, in vivo pharmacokinetic (PK) studies provide a more direct assessment of drug absorption, distribution, and systemic exposure. These studies help establish the bioavailability of inhaled formulations and are essential for determining therapeutic efficacy, supporting bioequivalence for generic products and confirming systemic safety, especially for corticosteroids or β -agonists. Pharmacokinetic parameters such as C_{max} (maximum concentration), T_{max} (time to reach C_{max}), and AUC (area under the curve) are measured in blood plasma following inhalation. These values are often compared with those from intravenous or oral administration to assess absolute or relative bioavailability. Importantly, combining PK data with in vitro aerosol and deposition profiles allows for the development of IVIVC models,

which can reduce reliance on extensive *in vivo* studies during product development. For locally acting inhaled drugs, however, pharmacodynamic endpoints or clinical trials may still be required to fully characterize efficacy.

REGULATORY LANDSCAPE AND MARKET OUTLOOK

The development, approval, and commercialization of dry powder inhalers (DPIs) require rigorous adherence to evolving regulatory frameworks, alongside a nuanced understanding of global market dynamics. Regulatory agencies such as the U.S. Food and Drug Administration (FDA), European Medicines Agency (EMA), and others provide guidance to ensure the safety, efficacy, and quality of DPI products (Table 2). Concurrently, the DPI market is expanding due to the increasing prevalence of respiratory diseases, technological advancements in inhalation devices, and a growing demand for patient-centric therapies. This section explores the global regulatory environment and assesses current trends shaping the DPI market⁵⁸.

Table 2: Comparative regulatory requirement for submission of DPIs between USFDA and EMA (Europe)

Aspect	FDA (U.S.)	EMA (Europe)
Overall Approach	Emphasizes stepwise approach: <i>In vitro</i> → Pharmacokinetics → Pharmacodynamics/clinical, if needed	Emphasizes weight-of-evidence: <i>In vitro</i> + <i>in vivo</i> demonstration of therapeutic equivalence
In Vitro Requirements	Strong emphasis; often sufficient if sameness in formulation/device	Required but often not sufficient alone for BE
Pharmacokinetics (PK)	Preferred when systemic absorption is measurable	Accepted when appropriate, especially for systemically acting drugs
Pharmacodynamic / Clinical Endpoint	Required only when <i>in vitro</i> and PK are not sufficient (e.g., corticosteroids)	Often required, especially for locally acting drugs (e.g., asthma/COPD treatments)
Device Similarity	Must match closely in resistance, operation, and patient interface; human factors studies may be required	Must be similar in design and use; more flexibility if therapeutic equivalence can be shown
Formulation Similarity (Q1/Q2)	Strongly preferred; differences must be justified with data	Required; Q1/Q2 sameness generally expected
Weight-of-Evidence	Allows <i>in vitro</i> + PK only in many cases (e.g., fluticasone/salmeterol)	Prefers <i>in vitro</i> + clinical endpoint study, especially for orally inhaled products (OIPs)
Guidance Style	Detailed Product-Specific Guidance (PSGs) available for many drugs	Class-level guidance with scientific advice encouraged for specifics
Local vs. Systemic Action	Focused on PK-based BE even for locally acting drugs if feasible	Emphasizes clinical endpoint studies for locally acting DPIs

Commercial DPI Products and Market Trends

The DPI market is experiencing robust growth, driven by increased disease prevalence, heightened awareness of respiratory health, and advancements in inhaler technologies. The global market for DPIs was valued at over USD 15 billion in recent years and is projected to grow at a CAGR of 6–8%, reaching over USD 25 billion by the early 2030s. Some of the most widely used commercial

DPI products include Advair Diskus® (fluticasone/salmeterol), Symbicort® Turbuhaler® (budesonide/formoterol), Spiriva® HandiHaler® (tiotropium bromide) and Trelegy Ellipta® (fluticasone/umeclidinium/vilanterol). These products have set benchmarks for performance and patient acceptance (Table 3). The Ellipta® platform, in particular, is recognized for its user-friendly design and multiple drug combinations. The pipeline is now expanding to include generic DPIs for blockbuster inhalers (e.g., Wixela Inhub® as a generic of Advair), biologic formulations for diseases like cystic fibrosis and pulmonary arterial hypertension and inhalable antibiotics and antivirals, especially in the context of rising antimicrobial resistance and respiratory pandemics.

Table 3: Illustrates the commercially available Dry Powder Inhalers

S No	Name of the API	Therapeutic Use	Brand Name & Manufactured By	Device type	Device Name	Inactive ingredients
1	Aclidinium Bromide	Used as maintenance treatment for COPD	Tudorza Pressair® & AstraZeneca	Multidose, breath-actuated DPI	PRESSAIR inhaler	Lactose monohydrate (Lactose) as the carrier
2	Aclidinium Bromide; Formoterol Fumarate	Used as maintenance treatment for COPD	Duaklir Pressair & Astra Zeneca	Multidose, breath-actuated DPI	PRESSAIR inhaler	Lactose monohydrate as the carrier
3	Albuterol Sulfate	Used to prevent and treat difficulty breathing, wheezing in asthma & COPD	ProAir® RespiClick® & Teva Pharmaceuticals	Multi-dose, breath-actuated DPI	RespiClick® inhaler	Alpha-lactose
4	Budesonide (Micronized API)	Treatment of asthma	Pulmicort Flexhaler & Astra Zeneca	Inhalation-driven multi-dose DPI	Flexhaler	Micronized lactose monohydrate
5	Fluticasone Furoate (micronized)	Used to prevent and control symptoms of asthma for better breathing in adults and children aged 5 years and older	Arnuity Ellipta & GlaxoSmithKline	A foil blister strip of powder -based DPI	Ellipta inhaler	Lactose monohydrate
6	Fluticasone Furoate; Umeclidinium bromide; vilanterol trifenate (micronized)	Used in COPD including chronic bronchitis and/or emphysema	Trelegy Ellipta & GlaxoSmithKline	Two foil blister strip of powder -based DPI	Ellipta inhaler	One Strip Contain API+ Lactose and Other Contains API + Lactose + Mg. Stearate
7	Fluticasone Furoate; Vilanterol Trifenate (micronized)	To treat asthma and COPD	Breo Ellipta & GlaxoSmithKline	Two foil blister strip of powder -based DPI	Ellipta inhaler	One Strip Contain API+ Lactose & Other Contains API + Lactose + Mg. Stearate
8	Fluticasone Propionate (micronized)	Indicated for the maintenance treatment of asthma as prophylactic therapy in patients	Flovent Diskus & GlaxoSmithKline	A foil blister strip of powder -based DPI	Diskus inhaler	Lactose monohydrate

		aged 4 years and older				
9	Fluticasone Propionate; Salmeterol Xinafoate (micronized)	To treat people with asthma and people with chronic obstructive pulmonary disease (COPD))	Advair Diskus & GlaxoSmithKline	A foil blister strip of powder -based DPI	Diskus inhaler	Lactose monohydrate
10	Fluticasone Propionate; Salmeterol Xinafoate	To treat Asthma	Airduo Respiclick & TEVA	Multidose Dry Powder Inhaler (MDPI) for oral inhalation	Deagglomeration & aerosolization of the drug particles as the formulation moves through the cyclone component of the device.	Lactose monohydrate
11	Levodopa (Spray dried powder)	To treat intermittent "off" episodes in advanced Parkinson's disease patients who are already taking carbidopa/levodopa	Inbrija & Acorda Therapeutics	inhaler is breath-actuated by the patient	NA	1,2-dipalmitoyl-sn-glycero-3-phosphocholine (DPPC), sodium chloride
12	Loxapine	Acute treatment of agitation associated with schizophrenia or bipolar I disorder in adults	Adasuve & Alexza Pharmaceuticals	provides rapid systemic delivery by inhalation of a thermally-generated aerosol of loxapine	NA	Excipient free
13	Mannitol	Indicated for the assessment of bronchial hyper responsiveness in adult and pediatric patients 6 years of age or older who do not have clinically	Aridol Kit & Methapharm, Inc	kit contains one, single patient use, DPI device & 3 consecutively numbered foil blister packs	NA	No inactive

		apparent asthma				
14	Mannitol (spray dried into particles of respirable size)	To treat Cystic Fibrosis	Bronchitol & Pharmaxis Ltd	dispersion into the airstream generated by the patient upon inhalation through the mouthpiece	NA	No inactive
15	Mometasone Furoate	Asthma symptoms in people 4 years of age and older	Asmanex Twisthaler & MSD International GmbH	cap-activated, inhalation-driven, Multidose DPI	NA	Anhydrous lactose
16	Salmeterol Xinafoate (Micronized)	To prevent asthma attacks or exercise-induced bronchospasm	Serevent & GlaxoSmithKline	a foil blister strip (powder mix of 12.5 mg per blister)	Diskus	Lactose monohydrate
17	Tiotropium Bromide	To treat long-term breathing problems, such as COPD or asthma	Spiriva & Boehringer Ingelheim Pharmaceuticals Inc	used to inhale the dry powder contained in the SPIRIVA capsule	Handi haler device	Lactose monohydrate
18	Tobramycin (Spray dried powder)	Cystic fibrosis patients whose lungs contain bacteria called <i>Pseudomonas aeruginosa</i>	Tobi Podhaler & Mylan	Capsule	PODHALER (device used to inhale the dry powder contained in the TOBI Podhaler capsule)	1,2-distearoyl-sn-glycero-3-phosphocholine (DSPC), calcium chloride & sulphuric acid (for pH adjustment)
19	Treprostinil	Approved for the treatment of pulmonary arterial hypertension and pulmonary hypertension associated with interstitial lung	Tyvaso DPI & United Therap	small, portable inhaler, single-dose Cartridges prefilled With medicine	Tyvaso DPI is administered using a single inhalation per cartridge	Carrier particles consisting of fumaryl diketopiperazine (FDKP)
20	Umeclidinium Bromide (Micronized)	To relieve the symptoms of COPD in adults	Incruse Ellipta & GlaxoSmithKline	Foil Blister Strip (powder blend of 12.5 mg per blister)	Plastic inhaler containing a foil blister strip	Magnesium stearate and Lactose Monohydrate

21	Umeclidinium Bromide; Vilanterol Trifenatate (Micronized)	To relieve the symptoms of COPD in adults	Anoro Ellipta & GlaxoSmithKline	plastic inhaler containing 2 foil blister strips	NA	One strip contains Umeclidinium bromide + Mg. Stearate + Lactose and other strip contains Vilanterol trifenatate + Mg. Stearate + Lactose
22	Zanamivir	To treat flu (influenza virus infection)	Relenza Rotadisk & GlaxoSmithKline	double-foil blisters	Diskhaler.	Lactose

RECENT ADVANCES AND EMERGING TRENDS IN DRY POWDER INHALERS (DPIS)

The landscape of dry powder inhaler (DPI) technologies is evolving rapidly due to growing demands for precision medicine, improved drug targeting, and user-friendly drug delivery systems. Recent innovations aim to overcome the limitations of conventional formulations and devices, opening new therapeutic avenues and expanding the scope of inhalation therapy beyond traditional small-molecule drugs⁵⁹. Highlighting in this section the key advancements and emerging trends that are reshaping the future of DPIS.

Nanoparticle-Based DPIS: Enhancing Drug Solubility and Lung Penetration

Nanoparticle-based formulations have emerged as a powerful strategy to enhance the performance of DPI systems, especially for poorly water-soluble drugs and molecules requiring deep lung deposition. Nanoparticles offer high surface area, improved dissolution rates, and controlled release profiles. When incorporated into DPIS, they facilitate better mucosal adhesion, cellular uptake, and systemic absorption. Common techniques for nanoparticle production include spray drying, supercritical fluid processing, and high-pressure homogenization. Carrier-free formulations using engineered nanoparticles or combination systems (e.g., drug-loaded nanoparticles blended with excipient microparticles) are gaining traction. Additionally, surface modification of nanoparticles with ligands or polymers is being explored to enable targeted delivery, particularly in diseases like lung cancer or multidrug-resistant tuberculosis. Despite their promise, challenges such as particle aggregation, aerosolization efficiency, and regulatory hurdles must be addressed for widespread clinical adoption⁶⁰.

Smart Inhalers and Digital Health Integration

Smart inhalers represent a paradigm shift in respiratory care by integrating sensors, wireless communication, and data analytics into DPI platforms. These devices monitor patient inhalation patterns, adherence, and environmental conditions in real-time, providing feedback to patients and healthcare providers through smartphone apps or cloud platforms. Key features of smart DPIS include dose tracking and reminders, inhalation flow rate monitoring, feedback on inhalation technique and integration with electronic health records. These innovations are particularly impactful in managing chronic respiratory diseases like asthma and COPD, where poor adherence and incorrect usage are common. Digital health integration not only improves clinical outcomes but also facilitates remote patient monitoring, personalized treatment adjustments, and participation in real-world evidence generation. Regulatory bodies such as the FDA and EMA are increasingly recognizing the value of digital inhalers in therapeutic monitoring and clinical trial

optimization, although data privacy and interoperability standards remain areas of ongoing development.

DPI-Based Vaccine Delivery: Toward Needle-Free Immunization

Dry powder inhalers are gaining attention as an innovative platform for pulmonary vaccine delivery, offering a non-invasive, thermostable, and needle-free alternative to traditional injection-based immunization. Key advantages of DPI-based vaccine delivery include enhanced mucosal immunity, especially in the respiratory tract, elimination of cold-chain requirements, improving access in low-resource settings and patient-friendly administration, which is particularly important for paediatric or needle-phobic populations.

Several preclinical and clinical studies have demonstrated promising results with live attenuated, inactivated, and subunit vaccines administered via DPIs. Technologies such as spray freeze-drying, thin-film freezing, and nanocarrier encapsulation are being explored to preserve vaccine antigenicity and enhance lung uptake. Notable examples include DPI formulations for influenza, tuberculosis, and more recently, COVID-19. However, regulatory pathways for inhaled vaccines are still being defined, and long-term safety, immunogenicity, and scalability remain areas of active research.

Biologics and Macromolecule Delivery via DPIs: Expanding Therapeutic Boundaries

The use of DPIs for delivering biologics (e.g., peptides, proteins, antibodies) and other macromolecules is a rapidly growing area, driven by the need for non-invasive routes of administration for these otherwise injection-dependent therapeutics. The lungs offer a large surface area, high vascularization, and minimal enzymatic activity, making them a promising route for systemic delivery of biologics. DPI formulations have been investigated for therapeutics such as insulin, monoclonal antibodies, interferons and nucleic acid-based therapies (e.g., siRNA, mRNA). To protect fragile biologics from degradation and maintain bioactivity, advanced formulation techniques such as lyophilization, spray drying with stabilizers, and liposomal or polymeric encapsulation are employed. Excipient selection is crucial for preserving structural integrity and ensuring aerodynamic performance. Challenges include low bioavailability, immunogenicity risks, and complex manufacturing processes, but ongoing research continues to make progress. The recent success of inhaled insulin (e.g., Afrezza®) demonstrates the clinical feasibility of this approach, paving the way for a broader application of DPI-based biologics in future therapies.

CHALLENGES AND FUTURE PERSPECTIVES

Despite significant progress in dry powder inhaler (DPI) technologies and formulation strategies, pulmonary drug delivery remains a complex and evolving field⁶⁰. Achieving consistent, efficient,

and targeted aerosol delivery is still constrained by multiple physiological, physicochemical, and technological challenges. These barriers necessitate continuous innovation and deeper scientific understanding to optimize treatment outcomes for respiratory and systemic diseases.

Physiological barriers and particle deposition constraints - One of the foremost challenges in inhalation therapy is navigating the intricate anatomy and physiology of the human respiratory tract. Factors such as airway branching, mucociliary clearance and the presence of pulmonary immune defenses significantly affect drug deposition and retention. The humid environment of the lungs and the presence of mucus layers can lead to premature particle aggregation or dissolution, thereby reducing drug bioavailability. While particles in the aerodynamic diameter range of 1–5 μm are generally considered optimal for alveolar deposition, they are also susceptible to rapid clearance by alveolar macrophages through phagocytosis. This delicate balance between achieving deep lung deposition and avoiding immune clearance remains a critical formulation challenge⁶¹.

Formulation limitations and safety considerations - To address deposition inefficiencies, extensive research has focused on engineering particle attributes such as size, morphology, and surface chemistry. Strategies include developing porous or low-density particles, modifying surface charges, and employing hydrophobic coatings. While these approaches can enhance aerosolization and reduce macrophage uptake, concerns regarding their long-term safety, biocompatibility, and immunogenicity persist, particularly with non-biodegradable excipients and surface-modified particles.

Manufacturing and technological barriers

Traditional dry powder production methods like jet milling and spray drying are widely used due to their scalability and cost-effectiveness. However, these techniques often produce powders with broad particle size distributions and inconsistent flow properties, which can compromise dose uniformity and aerosol performance. Emerging techniques such as spray freeze drying, supercritical fluid processing, and thin-film freezing offer more precise control over particle engineering, resulting in powders with superior dispersibility, aerodynamic behavior, and moisture stability. Despite these advantages, their widespread adoption is hindered by high production costs, complex process controls, and limited industrial scalability⁶².

Device handling and patient-related factors - Another layer of complexity stems from the interaction between patients and inhalation devices. Variability in inhalation technique, device priming, and flow rate dependency can significantly influence drug delivery efficiency. Misconceptions about device performance, particularly the assumption that all DPIs function identically regardless of patient effort, contribute to inconsistent therapeutic outcomes. There is a

growing need for user-friendly and breath-independent devices that ensure consistent dose delivery across diverse patient populations, including children, the elderly, and those with compromised lung function.

FUTURE PERSPECTIVES

To overcome existing challenges and unlock the full potential of pulmonary drug delivery, future efforts must focus on several fronts:

1. **Advanced Particle Design:** Continued exploration of biodegradable carriers, muco-inert coatings, and targeted delivery systems could enhance therapeutic efficacy while minimizing off-target effects.
2. **Integrated Smart Devices:** The incorporation of digital health technologies, such as sensors and feedback mechanisms into inhalers may improve adherence, monitor patient technique, and enable personalized dosing strategies.
3. **Mechanistic Understanding:** A deeper understanding of lung physiology, particle mucus interactions, and immune responses to inhaled materials will be essential for the rational design of next-generation formulations.
4. **Regulatory Harmonization:** Clearer global regulatory pathways for novel excipients, biologics, and nanoparticle-based inhalables will be vital to facilitate innovation and market access.

CONCLUSION

Dry powder inhalers (DPIs) have emerged as a vital platform for pulmonary drug delivery, offering advantages such as breath-actuated dosing, improved stability, and patient convenience. A comprehensive review of DPIs—from fundamental formulation principles, powder engineering, and device design to in vivo performance—highlights the critical role of particle size, morphology, and dispersion mechanisms in ensuring therapeutic efficacy. Despite the challenges posed by patient variability and formulation-device compatibility, advancements in carrier-free formulations, nanotechnology, and smart inhaler systems are driving the evolution of DPI technology. Looking ahead, the integration of personalized medicine and digital health tools holds promise for enhancing DPI performance, adherence, and clinical outcomes. Continued interdisciplinary research and regulatory alignment will be essential to fully realize the potential of dry powder inhalation therapies in both respiratory and systemic disease management.

ACKNOWLEDGEMENTS

Authors acknowledge Dr. Sudhakar Rao Vidiyala, President & CEO, Ascent Pharmaceuticals Inc. for his constant support and encouragement in writing this review article.

REFERENCES

1. Patton JS, Byron PR. Inhaling medicines: delivering drugs to the body through the lungs. *Nat Rev Drug Discov.* 2007;6(1):67–74.
2. Dureja H, Kumar V, Kumar N. Pulmonary drug delivery: A review. *Drug Invention Today.* 2011;3(2):441–448.
3. Xu Y, Dai H, Wang Y, et al. Insights into Inhalation Drug Disposition: The Roles of Pulmonary Drug Transporters and Metabolizing Enzymes. *Int J Mol Sci.* 2024;25(9):4671.
4. Cristea O, Dumitru R, Tudose C, et al. Inhalation Therapies in COPD—Adverse Drug Reactions Impact on Polypharmacy. *Eur J Clin Pharmacol.* 2022;78:1501–1512.
5. Islam N, Gladki E. Dry powder inhalers (DPIs)—A review of device reliability and innovation. *Int J Pharm.* 2008;360(1–2):1–11.
6. Carvalho TC, Peters JI, Williams RO. Influence of particle size on regional lung deposition – What evidence is there? *Int J Pharm.* 2011;406(1–2):1–10.
7. Telko MJ, Hickey AJ. Dry powder inhaler formulation. *Respir Care.* 2005;50(9):1209–1227.
8. Weers JG, Tarara TE. The Pulmonary Delivery of Inhaled Insulin: Advancements in Dry Powder Formulation Technology. *Respir Drug Deliv.* 2014;1:143–152.
9. Hickey AJ, Mansour HM, Telko MJ, et al. Physical characterization of component particles included in dry powder inhalers. I. Strategy review and static characteristics. *J Pharm Sci.* 2007;96(5):1282–1301.
10. Islam N, Cleary MJ. Developing an efficient and reliable dry powder inhaler for pulmonary drug delivery—A review for multidisciplinary researchers. *Med Eng Phys.* 2012;34(4):409–427.
11. Chrystyn H. Is the technique used for inhaled therapy correct in asthma management? *Eur Respir J.* 2006;27(3):535–537.
12. Pilcer G, Amighi K. Formulation strategy and use of excipients in pulmonary drug delivery. *Int J Pharm.* 2010;392(1–2):1–19.
13. Islam N, Cleary MJ. Developing an efficient and reliable dry powder inhaler for pulmonary drug delivery – A review. *Med Eng Phys.* 2012;34(4):409–427.
14. Telko MJ, Hickey AJ. Dry powder inhaler formulation. *Respir Care.* 2005;50(9):1209–1227.
15. Newman SP. Drug delivery to the lungs: challenges and opportunities. *TherDeliv.* 2017;8(8):647–661.

16. Weers JG, Tarara TE. The pulmonary delivery of inhaled insulin: Advancements in dry powder formulation technology. *Respir Drug Deliv.* 2014;1:143–152.
17. Hickey AJ. Inhalation aerosols: Physical and biological basis for therapy. 2nd ed. CRC Press; 2006.
18. Steckel H, Bolzen N. Alternative sugars as potential carriers for dry powder inhalations. *Int J Pharm.* 2004;270(1-2):297–306.
19. Chan AHY, Reddel HK, Apter A, et al. Adherence monitoring and e-health: How clinicians and researchers can use technology to promote inhaler adherence for asthma. *J Allergy Clin Immunol Pract.* 2013;1(5):446–454.
20. Leach CL. The CFC to HFA transition and its impact on pulmonary drug development. *Respir Care.* 2005;50(9):1201–1208.
21. Montfort WR. The Montreal Protocol: A success story of international cooperation. *Nature.* 2008;453(7199):413–417.
22. VikasKotkar, Dr.Hingane L.D., Prof. Latif Bagwan, Formulation and Evaluation of Dry Powder Inhaler, *IJRASET*, 2022, 10 (VI),4625-4637
23. M M. Hoppentocht, et al., Technological and practical challenges of dry powder inhalers and formulations, *Adv. Drug Deliv.Rev.* (2014),
24. Cheng YS. Mechanisms of pharmaceutical aerosol deposition in the respiratory tract. *AAPS PharmSciTech.* 2014;15(3):630–640. doi:10.1208/s12249-014-0092-0
25. Heyder J, Gebhart J, Rudolf G, Schiller CF, Stahlhofen W. Deposition of particles in the human respiratory tract in the size range 0.005–15 μm . *J Aerosol Sci.* 1986;17(5):811–825. doi:10.1016/0021-8502(86)90035-2
26. Chaurasiya B, Zhao YY. Dry Powder for Pulmonary Delivery: A Comprehensive Review. *Pharmaceutics.* 2020 Dec 28;13(1):31
27. Dry Powder for Pulmonary Delivery: A Comprehensive Review Birendra Chaurasiya 1,2, You-Yang Zhao
28. Laube BL, Janssens HM, de Jongh FHC, et al. What the pulmonary specialist should know about the new inhalation therapies. *Eur Respir J.* 2011;37(6):1308–1331.
29. Groneberg DA, Witt C, Wagner U, Chung KF, Fischer A. Fundamentals of pulmonary drug delivery. *Respir Med.* 2003;97(4):382–387.
30. Young, P. M., & Price, R. (2004). The influence of formulation variables on the performance of dry powder inhalers. *European Journal of Pharmaceutical Sciences*, 22(2–3), 235–242.

31. YahyaRahimpour, HamedHamishehkar. *Advanced Pharmaceutical Bulletin* 2(2): 183-187.
32. Steckel H and N Bolzen. *Int J Pharm* 270(1-2): 297-306
33. Saint-Lorant G, P Leterme A Gayot, and MP Flament. *Int J Pharm* 334(1-2); 85-91
34. Weers J, Clark A. The impact of inspiratory flow rate on drug delivery to the lungs with dry powder inhalers. *Pharm Res.* 2017;34(3):507–528.
35. Hickey AJ (ed.). *Pharmaceutical Inhalation Aerosol Technology*. 2nd ed. CRC Press; 2003.
36. Dalby RN, Suman JD. Inhalation therapy: Technological milestones in asthma treatment. *Adv Drug Deliv Rev.* 2003;55(7):779–791.
37. Lavorini F, Fontana GA, Usmani OS. New inhaler devices—the good, the bad and the ugly. *Respir Med.* 2014;108(6):772–780.
38. U.S. Food and Drug Administration (FDA). *Inhalation Drug Products: Chemistry, Manufacturing, and Controls Documentation—Guidance for Industry*. 2022.
39. Design, development, and technical considerations for dry powder inhaler devices Sagar Dhoble 1, Archana Kapse 1, Vaibhav Ghegade 1, Manasi Chogale 1, Vinod Ghodake 1, Vandana Patravale 1,†, Lalitkumar K. Vora
40. Weers, J. G., & Tarara, T. E. (2014). The PulmoSphere™ platform for pulmonary drug delivery. *Therapeutic Delivery*, 5(3), 277–295.
41. Niranjana, K., & Thielmann, F. (2012). Dry powder inhalers: Challenges and opportunities. *International Journal of Pharmaceutics*, 435(1), 1–4.
42. Borghardt, J. M., Weber, B., Staab, A., & Klotz, C. (2018). Predicting pulmonary pharmacokinetics from systemic data: A critical review. *European Journal of Pharmaceutical Sciences*, 115, 55–68.
43. Balasubramanian, J., Ung, K. T., & Stewart, P. J. (2020). Critical challenges in DPI formulation development: Drug-carrier interactions and dispersion performance. *Advanced Drug Delivery Reviews*, 157, 92–111.
44. Palem CR., Dudhipala N., Battu SK., Goda S., Repka MA., & Yamsani MR. (2015). Combined dosage form of pioglitazone and felodipine as mucoadhesive pellets via hot melt extrusion for improved buccal delivery with application of quality by design approach. *Journal of Drug Delivery Science and Technology*, 30.
45. Mariam Ibrahim Inhalation drug delivery devices: technology update *Medical Devices: Evidence and Research*
46. Stein, S. W., & Thiel, C. G. (2016). The history of therapeutic aerosols: A chronological review. *Journal of Aerosol Medicine and Pulmonary Drug Delivery*, 30(1), 20–41.

47. Chinna, Reddy P., Vamshi, Krishna L., Nishanth, Kumar N., Venkata Santhosh P., and Sridhar, G., (2024). Scale-Up Factors in the Development and Commercial Execution of Oral Solid Dosage Forms: A Current Industry Perspective. *J Pharmacol Pharm Res*, 7 (1) 1-22.
48. Pilcer, G., &Amighi, K. (2010). Formulation strategy and use of excipients in pulmonary drug delivery. *International Journal of Pharmaceutics*, 392(1–2), 1–19.
49. Keller, M., Müller, B. W., & Steckel, H. (2021). Advances and limitations in DPI device development: A systematic review. *Pharmaceutical Research*, 38(7), 1221–1234.
50. Draft Guidance for Industry: Bioavailability and Bioequivalence Studies for Nasal and Inhalation Products” (when applicable)
51. PSGs for drugs like fluticasone/salmeterol (Advair Diskus), budesonide, etc.
52. Guideline on the requirements for clinical documentation for orally inhaled products (OIP) including the requirements for demonstration of therapeutic equivalence between two inhaled products for use in the treatment of asthma and chronic obstructive pulmonary disease (COPD) in adults and for use in the treatment of asthma in children and adolescents” (CPMP/EWP/4151/00 Rev. 1)
53. Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations
54. Koullapis, P., Kassinos, S. C., Muela, J., et al. (2019). Regional aerosol deposition in the human airways: The SimInhale benchmark case and a critical review of in silico methods. *European Journal of Pharmaceutical Sciences*, 113, 77–94.
55. Sagaut, P. (2006). *Large Eddy Simulation for Incompressible Flows: An Introduction*. Springer Science & Business Media.
56. Ghosh, S., Hindle, M., & Longest, P. W. (2021). In silico modeling of dry powder inhalers: Challenges and opportunities. *Pharmaceutical Research*, 38, 521–538. <https://doi.org/10.1007/s11095-020-02985-1>
57. Tong, Z., Yang, R., & Yu, A. (2020). Numerical modeling of particulate systems in pharmaceutical engineering. *Advanced Powder Technology*, 31(10), 4088–4107. <https://doi.org/10.1016/j.appt.2020.07.002>
58. Zhou, Q., Morton, D. A. V., & Chan, H.-K. (2013). Drug–carrier interactions in dry powder inhaler formulations. *Expert Opinion on Drug Delivery*, 10(7), 1029–1043.
59. Tong, Z., Wang, W., & Yu, A. (2021). Particle–wall interactions in dry powder inhalers: Mechanisms and modeling. *Powder Technology*, 386, 74–85.

60. Rogueda P., Traini D. The future of inhalers: How can we improve drug delivery in asthma and COPD? *Expert Rev. Respir. Med.* 2016;10:1041–1044.
61. Williams R., Rankin N., Smith T., Galler D., Seakins P. Relationship between the humidity and temperature of inspired gas and the function of the airway mucosa. *Crit.Care Med.* 1996;24:1920–1929.
62. Dry Powder for Pulmonary Delivery: A Comprehensive Review Birendra Chaurasiya 1, 2 , You-Yang Zhao

AJPTR is

- Peer-reviewed
- bimonthly
- Rapid publication

Submit your manuscript at: editor@ajptr.com

