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Review Article

Inhalation-Based Novel Drug Delivery Systems: Advances and Applications

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ABSTRACT

Inhalation-based Novel Drug Delivery Systems (NDDS) have emerged as an efficient route for both local and systemic drug delivery. This review highlights various inhalation devices, their formulation aspects, quality control parameters, and clinical applications. Emphasis is placed on dry powder inhalers (DPI), metered dose inhalers (MDI), nebulizers, soft mist inhalers, breath-actuated devices, nasal inhalers, ultrasonic nebulizers, smart inhalers, and nanoparticle-based inhalers. Advances in particle engineering, device design, and targeted delivery systems have further enhanced therapeutic efficacy, patient compliance, and safety. Future prospects include integration of nanotechnology, personalized inhalation therapy, and AI-enabled smart devices for real-time monitoring.

INTRODUCTION

Inhalation therapy has been used for centuries to treat respiratory diseases. With the advancement in NDDS, inhalers now serve as a route for delivering

peptides, proteins, and systemic drugs. The pulmonary route offers large surface area, high vascularization, and avoidance of first-pass metabolism.

2. Dry Powder Inhalers (DPI):

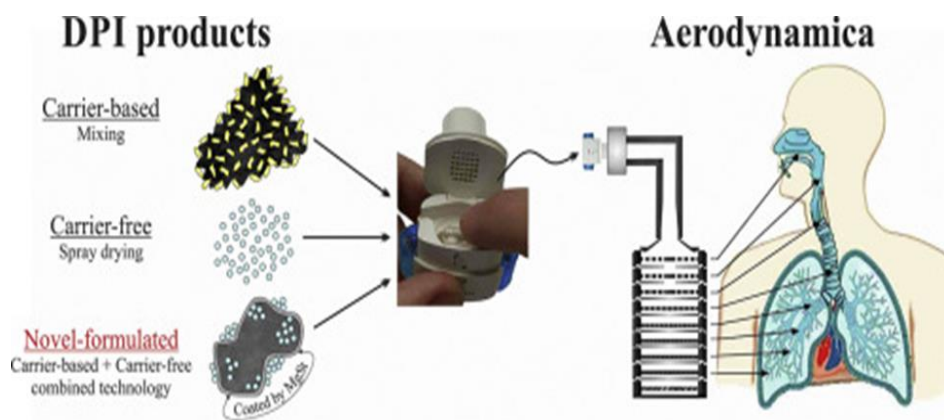
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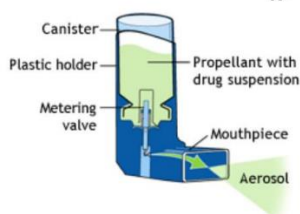




- Definition: Device delivering drug in micronized powder form without propellant.
- Formulation: Drug + carrier (lactose), micronized to 1–5 μm .
- Advantages: No propellant, stable, portable.
- Limitations: Requires patient's inspiratory effort.
- Applications: Asthma, COPD, pulmonary infections.

3. Metered Dose Inhalers (MDI):

Pressured Metered Dose Inhalers (pMDI)



- Canister
- Small reservoir
- Metering reservoir
- After pressure valve drug sprays
- Aerosol

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- Definition: Pressurized canisters releasing fixed drug dose via propellant.
- Formulation: Drug + propellant (HFA) + surfactants.
- Advantages: Compact, accurate dose.
- Limitations: Requires coordination of actuation & inhalation.
- Applications: Asthma, bronchospasm.

4. Nebulizers:



Nebulizer cup



Tracheostomy mask attached to nebulizer cup

Types: Jet, ultrasonic, mesh.

Advantages: 1. Suitable for infants, elderly, severe cases.

2. Allows administration of large drug doses.

3. No need for patient coordination between actuation and inhalation.

4. Can deliver drugs during tidal breathing (normal breathing).

5. Effective in emergency and hospital settings.

Limitations: Bulky, longer treatment time.

Applications: Acute asthma attacks, COPD, cystic fibrosis.

Definition:

A nebulizer is a drug delivery device that converts liquid medication into a fine mist or aerosol, which can be inhaled directly into the lungs through a mouthpiece or mask for local or systemic therapeutic effect.

5. Soft Mist Inhalers (SMI):



- Definition: Propellant-free device producing slow-moving fine mist.
- Advantages: Better lung deposition, easy to inhale.
- Applications: Chronic lung diseases.
- Mechanism of Action:
- The device contains a spring-loaded mechanism.
- When activated, the spring pushes liquid medication through a nozzle system.
- The nozzle converts the liquid into a fine mist at a slow velocity (around 1 m/s), giving the patient more time to inhale the drug deeply.

6. Breath-Actuated Inhalers:



1. Definition: Device releasing drug automatically on inhalation.
2. Advantages: No coordination needed, ideal for elderly.
3. Limitations: Costly, delicate mechanism.

Mechanism of Action:

- The device contains a mechanical or flow-triggered release system.
- Inhalation creates negative pressure inside the device.
- This triggers the release of the drug dose from the chamber into the inhaled air.

Applications:

1. Asthma maintenance therapy (e.g., budesonide, salbutamol).
2. COPD management.
3. Prevention of exercise-induced bronchospasm.
4. Delivery of combination inhaler medications (bronchodilator + corticosteroid).

7. Nasal Inhalers:

Definition: Delivers drugs via nasal mucosa for local/systemic effect. A nasal inhaler is a small, portable device designed to deliver volatile medicated vapours or powdered drugs directly into the nasal cavity for local or systemic therapeutic effects. It typically consists of a container with a medicated wick or powder chamber and an applicator tip for insertion into the nostril.

1. Applications: Migraine (sumatriptan), influenza vaccines, allergy relief.
2. Allergic rhinitis – Antihistamines and corticosteroid inhalers.
3. Migraine therapy – Sumatriptan nasal inhalers.
4. Common cold relief – Menthol, eucalyptus oil inhalers.
5. Nasal vaccination – Live attenuated influenza vaccines.
6. Herbal therapy – Ayurvedic and aromatic oil inhalers.

Types:

1. Aromatic Nasal Inhalers – Contain essential oils, menthol, or camphor for symptomatic relief (e.g., nasal congestion).
2. Powder Nasal Inhalers – Deliver micronized drug particles for systemic or local action.
3. Liquid Nasal Inhalers – Use a pump or spray to deliver liquid formulations.

Advantages:

1. Rapid absorption through the highly vascular nasal mucosa.
2. Non-invasive and painless.
3. Portable and easy to use anywhere.
4. Avoids first-pass metabolism for systemic drugs.
5. Provides both local (nasal congestion) and systemic (migraine therapy) effects.

8. Ultrasonic Nebulizers:

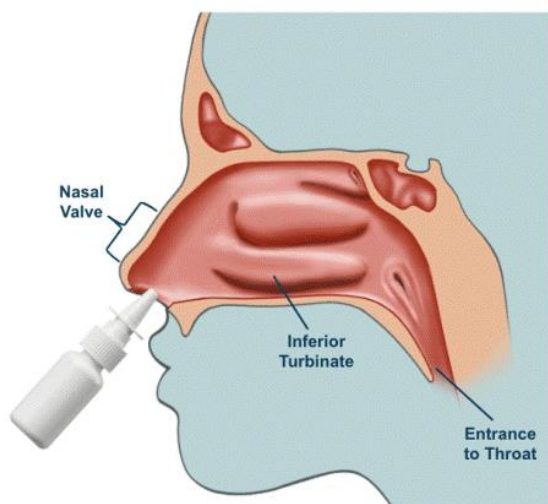


Definition: Uses ultrasonic vibrations to create fine mist.

Limitations: Heat generation may affect heat-sensitive drugs.

Advantages: Silent, fast treatment.

9. Pressurized Intranasal Sprays:



Definition: Metered sprays for nasal drug delivery. A pressurized intranasal spray is a metered-dose device that delivers a precise amount of liquid drug

formulation into the nasal cavity using a propellant or pump mechanism, for either local or systemic therapeutic effect.

Applications: Hormones, vaccines, pain relief.

Formulation Components:

- Active drug – Antihistamines, decongestants, hormones, vaccines, analgesics.
- Solvent system – Usually water, ethanol, or glycerin-based.
- Stabilizers & preservatives – Benzalkonium chloride, EDTA.
- Propellant (optional) – Hydrofluoroalkane (HFA) or mechanical pump system.

Advantages:

- Rapid onset of action due to rich vascular supply in nasal mucosa.
- Avoids first-pass hepatic metabolism.
- Non-invasive and painless.
- Portable and easy to use.
- Can be self-administered without medical assistance.

Limitations:

- Limited dose volume per spray (usually 25–200 μL).
- Potential nasal irritation with repeated use.
- Not suitable for patients with nasal congestion or obstruction.
- Requires proper spray technique for effectiveness. Applications:

Applications:

- Allergic rhinitis – Antihistamine nasal sprays (azelastine).
- Nasal decongestion – Oxymetazoline, xylometazoline.
- Hormonal therapy – Intranasal desmopressin, calcitonin.

- Vaccination – Live attenuated influenza vaccine (FluMist).
- Pain relief – Intranasal ketorolac for post-operative pain.
- Emergency therapy – Intranasal naloxone for opioid overdose.

10. Delivery Systems Targeted Pulmonary:

Definition: Using particle engineering for site-specific lung deposition. Targeted pulmonary drug delivery systems are specialized inhalation formulations and devices designed to deposit the drug specifically in the desired region of the respiratory tract (upper airways, bronchioles, or alveoli) to enhance local efficacy and minimize systemic side effects.

Example: Liposomes, microspheres.

Approaches for Targeting:

1. Particle Size Control:
 2. 1–5 μm → Deep lung (alveolar) deposition
 3. 5–10 μm → Central airway targeting
 4. 10 μm → Nasal/oropharyngeal region
5. Surface Modification.
6. Use of ligands or antibodies for targeting diseased lung cells.
7. Controlled Release Systems.
8. Microspheres, liposomes, and polymeric nanoparticles for sustained delivery.
9. Smart Aerosols.
10. pH-sensitive or enzyme-triggered drug release in diseased areas.



11. Smart Inhalers:



Definition: Digital devices with sensors to track usage and dose.

Applications: Asthma, COPD with adherence monitoring.

Working Principle:

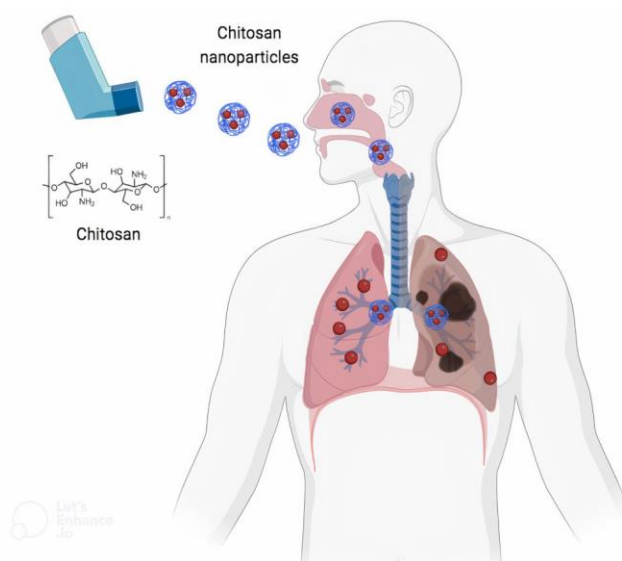
- A sensor is attached to or built into the inhaler device.

- When the patient inhales or actuates the inhaler, the sensor records the time, date, and inhalation parameters.
- Data is transmitted via Bluetooth or Wi-Fi to a smartphone app or cloud database.
- The system provides reminders, technique coaching, and adherence reports.

Advantages:

- Improved adherence – Reminds patients to take medication on time.
- Technique monitoring – Detects improper inhalation technique and gives guidance.
- Data sharing – Allows doctors to monitor usage remotely.
- Early warning – Identifies worsening symptoms and triggers alerts.
- Patient engagement – Motivates patients through usage statistics and goals.

12. Nanoparticle-Based Pulmonary Drug Delivery:



- Definition: Use of nanoparticles (polymeric, lipid) for targeted lung delivery.
- Advantages: Enhanced bioavailability, controlled release.
- Applications: Lung cancer therapy, tuberculosis, gene delivery.

Future Scope & Recent Advances:

- Development of inhalers for systemic diseases (diabetes – inhaled insulin)
- Integration of AI & IoT in smart inhalers
- Personalized inhalation therapy based on patient's lung function

1.Systemic Disease Treatment – Inhalers for diseases beyond respiratory disorders, such as inhaled insulin for diabetes and inhaled vaccines for infectious diseases.

2.AI-Enabled Smart Inhalers – Integration of artificial intelligence for dose adjustment and adherence monitoring.

3.IoT Connectivity – Real-time tracking of inhaler usage through smartphones for telemedicine applications.

4.Personalized Inhalation Therapy – Tailoring drug dose, particle size, and delivery method based on patient's lung function and disease severity.

5.Gene Therapy via Inhalation – Non-invasive pulmonary delivery of DNA, siRNA, and mRNA for genetic disorders and cancer.

6.Biologics and Biosimilars – Development of inhalation formulations for peptides, proteins, and monoclonal antibodies.

7.Environment-Friendly Devices – Propellant-free, recyclable inhalers to reduce environmental impact.

8.3D-Printed Inhalers – Custom-designed inhaler devices for individual patient needs.

9.Hybrid Devices – Combination of inhalation therapy with nasal delivery or buccal delivery in a single device.

10.Enhanced Particle Engineering – Use of nanotechnology, liposomes, and microparticles for targeted lung deposition with controlled release.

CONCLUSION:

1. Inhalation-based NDDS represents a rapidly evolving drug delivery route with both local and systemic applications.
2. These systems significantly improve drug targeting, patient compliance, and therapeutic outcomes.
3. Advanced formulations like nanoparticle systems and smart inhalers further enhance precision and monitoring.
4. Future research should focus on personalized inhalation therapy using AI and IoT integration.
5. The combination of innovative device design and advanced drug formulations has the potential to revolutionize pulmonary and systemic drug delivery.
6. Adoption of environmentally friendly, propellant-free devices will make inhalation NDDS more sustainable.
7. Expanding applications beyond respiratory disorders (e.g., diabetes, cancer therapy) makes this a versatile drug delivery platform.

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Conflict of Interest:

The authors declare no conflict of interest.

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