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Original Article

A Review: Nasopulmonary Drug Delivery System

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ABSTRACT

Nasal drug delivery has gained significant attention as a convenient, effective, and promising route for systemic drug administration. This approach is favored because of the nasal cavity's rich blood supply, large surface area, and its ability to bypass hepatic first-pass metabolism, intestinal metabolism, and degradation in the gastrointestinal tract.

The present review aims to present an overview of the naso-pulmonary drug delivery system, including its advantages and disadvantages, mechanisms of drug absorption, anatomical features of the nasal cavity and respiratory tract, factors influencing nasal absorption, various dosage forms, innovative formulations, and recent developments in nasal drug delivery technologies. The intranasal route has emerged as one of the most extensively explored areas in pharmaceutical research for the delivery of polar compounds, hormones, vaccines, proteins, and peptides. Owing to the favorable properties of the nasal mucosa for targeted delivery, various therapeutic agents can be administered intranasally to achieve local, systemic, and central nervous system (CNS) effects. Currently, naso-pulmonary drug delivery systems (NPDS) are being widely studied for direct drug transport to the brain and CNS to achieve rapid therapeutic responses.

Keywords: Nasopulmonary Drug Delivery ,Intranasal drug Delivery ,Pulmonary Drug Delivery, Respiratory Drug delivery

INTRODUCTION

The nasal route has been recognized as a promising method for drug administration, offering faster and more efficient absorption. This is because the nasal mucosa is more permeable to various compounds than the gastrointestinal tract, owing to the absence of pancreatic and gastric enzyme activity, the neutral pH of nasal mucus, and minimal dilution compared to gastrointestinal contents. Intranasal therapy has long been a recognized treatment method in the Ayurvedic system of Indian medicine. In recent years, many drugs have demonstrated improved systemic bioavailability when administered nasally compared to oral routes. At present, inhalation therapy is the preferred approach for managing respiratory conditions such as asthma, cystic fibrosis, and chronic obstructive pulmonary disease (COPD). These localized treatments enable the use of smaller doses while minimizing systemic side effects. Inhalation has long been the most traditional and widely used method for delivering medications to the lungs and airways. Drugs administered through this route serve three primary purposes: prevention, treatment of local or systemic diseases, and therapeutic management. Various inhalation devices—such as nebulizers, metered-dose inhalers, dry powder inhalers, and other aerosol-based technologies—are utilized for effective drug delivery. Intranasal drug delivery is increasingly acknowledged as a practical and dependable alternative to oral and parenteral routes. For many years, nasal administration has been commonly used for symptom relief and for the prevention or treatment of various nasal disorders. In this method, drugs are introduced through the nasal cavity, allowing for both topical and systemic delivery—depending on whether the medication acts locally within the nasal passages or enters systemic circulation to produce broader therapeutic effects.

Anatomy of Nose: -

The anatomy of the nose is essential for understanding nasal drug delivery, as its structure directly affects drug deposition, absorption, and clearance. The nose can be divided into external and internal parts, and each region has specific functions relevant to drug delivery.

1.External Nose

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Composed of bone and cartilage. Includes the nasal bridge, dorsum, tip, alae (sides), and nostrils (nares). Acts as the primary entry for air and inhaled drugs.

2. Internal Nose

The internal nasal cavity extends from the nostrils to the nasopharynx and is divided by the nasal septum into two chambers.

a. Nasal Vestibule

The anterior part of the nasal cavity. Lined with stratified squamous epithelium and contains hair (vibrissae) that filters large particles.

b. Respiratory Region

Makes up most of the nasal cavity. Lined with ciliated pseudostratified columnar epithelium with goblet cells that produce mucus. Highly vascularized, enabling rapid drug absorption. Contains turbinates/conchae (superior, middle, inferior):

Increase surface area for warming, humidifying, and filtering air. Direct airflow and affect drug deposition.

c. Olfactory Region

Located at the roof of the nasal cavity. Contains olfactory receptor neurons responsible for the sense of smell. Provides a direct pathway to the central nervous system, useful for nose-to-brain drug delivery.

3. Blood Supply

Nasal cavity is richly vascularized by branches of the internal and external carotid arteries, including:

- Sphenopalatine artery
- Anterior and posterior ethmoidal arteries
- Facial artery
- Dense vascular network facilitates rapid systemic absorption of drugs.

4. Lymphatic Drainage

Lymph vessels drain into the cervical lymph nodes. Plays a role in immune response and vaccine delivery.

5. Nasal Functions Relevant to Drug Delivery

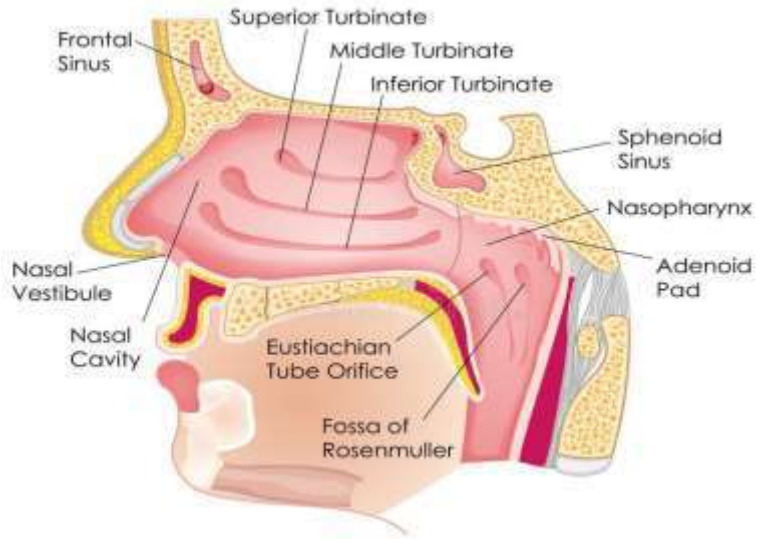
Filtration: Nasal hairs trap large particles.

Humidification and warming: Turbinates condition inhaled air.

Mucociliary clearance: Moves mucus and trapped particles to the pharynx; affects residence time of drugs.

Absorption: Rich vascularization and thin epithelial lining enhance systemic drug uptake.

If you want, I can create a labeled diagram of the nasal anatomy highlighting the regions important for drug delivery. This makes it much easier to visualize for NPDS purposes.



- **Factors Affecting on Nasopulmonary Drug Delivery:**

1. Physiological Factors:

Nasal and pulmonary anatomy: The structure of the nasal cavity (turbinate size, surface area, nasal passage shape) and respiratory tract (bronchial branching, alveolar surface area) affects deposition and absorption.

Mucociliary clearance: Rapid movement of mucus can remove the drug from the absorption site before it is absorbed, reducing bioavailability.

Enzymatic activity: Nasal and lung tissues contain enzymes (peptidases, proteases) that can degrade drugs, especially proteins and peptides.

Blood flow and vascularization: High vascularity in the nasal mucosa and lungs promotes rapid systemic absorption.

Nasal secretions and humidity: Excess mucus or nasal congestion can hinder drug deposition and absorption.

Pathological conditions: Conditions such as rhinitis, asthma, or COPD can alter deposition and absorption efficiency.

2. Physicochemical Properties of the Drug:

Molecular size and weight: Small molecules are absorbed more easily than large molecules like peptides and proteins.

Lipophilicity and solubility: Lipophilic drugs cross membranes more readily; hydrophilic drugs may require absorption enhancers.

Ionization/pH: Drugs in their unionized form are absorbed more effectively.

Stability: Drugs susceptible to enzymatic or chemical degradation may have reduced bioavailability.

3. Formulation Factors:

Type of dosage form: Dry powder, aerosol, or liquid formulations influence deposition and absorption.

Particle size: Ideal particle size for nasal delivery is 10–50 µm; for pulmonary delivery, 1–5 µm particles reach the alveoli effectively.

Use of excipients: Surfactants, stabilizers, and absorption enhancers can improve drug stability and uptake.

Viscosity and osmolarity: Affects residence time in the nasal cavity and absorption rate.

4. Device-Related Factors:

Inhaler design: The efficiency of aerosol generation, spray pattern, and plume velocity affects lung deposition.

Patient technique: Inhalation rate, breath-hold duration, and device handling impact the amount of drug delivered.

Nebulizer type: Jet, ultrasonic, or vibrating mesh nebulizers differ in droplet size and delivery efficiency.

- **Applications:**

1. Local Applications (Respiratory Disorders):

Drugs delivered via NPDS can act directly on the respiratory tract, improving therapeutic outcomes and reducing systemic side effects. Examples include:

Asthma: Inhaled corticosteroids (e.g., budesonide, fluticasone) and bronchodilators (e.g., salbutamol) for rapid relief.

Chronic Obstructive Pulmonary Disease (COPD): Combination therapies of bronchodilators and anti-inflammatory agents.

Cystic Fibrosis: Delivery of antibiotics (e.g., tobramycin) directly to the lungs to manage infections.

Allergic rhinitis and sinusitis: Intranasal corticosteroids and antihistamines for reducing nasal inflammation and congestion.

2. Systemic Applications:

NPDS can deliver drugs that normally have poor oral bioavailability, providing rapid systemic absorption:

Peptides and proteins: Insulin, calcitonin, and certain vaccines.

Pain management: Intranasal opioids or analgesics for rapid systemic relief.

Hormone replacement therapy: Drugs like desmopressin for systemic effect.

Cardiovascular drugs: For example, intranasal nitroglycerin for angina.

3. Central Nervous System (CNS) Delivery:

The nasal route provides a direct pathway to the brain via the olfactory and trigeminal nerves, bypassing the blood-brain barrier (BBB):

Neurodegenerative diseases: Intranasal delivery of insulin or neuroprotective peptides for Alzheimer's or Parkinson's disease.

Acute CNS conditions: Rapid administration of benzodiazepines (e.g., midazolam) for seizures.

Pain management: Opioids delivered intranasally can act quickly on the CNS.

4. Vaccination:

Intranasal vaccines utilize the nasal mucosa-associated lymphoid tissue (NALT) for immune response:

Influenza vaccines (e.g., live attenuated flu vaccine)
Experimental vaccines for respiratory pathogens

5. Miscellaneous Applications:

Smoking cessation: Nicotine sprays for rapid absorption.

Migraine management: Intranasal triptans for faster relief.

Emergency therapy: Rapid delivery of drugs in acute situations where oral or injectable routes are impractical.

MECHANISM:

The mechanism of drug absorption in the nasopulmonary drug delivery system (NPDS) depends on the route (nasal or pulmonary) and the physicochemical properties of the drug. Drugs can be absorbed locally in the respiratory tract or systemically via the blood. Here's a detailed explanation:

1. Absorption through the Nasal Route

a. Pathways of Absorption

1. Transcellular (through cells)

Lipophilic drugs pass directly through the nasal epithelial cell membrane. Small molecules and some peptides can diffuse across epithelial cells.

2. Paracellular (between cells)

Hydrophilic drugs pass through tight junctions between epithelial cells. Typically limited to small molecules due to the narrow intercellular spaces.

3. Olfactory Route (nose-to-brain)

Drugs can bypass the blood-brain barrier via olfactory neurons. Useful for delivering CNS-active drugs directly to the brain.

4. Trigeminal Nerve Pathway

Provides another route to the CNS, particularly for certain peptides and proteins.

b. Factors Affecting Nasal Absorption

Mucociliary clearance: Rapid movement of mucus can remove the drug before absorption.

Enzymatic degradation: Proteases in the nasal cavity can degrade peptides and proteins.

Molecular size and lipophilicity: Small, lipophilic molecules are absorbed more readily.

Formulation factors: Use of absorption enhancers, mucoadhesive agents, and pH adjusters can improve uptake.

2. Absorption through the Pulmonary Route

a. Mechanism

1. Deposition in the Airways

Particle size determines deposition:

>10 μm: Deposits in the upper airways (nasal cavity, trachea).
5–10 μm: Deposits in bronchi and bronchioles.
1–5 μm: Reaches alveoli for systemic absorption.

2. Absorption across Alveolar Epithelium

Alveolar epithelium is extremely thin (0.1–0.5 μm) and highly vascularized. Drugs diffuse rapidly into pulmonary capillaries, providing fast systemic absorption.

3. Endocytosis for Macromolecules

Large molecules (proteins, peptides, nanoparticles) can be absorbed via receptor-mediated endocytosis or transcytosis.

b. Factors Affecting Pulmonary Absorption

Particle size and shape (determines deposition site)
Formulation properties (solubility, hygroscopicity)
Breathing pattern (inhalation flow rate, breath hold)
Airway pathology (asthma, COPD, mucus production)

3. Overall Summary

Nasal route: Rapid absorption through highly vascularized epithelium; allows local, systemic, and CNS delivery.

Pulmonary route: Rapid systemic absorption via alveoli; ideal for local and systemic therapy.

Enhancement strategies: Use of absorption enhancers, mucoadhesive formulations, particle engineering, and proper inhaler design.

CONCLUSION:

The nasal drug delivery system represents a promising alternative route for administering various systemically active drugs with low bioavailability. It provides benefits such as increased patient acceptance and improved compliance compared to injectable (parenteral) drug administration. Although nasal drug delivery systems (NDDS) hold significant potential, they encounter challenges like rapid mucociliary clearance and restricted drug permeability. Nevertheless, continuous improvements in formulation techniques and delivery devices are expected to address these limitations.

REFERENCE

1. A J. Hickev. Pharmaceutical Inhalation Aerosol Technology, 2nd edition, Marcel Dekker, NY, 2004 Alagusundaram M., Deepthi N., Ramkanth S., Angala-parameswari S., Mohamed Saleem T.S., Gnanapra-kash K. Thiruvengadarajan V. S, Madhusudhana Chetty C, Dry Powder Inhalers - An Overview,Int. J. Res. Pharm. Sci. 2010, 1;1: 34-42
2. Armengot, M., Basterra, Macro,.Rev. Larngol.Octol. Rhinol. 1990, 111,219-226 Arora P, Sharma S, Garg S. Permeability issues in nasal drug delivery. Drug Discov Today 2002; 7,18, 967-975.
3. Aulton M.E. " Pharmaceutics - The science of dosage form design" Churchill Livingston., 494, 2002 Aurora J. Development of Nasal Delivery Systems: A Review.Drug Deliv Technol 2002; 2,7, 1-8.
4. Buri P. Hydrogels destines a la muqueuse nasale. Controle physiologique, Pharm. Acta Helv. 1966,41, 88-101.
5. Chien Y.W., Su K.S.E., Chang S.F., Nasal Systemic Drug Delivery, Ch. 1, MarcelDekker, New York, 1-77, 1989
6. Johnson NJ, Hanson LR, Frey WH. Trigeminal pathways deliver a low molecular weight drug from the nose to the brain and orofacial structures. Mol Pharm, 2010; 7: 884-93.
7. Svensson S, Olin AC, Hellgren J. Increased net water loss by oral compared to nasal expiration in healthy subjects. Rhinology, 2006; 44: 74-7.
8. Rudman KL, O'Brien EK, Leopold DA. Radiographic distribution of drops and sprays within the sinonasal cavities. Am J Rhinol Allergy, 2011; 25: 94-7.
9. 2. Illum. L., Jorgensen. H. Bisgard. Hand Rossing. N, Bioadhesivemicrospheres as a

potential nasal drug delivery system. Int. J. of Pharmaceutics, 189-199.
10. Akwete, A.L., Gupta, P.K., Eds.; Niven, delivery of biotherapeutics by inhalation aerosol. In Inhalation Delivery of Therapeutic Peptides and Proteins; Marcel Dekker, Inc., New York, 1997; 151-2
11. Patton, J.S. Mechanisms of macromolecule absorption by the lungs: Adv. Drug Delivery Rev, 1996; 3-36.
12. Rhidian, R., & Greatorex, B., Chest pain in the recovery room, following topical intranasal cocaine solution use. British Medical Journal Case Reports doi: 10.1136/bcr-2015- 20969
13. Slot, W.B., Merkus, Deventer, (1997). Normalization of plasma vitamin B12 concentration by intranasal hydroxocobalamin in vitamin B12- deficient patients. Gastroenterology. 113, 430-433.
14. Singh, L., & Khan, A. D., Nasal drug delivery: a promising way for brain targeting. The Pharma Research 13.2, 1-12.
15. S.G., Illum, L., Thomas, N.W., 1991. Nasal absorption in rats. II. Effect of enhancers on insulin absorption and nasal histology. International Journal Pharmaceutics. 76, 61-70
16. Ugwoke, M. I., Agu, R. U., Verbeke, N., & Kinget, R. (2005). Nasal mucoadhesive drug delivery: background, applications, trends and future perspectives. Advanced Drug Delivery Reviews, 57(11), 1640-1665.
17. Ugwoke, M. I., Verbeke, N., & Kinget, R. (2001). The biopharmaceutical aspects of nasal mucoadhesive drug delivery. Journal of Pharmacy and Pharmacology, 53(1), 3-22.
18. Zhou, M., Donovan, M.D., 1996. Recovery of the nasal mucosa following laureth-9 induced damage. International Journal of Pharmaceutics.130, 93-102.
19. Harris, A.S., (1993). Review: Clinical opportunities provided by the nasal administration of peptides. Journal of Drug Targeting 1, 101-116.
20. Hermann, N., (2015). Effectiveness of live attenuated influenza vaccines and trivalent inactivated influenza vaccines against confirmed influenza in children and adolescents in Saxony-Anhalt, 2012/13. Gesundheitswesen 77(7): 499-501
21. Knoester, P.D., Jonker, Pharmacokinetics and pharmacodynamics of midazolam administered as a concentrated intranasal spray. A study in healthy volunteers. British Journal of Clinical Pharmacology. 53, 501-507.
22. Kublik, H., & Vidgren, M. T., (1998). Nasal delivery systems and their effect on deposition and absorption. Advanced Drug Delivery Reviews, 29, 157-177.
23. Mahdi, M. H., Conway, B. R., (2015). Development of mucoadhesive sprayable gellan gum fluid gels. International Journal of Pharmaceutics, 488(1), 12-19.
24. Merkus, F. W. H. M., Schipper, (1993). Absorption enhancers in nasal drug delivery: efficacy and safety. Journal of Controlled Release, 24(1), 201-208.
25. Mundlia, J., & Mukesh, K. (2015). Nasal drug delivery: An overview. International Journal of Pharmaceutical Sciences and Research 6, 951-956.

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