



ISSN (E): 2320-3862  
ISSN (P): 2394-0530  
<https://www.plantsjournal.com>  
JMPS 2024; 12(1): 105-111  
© 2024 JMPS  
Received: 03-11-2023  
Accepted: 02-12-2023

**Siddhiraj More**  
Students, Ashokrao Mane  
institute of Pharmacy, Ambap,  
Maharashtra, India

**Abhishek Desai**  
Assistant Professor, Ashokrao  
Mane Institute of Pharmacy,  
Ambap, Maharashtra, India

**Nilesh Chougule**  
Assistant Professor, Ashokrao  
Mane Institute of Pharmacy,  
Ambap, Maharashtra, India

**Corresponding Author:**  
**Siddhiraj More**  
Students, Ashokrao Mane  
institute of Pharmacy, Ambap,  
Maharashtra, India

# Journal of Medicinal Plants Studies

[www.PlantsJournal.com](http://www.PlantsJournal.com)

## A role of nasal in the raputic management

**Siddhiraj More, Abhishek Desai and Nilesh Chougule**

### Abstract

Nasal medication administration has become a key point of research due to its convenience, reliability, and encouraging future for the systemic delivery of medication. This method proves particularly beneficial for individuals with limited oral efficacy, requiring injection for optimal effectiveness. In comparison to alternative non-invasive drug administration systems, the nasal route boasts distinct advantages. This comprehensive review delves into various aspects of nasal delivery systems, providing an in-depth exploration of their potential and limitations. This review's goal is to provide a comprehensive overview of the nasal medication delivery system by covering a wide range of subjects. These include elucidations on the benefits and restrictions of nasal medication administration, the intricate mechanisms underlying drug absorption through the nasal cavity, the anatomical features of the nasal cavity influencing drug delivery, important elements influencing nasal medication absorption and techniques used to improve absorption. In addition, the paper addresses methods for prolonging the half-life of medication formulations in the nasal cavity, which enhances absorption in general. It explores novel medication compositions, various kinds of nasal drug delivery devices, and their uses in the treatment of various diseases. Additionally, the review encompasses recent advancements in nasal delivery methods, providing insight into the most recent advancements in this area. By covering these many aspects, the study hopes to provide a thorough resource for scholars, professionals, and hobbyists interested in understanding the intricacies of nasal drug delivery, thereby contributing to the ongoing dialogue and progress in this important area of pharmaceutical research.

**Keywords:** Nasal medication administration, drug delivery, pharmaceutical research, requiring injection

### Introduction

Because nasal drug delivery has so many benefits, it has become a focus of pharmaceutical science research and development. The nasal cavity provides a unique and efficient pathway for medication absorption because of its huge surface area and abundance of blood vessels. Rapid drug absorption and the delivery of a wide range of therapeutic agents, including more complex macromolecules like peptides, proteins, hormones, and vaccines, are made possible by this vascular-rich environment. The capacity to evade first-pass metabolism, a procedure in which medications undergo partial hepatic metabolism before to systemic circulation, is a significant benefit of nasal drug delivery. Because of the increased bioavailability that results, the nasal route is especially appealing for medications that experience significant hepatic metabolism when taken orally. Notable is the nasal mucosa's permeability to a broad variety of compounds, in contrast to the gastrointestinal tract. This trait is explained by the lack of pancreatic and stomach enzymatic activity as well as the decreased interference from gastrointestinal contents. Consequently, nasal delivery of drugs may lead to pharmacokinetic profiles that are more consistent and predictable. Nasal drug delivery has historical roots in addition to its contemporary uses. This is evident in conventional medical systems such as Ayurveda, where nasal administration, or Nasya karma, has been acknowledged as a successful therapeutic approach. Although the nasal route has many advantages, there are drawbacks and restrictions as well. When optimizing nasal drug delivery, factors like individual differences in nasal anatomy, possible irritability to the nasal mucosa, and the requirement for precise formulation adjustments are taken into account. Research in this area is still concentrated on creating novel drug delivery systems, fine-tuning formulations, and comprehending the complexities of nasal physiology. The field of pharmaceuticals is finding nasal drug delivery to be more valuable and adaptable as a result of the continuous advancements that are broadening its scope [1-8].

### Options to use the nasal cavity for medical delivery

The nose's wide surface area and convenient accessibility make it a promising candidate for medicine administration. The primary responsibility of pharmaceutical product development is closely linked to its intended therapeutic uses. Product development takes into account the intended use, which includes:

- Local delivery
- Systemic delivery
- Single or repetitive administration.

In addition, the nasal route has benefits like self-administration, bypassing first-pass metabolism, and quick onset of action, which makes it appealing in some drug delivery situations. The targeted therapeutic outcomes will determine whether local or systemic delivery is preferred, and the nasal cavity offers a flexible and adaptable option for optimizing drug administration strategies.

#### Local delivery

When it comes to localized or topical treatments, nasal delivery makes sense because it can reduce the risk of systemic adverse effects in contrast to oral dosage. This feature lowers the risk of systemic toxic effects by enabling the effective use of relatively lower doses through the nasal route. Key therapeutic drug classes that are commonly administered via nasal delivery include antihistamines and corticosteroids to treat allergic rhinitis, as well as decongestants for the treatment of nasal cold symptoms. Not only does nasal delivery reduce systemic side effects, but it also has advantages like enhanced bioavailability and a quicker beginning of the action.

The nasal route is used to provide drugs efficient because it avoids first-pass metabolism and has direct access to the bloodstream. These characteristics make nasal administration especially attractive for medications with known gastrointestinal side effects or for conditions that need immediate relief. Moreover, the nasal cavity's rich vascularization and permeability aid in the efficient absorption of a variety of medications, thereby enhancing the range of therapeutic uses. Because of this, nasal drug delivery is a versatile and adjustable technique that may be applied to fulfil specific medical needs while lowering the possibility of systemic side effects that are frequently linked to other routes of administration.

#### Systemic delivery

When it comes to obtaining systemic drug availability, intranasal drug administration proves to be more successful than oral and intravascular routes. This process guarantees both rapid and sustained drug absorption. Among the notable therapeutic classes administered intravenously are hormones, cardiovascular medications, analgesics, anti-inflammatory agents, and antiviral medications. Examples that are readily available on the market, such as sumatriptan and zolmitriptan, demonstrate the effectiveness of intranasal medication therapy for ailments like cluster headaches and migraines. The intranasal route presents a flexible and effective way to administer medication with potential uses in a wide range of therapeutic domains<sup>[11-14]</sup>.

#### Nasal vaccines

The nasal mucosa is a focal point for vaccination research because it serves as the first point of contact for inhaled antigens during inhalation, especially when it comes to

respiratory infections. In contrast to the traditional parenteral route, nasal vaccination presents a promising alternative that may increase systemic concentrations of nasal secretory immunoglobulin A and particular immunoglobulin G. Intranasal vaccines have proven to be effective in protecting humans against a range of pathogens, surpassing their theoretical potential. Group B meningococcal native, attenuated respiratory syncytial virus, parainfluenza 3 virus, proteosoma influenza, and influenza vectored by adenovirus are a few examples of vaccines that target the influenza A and B viruses. This achievement demonstrates how adaptable and powerful the intranasal route is at triggering immune responses against a variety of respiratory pathogens. Intranasal vaccination is a more patient-friendly choice due to its practical benefits, which include ease of administration, the ability for self-administration, and a decreased dependency on needles. Expanding research on nasal vaccination presents a dynamic field that could transform immunization strategies, especially when it comes to respiratory health<sup>[15-17]</sup>.

#### Nasal route: Central Nervous System (CNS) delivery

By directly accessing the olfactory system to the central nervous system (CNS). Neuroepithelium, the intranasal route presents a promising option to deliver medication to the brain. The potential applications of this method have been demonstrated by its exploration in a variety of neurological conditions. Notable examples include the administration of medications via the nasal route for the management of epilepsy, brain tumors, Alzheimer's disease, pain, and sleep disturbances. Intranasal medication administration to the central nervous system (CNS) has additional advantages, such as a rapid commencement of action, circumvention of the blood-brain barrier, and perhaps fewer systemic adverse effects. This strategy is appealing for conditions that require focused neurological interventions because it offers a non-invasive way in order to get therapeutic brain concentrations. The intranasal route stands out as a dynamic area for drug delivery innovations as this field of study advances, with the potential to address a variety of neurological disorders more effectively and with fewer systemic complications<sup>[18-19]</sup>.

#### Physiological and anatomical aspects for intranasal deliver

##### Anatomy

The human skull is divided into two parts that serve different purposes and are meant to protect the sensitive structures inside. Enclosing and protecting the brain is one of these sections, the neurocranium. The other part is called the viscerocranium, and it is composed of several distinct bones that make up the jaw and face skeleton, shielding the nasal cavity, mouth, and eyes. The nasal cavity is composed of five anatomically separate regions: The nasal vestibule, atrium, respiratory area, olfactory region, and nasopharynx (see Table 1). The nasal septum divides each nasal cavity into two symmetrical parts, which is made consists of cartilage and bone, with a volume of around 7.5 mL and a surface area of roughly 75 cm<sup>2</sup>. It extends posteriorly to the nasopharynx at the nasal vestibule, the most anterior part of the nasal cavity that exits at the face through the nostrils. Between the vestibule and the respiratory region, the atrium acts as a transitional area. The lateral walls of the nasal cavity is divided into three regions, referred to as the inferior (C1), middle (C2), and superior (C4) nasal turbinates, by the respiratory area, which comprises the bulk of the nasal cavity. These turbinates in humans provide the nasal cavity a

relatively small volume but a remarkably large surface area of about 150 cm<sup>2</sup>. The respiratory region, being well-blooded and receiving the most amount of nasal secretions, is especially favourable for compound permeation. The ciliated olfactory nerve cells that detect scent are found in the olfactory area, which is situated above the superior nasal turbinate. The olfactory epithelium is 200-400 mm<sup>2</sup> in total surface area [20-23].

#### The utilization of nasal drug delivery in the systemic circulation presents several advantages

1. It avoids the first-pass metabolism of the liver.
2. Compared to parenteral routes, improved patient compliance is attained because of the drug's easy accessibility and needle-free application, which permits self-medication without the assistance of trained personnel.
3. The nasal approach avoids the gastrointestinal tract's medication breakdown.
4. It is possible to increase the bioavailability of big drug molecules via the nasal route by using absorption enhancers.
5. It is simple to achieve a fast onset of action and rapid drug absorption.
6. For small drug molecules, the nasal route shows good bioavailability.
7. Drugs with poor stability in gastrointestinal fluids are suited for nasal delivery.
8. Research suggests that the nasal route is a useful substitute for the parenteral route, particularly for medications containing proteins and peptides.
9. Polar compounds that are poorly absorbed orally are especially well-suited for nasal administration.
10. Compared to parenteral medication, it is more convenient for patients, particularly those undergoing long-term therapy.

#### Drawbacks [24-25]

1. The gastrointestinal tract provides more surface area than the nasal cavity for absorption does.
2. In contrast to the oral delivery method, there is a chance of irritation.
3. The ingredients and substances included in the dosage form have the potential to cause irreversible harm to the nasal mucosa's cilia as well as localized side effects.
4. Ineffective administration methods could cause the

dosage form to mechanically leak into the lungs or other respiratory tract organs.

5. At high concentrations, some surfactants that are used as chemical enhancers have the potential to disrupt and dissolve the membrane.

#### Constraints in Nasal Drug Delivery [26]

1. Both extra ingredients and compounds in the dosage form have the potential to cause permanent harm to the cilia in the nasal mucosa as well as to cause local side effects.
2. An improper method of administration could cause the dosage form to mechanically disappear from other respiratory system organs, like the lungs.
3. At high concentrations, some surfactants used as chemical catalysts can cause membrane disruption or dissolution.

#### Advantages of Nasal Drug Delivery [27]

- Within the limited volume of 25-200 µL, medications that are not absorbed by oral effectively administered into the nasal cavity.
  1. This method cannot be used to deliver molecules with a high molecular weight and a mass cut-off of roughly 1 kDa.
  2. Nasal medication delivery may be negatively impacted by pathological disorders.
  3. This route shows significant interspecies variability.
  4. The permeability of the medication may be impacted by regular defence mechanisms like ciliary beating and mucociliary clearance.
  5. The permeability of drugs is impeded by an enzymatic barrier.
  6. Medicines have the potential to irritate the nasal mucosa.
  7. At this point, models are less developed and mechanisms are not fully understood.
  8. Promotes better patient adherence.
  9. Reduces the possibility of overdosing.
  10. Aids in the quick start of therapeutic action. Elements affecting medication absorption through the nose. Numerous factors indicated in Table 2 influence the degree and pace at which drugs are absorbed through the nasal passages. These elements are essential to the design of the intranasal administration device and formulation.

**Table 1:** Structural characteristics of different nasal regions and their influence on nasal cavity permeability

Region	Structural Features	Permeability
Nasal Vestibule	- Hairs on the nose (vibrissae) - Squamous, keratinized, and stratified epithelial cells - There are sebaceous glands	- Least permeable (The existence of keratinized cells, which are dehydration-resistant and resilient to environmental toxins)
Atrium	Section transepithelial - Anterior stratified squamous cells - Pseudostratified cells posteriorly containing microvilli	- Less permeable due to its tiny surface area and anteriorly arranged stratified cells.
Respiratory Region (Inferior, Middle, Superior Turbinates)	- Microvilli-adorned pseudostratified ciliated columnar cells - Generous surface area - Goblet cells, nasolacrimal duct, and seromucous glands are present. - Abundant blood supply to warm and humidify inspired air	- Most permeable (high surface area, many blood vessels)
Olfactory Region	- Scent perception is sensed by ciliated olfactory nerve cells. - Gets the trigeminal nerve's ophthalmic and	- Easy access to the brain fluid

	maxillary divisions	
Nasopharynx	- Squamous epithelium is found in the bottom section while ciliated cells are found in the upper part.	- Gets discharge of the nasal cavity

### Mechanism of nasal drug absorption

Out of the various mechanisms that have been suggested, two main ones have been taken into consideration. The first pathway is the paracellular route, which is an aqueous means of transport. Among this mechanism's salient features are:

1. This path is distinguished by a sluggish and passive procedure.
2. The molecular weight of substances that are soluble in water and intranasal absorption have an inverse log-log relationship.
3. It has been noted that medications with molecular weights greater than 1000 Daltons have poor bioavailability. The transcellular process, also referred to as the lipoidal route of transport, is the second pathway. Lipophilic medications are transported via this pathway, which shows a rate dependence on lipophilicity. For example, the natural biopolymer chitosan, which is derived from shellfish, can open [28, 29].

### Methods to improve availability of drug in nasal delivery

Various approaches utilized to improve medication accessibility in the nasal mucosa include:

1. An extended duration of nasal residency.
2. An increase in nasal absorption.
3. A drug's physicochemical properties can be altered by altering its structure.

### To enhance nasal residence time

It is possible to postpone the mucociliary clearance mechanism, which is intended to quickly remove materials and foreign objects from the nasal mucosa. One method involves applying the medication to the front part of the nasal cavity; the dose type utilized largely determines the result. Furthermore, nasal drug delivery enhancers include formulations with polymers such polyacrylic acid, hydroxypropyl methylcellulose, or methylcellulose, which are categorized as distinct substances-can be created. These polymers are added, which makes the formulation more viscous and functions as a bio adhesive with mucus. It's crucial to remember that longer residence times do not always translate into higher absorption. An analogous viscosity insulin solution containing carbopol and carboxymethylcellulose (CMC) serves as an example of this idea. In this instance, absorption is improved by carbopol, but insulin absorption is not improved by the CMC solution. Retention in absorption is caused by the drug's slow diffusion out of the matrix as a result of the increased viscosity with CMC. On the other hand, carbopol opens intracellular junctions to improve absorption. Using biodegradable microspheres as drug delivery vehicles is another efficient way to extend nasal residence time. When water is present, these microspheres expand, increasing viscosity and extending the duration of nasal residence time.

### Improving Nasal Absorption

When polar medications are Coad ministered using an enhancer of absorption that facilitates medication transfer across the nasal membrane, nasal absorption can be significantly improved. Combining a bio adhesive effect with

an absorption-enhancing activity can also increase the duration of the formulation's residence time in the nasal cavity, increasing the efficacy of nasal medication delivery systems. Numerous absorption enhancer systems have been studied in animal models, with notable improvements in drug absorption through the nose observed, especially in rabbit and dog models. These beneficial effects might result from variations in the structure and morphology of the nasal cavity, as well as from the use of sedatives or anesthetics, which can affect the mucociliary clearance process [31]. For example an absorption enhancer, dimethyl- $\beta$ -cyclodextrin, was employed in a rat investigation on nasal insulin administration, and the results showed an amazing 100% bioavailability when compared to subcutaneous injection. But when tested on humans and rabbits, the bioavailability in both species decreased almost to zero. Additional enhancers include fatty acids, bile salts, surfactants, and specific Cells' phospholipid bilayer structure is changed by phospholipids and lysophospholipids, removing the mucosa's outer layer, or leaching out proteins. This facilitates better drug transcellular transport, and it has been found that membrane damage and bioavailability are directly correlated [32]. Enhancers such as chitosan, cyclodextrins, and phospholipids that momentarily open tight junctions between cells can have an absorption-enhancing effect greater than any mucosal modifications. There are two types of mechanisms of absorption enhancement: Membrane effects, which involve enhancers affecting the nasal mucosa's surface, and physicochemical effects, which involve enhancers changing the drug's weak ionic interactions, partition coefficient, or solubility.

### Modifying Drug Structure

A viable approach to improving nasal absorption is to alter the structure of the drug without sacrificing pharmacological potency. This strategy involves modifying physicochemical characteristics that are beneficial to nasal drug absorption, like pKa and molecular weight, solubility, and size [33].

The specific therapeutic requirements of the medication molecule, the intended time of action, and the course of treatment all influence the design of nasal formulations. Controlled-release as well as it is possible to administer conventional-release drugs by nasal route. The method of drug delivery-local or systemic-influences the selection of pharmaceutical excipients. Numerous studies investigating these delivery methods and the following list of key elements is the outcome of the creation of several nasal formulations.

### Nasal Drops

These constitute an easy-to-use and practical nasal drug delivery system. Nasal drops are frequently advised for the control of regional circumstances. They are administered using a pipette or squeeze bottle. Problems with this system include non-specific loss in the nasal or lower back area, mucosal dysfunction, and microbial growth. The lack of dose precision, however, is a significant drawback that makes nasal drops less appropriate for prescription products. According to certain reports, nasal sprays are less effective than nasal drops at putting human serum albumin within the nasal cavity [34-36].

**Table 2:** Influences on the delivery of intranasal medication

Biological factors	Formulation-related factors	Strategies to overcome them
Biochemical changes	Physicochemical properties of the drug	Prodrugs
Refer to the enzymatic barrier of nasal mucus	Lipophilicity	Enzyme inhibitors
Which include oxidative and conjugative	Chemical form	Absorption enhancers
Enzymes, peptidases, and proteases	Polymorphism	Mucoadhesive drug delivery systems
Physiological factors	Molecular weight	Novel formulation forms
Blood supply and neuronal regulation	Partition coefficient and pKa	
Nasal secretions	Solubility and dissolution rate	
Nasal cycle	Physicochemical properties of formulation	
pH of the nasal cavity	pH and mucosal irritancy	
Mucociliary clearance and ciliary beat frequency	Osmolarity	
Pathological conditions	Viscosity/density	
Common cold	Drug distribution	
Rhinitis	Area of nasal membrane exposed	
Atrophic rhinitis	Area of solution applied	
Nasal polyposis	Dosage form	
Environmental factors	The physical form of the formulation	
Temperature	Types of dosage form and delivery systems	
Humidity	Nasal drops	
	Solution sprays	
	Suspension sprays	
	Powders	
	Gels	
	Emulsions and ointments	
	Specialized systems, for example, microspheres, liposomes, etc.	

### Nasal Sprays

Nasal sprays with metered dose pumps and actuators provide accurate dosing through formulations as solutions or suspensions. The morphology and particle size of the drug (for suspensions) as well as the formulation's viscosity influence selecting a pump and actuator combination<sup>[37]</sup>.

### Nasal Gels

The thickened liquids or suspensions with high viscosity known as nasal gels have garnered attention as a result of recent developments in dosing devices. Their advantages include lessening anterior leakage, lowering taste impact, reducing post-nasal drip, reducing irritation with emollient excipients, and focusing on the mucosa for improved absorption<sup>[38-39]</sup>.

### Nasal Powder

When problems with drug stability make solution and suspension formulations unfeasible, this dosage form is taken into consideration. Nasal powders have benefits like better stability and formulations without preservatives. A number of variables, including solubility, particle size, aerodynamic characteristics, nasal irritation, and the drug's local application, affect suitability<sup>[40]</sup>.

### Liposomes

Liposomes are phospholipid vesicles that include one or more aqueous compartments enclosed in a bilayer that can be utilized to adsorb or entrap medications.

### Microspheres

Microspheres are essential for nasal drug delivery because they improve absorption, offer sustained release, and shield the medication from enzymatic breakdown<sup>[41]</sup>.

### Evaluation of nasal formulations

In order to guarantee nasal formulations' safety, effectiveness, and usefulness, a comprehensive evaluation process is employed. A thorough evaluation is influenced by several important factors, including:

**1. Pharmacokinetic Studies:** These investigations shed light

on the drug's distribution, metabolism, excretion, and absorption (ADME) when administered via the nasal route. Pharmacokinetic parameters aid in assessing the formulation's overall performance and bioavailability.

**2. Biocompatibility and Safety:** In order to guarantee patient safety, it is essential to evaluate the formulation's effect on nasal tissues, including any potential for irritation, inflammation, or negative reactions.

**3. Mucociliary Clearance Studies:** Knowing how the formulation affects mucociliary clearance aids in assessing how long it stays in the nasal cavity, which influences therapeutic effectiveness and absorption.

**4. In vivo Imaging:** To see the distribution and destiny of the nasal formulation inside the nasal cavity, one can make use of modern imaging techniques such as magnetic resonance imaging (MRI) or positron emission tomography (PET).

**5. Patient Acceptance and Compliance:** The success of nasal drug delivery is greatly dependent on factors that affect patient acceptance, comfort, and compliance, such as tolerability and ease of administration.

**6. Formulation Stability:** Keeping the formulation safe and effective over time requires taking into account variables like temperature, light, and storage conditions.

**7. Analytical Techniques:** Sturdy analytical techniques are used to evaluate the nasal formulation's quality, purity, and consistency. This covers methods for drug quantification such as high-performance liquid chromatography (HPLC).

**8. Comparative Studies:** When available, comparative evaluations made against reference formulations or established standards offer useful benchmarks for evaluating the effectiveness of the nasal formulation.

**9. Patient Feedback and Experience:** By getting input from patients about how they felt about the nasal formulation, the product is improved and any problems with taste, smell, or

general comfort are resolved.

**10. Regulatory Compliance:** The authorization and marketing of nasal formulations depend critically on compliance with regulatory requirements and standards. This entails carrying out research in compliance with legal specifications.

#### Studies on *in vitro* nasal permeation

Different methods are used to evaluate how well formulations of drugs diffuse through the nasal mucosa. The following describes the two main approaches for examining the drug's diffusion profile.

#### *In vitro* Diffusion Studies

A glass *in vitro* nasal diffusion cell has a 60 ml capacity, a flanged top (approximately 3 mm), and a recipient chamber that is water-jacketed. The lid has a donor tube chamber, a thermometer, and three sampling apertures. The donor chamber tube is used; it is 10 cm long and has a 1.13 centimetre interior diameter. The sheep nasal mucosa is separated from the underlying bone tissues after blood is extracted, and it is then washed in distilled water that has been injected with gentamicin. After that, the donor chamber tube is attached to it. The chamber of the recipient diffusion medium is where the tube is supposed to come into contact. 0.5 ml samples are taken out of the recipient chamber at predetermined intervals, replaced appropriately, and their drug content is determined using the proper analytical method. The experiment is conducted with the temperature kept at 37 °C. Studies conducted *in vitro* showed that in just two minutes, about 95.2% of the medication was discharged from the mixture [42].

#### *In vivo* Nasal Absorption Studies

Animal Models for Research on Nasal Absorption: Two types of animal models are employed: *in vivo* (whole animal) and *ex vivo* (isolated organ perfusion).

Rat, rabbit, monkey, and dog models are examples of *in vivo* models commonly used [43-44].

*Ex Vivo* Nasal Perfusion Models: The *in vivo* rat model is mimicked in terms of surgical preparation. During In order to minimize medication solution loss during perfusion tests, a funnel is placed in between the reservoir and the nose. The drug solution is pushed through the rat's nasal cavity at 37 °C using a peristaltic pump. The residual drug concentration in the perfusing solution is monitored in order to compute drug absorption. Drug activity during the experiment may be impacted by stability concerns, especially for peptides and proteins that could aggregate and undergo proteolysis. *In vivo* nasal perfusion studies using rabbits that have been anesthetized with parenteral urethane-acepromazine are a common practice. The procedure includes cannulating the trachea, closing the nasopalatine tract, and making a midline incision in the neck. Recirculating the medication in an isotonic buffer solution

#### Recent Advancements in Pulmonary Drug Delivery Formulations [47-48]

- Aerosolized Insulin.
- Using Nicotine Aerosol to Quit Smoking.
- Using Nicotine Aerosol to Quit Smoking.
- Aerosols for Angina Treatment - Aerosol Gene Therapy
- Chromatography in the Management of Cancer.
- Aerosol Pentamidine.
- Aerosol of Gentamicin.
- Aerosol Ribavirin.

- Heparin with a lower molecular weight delivered to the heart.
- Managed Substance Administration to Lungs.
- Drug Delivery to the Pulmonary System for Bone Disorders.
- Inhaled Antibiotics for Respiratory Infections.
- Corticosteroid Inhalers for Asthma Management.
- Bronchodilators for Chronic Obstructive Pulmonary Disease (COPD).
- Novel Inhalable Vaccines.
- Targeted Therapies for Pulmonary Hypertension.
- Antifungal Aerosols for Pulmonary Mycosis.
- Inhaled vasodilators for pulmonary arterial hypertension.

#### Conclusion

The nasal cavity, characterized by its expansive surface area and highly vascularized mucosa, emerges as a promising avenue for drug absorption. The direct entry getting medications into the bloodstream through the intricate network of blood arteries gets around the barriers posed by first-pass metabolism. The growing corpus of research on nasal medication delivery highlights its potential to address complex problems in drug administration and pharmaceutical manufacture. Given the ever-changing environment of nasal medication administration and the obvious advantages it provides, a wide range of innovative nasal solutions are expected to be introduced onto the market in the near future. This signifies a transformative phase in drug delivery, harnessing the unique attributes of the nasal route to enhance therapeutic outcomes and cater to the evolving demands of pharmaceutical science and healthcare. As research and development in this field continue to flourish, the realization of innovative nasal formulations holds promise for addressing complex drug delivery needs and expanding the scope of therapeutic possibilities.

#### References

1. Hicke AJ. Pharmaceutical Inhalation Aerosol Technology. 2<sup>nd</sup> Ed. New York: Marcel Dekker, Inc; c2004.
2. Sharma PK, Chaudhari P, Kolsure P, Ajab A, Varia N. Recent trends in nasal drug delivery system - An overview. ARPB, 2006, 5(4).
3. Ramadan HH, Sanclement JA, Thomas JG. Chronic rhinosinusitis and biofilms. Otolaryngol Head Neck Surg. 2005;132:414-7.
4. Mahita B, Vinod K. A clinicopathological study of allergic rhinitis. Asian J Pharm Clin Res. 2017;10:186-91.
5. Shanu T, Nitin S, Sharma PK. A review on application of natural bio adhesive polysaccharides for intranasal drug delivery. Int J A.PS.BMS. 2012;1:80-94.
6. Zaheer A, Swamy S. Mucoadhesive polymers: Drug carriers for improved nasal drug delivery. Indian J Novel Drug Deliv. 2012;4:2-16.
7. Vyas SP, Khar RK. Targeted and Controlled Drug Delivery Novel Carrier System. 1<sup>st</sup> Ed. New Delhi: CBS Publishers and Distributors; c2006. p. 173, 249, 331, 417.
8. Mahalaxmi R, Kumar DS, Shirwaikar A. Preparation of mucoadhesive microsphere for nasal delivery by spray drying. Indian J Pharm Sci. 2007;69:651-7.
9. Pires A, Fortuna A, Alves G, Falcão A. Intranasal drug delivery: How, why and what for? J Pharm Pharm Sci. 2009;12:288-311.
10. Varshosaz J, Sadrai H, Heidari A. Nasal delivery of insulin using bio adhesive chitosan gels. Drug Deliv. 2006;13:31-8.

11. Patil SB, Sawant KK. Development, optimization and *in vitro* evaluation of alginate mucoadhesive microspheres of carvedilol for nasal delivery. *J Microencapsul.* 2009;26:432-43.
12. Ding WX, Qi XR, Fu Q, Piao HS. Pharmacokinetics and pharmacodynamics of sterylglucoside-modified liposomes for levonorgestrel delivery via nasal route. *Drug Deliv.* 2007;14:101-4.
13. Costantino HR, Illum L, Brandt G, Johnson PH, Quay SC. Intranasal delivery: Physicochemical and therapeutic aspects. *Int J Pharm.* 2007;337:1-24.
14. Langley JM, Halperin SA, McNeil S, Smith B, Jones T, Burt D, *et al.* Safety and immunogenicity of a proteosome-trivalent inactivated influenza vaccine, given nasally to healthy adults. *Vaccine.* 2006;24:1601-8.
15. Van Kampen KR, Shi Z, Gao P, Zhang J, Foster KW, Chen DT, *et al.* Safety and immunogenicity of adenovirus-vectored nasal and epicutaneous influenza vaccines in humans. *Vaccine.* 2005;23:1029-36.
16. Greenberg DP, Walker RE, Lee MS, Reisinger KS, Ward JI, Yogev R, *et al.* A bovine parainfluenza virus type 3 vaccine is safe and immunogenic in early infancy. *J Infect Dis.* 2005;191:1116-22.
17. Garmise RJ, Staats HF, Hickey AJ. Novel dry powder preparations of whole inactivated influenza virus for nasal vaccination. *AAPS Pharm Sci Tech.* 2007;8:E81.
18. Illum L. Transport of drugs from the nasal cavity to the central nervous system. *Eur J Pharm Sci.* 2000;11:1-8.
19. Merkus P, Ebbens FA, Muller B, Fokkens WJ. The 'best method' of topical nasal drug delivery: Comparison of seven techniques. *Rhinology.* 2006;44:102-7.
20. [No Author]. Lung. Available from: <https://en.m.wikipedia.org/wiki/Lung>
21. Aulton ME. *Pharmaceutics - The Science of Dosage Form Design.* New York: Churchill Livingstone; c2002, 494.
22. 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.
23. Svensson S, Olin AC, Hellgren J. Increased net water loss by oral compared to nasal expiration in healthy subjects. *Rhinology.* 2006;44:74-7.
24. Dey S, Mahanti B, Mazumder B, Malgope A, Dasgupta S. Nasal drug delivery: An approach of drug delivery through nasal route. *Pelagia Res Lib.* 2011;2:94-106.
25. Molinari G, Colombo G, Celenza C. Respiratory allergies: A general overview of remedies, delivery systems, and the need to progress. *ISRN Allergy.* 2014;2014:326980.
26. Illum L. Nasal delivery. The use of animal models to predict performance in man. *J Drug Target.* 1996;3:427-42.
27. Ravikumar R, Balan R, Ganesan N, Thiruvengadam D. Recent modalities in drug delivery via inhalation therapy - An advanced treatment strategy for pulmonary carcinoma. *Int J Pharm Pharm Sci.* 2015;7:8-21.
28. Aulton ME. *Pharmaceutics - The Science of Dosage Form Design.* New York: Churchill Livingstone; c2002, 494.
29. 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.
30. Svensson S, Olin AC, Hellgren J. Increased net water loss by oral compared to nasal expiration in healthy subjects. *Rhinology.* 2006;44:74-7.
31. Illum L. Nasal delivery. The use of animal models to predict performance in man. *J Drug Target.* 1996;3:427-42.
32. Hussain AA, Hirai S, Bawarshi R. Nasal absorption of propranolol in rats. *J Pharm Sci.* 1979;68:1196.
33. Djupesland PG, Skretting A. Nasal deposition and clearance in man: Comparison of a bidirectional powder device and a traditional liquid spray pump. *J Aerosol Med Pulm Drug Deliv.* 2012;25:280-9.
34. Kaye RS, Purewal TS, Alpar OH. Development and testing of particulate formulations for the nasal delivery of antibodies. *J Control Release.* 2009;135:127-35.
35. Hardy JG, Lee SW, Wilson CG. Intranasal drug delivery by spray and drops. *J Pharm Pharmacol.* 1985;37:294-7.
36. Haque S, Md S, Sahni JK, Ali J, Baboota S. Development and evaluation of brain-targeted intranasal alginate nanoparticles for treatment of depression. *J Psychiatr Res.* 2014;48:1-2.
37. Watson J, Wright S, Lucas A, Clarke KL, Viggers J, Cheetham S, *et al.* Receptor occupancy and brain free fraction. *Drug Metab Dispos.* 2009;37:753-60.
38. Watson J, Wright S, Lucas A, Clarke KL, Viggers J, Cheetham S, *et al.* Receptor occupancy and brain free fraction. *Drug Metab Dispos.* 2009;37:753-60.
39. Dinanath G, Padmini K, Dipak M, Namdeo J. Development of particulate mucoadhesive gel for intranasal delivery. *Asian J Pharm Clin Res.* 2017;10:222.
40. Giuliani A, Balducci AG, Zironi E, Colombo G, Bortolotti F, Lorenzini L, *et al.* *In vivo* nose-to-brain delivery of the hydrophilic antiviral ribavirin by microparticle agglomerates. *Drug Deliv.* 2018;25:376-87.
41. Özer AY. The importance of intranasal route for application of drugs and nasal drug delivery systems. *Pharm JTPA.* 1990;30:136-47.
42. Deleu D, Hanssens Y. Current and emerging second-generation triptans in acute migraine therapy: A comparative review. *J Clin Pharmacol.* 2000;40:687-700.
43. Zhang H, Lin CW, Donovan MD. Correlation between nasal membrane permeability and nasal absorption rate. *AAPS Pharm Sci. Tech.* 2013;14:60-3.
44. Pelgrim GJ, Das M, Haberland U, Slump C, Handayani A, Tuij VS, *et al.* Development of an ex vivo, beating heart model for CT myocardial perfusion. *Biomed Res Int.* 2015;2015:8.
45. Thornton-Manning JR, Dahl AR. Metabolic capacity of nasal tissue interspecies comparisons of xenobiotic-metabolizing enzymes. *Mutat Res.* 1997;380:43-59.
46. Stevens J, Ploeger BA, Van der Graaf PH, Danhof M, De Lange EC. Systemic and direct nose-to-brain transport pharmacokinetic model for remoxipride after intravenous and intranasal administration. *Drug Metab Dispos.* 2011;39:2275-82.
47. Bhavane R, Karathanasis E, Annapragada AV. Agglomerated vesicle technology: A new class of particles for controlled and modulated pulmonary drug delivery. *J Control Release;* c2003. p. 15-28.
48. Le Brun PPH, De Boer AH, Heinemann HGM, Frijlink HW. A review of the technical aspects of drug nebulization. *Pharm World Sci.* 2000;22(3):75-81.