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Advantages of Nasal Drug Delivery System

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Abstract: *The nasal drug delivery system has received a lot of interest as a non-invasive and effective way to provide medications. Its distinct benefits include quick absorption due to the nasal mucosa's extensive vascularization, bypassing first-pass metabolism, and increased bioavailability when compared to oral administration. This approach is especially useful for administering medications that have little gastrointestinal stability or are destroyed by hepatic enzymes. The nasal route offers an alternative to systemic medication administration, particularly for individuals who have difficulties swallowing pills or injections.*

Furthermore, the nasal cavity's closeness to the brain makes it an appealing alternative for treating central nervous system problems, as medications can traverse the blood-brain barrier via the olfactory and trigeminal pathways. Nasal administration is also simple, patient-friendly, and inexpensive, with minimum pain. Advances in formulation technology, such as nanoparticles and mucoadhesive compounds, have improved medication retention and effectiveness. Despite its potential, issues including mucosal irritation and low medication volume must be addressed. Overall, the nasal medication delivery system is a potential tool for increasing treatment results and patient compliance.

Keywords: Systemic bioavailability, Patient compliance, First pass effect, Absorption enhancer, Intranasal drug delivery

I. INTRODUCTION

In Ayurvedic medicine, intranasal therapy is a commonly used therapeutic method. Nasal delivery of medicines has been found to have higher systemic bioavailability compared to oral administration. Biotechnology has led to the development of several protein and peptide drugs to treat various ailments. These medications are not suited for oral delivery as they are destroyed in the gastrointestinal system or metabolized by first pass action in the liver. Long-term treatment might be inconvenient, even with parenteral administration. Intranasal medication delivery appears to be a potential option for administering these medicines. This page provides an overview of the design and development.

The nasal septum, a bone and cartilage barrier, divides the nasal cavity into two symmetrical halves. Each side opens via the nostrils and links to the mouth via the nasopharynx. The nasal cavity has three primary regions: the nasal vestibule, respiratory area, and olfactory region. The nasal cavity's lateral walls fold, resulting in a surface area of around 150 cm. The nasal cavity is lined with a mucous membrane that is separated into non-olfactory and olfactory epithelium. The non-olfactory area consists of skin-like cells in the nasal vestibule and airway epithelium.(fig.1)

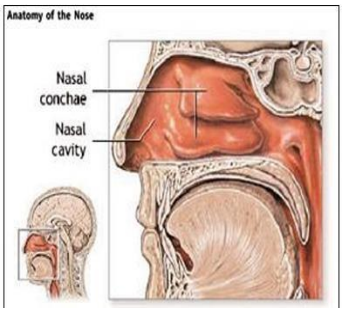

Fig 1: Anatomy and Physiology of Nasal Cavity.

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Anatomy and Physiology of the Nasal Cavity

The nasal cavity is a complex structure with several anatomical targets for therapeutic purposes. The nasal cavity is the most cephalic component of the respiratory system, primarily responsible for olfaction and air conditioning. The nasal cavity is located between the base of the skull and the roof of the mouth.

The nasal cavity is supported by the ethmoid, maxillary, and inferior conchae bones both above and laterally.

The nasal cavity contains a capacity of 15-20 mL and a surface area of around 150 cm. The nasal septum separates the human nasal cavity, which spans 12-14 cm from nostril to nasopharynx. Filtering, warming, and humidifying breathed air. The inferior, middle, and superior turbinate have a total mucosal surface area of around 160 cm².

The nasal cavity consists of two irregular air spaces joined at the bottom by the nasopharynx, the upper section of the throat, and separated by the septum. It is limited by bones and kept together by connective tissue.

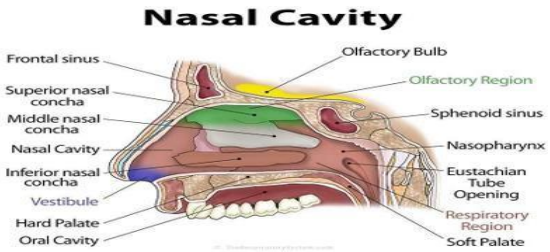

Fig 2: Anatomy of Human Nasal Cavity.

Advantages of Nasal Drug Delivery Systems

- The gastric tract does not degrade drugs.
- Hepatic first-pass metabolism is missing.
- Drug absorption and activity can occur quickly.
- Absorption enhancers and other approaches can improve the bioavailability of bigger medication molecules.
- Nasal bioavailability of smaller medication molecules is excellent.
- Nasal medication administration can transport drugs that are not taken orally into the systemic circulation.
- Research suggests that the nasal route is a viable alternative to parenteral administration for protein and peptide medicines.
- Convenient for patients, particularly those on long-term treatment, compared to parenteral medications.
- Increased nasal mucosal surface area for dosage absorption.
- Rapid medication absorption through highly vascularized mucosa.
- Quick action
- Easy to administer, non-invasive.
- Avoidance of GI tract and first-pass metabolism.
- Improved bioavailability.
- Lower dosage and less negative effects
- Minimal aftertaste.
- Increased convenience and compliance
- Self-administration.
- New patent coverage for medication compositions is due to expire.

Traditional nasal medication delivery systems have benefits over injection or oral administration, but face limitations in effectiveness and applicability.

Limitations

- It is currently unclear whether the absorption enhancers utilized in nasal drug delivery systems are histologically harmful.

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- Due to the potential for nose irritation, it is somewhat inconvenient for patients in comparison to oral delivery methods.
- In comparison to the GIT, the nasal cavity offers a lesser absorption surface area.

Nose To Brain Drug Delivery System

Nasal administration is a useful method for delivering drugs that have low oral bioavailability. Intranasal delivery has several advantages. Rapid absorption without enzymatic degradation and first-pass metabolism leads to increased bioavailability and faster onset of pharmacological effects. This channel connects the brain to the external environment, allowing for direct targeting of drugs. The nasal cavity is divided into two zones for drug delivery: the olfactory region around the nostrils and the respiratory area higher up in the nares. The "Nose to Brain Approach" refers to the direct delivery of drugs from the nose to the brain through olfactory and trigeminal nerves. This method allows medications to pass the blood-brain barrier and enter the brain directly. The olfactory mucosa receives blood from the anterior and posterior ethmoidal arteries, minor branches of the ophthalmic artery. The respiratory mucosa receives blood from the sphenopalatine artery, a branch of the maxillary artery. Medication delivered through the nose can go from systemic circulation to the brain via the blood vessels that feed the nasal cavity. The trigeminal nerve route connects the nose, medulla, pons, and spinal cord in the posterior brain. Additionally, it has restricted access to the olfactory bulb.

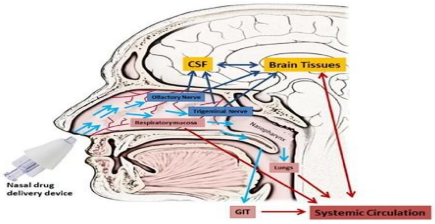

Fig 3: Nose To Drug Delivery System

Nasal Drug Absorption

Mechanism of Drug Absorption

The following are some of the processes that have been suggested for medication absorption via the nasal route. The first process uses an aqueous transport pathway, sometimes referred to as the paracellular pathway. This is a passive and slow path. The molecular weight of water-soluble substances and intranasal absorption have an inverse log-log relationship. For drugs with molecular weights more than 1000 Daltons, poor bioavailability was noted. The transport of lipophilic medications that exhibit a rate dependence on their lipophilicity is accomplished by the

second mechanism, which involves transport via a lipoidal pathway and is also referred to as the transcellular process. Additionally, drugs can pass across cell membranes through tight junction opening or carrier-mediated active transport. For instance, chitosan, a naturally occurring biopolymer derived from shellfish, helps to transport drugs by creating tight connections between epithelial cells.

Nasal distribution of medicines is a promising option for low-dose drugs with poor gastrointestinal stability or substantial first-pass effects when administered orally. The nose-to-brain (N2B) route allows for medication administration into the CNS through the nasal cavity's innervation, including the olfactory nerve and the trigeminal nerve.

Trans nasal drugs must pass past the epithelial cell layer to reach the circulation and exert their pharmacological effects. The nasal epithelium's strong connections at the apical surface allow medications to potentially pass its barrier.

The nasal mucosa, with its highly vascularized epithelium, provides a non-invasive route for delivering medicines with limited bioavailability.

Mucus is the primary pathway for medication absorption in the nasal cavity. Fine particles easily pass through the mucus layer, but larger particles may struggle to do so. The solute is attracted to the mucus layer, which influences diffusion and includes the specialized protein mucin.

Exogenous variables, including biological and environmental factors, can affect the shape of the mucus covering. They achieve this by penetrating the fifth cranial nerve, also known as the olfactory nerve. These processes enhance medicine stability and mucus solubility, as well as facilitate material penetration through intracellular or paracellular routes.

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The mucosa absorbs nutrients through two main mechanisms. There are two types of transport: transcellular (by vesicle carriers) and paracellular (via open tight junctions between cells).

To Enhance the Nasal Absorption

The absorption enhancer's mechanism of action involves speeding up the drug's passage through the nasal mucosa. Many enhancers work by changing the shape of epithelial cells in some way, but they should do so without harming the nasal mucosa or changing it permanently. The following are general requirements for the perfect penetration enhancer:

- It ought to result in a noticeable improvement in the drug's absorption.
- The tissue shouldn't be permanently harmed or altered.
- It must be harmless and nonirritating.
- It should work well in small doses.
- When absorption is necessary, the boosting effect need to take place.
- The impact ought to be transient and reversible.
- It must work well with other excipients.

Penetration Enhancers Are Classified as Follows:

- Solvents
- Alkyl Methyl Sulphoxides
- Dodecyl Azacycloheptan-2-one
- Surfactants

Penetration Enhancers' Mechanism:

- Increasing the permeability of cell membranes.
- Intracellular aqueous channel development and tight junction opening.
- Increasing the charged drug's lipophilicity by ion pair formation.
- Proteolytic activity inhibition.

To Alter a Drug's Structure In Order To Alter Its Physicochemical Characteristics:

One of the profitable strategies to increase nasal absorption is to modify the drug's structure without affecting its pharmacological efficacy. In this case, changes to physiochemical characteristics including solubility, PKA, molecular weight, and molecular size are advantageous for nasal drug absorption

Intranasal Medical Drug Delivery Devices

Powder-Based Devices:

Powders have a propensity to stick to the surface of the moist nasal mucosa before dissolving and cleaning when used in conjunction with bio adhesive agents. This can improve absorption, decrease clearance rates, and reduce ciliary movement.

Liquid Formulation Devices:

Although aqueous solutions are the most widely used kind of liquid nasal formulations, suspensions and emulsions can also be used. For topical treatments, such as when humidification is used to combat the dryness and crusting that commonly accompany chronic nasal disorders, liquid formulations are believed to be particularly helpful.

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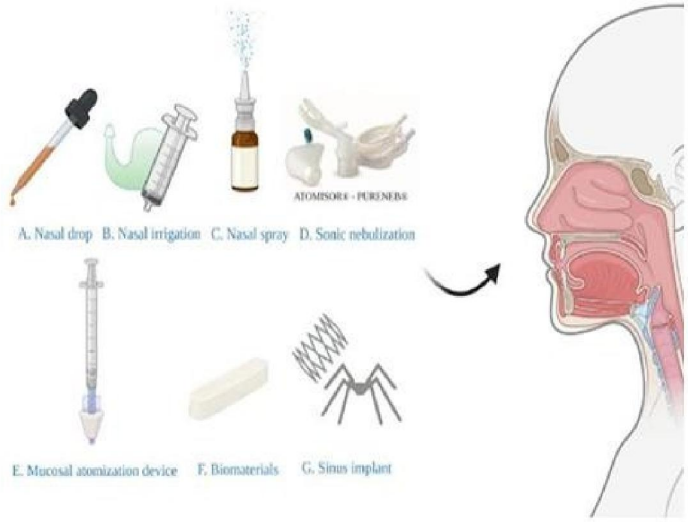

Fig 4: Nasal Drop

Sprays and Solutions:

The functioning of the device is described below. An external pneumatic pressure application is applied to a central reservoir, which drives the NP-drug suspension toward a nozzle. Airflow surrounds the drug stream from the internal air ducts on either side of the apparatus. As it leaves the nozzle, expansion in the liquid-air contact causes the two-phase flow to fragment and nebulize.

Fig. 5: Nasal Spray

Systems For Nasal Drug Delivery System

Nasal Gels:

These thickening solutions or equivalents have a high viscosity. Nasal gel has a number of benefits, including lowering pre-formulation leakage, lowering discomfort through the use of calming excipients, and improving intake by targeting the mucosa. Because of its higher viscosity, nasal gel also reduces post-nasal flow, pre-formulation leaks, and the flavor effect from eating less.

Nasal gels are thickened liquids or suspensions with a high viscosity. This technique was not very popular until the development of a precise dosage device. A nasal gel's benefits include lowering post-nasal drip because of its high viscosity, lowering the taste impact because swallowing is lessened, lowering anterior formulation leakage, lowering irritation by using calming/emollient excipients, and targeting the mucosa for improved absorption.

Entsol Nasal Gel:

This drug-free, hypoteric saline gel contains vitamin E and aloe. It soothes and moisturizes dry, congested, and irritated nasal passages. By quickly and efficiently lowering swelling and edema, Entsol nasal gel also aids in the relief of nasal

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congestion. It is perfect for dries up the those who use CPAP devices to treat sleep apnea because the continuous airflow nasal passages. Additionally, it is especially helpful for people with sinusitis or nasal allergies as well as in dry, low-humidity environments as inside during the winter and in some arid western states.

Squeezed Bottle:

Fig 6: Squeezed bottle for nasal drug delivery

Squeezed nasal containers are the most popular method of administering decongestants. Included is a soft metal container with a simple gas inlet. Because of the little punch that forces air out of the container, some of the contents of the plastic bottle are atomized

Nasal Powder:

If solution and suspension dosage forms cannot be created, for example, because of poor drug stability, this dosage form may be created. The nasal powder dose form has the advantages of greater formulation stability and no preservative. However, the solubility, particle size, aerodynamic characteristics, and nasal irritancy of the active ingredient and/or excipients determine whether the powder formulation is appropriate. Another benefit of this technique is the local drug application. However, formulation scientists and device makers face several difficulties, including nasal mucosa irritation and metered dose administration (Tabel 1)

Drugs	Delivery devices
ACTH	Insufflator, Nebulizer(De Vilbis No.40)
Adrenal corticosteroids	Nasal spray, Nasal drop, Nasal gel, Insufflators, Submucosal injection into the anterior tip of inferior turbinate, Metered dose aerosol.
Antihistamines	Nasal spray, Nasal drop.
Atropine	Nasal drop,Nasal spray, nasal aerosol.
cocaine	Nasal spray ,Nasal drops, Cotton pledget Gauge pack tail, Insufflator, Rubbing with cocaine mud
gentamycin	Nasal spray
glucagon	Nasal drop
insulin	Metered pump sprayer, Metered dose aerosolized spray, Fixed volume aerosol spray, Nasal spray, Nasal drops, Cotton pledget.
dopamin	Nasal spray
ipratropium	Nasal spray
LHRH	Nasal spray
Nicotine	Tobacco snuff, Injected into dog's frontal sinus.
Nitroglycerin	Metered dose spray
methacholine	Nasal aerosol, Nose drops.
Meclizine HCL	Nose drops
Isosorbide dinitrate	Nasal spray (IsoMack spray)
Naloxone	Micropipette
Lypressin	Nasal spray
Penicillin	Nebulizer(De Vilbiss No.40) Aerosol with intermittent negative pressure in the nasal passage and nasal accessory sinuses Aerosol with a balance calibrated suction and pressure
Penagastrin	Insufflators, snuff
Phenylephrine	Nasal drop
Propranolol	Micropipette
Prostaglandins	Nasal drop
Scarlet fever toxin	Nasal spray
Testosterone	Micropipette
Vaccines	Inhalation aerosol, Nasal spray, Nasal drop, Nasal aerosol spray, Nebulizer, aerosol
Vitamin B12	Nasal drop insufflators

Table 1: Delivery Means and Devices for Intra Nasal Administration Of Drug

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Objectives of Advantageous of Nasal Drug Delivery System

The Goal of Advantageous Nasal Drug Delivery System is :

1. Improved medication Absorption: Use the nasal mucosa's strong vascularization to provide quick and efficient medication absorption, resulting in increased bioavailability.
2. Non-Invasive Administration: Offer a pleasant and patient-friendly alternative to injections, which increases patient compliance.
3. Targeted Drug administration: Allow for direct administration of medications to the central nervous system (CNS) via the olfactory and trigeminal pathways for disorders such as migraines and neurodegenerative diseases.
4. Increased Stability: Protect sensitive medications, such peptides and proteins, against enzymatic breakdown in the gastrointestinal system.
5. Reduced adverse Effects: Localized medicine administration for nose and sinus disorders helps to reduce systemic adverse effects.
6. Cost-Effectiveness: Reduce healthcare expenditures by reducing the requirement for skilled administrative workers.
7. Sustained Release Potential: Allows for the creation of formulations that extend medication release, minimizing the need for frequent doses.

II. CONCLUSION

The nasal drug delivery system offers several advantages, making it a promising route for medication administration. This approach bypasses the gastrointestinal tract and first-pass metabolism, ensuring faster and more efficient drug absorption directly into the systemic circulation. The nasal mucosa's high vascularization and large surface area contribute to rapid onset of action, which is particularly beneficial for treating acute conditions like migraines, seizures, or allergic reactions. Additionally, it enables non-invasive delivery of drugs, enhancing patient compliance compared to injectable routes.

Nasal delivery is also advantageous for delivering drugs that are poorly absorbed orally, including peptides, proteins, and vaccines. The system's ability to penetrate the blood-brain barrier provides a unique opportunity for treating central nervous system (CNS) disorders, such as Alzheimer's or Parkinson's disease, by delivering drugs directly to the brain.

Moreover, nasal drug delivery reduces the risk of gastrointestinal side effects and degradation by digestive enzymes, preserving the drug's integrity and bioavailability. It is also cost-effective, as it often requires lower doses and eliminates the need for complex formulations.

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