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Review Article

Review on Naso-Pulmonary Drug Delivery System

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ABSTRACT

Nasal drug delivery has received a great deal of attention as a Convenient, reliable and promising method for the systemic Administration of drugs. This is due to high vascularity, large surface Area, the avoidance of hepatic first pass metabolism, gut wall Metabolism and/or destruction in gastrointestinal. the application of nasopulmonary drug delivery systems a little bit challenging. Studying the parameters of nano- or microparticles (such as particle shape, size, stealth ability from the immune clearance mechanisms, etc.) that enable them to reach the desired site of action via the nasopulmonary route is very crucial and provides important information, which should be taken into account while preparing a nasopulmonary drug delivery system .Nasopulmonary delivery system (NPDS) has produced a significant interest as a simple, reliable, and promising approach for the systemic administration of pharmaceuticals. The intranasal route can improve patient convenience, comfort, and compliance because it is basically painless and simple for the physician or patient to use. It is also described how nasopulmonary medication delivery devices might be used to treat a variety of Illnesses, including allergies, respiratory issues, and systemic problems. In order to maximize the Effectiveness and safety of nasopulmonary drug delivery systems. Many drug delivery devices for nasal application of liquid, semisolid and solid formulation are investigated to Deliver the drugs to the treat most crisis CNS diseases (i.e. Parkinson's disease, Alzheimer's disease) because it Requires rapid and/or specific targeting of drugs to the brain.

INTRODUCTION

The most convenient and favored method of medicine delivery is oral administration due to its simplicity in manufacturing and administration. Inadequate gastric absorption prompted research on alternative medication delivery systems. The term "Nasya" refers to the ancient Indian ayurvedic medical system use of the nasal route for medicament administration. This day intranasal drug delivery is thought to be more reliable and successful than parental and oral medicine delivery techniques. Without a doubt intranasal

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Drug administration has been used widely for a very long time to treat, prevent or alleviate the symptoms of topical nose illness [2]. The medication being given and The intended place of action determine the kind of device that is used Breathold dilation, Leukotriene inhibitors and inhaled corticosteroid are among the several treatment that are Frequently given utilizing NPPDS for treatment of asthma Nasal Decongest: you can use Nasal spray that contain decongestant to treat nasal congestion brought on by allergies or Other like common cold; prescription drug for migranes such as the nasal spray, harmone Replacement therapy such as the administration of estrogen and testosterone is used for Harmone replacement therapy in the form of nasal spray . It has been suggested that using the nasal mucosa as an administration route could Increase and speed drug absorption. The reason for this is Because of its big surface area, porous endothelium membrane, high blood flow overall, ability to evade first pass metabolism, and convenient accessibility. Recent year have seen a significant amount of research on the nasal delivery of medication for systemic treatment, including peptide and protein medicines, among many other molecules [4]. Many researchers have recently tried to deliver medication to the central nervous system via the nose. However, the formulation inadequate contact with the nasal mucosa is the main drawback of administrating medication via the nasal route. In an attempt to improve nasal drug absorption numerous attempts have been undertaken recently to lengthen the duration of drug formulation residence the duration of drug formulation residence in the nasal cavity. Because of nasal mucosa high degree of permeability and vascularization researchers have been interested in using the nasal route for systemic pharmaceutical distribution. Numerous scholars have examined the vascular Nature and structural features of the nasal membrane in reaction to drug administration. The septum divides the nose into two nasal chambers. Each cavity has a surface area of roughly $75cm^2$ and a capacity of around 7.5ml. The vestibular, respiratory and olfactory region of nose are its three distinct function regions. The respiratory area is the most crucial for systemic medication distribution among them. Basal mucus containing goblet, ciliated columnar and non-ciliated columnar cell type make up the respiratory epithelium. To transfer particle to the pharynx area for ingestion, the cilia move in wave-like manner. Furthermore, almost 300 microvilli cover the cell in these area, offering a sizable surface area for absorption. The lamina propria lies behind the epithelium, blood vessels, nerves, mucus secretary gland, and Serous gland may be located here [1].

A layer of mucus covers the nasal tube epithelium, this layer is replaced ever ten to fifteen minutes. In adult, the PH of mucosal secretion ranges from 5.5- 6.5, while in children it ranges from 5.0 to 6.7. Particular are caught in mucus layer and subsequently expelled from the nasal cavity by the cilia. Every 20 minutes, the mucus in the nose clear the particle moving through the pace of about 5-6mm/min. Numerous enzymes are also found in nasal cavity. These isoforms of cytochrome P450 enzyme have been found in human-CYPIA, CYP2A, CYP2E Additional enzyme found in human nose include glutathione s-transferase and carboxylesterase. In recent years, a workable solution for administering drugs through the nose has emerged: the Nasopulmonary drug delivery system. This comprehensive review looks into the potential applications and benefits of the drug delivery system as well as its future prospects [3]. A nasal-pulmonary drug delivery system is one non-invasive method of getting medication into the lungs through the nose (NPDDS). These systems have the following advantages over traditional oral and injectable drug delivery methods: rapid absorption because of the large surface area and high vascularity of the nasal and

pulmonary mucosa; first-pass metabolism avoidance drugs administered through the NPDDS bypass the liver, which can lower the bioavailability of certain drugs targeted delivery [5].

2. ADVANTAGES: -

- **Fast on set of Action: -**

Compare to oral administration nasal medication delivery has a speedier therapeutic impact and faster absorption because of nasal cavity thin mucosal barrier.

- **Avoidance of first pass Metabolism: -**

When are administered by the nasal route, they avoid the liver first pass Metabolism, which increases their bioavailability and maintain more stable plasma concentrations than when that are administered orally.

- **Non-invasive Administration: -** Because nasal drug delivery is generally well tolerated and non-invasive, it is appropriate for individual who may have trouble swallowing pills or who need to take their medication frequently.
- **Administration Ease: -**Nasal medication delivery is easy to use and convenient, frequently requiring little effort from the patient and no special equipment to administer, which can enhance patient compliance
- **Localized Drug Delivery: -** By delivering medication specifically to certain area of lungs or nasal cavity, nasal drug delivery minimizes systemic exposure and lower the possibility of systemic side effects.

3. DISADVANTAGES: -

1. Pathological disorder as allergic or cold can drastically change the nasal bioavailability
2. It is currently unclear whether the absorption enhancer utilizes in nasal drug delivery systems are histologically harmful.
3. Comparatively inconvenient for patients in comparison to oral administration method due to potential for nasal discomfort
4. In comparison to GIT, the nasal cavity offers a lower surface area for absorption.

4.Anatomy and Physiology of Nasal

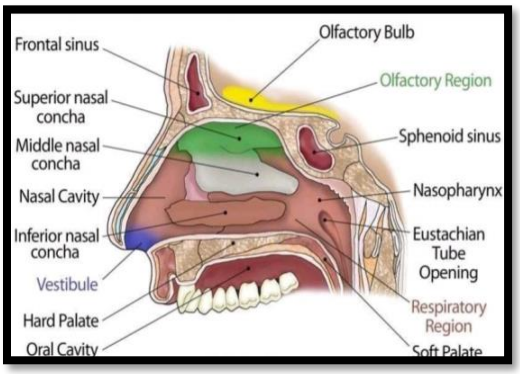

Fig 1. Anatomy and Physiology of Nose

Nasal passages the intricate anatomical structure is situated between the nasopharynx and nostrils. It performs multiple activities including as breathing olfaction (smell perception) and airborne particles filtration. When it comes to nasal medicine administration its content and structure are particularly important [10]. The nasal cavity content and structure are summarized as follows: -

- **Nasal Vestibule: -**This area of nasal cavity, which is the most anterior, is coated with skin that has sebaceous gland and hair follicles. Hair serves as the filter to remove bigger particles from inspired air.
- **Nasal Septum**: - Made of bone posteriorly and cartilage anteriorly, the nasal septum divides the nasal cavity in half. There are

blood artery and a mucus" membrane lining the septum.

- **Nasal Turbinate's (conchae): -** Each side of nasal cavity contain three pairs of nasal turbinates (superior, middle, inferior). The nasal cavity surface area is increase by this bony projection coated in vascular mucosa, which also aid in filtering, heating and humidifying inspired air.
- **Nasal Mucosa**: - Pseudotratified ciliated columnar epithelium makes up the respiratory mucosa that lines the nasal cavity. This mucosa is made up of ciliated cell, brush cell, basal cell, and goblet cell, which produces mucus, foreign objects and pathogens are captured and eliminated by mucus layer, and are then propelled into the pharynx for expectoration or swallowing by ciliary action.
- **Blood flow**: - The internal and exterior carotid artery branches provide the nasal cavity with a plenty blood flow. The nasal mucosa large vasculature makes it easier for medication to be absorbed quickly when taken internally.
- **Nerves**: - The trigeminal nerves (CNV), which control feeling (touch, pain, temp) and reflexes like sneezing and nasal congestion, has branches that innervate the nasal cavity.
- **Olfactory region**: - It is located in superior aspect of nasal cavity, is home to olfactory receptor that are important for smell perception Specialized olfactory epithelium containing olfactory sensory neuron line this area.
- **Nasopharynx**: - It connects the nasal cavity to the throat, is formed by the posterior portion of nasal cavity opening into it. This area facilitates the flow of food and air as well as drainage of nasocrimal duct [11-12].

5. Mechanisms of Drug Delivery in Nasal Drug Delivery System

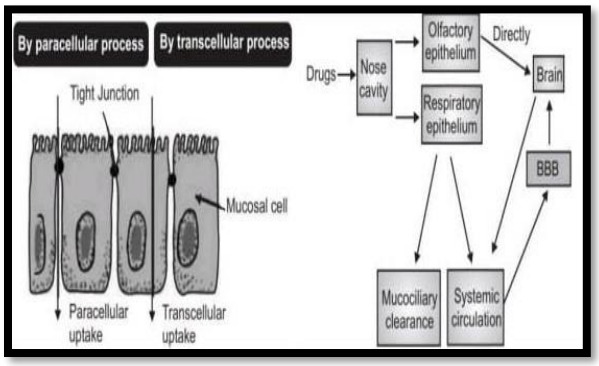

Fig 2. Mechanisms of Drug Delivery in Nasal Drug Delivery System [26]

The nasal mucosa, a highly vascularized and porous membrane lining the nasal cavity, is the barrier that medication must pass through in order to be absorbed through the nasal route. With its huge surface area and direct access to blood stream, the nasal mucosa is advantageous. Optimizing drug delivery in nasal drug delivery systems entails a number of crucial steps design to make it easier for medication to be transported effectively from the nasal cavity into the blood stream or to specific location inside the respiratory duct. When using ups administration, the medication is usually sprayed into nasal cavity as a liquid or as a powder. Subsequently, the medication interacts with nasal mucosa which is abundant in blood vessels and provide a sustainable surface area for medication absorption. Drug is influenced by several factors, drug physicochemical qualities, formulation features and nasal epithelial integrity all affect medication absorption in nasal mucosa [16-17]. There are two ways for the medication molecule to pass through nasal mucosa: -

- **Transcellular pathway**: - lipophilic medication preferentially take up space in lipid bilayer of cell membrane where they breakdown path. They go straight through the nasal mucosa lining epithelial cell.
- **Paracellular pathway: -** This pathway is mainly used by hydrophilic medicine, which have difficulty passing through the cell membrane. They traverse the gap in between epithelial [20,21].

Table 1: - Mechanism of Pathways6. A) Factors Influencing Drug Absorption and Bioavailability:

Mechanisms	Description
Transcellular pathway	Drug that are lipophilic cross the membrane of epithelial cell directly
Paracellular pathway	Drug that are hydrophilic can go across the gap between epithelium cell.

Factors Related to Drug

Lipophilicity: - The compound usual rise in penetrations through the nasal mucosa corresponds with an increase in lipophilicity. The nasal mucosa has been seen to possess certain hydrophilic characteristics; nonetheless it seems that these mucosa are predominantly lipophilic in nature, and the lipid domain is crucial for the barrier function of these membrane [3].

Chemical Form: - A drugs chemical Form may play a significant role in influencing absorption. The drugs absorption may change, for instance if it is transformed into an ester or salt. Huang etal's study looked at how a drug structural alteration affected absorption. It was shown that in-situ nasal absorption of L-tyrosine carboxylic acid ester was considerably higher than that of L -tyrosine itself [3].

Polymorphism: - Drug solubility and dissolution rate, consequently the medication absorption across biological membranes is known to be impacted by polymorphism [3].

Molecular weight: - When it comes to lipophilic molecule, the molecular weight and drug penetrations have a direct relationship, while the relationship for water soluble compounds is inverse yammato et. Al and fisher et. Al suggests that the physicochemical properties do not have impact on drug permeation of less than 300 Da [3].

Drug solubility and dissolution rate: - When it comes to measuring nasal absorption from powder and suspension, solubility and dissolution rate play a significant role. Before being absorbed, the particle that have lodge in nasal cavity must be dissolved. No absorption occurs if a medication is eliminated or stay in form of particle [3].

B) Factors Related to Formulation

1] Physicochemical properties of formulation

- **pH and mucosal irritancy: -** A drug penetration may be impacted by the PH of the nasal surface as well as the formulation. The pH of nasal formulation should be adjusted to 4.5-6.5in order to prevent nasal irritation. This is not only preventing irritation but also efficient drug penetration and inhibit the growth of bacteria [3].
- **Osmolarity**: - Rats' absorption of secretin was examined by Oliwaki et., who discovered that at 0.462 M sodium chloride concentration, absorption reached its maximum, as it was noted that at this salt concentration, the nasal epithelial mucosa shrank [51]. This leads to increased compound penetration as a result of structural alterations, and the use of sorbitol as an osetoregulatory drug further supported this. Because of the consequent decrease in 52) anal permeability of secretin, as reported by the authors, isotonic solutions are typically recommended for administration [3].
- **Viscosity**: - The longer the medication is in touch with the nasal mucosa due to the increased viscosity of the formulation, the longer the time it takes for permeation. In addition, very viscous formulations change a

drug's capacity to pass through the body by interfering with regular processes such ciliary beating and mucocilliary clearances [3].

7. The Theories of Nasopulmonary Drugs Delivery System: -

The term "Nasopulmonary drug delivery" describes the administration of medications via the nasal canal, which targets the lungs and the upper respiratory system. This method has a number of benefits, including non-invasive delivery, a quick start of action, and avoidance of first-pass metabolism. The pulmonary medication delivery mechanism is the subject of five theories. For the pulmonary drug delivery route, the following 5 theories are taken into consideration for the delivery of the medication:

•Electronic Theory
•Adsorption Theory
•Wetting Theory
•Diffusion Theory
• Fracture Theory

Nasopulmonary drug delivery systems are based on a number of theories that optimize medication deposition, absorption, and effectiveness in the nasal and pulmonary areas. The idea of mucocilliary clearance, which controls the passage of mucus and other particles through the respiratory epithelium, is one well-known theory. While pulmonary drug delivery systems must take into consideration clearance mechanisms in the lungs to achieve optimal drug deposition and retention, nasal drug delivery systems must overcome application this clearance mechanism to ensure sufficient drug retention and absorption in the nasal cavity. Particle size and aerodynamic behavior are the focus of another hypothesis, which highlights the need of maximizing particle size distribution and aerodynamic characteristics to enable effective medication delivery to both the nasal and pulmonary areas. 13–16, There is discussion on these theories [1]. Tablet The list of description of theory of pulmonary drug delivery systems with its application.

Table 2: **The Theories of Nasopulmonary Drugs Delivery System**

Theory	Description	Applications	Marketed Drug
Electronic theory	Drug particle interaction and lung surfactant according to its electrical qualities	Forecast the stability and dispersion of medications particle breathed into the fluid lining the lungs.	TOBI podhaler (Tobramcyin Inhalation powder)
Absorption theory	Drug particle adhering to the lung surface while teased on intermolecular force	Create medication formulation with the best possible surface characteristic s to improve lung retention	Respimat (Tiotropium bromide inhalation spray)
Wetting theory	Drug particle dispersion on the lung surface as a function of contact angle and surface tension	Create medication composition for enhancing lung absorption that distribution efficiency medication absorption	Spiriva Handi haler (Tiotropium bromide inhalation powder)
Diffusion theory	Drug molecular go from the surface into the blood stream	Achieve sustained medication delivery to the lung and	Adavair Diskus (fluticasone propionate)
Fracture Theory	Drug Particles breakdown into smaller pieces as a result of the lung mechanical stresses	Create medication formulation for effective drug delivery that can endure mechanical stress and retain their integrity	Pulmicort flexhaler (budesonide inhalation powder)

These are the five theories for medication distribution and absorption for treating a specific condition, along with a few commercially available drug items listed in Table 2 above. Furthermore, Nasopulmonary drug delivery is greatly influenced by theories of drug solubility, permeability, and formulation properties, which direct the creation of formulations that can improve drug solubility and penetration. Targeted distribution to particular respiratory tract areas and via mucosal barriers.

8. Advancement in Nasopulmonary Drug Delivery System

8.1. Formulation strategy for enhanced drug delivery: -

The various dosage forms available for the delivery of drugs to treat specific Diseases, Medical devices known as inhalers are used to administer medication directly to the lungs. This allows for the targeted and efficient treatment of a number of respiratory disorders, including cystic fibersis, asthma, and chronic obstructive pulmonary disease (COFD). Compared to oral or injectable drugs, they provide a number of benefits, such as a quicker onset of action, fewer systematic side effects, and better patient compliance.

There are various varieties of inhalers, each having a unique mode of action, benefits, and drawbacks.

Type of inhaler formulation: - They are of 3 types

Metered Dose inhaler: -MDI use a propellant to propell a pre-measured dosage of medication They are frequently used in the treatment of asthma and chronic obstructive Pulmonary disorder (COPD).

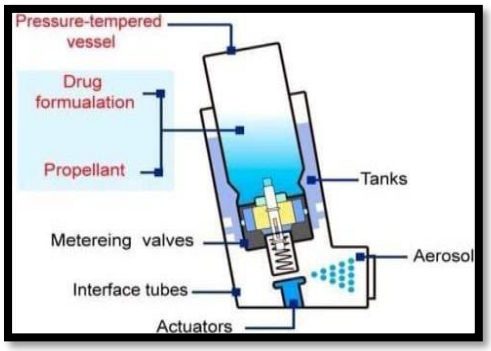

Fig 3. The Composition of metered Dose inhaler [27

Dry Powder Inhaler: - the patient's inspiratory effort disperses a dry powder formulation delivered by DFIs. They are frequently applied to medications that exhibit solution instability or propellant sensitivity

Nebulizer: - L A fine mist of suspension or solution nebulizer and inhaled over a sufficient period of time. They are usually prescribed for those who are unable to successfully use MDI or DPI for patient with severe respiratory disorder. Below list the various formulation types together with their respective doses form and modes of action.

Table 3: Type of Inhalers

Inhaler types	MOA	Marketed drug
Metered dose inhaler	Delivers a premeasured dose medication in a propellant driven spray	ProAir HFA of Ventolin HFA

Dry powder inhaler	Delivers a dry powder formulation that is dispersed by the patient's impiratory effort.	Advairs diskus, spiriva Handi haler
Nebulizer	Generate a fine mist of medication that is inhaled over a longer period.	Omron microAIR nebulizer

There are some important marketed products with different types of inhalers in formulation as per table 3 will discuss briefly.

8.2. Novel Drug Delivery device and Technologies

The several novel drug delivery devices and technologies have been developed to enhance drug delivery to the nasal and pulmonary regions. The some of them as examples discussed below followings

Nasal Spray with Microfluidic Systems: -

Microfluidic systems integrated into nasal spray devices allow for precise control aver droplet size and distribution, optimizing drug deposition and absorption in the natal cavity.

Nasal powder inhaler: -

These devices offer benefits like increased patient satisfaction and drug stability by directly delivering powdered formulation to the nasal mucosa Ease of use in contrast to conventional liquid doses Spray.

Nasal Drug delivery systems with Nanotechnology: -

Nasal Drug Delivery System based on nanoparticles provide targeted and regulated drug administration to certain areas of the nasal cavity, increasing the availability and Effectiveness of treatment.

Nasal implant and insert: -

these are inserted inside. he nasal cavity to deliver prolonged, sustained medication release, providing a practical, noninvasive substitute for regular dosing.

Nasal Aerosol Device with vibrating mesh: -

Vibrating mesh technique in nasal Aerosol devices produces small Aerosol particles with a restricted size distribution, enhancing medication deposition increasing medication absorption and the nasal cavity.

Nasal pump with smart inhaler technologies: -

intelligent inhaler utilising technology built into nasal pumps, customized treatment plans are made possible by real-time monitoring of drug delivery parameters like dosage, frequency, and patient adherence. In contrast to others, nasal grace devices connected to nasal spray pumps aid in improving medicine administration by regulating the spray pattern and lowering variability in nasal**.** Deposition, guaranteeing reliable and effective drug absorption. Mucoadhesive formulations in nasal administration systems stick to the nasal mucosa, optimizing contact time and boosting medication absorption to improve therapeutic effects.Pulmonary drug delivery devices vices with a dry powder inhalers (DPIs), DPis deliver drug formulations directly to the lungs in the form of dry powder, offering improved stability and ease of use compared to traditional nebulizers and nasal delivery. Systems with inhaled corticosteroids (ICS), HS S formulations delivered via nasal sprays or inhalers are used to treat respiratory conditions such as asthma and chronic obstructive pulmonary disease (COPD), providing localized anti- Inflammatory effects with reduced systemic side effects These novel drug delivery devices and technologies hold great promise for improving the efficacy, safety, and patient adherence of nasal and pulmonary drug delivery

systems, offering innovative solutions for the treatment of various respiratory and Systemic diseases [14].

8.3. Formulation Approaches in Nasopulmonary Drug Delivery System

The following are the most popular formulation approaches used in Nasopulmonary drug delivery systems:

1)Nasal Gels
2) Nasal Drops,
3) Nasal Spray
4) Nasal powder,
5) Liposomes
6) Microspheres

The goal of these formulation approaches is to maximize patient compliance and drug efficacy by addressing the particular difficulties involved in delivering medications to both the nasal and pulmonary regions. One approach is to create multifunctional formulations that can effectively target both sites of delivery. For example, formulations based on nanoparticles can be designed to encapsulate drugs and facilitate their transport across mucosal barriers in the nasal cavity while also enacting deposition and absorption in the hings upon inhalation.

1)Nasal Drops: -One of the easiest and most practical nasal administration systems ever created is nasal drops. Because of this system's primary drawback—its lack of dose precision— nasal drops might not be appropriate for use with prescription medications. [53] According to reports, albumin from nasal drops deposits Baxman's nose more effectively than nasal spray [6].

Fig 4. Nasal Drops [28].

2) Nasal Spray: - Nasal sprays can be formulated with either solution or suspension. A nasal spray can precisely provide a dosage between 25 and 200 µl thanks to the availability of metered dose pumps and actustant. The choice of pump and actuator assembly is determined by the viscosity of the formulation, the drug's particle size and shape (for suspicions), and other factors. Sprays that are liquid or dissolved are preferable to those that are powdered since the latter cause muscular irritation [7]

Fig 5. Nasal Spray [29].

1) **Nasal gel**: - A nasal gel's benefits include reducing post-nasal to high viscosity through drip technique, lessening the impact of taste, which reduces swallowing, redacting anterior formulation leakage, reducing irritation through the use soothing molecule excipients, and delivering the gel directly to the mucosa for improved absorption [8].

Fig 6. Nasal Gels [30]

4) Nasal Powder -If solution and pill dosage forms cannot be developed, for example, because of insufficient drug Stability, this dosage form might be created. The greater stability of the formulation and the lack of preservative are the benefits of the nasal powder dosage forms. However, the solubility, particle Size, aurodynamic properties, and nasal irritability of the active medication and/or excipients Determine the mutability of the final powder formulation. Benefit of this approach is the ability to Apply drugs locally, although communication Scientists and device makers may face obstacles due nasal mucosa irritancy and individualized dose delivery [9].

Fig 7. Nasal Powder [31]

Table. The several formulations Approaches in Nasopulmonary Drug Delivery System with its example, Application and disadvantage and. Strategies to overcome Disadvantage

Table 4:- Formulation Approach

Formulation approach	Applications	Marketed drug	Strategies to over come disadvantage
Nasal gel	Extended duration of medication release and residence the nasal cavity	Musinex sinusmax full force nasal gel	Using less viscous and biocompatible gelling agent
Nasal drops	Management of small straight	Otrivias nasal drops afrin nasal drops	A kind of dropper with accurate dosage control

	forward and practical volume		
Nasal spray	Often utilized Become it's simple to administer for a variety of medication	Flonase nasal spray, nasal spray	Using controlled release formula or mucoadhesive polymer
Liposomes	Boost the bioavailability and absorption of drug	None currently marketed for nasal delivery	Use formulation with stable liposomes and controlled release
Microspheres	Regulated medication release and	None currently marketed	Using biodegradable and highly

8.4. The Evaluation of Nasopulmonary drug delivery

The various assessments that were carried out for the Nasopulmonary medication dose forms. A comprehensive method is employed to appraise Nasopulmonary drug delivery systems in order to determine their clinical applicability, safety, and effectiveness. To guarantee the best possible aerosolization and deposition of the medication inside the respiratory tract, the physicochemical parameters of the formulation are examined first. Aerodynamic and particle size distribution are characterized using methods like cascade impaction. Behavior, which are essential factors in determining lung penetration and deposition efficiency, Second, preclinical research is done to look at the given drug's pharmacokinetics and Pharmacodynamics. To evaluate drug clearance, tissue distribution, and systemic absorption after nasal delivery, animal models are used. Furthermore, effectiveness research in pertinent illness models provide light on the prospective therapeutics potentials of the drug delivery systems. Table 5. The several list of evaluation of Nasopulmonary Drug Delivery System.

Table 5: - Evaluation Parameter

Parameter	Description	Procedure	Equations
Fine particle fraction	Represent the proportion of particle that reach the lower always with an aerodynamic diameter smaller than micrometer which have higher chance	Calculated from ASPD data	FPF (mass of particle<5 um) (total mass of particle) ×100%
	Represent the total quantity of medication that the gadget has discharged	Utilizing gravimetric analysis or a dosage collection chamber for measurement	ED= (mass of drug collected) (number of actuation)
	Delivered dome represent the dosage of medication that enter the patient's lungs	Measurement in Vivo techniques or with the use of a breathing simulations	DD= (mass of drug deposited in lungs) (numbers of actuation)

	Evaluate the of uniformity drug in each composition dosage	Measured with different analytical techniques or high performance liquid chromatography (HPLC)	DCU (standard deviation of drugs content) (mean drug content) ×100%
	Demonstrate the connection Between in Vivo pharmacokinetic characteristic s and invitro performance metrics (Such as FFF and APSD) {for instance the medication content in plasma	Utilizing statistical analysis, one may correlate in Vivo and in Vitro data	

According to the guidelines for the assessments, these are the evaluated Nasopulmonary drug delivery vesicles in Table 7 above. Validating the effectiveness of Nasopulmonary medication delivery systems in human beings is mostly dependent on clinical studies. Drug absorption, bioavailability, and pharmacokinetic characteristics are assessed in vivo using pharmacokinetic evaluations. Moreover, effectiveness trials assess the drug delivery system's capability for managing diseases and producing therapeutic results in patient groups. The safety monitoring makes sure that any unfavorable incidents or side effects connected to nasal delivery are recognized and treat Additionally, from the standpoint of the end-user, patient centered studies assess the acceptability and usefulness of nasal medication delivery systems.

9. Potentials Application of Nasopulmonary drug delivery systems

Because nasopharyngeal drug delivery devices effectively target both the upper and lower respiratory tracts, they offer great potential for a variety of therapeutic applications. One possible application is in the management of respiratory conditions such cystic fibrosis, asthma, and chronic obstructive pulmonary disease (COPD). The potential applications for Nasopulmonary drug delivery systems (NDDS) are numerous. Applications, such as Local administration to the lungs and nose NDDS can be used to locally provide medication to the nose and lungs in order to treat a range of respiratory disorders, including asthma, COPD, allergies, and infection. Systemic Delivery: NDDS may also be used to provide medications in a way that disperses them throughout the body by absorbing them into the circulation. Nasopulmonary drug delivery systems (NDDS) are a promising new approach for the treatment of respiratory disorders. NDDS allow drugs to be delivered directly to the nose and lungs where they can be absorbed into the bloodstream or act locally. This can be helpful for delivering drugs that are poorly absorbed from the gut or that need to be delivered quickly. Delivery to the dog NDDS can also be med to deliver drugs directly to the brain. This can be useful for treating conditions like Parkinson's disease, Alzheimer's disease, and brain tumors. Journal of Drug Delivery & Therapy [24].

9.1. Treatment of Nasopulmonary disorder

Novel and promising method for treating respiratory illnesses is the use of Nasopulmonary Drug Delivery devices (NDDS). These devices allow medications to be sent directly to the nose

and lungs, where they can either act on the respiratory system or be absorbed into the circulation currently.

Asthma: - NPDDS are being utilized locally to treat a range of respiratory conditions, such Inhalation Many asthma treatments, including bronchodilators, corticosteroids, and anti-inflammatory agents, can be administered by NDDS.

Chronic obstructive pulmonary disease: -COPD or chronic obstructive pulmonary disease, NDDS can be used to administer bronchodilators along with other COPD treatments. NDDS have been shown to improve lung function and quality of life in patients with COPD.

Cystin fibrosis: - Antibiotics and NDDS can be used to treat cystic fibrosis. Additional drugs to address cystic fibrosis. In individuals with cystic fibrosis, NDDS have been demonstrated to enhance lung function and lower the frequency of exacerbations.

Lung Cancer: - The distribution of chemotherapy medications to treat lung cancer is being studied using NDDS. NDDS may lessen side effects and increase the effectiveness of chemotherapy [24]. Apart from the aforementioned respiratory problems, NDDS is also being researched for treating other ailments including diabetes, pain, and neurological issues. The numerous types of respiratory illness treated with Nasopulmonary medication delivery mentioned in the given. Table 6. The list Of Nasal Drug Delivery examples and their treated respiratory disorder.

Table 6: - Nasal Drug Delivery Example

Nasal drug delivery example	Respiratory disorder
Flunasae nasal spray	Allergic rhinitis (high fever)
Nasal influenza vaccine	Influenza
Ipratropium bromide nasal spray	Asthma and chronic obstructive pulmonary disease (COPD)
Budesonide nasal spray	Asthma and allergic rhinitis
Beclonethasone disproportionate nasal spray	Allergic rhinitis and COPD

10. Future perspective and Challenges

With several possible uses, NDDS is a drug delivery system that shows promise. NDDS has a bright future ahead of it, and in the years to come, major advancements in this subject should be expected. The following are some major themes that might influence how NDDS develops in the future:

Increase use of Nanotechnology: -Nanomaterials can enhance medication solubility, permeability, and targeting, among other benefits for NDDS. In the future, we may anticipate seeing more nanomaterials used in the creation of new NDDS systems.

Development of personalized NDDS system: - These systems may be modified to meet the unique requirements of every patient. This may be accomplished by accounting for variables including the patient's age, gender, and disease state. In the future, we should anticipate seeing more customized NDDS systems being created.

Use of NDDs for delivery of complex drug: - such proteins and vaccines, that are challenging to provide by conventional routes of administration, can be delivered via NDDS systems. In the future, we should anticipate seeing NDDS employed to provide a progressively greater variety of complicated medications. These are a few potential future developments for the nasal medication delivery system [24].

10.1 Regulatory Consideration and safety profile

Addressing regulatory issues and ensuring the safety profiles of Nasopulmonary medication delivery devices are crucial in this field. This

expert discussion seeks to highlight the significance of following legal requirements and having a strong safety record in the creation and use of these technologies. The US Food and Drug Administration (FDA) oversees nasal drug delivery systems (NDDS) as medical devices. In general, NDDS has a decent safety record. On the other hand, there are a few possible adverse effects, including nasopharyngeal irritation, dry nose, headache, nausea, and coughing. In terms of cares, More severe adverse effects from NDOS include allergic reactions. elevated intracranial pressure, and seizures. Nasopulmonary medication delivery systems are developed and used with regulatory concerns and safety profiles in mind. Ensuring the effectiveness, quality, and safety of these systems requires strict adherence to regulatory requirements and the completion of thorough safety evaluations. Drug delivery may be advanced and patient care improved by putting a high priority on regulatory Compliance and upholding strong safety profiles [23]

11. CONCLUSION

With several possible uses, NDDS is a drug delivery system that shows promise. NDDS has a bright future ahead of it, and in the years to come, major advancements in this subject should be expected. Many benefits come with using the Nasopulmonary route, including as non-invasive administration, quick absorption, and avoidance of first pass metabolism. Moreover, the nasal cavity is a great route for systemic medication distribution due to its abundant blood supply and wide surface area. To maximize this delivery's effectiveness, however, issues including nasal mucocilliary clearance and restricted drug permeability must be resolved. The Nasopulmonary route has considerable potential for the future of medication administration due to continuous developments in formulation technology and nasal drug delivery devices. To fully use this route's promise and convert it into therapeutic applications, more investigation and development work are necessary.

REFERENCES

1. Pal, Rahul, et al. "The Comprehensive Review: Exploring Future Potential of Nasopulmonary Drug Delivery Systems for Nasal Route Drug Administration." Journal of Drug Delivery and Therapeutics 14.3 (2024): 126-136.
2. Kalwale .O, A Review on Nasopulmonary Drug Delivery System : International journals of Pharmaceutical Research and Application, Volume 8 , (2023)
3. Jadhav, Kisan R., et al. "Nasal drug delivery system-factors affecting and applications." Current drug therapy 2.1 (2007): 27-38.
4. Niven, Ralph W. "Delivery of biotherapeutics by inhalation aerosol." Critical Reviews™ in Therapeutic Drug Carrier Systems 12.2-3 (1995).
5. Choudhury R., Deshmukh. A, Sahu. V, "Nasopulmonary Drug Delivery System -A Novel Approach ": World journal of Pharmaceutical Research, Volume.9, Amravati (2020)
6. Patel RS, McGarry GW. Most patients overdose on topical nasal corticosteroid drops: an accurate delivery device is required. J Laryngol Otol 2001; 115: 633-635.
7. Ishikawa F, Katsura M, Tamai I, Tsuji A. Improved nasal bioavailability of electron by insoluble powder formulation. International J Pharm 2001; 224: 105-114. junginger HE. Mucoadhesive hydrogels. Pharmaceutics Industries 1956; 53: 1056-1069.
8. Aurora J. Development of Nasal Delivery Systems: A Review Drug Delivery Technol2002; 2(7): 1-8.
9. Scherließ, R. "Nasal formulations for drug administration and characterization of nasal preparations in drug delivery", Therapeutic Delivery, 2020; 11(3); 183-191.

10. Ghori, M. U., Mahdi, M. H., Smith, A. M, & Conway, B. R."Nasal drug delivery systems: An overview", American Journal of Pharmacological Sciences, 2015; 3(5): 110-11
11. Lavorini F. The challenge of delivering therapeutic aerosols to asthma patients. International Scholarly Research Notices. 2013;2013
12. Zubair M, Abdullah MZ, Ismail R, Shuaib IL, Hamid SA, Ahmad KA. "A critical overview of limitations of CFD modeling in nasal airflow", Journal of Medical and Biological Engineering.2012; 32(2); 77-84
13. Geller, D. E. "Comparing clinical features of the nebulizer, metered- dose inhaler, and dry powder inhaler", Respiratory care, 2005; 50(10): 1313-1322
14. Pandey, P., Pal, R., Singh, S., & Gupta, H., "THE CURRENT STATUS IN MUCOSAL DRUG Delivery System (MDDS) Future Prospectus In Delivery: A Systematic Review", 2023; https://doi.org/10.47760/ijpsm.2023.v08110. 00716.Chaudh ari, R., Deshmukh, A., Sahu, V., Pharm, B., & Pote, P. R. "NASO Pulmonary Drug Delivery System-A Novel Approach", World J Pharmaceutical Res, 2020; 9; (10.20959).
15. https://solutionpharmacy.in. (2022, February 21).
16. Pal, R., Pandey, P., & Nogai, L. "The Advanced Approach in the Development of Targeted Drug Delivery (TDD) With Their Bio- Medical Applications: A Descriptive Review", International Neurourology Journal, 2023; 27(4); 4058. DOI:
17. Serralheiro, A., Alves, G., Sousa, J., Fortuna, A., & Falcon, A. "Nose as a route for drug delivery". Nasal Physiology and Pathophysiology of Nasal Disorders, 2013; 191-215.
18. Alabsi, W., Eedara, B. B., Encinas-Basurto, D., Polt, R., & Mansour, H. M. "Nose-to-brain delivery of therapeutic peptides as nasal aerosols", Pharmaceutics, 2023; 14(9); 1870. PMid:36145618 PMCID: PMC950208721
19. Handa, M., Tiwari, S., Yadav, A. K., Almalki, W. H., Alghamdi, S., Alharbi, K. S., … & Beg, S. "Therapeutic potential of nanoemulsions as feasible wagons for targeting Alzheimer's disease", Drug Discovery Today, 2021; 26(12), 2881-2888.
20. Couroux, P., Kunjibettu, S., Hall, N., & Wingertzahn, M. A. "Onset of action of ciclesonide once daily in the treatment of seasonal allergic rhinitis", Annals of Allergy, Asthma & Immunology, 2009; 102(1); 62-68. PMid:19205288
21. Lareau, S. C., Fahy, B., Meek, P., & Wang, A. "Chronic obstructive pulmonary disease (COPD)", American journal of respiratory and critical care medicine, 2019; 199(1); P1-P2 Pandey, P., Pal, R., Thakur, S. K., Sharma, V., Chanana, A., & Singh, R. "Future Aspects & Modification in Carbon- Nanoparticles in Treatment and DIAGNOSIS", 2022; 12(2); 307-324
22. https://www.researchgate.net/figure/Anatomy-AndPhysiology-of-Nose_fig1_340889125
23. https://www.sciencedirect.com/science/article/abs/pii/S 002432051730663X
24. https://www.mdpi.com/1422-0067/25/6/3261
25. https://www.apollopharmacy.in/otc/otrivin-moisturisingadult-nasal-drops-10ml
26. https://www. Co .in/products/otrivin-nasal-spray/
27. https://www.walgreens.com/store/c/walgreens-salinenasal-gel/ID=300434400-product
28. https://www.google.com/imgres

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