WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
Coden USA: WJPRAP Impact Factor 8.453
Volume 15, Issue 2, 520-540. Review Article ISSN 2277–7105

NOSE TO BRAIN DRUG DELIVERY SYSTEM: A REVIEW

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Article Received on 15 Dec. 2025,
Article Revised on 05 Jan. 2026,
Article Published on 16 Jan. 2026,

https://doi.org/10.5281/zenodo.18264725

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How to cite this Article: Mansi S. Mundhe[1], Anil B. Panchal*[2], Vishal S. Madankar[3] (2026). NOSE TO BRAIN DRUG DELIVERY SYSTEM: A REVIEW. World Journal of Pharmaceutical Research, 15(2), 520–540.

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ABSTRACT

Nose-to-brain drug delivery has emerged as a promising non-invasive strategy to bypass the blood–brain barrier (BBB), enabling rapid and targeted transport of therapeutic agents directly to the central nervous system (CNS). This route utilizes the unique anatomical and physiological connections of the olfactory and trigeminal nerves, offering a direct pathway for drugs to reach various brain regions while minimizing systemic exposure. Recent advances in formulation science—including nanoparticles, liposomes, polymeric carriers, in situ gels, and mucoadhesive systems—have significantly enhanced drug retention, permeability, and stability within the nasal cavity. These innovations address major challenges such as mucociliary clearance, limited absorption surface area, enzymatic degradation, and variability in nasal physiology. Nose-to-brain delivery has shown strong potential in the treatment of neurological disorders such as Alzheimer's disease, Parkinson's disease, epilepsy, brain tumors, and acute CNS conditions, providing improved onset of action and enhanced therapeutic efficacy. Despite its advantages, translation to clinical practice remains limited due to formulation constraints, safety concerns, dose reproducibility, and a lack of standardized regulatory pathways. This review summarizes current mechanisms, formulation strategies, therapeutic applications, and future prospects of nose-to-brain drug delivery systems, highlighting their growing relevance in modern neurotherapeutics.

KEYWORDS: Nasal drug delivery, trigeminal pathways, nanotechnology, Parkinson's disease, nose to brain drug delivery.

INTRODUCTION

Because the blood–brain barrier (BBB) restricts the entry of therapeutic substances into the central nervous system (CNS), getting medications to the brain is still one of the biggest problems in pharmaceutical research. In neurological illnesses, conventional medication delivery methods frequently fall short of achieving adequate brain concentrations, resulting in less-than-ideal therapeutic results.[1] By directly transporting medications from the nasal cavity to the brain through the olfactory and trigeminal nerve pathways, the nose-to-brain drug delivery device has become a viable non-invasive method of overcoming the blood-brain barrier. This novel approach has enormous promise for treating neurological disorders such brain tumors, Parkinson's disease, and Alzheimer's disease. Prior research has shown that intranasal delivery offers minimal systemic side effects, good bioavailability, and quick absorption.[2] According to research, the nasal route essentially circumvents the BBB by providing direct access to the central nervous system. Drug stability, retention duration, and targeted delivery effectiveness have all been further enhanced by the combination of biomaterials and nanocarriers. Despite these developments, there are still issues with overcoming mucociliary clearance, obtaining consistent medication distribution, and comprehending the exact mechanisms of transport across nasal-brain pathways. To improve the accuracy and effectiveness of medication delivery, current research is still concentrating on developing new carriers and refining formulation methods.[3]

Anatomy of Nose

A flexible septum divides the two lobes that make up the human nose. Each lobe has a volume of roughly 7.5–9 mL, and the combined volume of the two lobes is roughly 16–19ml. The nose inside surface area is roughly 180 cm^2. The nose is classified into three main categories from the perspective of drug administration.[4]

Vestibular region

Respiratory region

Olfactory region

The aforementioned areas are where drug absorption occurs when drugs are delivered through the nasal route in different forms, such as nasal drops, nasal sprays, or nasal emulsions.

1. Vestibular Region

It is found where the nostrils open. It is made up of tiny nasal hair. Nasal hair's primary job is to filter out airborne particles. It doesn't significantly affect how well medications are absorbed.[4]

2. Respiratory Region

Drug absorption primarily occurs in the respiratory area. It includes a significant number of blood vessels in the respiratory mucosa.

The majority of medications enter the systemic circulation through the respiratory system.[5]

3. Olfactory region

It has a surface area of roughly 10–11 cm2 and is crucial for the direct absorption of drugs into the CSF and brain tissues.

Numerous olfactory nerve terminals make up the olfactory area.

Although this area is in charge of delivering medication to the brain, the precise mechanism at play is yet unclear.[5]

The mucus layer covering the nose's epithelium serves to both calm the epithelial cells and trap foreign particles. The ciliary movement removes mucus from the epithelium. Cilia travel a distance of one centimeter in 15 to 20 minutes. In healthy adults, the pH of mucosal secretions is between 5.5 and 6.5, while in youngsters, it is between 5.0 and 6.7.[6]

MECHANISM OF DRUG DELIVERY FROM NOSE TO BRAIN

In the olfactory region of the nose, the drug interacts with the nerve endings found at the olfactory receptors and also engages with trigeminal neurons to a certain extent. Following its interaction with the nerve endings, the drug travels toward the brain through both extracellular and intracellular transport mechanisms, following the pathways of the olfactory cells. Ultimately, the drug reaches the cribriform plate and subsequently enters the olfactory bulb and cerebrospinal fluid (CSF). Once in the CSF, the drug mixes with the spinal fluid and is distributed throughout the brain and central nervous system (CNS). The clearance of the drug from the CNS to the peripheral nervous system (PNS) occurs in the opposite direction using the same mechanisms.

Sometimes a medication that is absorbed from the respiratory area of the nose is held in the venous supply rather than entering the systemic circulation through the nasal route and

swiftly moving to the brain and CNS arteries. Countercurrent transfer is the term used to describe this medication transfer method.[7]

The following pathways allow medicines to enter the brain through the nose

Trigeminal route

Substances travel along different branches of the trigeminal nerve that supply the nasal respiratory mucosa, which is known as the trigeminal pathway. These include the posterior nasal and nasopalatine nerves, which emerge from the maxillary branch, and the ethmoidal nerve, which originates from the ophthalmic branch. These nerves extend to the brainstem's trigeminal nuclei after joining the trigeminal ganglion. Additionally, there is evidence that some sensory neurons in the trigeminal ganglion transmit direct projections to the olfactory bulb from terminals in the nasal epithelium. Studies have shown that substances can reach the trigeminal nerve following intranasal delivery. For example, within three minutes of treatment, a GLP-2 derivative was found in the pons' primary sensory nucleus of the trigeminal nerve, suggesting quick intracellular axonal transport. The involvement of extracellular transport mechanisms in this pathway has also been confirmed by the observation of insulin in the trigeminal nerve's perineural region.[8,9]

Systemic pathway

The systemic circulation can potentially carry drugs from the nasal cavity to the brain. A part of the medication gets absorbed into the bloodstream because the respiratory epithelium has a denser blood vessel network than the olfactory mucosa. Both continuous and fenestrated endothelial cells are found in the respiratory region, allowing both big and small molecules to enter the bloodstream. These chemicals can enter the bloodstream and go to the central nervous system (CNS) via passing through the blood–brain barrier (BBB). Small, lipophilic compounds readily enter the bloodstream and pass through the BBB more efficiently than large, hydrophilic ones. through a process called counter-current exchange, the active medication is dispersed throughout the body following systemic absorption, enters the nasal blood vessels, and is swiftly delivered to the carotid arteries that supply the brain and spinal cord.[10,11]

Blood circulation pathway

Low-molecular-weight and lipophilic medicines primarily reach the brain after being absorbed into the systemic circulation via the thick capillary network present in the lamina propria of the nasal respiratory area. But even after entering the bloodstream, these

medications still have to pass across the blood–brain barrier (BBB) in order to reach the central nervous system (CNS), which frequently reduces their effectiveness as treatments. Therefore, depending on its physicochemical properties, the formulation utilized, and the particular route of delivery that establishes the primary pathway involved, a medication may eventually reach the central nervous system (CNS) through one or more potential transport routes following intranasal administration.[9,12]

Pathways involving cerebrospinal fluid and lymphatics

Nasal medication delivery is significantly influenced by the lymphatic and cerebrospinal fluid (CSF) systems. Drugs can enter the central nervous system (CNS) directly through the perineurial gaps surrounding the olfactory nerve, and the nasal lymphatic network is connected to the CSF. Studies have demonstrated that administering Nao-Qing microemulsion intranasally improves medication absorption and has a quick therapeutic impact.[13,14]

Olfactory Pathway

The intracellular and extracellular pathways are the two primary processes that make up the olfactory route. Olfactory receptor neurons absorb nanoparticles, which are subsequently carried within the neuron by endocytic vesicles involving olfactory ensheathing cells (OECs), initiating the intracellular (olfactory nerve) pathway.

These chemicals are eventually released by mitral cells through exocytosis. There are two types of extracellular pathways: paracellular and transcellular. Substances travel through the basement membrane and the gaps between sustentacular cells (SUS) in the paracellular route. The transport of tiny, hydrophilic molecules is mostly facilitated by this pathway, which is independent of receptor binding. On the other hand, hydrophobic nanoparticles can traverse the sustentacular cell membrane via receptor-mediated endocytosis or passive diffusion thanks to the transcellular pathway.[11,15]

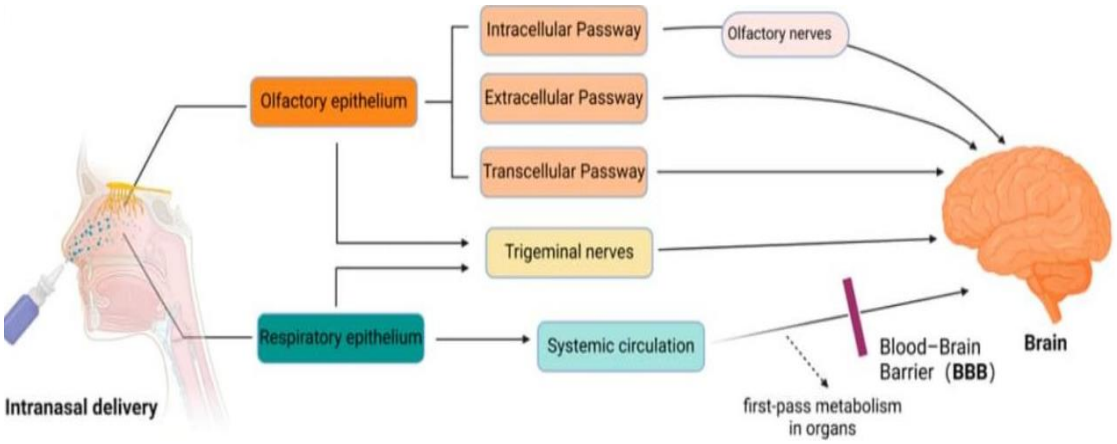

Fig. 1: Nose to Brain Delivery Pathway.

Advantages of Nasal Drug Delivery System

1. The nasal mucosa provides an extensive surface area to hold the drug or dosage form, which enhances the drug's absorption efficiency.

2. The nasal mucosa contains a dense network of blood vessels, enabling rapid and efficient absorption of drugs into the systemic circulation.

3. Rapid onset of action: The nasal mucosa's rich blood supply and wide surface area allow drugs to be absorbed swiftly, resulting in a quick therapeutic response.

4. Non-invasive: Nasal drug delivery is simple and does not require injections, allowing patients to self-administer the medication conveniently.

5. Bypass BBB: Nasal delivery enables drugs that cannot cross the blood–brain barrier to reach the brain. Through the olfactory pathway, drugs can be transported directly from the nasal cavity to the brain and cerebrospinal fluid, avoiding the BBB.

6. Improved drug utilization with fewer side effects: Nasal administration avoids first-pass hepatic metabolism, allowing lower drug doses to achieve the desired therapeutic effect while reducing the likelihood of adverse reactions.

7. Systemic and CNS drug delivery: Nasal administration can provide both systemic therapeutic effects and targeted delivery to the brain. Drugs absorbed through the respiratory region enter systemic circulation, while those taken up via the olfactory epithelium can reach the central nervous system and brain tissues.[16]

DRUG FORMULATION FOR NOSE‐TO‐BRAIN DELIVERY

Finding a suitable drug formulation that delivers the medication in a stable, safe, and efficient way is another crucial component of drug discovery. Drugs can be prepared as gels, powders, or liquids for nose-to-brain delivery. Moreover, biological characteristics like as charge, pH,

and particle size can be changed. It is feasible to increase brain absorption by more than ten times by formulation optimization.[17]

Particle size is a key factor in determining neuronal absorption, as previously mentioned. Additionally, after application, different-sized particles also disperse differently within the nasal cavity; this issue can be resolved by refining the formulation. Micro-particles 10 μm in size enter the olfactory region more frequently than particles 2 μm in size in a 3D model of the human nose.[18]

The particles with the largest olfactory deposition were 8–12 μm in size.[19] Consistent with these results, another study found that diffusive 1-nm particles and inertial 10-μm particles have higher olfactory deposition than particles in the size range of 10 nm–2 μm. This was likely caused by the Brownian motion of 1-nm particles and the inertial force of 10-μm particles.[20] This is in line with a different study that discovered that particles as small as 1-2 nm had the maximum olfactory deposition.[21]

The pH of the formulation must be adjusted to prevent nasal irritation and ensure effective drug absorption from the nasal mucosa.[22] Although the nasal mucosa has a pH of around 6.3,[23] research has shown that nasal formulations are better absorbed at pH values below 4.79.[24] Additionally, the pH of the nasal formulation should be slightly acidic to avoid discomfort and preserve microbial defense since lysozymes in nasal secretions efficiently kill bacteria at acidic pH but become inactive at alkaline pH, leaving tissue susceptible to infection.[25] Intranasal formulations should preferably have a pH level between 4.5 and 6.5 due to the benefits of an acidic pH and the physiological environment of the nose. This is crucial to prevent negative effects on the mucosa or ciliary movement.[26]

Furthermore, the transport efficiency of intranasal medications is influenced by their lipophilicity, molecular weight, and surface charge. Higher drug concentrations in the CSF following intranasal delivery are associated with increasing lipophilicity.[27] Furthermore, decreased molecular weight of drugs is associated with higher drug concentrations in the CSF.[28] Compared to cationic carriers, anionic drug carriers offer a 20% improvement in drug targeting efficiency.[29]

Formulations in powder, gel, or solution

The short residence period of solutions in the nasal cavity is a clear drawback. When compared to liquids, gels with a higher viscosity stay in the mucosa longer and deliver far larger medication concentrations in the brain.[30,31] Gels that react to temperature, ions, or pH with increased viscosity are being developed in order to extend the residency duration of gels and prevent the medication from being cleared quickly.[32,33] In comparison to a non-thermo-responsive gel, a thermo-responsive gel that becomes viscous at 32 °C not only raises medication concentrations in the brain but also maintains those concentrations for a longer amount of time.[34] Additionally, the formulation may contain mucoadhesive agents, which can enhance biodistribution by lengthening the brain's retention period and raising the brain/blood ratio.[35] In most cases, liquids or gels were utilized, but a few research also looked at powder formulations. Some studies demonstrated the superiority of powders, while others found better delivery results using alternative formulations, depending on a variety of criteria, including the medicine delivered. Powders appear to act faster than solutions in administering L-3,4-dihydroxyphenylalanine (L-DOPA) to Parkinson's patients, which may be advantageous depending on the therapy aim.[36] Two distinct nasal powders administered with an active delivery device yield direct transport rates that exceed 60%.[37] However, additional research revealed that eutectic formulations were better than powders.[38]

Nanoparticle‐mediated nose‐to‐brain delivery

Vectors are frequently utilized in the treatment of CNS disorders, but effective delivery to the brain is difficult, whether employing powders, sprays, solutions, or gels. Notably, adeno-associated viruses are the most frequently employed carriers in the field of neurodegenerative illnesses. Nevertheless, they have certain drawbacks, including low loading capacity, challenging vector production, and inflammatory reactions.[39,40,41] non-viral vectors are safer for patients and do not have these drawbacks. In order to improve the brain bioavailability of different medications, numerous studies have investigated non-viral carriers like liposomes or nanoparticles. Nanoscale carriers have already been shown to enhance the stability of active chemicals while facilitating the transfer of drugs to the brain. Compared to the free drug, paclitaxel and miltefosine-loaded lipid nanoparticles increased drug concentration in the mouse brain by five times.[42] Numerous studies have shown that nanoparticle-mediated distribution is superior to ordinary delivery in terms of both therapy efficacy and pharmacokinetic parameters.[43,44,45] Nanoparticles can be made from a variety of materials. Depending on the intended use, materials should be carefully chosen. Nanoparticles must be

non-toxic to the brain or nasal mucosa in order to enter the brain and enter target cells. In the meanwhile, they might directly impact the medication's effectiveness. For example, tyrosine alteration on siRNA therapeutic nanoparticles increases the effectiveness of siRNA-mediated knockdown.[46] The biocompatibility of nanoparticles is also influenced by their linear or branching form.[46,47] Furthermore, a meta-analysis revealed that when it comes to improving the brain bioavailability of medications, lipid nanoparticles are noticeably better than polymeric nanoparticles[48] Furthermore, the characteristics of nanoparticles can be influenced by their coating; in vitro, chitosan coating seems to enhance mucoaffinity and diffusion efficiency. In conclusion, there are a number of approaches to alter nanoparticles and enhance a drug's nose-to-brain distribution.[49]

FACTORS TO BE CONSIDERED IN DEVELOPMENT OF NASAL DRUG DELIVERY SYSTEM

When developing a nasal drug delivery system, several elements are thought to be crucial. These are regarded as such because even little changes in these variables have the potential to significantly impact the therapeutic efficacy of dose forms.[50]

These factors below mentioned

1. Physicochemical factors

Chemical form

Molecular weight

Polymorphism

Lipophilicity

2. Formulation-related factors

pH of formulation

Osmolarity

Gel forming carrier used

Solubilizers

Dose concentration

3. Physiological factors

Nasal blood flow

Mucocilliary clearance

Enzymatic degradation

Pathological conditions

Chemical form of drug

When creating intranasal dosage forms, the drug's chemical form is more crucial. It has an impact on both stability and medication absorption. Certain medications are more soluble in their complex or salt form than in their pure version.[51,52]

Molecular Weight

Because only compounds with lower molecular weight can be employed for brain targeting, molecular weight is one of the most crucial criteria. Drugs up to a molecular weight of 1000 Da can be administered when discussing intranasal medication delivery for brain targeting. Drugs with molecular weights under 300 Da can pass through the nasal epithelium without being greatly impacted by physicochemical considerations.[53]

Polymorphism

Many chemical compounds are found in nature in several forms. They exist in several states, including stable, metastable, and unstable. The metastable form of the medication is employed for dose formulation due to its maximal solubility and appropriate stability.[54]

Lipophilicity

The drug's capacity to be absorbed from the mucosal surface depends on its lipophilic nature. In general, it is dependent on the drug's hydrophilic lipophilic balance (HLB). The medicine must pass through the phospholipid bilayer membrane in order to enter the brain or systemic circulation. Highly lipophilic medications can therefore readily cross this membrane.[55]

pH of Formulation

The nasal mucosa has a pH between 5.5 and 6.5. This pH range should be covered by the formulations created for intranasal delivery. Lysozyme, an enzyme found in nasal mucosa, is in charge of eliminating a wide range of microorganisms. Any medication that changes the pH of the nasal cavity may cause an infection since lysozyme is still active at acidic ph. Nasal pH is crucial for the following key functions

Provides a unionized version of the medication for absorption.

Preserves the characteristics and functions of excipients.

Prevents microbial growth and infection in the nasal cavity.

Preserves regular ciliary activity and prevents irritation of the nasal mucosa.[51]

Tonicity

The concentration of a solution in relation to bodily fluids is measured by its tonicity. The nasal mucosa's ability to absorb drugs can be impacted by tonicity. Previous research has shown that hypertonic medication solutions reduce the nasal mucosa and improve absorption. Additionally, hypertonic solutions prolong the duration of drug occupancy and reduce the normal ciliary activity.[56]

Gelling Agent

Gelling agents are compounds that increase a formulation's viscosity. The longer the medication stays in the nasal cavity, the greater its gelling capacity. Research indicates that medications with high molecular weight do not exhibit a substantial increase in absorption from the nasal mucosa, while dosage forms with high viscosity and less molecular weight that are meant to be taken through the intranasal route are better absorbed.[57]

Solubilizers

Although high aqueous solubility of medications is undesirable, the soluble form of the drug is ideally thought to be better for absorption. When the medications are meant to be absorbed through the nasal cavity, they should be sufficiently fat soluble. Aqueous solvents and cosolvents including alcohol, glycerol, medium chain glycerides, and labra sol can be employed for this. Cyclodextrin complexation and the use of nonionic surfactants are two more methods to solve this issue. Nasal irritation must be taken into account when using these substances.[58]

Drug Concentration

While this wasn't always the case, some research indicated that drug absorption increased as drug concentration increased. When drug absorption occurs in accordance with a concentration gradient, there is an increase in drug absorption as concentration rises; however, when absorption is carrier mediated, there is no discernible increase in absorption as concentration rises.[59]

Nasal Blood Flow

There are a lot of blood vessels in the nasal mucosa. It contributes significantly to the humification of breathed air. Blood arteries facilitate the quick absorption of medication molecules from the nasal mucosa.[51]

Mucocilliary Clearance

Dust, allergies, and other foreign objects are naturally removed from the nose passage through a process known as Mucocilliary clearing. This clearance has an indirect impact on the absorption process and the residence period of dose forms. Certain bio adhesive polymers, like chitosan, carbopol, and HPMC, are utilized in formulations to get around this.[60]

Enzymatic Degradation

Nasal route comprises a number of enzymes that may degrade the medications during administration through nasal cavity; proteins are predominantly destroyed by the protease enzyme, which break the protein structure into peptones. Endopeptidases like serine and cysteine proteases disrupt the peptide molecule's internal structure, making the medication ineffective, while exopeptidases like mono and diamino peptidases split the protein molecule from its C- and N-terminal.[51]

Pathological Conditions

Drug Mucocilliary clearance and absorption tendency are impacted by pathological situations such nasal allergies, allergic rhinitis, nasal infection, and nasal surgery. Due to increased nasal cavity outflow, the intranasal route cannot be utilized during a cold or the flu. Drug absorption may be impacted by pathological disorders that may change the pH of the nose.[51]

NASAL DRUG DELIVERY CHALLENGES IN CONVENTIONAL CNS DRUG DELIVERY

Mucociliary Clearance: Drug formulations and foreign particles are quickly removed by the nasal mucosa, which shortens the duration of drug residence and improves absorption efficiency in the nasal cavity.[61]

Enzymatic Degradation: Before medicines, peptides, and proteins enter the brain's olfactory or trigeminal pathways, they can be broken down by enzymes found in the nasal mucosa.[62]

Limited Absorption Surface: The nasal cavity's effective surface area for drug absorption is significantly lower than the gastrointestinal tract's, which limits the dosages of big molecules or poorly soluble medications.[63]

Variability in Nasal Physiology: Drug absorption and bioavailability can be greatly impacted by variations in mucus composition, nasal airflow, and medical disorders (such as rhinitis).[62]

Patient-related Factors: Drug delivery success and repeatability are impacted by nasal congestion, anatomical differences, and incorrect administration method.[61]

Potential Local Adverse Effects: Frequent intranasal delivery may irritate or inflame the nasal mucosa, which could compromise long-term safety and patient compliance.[63]

SAFETY CONSIDERATIONS

Mucosal Irritation and Damage: The nasal mucosa may become irritated, inflamed, or ulcerated as a result of repeated intranasal delivery. This could weaken the nasal barrier and make the nose more vulnerable to infection.[64]

Immunogenicity: Allergic reactions or long-term inflammatory consequences may result from immunological responses triggered by nanocarriers and other delivery mechanisms.[64]

Toxicity of Nanomaterials: To avoid buildup and possible toxicity in neural tissues, the biocompatibility, biodegradability, and clearance of nanocarriers must be carefully assessed.[65]

Off-Target consequences: When medications or nanocarriers are distributed non-specifically, they may unintentionally interact with peripheral tissues or other parts of the central nervous system, resulting in toxicity or adverse consequences.[66]

Stability of Formulation: To avoid breakdown or aggregation that could damage the nasal mucosa or result in inconsistent dosing, formulations must be stable both during storage and after delivery.[64]

Regulatory and Ethical Concerns: To establish safety, efficacy, and ethical approval, extensive preclinical and clinical research is necessary, particularly for innovative nanocarrier systems and biologics.

CURRENT CHALLENGES

Limited Knowledge of Transport Mechanisms: Despite progress, the precise mechanisms and dynamics of nanoparticle translocation from the nasal mucosa to the brain remain unclear.[67]

Formulation Stability and Scalability: Manufacturing complicated nanocarriers presents difficulties in maintaining stability, homogeneity, and scalability.[64]

Variability in Patient Response: Drug absorption is impacted by anatomical and physiological variations, making uniformity across a range of patient groups challenging.[62]

Limited Clinical Translation: Due to safety concerns and regulatory obstacles, only a small number of nanocarrier-based nasal systems have reached commercialization; the majority are in experimental or early clinical stages.[64]

Potential Toxicity and Long-Term Effects: Long-term safety information is currently insufficient, and research on the toxicity profile of nanomaterials is still ongoing.[65]

PROSPECTS FOR THE FUTURE

Biocompatible and Smart Nanocarriers: Creating non-toxic, biodegradable, and stimuli-responsive nanocarriers can improve targeting effectiveness and safety.[65]

Personalized medicine: Response consistency and safety can be enhanced by customizing nasal formulations according to each patient's unique nasal anatomy, physiology, and pathology.[64]

Advanced Monitoring and Imaging: Safer and more effective treatment will be made possible by the integration of imaging modalities and biosensors to track delivery, drug release, and biodistribution in real-time.[66]

Regulatory Frameworks: Clinical translation will be accelerated by establishing uniform regulations, safety standards, and testing procedures unique to intranasal nanotechnologies.[62]

Multimodal Delivery Systems: By combining nasal delivery with additional methods or technologies (such as magnetic guidance or targeted ultrasound), treatment safety may be increased by improving penetration and lowering systemic exposure.[68]

CONCLUSION

Nose-to-brain drug delivery represents a promising alternative to conventional routes for targeting the central nervous system, primarily due to its ability to bypass the blood–brain barrier and provide rapid therapeutic action. Advances in formulation technologies—such as nanocarriers, mucoadhesive systems, and in situ gels—have significantly improved drug stability, residence time, and penetration across nasal pathways. These innovations offer new opportunities for treating a wide range of neurological disorders, including neurodegenerative

diseases, brain tumors, and acute CNS conditions. Despite its potential, several challenges remain, including variability in nasal physiology, limited dosing capacity, mucociliary clearance, and the need for more comprehensive clinical data. Regulatory standardization and long-term safety assessments are also essential for successful clinical translation. Overall, nose-to-brain delivery continues to evolve as an innovative and effective strategy in neurotherapeutics. With ongoing research and technological advancements, it holds the potential to transform CNS drug delivery and improve patient outcomes in the coming years.

ACKNOWLEDGEMENTS

The authors express gratitude to Dr. Sampat D. Navale, Principal of Delight college of Pharmacy for their constant support throughout this review.

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