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Innovative Nasal Drug Delivery Systems for Effective Brain Targeting and Blood-Brain Barrier Overcoming

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Keywords

Intranasal drug delivery, Blood-brain barrier, Central nervous system, Brain targeting, Neurotherapeutics.

Abstract

Central nervous system disorders remain among the most challenging conditions to treat due to the restrictive nature of the blood-brain barrier, which significantly limits the delivery of therapeutic agents to the brain. Traditional systemic drug delivery methods often result in low brain bioavailability and increased systemic side effects. In recent years, intranasal drug delivery has gained attention as a non-invasive and efficient route for targeting the brain, bypassing the blood-brain barrier and providing faster therapeutic action. Advancements in nasal delivery technologies such as breath-powered devices, magnetophoretic systems, iontophoresis, and nanocarrier-based formulations have shown promising results in enhancing drug retention in the brain while minimizing peripheral exposure. These methods support the delivery of a wide range of therapeutic agents, including small molecules, peptides, proteins, stem cells, and genetic material, making them suitable for the treatment of neurodegenerative diseases, psychiatric disorders, brain tumours, and other central nervous system conditions. The evolving field of nasal drug delivery offers significant potential to revolutionize central nervous system therapeutics by improving treatment efficacy, patient compliance, and safety. Continued research and clinical validation will further establish intranasal delivery as a cornerstone in the management of complex brain disorders.

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1. Introduction

The nasal route of drug delivery has gained significant attention as a non-invasive method for targeting the central nervous system (CNS). This method provides a promising alternative to traditional routes of drug administration, such as oral or intravenous delivery, by offering direct access to the brain while bypassing the blood-brain barrier (BBB). The ability to deliver drugs directly to the CNS via the nasal route holds great potential for treating various neurological disorders, including neurodegenerative diseases like Alzheimer's disease (AD), Parkinson's disease, and other CNS-related conditions. In addition to bypassing the BBB, intranasal (IN) drug delivery offers several advantages, such as a faster onset of action, reduced systemic side effects, and ease of administration [1]. The olfactory region in the nasal cavity plays a key role in the nasal-to-brain pathway, allowing drugs to reach the brain directly through the olfactory and trigeminal nerves. This direct route not only provides a mechanism to overcome the BBB but also ensures that drugs can target specific regions of the brain quickly and efficiently. The BBB, a selective permeability barrier, restricts the entry of most therapeutic drugs into the brain from the bloodstream, posing a significant challenge for drug delivery. Traditional drug administration methods often fail to provide effective treatments for brain diseases because of this limitation. By using the nasal cavity as a gateway, intranasal delivery circumvents this barrier and provides a potential solution for the treatment of CNS disorders [2], [3].

One of the major benefits of nasal delivery is the rapid absorption and distribution of drugs in the brain. The nasal mucosa allows for quick access to several brain regions, including the olfactory bulb, cortex, hippocampus, and hypothalamus. This direct route ensures that therapeutic agents can act rapidly on their intended targets within the brain, making it ideal for treating acute neurological conditions. Furthermore, intranasal delivery reduces the risk of systemic side effects by limiting the exposure of the drug to the rest of the body. This characteristic is particularly important for drugs that have the

potential for systemic toxicity or adverse effects. In many cases, the nasal route can be used to deliver large molecules or peptides that would otherwise struggle to cross the BBB through conventional methods [4], [5].

Over the past few years, numerous studies have highlighted the potential of intranasal drug delivery for treating neurological disorders. For example, certain peptide agonists, such as exendin (1-9), have been delivered intranasally to improve cognitive function in animal models of memory impairment. Additionally, peptides like NAP (NAPVSIPQ), derived from the activity-dependent neuroprotective protein, have demonstrated neuroprotective effects and improved memory in animal models of Alzheimer's disease. Other promising compounds, such as galanin-like peptide (GALP), have been shown to regulate eating behavior and have therapeutic potential in treating obesity when delivered intranasally [6], [7].

Intranasal delivery has also been explored for its role in treating inflammation and neurodegenerative diseases. For instance, interferon-beta, an anti-inflammatory cytokine, has been tested via intranasal administration as a treatment for multiple sclerosis. Intranasal delivery led to higher concentrations of interferon-beta in the brain compared to intravenous delivery, demonstrating the ability of the nasal route to deliver therapeutic agents effectively to CNS targets. Similarly, leptin, a neuropeptide involved in regulating appetite, has been successfully delivered intranasally to bypass the BBB and influence the hypothalamus, a key brain region involved in appetite control [8], [9].

Despite the promising results seen in preclinical and clinical studies, there are still challenges in translating intranasal drug delivery to widespread clinical use. The nasal cavity is a complex environment, and several factors can affect drug absorption, including the thickness of the nasal mucosa, the presence of mucus, and enzymatic degradation. These factors can hinder drug penetration and reduce the efficacy of nasal drug delivery [10]. Additionally, because the structure and thickness of nasal tissues vary across species, extrapolating data from animal models to humans can be difficult, making it challenging to predict how drugs will behave in clinical settings. Furthermore, the clearance of mucus and the potential for enzymatic breakdown of drugs within the nasal cavity must be addressed to optimize drug delivery [11].

To overcome these challenges, researchers are exploring innovative strategies to improve nasal drug delivery. These strategies include the development of formulations that enhance drug absorption, such as mucoadhesive formulations or absorption enhancers. Advances in nanoparticle-based drug delivery systems are also being explored to improve the stability, bioavailability, and targeting efficiency of drugs delivered via the nasal route [12].

Intranasal drug delivery holds significant promise as a non-invasive method for delivering therapeutic agents directly to the brain, bypassing the blood-brain barrier and minimizing systemic side effects. This delivery route has shown potential in the treatment of various neurological disorders, including Alzheimer's disease and other CNS-related conditions [13], [14]. While there are still challenges in optimizing drug absorption, formulation development, and clinical translation, the continued research into nasal drug delivery systems offers great potential for the development of novel therapies for brain diseases [15]. While existing reviews separately discuss nasal formulations or delivery devices, this article uniquely brings together cutting-edge delivery platforms (e.g., iontophoresis, magnetophoretic systems) and formulation-based strategies (e.g., polymeric nanoparticles, exosomes, stem cell carriers), highlighting their convergence for efficient brain targeting. This integrative approach identifies underexplored areas and suggests translational frameworks for future research [16], [17].

2. Methodology and Article Selection Criteria

A structured literature search was conducted using databases such as PubMed, ScienceDirect, Scopus, and Google Scholar. Keywords included “intranasal drug delivery,” “brain targeting,” “blood-brain barrier,” “nanocarriers,” and “CNS therapeutics.” Articles published between 2010 and 2024 were included. Selection criteria focused on studies demonstrating innovation in nasal delivery mechanisms, brain bioavailability, and therapeutic application in CNS disorders. Both preclinical and clinical studies were considered. Non-English articles and those unrelated to nasal delivery were excluded [18].

3. Intranasal Drug Delivery

The treatment of central nervous system (CNS) disorders such as Alzheimer’s disease, Parkinson’s disease, and other neurodegenerative or psychiatric conditions continues to be a major therapeutic challenge. Despite advances in medicine, most available treatments are symptomatic and fail to halt disease progression [19]. One of the primary limitations in treating CNS diseases is the blood-brain barrier (BBB), a highly selective membrane that prevents approximately 98% of small-molecule drugs and nearly all large biomolecules from reaching the brain. This has led to a persistent gap in the availability of effective, targeted treatments for CNS disorders. As a result, there is a growing interest in intranasal drug delivery as a non-invasive, rapid, and direct route for transporting drugs to the brain, bypassing the restrictive nature of the BBB [20], [21]. The nasal cavity offers a highly vascularized surface and direct access to the brain via the olfactory and trigeminal neural pathways. Additionally, innovations such as breath-powered bi-directional devices, magnetophoretic systems, nanocarrier-based formulations, and mucoadhesive technologies have further expanded the potential of nose-to-brain delivery. These approaches enhance drug bioavailability, reduce systemic side effects, and offer a more targeted and effective method of therapy. Given the increasing prevalence of CNS diseases and

the shortcomings of conventional treatment modalities, it is crucial to investigate and consolidate current research on intranasal drug delivery technologies. The objectives of this study are to explore the limitations of conventional CNS drug delivery, review current intranasal drug delivery methods, evaluate their advantages and effectiveness, and highlight their potential in treating diseases like Alzheimer's. By understanding and leveraging these advanced delivery strategies, the study aims to support the development of more efficient, targeted, and patient-friendly therapeutic approaches for managing and potentially modifying the course of CNS disorders [22], [23].

3.1. Approaches For Nose to Brain Drug Delivery

Nose-to-brain drug delivery offers a promising alternative to bypass the blood-brain barrier for treating central nervous system disorders. Various advanced techniques have been developed, including breath-powered bi-directional delivery, magnetophoretic systems, iontophoresis, and nanocarrier-based formulations. These approaches enhance drug targeting to the brain while minimizing systemic side effects. They allow rapid onset of action and improved patient compliance due to their non-invasive nature. Optimizing formulation parameters and delivery mechanisms is key to improving therapeutic outcomes in neurological conditions [24], [25].

Table 1 summarizes key studies on nose-to-brain drug delivery strategies for the treatment of various central nervous system (CNS) disorders. It highlights the different drugs and therapeutic compounds investigated, along with the corresponding formulation technologies employed to enhance their delivery to the brain. The table illustrates a variety of innovative approaches, including nanoparticle-based systems, liposomal formulations, mucoadhesive gels, breath-powered devices, magnetophoretic nanoparticles, and thermoresponsive in situ gels [26]. These strategies have been applied across multiple CNS conditions such as Alzheimer's disease, Parkinson's disease, neuroinflammation, and autism spectrum disorders. The reported outcomes demonstrate significant improvements in brain bioavailability, targeted delivery, and therapeutic efficacy, often with reduced systemic side effects. Collectively, these studies underscore the potential of intranasal delivery as a non-invasive and effective route for CNS drug administration, providing a promising alternative to conventional systemic therapies that are limited by the restrictive nature of the blood-brain barrier [27], [28].

Table 1: Studies on nose to brain drug delivery for treating CNS disorders.

S. No.	Drug / Compound	Formulation / Technology	CNS Disorder / Model	Key Findings / Outcomes	References
1.	Rivastigmine	Nanoparticle-based nasal spray	Alzheimer's disease (rodent model)	Enhanced brain bioavailability, improved cognitive function	[29]
2.	Dopamine	Liposomal nasal formulation	Parkinson's disease (rat model)	Increased striatal dopamine levels, reduced motor deficits	[30], [31]
3.	Insulin	Mucoadhesive nasal gel	Alzheimer's disease	Improved memory and learning, bypassed BBB efficiently	[32]
4.	Oxytocin	Breath-powered bi-directional nasal device	Autism spectrum disorder	Rapid CNS delivery, improved social behavior in preclinical studies	[33], [34]
5.	Curcumin	Magnetophoretic nanoparticle system	Neuroinflammation	Targeted brain delivery, reduced inflammatory markers	[35], [36]
6.	Levodopa	Chitosan-based mucoadhesive nanoparticles	Parkinson's disease	Sustained release, improved motor performance	[37]
7.	Galantamine	Nanoemulsion nasal spray	Alzheimer's disease	Higher brain uptake, reduced systemic side effects	[38], [39]
8.	Peptide drugs	Thermoresponsive in situ gel	Neurodegenerative disorders	Controlled release, enhanced nose-to-brain transport	[40], [41]

3.2. Comparative Overview of Nasal Drug Delivery Strategies for CNS Targeting

The development of nasal drug delivery systems for targeting the brain has seen significant innovation in recent years, with multiple techniques showing promise in overcoming the blood-brain barrier. Each method offers unique advantages depending on the therapeutic need, drug properties, and desired targeting site within the central nervous system [42]. Comparing these approaches in terms of their mechanisms, benefits, and limitations provides a clearer understanding of how they contribute to enhancing drug bioavailability, reducing systemic exposure, and offering non-invasive alternatives to traditional routes. A comparative summary of these advanced nasal drug delivery technologies is provided in Table 2 highlighting the strengths and limitations of each method for better clinical and research insight. Figure 1 shows a representative illustration of the drug transport route for nose-to-brain delivery. It highlights the pathway through which drugs are absorbed via the nasal mucosa and directly reach the brain, bypassing the blood-brain barrier [43], [44].

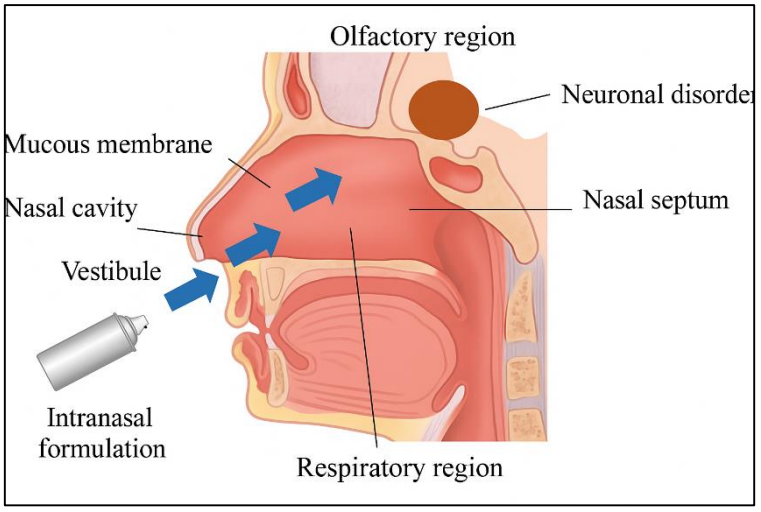

Figure 1: Representative illustration of the nose-to-brain drug transport pathway, showing direct and indirect routes bypassing the blood-brain barrier for targeted delivery to the central nervous system

Table 2 provides a comparative overview of advanced nasal drug delivery technologies developed to enhance brain targeting. These approaches are designed to overcome the challenges posed by the blood–brain barrier while maintaining a non-invasive route of administration. Breath-powered bi-directional technology utilizes exhalation-driven positive oropharyngeal pressure to open the nasal valve and improve drug deposition into upper nasal regions, particularly the olfactory area, thereby enhancing delivery efficiency and targeting [45]. Its benefits include non-invasiveness and improved airflow, although the method depends heavily on proper patient use, and device resistance may affect drug flow. Magnetophoretic olfactory delivery employs magnetic fields to guide ferromagnetic drug particles to the olfactory bulb, allowing for bypass of the blood–brain barrier and focused targeting. While promising, it requires strong magnetic gradients and involves complex device design [46], [47].

Iontophoresis uses a mild electric current to drive charged molecules across the nasal mucosa, enhancing penetration for drugs with poor permeability. This technique is efficient and non-invasive, but it is limited by the need for specialized electrical equipment and by drug type compatibility [48]. Protein and peptide delivery through the nasal mucosa allows direct brain targeting, avoids first-pass metabolism, and provides a rapid onset of action. However, the instability of proteins and susceptibility to enzymatic degradation restrict its applicability. Similarly, DNA plasmid delivery via nanoparticles offers potential for gene therapy and targeted genetic intervention in neurological diseases by bypassing the blood–brain barrier. Despite its promise, it poses risks of immune response and other gene therapy-related safety issues [49].

Stem cell delivery through the nasal route is an emerging strategy for neuroregeneration and treatment of neurodegenerative conditions. It offers a non-invasive means to transport viable stem cells into the CNS, supporting tissue repair and recovery. However, maintaining stem cell viability, avoiding immune rejection, and minimizing tumor formation remain significant challenges. Overall, these advanced nasal delivery systems demonstrate considerable potential for brain targeting, but their translation to clinical application requires overcoming limitations related to device design, safety, and drug or cell stability [50], [51].

Table 2: Comparative Overview of Advanced Nasal Drug Delivery Technologies for Brain Targeting.

S. No.	Nasal Delivery Technology	Mechanism	Benefits	Limitations	References
1.	Breath-Powered Bi-Directional Technology	Utilizes positive oropharyngeal pressure from exhalation to open nasal valve and increase nasal cavity airflow.	Enhances nasal airflow and drug delivery efficiency, non-invasive, targeted delivery to CNS.	Requires precise user operation, and resistance from device may impact drug flow.	[52], [53]
2.	Magnetophoretic Olfactory Delivery	Uses magnetic fields to guide ferromagnetic drug particles through nasal passages to olfactory area.	Focused delivery to the olfactory bulb, potentially bypassing BBB for direct CNS access.	Requires high magnetic gradients, potential complexity in device design.	[54], [55]
3.	Iontophoresis	Uses an electric current to drive charged drug molecules across the nasal mucosa.	Non-invasive, enhances drug penetration, particularly for molecules with low BBB permeability.	Requires electrical equipment, may not be suitable for all drug types.	[56]
4.	Protein/Peptide Nasal Delivery	Delivers proteins and peptides via the nasal mucosa to the brain, bypassing the BBB.	Effective for brain-targeted protein delivery, avoids first-pass metabolism, fast onset of action.	Limited to specific types of proteins, potential issues with stability and enzymatic degradation.	[57], [58]
5.	DNA Plasmid Delivery	Uses nanoparticles to deliver genetic material (DNA plasmids) through the nasal route to the brain.	Potential for gene therapy, bypasses BBB, enables targeted genetic intervention for neurological diseases.	Risk of immune response, potential gene therapy-related issues.	[59]
6.	Stem Cell Delivery	Intranasal administration of stem cells to promote CNS repair and regeneration.	Non-invasive method for delivering stem cells for neurodegenerative diseases and injury repair.	Complex regulation of stem cell viability, risk of tumor formation, and immune rejection.	[60], [61]

4. Anatomical and Physiological Considerations of the Nasal Cavity

The nasal cavity is a highly vascularized structure lined with respiratory and olfactory mucosa, playing a vital role in air filtration, humidification, and drug absorption. Its close connection to the olfactory and trigeminal pathways enables direct nose-to-brain transport, bypassing the blood–brain barrier for rapid and targeted drug delivery [62].

4.1. Nasal mucosa structure

The nasal mucosa is a specialized tissue lining the nasal cavity, consisting of epithelial cells, a basement membrane, and an underlying lamina propria rich in blood vessels and glands. It is divided into respiratory and olfactory regions. The respiratory epithelium is pseudostratified ciliated columnar with goblet cells that secrete mucus, aiding in humidification and filtration of inhaled air. The olfactory epithelium contains sensory neurons responsible for smell and provides a direct route to the brain. The rich vascularization facilitates rapid systemic and brain absorption of drugs, while the mucociliary clearance mechanism helps in protecting against pathogens and foreign particles [63], [64].

4.2. Olfactory vs. respiratory region

The nasal cavity is divided into olfactory and respiratory regions, each with distinct roles. The olfactory region, located in the upper nasal cavity, contains specialized sensory neurons that connect directly to the brain via the olfactory bulb, enabling nose-to-brain drug transport. In contrast, the respiratory region covers most of the nasal cavity and is lined with ciliated epithelium and goblet cells, primarily responsible for air filtration,

humidification, and systemic drug absorption due to its rich vascular network. While the olfactory region is crucial for direct brain targeting, the respiratory region supports efficient systemic uptake and Nasal–brain pathways primarily involve the olfactory and trigeminal nerves, which enable drugs to bypass the blood–brain barrier and reach the central nervous system directly. The olfactory pathway transports drugs through the olfactory epithelium to the olfactory bulb, allowing rapid access to brain regions. The trigeminal pathway connects the nasal respiratory epithelium to deeper brain structures, including the brainstem, via the trigeminal nerve branches. Together, these pathways provide direct and indirect routes for nose-to-brain delivery, enhancing drug targeting efficiency and reducing systemic exposure, making them highly valuable for treating neurological disorders through intranasal administration [67].

5. Factors Affecting Nasal Drug Delivery and Brain Targeting

Nasal drug delivery and brain targeting are influenced by multiple factors, including the drug's physicochemical properties (such as molecular weight, lipophilicity, and charge), formulation characteristics (like particle size, pH, and viscosity), and biological factors (such as mucociliary clearance and enzymatic activity). These determine the drug's absorption, retention time, and overall targeting efficiency [68].

5.1. Physicochemical properties of the drug

The physicochemical properties of a drug play a crucial role in determining its nasal absorption and brain targeting efficiency. Drugs with low molecular weight generally diffuse more easily across the nasal mucosa, while highly lipophilic molecules show better membrane permeability and enhanced brain uptake. Conversely, large or hydrophilic compounds may require carrier systems for efficient delivery. The surface charge also influences mucosal interaction—positively charged molecules exhibit stronger adhesion to the negatively charged mucosa, improving retention and absorption, whereas negatively charged molecules may face electrostatic repulsion [69], [70].

5.2. Formulation factors

6.1. Mucoadhesive systems

Mucoadhesive systems are advanced nasal formulations designed to prolong drug residence time in the nasal cavity by adhering to the mucosal surface. They improve absorption, enhance bioavailability, and reduce drug clearance caused by mucociliary action. Common mucoadhesive agents include chitosan, carbopol, and hyaluronic acid, which facilitate intimate contact between the formulation and nasal epithelium. This increases drug permeation and ensures sustained release for efficient brain targeting. Mucoadhesive systems are particularly beneficial for peptides, proteins, and drugs with poor permeability across the nasal mucosa [76].

mucociliary clearance [65], [66].

4.3. Nasal–brain pathways

Formulation factors significantly influence the efficiency of nasal drug delivery and brain targeting. Particle size affects deposition and absorption, with smaller particles enhancing mucosal penetration and brain uptake. The pH of the formulation should match nasal pH (approximately 4.5–6.5) to avoid irritation and ensure drug stability. Optimal viscosity improves mucosal contact time without hindering diffusion, enhancing retention and absorption. Additionally, suitable excipients such as permeation enhancers, mucoadhesive agents, or stabilizers can improve drug solubility, protect against enzymatic degradation, and facilitate better transport across the nasal mucosa for effective brain targeting [71], [72].

5.3. Biological factors

Biological factors play a crucial role in determining nasal drug absorption and brain targeting. Mucociliary clearance rapidly removes foreign particles and formulations from the nasal cavity, which can reduce drug residence time and absorption. Enzymatic activity within the nasal mucosa may degrade sensitive drugs, particularly peptides and proteins, limiting their effectiveness. Interspecies variability in nasal anatomy, physiology, and enzyme expression affects drug absorption patterns, making it challenging to extrapolate animal data to humans. Understanding these biological factors is essential for optimizing formulation design and ensuring consistent therapeutic outcomes in nasal drug delivery [73].

6. Recent Advances in Nasal Formulation Technologies

Recent advances in nasal formulation technologies focus on enhancing drug stability, absorption, and targeted brain delivery. Innovative systems such as mucoadhesive formulations, thermoresponsive gels, lipid and polymeric nanoparticles, exosomes, and cell-based carriers improve retention time, protect drugs from degradation, and enable efficient nose-to-brain transport. These technologies offer promising solutions for treating complex neurological disorders [74], [75].

6.2. Thermoresponsive gels

Thermoresponsive gels are innovative nasal drug delivery systems that remain in liquid form at room temperature but transform into a gel upon exposure to nasal cavity temperature. This sol–gel transition enhances drug retention, reduces mucociliary clearance, and provides sustained drug release. Polymers such as poloxamers, chitosan derivatives, and carbopol are commonly used to develop these systems. Their gelling property ensures better contact with the nasal mucosa, improving absorption and brain targeting. They are especially useful for peptides, proteins, and controlled-release therapies [77], [78].

6.3. Lipid and polymeric nanoparticles

Lipid and polymeric nanoparticles are advanced carriers used in nasal drug delivery to enhance stability, bioavailability, and brain targeting. Lipid-based systems like solid lipid nanoparticles and nanostructured lipid carriers provide high drug loading, controlled release, and protection from enzymatic degradation [79]. Polymeric nanoparticles, prepared from biocompatible polymers such as PLGA and chitosan, improve mucoadhesion and permeability across nasal mucosa. These nanosystems facilitate efficient nose-to-brain transport, minimize systemic side effects, and are suitable for delivering small molecules, peptides, proteins, and nucleic acid-based therapeutics [80].

6.4. Exosomes and cell-based carriers

Exosomes and cell-based carriers represent emerging nasal drug delivery systems with remarkable potential for brain targeting. Exosomes, naturally secreted nanovesicles, possess intrinsic biocompatibility, low immunogenicity, and efficient cellular uptake, enabling the delivery of proteins, peptides, RNA, and drugs across the nasal mucosa. Cell-based carriers, including stem cells and engineered immune cells, act as delivery vehicles that can cross biological barriers and release therapeutic agents at targeted brain sites. These systems offer promising strategies for treating neurodegenerative diseases and genetic or inflammatory brain disorders [81].

7. Clinical Studies and Translational Challenges

Several clinical studies on intranasal drug delivery have shown promising results in improving brain targeting and therapeutic outcomes. However, challenges such as interspecies variability, formulation stability, large-scale production, safety, and regulatory approval hinder smooth clinical translation. Ensuring patient compliance and long-term efficacy remains crucial for widespread adoption [82].

7.1. Completed or ongoing clinical trials

Numerous clinical trials have explored intranasal delivery for CNS disorders, including Alzheimer's, Parkinson's, depression, and multiple sclerosis. Intranasal insulin and oxytocin have shown positive outcomes in improving cognition and social behavior, while interferon-β demonstrated enhanced brain targeting [83]. Ongoing trials are investigating nanoparticle-based and mucoadhesive formulations for safer, more effective therapies. These studies highlight the translational potential of nasal drug delivery but emphasize the need for standardized protocols, long-term safety data, and larger patient populations for clinical validation [84], [85].

7.2. Safety, efficacy, regulatory status

The safety and efficacy of intranasal drug delivery depend on formulation type, excipients, and long-term mucosal tolerance. Many studies reports reduced systemic toxicity and improved therapeutic outcomes compared to conventional routes. However, variability in absorption and mucociliary clearance remains a concern [86]. Regulatory approval is still limited, with only a few intranasal products reaching the market. Stringent evaluation of pharmacokinetics, toxicity, scalability, and patient compliance is required to establish clear regulatory guidelines for widespread clinical adoption of these advanced systems [87].

7.3. Scale-up and patient acceptability

Scaling up intranasal formulations poses challenges due to complex manufacturing, stability issues, and the need for reproducible drug delivery performance. Advanced systems like nanoparticles, gels, and exosomes require stringent quality control for large-scale production. Patient acceptability is generally high because the nasal route is non-invasive, painless, and easy to administer, improving compliance. However, factors such as formulation viscosity, odor, irritation potential, and device usability must be optimized to ensure comfort, safety, and consistent therapeutic outcomes in real-world applications [88].

8. Discussion

Intranasal drug delivery has emerged as a promising non-invasive approach for bypassing the blood–brain barrier (BBB) and directly targeting the central nervous system (CNS). The reviewed literature and recent advancements highlight how innovative formulation technologies, including mucoadhesive systems, thermoresponsive gels, lipid/polymeric nanoparticles, and exosome-based carriers, significantly improve drug stability, retention, and brain uptake. These systems address the inherent limitations of nasal physiology, such as mucociliary clearance and enzymatic degradation, by prolonging residence time and enhancing absorption [89], [90].

Mucoadhesive systems increase formulation contact with the nasal mucosa, thereby improving bioavailability of poorly permeable drugs. Thermoresponsive gels provide sustained release through in situ gelling, reducing clearance and ensuring controlled drug delivery. Similarly, lipid and polymeric nanoparticles not only protect drugs from degradation but also enable efficient nose-to-brain transport of both small molecules and biologics. More recently, exosomes and cell-based carriers have demonstrated unique advantages in targeted delivery due to their natural biocompatibility, making them particularly valuable in treating neurodegenerative and genetic disorders [91].

Clinical investigations further validate the translational potential of intranasal therapies. Trials involving intranasal insulin, oxytocin, and interferon-β have shown improvements in cognitive, behavioral, and neurological outcomes, confirming the feasibility of this route. However, despite promising findings, challenges remain in safety evaluation, formulation reproducibility, large-scale manufacturing, and patient variability. Regulatory approvals are limited, as robust pharmacokinetic, toxicity, and long-term efficacy data are still required [92].

From a patient perspective, intranasal delivery is highly acceptable due to its ease of use, non-invasiveness, and rapid therapeutic action. Nonetheless, formulation-related factors such as viscosity, irritation potential, and device design must be optimized for better compliance. Translational success will depend on harmonizing formulation strategies with regulatory standards, ensuring scalability, and validating efficacy across diverse populations [93].

Overall, intranasal delivery technologies represent a paradigm shift in CNS therapeutics. With continued innovation and clinical validation, these systems hold the potential to revolutionize treatment approaches for complex neurological and psychiatric disorders by offering safer, more effective, and patient-friendly alternatives to conventional drug delivery routes [94].

Conclusion

Intranasal drug delivery offers a highly promising strategy for overcoming the challenges of brain targeting imposed by the blood–brain barrier. Recent advances such as mucoadhesive systems, thermoresponsive gels, lipid and polymeric nanoparticles, and exosome-based carriers have significantly improved drug stability, retention, and transport efficiency to the CNS. Clinical studies further demonstrate encouraging outcomes, though issues of safety, large-scale production, and regulatory approval remain. With continued innovation and translational research, intranasal delivery has the potential to establish itself as a reliable, patient-friendly, and effective approach for treating diverse neurological and psychiatric disorders.

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Author Contribution

UF; Conceptualized the study, **SA;** Visualization, and **NS;** Prepared the manuscript draft.

Conflict of Interest

No conflicts of interest are disclosed by the authors.

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1. S. H. Jeong, J. H. Jang, and Y. B. Lee, “Drug delivery to the brain via the nasal route of administration: exploration of key targets and major consideration factors,” 2023. doi: 10.1007/s40005-022-00589-5.
2. F. Laffleur and B. Bauer, “Progress in nasal drug delivery systems,” 2021. doi: 10.1016/j.ijpharm.2021.120994.
3. T. Ali, “Chromatography and Spectroscopic Characterization of Nano-Carrier Pharmaceuticals,” Pharm. Nanotechnol., 2024, doi: 10.2174/0122117385319695240911115239.
4. H. B., K. M., R. B. Sree, V. A., and P. K., “An Overview on Nasal Drug Delivery System,” Asian J. Pharm. Res., 2022, doi: 10.52711/2231-5691.2022.00041.
5. Shadab Ali, Sayad Ahad Ali, Mukesh Kumar, Iram Jahan, and Jiyaul Hak, “Emerging Strategies for Targeted Drug Delivery across the Blood–Brain Barrier in Neurological Disorder,” Curr. Pharm. Res., pp. 1–14, 2025, doi: 10.63785/cpr.2025.1.1.114.
6. K. Sasaki et al., “Effective nose-to-brain drug delivery using a combination system targeting the olfactory region in monkeys,” J. Control. Release, 2023, doi: 10.1016/j.jconrel.2023.06.005.
7. Mukesh Kumar, Shadab Ali, and Smriti Gohri, “Microsponge Drug Delivery Systems: Advancing Methotrexate Delivery for Rheumatoid Arthritis Management,” Curr. Pharm. Res., pp. 15–29, 2025, doi: 10.63785/cpr.2025.1.1.1529.
8. Y. Liu and D. Wu, “Bi-directional nasal drug delivery systems: A scoping review of nasal particle deposition patterns and clinical application,” 2023. doi: 10.1002/lio2.1190.
9. Tarmeen Ali, “Nanomedicine Approaches to Overcome Barriers in Pulmonary Drug Delivery for Respiratory Diseases,” Curr. Pharm. Res., pp. 30–44, 2025, doi: 10.63785/cpr.2025.1.1.3044.
10. [10] A. Thakar et al., “Chloroquine nasal drops in asymptomatic & mild COVID-19: An exploratory randomized clinical trial,” Indian J. Med. Res., 2021, doi: 10.4103/ijmr.IJMR_3665_20.
11. S. Cunha, B. Forbes, J. M. S. Lobo, and A. C. Silva, “Improving drug delivery for alzheimer’s disease through nose-to-brain delivery using nanoemulsions, nanostructured lipid carriers (NLC) and in situ hydrogels,” 2021. doi: 10.2147/IJN.S305851.
12. S. Ul Islam, A. Shehzad, M. Bilal Ahmed, and Y. S. Lee, “Intranasal delivery of nanoformulations: A potential way of treatment for neurological disorders,” 2020. doi: 10.3390/molecules25081929.
13. Z. Xu et al., “Effect of short-course glucocorticoid application on patients with chronic rhinosinusitis with nasal polyps,” World Allergy Organ. J., 2020, doi: 10.1016/j.waojou.2020.100131.
14. Shadab Ali, Smriti Gohri, Sayad Ahad Ali, and Mukesh Kumar, “Nanotechnology for Diabetes Management: Transforming Anti-diabetic Drug Delivery Systems,” Curr. Pharm. Res., pp. 45–59, 2025, doi: 10.63785/cpr.2025.1.1.4559.
15. R. Maher, A. Moreno-Borrallo, D. Jindal, B. T. Mai, E. Ruiz-Hernandez, and A. Harkin, “Intranasal Polymeric and Lipid-Based Nanocarriers for CNS Drug Delivery,” 2023. doi: 10.3390/pharmaceutics15030746.

16. L. A. Keller, O. Merkel, and A. Popp, “Intranasal drug delivery: opportunities and toxicologic challenges during drug development,” Drug Deliv. Transl. Res., 2022, doi: 10.1007/s13346-020-00891-5.
17. Bhanu Pratap and Pankaj Singh Jadaun, “Hydrogel Microneedles: A Breakthrough in Disease Treatment and Drug Delivery Systems,” Curr. Pharm. Res., no. 204101, pp. 60–77, 2025, doi: 10.63785/cpr.2025.1.1.6077.
18. J. Busner et al., “Clinician-and Patient-reported Endpoints in CNS Orphan Drug Clinical Trials: ISCTM Position Paper on Best Practices for Endpoint Selection, Validation, Training, and Standardization,” 2021.
19. S. Trabut, H. Friedrich, M. Caversaccio, and S. Negoias, “Challenges in topical therapy of chronic rhinosinusitis: The case of nasal drops application – A systematic review,” Auris Nasus Larynx, 2020, doi: 10.1016/j.anl.2020.05.026.
20. V. A. Duong, T. T. L. Nguyen, and H. J. Maeng, “Recent Advances in Intranasal Liposomes for Drug, Gene, and Vaccine Delivery,” 2023. doi: 10.3390/pharmaceutics15010207.
21. K. Singh et al., “Recent Advances in the Synthesis of Antioxidant Derivatives: Pharmacological Insights for Neurological Disorders,” Curr. Top. Med. Chem., vol. 24, no. 22, pp. 1940–1959, 2024, doi: 10.2174/0115680266305736240725052825.
22. S. Meirinho, M. Rodrigues, A. O. Santos, A. Falcão, and G. Alves, “Self-Emulsifying Drug Delivery Systems: An Alternative Approach to Improve Brain Bioavailability of Poorly Water-Soluble Drugs through Intranasal Administration,” 2022. doi: 10.3390/pharmaceutics14071487.
23. Robin Singh, “Revolutionizing Antimicrobial Therapies Through Biofilm-Targeted Nanomedicine,” Curr. Pharm. Res., pp. 78–97, 2025, doi: 10.63785/cpr.2025.1.1.7897.
24. J. Zhao, J. Yang, J. Jiao, X. Wang, Y. Zhao, and L. Zhang, “Biomedical applications of artificial exosomes for intranasal drug delivery,” 2023. doi: 10.3389/fbioe.2023.1271489.
25. M. R. Khan, D. Kumar, S. Shamim, K. Sunand, S. Sharma, and G. Rawat, “Ethnopharmacological relevance of Citrus limon (L.) Burm. f. as adjuvant therapy,” Ann. Phytomedicine An Int. J., vol. 12, no. 2, pp. 169–179, 2023, doi: 10.54085/ap.2023.12.2.19.
26. E. Santoro, P. Kalita, and P. Novak, “The role of saline nasal sprays or drops in nasal hygiene: a review of the evidence and clinical perspectives,” Rhinol. Online, 2021, doi: 10.4193/rhinol/20.072.
27. T. P. Crowe and W. H. Hsu, “Evaluation of Recent Intranasal Drug Delivery Systems to the Central Nervous System,” 2022. doi: 10.3390/pharmaceutics14030629.
28. Rinki Vishwas, “Peptide-Based Therapeutics in Fungal Infections: Challenges and Innovations,” Curr. Pharm. Res., no. 250001, pp. 98–115, 2025, doi: 10.63785/cpr.2025.1.1.98115.
29. S. Reilly, S. Dhaliwal, U. Arshad, A. Macerollo, N. Husain, and A. Da Costa, “The effects of rivastigmine on neuropsychiatric symptoms in the early stages of Parkinson’s disease: A systematic review,” 2024. doi: 10.1111/ene.16142.
30. K. M. Costa and G. Schoenbaum, “Dopamine,” 2022. doi: 10.1016/j.cub.2022.06.060.
31. J. Neumann, B. Hofmann, S. Dhein, and U. Gergs, “Role of Dopamine in the Heart in Health and Disease,” 2023. doi: 10.3390/ijms24055042.
32. G. Barszcz, D. Bartusik-Aebisher, and D. Aebisher, “Insulin,” in The Biochemical Guide to Hormones, 2023. doi: 10.5040/9798400605284.ch-051.
33. S. Buckley et al., “Maternal and newborn plasma oxytocin levels in response to maternal synthetic oxytocin administration during labour, birth and postpartum – a systematic review with implications for the function of the oxytocinergic system,” BMC Pregnancy Childbirth, 2023, doi: 10.1186/s12884-022-05221-w.
34. Shamim, S. Ali, T. Ali, H. Sharma, B. N. Kishor, and S. K. Jha, “Recent Advances in Monodisperse Gold Nanoparticle Delivery, Synthesis, and Emerging Applications in Cancer Therapy,” Plasmonics, vol. 20, no. 1, 2025, doi: 10.1007/s11468-024-02732-4.
35. M. Urošević, L. Nikolić, I. Gajić, V. Nikolić, A. Dinić, and V. Miljković, “Curcumin: Biological Activities and Modern Pharmaceutical Forms,” 2022. doi: 10.3390/antibiotics11020135.
36. Manisha Dev and Pallavi Chandel, “Nanostructured Lipid Carriers in Pulmonary Drug Delivery: Progress and Prospects,” Curr. Pharm. Res., pp. 131–143, 2025, doi: 10.63785/cpr.2025.1.1.131143.
37. V. Leta et al., “Gastrointestinal barriers to levodopa transport and absorption in Parkinson’s disease,” 2023. doi: 10.1111/ene.15734.
38. C. N. Metz and V. A. Pavlov, “Treating disorders across the lifespan by modulating cholinergic signaling with galantamine,” 2021. doi: 10.1111/jnc.15243.
39. A. K. Jaiswal et al., “Multi-targeted therapeutic exploration of Tamarix gallica flowers for anti-ulcer activity and associated complications,” J. Ayurveda Integr. Med., vol. 15, no. 4, p. 100947, 2024, doi: 10.1016/j.jaim.2024.100947.
40. X. Ji, A. L. Nielsen, and C. Heinis, “Cyclic Peptides for Drug Development,” 2024. doi: 10.1002/anie.202308251.
41. X. Luo et al., “Advancements, challenges and future perspectives on peptide-based drugs: Focus on antimicrobial peptides,” 2023. doi: 10.1016/j.ejps.2022.106363.
42. E. Taha, A. Shetta, S. A. Nour, M. J. Naguib, and W. Mamdouh, “Versatile Nanoparticulate Systems as a Prosperous Platform for Targeted Nose-Brain Drug Delivery,” 2024. doi: 10.1021/acs.molpharmaceut.3c00588.
43. E. Gasthuys et al., “Pediatric Pharmacology of Desmopressin in Children with Enuresis: A Comprehensive Review,” 2020. doi: 10.1007/s40272-020-00401-7.
44. Abhinay Tiwari, Anshu, Chirag Kumar, and Moh. Zaid, “Unravelling the Herbal Formulation of

Floating Microspheres for Gut Microbiome Modulation: Curren1Abhinay Challenges and Future Prospects," Curr. Pharm. Res., pp. 144–162, 2025, doi: 10.63785/cpr.2025.1.1.144162.
45. R. Pal et al., "The Comprehensive Review: Exploring Future Potential of Nasopulmonary Drug Delivery Systems for Nasal Route Drug Administration," J. Drug Deliv. Ther., 2024, doi: 10.22270/jddt.v14i3.6444.
46. F. Meier-Gibbons and M. Töteberg-Harms, "Follow-up studies of the classical landmark studies in Glaucoma," 2023. doi: 10.1097/ICU.0000000000000926.
K. Singh et al., "Deciphering the Genetic Landscape: Exploring the Relationship Between HLA-DQA1, HLA-DQB1, and HLA-DRB1 Genes in Diabetes Mellitus," Curr. Pharmacogenomics Person. Med., vol. 21, pp. 1–11, 2024, doi: 10.2174/0118756921310081240821065036.
47. O. Equils, K. Lekaj, A. Wu, S. Fattani, G. Liu, and L. Rink, "Intra-nasal zinc level relationship to COVID-19 anosmia and type 1 interferon response: A proposal," 2021. doi: 10.1002/lio2.513.
48. M. Schwarz et al., "Speech pathology prescribing in the outpatient setting: A review of requirements, considerations and barriers," 2022. doi: 10.1111/1460-6984.12756.
49. S. Nakhaee, F. Saeedi, and O. Mehrpour, "Clinical and pharmacokinetics overview of intranasal administration of fentanyl," 2023. doi: 10.1016/j.heliyon.2023.e23083.
50. Shivmohan, Gurpreet Kaur, Shivam Kumar, and Nisha, "Neuroprotective Effects of Seaweeds in Alzheimer's Disease: A Review," Curr. Pharm. Res., pp. 13–28, 2025, doi: 10.63785/cpr.2025.1.1.137149.
51. C. Wallick, K. Shulman, S. Siegert, L. Yedigarova, and C. Yonan, "Breath-powered nasal delivery of sumatriptan powder (AVP-825): an exploratory analysis of rapid response in migraine patients grouped by prior triptan history from the phase 3 TA rget study," J. Manag. care Spec. Pharm., 2015.
52. P. Kumar et al., "Fused Deposition Modeling 3D-Printed Scafolds for Bone Tissue.pdf," Appl. Biochem. Biotechnol., vol. 12, no. 22, pp. 1–11, 2024, doi: 10.54085/ap.2023.12.2.19.
53. N. Pradakis, N. Maniotis, and T. Samaras, "Computational Study of Magnetic Particle Motion inside the Nasal Cavity under the Impact of an External Magnetic Field for Biomedical Applications," Micromachines, 2022, doi: 10.3390/mi13111816.
54. P. Das, D. Kumar, V. Gupta, S. Gupta, R. Tanwar, and K. Behmani, "Sphingosomes: Advancements and Emerging Applications in Advanced Drug Delivery Systems," Curr. Pharm. Res., vol. 1, pp. 199–208, 2025, [Online]. Available: https://cpr.org.in/index.php/files/article/view/134/83
55. S. M. Hosseini et al., "A comparative evaluation of aluminum chloride hexahydrate gel iontophoresis versus tap water iontophoresis in people with primary palmar hyperhidrosis: A randomised clinical trial," Indian J. Dermatol. Venereol. Leprol., 2024, doi: 10.25259/IJDVL_975_2022.
56. J. Maeng and K. Lee, "Systemic and brain delivery of antidiabetic peptides through nasal administration using cell-penetrating peptides," 2022. doi: 10.3389/fphar.2022.1068495.
57. B. Pratap, S. Shamim, and S. Ali, "Formulation and Characterisation of Herbal Ethosomal Gel of Luliconazole and Clove Oil for Modified Drug Diffusion to the Skin," Res. J. Pharm. Technol., vol. 18, no. 8, pp. 3501–3508, 2025, doi: 10.52711/0974-360X.2025.00504.
58. Y. Zhu et al., "Multi-step screening of DNA/lipid nanoparticles and co-delivery with siRNA to enhance and prolong gene expression," Nat. Commun., 2022, doi: 10.1038/s41467-022-31993-y.
59. H. Duan, Y. Liu, Z. Gao, and W. Huang, "Recent advances in drug delivery systems for targeting cancer stem cells," 2021. doi: 10.1016/j.apsb.2020.09.016.
60. Shukar Singh, Gursewak Singh, Tawqeer Shafi, and Shafkat Hussain Malik, "Overview of Peptic Ulcer Disease: Epidemiology, Causes, Pathophysiology, and Clinical Importance," Curr. Pharm. Res., pp. 68–79, 2025, doi: 10.63785/cpr.2025.1.2.184192.
61. S. V. Prasad, P. Sudheer, and K. B. C. Shetty, "Current advances in nose to brain drug delivery," 2023. doi: 10.29090/psa.2023.03.23.477.
62. N. H. Mehta et al., "The Brain-Nose Interface: A Potential Cerebrospinal Fluid Clearance Site in Humans," 2022. doi: 10.3389/fphys.2021.769948.
63. Murari Kumar Maharaj, Aman Kumar, Tawqeer Shaf, and Shafkat Hussain Malik, "Mouth-Dissolving Films: A Novel Approach for Oral Drug Delivery in Diabetic Management," Curr. Pharm. Res., pp. 80–87, 2025, doi: 10.63785/cpr.2025.1.2.193199.
64. A. Maaz, I. S. Blagbrough, and P. A. De Bank, "In vitro evaluation of nasal aerosol depositions: An insight for direct nose to brain drug delivery," 2021. doi: 10.3390/pharmaceutics13071079.
65. A. Anand et al., "Neuroprotective Efficacy and Complementary Treatment with Medicinal Herbs: A Comprehensive Review of Recent Therapeutic Approaches in Epilepsy Management," CNS Neurol. Disord. - Drug Targets, vol. 24, no. 1, pp. 60–73, 2024, doi: 10.2174/0118715273332140240724093837.
66. J. Cui et al., "Inhalation Aromatherapy via Brain-Targeted Nasal Delivery: Natural Volatiles or Essential Oils on Mood Disorders," 2022. doi: 10.3389/fphar.2022.860043.
67. M. Raghav, V. Gupta, R. Awasthi, A. Singh, and G. T. Kulkarni, "Nose-to-brain drug delivery: Challenges and progress towards brain targeting in the treatment of neurological disorders," 2023. doi: 10.1016/j.jddst.2023.104756.
68. C. de Barros et al., "Formulation, design and strategies for efficient nanotechnology-based nasal delivery systems," RPS Pharm. Pharmacol.

Reports, 2022, doi: 10.1093/rpsppr/rqac003.
69. S. et al. Singh, K., Gupta, J. K., Chanchal, D. K., Khan, S., Varma, A., Shanno, K., Kumar, S., & Shamim, "Deciphering the Genetic Landscape: Exploring the Relationship Between HLA-DQA1, HLA-DQB1, and HLA-DRB1 Genes in Diabetes Mellitus," Curr. Pharmacogenomics Person. Med., vol. 21, no. 3, pp. 1–11, 2024, doi: 10.2174/0118756921310081240821065036.
70. M. Gao, X. Shen, and S. Mao, "Factors influencing drug deposition in the nasal cavity upon delivery via nasal sprays," 2020. doi: 10.1007/s40005-020-00482-z.
71. Imanshu, Mohita Thakur, and Deepika Bhatia, "Gingko biloba Herbal Plant Used for Treating Dementia and Alzheimer's Disease," Curr. Pharm. Res., pp. 105–115, 2025, doi: 10.63785/cpr.2025.1.2.215224.
72. H. A. Abo El-Enin et al., "Assessment of Nasal-Brain-Targeting Efficiency of New Developed Mucoadhesive Emulsomes Encapsulating an Anti-Migraine Drug for Effective Treatment of One of the Major Psychiatric Disorders Symptoms," Pharmaceutics, 2022, doi: 10.3390/pharmaceutics14020410.
73. T. To Quoc et al., "Development and Evaluation of an FDM Printed Nasal Device for CPZ Solid Nanoparticles," Molecules, 2023, doi: 10.3390/molecules28114406.
74. S. Chawla, R. Gupta, S. K. Jha, and K. T. Jha, "Stereoisomerism in Chemistry and Drug Development: Optical, Geometrical, and Conformational Isomers," Med. Chem. (Los. Angeles)., 2025, doi: 10.2174/0115734064366389250923044201.
75. R. Kumar, T. Islam, and M. Nurunnabi, "Mucoadhesive carriers for oral drug delivery," 2022. doi: 10.1016/j.jconrel.2022.09.024.
76. B. Sipos, G. Katona, F. M. Szarvas, M. Budai-Szűcs, R. Ambrus, and I. Csóka, "Development of Vinpocetine-Loaded Nasal Polymeric Micelles via Nano-Spray-Drying," Pharmaceuticals, 2023, doi: 10.3390/ph16101447.
77. A. et al. Kumar, J., M., T., Musayev, "Stimuli-responsive Hydrogels for Targeted Antibiotic Delivery in Bone Tissue Engineering," AAPS PharmSciTech, vol. 26, no. 217, pp. 1–23, 2025, doi: https://doi.org/10.1208/s12249-025-03218-0.
78. R. K. Yadav, K. Shah, and H. K. Dewangan, "Intranasal drug delivery of sumatriptan succinate-loaded polymeric solid lipid nanoparticles for brain targeting," Drug Dev. Ind. Pharm., 2022, doi: 10.1080/03639045.2022.2090575.
79. S. Raman, A. A. Khan, and S. Mahmood, "Nose to brain delivery of selegiline loaded PLGA/lipid nanoparticles: Synthesis, characterisation and brain pharmacokinetics evaluation," J. Drug Deliv. Sci. Technol., 2022, doi: 10.1016/j.jddst.2022.103923.
80. C. Surya Kumari, N. Srinavas Rao, S. Asha Begham, S. Suresh Babu, G. Durga Rao, and K. Venketeswara Rao, "FORMULATION TECHNIQUES OF LIPID BASED NANOPARTICLES: SLN/NLCS, ITS EVALUATION AND APPLICATIONS," Int. J. Res. Pharm. Chem., 2020, doi: 10.33289/ijrpc.10.1.2020.10(26).
81. Y. Gu, B. Schwarz, A. Forget, A. Barbero, I. Martin, and V. Prasad Shastri, "Advanced bioink for 3D bioprinting of complex free-standing structures with high stiffness," Bioengineering, 2020, doi: 10.3390/bioengineering7040141.
82. G. M. Keserű, "Az akadémiai-ipari együttműködések szerepe a gyógyszerfejlesztésben pandémia idején," Sci. Secur., 2021, doi: 10.1556/112.2021.00029.
83. T. Lapidot et al., "A Novel Faster-Acting, Dry Powder-Based, Naloxone Intranasal Formulation for Opioid Overdose," Pharm. Res., 2022, doi: 10.1007/s11095-022-03247-5.
84. P. Kumar et al., "Trends of Nanobiosensors in Modern Agriculture Systems," Appl. Biochem. Biotechnol., vol. 197, no. 1, pp. 667–690, 2024, doi: 10.1007/s12010-024-05039-6.
85. A. M. Salapatek, N. Werkhäuser, B. Ismail, R. Mösges, E. Raskopf, and A. Bilstein, "Effects of ectoine containing nasal spray and eye drops on symptoms of seasonal allergic rhinoconjunctivitis," Clin. Transl. Allergy, 2021, doi: 10.1002/clt2.12006.
86. J. Errecalde et al., "Safety and Pharmacokinetic Assessments of a Novel Ivermectin Nasal Spray Formulation in a Pig Model," J. Pharm. Sci., 2021, doi: 10.1016/j.xphs.2021.01.017.
87. S. Jacob, A. B. Nair, and J. Shah, "Emerging role of nanosuspensions in drug delivery systems," 2020. doi: 10.1186/s40824-020-0184-8.
88. D. Yadav, K. Kashyap, K. Atwal, and C. Singh, "Polymer nanoparticles of [(1-methyl-(S)-4,5-dihydroorotyl)-histidyl-prolinamide] as a potential central nervous system antidepressant formulation and their scale-up studies," Iran. Polym. J. (English Ed., 2024, doi: 10.1007/s13726-023-01271-9.
89. S. A. Ali, S. Ali, S. Rastogi, B. Shivhare, and M. Muztaba, "A Comprehensive Review on Advancements in Nanocarriers-Based Peptide Delivery for Cancer Therapeutics," Micro Nanosyst., vol. 17, no. 4, pp. 283–297, 2025, doi: 10.2174/0118764029358553250325040749.
90. Y. Mehmood et al., "Remdesivir nanosuspension for potential nasal drug delivery: determination of pro-inflammatory interleukin IL-4 mRNA expression and industrial scale-up strategy," J. Nanoparticle Res., 2023, doi: 10.1007/s11051-023-05784-5.
91. M. Naga Sujan, A. B. Patil, and D. V. Gowda, "A review on methods of preparation and characterisation of the solid lipid nanoparticles," 2020. doi: 10.5958/0974-360X.2020.00610.1.
92. P. P. Yeung et al., "Cariprazine in Pediatric Patients with Autism Spectrum Disorder: Results of a Pharmacokinetic, Safety and Tolerability Study," in Journal of Child and Adolescent Psychopharmacology, 2023. doi: 10.1089/cap.2022.0097.
93. C. Nadvornik et al., "Effect of Antibiotic Eye

Drops on the Nasal Microbiome in Healthy Subjects—A Pilot Study," Antibiotics, 2023, doi: 10.3390/antibiotics120305