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# Drug Delivery from Nose to Brain

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## Introduction

Over the last few decades, nose-to-brain medication administration has piqued attention as a potential treatment for a variety of CNS illnesses and psychiatric disorders. Several nasal formulations have been created to bypass the blood-brain barrier and deliver medications directly to the CNS via the olfactory and trigeminal pathways. However, medication absorption by the nasal mucosa is poor, and the volume of the nasal cavity is small, making nose-to-brain drug transport difficult. These issues could be addressed using formulations based on solid lipid nanoparticles (SLNs) or nanostructured lipid carriers (NLCs), which are excellent nose-to-brain drug delivery methods that increase drug solubility and penetration, extend therapeutic activity, and reduce enzymatic degradation. SLNs and NLCs nose-to-brain delivery methods have been studied in vivo pharmacokinetics and pharmacodynamics by several research groups. This review was conducted to provide an overview of these studies and to highlight research on SLN and NLC-based formulations for the treatment of CNS illnesses like neurodegenerative diseases, epilepsy, and schizophrenia. Based on assessments of their pharmacokinetic properties and toxicities, we evaluate the efficacies and brain targeting efficiency of these formulations, point out certain gaps in current knowledge, and recommend future developmental targets.

## Description

Drug development for CNS diseases and psychiatric disorders is difficult due to drug side effects, the brain's complexity, and, most importantly, the lack of effective ways for delivering pharmaceuticals across the blood-brain barrier (BBB) [1,2]. The BBB, which is made up of densely linked endothelial capillary cells, protects the CNS from infections and solutes in the blood [3]. Different ways exist for solute molecules to penetrate the BBB. Passive diffusion allows several lipid-soluble compounds to enter the brain. Lipophilicity of the chemical determines the rate and degree of penetration into the brain in this mechanism. Many of these compounds, however, are often pushed back into the circulatory system via efflux pumps found in the BBB.

Carrier-mediated transport transports small polar molecules such amino acids, glucose, nucleosides, and organic anions and cations. Receptor-mediated transcytosis is another route that transfers big molecules including iron, insulin, and leptin [4]. The penetration of a molecule over the BBB is influenced by its molecular weight, lipophilicity, H bond donors and acceptors, charge, and polar surface area, similar to Lipinski's rule of five [5]. As a result, only a few hydrophobic and low molecular weight compounds can traverse the BBB, while others are hindered by the BBB's barrier properties, making it challenging to produce medications that target the brain.

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## Conclusion

They increase nasal retention, reduce mucociliary clearance, improve drug solubility and permeability, minimise drug enzymatic degradation, and improve nasomucosal biocompatibility, SLN and NLC-based formulations have been developed and evaluated for nose-to-brain delivery in various studies. A growing body of evidence suggests that SLNs and NLCs are effective drug delivery systems capable of delivering medications to the brain via direct channels. However, several obstacles must be overcome, as promising SLN and NLC-based formulations in the preclinical stage may fail in the clinical stage for a variety of reasons. For starters, human and animal nasal canals are anatomically different. The length, surface area, volume, histology, and geometry of the nasal cavity vary by species and influence drug retention and absorption. Because of their low cost and accessibility, rats and mice were employed in the bulk of the studies included in this review for PK and PD studies. Their nasal cavities, on the other hand, are quite different from those of humans and other animals including rabbits, sheep, monkeys, and dogs. Rats and mice have small nasal orifices, which make intranasal delivery challenging, but rabbits, lambs, primates, and dogs have much bigger ones. Humans, rabbits, lambs, and primates have an olfactory region that occupies 10% of the nasal cavity, but mice, rats, and dogs have an olfactory region that occupies up to 50% of the nasal canal. Second, IN administration quantities vary by species, ranging from 10 L for mice to 40-50 L for rats and higher amounts for other larger animals. Micropipettes, syringes, nasal atomizers, sprays, and cannulas are also employed for administration, which may impact overall drug absorption and therapeutic benefits. Third, multiple methodologies have been employed to evaluate the brain targeting efficiencies of created formulations, and distinct experimental procedures for PK investigations on nose-to-brain transport by IN injection vary among research groups. As a result, PK studies on formulations designed for nose-to-brain distribution should be standardised to some extent.

## Conflict of Interest

None.

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