

# Kinetics Aspects in Design and Release of Nasal Drug Delivery Systems

Shubham Choudante<sup>1\*</sup>, Priya Deshmukh<sup>2</sup>, Vaishali Kadam<sup>1</sup>, Harshal Tare<sup>3</sup>

<sup>1</sup>Saraswati Institute of Pharmacy, Pangri Nanded, Maharashtra, India.

<sup>2</sup>Department of Quality Assurance, School of Pharmacy, SRTM University, Nanded, Maharashtra, India.

<sup>3</sup>Dr. Harshal Tare (OPC) Pvt. Ltd., Jalgaon, Maharashtra, India.

Received: 21<sup>st</sup> May, 2024; Revised: 01<sup>st</sup> June, 2024; Accepted: 10<sup>th</sup> June, 2024; Available Online: 25<sup>th</sup> June, 2024

## ABSTRACT

The traditional school of Indian medicine includes a sort of nasal therapy known as Nasya karma. There is a lot of recent interest in using the nasal route for administering difficult medications including tiny polar compounds, vaccines, hormones, peptides, and proteins. Nasal drug molecules are highly suited for systemic distribution and the absence of hepatic first-pass metabolism. Vaccination through the nose is thought to be a straightforward and economical method with improved patient compliance, and it may also provide immunity at numerous distant mucosal locations. Microparticle, nanoparticle, and liposomal nasal vaccination delivery technologies are now in development and show protection in animal models. Both pharmacokinetics & pharmacodynamics of nasal administration devices have been studied *in-vivo* by a number of different research organizations. The purpose of this review was to summarise these studies and bring attention to the work done on nasal-based formulations to better treat conditions like epilepsy, schizophrenia, and neurodegenerative diseases.

**Keywords:** Nasal delivery, Pharmacokinetics, Nose to CNS Delivery, Nasal vaccines.

International Journal of Drug Delivery Technology (2024); DOI: 10.25258/ijddt.14.2.00

**How to cite this article:** Choudante S, Deshmukh P, Kadam V, Tare H. Kinetics Aspects in Design and Release of Nasal Drug Delivery Systems. International Journal of Drug Delivery Technology. 2024;14(2):1191-1197.

**Source of support:** Nil.

**Conflict of interest:** None

## INTRODUCTION

Drugs that are effective at low doses and have no minimum oral bioavailability are good candidates for nasal medication administration. In contrast to oral delivery, which is subject to first-pass clearance by the liver, the nasal route is safe for self-administration and requires no special preparation. There are now two categories of drugs available for nasal administration. The first group includes OTC medications used for the treatment of nasal mucosa and sinuses. The second group consists of the very few medications that can be absorbed through the nasal passages to have systemic effects. Compounds that are poorly absorbed after oral administration, are unstable in the gastrointestinal tract and undergo substantial biotransformation are prime candidates. Therefore, peptides and protein medicines in particular, may benefit from a potential new delivery method: the nasal cavity<sup>1</sup>.

### Mechanism of Drug Absorption

The following two methods are the most commonly considered, while others have been proposed. The first is the transfer via an aquatic pathway, also called the paracellular pathway. This is a slow and inactive path. Intranasal absorption of water-soluble substances is proportional to the inverse of their molecular weight. Drugs with molecular weights over 1000 Daltons were

shown to have low bioavailability. Lipophilic medications that exhibit a rate dependency on their lipophilicity are transported by transcellular process, which involves transport via a lipoidal pathway. Active transport of drugs through cell membranes via the opening of tight junctions is another mechanism.<sup>2</sup> The cell types are given in Figure 1.

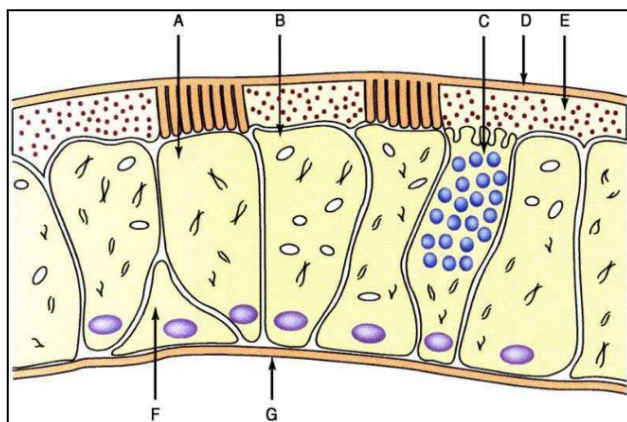
### Nasal Administration

Insufflation through nose passages, more often known as “snorting,” is a common method of medication administration. It can be used topically or injected into the body. Nasal sprays, like decongestants used to treat the common cold and allergies, are locally acting medications with low systemic effects. Nasal sprays are a convenient delivery method for a variety of systemically active pharmaceuticals, including those used to treat migraines, overdoses, seizures, nicotine addiction, and hormonal imbalances<sup>3</sup>(Figures 2, and 3).

### Advantages of Nasal Systemic Drug Delivery

The nasal cavity is lined with a thin mucosa that is rich in blood vessels. Therefore, it is conceivable for a drug molecule to bypass the liver and intestines and enter the systemic blood circulation via fast transport *via* a single epithelial cell layer. For smaller molecules, this usually happens within 5 minutes. Crushing or crushing pills or capsules and inhaling

\*Author for Correspondence: shubhamchoudante2@gmail.com



**Figure 1:** Cell types of the nasal epithelium showing ciliated cell (A), non-ciliated cell (B), goblet cells(C), gel mucus layer (D), sol layer (E), basal cell (F) & basement membrane (G)

the resulting powder is an alternative to oral delivery that can lead to a faster onset of effects. This method of administration is also useful for drugs that have a low rate of oral absorption or that are significantly broken down in the liver and intestines.<sup>4</sup>

#### Disadvantages of Nasal Drug Delivery System

Nasal administration is ideal for potent drugs because just a small amount is required. Because of the risk of permanent damage to the nasal epithelium, medications that require constant and frequent administration are less preferred. It has also been established that the amount of drug absorbed following nasal administration varies greatly. Nasal mucosal sensory irritation, the amount of liquid that is eaten rather than retained in the nasal cavity, and the actuation mechanism utilized to direct the spray are all potential contributors to variability. However, absorption *via* nasal delivery should be equally as varied as following oral dosing.<sup>5</sup>

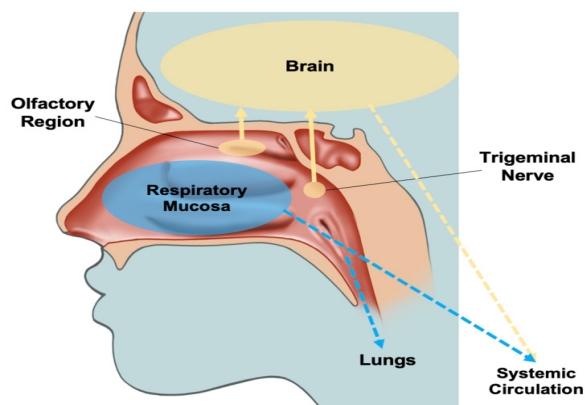
#### Formulations Based on Nasal Drug Delivery Systems

Nasal preparations available without a prescription are often solutions used to alleviate the symptoms of allergies and the common cold that manifest in the nose. A simple medication solution will do, as it will allow for more uniform distribution over a larger region. Such a formulation has a short nasal residence duration (between 3 and 20 minutes), with a lot of variation between people.

#### Liquid Dosage Forms

##### *Nasal drops*

It is a popular and effective method of administration because of its ease of use and portability. The lack of dosage precision is the fundamental drawback of this approach. Almotriptan malate nasal solutions were made in phosphate buffer with varying concentrations of HPMC E15. Franz diffusion cells equipped with dialysis membranes were used for *in vitro* permeation research, and the nasal mucosal layer of sheep was used for *ex vivo* permeation studies. Radioactive <sup>99m</sup>Tc was added to the formulations so that the nasal residence time in rabbits could be measured. Rats were tested for



**Figure 2:** Intranasal systemic delivery

nasal discomfort. Almotriptan release was not slowed in formulations made with HPMC E15 5% w/v. Research using gamma scintigraphy revealed a lengthened duration spent in the drug's system compared to control solutions. There was no evidence of nose discomfort, and the formulations held up well over a three-month period.

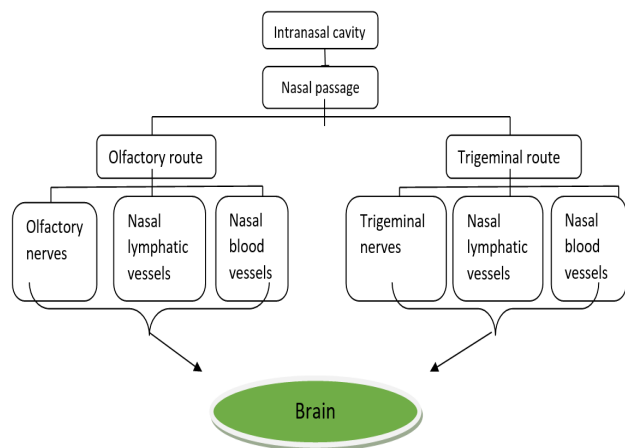
##### *Nasal sprays*

It is made from either a solution or a suspension. Metered dose pumps and actuators make it possible for a nasal spray to accurately administer a dose between 25 and 200 L. There hasn't been as much research done on nasal emulsions, microemulsions, or intranasal emulsions as there has been on other liquid nasal delivery techniques. Because of their high viscosity, nasal emulsions are ideal for targeted delivery. Dosages in semi-solid state nasal drug delivery systems often make use of semi-solid systems.

##### *Nasal gels*

Nasal gels are highly viscous liquids or suspensions that are administered by the nose. Nasal gels have many benefits, including less post-nasal drip due to their high viscosity, less swallowing and hence less flavor influence, and less anterior leakage of the formulation. Pills and capsules

In terms of morbidity and cost to society and the economy, allergic rhinitis (AR) is a major problem. When nasal congestion is a prominent symptom, intranasal corticosteroids are often prescribed. Varied intranasal corticosteroids have varied structures and pharmacokinetic and pharmacodynamic features, which must be taken into account when comparing their efficacy and safety profile in the treatment of AR. These medications have expanded dramatically. In the case of allergic respiratory illnesses, research has shed light on the medications' methods of action, pharmacologic qualities, and clinical impact. While current intranasal corticosteroids are very effective, it would be great to see even more advanced formulations introduced that have a better efficacy/safety profile. The new nasal spray form of the corticosteroid fluticasone furoate has improved affinity and a novel side-actuated delivery system. It's a promising option for treating



**Figure 3:** Nasal delivery to brain

rhinitis because it's highly effective when used topically and has a low risk of producing systemic side effects.

#### *Nasal suspensions and emulsions*

It's interesting to note the underutilization and under-researched aspects of nasal medication delivery techniques that utilize suspensions. Nasal drug delivery can offer advantages in terms of rapid onset of action, avoidance of first-pass metabolism, and potential for local or systemic drug effects depending on the formulation. Let's discuss the two points you mentioned:

- *Nasal aqueous suspension of loteprednol etabonate*

Loteprednol etabonate is a corticosteroid with anti-inflammatory properties often used in ophthalmic preparations. The use of a nasal aqueous suspension of this drug for allergic rhinitis is an interesting concept. Nasal suspensions may allow for prolonged contact with the nasal mucosa, potentially enhancing drug absorption and local therapeutic effects. Similar to ophthalmic suspensions, which are well-established in the market, nasal suspensions could be designed to provide sustained drug release in the nasal cavity.

- *Nasal insulin delivery with absorption enhancers*

The idea of using a nasal solution for insulin administration is also intriguing. Nasal delivery of insulin could provide a non-invasive alternative to subcutaneous injections, which are the standard route of administration for insulin. The use of absorption enhancers, such as soybean-derived steryl glycoside and sterols, to improve the bioavailability of insulin through the nasal mucosa is a promising approach. Achieving pharmacological bioavailabilities of 6.7 and 11.3% with these enhancers suggests that nasal delivery of insulin could be a viable option, although further research and development would be necessary to refine the technique.

Both of these examples highlight the potential of nasal drug delivery as an alternative or complementary route to traditional administration methods. However, emulsions are preferred over suspensions for improving the bioavailability of

poorly soluble medicines when it comes to oral drug delivery, and the same is true for nasal formulations. Solubilization of the medication and the presence of lipophilic absorption enhancers have been linked to the improvement in absorption observed. In 2015, Klang et al. employed a nano-suspension to enter the brain via the nasal passages. When created as a nanosuspension, particles between 1 and 500 nm in size were able to cross BBB. Researchers have also claimed success with nanoemulsions delivered via the nasal route for use in brain targeting<sup>6</sup>.

### **Solid Dosage Forms**

#### *Nasal powders*

If it is impossible to create a drug-stable liquid dosage form, like a solution or suspension, then a powder form could be created. Nasal powder has the benefits of being a preservative-free formulation with excellent medication stability. However, the active medication and/or excipient's characters will determine the acceptability of the powder formulation.

There are a number of different polymers that can be used as mucoadhesive agents. All of the materials were chosen because of their low toxicity. Therefore, we selected excipients that are either listed in the FDA's inactive ingredient database. Next-generation products are being researched that take advantage of the advantages of nasal administration, such as the presence of immune-competent cells, a direct route to the brain, and the ease of access to the relatively permeable mucosa. However, there is a lack of accessible *in-vitro* systems that may be used to characterize this effect. This research aimed to determine how well various approaches to studying the impact on contact time might be applied to the process of selecting excipients for powder formulations. An additional method for gauging the unpleasantness of powders' proximity to the mucosa was developed: the slug mucosal irritation assay. These techniques are thought to be helpful for competitive screenings during the preformulation stage of product creation.<sup>7</sup>

#### *Novel drug formulations*

In order to improve intranasal drug delivery, several arguments have been presented in favor of creating nasal formulations with novel formulations. Nasal absorption enhancers, mucoadhesive polymers, and enzymatic inhibitors are all examples of systems that can be used to boost important activities.

#### *Liposomes*

Phospholipid bilayers enclose one or more aqueous compartments in which medications or other compounds can be encapsulated to form vesicles known as liposomes. In addition to its efficacy, liposomal drug delivery systems have other benefits, such as being able to encapsulate molecules of varying sizes, hydrophilicity, and pKa values. Nasal administration of peptides like insulin and calcitonin has been shown to improve their uptake by improving membrane penetration. This has been linked to the fact that our ability to retain peptides in the nose is improving.

Additionally, liposomal drug delivery methods were

reported to be beneficial for non-peptide medications, such as nifedipine, in addition to the influenza vaccination. Various liposome compositions are available for use. The study found that intranasal administration of a liposome solution of levonorgestrel resulted in a quick onset of action and prolonged delivery of the drug. Acyclovir in a liposomal gel showed promising outcomes when administered *via* the nasal route. Direct absorption *via* the nasal mucosa was made possible by the application of a liposomal gel, which not only increased the drug's time in contact with the absorptive site. Liposomal formulations were compared to a free medication suspended in gel, leading to these findings.

#### Nanoparticles

There has been a lot of buzz around nanotechnology recently. Improvements in medication administration in the nose are the focus of current research into nanoparticle systems. Nanoparticles are also known as nanosatellites. Therapeutic applications for these macromolecular materials include serving as carriers for dissolving, entrapping, encapsulating, adsorbing, or chemically attaching the active component. Only the tiniest nanoparticles are able to permeate the paracellular pathway in a significant amount. Using nanoparticles for intranasal medication delivery has had mixed outcomes. It's been shown in numerous studies that nanoparticle compositions greatly improve drug delivery through the nasal passages. However, recent research has shown that nanoparticle technologies may be best for nasal vaccination administration.

#### Microspheres

Formulations for nasal medication administration have made extensive use of microsphere technology. Microspheres offer benefits for intranasal drug delivery since they are often made from mucoadhesive polymers (chitosan alginate). Microspheres may potentially prevent the drug from being metabolized by enzymes and maintain drug release.

Microspheres of tramadol HCl were developed by Veena B *et al.* for rapid administration in the brain. In the microsphere formulations, they used a mucoadhesive polymer with a lower viscosity grade HPMC (E15) and experimented with varied drug-to-polymer ratios. Spray-dried microspheres were studied in rabbits for radio imaging and histopathology. The drug was molecularly dispersed and changed into an amorphous form, as shown by DSC and XRD studies. Microspheres were measured using a scanning electron microscope (SEM), which confirmed their spherical shape and smooth surface. Nasal mucosa is undamaged by the microspheres and they adhere well enough to the mucosa to be used. Optimization of the formulation resulted in a 94% drug release after 90 minutes *in-vitro*. According to the MRI results, the drug was really located in the brain.

#### Drug release in-vivo nasal kinetics

DTE is a critical parameter that measures the proportion of the administered drug that reaches the brain. It provides a quantitative assessment of how efficiently the drug is targeted to the brain following nasal administration. DTP represents the

percentage of the administered drug that successfully crosses the blood-brain barrier (BBB) and enters the brain tissue. A higher DTP indicates better drug transport to the brain. The effectiveness of nose-to-brain delivery methods relies heavily on the DTE and DTP. Drug brain uptake after intravenous (IN) delivery as a percentage (DTE%).

$$DTE\% = \frac{(AUC_{brain,IN})/(AUC_{blood,IN})}{(AUC_{brain,IV})/(AUC_{blood,IV})} \times 100$$

where the AUC is calculated over the course of the whole research (AUC<sub>0-t</sub>). The values of DTE% might be anywhere from 0 through. If the DTE% is more than or equal to 100, then brain targeting was successful. Values in the Log10 (DTE %) form are also employed.

DTP% is the fraction of a drug that makes it all the way to the brain without going through the digestive system.

$$DTP\% = \frac{AUC_{brain,IN} - \left(\frac{AUC_{brain,IV}}{AUC_{blood,IV}} \times AUC_{blood,IN}\right)}{AUC_{brain,IN}} \times 100$$

By deducting this value, we may calculate the amount of medication that crossed the BBB from the blood and entered the brain indirectly.

$$DTP\% = \left(1 - \frac{100}{DTE\%}\right) \times 100$$

Theoretically, DTP% numbers can be anything from 0 to 100. DTP% = 0 if no drugs are shipped via direct routes. However, DTP% numbers are sometimes 0 due to DTE% values being 100. When the DTP% is high, it shows that the medication is being taken directly to the brain. A high DTP% value suggests that a drug has difficulty crossing the BBB, while a value of 100 implies that the medication cannot cross the BBB (AUC<sub>brain,IV</sub> = 0). DTE% and DTP% are typically calculated using the AUC values of free medicines (IN). However, in certain cases, the AUC values of SLNs or NLCs (IN) have been used instead. To eliminate this disparity, we recalculated the DTE% and DTP% values that were used in these analyses.

However, in the case of very low AUC<sub>blood,IN</sub>, DTE% and DTP% may be elevated despite a low AUC<sub>brain,IN</sub>. This is because DTE% and DTP% are valuable measurements for determining brain targeting by IN formulations. As a result, we use certain further criteria. Drug buildup in the brain following IN delivery is symbolized by the sign B<sub>IN/IV</sub>, where IV stands for intravenous.

$$B\%_{IN/IV} = \frac{AUC_{brain,IN}}{AUC_{brain,IV}} \times 100$$

If the B<sub>IN/IV</sub> number is greater than 100, more of the medication has been deposited in the brain after IN administration than after IV treatment.<sup>8,9</sup>

#### Nasal to brain drug delivery system

Drugs taken *via* the intranasal route reach the brain quickly and efficiently because they travel directly from the nose to the skull.

The enormous barriers to delivering medications selectively and effectively to the brain are a major cause of the difficulties in treating brain illnesses. The main obstacle to getting the medicine to the brain is BBB. Bypassing BBB & delivering treatments directly to the brain is made easier through intranasal delivery, which is both non-invasive and easy. The nasal mucosa must be quickly and efficiently crossed when a medicine is administered in this manner. Drug deposition, drug absorption, and drug clearance issues can arise due to the complexity of the nose. With no need to worry about the blood-brain barrier (BBB) or gastrointestinal (GI) exposure, the intranasal route stood out as a promising alternative for therapeutic brain targeting (Martins, Collaborators, 2019). Since its inception in 1989 with the purpose of delivering neurotrophic factors to the brain, intranasal drug delivery has emerged as a promising new option for direct CNS drug administration. It was hypothesized that big, polar medicines may be administered directly to CNS using this method. The nasal cavity is only an opening via which sensory nerve fibers can reach the central nervous system, making this a real possibility.

#### *Advantages*

- Almost all macromolecular medications and more than 98% of small molecule pharmaceuticals are thought to be impermeable by the blood-brain barrier. However, this route can transport the drug straight to the brain.
- Through this pathway, the digestive system and the liver are bypassed.
- Deposition of medication in the nasal cavity increases the likelihood that it will be taken up by cells lining the olfactory or trigeminal nerve pathways or absorbed into the systemic circulation rather than being broken down by enzymes and cleared quickly by the mucociliary system.

#### *Limitations*

- Dose-volume is the limitation for this system. For liquids, it is 100 to 250  $\mu\text{L}$ , and for powders 20 to 50 mg and depends on the bulk density of the powder.
- Only very powerful medications are practical candidates for this approach.
- It is important to prevent the breakdown of drugs that are metabolized by nasal enzymes.
- The nasal cavity should not be irritated by the drug's composition.
- To administer medication directly into the brain, a nasal delivery device is necessary.

#### *Mechanism of nose-to-brain drug transport*

The nasal cavity is the first part of the respiratory system and the starting point for airflow into the body. The nasal septum separates the two halves of this space. The mucous membrane lines the cavity's interior and serves as the body's first line of defense against invading organisms, poisons, pathogens, and allergens. There are three distinct areas within the nasal cavity: the vestibular area, the respiratory area, and the olfactory area. The back of the nose and the front of the nose are the two primary sections of the nasal cavity. The vestibular region, commonly

referred to as the nostril openings is located in the nasal cavity's anterior half, whereas the posterior region is rich in olfactory sensory neurons that perceive smell. Both a base supporting cell layer and an olfactory epithelium make up the olfactory layer. The olfactory neuroepithelium is a one-of-a-kind structure that connects CNS to the atmosphere. Therefore, the olfactory route is extensively investigated to circumvent the BBB and deliver the medication directly to the CNS. The trigeminal nerve, on the other hand, links the nasal cavity to the frontal lobes and parietal lobes of the brain. The olfactory and respiratory epithelia are well-known sites of molecular absorption. Transcellular transport is used to move the molecules from the olfactory region to the olfactory bulb. Trigeminal nerves carry molecules from the nasal respiratory epithelium to the brain. Once inside the brain, it is carried by extracellular convective bulk flow or perivascular pathways to other regions.

Nasal cavity formulations are most commonly utilised as simple solutions or gels. When compared to other types of particulate delivery systems, emulsions and nanoparticles and were utilised more frequently.

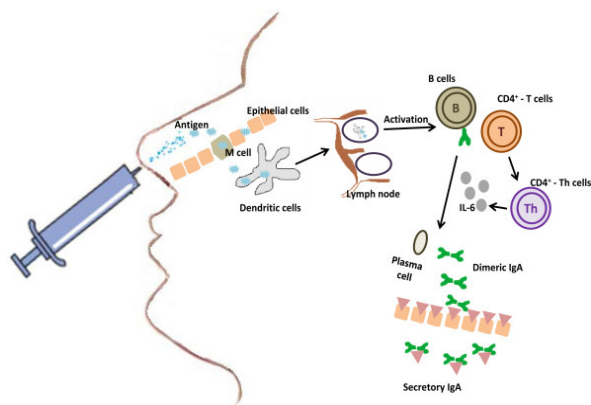
Using magnetic resonance imaging, researchers determined that the typical human nasal cavity has a volume of 16,449.81 and 4288.42  $\text{mm}^3$ , and that the area of the nostril entrance is 357.83 and 108.09  $\text{mm}^2$ . The size of the nasal cavity was found to be positively correlated with the size of the nostril aperture. There was no difference between the sexes in terms of average nasal cavity volume.

Human investigations have shown that intranasal insulin is present in the cerebrospinal fluid, where it enhances cognitive function in those with Alzheimer's disease. These results show that the nasal-to-cognitive pathway is useful in humans, especially when it is desirable to minimize drug activity in the periphery.

The nasal route has been quite successful in treating epilepsy. Different nanoformulations of antiepileptic medicines exist. Nanostructure lipid carriers are utilized to create commonly prescribed medications like valproic acid and lamotrigine. Both nanostructure lipid carriers and solid lipid nanoparticles of carbamazepine are commercially accessible. Oxcarbazepine, another vital medication, is available in emulsified form. The nanoliposomal formulations of lamotrigine and olanzapine are particularly exciting.

AptarPharma has developed the first nasal rescue medication for epileptic patients using its Unidose Liquid System. It can be used in treatments when a tiny but exact dose of the medicine must be administered all at once.

Intra-nasal lamotrigine-PLGA nanoparticles have been created to treat neuropathic pain. Using a modified nanoprecipitation approach involving high-velocity homogenization & ultra-sonication, the LTG-PLGA nanoparticles were produced. The generated LTG-PLGA nanoparticles had an entrapment efficiency (EE) of 84.871.2% and a drug loading of 10.210.89%. Nanoparticles that were created have a mean particle size of 184.6 nm. Biodistribution studies estimated medication concentrations in the blood and brain using several pharmacokinetic factors. The result



**Figure 4:** Schematic representation of immune response induction after nasal immunization

attained had a  $C_{max}$  of 3.82%/g and a  $T_{max}$  of 1.5 hours. This study demonstrated that nasal administration of lamotrigine was successful. In this investigation, nanoemulsions serve as a model carrier for fluorescent bioimaging methods. Two standard probes, DiR and coumarin-6 (C6), are embedded to represent the cargos, and two new types of environment-responsive dyes, P2 and P4, are activated by an on-off signal to identify NEs in biological tissues. Delivery was also shown to be higher in all of the examined regions of the brain, suggesting that the synthesized nanogel may be able to circumvent some of the most pressing problems caused by insulin-free administration.

Paliperidone-loaded microemulsion for intranasal distribution was investigated as a potential treatment for schizophrenia using the spontaneous micro emulsification technique. Swiss albino rats were used to study pharmacokinetics in the central nervous system.

The use of nanoparticles to facilitate direct drug delivery from the nasal cavity to the brain has been studied intensively over the past decade for its potential to improve the treatment of neurological disorders. PEGylation was examined for the first time as a mucus penetration booster. The research was conducted to determine if polycaprolactone (PCL) nanoparticles (PCL-NPs) enclosing bexarotene, a putative neuroprotective chemical, could be delivered from the nose to the brain. These findings supported the hypothesis that PEGylation of PCL nanoparticles with PCL-PEG5% could improve intranasal medication delivery to the brain by decreasing NP interactions with mucus.<sup>10</sup>

Nasal *in-situ* gel with methylcellulose as the basis is a new delivery system for the anti-Parkinson's medication piribedil. PBD was instilled in the olfactory area of the nose through intranasal administration utilizing a cannula-microtip combination. Researchers found that intranasal administration of PBD has benefits above the standard oral treatment.<sup>11</sup>

#### *Approaches to facilitate nose-to-brain delivery*

The following facts illustrate the variety of methods employed to facilitate medication administration via the nasal route to the brain, as well as the existence of methods to prevent such drug delivery.

#### *Strategies for nose-to-brain drug delivery*

To facilitate nose-to-brain delivery

To block nose-to-brain delivery

- Permeation enhancers
- Induction of efflux transporters
- Enzyme inhibitors
- Chemical structural change
- P-glycoprotein inhibitors
- Increasing the size of nanoparticles
- Prodrugs
- Site of deposition
- Inhibitors of the mucociliary clearance
- Inhibiting endocytosis
- Nanoparticles
- Using lidocaine
- Cell-penetrating peptides
- Magnetophoresis
- Eutectic mixtures
- Ultrasound
- Vasoconstrictors
- Devices

#### *Challenges in nose to brain delivery system*

The nasal passage has a lower surface area than the oral cavity, therefore, less of the medication enters the bloodstream. Significant obstacles to intranasal drug delivery include the short contact length, etc.

#### *Intranasal vaccine*

Immunizations given through the nose, or intranasally are less invasive and more practical than other delivery methods. Antigens, patient characteristics, and commercial considerations all play a role in determining which delivery mechanism is used. Nasal vaccine can be administered in a variety of ways. Vaccine delivery technologies for mucosal vaccines has progressed. The oral and nasal methods of mucosal immunization are the most popular and widely available. Snuff, cocaine, and other hallucinogens and psychotropics have all been used in the nose for decades. Similarly, antihistamines, antibiotics, and non-peptide medicines have all been used intranasally for their local effect on the mucosa for quite some time. Initially released in 2001, the first nasal influenza vaccination was taken off the market due to safety concerns. In 2003, a syringe-sprayer-based intranasal vaccine called Flumist was introduced. Nasal immunization, for example, elicits powerful immunoglobulin A (IgA) secretion in the respiratory system, demonstrating how delivery and route of administration both contribute to a vaccine's success. Compared to parenteral and oral administration, nasal delivery of vaccinations has been proven to yield higher systemic bioavailability and protection from gastrointestinal enzymes. Vaccines administered *via* the nose have a greater overall efficiency because they operate as a "first entry block," preventing pathogens from entering the body while also infiltrating the mucosal surface and eliciting local microbial-specific immune responses. Furthermore, mucosal

absorption of vaccines into the blood circulatory system can be a fast process. Due to its high concentration of T cells, B cells, and plasma cells, as well as its ability to elicit antigen-specific systemic and mucosal adaptive immune responses, vaccination through this route is optimal. The absence of needles in the distribution process increases patient compliance.<sup>12</sup>

#### *Benefits and challenges of developing nasal vaccines*

There are a number of benefits to administering vaccines through the nose, making it a viable option (Figure 4).

- Nasal absorption is enhanced by the presence of many microvilli in the nasal epithelium.
- Needles and syringes are unnecessary for nasal immunisation.

#### **CONCLUSION**

From this review, it can be concluded that now a days, researchers are putting a lot of emphasis on finding better ways to deliver medications. Due to their sensitivity or high molecular weight, many newly developed medicines have extremely low oral bioavailability. It is necessary to find an alternate route that avoids the hepatic first pass effect, the entire gastrointestinal tract, and stomach acid. Opting for nasal medication administration could be a powerful alternative. Numerous anastomoses and redundancy in blood flow make the nose a very vascular structure. When a drug is applied to the nose, cilia in the nasal cavity move it to the gastrointestinal (GI) tract, where it can also be absorbed. This process, called mucociliary clearance (MC), can be assumed to follow first-order kinetics. The mucus adhesion system can help drugs stay at the absorption site longer, while the mucus penetration system can help distribute particles more widely and penetrate them deeper. The nasal epithelium is highly permeable and vascularized, which can help drugs enter the body. When certain medications cross the nasal mucosa, they can be transported through the lymph capillaries, which are part of a well-developed lymphatic network.

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