Review Article

Nasal Drug Delivery System - An Overview

Senthil kumar K[1*], Manoj Varma G[1], Vudaykiran A[1], R Arun kumar[1] and B Sudhakar[2]

[1]Sri Adichunchanagiri College of Pharmacy, B.G. nagara, Karnataka, India.
[2]Scientific manager, The Himalaya Drug Company, Bangalore, Karnataka, India.

INTRODUCTION

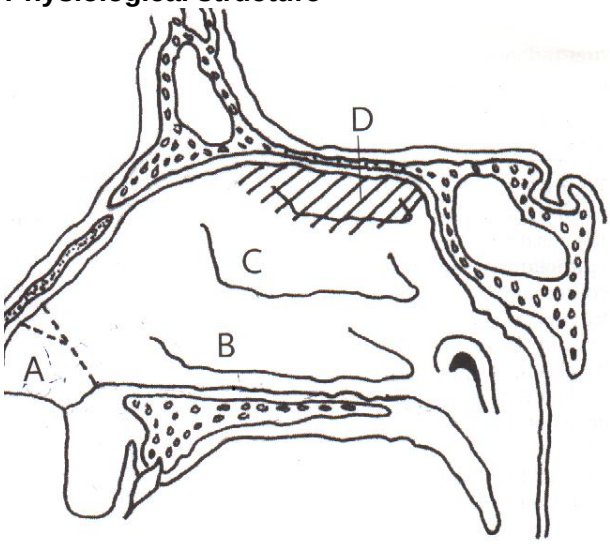
Certain drugs are delivered to the nasal cavity because their intended site of action. These are administrated as nasal drops or sprays for a local effect. Such drugs in clinical use include decongestants, antibiotics and mucolytics.

The nasal cavity may also be exploited as a route of entry into the systematic circulation, either because the absorption profile of the drug is appropriate to its clinical application or destroyed in the gastrointestinal fluids or metabolized in the wall of the gastrointestinal tract or undergo extensive biotransformation by the liver during their first passage around the circulation.

Structure and physiology of the nasal cavity

The nasal cavity 12-14 cm, from the nostril to the nasopharynx (throat) and is divided laterally, by the nasal septum.

Physiological structure



A-Nasal vestibule, B-Inferior turbinate, C-Middle turbinate, D-Superior turbinate

The nasal vestibule has the smallest cross-sectional area in the respiratory tract (approximately 0.3cm2on each side) and extends from the entrance of the nostrils, which are guarded by long vibrissae (hair), to the anterior ends of the inferior turbinate. The olfactory region of the nose is located towards the roof of the nasal cavity. The nasal mucosa is highly vascular.

Olfaction

One of the functions of nose in man is that of olfaction. It is about 10 cm. The olfactory region of the nose is a small patch of tissue containing the smell receptors. It is located towards the roof of the nasal cavity and is lined with non-ciliated neuro-epithelium. Approximately 20% of the air flowing through the nasal cavity is directed upwards to the olfactory region.

Modification of inspired air

The principal function of the nasal cavity in man is that of air conditioning. The anatomy of the nose permits intimate contact between the inspired air and the mucosal surface enabling the air to be warmed and humidified by the vasculature and secretions of the epithelium.

- Inspired air of 23 C and 40% relative humidity can be brought to 320C and 98% relative humidity upon inhalation via the nose.
- An additional form of air conditioning is concerned with the removal of particulate, such as dust, micro organisms and allergens, from the inspired air.
- The efficiency of particle removal from the air-steam is dependent on a

number of factors including the aerodynamics diameter of the inhaled particles:

- Particles greater than 10µm are generally filtered out by the vibrissae (hair) at the nostrils.
- Smaller particles (approximately 5-10µm) tend to deposit in the nasal passage and are subsequently cleared by the process of mucociliary clearance.
- Particles less than 2µm are not normally filtered out and may enter the lungs.

Mucociliary clearance

Mucociliary clearance contributes to the body's defence mechanisms by entrapping potentially hazardous substance, such as dust and micro organisms, with in the viscoelastic mucus blanket lining the nasal passage.

Efficient mucociliary clearance on a successful relationship between the:

- Periciliary fluid
- Mucus
- Cilia

Changes in any of these three parameters can alter the characteristics of clearance.

Periciliary fluid

Periciliary fluid is a watery, ionic solution maintained by transepithelial ion-transport that provides an environment within the cilia is able to beat. It also provides a reservoir of fluid for the humidification of inspired air.

Mucus

The mucus plays a number of important physiological roles:

- It entraps substance entering the nasal cavity and participates in the removal of particulates via mucociliary clearance. This process protects the underlining mucosa.
- The capacity of the mucus to hold water permits the humidification of the inspired air and also aids heat transfer, since water is a better conductor of heat than air.
- Approximately 1.5-2 litres of mucus is secreted daily by goblet cells and serous glands within the nasal cavity.

Composition of mucus

Water: 90-95%
Salt : 1-2%
Mucin: 2-3%
Proteins, enzymes, antibiotics etc.

Cilia: The beat cycle of respiratory tract cilium is composed of three phases:

Effective stroke

The cilium maximizes its height enabling the "ciliary crown" at its tip to interact with the under-surface of the mucus gel which is then propelled forward as the cilium moves through an almost planar arc.

Rest phase

At the end of the effective stroke the cilium disengages from the mucus gel and enters the rest phase where it lies parallel to the epithelium pointing in the direction of the mucus flow. This position is believed to discourage any reversal of mucus movement.

Recovery stroke

The cilium "unrolls" within the periciliary fluid ready for the next effective stroke. Undergoing the recovery stroke beneath the mucus layer prevents traditional mucus transport.

Limitation

1. The histological toxicity of absorption enhancers used in nasal drug delivery system is not yet clearly established.
2. Relatively inconvenient to patients when compared to oral delivery systems since there is a possibility of nasal irritation.
3. Nasal cavity provides smaller absorption surface area when compared to GIT.
4. Frequent use of this route results in mucosal damage (e.g. infection, anosmia).
5. Nasal congestion due to cold or

allergies may interfere with this method of delivery.

Mechanism of Drug Absorption

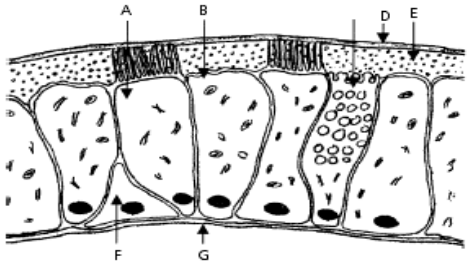


Figure 2 Cell types of the nasal epithelium showing ciliated cell (A), nonciliated cell (B), goblet cell (C), gel mucus layer (D), sol layer (E), basal cell (F) and basement membrane (G).

Paracellular route

The first mechanism involves an aqueous route of transport, between adjacent epithelial cells via the mechanisms of passive which is also known as the paracellular route, this route is slow. There is an inverse log-log correlation between intranasal absorption and the molecular weight of water-soluble compounds. Para-cellular permeability of the nasal epithelium is approximately the same as that of the intestine. Poor bioavailability was observed for drug with a molecular weight greater than 1000 Daltons.

The second mechanism involves transport through a lipoidal route is also known as the transcellular process and is responsible for the transport of lipophilic drugs that show a rate dependency on their lipophilicity. Drug also cross cell membranes by an active transport route via carrier-mediated means or transport through the opening of tight junctions. For examples, chitosan, a natural biopolymer from shellfish, opens tight junctions between epithelial cells to facilitate drug transport.

Trans-cellular route

Trans-cellular passive diffusion, for most conventional drug molecules, which tend to be small and lipophilic, absorption, occurs transcellularly, by passive diffusion across the cell of the epithelium.

Carrier-mediated processes

Active transport mechanisms for di and tri-peptides, as well as L-amino acids, have been demonstrated in the nasal epithelium.

Endocytic processes

Most compounds of interest for nasal delivery have a molecular weight in excess of 1,000 Da and unit recently were thought to cross the cells endocytically.

Formulation factors affecting nasal bioavailability

1. Physical and chemical parameters

Physiological factor associated with the drug for nasal drug delivery, it has been suggested that two mechanisms of absorption exist, based on the physiological properties of the drug:

- **Fast rate-which is dependent on the lipophilicity of the drug**

  Lipophilic drugs such as propanolol, 17-oestradiol, naloxone and testosterone are absorbed rapidly and completely from the nasal cavity. In contrast, their oral bioavailability ranges from 25% for propranolol to less than 1% for progesterone.

- **Slower rate-which is dependent on the molecular weight**
  - o Unlike the most small drug molecules, some drugs and peptides do not cross the nasal membrane efficiently. As a result the nasal bioavailability in simple solution formulation is very low. The low nasal absorption can be attributed to poor membrane permeability due to molecular size.
  - o The slower rate of absorption (probably via the Paracellular route and also sub – optimally via the trancellular route) is considered to provide adequate absorption of low molecular weight polar compounds. Above a molecular weight of 1,000Da the nasal absorption of

compounds declines. Thus the absorption of hydrophilic drug is more variable than that of lipophilic compounds and certain salts.

- Ex: Sodium cromoglycate is rapidly absorbed across the nasal mucosa.

- **Concentration**

The higher the drug concentration, the steeper the concentration gradient driving the absorption process and the faster the drug will be absorbed. Therefore if the drug is formulated as a solution, the highest concentration possible should be chosen that is compatible with an accurate and reproducible dosing volume. However, care must be taken, as high local drug concentration over extends periods of time may also cause sever local irritation or adverse tissue reactions.

- Nasal absorption of L-Tyrosine was shown to increase with drug concentration in nasal perfusion experiments.
- In another study, aminopyrine was found to absorb as a function of concentration.

In contrast, absorption of salicylic acid was found to decline with concentration. This decline is likely due to nasal mucosa damage by the permanent.

2. Effect of perfusion rate

The perfusion rate increases the nasal absorption is first increases and then reaches a plateau level that is independent of the rate of perfusion.

3. Effect of perfusate volume

As the volume of the perfusate solution increases, the first order rate of Phenobarbital from the perfusion solution has been observed to decrease. Results from studies using drugs with different molecular structures suggested that the intrinsic rate constant varies from one drug to another.

4. Effect of solution pH

Adults have pH 5.52-6.5; infants have pH 5.0-6.7, increased nasal absorption at decreased pH due to unionized condition of the drug. Decreased nasal absorption at increased pH due to ionization of penetrant molecule.

The pH of a nasal formulation is important for the following reasons

- To avoid irritation of nasal mucosa;
- To allow the drug to be available in unionized form for absorption;
- To prevent growth of pathogenic bacteria in the nasal passage;
- To maintain functionality of excipients such as preservatives; and
- To sustain normal physiological ciliary movement.

5. Factors associated with the dosage form

- Drugs to be administered to the nasal cavity are generally formulated as nasal drops, nasal sprays, aerosol spray, and the insufflators.
- Nasal drops which deposits a film of drug solution. Nasal sprays which deposit an aerosol particles, droplets, or particle suspended in drops.
- The extent and deposition of an aerosol from a nasal spray will depend upon:
- Aerodynamic diameter of the particle (which is also function of droplet size, shape and density).
- Particle charge (which depend on the drug, formulation excipients and method of aerosolization).
- The velocity at which the particle is moving (which depends on respiratory patterns).
- Deposition mechanisms in the nose include inertial impaction,

sedimentation, diffusion, interception and electrostatic attraction.

- The structure and physiology of the nasal cavity with the small cross-section for airflow and sharp curves suggests that inertial impaction is the most significant mechanism for drug deposition in the nasal cavity.
- Nasal drops disperse a drug solution throughout the length of the nasal cavity from atrium to nasopharynx, offering a relatively large area for immediate absorption.
- Nasal sprays tend to deposit at the front of the nasal cavity with little of the dose reaching the turbinate.
- The metered dose nebulizer has recently been introduced as a nasal drug delivery device that operates by mechanical actuation and delivers a predetermine volume with precision into the nasal cavity. The dose of active ingredient administered intranasally depends upon the volume of drug solution delivered at each actuation and the concentration of drug in the formulation.
- The bioadhesive powder dosage form and a mucoadhesive powder spray formulation for the nasal delivery of insulin. Studies conducted in rabbits and dogs indicated that the bioadhesive powder dosage produces drug absorption that is more effective and less irritating than the liquid forms.

6. Distribution

The mode of administration could influence the distribution of drug in the nasal cavity, which in turns determines the efficacy of its absorption. The distribution of drug following intranasal administration by different types of nasal delivery systems, including nasal drops, a plastic bottle nebulizer, an atomized pump, and a metered dose pressurized aerosol was evaluated the atomized pump was found to be the best nasal delivery system because it delivered a constant dose and achieved a very uniform distribution on the nasal mucosa.

7. Deposition

With nasal breathing all particles having an aerodynamic size of 10-20µm are found to be deposited on nasal mucosa. One should avoid deposition in both the poorly absorptive striated epithelium of the anterior atrium and in the posterior nasopharyngeal region, which leads to drug loss to the stomach by swallowing. Insoluble particles if deposited in the main nasal passage are likely to be transported posteriorly by ciliary movement and dispatched to the stomach.

Among the 3 mechanism usually taken into consideration when one assesses the deposition of particles in the respiratory tract i.e. inertia, sedimentation and diffusion, inertia deposition was found to be a dominant mechanism is nasal deposition particles with an aerodynamic diameter of 50 µm or greater do not enter the nasal passage. The site of drug deposition with in the nasal cavity depends upon the type of delivery system used and the technique of administration applied. The particles once deposited at the anterior region of the nasal cavity may be again conveyed posteriorly by inhaled air; ciliary movement and diffusion in the mucous layer.

8. Enhancement in absorption

Factors that affect the delivery of drug across nasal mucosa such as surfactants, dose pH, osmolarity, viscosity, particle size and nasal clearance, drug structure can be used to advantage to improve absorption.

9. Structural modification

The chemical modification of the molecule structure of a drug has been often used to modify the physicochemical properties of the drug and hence it could also be utilized to enhance the nasal absorption of a drug.

10. Salt formation
The drug could be converted to form a salt or an ester for achieving better trans-nasal permeability such as formation of a salt with increased solubility.

11. Formulation design
Proper selection of formulation excipients could improve stability or enhance the nasal absorption of drugs.

12. Surfactants: They modify permeability of nasal mucosa to increase absorption,

Mechanism of action

- Inhibit the aminopeptidase activity.
- Formation of transient hydrophilic pores in ciliary.
- Reduce viscosity of mucus.
- Remove epithelial cells which act as barrier.
- Solubilize drug in bile salt micelles and create transmembrane concentration gradient to facilitate absorption.

Ex: sodium lauryl sulphate, polyacrylic acid, sodium glycolate, lysophosphatidyl choline.

13. Bioadhesive polymer
Turbinates are the principal sites for the systemic absorption of intranasally delivered drug; these are also an area of high mucociliary clearance, especially in the highly ciliated middle and posterior region. Thus drug deposited in the anterior region of the nasal cavity may be expected to clear less rapidly and have a greater opportunity to be absorbed. They increase the residence time of drug in the nasal cavity.

Mechanism of action
Polymer absorbs water from mucus swells gel bond formation with in polymer and glycoprotein chain.
Ex: methyl cellulose, hydroxyl propyl cellulose etc,

Use of bio-adhesives
Bio-adhesives adhere to biological substrates such as mucus or tissue. Bio-adhesives are proposed to influence drug bioavailability by:
Decreasing the rate of clearance from the absorption site thereby increasing the time available for absorption.
Increasing the local drug concentration at the site of adhesion/ absorption.
Protecting the drug from dilution and possible degradation by nasal secretions.

A number of different bio-adhesive formulations are possible:

a) Bio-adhesive solutions/suspensions
Many viscosity enhancers are also considered to be bio-adhesive and putative bio-adhesive polymer gels, including methyl-cellulose sodium carboxy methyl cellulose chitosan, carbopol 934p and pluronic F127, have been shown to decrease the rate of mucociliary clearance. By reducing or abolishing ciliary motility the rate of clearance of the drug from the nasal cavity is reduced.
Some bio-adhesives, such as carbomers have also been shown to complex with mucus, increasing the viscoelasticity.

b) Dry powder bio-adhesives
A slightly different approach is to deliver the active drug in a dry powder carrier system
Ex: microcrystalline cellulose, hydroxyethyl starch, cross linked dextran, microcrystalline chitosan, carbomer, pectin, or alginic acid.
The polymer absorbs water upon contact with the nasal mucosa and swells to become a viscous gel, often demonstrating bio-adhesive properties. Such systems can remain in the nasal cavity for as long as six hours.

c) Colloidal bio-adhesives
Bio-adhesive micro-spheres composed from a variety of materials such as starch, carbomer,

hyluronan esters, and dextrin have been used to prolong the retention time of the drug within the nasal cavity. The clearance half-life of micro-spheres can be in the order of 3-4 hours, in comparison with 15 min. for a simple solution.

Ex: Gentamycin, insulin and Desmopressin.

14. Buffer capacity

Nasal formulations are generally administered in small volumes ranging from 25 to 200µL with 100 µL being the most common dose volume. Hence, nasal secretions may alter the pH of the administered dose. This can affect the concentration of unionized drug available for absorption.

15. Gelling/Viscofying agents or Gel-Forming Carriers

Agents that decrease the viscoelasticity of mucus. A drug carrier such as hydroxypropyl cellulose was effective for improving the absorption of low molecular weight but did not produce the same effect for high molecular weight peptides a fo esU . netfo si sreirrac fo noitanibmoc lasan(ytefas a morf noitadnemmocer .weiv fo tniop)ycnatirri

Ex: anionic and cationic surfactants and bile salts have been shown to increase absorption.

16. Solubilisers

Aqueous solubility of drug is always a limitation for nasal drug delivery in solution conventional solvents such as glycols, small quantities of alcohol, Transcutol (diethylene glycol monoethyl ether), medium chain glycerides and Labrasol (saturated polyglycolyzed C8-C10 glycerides) can be used to enhance the solubility

of drugs. Other options include the use of surfactants or cyclodextrins such as HP-β-cyclodextrin that serve as a biocompatible solubilizer and stabilizer in combination with lipophilic absorption enhancers.

17. Antioxidants

Sodium metabisulphite, sodium bisulfite, butylated hydroxytoluene and tocopherol. Usually, antioxidants do not affect drug absorption or cause nasal irritation. Chemical/physical interaction of antioxidants and preservatives with drugs, excipients, manufacturing equipment and packaging components should be considered as part of the formulation development program.

18. Enzymatic degradation

Cytochrom P-450 monooxygenase: this enzyme metabolises compounds such as nasal decongestants, nicotine, cocaine, phenacetin etc.

Leucine aminopeptidase metabolises hydrolyses insulin (zinc free).

Hydrolylases metabolises progesterone and testosterone.

Enzyme inhibitors can be added to nasal formulation to prevent enzymatic degradation.

19. Alteration of properties of mucosa layer

Opening tight junctions between epithelial: Substances that sequester extra-cellular calcium ions, which are required to maintain tight junction integrity

Ex: EDTA, bile salts will cause the tight junctions to open. Thus the paracellular route becomes leakier, permitting increased absorption of substances that use this route.

20. Increasing the membrane fluidity by

Various types of penetration enhancers have been evaluated for organic drugs including surfactants, bile salts, chelators, fatty acid salts, phospholipids, glycyrrhetenic acid derivatives, cyclodextrins and glycols. Polyoxyethylene-9-lauryl ether (BL-9) in saline solution improves the nasal absorption of hydralazine in both in-situ and in vivo nasal absorption studies in rats.

An added benefit of having the drug at higher concentration is that the same dose can be achieved in a smaller volume of solution.

Penetration enhancer may also promote delivery by increasing drug stability, due to

the enhancer decreasing the activity of enzymes which may degrade the drug.
E.g.:-

- Polysorbate 80 (1 %) in saline solution was observed to promote the nasal absorption of atropine and hyoscine from nasal solution. The absorption was rapid, complete and uniform with addition of sodium lauryl sulphate.
- A nasal formulation of meclizine (50 mg/ml) prepared in propylene glycol and 10 % glycerol results in 50 % of nasal drug absorption, which is equivalent to I.V. therapy.
- The nasal absorption of gentamycin (60 mg/ml in saline solution) in humans has observed to increase by incorporation of 1 % sodium glycocholate and peak serum levels were achieved in 30-60 min.
- Insulin is poorly absorbed from nasal mucosa. Among medium chain fatty acids, sodium caprylate (1%) exhibit the strongest promoting effect.
- The fatty acids show higher hemolytic activity than glycocholate. The compound carbenoxolone, glycerrhetenic acid salt has structures similar to triterpenes and show promoting effect similar to bile acids and saponins.

21. Increasing contact time at absorption site

Prolonging the contact time between the drug and its absorption site is likely to increase the bioavailability of the drug. Since drugs may be cleared from the nasal cavity by mucociliary clearance, swallowing and/ or by metabolism, the inhibition or the avoidance of these clearance mechanisms should result in increased absorption. These includes,

22. Reducing rate of mucociliary clearance

An alternative approach is to reduce the rate of mucociliary clearance and hence increase the retention time of the drug. This can be achieved by including an excipient in the formulation with a reversible ciliostatic effect, such agents include certain preservatives.

23. Miscellaneous methods

Altering the osmotic pressure (tonicity) of formulations: Alteration of osmotic pressure and pH beyond a certain range might be expected to result in damage to the epithelium and hence increase its permeability to xenobiotics.

Delivering the drug as a dry powder: Drugs in the form of a powder (but without a bio-adhesive carrier) show better absorption.
Ex: Freeze dried insulin has been shown to be better absorbed as a powder than in solution.

24. Nasal residence time

One way of delaying clearance is to apply the drug to the anterior part of the nasal cavity, an effect that is largely determined by the type of dosage form used. The preparation could also be formulated with polymers such as methylcellulose, hydroxy propyl methyl cellulose or polyacrylic acid, in which incorporation of polymer increases viscosity of the formulation and also acts as a bio adhesive with mucus. Increase in residence time does not necessarily lead to increase the absorption.
E.g.: Insulin solution with similar viscosity containing carbopol and CMC. Here carbopol enhance the absorption whereas CMC solution doesn't enhance the absorption of insulin. If we increase the viscosity, slow diffusion of drug from matrix causes retention in absorption with CMC. In case of carbopol causes enhancement of absorption due to opening the intracellular junctions.
One more lucrative way to increase the nasal resistance time is using biodegradable microspheres as a carrier for drug delivery. Biodegradable microspheres swell in presence of water thereby increasing the viscosity.

General requirement of an ideal penetration enhancer are as follows

1. It should lead to an effective increase in the absorption of the drug
2. It should not cause permanent damage or alteration to the tissue
3. It should be non irritant and non-toxic.
4. It should be effective in small quantity
5. The enhancing effect should occur when absorption is required
6. The effect should be temporary and reversible
7. It should be compatible with other excipients.

Advantages of nasal drug delivery system

1. Large surface area
The nasal cavity offers a relatively large surface area (approximately 160cm2) for drug absorption.

2. Rich blood supply
The highly vascular surface of the nasal mucosa ensures rapid absorption and onset of action as well as the maintenance of sink conditions.

3. Low metabolic activity
The metabolic activity of the nasal cavity towards peptides and proteins is less than that of the GI tract, making this route an attractive alternative to the oral delivery of these moieties. In contrast to the oral route this route avoids degradation in the intestinal wall or the liver prior to the drug reaching the systemic circulation.

4. Accessibility
The nasal cavity offers a readily accessible surface for drug delivery.

5. Ease of administration
Nasal devices such as metered dose nasal sprays are simple for the patient to use and might be expected to be more acceptable to the patient than the use of pessaries or suppositories for the intravaginal and rectal delivery routes respectively.

6. Intestinal alternative
The nasal may become a useful alternative to the intestinal route for drug absorption in situations where use of the GI route is unachievable.
Ex: - Patients with nausea and vomiting
- Patients with swallowing difficulties and /or children
- Drugs those are unstable in the GI fluids
- Drugs that undergo extensive first pass effects in the gut wall or liver.

Disadvantages of nasal drug delivery system

1. Mucociliary clearance
Mucociliary clearance reduces the retention time of drugs within the nasal cavity and thus the opportunity for absorption.

2. Mucus barrier
Drug diffusion may be limited by the physical barrier of the mucus layer and the binding of drugs to mucins.

3. Metabolic activity
While metabolic activity of the nasal cavity towards peptides and proteins is less than that of the GI tract it should be recognized that the nasal mucosa and secretions do have the ability to degrade drugs and that measures may be necessary to overcome this.

4. Limited to potent molecules
For drugs of a high molecular weight (which are thus poorly absorbed) the route is limited only to potent drug molecules, typically those with effective plasma concentration in the ng/ml (or lower) range.

5. Lack of reproducibility
Diseases such as the common cold and hay fever are recognized to alter the condition of the nose either increasing or decreasing mucociliary clearance or altering the

permeability of the absorbing mucosa.

6. Adverse reaction

Locally irritating or sensitizing drugs must be used with caution in this route. Nasal epithelia and in particular the cilia are highly sensitive and fragile. Damage to the epithelium could result in compromised mucociliary clearance which is associated with respiratory disease.

Delivery Systems

Current technologies for nasal drug delivery are concerned with, the local delivery of drugs such as decongestants, antibiotics and mucolytics for treatment of conditions of the nasal cavity. The systemic delivery of low molecular weight drugs (<500Da) including therapeutic peptides.

Delivery devices currently in use include nasal sprays and drops. The selection of delivery system depends upon the drug being used, proposed indication, patient population and last but not least, marketing preferences.

Nasal Drops

Nasal drops are one of the most simple and convenient systems developed for nasal delivery. The main disadvantage of this system is the lack of the dose precision and therefore nasal drops may not be suitable for prescription products. It has been reported that nasal drops deposit human serum albumin in the nostrils more efficiently than nasal sprays.

Upon the instillation of one or more drops of drug solution either from a dropper with a flexible (rubber) teat or directly from a “squeezable” plastic container into the nasal cavity.

Nasal drops, if administered correctly deposit drug throughout the nasal cavity, which offers a larger effective area for immediate absorption than if the drug is delivered in form of a spray. Some drug is certainly deposited on the ciliated regions of the mucosa and is therefore immediately available for clearance.

A proportion of the dose actually deposits at the nasopharynx where it may be immediately swallowed and is therefore not available for nasal absorption.

Ex: meclizine HCl,

Nasal sprays

Nasal sprays are available as squeeze bottles which would not be expected to give reproducible dosing. They are also available as metered dose devices which would be expected to give more reproducible dosing as a mechanical actuation delivers a pre-determined volume to the patient. Thus the dose of drug received by the patient will be dependent on the concentration of drug in the formulation.

Nasal sprays tend to deposit at their impaction site, in the anterior, non-ciliated regions of the nasal cavity, where air-flow associated with inspiration is high and mucociliary clearance is slow or erratic. Thus a drug moiety depositing in this region is cleared slowly and is transported over a large area en route to the pharynx. These factors promote drug absorption.

Ex: atropine, penicillin, hyoscine etc,

Both solution and suspension formulations can be formulated into nasal sprays. Due to the availability of metered dose pumps and actuators, a nasal spray can deliver an exact dose from 25 to 200. The particles size and morphology (for suspensions) of the drug and viscosity of the formulation determine the choice of pump and actuator assembly.

Nasal sprays V/S nasal drops

With both drops and sprays, about 40% of the administered dose is cleared rapidly within 20 min. then a second slower phase of clearance follows. In this second slower phase clearance of the drops is much faster than clearance of the spray, probably because most of the spray deposits on non ciliated regions. Due to the faster clearance nasal drops are more suitable for drug moieties which are rapidly absorbed.

Drug molecules which diffuse across the nasal epithelium relatively slowly will need a longer contact time and may therefore be better administered as spray. The bioavailability of the peptide drug

desmopressin is greater from a metered dose nasal spray than from drops.

Nasal Powder

This dosage form may be developed if solution and suspension dosage forms cannot be developed e.g., due to lack of drug stability. The advantages to the nasal powder dosage form are the absence of preservative and superior stability of the formulation. However, the suitability of the powder formulation is dependent on the solubility, particles size, aerodynamic properties and nasal irritancy of the active drug and /or excipients. Local application of drug is another advantage of this system.

Nasal Gels

Nasal gels are high-viscosity thickened solutions or suspensions. Until the recent development of precise dosing device, there was not much interest in this system. The advantages of a nasal gel includes the reduction of post-nasal drip due to high viscosity, reduction of taste impact due to reduced swallowing, reduction of of anterior leakage of the formulation, reduction of irritation by using soothing/emollient excipients and target to mucosa for better absorption.

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