



# REVIEW ARTICLE ON NASAL DRUG DELIVERY SYSTEM

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## 1. ABSRTACT :

Nasal drug administration has been used as an alternative route for the systemic availability of drugs restricted to intravenous administration and improved patient compliance and comfort.<sup>1</sup> In ayurvedic system, intra nasal is accepted form of treatment. Nasal route is useful for the drugs which are unstable on oral administration because they are significantly degraded in GIT or metabolized by first pass effect in liver. also useful for long term therapy.<sup>2</sup>

## 2. KEYWORDS :

Nasal, mucoadesive, invivo.

## 3. INTRODUCTION :

The history of nasal drug delivery dates back to earlier topical applications of drugs using for local effects. Nasal therapy also called 'Nasya karma' has been recognized form of treatment in the Ayurvedic system of Indian medicines.<sup>2,10</sup> Nasal route is easily accessible, convenient, and a reliable with a porous endothelial membrane and a very vascularized epithelium that provides a rapid absorption of compounds into the systemic circulation, avoiding the hepatic first pass elimination. In addition, intranasal drug delivery use to make dose reduction, rapid attainment of therapeutic blood levels, quicker onset of pharmacological activity, and fewer side effects.<sup>2,11,12</sup> The nasal delivery seems to be a easy and useful way to circumvent the obstacles for blood-brain barrier (BBB) allowing the direct drug delivery in the biophase of central nervous system (CNS) active compounds. It has also been considered to the administration of vaccines.<sup>12,13</sup> Other attractive features include the rather large surface area of the nasal cavity and the relatively high blood flow, which promotes rapid absorption. intranasal administration has much more potential.<sup>6</sup>

Advantages of nasal drug delivery system<sup>15,16,17</sup>

1. Absorption of drug is rapid via highly vascularised mucosa.
2. Availability of large nasal mucosal surface area for dose absorption.
3. Onset of action is rapid.
4. Non invasive and easy for administration.
5. Bypass the BBB.
6. Degradation of drug observed in GIT is avoided.
7. Hepatic first pass metabolism is absent.
8. Nasal bioavailability of small drug molecules is good.
9. Bioavailability of drug molecules greater in size can be increased by means of absorption enhancers.

10. Unsuitable drug candidates for oral route can be successfully given via nasal route.
11. Alternate to parenteral route especially for proteins and peptides.
12. Convenient route for the patient on long term therapy.
13. Improved bioavailability.
14. Side effects are reduced due to low dose.
15. Patient convenience and compliance is improved.
16. A self-administration is possible.
17. Direct transport into systemic circulation and CNS is Possible.
18. Offers lower risk of overdose
19. Does not have any complex formulation requirement

#### 4. Profile of an 'ideal' drug candidate for nasal delivery<sup>18</sup>

An ideal nasal drug candidate should possess the following properties:

1. Appropriate aqueous solubility to provide the desired dose in a 25–150 ml volume of formulation administration per nostril.
2. Appropriate nasal absorption properties.
3. No nasal irritation from the drug.
4. A suitable clinical principle for nasal dosage forms, e.g. rapid onset of action.
5. Low dose. Generally, below 25 mg per dose.
6. No toxic nasal metabolites.
7. No unpleasant odors/aroma associated with the drug.

#### 5. Anatomy and physiology of nose

The nose is the primary entrance to the respiratory tract, allowing air to enter into the body for respiration.<sup>19</sup> The nose serves as the mean of bringing warm humidified air into the lungs. It is the initial organ for filtering out particles in the inspired air, and it also serves to provide a first-line immunologic defence as it brings the inspired air into contact with the mucous-coated membrane. The nose has three important regions: vestibular, turbinate and olfactory regions. The vestibular region is the antecedent part of the nose and it is the narrowest part of the nasal cavity. The vibrissae cover most of this area which renders it liable of filtering out particles with an aerodynamic particle size larger than 10 µm that may be inhaled with air. In the vestibular region, the surface lining changes from skin, at the first part of the passage, to a stratified squamous epithelium.<sup>20</sup> The turbinate region is a large vascular part of the nose and can be divided into superior, middle and inferior regions. It is bounded with a pseudostratified columnar epithelium. It consists of mucus secreting, ciliated, non-ciliated and basal cells. The ciliated and non-ciliated cells are covered with non-motile microvilli, which are capable for increasing the surface area, thus, this is the region where the drug absorption is optimal. Ciliated cells are shield with approximately 100 motile cilia which are responsible for mucus transport so mucociliary clearance prevails. Once drug (as particles or in solution) find their way to the mucociliary area, they will be cleared from nasal cavity and then have limited access to the absorption site.<sup>21,22</sup>

#### 6. Factors affecting nasal drug absorption

##### 6.1 Physicochemical properties of the drug

The rate and extent of drug absorption may depend upon many physicochemical factors including the partition coefficient of the drug, the pKa, the molecular weight of the drug, perfusion rate and perfusate volume, and solution pH and drug concentration.<sup>23</sup>

##### 6.2 Mucociliary clearance

Particles are capture in the mucus layer are transported with it thus, effectively cleared from the nasal cavity. The integrate action of mucus layer and cilia is called mucociliary clearance. This is an important, nonspecific physiological defence mechanism of the respiratory tract to protect the body against noxious inhaled materials<sup>24</sup>. The normal mucociliary transit time in humans has been reported to be 12 to 15 minutes<sup>25</sup>.

## 7. Excipients used in nasal formulations<sup>16</sup>

### 7.1 Bioadhesive polymers

Compound that is able to interacting with biological material through interfacial forces and being retained on such material for prolonged periods of time is called as bioadhesive.

### 7.2 Gelling agent<sup>26</sup>

As per a study by Pennington et al. enhancing solution viscosity may provide a means of prolonging the therapeutic effect of nasal preparations.

### 7.3 Penetration enhancer

Chemical penetration enhancers are extensively used in the nasal drug delivery. Such as Buffers solubilizers.

### 7.4 Preservatives

Many nasal formulations are aqueous based so needs preservatives to prevent microbial growth. Parabens, phenyl ethyl alcohol, benzalkonium chloride, EDTA and benzoyl alcohol are some of the usually used preservatives in nasal formulations.

### 7.5 Antioxidants

A small quantity of antioxidants may be need to prevent drug oxidation.<sup>2</sup>

## 8. Evaluation of nasal drug formulations<sup>26, 27</sup>

### 8.1 Determination of pH

### 8.2 Measurement of Viscosity

### 8.3 Assessment of Mucoadhesive Properties

## 9. In vitro nasal permeation studies

Many approaches used to determine the drug diffusion through nasal mucosa from the formulation.

### 10. In vitro diffusion studies

The nasal diffusion cell is fabricated in glass. The water-jacketed recipient part of chamber having total capacity of 60 ml and a flanged top of about 3mm; the lid has 3 opening, each for sampling, thermometer, and a donor tube chamber. Samples (0.5 ml) from recipient chamber are with draw at predetermined intervals of time. The samples are estimated for drug content by suitable analytical method.

### 11. In Vivo Nasal Absorption studies Animal models for nasal absorption studies

The animal models used for nasal absorption studies can be of two types, viz., whole animal or in vivo model and an isolated organ perfusion or ex vivo model.

## 12. Conclusion

Over last decade, the nasal cavity has become one the favourable and potentially versatile route for delivering drugs. In particular, its unique capability of extending the drug release, by passing the hepatic firstpass metabolism and direct delivery of drugs to brain holds great promise in the field of drug delivery.

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